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Key issues affecting the current status of infectious diseases in Chinese cattle farms and their control through vaccination

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ABSTRACT

Infectious diseases can have a major impact on the profitability of the cattle industry. To determine the occurrence of bovine infectious diseases in China and the adoption of vaccination to control them, a national-wide questionnaire and focus group meeting were performed. The questionnaire was administered to 189 farmers including 93 dairy farmers, 80 beef cattle farmers and 16 yak farmers. Since it is compulsory to vaccinate cattle against foot and mouth disease, the coverage of vaccination to this disease was the highest (100% of dairy and yak farms and 92.5% of beef farms). However, the implementation of vaccination against other diseases was vastly different between cattle types with less than 50% of farms adopting vaccination (except brucellosis vaccine in yak farms). In a focus group meeting of 36 cattle experts on the key issues affecting the frequency of infectious diseases in cattle and the vaccination practices adopted on Chinese cattle farms, the lack of effective vaccines against single or multiple pathogens, a lack of tools for the early and correct diagnosis of disease, difficulties in licensing novel vaccines and diagnostic agents, low efficiency in disseminating knowledge on diseases and control products to producers were identified as key issues. In conclusion, except for FMD, the control of most infectious diseases of cattle in China requires improving. Development of improved control measures and diagnostic tests along with the development and implementation of educational material for producers on cattle diseases should be given priority.

1. Introduction

Infectious diseases of cattle have a deleterious effect on production, restrict access to international export markets and can potentially have a direct impact on public health. Only two infectious diseases (rinderpest and contagious bovine pleuropneumonia) have been eradicated from China in 1956 and 1996, respectively with rinderpest being declared eradicated globally in 2011 (https://www.oie.int/en/animal-health-in-the-world/official-disease-status/cbpp/; https://www.oie.int/en/animal-health-in-the-world/official-disease-status/rinderpest/) [1]. Zoonotic diseases, such as bovine brucellosis and bovine tuberculosis (bTB), have been endemic in China for a long time [2]. However due to poor biosecurity adopted on cattle farms and frequent animal movements between farms, counties and provinces [3], a test and slaughter strategy alone is unlikely to be effective for the control and eradication of these diseases. In 2012 the Chinese Government established a list of 16 priority epidemic diseases of livestock to be controlled and consequently allocated more resources to the control of these diseases than to others [4]. However, it is likely that the diseases considered by livestock producers to be of significance to their animals are different to those considered as priorities by the government [5]. In addition, emerging or reemerging diseases may occur in China, such as *Mycoplasma bovis* pneumonia which was first reported in 2008 [6]; and lumpy skin disease (LSD) reported in August 2019 [7]. Furthermore many endemic infectious diseases, such as bovine ephemeral fever (BEF) [8], infectious bovine rhinotracheitis (IBR) [9] and bovine viral diarrhea (BVD)

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[10] also affect livestock productivity. Some of these diseases can be controlled or prevented by the judicial use of vaccines and/or by strengthening biosecurity.

Although a voluntary eradication program for the listed priority diseases of cattle was initiated in 2015, only several semen collection stations and some dairy herds have been actively involved in the program (Center for Animal Disease Control and Prevention in China, CADC). On most cattle farms the strategic implementation of efficacious vaccination is an attractive and effective choice for the prevention and control of infectious diseases, resulting in improved cattle health and welfare and reduced zoonotic transmission of disease resulting in improved public health [11]. Vaccination against *Brucella* spp. has been demonstrated to effectively control brucellosis in the cattle population and subsequently reduce its impact on the health burden of the human population [12]. In order to successfully control cattle diseases via vaccination, China has allocated significant resources for the development of effective local vaccines (http://vdts.ivdc.org.cn:8081/cx/). For example, the killed trivalent vaccine against foot and mouth disease virus types O, A and Asia I was licensed in 2013 and an inactivated combined vaccine against IBR and BVD was licensed in 2016 (http://vdts.ivdc.org.cn:8081/cx/#). However the knowledge, attitudes and practices (KAPs) of cattle owners/managers must also be considered to understand why they would or would not adopt vaccination as a method for disease control in livestock.

