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Original article

Effectiveness of simulated interventions in reducing the estimated prevalence of *E. coli* O157:H7 in lactating cows in dairy herds

Bouda VOSOUGH AHMADI[a]*, Klaas FRANKENA[b], Joanne TURNER[c], Annet G.J. VELTHUIS[a], Henk HOGEVEEN[a,d], Ruud B.M. HUIRNE[a]

[a] Business Economics Group, Wageningen University, Hollandseweg 1, 6706 KN Wageningen, The Netherlands
[b] Quantitative Veterinary Epidemiology Group, Wageningen Institute of Animal Science, Wageningen University, PO Box 338, 6700 AH Wageningen, The Netherlands
[c] Department of Veterinary Clinical Science and Animal Husbandry, The University of Liverpool, Leahurst, Neston, South Wirral CH64 7TE, United Kingdom
[d] Department of Farm Animal Health, Faculty of Veterinary Medicine, Utrecht University, Yalelaan 7, 3584 CL Utrecht, The Netherlands

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Abstract – A transmission model developed to investigate the dynamics of *Escherichia coli* O157:H7 bacteria in a typical Dutch dairy herd was used to assess the effectiveness of vaccination, diet modification, probiotics (colicin) and hygienic measures as to water troughs and bedding, when they are applied single or in combination, in reducing the prevalence of infected animals. The aim was to rank interventions based on their effectiveness in reducing the baseline prevalence of infected animals in the lactating group. The baseline prevalence of the lactating group and the within-herd prevalence were estimated by the model to be 5.02% and 13.96% respectively. The results show that all four interventions, if applied to all four animal groups or only to young stock, are the most effective and will reduce the baseline prevalence by 84% to 99%. In general, combinations of hygiene (applied in all groups) and one other intervention had the highest effectiveness in reducing prevalence in the lactating group. Vaccination and diet modification show a slightly higher effectiveness than colicin and hygiene.

***Escherichia coli* O157:H7 / on-farm intervention / dairy-beef herd / effectiveness**

1. INTRODUCTION

Escherichia coli O157:H7 (VTEC O157 in this paper) is one of hundreds of strains of the bacterium *E. coli* that is found regularly in the faeces of healthy cattle [2,5,21]. It can be transmitted to humans through direct contact with faeces and by consumption of contaminated beef and dairy products [1, 6, 16, 18]. A human infection is associated with a wide range of symptoms, including asymptomatic shedding, non-bloody diarrhea and hemorrhagic colitis, life-threatening complications such as hemolytic-uremic syndrome (HUS), particularly in children under five

* Corresponding author:
Bouda.Vosough-Ahmadi@wur.nl

years, thrombotic thrombocytopenic purpura (TTP) in elderly people, and death [13]. The incidence of human infection with VTEC O157 in the Netherlands is estimated to be 1 251 cases per year [14]. The severe health consequences of human infection make preventive strategies important.

Dairy and beef cattle are known as the main reservoirs of VTEC O157 and the bacteria can be found at several locations on the farm including other animals, water, soil and feed. Beef is known as one of the main transmission vehicles to consumers. Interventions that reduce the risk of beef becoming contaminated with VTEC O157 can be applied at the farm and transport level (i.e., pre-harvest interventions) and/or at slaughter and processing levels (i.e., post-harvest interventions). Reducing the number of infected lactating cows is a good approach in reducing the level of beef-borne human VTEC O157 infections, because a large proportion of the beef consumed in the Netherlands originates from culled and slaughtered (domestic) dairy cows.

Some farm attributes (e.g., water and sediments in water troughs) have been frequently reported as main on-farm risk factors for VTEC O157 transmission and based on that, appropriate biosecurity interventions have been suggested [7]. Also measures that reduce the concentration of VTEC O157 shed in the faeces of infected cattle, such as probiotics and vaccination, were identified as effective interventions [4]. However, little is known about the capability of these interventions in reducing the prevalence of infected animals in the beef producing group (i.e., lactating cows) as well as in the whole herd.

Understanding the transmission and survival process of food-borne pathogens in a highly managed and complex system, such as a modern dairy farm, requires a framework to cover all the aspects. Moreover, evaluating the interventions by direct implementation is often costly and interruptive of the routine farm practice. Thus, epidemiological models that simulate the dynamics of food-borne bacterial populations in a representative herd (e.g., VTEC O157 and *Salmonella* spp.) [23, 24, 27] are important tools to estimate the effectiveness of interventions in the whole herd and in specific groups of animals (e.g., lactating group). In such a modelling approach, population dynamics of the concerned pathogens and the effect of management of the farmer on the dynamics are simulated using a combination of numerical and analytical techniques. This type of model has been used to investigate the long term behaviour of food-borne pathogens, such as *Salmonella* infections in livestock, and to develop potentially more effective intervention strategies [26]. Intervention strategies against VTEC O157 can be categorized into antibacterial, probacterial, dietary and management strategies [4]. In this study, based on the literature, we selected one intervention from each of the categories mentioned which were the following: vaccination, probiotics (i.e., colicin), diet modification and more frequent replacing and cleaning bedding materials and water troughs.

The objective of this study was to rank interventions based on their effectiveness in reducing the baseline prevalence of infected animals in the lactating group and the herd as a whole.

2. MATERIALS AND METHODS

2.1. General description of the model

A VTEC O157 transmission model that was developed to investigate the population dynamics of *E. coli* O157:H7 in a typical United Kingdom dairy herd [23] was used to assess the effectiveness of four on-farm interventions in the Netherlands. Figure 1 represents the model structure.