Disease control through adoption of vaccination can, however, be problematic as some new diseases, such as *Mycoplasma bovis* pneumonia, cannot currently be controlled by vaccines, while others, such as pasteurellosis, require strain specific vaccines [13], and immunity induced against some diseases can be short lived requiring regular revaccination [14].

The study described in this manuscript was undertaken to provide insight into the uptake of vaccination against bovine diseases by livestock producers and to identify the need for future vaccine development.

2. Material and methods

2.1. Questionnaire

A questionnaire was designed to gather information on the use and administration of vaccines on cattle farms in China. It was developed and assessed by 5 experts from the National beef yak industry technology system and the National dairy industry technology system. After refining the questionnaire was pretrialed on 15 farmers, and then finalized and administered over a 30 day-period from June 1st to 30th, 2019. The survey was administered using Wenjuanxing online survey software (https://www.wjx.cn/). All participants were informed of the purpose of the questionnaire.

The questionnaire covered three broad categories: (1) general information about the respondents and their farms; (2) farm type and livestock numbers; and (3) vaccination information (Appendix 1) and took approximately 5 min to complete.

2.2. Sample size and questionnaire delivery

The study population was sourced from the China Dairy Data Report 2018 and the National Beef Cattle Industrial Technology System investigation, and represented three categories of cattle: dairy, beef and yaks. A total of 53,595 cattle farms with a herd size $\geq$ 20 head were eligible for inclusion in this survey. The minimum number of cattle farms to survey (97) was determined using Epitools [15] assuming an estimated vaccine adoption level of 50%, a precision of 10% and 95% confidence intervals.

The link to the online questionnaire was either delivered via the social media platform Wechat to livestock owners, emailed to cattle enterprise managers, or emailed to staff of the Center for Animal Disease Control and Prevention in each province and experts at universities or veterinary medicine institutions, for forwarding to local cattle keepers. At least one person was identified in each of the 31 provincial administrative regions of China to act as a "go-between" the research team and the producers. These contact persons were responsible for inviting potential respondents to participate in the online survey by providing the survey link. The location of the respondents was mapped (Fig. 1) using *ArcGIS 10.2* (ESRI, Redlands, CA, USA).

2.3. Focus group seminar

After the questionnaire was completed and the responses analyzed, a focus group of 36 veterinary/livestock experts from animal vaccine companies (12), academics working on bovine diseases at universities/research institutes (10), veterinarians/managers at large cattle enterprises (9) and 5 government officers responsible for disease surveillance in cattle was conducted on the August 23th, 2019. All the participants were considered experts in cattle and/or cattle diseases and had extensive experience. In the focus group a facilitator was responsible for guiding the meeting. A list of cattle diseases was presented to the focus group based on the responses from the farmer questionnaire and from published literature. The participants were asked to rank the importance of these diseases and to provide information on factors resulting in increased or decreased severity of disease and methods to improve disease control.

2.4. Statistical analyses

The study variables investigated were categorized under three broad categories. Category 1 comprised farm and participant variables and included: (1) participants' position, and (2) farm location. Category 2 variables included: (1) farm type (dairy, beef, yak), (2) number of stock on the farm, (3) proportion of cows, heifers and calves on the farm. Category 3 variables included (1) cattle vaccines currently or previously used on the farm, (2) time of vaccination, (3) what other diseases the participants thought needed controlling or vaccines that needed developing/improving.

For age, animals $\leq$ 6 months were classified as calves, females > 6 months – 2.5 years were classified as heifers, and adults > 2.5 years as adults.

A datasheet was created using Microsoft Excel 2010 (Microsoft, Redmond, USA) and data on questionnaire responses were transferred directly from the Wenjuanxing online survey software to this spreadsheet. Chi-square and Fisher's exact tests were used to test the significance of variables of interest in different classes of animals and types of cattle farms. A p value < 0.05 was classified as having statistical significance. All statistical analyses were conducted in *SPSS* version 24.0 (IBM Corporation, Armonk, NY, USA).