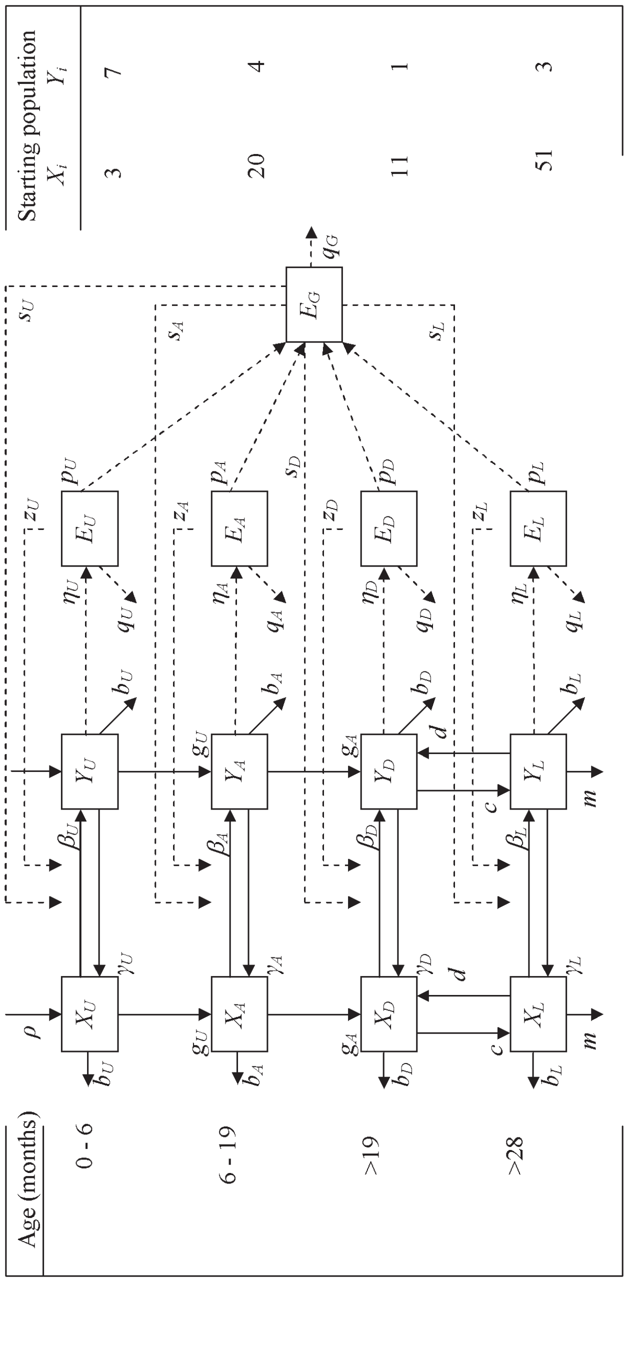

Figure 1. Schematic overview of the model and the relationships modelled between the groups and general and specific environments.

The four management groups in the model are young stock under-six-months old (U), young stock above-six-months old (A), dry (D) and lactating (L) adult cattle. Susceptible (X) and infected (Y) animals pass from the under-six-month group to the above-six-month with a maturation rate of (g_i), then to the dry group and finally to the lactating group as they grow older. At the end of lactation, animals re-enter the dry group and this cycle continues (parameters c and d in the model) until lactating animals are culled (denoted by m). Besides this, an animal death rate was included in the model for each group (denoted by b_i, i indicating the group).

Within each group i direct host-to-host transmission occurs and susceptible animals move to the infectious group with rate β_i and recover with rate γ_i. Infected animals (Y_i) shed infectious doses (η_i) (it is assumed that 100 colony forming units (CFU) represent one infectious dose) into their group-specific environments (E_i) during their infectious period [23]. The term 'infected' is used to denote animals that shed more bacteria than they initially ingested, as a result of colonisation. An animal that sheds bacteria, without amplification of the number of bacteria, was considered to be of little importance. Animals do not gain immunity, so when shedding stops they return to the susceptible group. There is a flow of bacteria from each group-specific environment to the 'general' environment (E_G) that poses a risk to all groups, which is expressed in the pooling rate (p_i). The general environment represents personnel or equipment that routinely come into contact with the various groups and provides a route of transmission between all groups. Susceptible animals can become infected by ingesting infectious units from either their group-specific environment (represented by the group-specific environment indirect-transmission parameter z_i), perhaps from contaminated bedding, feed and water troughs, or from the general environment (represented by general environment indirect-transmission parameter s_i). A daily death rate (q_i) of bacteria was incorporated in the model for both the group-specific and general environment. This represents natural bacterial elimination or the effect of any bactericidal intervention (e.g., cleaning water troughs or changing/cleaning the bedding material). The model also includes pseudovertical transmission (ρ, representing transmission from dam to calf within the first hours after birth).

The model was run for a period of 1 000 days. The initial numbers of infected animals in groups in U, A, D and L were 7, 4, 1, and 3 respectively. These numbers correspond to the numbers of infected animals in each group when the baseline model is at equilibrium (i.e., when the proportion of infected animals in each group becomes constant after introducing one infected animal to a negative herd). The exchange of animals between susceptible and infectious groups was calculated using differential equations. Also, two transition matrices were used to calculate the time spent in each group and each environment. For details of the differential equations and matrices see Turner et al. [23].

2.2. Input

Table I and the first column of Table II represent the values of the input parameters. There are three categories of input variables in the model. The first category is related to the general dairy-farm management such as total herd size (N), maturation rate (g_i) of the animals, rate of flow from dry to lactating (c) and vice versa (d). The values used for these parameters were according to Dutch dairy practice. The average total herd size in the Netherlands was estimated to be 100, and the average milking period, dry period and maturation age were reported to be 345, 60 and

Table I. Input parameters and values that were not affected by interventions.

Parameter		Unit	Value	Parameter		Unit	Value
N	Total herd size	Animal	100	η	Shedding rate	Units/day	
ρ	Pseudovertical transmission		0.46		$\eta_U, \eta_A, \eta_D, \eta_L$		$k_i \times f_i \times 10$
g	Maturation rate	Animal/day		*p*	Pooling rate	Units/day	
	g_U		0.00556		p_U, p_A, p_D, p_L		0.00025
	g_A		0.00178	β	Direct tr.	Per animal/day	
c	Flow from dry to lactating	Animal/day	0.0166		β_U		0.0256
d	Flow from lactating to dry	Animal/day	0.0029		β_A		0.0013
b	Death rate	Animal/day			β_D		0.0034
	b_U		0.000137		β_L		0.0009
	b_A		0.000023	*z*	G-specific indirect-tr.	Per animal/day	
	b_D		0.000046		z_U		2.132×10^{-10}
	b_L		0.000046		z_A		4.681×10^{-12}
m	Culling rate	Animal/day	0.0008		z_D		1.652×10^{-8}
					z_L		1.484×10^{-8}
f	Faecal shedding	kg/day		*s*	General indirect tr.	Per animal/day	
	f_U		4.9		s_U		$0.01z_U$
	f_A		12.6		s_A		$0.005z_W$
	f_D and f_L		37.1		s_D		$0.01z_D$
					s_L		$0.02z_L$

Table II. Input parameters and values that were affected by interventions.

Parameter		Unit	Baseline	With-intervention				
				Vaccine (a)	Vaccine (b)	Diet modification[b]	Colicin	Hygiene[c]
γ	Recovery rate	Animal/day						
	γ_U and γ_A		0.068	0.090	0.068	0.068	0.068	–
	γ_D & γ_L		0.106	0.090	0.106	0.106	0.106	–
k	Concentration	CFU/g						–
	k_U and k_A		3.367×10^5	0.0	3.367×10^4	0.0	2.439×10^4	–
	k_D and k_L		7.0×10^1	0.0	7.0	0.0	5.07	–
q	Death rate of organism	Units/day						
	q_U, q_A, q_D		0.1395	–[a]	–		–	0.631
	q_G		0.1395	-	–		–	0.139
	q_L		0.5075	–	–		–	0.631

[a] '–' means there was no change.
[b] Consists of HFNM (high-forage no-monensin), HFM (high-forage, plus monensin), HGNM (high-grain no-monensin) and HGM (high-grain plus monensin).
[c] Hygiene consists of replacement of bedding (*q*: 0.46) and cleaning water troughs (*q*: 0.169).

745 days respectively [12]. The second category consists of the direct-transmission rates of VTEC O157 from animal to animal (β_i) in the various groups. No Dutch specific data were available for these parameters. Turner et al. [23] assumed values for these parameters that were updated in their more recent paper [24]. The latter parameter values were used in our study. The third category includes the group-specific (z_i) and general (s_i) indirect-transmission parameters, faecal-shedding rate (η_i), recovery rate (γ_i) and death rate (q_i) of pathogen. η_i, γ_i and q_i were deemed to be affected by intervention measures (see next section). Transmission parameters were considered density-dependent and their values were calculated for a herd size of 100.

2.3. Interventions

Two selection criteria for interventions were applied: (i) interventions should be effective according to the literature and (ii) quantitative data of their impact on the model input parameters should be available. In this way, four interventions were considered: vaccination, modified diet in reducing the concentration of bacteria in the gastrointestinal tract, adding probiotics (colicin) to the diet, and application of better hygienic measures, consisting of more frequent cleaning of water troughs and replacement of bedding material. Three of the input parameters (η_i, γ_i and q_i) can be affected by these interventions. The faecal shedding rate η_i is the product of the bacterial concentration K_i (i.e., CFU/g) and the quantity of faeces produced per day. Vaccination affects both faecal shedding and the recovery rate. However, diet modification and colicin only affect the shedding rate. Hygiene only affects the pathogen death rate (q_i). Table II shows the values of the input parameters affected. The details of the selected interventions are described in the following sections.

2.3.1. Vaccination

A substantial amount of research was carried out to develop new vaccines against VTEC O157 [8–10, 17]. Potter et al. [17] describes a recently developed vaccine, which was successfully tested in an experimental study. This vaccine raises antibodies that interfere with gut colonisation of the host (cattle or other hosts) by VTEC O157. In a trial, 3 doses of the vaccine were administered at 3-week intervals during 106 days. The results showed a 10-fold reduction in log number of CFU bacteria/gram of faeces of calves and yearlings. The shedding duration was at maximum 11 days for the vaccinated groups. This implies a higher recovery rate for young stock (i.e., under-six-months old (U) and above-six-months old (A) groups) and a slightly lower recovery rate for dry and lactating groups. We used these experimental data as the effect of the vaccine mentioned in this study and we called it vaccine (a). Vaccine (b) is an imaginary type of vaccine that produces a 10-fold reduction in the shedding rate without affecting the recovery rate. We used vaccine (b) to evaluate the sensitivity of the model to recovery rate.