3. Results

3.1. Response rate and job duties of the respondents

Of the 208 responses obtained, 189 (90.9%) were included in the analysis with 19 excluded due to inadequate/incomplete information. Of the valid responses, 49.2% (93/189) were from dairy farms, 42.3% (80/189) from beef farms, and 8.5% (16/189) from yak farms. Of the respondents 55% (104/189) were directly responsible for the management of the cattle farms, 21.7% (41/189) were veterinarians and 21.2% (40/189) were livestock workers.

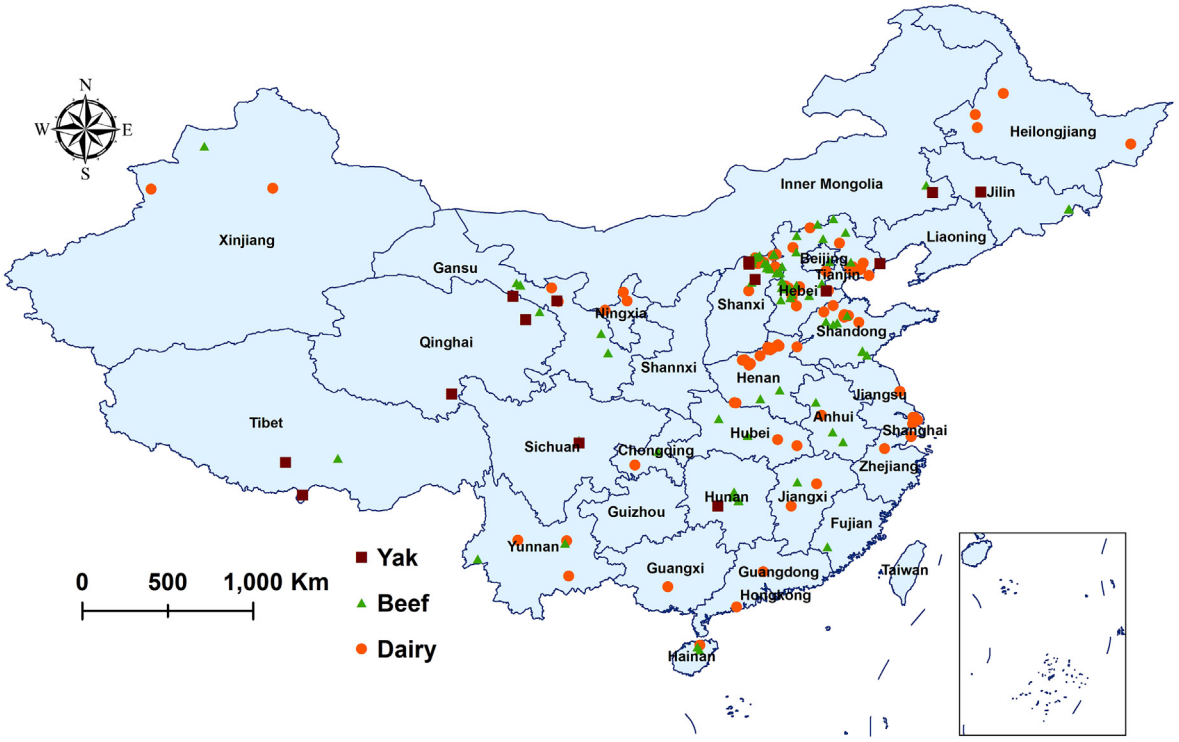

Fig 1. Geographical distribution of different type of farms in this survey.

3.2. Farm characteristics

70% responders were involved with herds that were classified as either medium (301–999 head) or large (≥1000) herds. Dairy farms had a significantly larger herd size than beef and yak farms, with approximately 90% (82/91) dairy farms containing > 300 head. In contrast significantly more beef herds were categorized as small (≤300 head) (41.3% – 33/80) (Table 1).

The surveyed herds were distributed in most of the provincial administration regions (28/31) of mainland China (Fig. 1). Overall, 41.3% (78/189) of the cattle farms surveyed were located in northern China, with only 3.2% (6/189) situated in southern China. Dairy and beef farms included in this study were similarly distributed; however yak farms were mainly distributed in the northern, northwestern and southwestern regions of China (Fig. 1 and Table 1).

The make-up of dairy, beef and yak herds is summarized in Table 2. Adult cattle were the most common age group in all three cattle types.