2.3.2. Diet modification

Diet and feeding practices are considered to be important factors affecting faecal shedding of VTEC O157. Diets containing high forage or high grain are mentioned in the literature as influential factors. In an experimental study, the effect of four feed rations, namely high-forage no-monensin (HFNM), high-forage with-monensin (HFM), high-grain no-monensin (HGNM) and high-grain with-monensin (HGM), on the number of bacteria shed as well as the effects on the shedding duration (recovery rate) were studied [25]. Monensin is used in some countries to increase milk production, to improve feed efficiency and to control ketosis and bloat. Because all the rations mentioned reduced the shedding rate to below the detection level after a period of time (between 19 and 68 days), we assumed that the concentration of bacteria in the faeces would be below the detection level by switching from the normal diet to these modified diets. Because the baseline values of the recovery rates used in the model were very close to the recovery rates observed in the experimental study [25], the baseline values were used.

2.3.3. Probiotics

Probiotics or competitive exclusions (CE) are capable of reducing pathogenic microorganisms in livestock [3, 19, 20, 28]. The ability of colicinogenic *E. coli* that produce colicin E7 (DNase) in reducing the prevalence of VTEC O157 in cattle has been investigated [20]. Young cattle were infected with high doses of VTEC O157 and colicinogenic *E. coli* was added to the diet to produce colicin. In the treated group an average 1.14 log CFU reduction of bacteria per gram of faeces could be observed. Based on these results, we considered a 1.14 log CFU reduction of bacteria shed by administration of colicinogenic *E. coli* to cows. Because the length of the reference study [20] was the same for treated and control groups (24 days), and both groups were positive in faeces to the end of the study, we assumed that there is no change in the shedding period and consequently the recovery rate in the model.

2.3.4. Hygiene

Hygienic measures affect daily death rate (q_i) of the pathogen in the group-specific environment and the general environment on a dairy farm. An exponential decay rate can be used in modelling the death of the bacteria outside the host (e.g., in faeces). In this model, we chose to incorporate the additional loss due to removal of faeces by increasing the baseline exponential decay rate. For simplicity, we assumed that this parameter depends on two factors: (i) contaminated bedding and (ii) contaminated water troughs. The total effect of increasing the frequency of bedding replacement/cleaning and water trough cleaning is considered a hygienic measure in reducing the prevalence of VTEC O157 infected animals. The data of Scott et al. [22] and Davis et al. [11] were used to determine the bacterial death rate in water and bedding materials respectively, using formula 1:

$$C = \mathrm{I}\mathrm{e}^{-q\gamma} \quad (1)$$

where C is the number of CFU bacteria per millilitre of water or per gram of bedding, e is the base of natural logarithm, I is the intercept or initial number of bacteria, q is the reduction rate and γ is the time scale. Using formula 1, we estimated that increasing the frequency of replacing bedding (in a straw yard housing system) or cleaning (in a cubicle housing system) from one to two times per week results in a death rate of 0.46 infectious units per day. This was done by fitting an exponential distribution to the data (i.e., initial number of CFU in the environment corresponding to the time unit (day) of the study) reported by Davis et al. [11]. Following the same procedure and using the data obtained by Scott et al. [22], it was estimated that increasing the frequency of cleaning the water troughs from once per month to four times per month results in a death rate of 0.17 infectious units per day. The parameter q in the model is assumed to relate to both water and bedding. Therefore, by increasing the cleaning or replacing frequency, the death rate will increase. Thus, the total death rate will be 0.63 infectious units per day, due to both interventions.

2.3.5. Combination of interventions

A combination of two or more pre-harvest interventions can also be applied in practice. However, some of the interventions considered in the model exert an effect on the same input parameters of the model (e.g., shedding rate is affected by vaccination, diet modification and colicin) and therefore determining the combined effect of two or more interventions on one input parameter is very difficult. Thus, combinations of hygiene and one of the other three interventions were examined. We assumed that improved hygiene is applied in all groups (U, A, D and L) when it is combined with other interventions. The model was run using single interventions (i.e., using only one intervention in one or more animal groups) and combinations of hygiene with other interventions (i.e., hygiene was applied in all animal groups and other interventions were applied in one or more animal groups).

2.4. Output

Prevalences within the lactating-group (P_{lact}) and the herd (P_{herd}) were the model's output of interest. The effectiveness of interventions is defined as the relative change of P_{lact} and P_{herd} from the baseline. Thus, the effectiveness was measured as the following:

$$Eff_{lact} = {(BP_{lact} - P_{lact})}/{BP_{lact}};$$
$$Eff_{herd} = {(BP_{herd} - P_{herd})}/{BP_{herd}} \quad (2)$$

Where Eff_{lact} and Eff_{herd} denote the effectiveness in the lactating group and herd and BP_{lact} and BP_{herd} denote the baseline outputs (they are the prevalences without any intervention) of the model.

2.5. Sensitivity analysis

The robustness of the outputs was examined by changing the following input parameters: direct transmission parameter (β_i), group-specific indirect transmission parameter (z_i) and the herd size (N). We changed only one of the parameters at a time. For the direct transmission parameter and group-specific indirect transmission parameter ± 10-fold of the default input values were examined, while for the herd size a minimum value of 75 and a maximum value of 125 were examined.

3. RESULTS

3.1. Baseline prevalence and with-intervention prevalences

The model was run for 1 000 days for without- and with-intervention situations. The baseline lactating group prevalence and herd prevalence were 5.02% and 13.96% respectively. The results of implementing the four studied interventions and the combination of hygiene with vaccination (a) are presented in Table III.