3.3. Vaccine usage and administration protocols

All but two (yak farms) of the 189 surveyed farms (98.9% – 187/189) had previously or currently vaccinated some or all of their livestock. The most frequently used vaccine was against FMD (96.8%, 181/189), followed by brucellosis vaccine (41.7%, 74/187) and bovine ephemeral fever (BEF) vaccine (25.1%, 47/187). Other diseases vaccinated included bovine viral diarrhea (BVD, 18.2%), bovine hemorrhagic septicemia (BHS, 16.6%), anthrax (14.4%), clostridial diseases (CD, 13.4%) and infectious bovine rhinotracheitis (IBR, 11.8%) (Table 3).

Table 1
Information on respondents to the questionnaire.

	Type of cattle raised			
	Total % (n/total)*	Dairy % (n)	Beef % (n)	Yak % (n)
Job duty				
Farm manager	56.2 (104/185)	52.7 (48/91)	64.1 (50/78)	37.5 (6/16)
Veterinarian	22.2 (41/185)	24.2 (22/91)	20.5 (16/78)	18.8 (3/16)
Worker	21.6 (40/185)	23.1 (21/91)	15.4 (12/78)	43.7 (7/16)
Farm size (number of head)				
Small (≤300)	28.2 (51/181)	9.9 (9/91)	41.3 (33/80)	90.0 (9/10)
Medium (301–999)	40.3 (73/181)	54.9 (50/91)	27.5 (22/80)	10.0 (1/10)
Large (≥1000)	31.5 (57/181)	35.2 (32/91)	31.3 (25/80)	0.0 (0/10)
Location				
Northeast China	3.7 (7/189)	4.3 (4/93)	2.5 (2/80)	6.3 (1/16)
Northern China	41.3 (78/189)	31.2 (29/93)	53.8 (43/80)	37.5 (6/16)
Central China	13.8 (26/189)	18.3 (17/93)	10.0 (8/80)	6.3 (1/16)
Eastern China	20.6 (39/189)	29.0 (27/93)	15.0 (12/80)	0.0 (0/16)
Southern China	3.2 (6/189)	4.3 (4/93)	2.5 (2/80)	0.0 (0/16)
Southwest China	7.4 (14/189)	5.4 (5/93)	6.3 (5/80)	25.0 (4/16)
Northwest China	10.1 (19/189)	7.5 (7/93)	10.0 (8/80)	25.0 (4/16)

[#]Difference in denominators (responses) is associated with some questions not being answered by all respondents.
* Number of responses compared to all responses for that category.

Table 2
Proportion of different ages of cattle in the three categories of farms surveyed.

		Dairy farms		Beef cattle farms		Yak farms	
		No.	Percentage	No.	Percentage	No.	Percentage
Adults (>2.5 year)	≥70%	4	4.3%	9	11.3%	2	12.5%
	≥50%,<70%	70	75.3%	23	28.8%	6	37.5%
	≥10%,<50%	15	16.1%	20	25.0%	3	18.8%
	<10%	1	1.1%	10	12.5%	0	0.0%
	no information	3	3.2%	18	22.5%	5	31.3%
Heifers (6–2.5 years)	≥50%	7	7.5%	23	28.8%	5	31.3%
	≥30,<50	54	58.1%	19	23.8%	1	6.3%
	≥10,<30	28	30.1%	20	25.0%	4	25.0%
	<10	1	1.1%	2	2.5%	1	6.3%
	no information	3	3.2%	16	20.0%	5	31.3%
Calves (<6 months)	≥20%	19	20.4%	31	38.8%	6	37.5%
	≥10,<20	54	58.1%	17	21.3%	4	25.0%
	<10	17	18.3%	12	15.0%	1	6.3%
	no information	3	3.2%	20	25.0%	5	31.3%

3.4. Focus group meeting

In the focus group meeting, 83.3% of the experts regarded FMD as the most important disease to China's cattle industry. Of other diseases BVD was identified as the most important because of its negative effect on production resulting in a higher perinatal mortality level of calves and reduced milk yield and growth rate. Brucellosis was ranked as the third most important disease by 42.9% experts. 33.3% of the experts believed that respiratory diseases, bovine tuberculosis and bovine hemorrhagic septicemia were endemic in some parts of China and required measures to mitigate the risk of their spread.