Table III shows that hygiene was most effective if it was applied to the whole herd (i.e., all animal groups) or to young stock (above and under-six-month old groups; U+A). Application of hygiene in the above-six-month old group plus lactating group (A+L) was more effective in reducing the P_{lact} than hygiene in only one of the groups or only in the adult groups of cows (D+L). The highest effect of hygiene on P_{herd} was achieved when it was applied in all the groups (U+A+D+L, ΔP_{herd}: 46.6%), although the same effect is obtained when implemented only to young stock groups (U+A, ΔP_{herd}: 45.3%).

The results in Table III show that vaccination (a) has the highest efficacy in reducing P_{lact} when implemented in all the animal groups (i.e., U+A+D+L, ΔP_{lact}: 99.9%) or when implemented to young stock only (i.e., U+A, ΔP_{lact}: 99.3%). Vaccination (a) applied in the above-six-month old group plus lactating group (A+L) has

Table III. Relative reduction of lactating-group prevalence (P_{lact}) and herd prevalence (P_{herd}) from the baseline prevalences (baseline lactating-group prevalence was 5.02% and baseline herd prevalence was 13.96%) by implementing hygiene, vaccination (a) and vaccination (b), implementing diet modification and implementing colicin in various groups.

Interventions and implemented groups[a]	ΔP_{lact}(%)	ΔP_{herd}(%)	Interventions and implemented groups[a]	ΔP_{lact}(%)	ΔP_{herd}(%)
Additional hygiene			Diet modification		
U+A+D+L	89.6	46.6	U+A+D+L	99.6	54.6
U+A	84.4	45.3	U+A	98.9	54.3
A+L	62.1	32.6	A+L	84.0	39.1
A	48.7	29.9	D+L	63.2	14.0
U	30.1	14.9	L	61.7	12.6
D+L	25.3	6.3	A	53.7	32.7
L	22.3	4.5	U	39.4	21.8
D	3.7	1.9	D	4.1	2.2
Vaccination (a)			Colicin		
U+A+D+L	99.9	63.8	U+A+D+L	98.5	52.3
U+A	99.3	63.6	U+A	94.4	51.4
A+L	78.8	40.8	A+L	82.9	38.3
A	53.5	35.6	D+L	61.3	13.6
D+L	50.2	11.1	L	59.8	12.2
L	48.7	10.0	A	52.0	31.9
U	43.5	31.0	U	36.1	19.3
D	3.0	1.6	D	4.1	2.8
Vaccination (b)			Additional hygiene plus vaccination (a)[b]		
U+A+D+L	97.8	51.4	U+A+D+L	99.9	63.8
U+A	92.6	50.2	U+A	99.6	63.8
A+L	82.2	37.9	A+L	95.9	52.0
D+L	60.6	13.4	A	92.9	51.4
L	59.1	12.0	D+L	93.7	47.4
A	51.3	31.6	L	93.7	47.4
U	34.9	18.4	U	97.0	60.0
D	4.1	2.2	D	89.6	46.6

[a] U: under-six-month age group; A: above-six-month age group; D: dry group; L: lactating group.
[b] Additional hygiene was applied to all groups (i.e., whole farm) and vaccination (a) was applied to single and combined groups.

a lower effectiveness (78.8%) in reducing the lactating group prevalence. Vaccination (a) applied in other groups such as above-six-month old group (A), adult groups (D+L), lactating group (L,) under-six-month old (U) and dry group (D) has a relatively low effectiveness in reducing P_{lact} (< 54%). The highest effect of vaccination (a) on P_{herd} is when it is implemented in all groups or in young stock only (ΔP_{herd}: 63.8%). Vaccination (a) when it is applied only in under-six-month old (U) group shows a relatively high reduction in P_{herd} (ΔP_{herd}: 31%) compared to its application in adults (D+L), lactating (L) and dry (D) groups. Also combination of vaccine (a) in under-six-month old (U) group and hygiene in the whole herd shows a 60% reduction in P_{herd}.

Vaccination (b) shows a slightly lower effectiveness than vaccination (a), indicating that a shorter shedding period has an effect on the effectiveness of the vaccine in reducing the prevalence. Table III shows that, similar to vaccine (a), using vaccine (b) in all groups has the highest effectiveness (97.8%) and using it in young stock (U+A) has the second best effectiveness. Vaccine (b) in above-six-month old plus lactating groups (A+L) and in adult groups (D+L) show 82.2% and 60.6% effectiveness. In general, vaccine (a) reduces the shedding period for groups U and A, but actually slightly increases the shedding period for groups D and L. Also, vaccine (b) differs from vaccine (a) in two ways. Vaccine (b) could be less effective just because it does not reduce the shedding rate as much as vaccine (a). However, it is probably a combination of both factors that leads to vaccine (b) being less effective than vaccine (a).

Feeding a modified diet to the lactating group shows 61.7% effectiveness to P_{lact}. This was very close to the effect (63.2%) of feeding a modified diet to all adult animals of the farm (D+L). However, the effects on P_{herd} were low (14.0% and 12.6%). Feeding a modified diet was most effective when it was fed to all the groups or to young stock (U+A) (99%).

Colicin reduced the P_{lact} by 59.8% when it was applied in the lactating group only. Its effect on P_{herd} was slightly higher than vaccinations (a) and (b).