The important factors affecting the control of cattle' diseases in China were considered to be:

1. Lack of effective vaccines against single or multiple pathogens

It was recognized that farmers wanted vaccines that: had a high efficacy; covered a wide range of pathogens; and were easy to administer on-farm. The participants considered that there was a need for development of vaccines against multiple diseases, especially bovine respiratory diseases, diarrhea diseases, pasteurellosis, and clostridial disease in China.

2. Difficulties in receiving approval for newly developed vaccines and diagnostic kits

The long period to receive registration approval for new vaccines and diagnostic kits and consequently the time to reach market (approximately 5 years) was considered an obstacle for manufacturers. This was considered to hinder the development of vaccines and diagnostic kits resulting in less effective disease control.

3. Low level of knowledge on disease and control products

It was exclusively agreed that most farm workers had a low level of education and training and therefore were less aware of disease and necessary control measures. So the training was needed. The participants also considered that some chronic diseases, such as paratuberculosis, which often initially presented without apparent clinical signs, were overlooked by farmers and even though commercial vaccines may be available for their control uptake was low.

4. Discussion

This investigation firstly describes the latest information on vaccine usage in a sample of dairy and beef cattle and yak farms in China and then focuses on potential challenges in developing and ensuring vaccination protocols are followed.

The high adoption of vaccines by cattle farmers (98.9%) in this survey is most likely attributed to the intensive management systems adopted for dairy and beef cattle (CADC). In contrast yaks are raised predominantly under an extensive pastoral production system which may account for two of the yak farms not implementing vaccination as a method of controlling infectious diseases in their livestock. Intensive farms with a larger herd size are more likely

Table 3
Vaccine usage and administration protocols adopted among Chinese cattle farms.

	Farm Type			
	Total, % (n)*	Dairy, % (n)	Beef, % (n)	Yak, % (n)
Have you vaccinated your cattle in the past year?				
Yes	98.9 (187/189)	100.0 (93/93)	100.0 (80/80)	87.5 (14/16)
Have you used the following individual vaccines in the past year?				
Yes, Foot-and-month disease	96.8 (181/187)	100.0 (93/93)	92.5 (74/80)	100 (14/14)
Yes, Brucellosis	41.7 (78/187)	46.2 (43/93)	33.8 (27/80)	57.1 (8/14)
Yes, Bovine ephemeral fever	25.1 (47/187)	36.6 (34/93)	15.0 (12/80)	7.1(1/14)
Yes, Bovine haemorrhagic septicaemia	16.6 (31/187)	8.6 (8/93)	21.3 (17/80)	42.9 (6/14)
Yes, Anthrax	14.4 (27/187)	11.8 (11/93)	12.5 (10/80)	42.9 (6/14)
Yes, Clostridium disease	13.4 (25/187)	8.6 (8/93)	20.0 (16/80)	7.1 (1/14)
Yes, Infectious bovine rhinotracheitis	11.8 (22/187)	15.1 (14/93)	8.8 (7/80)	7.1 (1/14)
Yes, Bovine viral diarrhea	18.2 (34/187)	22.6 (21/93)	12.5 (10/80)	21.4 (3/14)
What route of administration did you use?				
Use recommended route(s)#	74.3 (139/187)	68.8 (64/93)	82.5 (66/80)	78.6 (11/14)
What frequency of vaccination did you use?				
Recommended frequency as per vaccine manufacturers	89.2 (124/139)	92.2 (59/64)	87.9 (58/66)	72.7 (8/11)

* Include dairy, beef and yak respondents.
\# Recommended routes include intramuscular, subcutaneous and oral routes.

to adopt measures to maintain the health of the animal populations and hence allocate more resources to disease prevention [16].

As FMD is a highly contagious disease which can have a devastating impact on the livestock industry, it has been classified as a disease requiring compulsory immunization in China [17]. After the implementation of mass vaccination, the incidence of outbreaks of FMD reduced significantly in China, however sporadic cases still occur, most likely due to the introduction of new viral strains not included in the vaccines used or a failure to achieve 100% vaccination coverage [17,18]. This was supported by the findings of the current study where 2 yak farmers did not vaccinate their herd against FMD, presumably because of economic reasons and/or a lack of understanding of the potential impact of the disease. This highlights the need for specific training and education material for cattle producers throughout China.