In Figures 2 and 3, the reduction in lactating group prevalence on the horizontal axis is graphed against the reduction in herd prevalence on the vertical axis. Figure 2 illustrates the interventions that were able to reduce the P_{lact} to < 1% and P_{herd} to < 9%. This figure represents interventions that were the best in reducing both P_{lact} and P_{herd}. Each number corresponds to a particular intervention strategy, as described in Appendix I. The majority of the best interventions are a combination of hygiene with other interventions. However, there are some exceptions. Vaccination (a) in all groups (15) and vaccination (a) in U+A (16) are single interventions that effectively reduced both P_{lact} and P_{herd}. Modified diet in U+A (32), vaccination (b) in all groups (23) and colicin in all groups (39) are other single interventions that were effective in reducing P_{lact} by > 98% and to a lower extent P_{herd}. Implementing hygiene in all groups (7) as well as implementing it in young stock only (8) shows a relatively good effectiveness in reducing P_{lact} by almost 90%.

Figure 3 illustrates the interventions that were able to reduce P_{lact} to a value between 1% and 5.02% (i.e., baseline) and P_{herd} to a value between 8% and 13.96% (i.e., baseline). None of the combined interventions falls under these limits. The best intervention in this figure in reducing both P_{lact} and P_{herd} is vaccination (a) in the above-six-month old group plus the lactating group (A+L) (14). Hygiene in the above-six-month old group plus lactating group (A+L) (6) is the second best intervention. In general, the application of hygienic measures shows a lower effect on

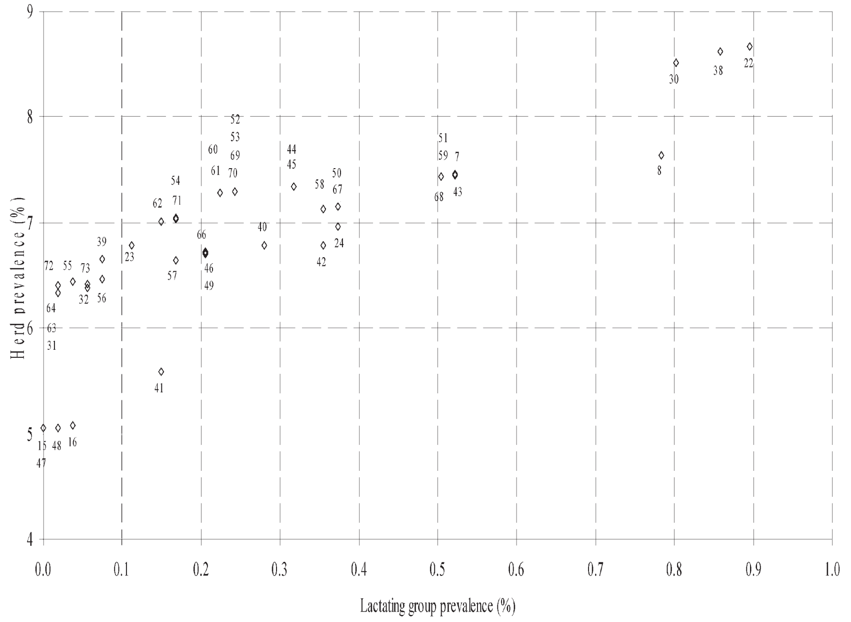

Figure 2. The reduction in lactating group prevalence on the horizontal axis is graphed against the reduction in herd prevalence on the vertical axis. Given are the interventions that were able to reduce the P_{lact} to < 1% and P_{herd} to < 9%. Each number corresponds to a particular intervention strategy, as described in Appendix I.

P_{herd} than the effect of the other interventions (see Tab. III).

According to Figure 2, the top ten interventions in reducing P_{lact} were 15, 47, 48, 16, 31, 63, 64, 72, 55 and 32. These interventions reduce P_{lact} to a value < 0.1%. These interventions were either single interventions in all groups, only in young stock groups or as a result of a combination of hygiene in all groups and other interventions.

3.2. Sensitivity analysis

Figure 4 shows the result of the sensitivity analysis for the three input parameters of the model. The lactating group prevalence is very sensitive to direct transmission parameters as well as group-specific indirect transmission parameters. However, it is not sensitive to the herd size. The results of the sensitivity analysis of the herd prevalence showed the same pattern of sensitivity to the direct transmission parameter and group-specific transmission parameter.

4. DISCUSSION

In this study, we evaluated the effectiveness of four interventions in reducing the prevalence of *E. coli* O157 in either the lactating group or the whole dairy herd, using a deterministic transmission model and quantitative input data. The deterministic essence of the model cannot capture the spontaneous fade-out of the infection that is possible in reality. The

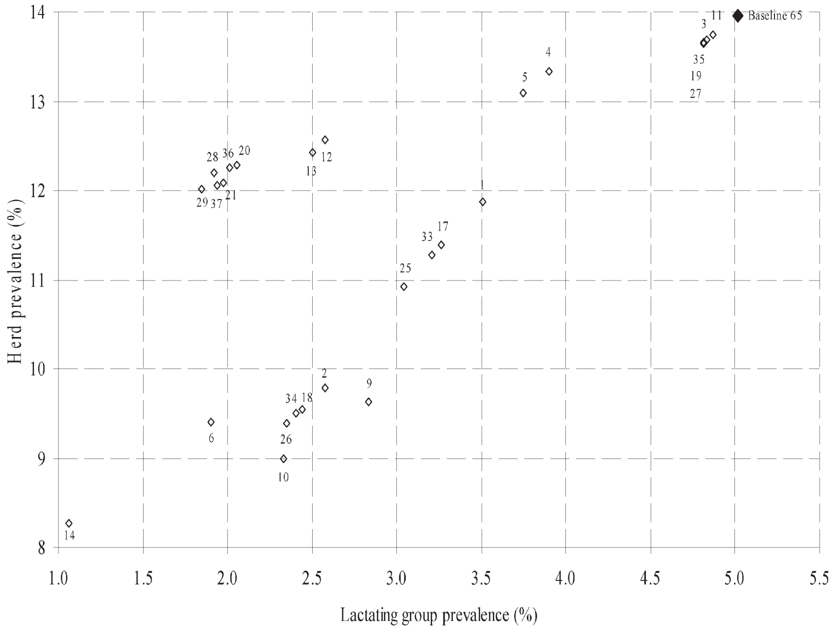

Figure 3. The reduction in lactating group prevalence on the horizontal axis is graphed against the reduction in herd prevalence on the vertical axis. Given are the interventions that were able to reduce P_{lact} from > 1% to < 5.02% (i.e., baseline) and, to reduce P_{herd} from > 8% to < 13.96% (i.e., baseline). Each number corresponds to a particular intervention strategy, as described in Appendix I.

parameters related to indirect-transmission parameters (i.e., shedding rate, animal recovery rate and pathogen death rate) were assumed to be affected by the interventions considered in this study. However, the direct-transmission parameters might also be affected by the interventions, but this was not included in this study, mainly due to the lack of quantitative data. On the contrary, the results of the sensitivity analysis showed that the output is very sensitive to the direct-transmission parameters. Therefore, the effectiveness of interventions might have been underestimated. Our current knowledge about the direct-transmission parameters is limited. Therefore, field studies are recommended to obtain reliable estimates for these parameters. Also, splitting the herd into two groups of young stock and two groups of adults is a simplification of the real Dutch dairy farming system that in many cases consists of more than four groups of young stock. This fact increases the number of transmission routes of the pathogen between the groups and its inclusion in epidemiological models requires much more precise field data, which are lacking.

The baseline lactating group prevalence and herd prevalence were estimated by the model to be 5.02% and 13.96% respectively. These figures were close to the real prevalence estimations. The real lactating group prevalence was estimated to be 2.2% to 10.7% [15]. The same study estimated the real herd prevalence to be 0.8% to 22.4% in the Netherlands. Implementing vaccination, diet modification and colicin

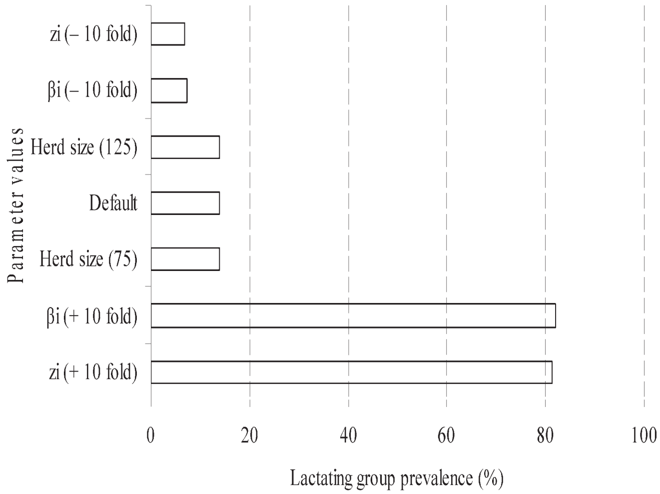

Figure 4. The results of the sensitivity analysis of the impact of the three input parameters of the model, which were not affected by the interventions. Given are the estimated prevalences in lactating group. For direct transmission parameter (β_i) and group-specific indirect transmission parameter (z_i)±10-fold of the default input values were examined, while for herd size a minimum value of 75 and a maximum value of 125 were examined.

in all animal groups or only in young stock are all effective interventions in reducing the baseline P_{lact} by > 90%. This was in accordance with the literature [17, 20, 23, 25]. Previous studies [23, 24] show that implementing on-farm interventions in the entire animal groups of the farm (U+A+D+L) or only in young stock groups (U+A) are the most effective interventions when targeting at P_{lact}. One reason for this could be that the number of bacteria shed by young stock is higher than that shed by adult cattle and interventions considered here mainly affect this parameter. Implementing hygiene only in all groups or in young stock reduces P_{lact} by 89% and 84%, respectively. This was less effective than the other three interventions, but still was a noticeable reduction in P_{lact}. Given the fact that hygiene, (i.e., cleaning water troughs and replacing/cleaning bedding materials more frequently), only affects the bacterial death/removal rate and not the shedding rate, it can be considered a simple and easy-to-apply method. Moreover, a combination of implementing hygiene in all groups and application of one of the other three interventions in one or more animal groups is very effective (> 89% reduction in prevalence).

The results also indicate that implementing diet modification, colicin and vaccination (b) in group L is slightly more effective than implementing them only in the above-six-month old young stock groups (59%–61% versus 51%–53%). This was inconsistent with the finding of Turner et al. [24] that suggests that the best approach to decrease P_{lact} is in reducing the shedding rate and the shedding period in the young stock group (weaned group in their study). One reason for this discrepancy might be that we used Dutch specific input parameters, particularly for the dairy practice parameters instead of UK specific values. There are differences between the two country values mainly in maturation rate, flow from dry to lactating groups and vice versa as well as culling rate. Nevertheless our findings show that the best target group in reducing the herd prevalence (P_{herd}) is the young stock above six-month old group (A), which was consistent with the findings of Turner et al. [24] under UK conditions.