Infection with brucellosis can severely affect reproductive performance and reduce milk yield of livestock, as well as having a detrimental impact on human health. The animal-level seroprevalence of brucellosis in dairy cattle in China was reported to be 2.6% (95% CI 2.4–2.8) during the period 2013–2018; although it was higher in northern China with a seroprevalence > 10% [19]. An investigation in Hubei province showed a 34.9% (95% CI: 28.5, 41.8) to 51.4% (95% CI: 48.2, 54.6) real prevalence in dairy cows [2]. A study in yaks from Tibet in 2017 reported an animal-level seroprevalence of 2.8% (95% CI 2.0–3.7) and a herd-level prevalence of 18.2% (95% CI 12.9–24.6) [20]. The high prevalence of this disease in China may account for the finding that 41.3% of the surveyed farms vaccinate their cattle against brucellosis, with these farms being concentrated in the endemic areas of northern China. The findings of the study of Wang et al (2020) indicated that some dairy herds privately arranged vaccination of their animals, presumably due to the potential impact of this disease on their herd [2]. In China, two commercial vaccines are used in cattle, *Brucella abortus* 19 strain (A19) and *Brucella suis* 2 strain (S2). Although A19 strain is widely used with a high protective efficacy, it has some limitations as it is potentially infective for humans and may induce abortion in pregnant cattle [21]. The biosecurity and biosafety of vaccines has received heightened attention, especially after the 2019 brucellosis vaccine leak event that resulted in thousands of people being exposed to the live vaccine strain in Lanzhou (http://wsjk.gansu.gov.cn/single/11067/81007.html). Such an event highlights the need to develop safer and more effective vaccines to mitigate against brucellosis both in humans and livestock.

BEF is an arthropod-borne seasonal viral disease in cattle that can lead to a transient drop in milk production and a loss of meat production [22]. In the current study more dairy producers adopted vaccination against BEF vaccine than beef producers (36.6% vs 15.0%, Table 3). Also in this study more producers were found to vaccinated against BVD than IBR. BVD produces obvious signs of diarrhea, especially in calves, compared with IBRV which is one of the pathogens involved in bovine respiratory disease (BRD) [23]. In contrast to other diseases more yak farms than beef or dairy farms implemented vaccination coverage against BHS and anthrax. Both of these diseases are potentially fatal and endemic in Tibet and Qinghai [24], where yaks are predominantly concentrated in China. These vaccination results are not surprising as producers are more likely to be concerned about diseases with obvious clinical signs than those with minor or subclinical presentations. This highlights the need in China for the development of material to educate farmers about the impacts of diseases with subclinical clinical signs which can reduce livestock productivity and potentially be zoonoses.

Surprisingly in this study only 74.3% of producers used the administration route recommended by the relevant vaccine manufacturer. Such a practice may restrict the development of protective immunity against disease or may result in side effects such as permanent serological titers or abortions when the *Brucella* vaccine A19 is given intramuscularly rather than subcutaneously [25]. This again highlights the need for development and implementation of education programs for cattle producers in China.

As well as implementing vaccinations there is a need for the prompt reporting by producers to the local veterinarians/authorities when disease occurs, followed by the rapid and accurate diagnoses of disease for effective disease control. Vaccination is only one aspect of control of infectious diseases and needs to be partnered with strengthening on-farm biosecurity, expanded surveillance and monitoring programs [26] and increased awareness about diseases.

5. Conclusion

FMD is the most commonly disease vaccinated against in cattle, followed by brucellosis. There is a need for developing vaccines to protect against multiple pathogens, particularly those associated with respiratory disease and diarrhea in cattle in China along with developing vaccines against brucellosis that are both safe to administer and efficacious. Further education of producers is required to ensure that they are aware of the diseases affecting cattle and follow the recommended protocols developed by vaccine manufacturers.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.vaccine.2021.05.078.

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