In our reference study [25] for diet modification, a combination of high forage/high grain with monensin was used. In principle, the use of ionospheres such as monensin is prohibited in the Netherlands. However, we included it as a potential intervention that might be considered in the future. Also, both diets evaluated by Van Baale et al. [25] are not commonly used in the Netherlands. Because there has not been a specific Dutch study on reducing the shedding concentration via diet modification, we used the results of the above study as our basis. It is clear that switching the current routine diet on the Dutch dairy farms to the diets used in this study will be interruptive and costly. Therefore, until a specific Dutch experimental study of the effect of diet modification on the concentration of VTEC O157 shed is performed, diet modification cannot be strongly advised for practice. Moreover, we assumed that the new diet reduces only the shedding rate as a result of hindering colonisation of the bacteria in the GI tract. However, we might expect that the duration of shedding and consequently recovery period are also reduced. This was not included in the model to avoid adding complexity by using uncertain data or making more assumptions.

Probiotics and mainly colicin are mentioned as effective interventions to control VTEC O157 at the farm level [20]. However, our results show that colicin is only effective when it is administered at least in the above six-month old group (A) and under six-month old group (U). This is most probably due to the fact that the recovery period of the animals in the study by Shamberger et al. [20] was longer than the default value used in the model.

The results show that implementing the hygienic intervention in young stock plus lactating groups (A+L) has closely the same effect as implementing modified diet in group L. Thus, the decision about which intervention to be used should also take implementation costs into account.

Selecting the best intervention and the best target group will still depend on the result of a cost-effectiveness analysis as well as a utility analysis of the decision makers in the field. We therefore recommend that first, conditions and limitations of the modelling approach should be considered when interpreting these results and second, further field studies should be done to prove the assumptions and to assess the cost-effectiveness of the on-farm interventions.

The objective of this paper was to rank simulated interventions based on their effectiveness in reducing the baseline prevalence of infected animals in the group of lactating-dairy cattle. The first conclusion is that combinations of hygiene in all groups and one other intervention are in the top ranking of interventions in reducing the lactating group prevalence and to a lower extent the herd prevalence. The second conclusion is that implementing each four single interventions studied in all the animal groups of the farm (whole herd) or only in young stock groups are the second top ranking interventions. The third conclusion is that vaccination, diet modification and colicin E7 are estimated to be more effective than hygiene in reducing P_{lact} given our assumptions used in this study. The results show that in some cases single interventions are as effective as combined sets. The result of this paper gives an insight into the interventions that can be considered for implementation. It also shows that field data are still lacking that could enable an even better judgement on the effectiveness of interventions.

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Appendix I. Numbers related to interventions and implemented groups mentioned in Figure 2 and Figure 3.

#	Intervention - group	#	Intervention - group	#	Intervention - group	#	Intervention - group
1	Hygiene - U	20	Vaccine (b) - L	39	Colicin - U+A+D+L	58	Hyg. & diet - A
2	Hygiene - A	21	Vaccine (b) - D+L	40	Colicin - UA	59	Hyg. & diet - D
3	Hygiene - D	22	Vaccine (b) - A+L	41	Hyg. & vacc. (a) - U	60	Hyg. & diet - L
4	Hygiene - L	23	Vaccine (b) - U+A+D+L	42	Hyg. & vacc. (a) - A	61	Hyg. & diet - D+L
5	Hygiene - D+L	24	Vaccine (b) - U+A	43	Hyg. & vacc. (a) - D	62	Hyg. & diet - A+L
6	Hygiene - A+L	25	Diet - U	44	Hyg. & vacc. (a) - L	63	Hyg. & diet - U+A+D+L
7	Hygiene - U+A+D+L	26	Diet - A	45	Hyg. & vacc. (a) - D+L	64	Hyg. & diet - U+A
8	Hygiene - U+A	27	Diet - D	46	Hyg. & vacc. (a) - A+L	65	Baseline
9	Vaccine (a) - U	28	Diet - L	47	Hyg. & vacc. (a) - U+A+D+L	66	Hyg. & col. - U
10	Vaccine (a) - A	29	Diet - D+L	48	Hyg. & vacc. (a) - U+A	67	Hyg. & col. - A
11	Vaccine (a) - D	30	Diet - A+L	49	Hyg. & vacc. (b) - U	68	Hyg. & col. - D
12	Vaccine (a) - L	31	Diet - U+A+D+L	50	Hyg. & vacc. (b) - A	69	Hyg. & col. - L
13	Vaccine (a) - D+L	32	Diet - U+A	51	Hyg. & vacc. (b) - D	70	Hyg. & col. - D+L
14	Vaccine (a) - A+L	33	Colicin - U	52	Hyg. & vacc. (b) - L	71	Hyg. & col. - A+L
15	Vaccine (a) - U+A+D+L	34	Colicin - A	53	Hyg. & vacc. (b) - D+L	72	Hyg. & col. - U+A+D+L
16	Vaccine (a) - U+A	35	Colicin - D	54	Hyg. & vacc. (b) - A+L	73	Hyg. & col. - U+A
17	Vaccine (b) - U	36	Colicin - L	55	Hyg. & vacc. (b) - U+A+D+L		
18	Vaccine (b) - A	37	Colicin - D+L	56	Hyg. & vacc. (b) - U+A		
19	Vaccine (b) - D	38	Colicin - A+L	57	Hyg. & diet - U		