

Milk quality assurance programmes for paratuberculosis: stochastic simulation of within-herd infection dynamics and economics

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ABSTRACT

A bulk milk quality assurance programme for *Mycobacterium avium* subsp. *paratuberculosis* (MAP) in dairy herds was simulated with a stochastic simulation model (JohneSSim). Herds were certified as 'low-MAP bulk milk' if, with a certain probability, the concentration of MAP in bulk milk did not exceed a maximum acceptable concentration (MAC). The MAC, less than 10^3 MAP per litre, was based on pasteurisation studies. The programme starts with an intake procedure; test-negative herds enter a surveillance procedure and test-positive herds enter a control procedure. The aim of this study was to simulate combinations of various intake, surveillance and control procedures to evaluate their epidemiological and economic effects in a population of closed Dutch dairy herds.

The results showed that herd examinations by ELISA for intake and surveillance effectively ensure the quality of 'low-MAP bulk milk': >96% of simulated certified herds were below the MAC. Preventive management measures had little influence on the MAP bulk milk concentration in herds certified as 'low-MAP bulk milk', but had an important positive effect on the number of certified herds. Culling of test-positive animals based on biennial faecal culture was more effective than culling based on annual ELISA. Average total discounted costs for 20-year participation in a programme consisting of intake by ELISA, surveillance by biennial ELISA and control by biennial faecal culture were $\text{€}6 \cdot 10^3$ per herd. On average, additional preventive measures increased these costs to $\text{€}40 \cdot 10^3$ per herd.

This study showed that a bulk milk quality assurance programme based on MAP concentrations for closed Dutch dairy herds is feasible and provided decision-makers with information on the cost-effectiveness of different programmes.

Keywords: cattle, paratuberculosis, stochastic simulation model, certification, surveillance.

INTRODUCTION

Mycobacterium avium subsp. *paratuberculosis* (MAP) infections in cattle are of concern to the dairy industry in part due to the as-yet-unresolved issue of its potential role in Crohn's disease in humans (Anon. 2000, Chacon et al. 2004, Herrewegh et al 2004). If MAP is causally implicated, then milk is a possible vehicle by which humans may acquire the infection, because MAP has been detected in raw milk and may not be effectively inactivated by pasteurisation (Sweeney et al., 1992b, Streeter et al. 1995, Grant et al. 1996, Millar 1996, Sung and Collins 1998, Grant et al. 1999, Giese and Ahrens 2000, Corti and Stephan 2002, Gao et al. 2002, Grant et al. 2002a & b, MacDonald et al. 2002, Pillai and Jayaro 2002, Sevilla et al. 2002, Rademaker (NIZO food research, the Netherlands) personal communication 2004). A milk quality assurance programme for paratuberculosis in dairy herds may reduce the potential risk of MAP transmission to humans through consumption of milk and milk products.

Certification-and-surveillance programmes for MAP-free herds have been developed in several countries (Kennedy et al. 2001). These programmes generally aim at providing buyers with a low risk of acquiring the infection through trade of cattle. In the Netherlands, a certification-and-surveillance programme has been

developed in which herds can obtain 'MAP-free' status following five negative annual herd examinations (the first herd examination by ELISA and faecal culture of ELISA-positive animals, the 2nd through 5th examination by pooled faecal culture; Benedictus et al., 1999). Control programmes for MAP-infected herds generally aim at its elimination. These certification, surveillance and control programmes are inherently expensive and participation is often restricted to a minority of herds. By July 1st, 2005, only 473 of approximately 23.000 Dutch dairy herds had obtained 'MAP-free' status. An alternative control approach is to develop a milk quality assurance programme that focuses on reducing the concentration of MAP in bulk milk rather than eradication of MAP infection from cattle. Herds in a milk quality assurance programme can be certified as 'low-MAP bulk milk' if, with a certain probability, the concentration of MAP in bulk milk does not exceed a pre-set maximum acceptable concentration. This does not necessarily mean that the herd is free of MAP infection. Thus, such a milk quality assurance programme might possibly be run at considerably lower costs than the current Dutch certification, surveillance and control programme. Therefore, the aim of this study was to simulate different milk quality assurance programmes to evaluate their epidemiological effects and economic consequences for a population of closed Dutch dairy herds.

A milk quality assurance programme was simulated, starting with an intake testing procedure. Test-negative herds enter a surveillance program and test-positive herds enter a control program. Herds that are found to be test positive during surveillance shift to the control program. The control program aims to suppress the infection in the herds, such that the milk quality can be guaranteed and the herd can move to the surveillance program. Different milk quality assurance programmes were simulated with a stochastic model JohneSSim (Groenendaal et al. 2002). Varied alternative test schemes based on herd examinations by serology (ELISA) or individual faecal culture (IFC) were simulated. All programmes were simulated with and without preventive management measures taken by all participating herds. The simulation assumed all herds were closed.

MATERIALS AND METHODS

The JohneSSim model. The JohneSSim model is a stochastic and dynamic simulation model that simulates (a) herd dynamics, (b) disease dynamics within the herd, (c) control of Johne's disease and (d) economic consequences at the herd level. The herd dynamics of a typical Dutch dairy herd and the infection and disease process in a 20-year period are simulated. The model and its use to study certification and surveillance programmes have been described in detail (Groenendaal et al. 2002, Weber et al. 2004). Repeated runs of the model provide insight into the variation in outcome at the farm level. Results at a higher aggregation level (e.g. national level) are obtained by simulating different types of dairy herds and aggregating the results according to their relative abundance. Both infected and non-infected herds are simulated.

Assumptions in JohneSSim model for present study. All herds were assumed to be closed (i.e. no purchase of animals and no new introductions of MAP). Herd size was assumed to be 65 adults (≥ 2 yr.) initially, and to increase by 5% per annum. Eighty to 100% of heifer calves were raised in the herd, while a surplus of heifers was sold shortly before 1st calving. Mean annual milk production was 8000 kg. Initial herd-level true prevalence was assumed to be 0.30, based on a recent study in the Netherlands (van Weering (AHS, the Netherlands), personal communication, 2004). The assumed distribution of the initial within-herd true prevalence in infected herds is shown in Fig 1. Economic assumptions on losses caused by infection with MAP, costs of participation in the quality assurance programme and costs of preventive management measures were updated (Tables 1-3). All costs were discounted at a real interest rate (approximated by interest rate minus inflation rate) of 5% per year. Assumptions on test characteristics are shown in Table 4. Preventive management in the simulated herds was set to reflect the distribution of management practices in the Dutch dairy industry ('background' management; Groenendaal et al. 2002). Assumptions on effectiveness of additional preventive management measures, imposed on the 'background' management, have been described in detail previously (Groenendaal et al. 2002). By default, effective separation of young stock from adult cattle was assumed to reduce incidence through faecal contamination of the environment by 90%.

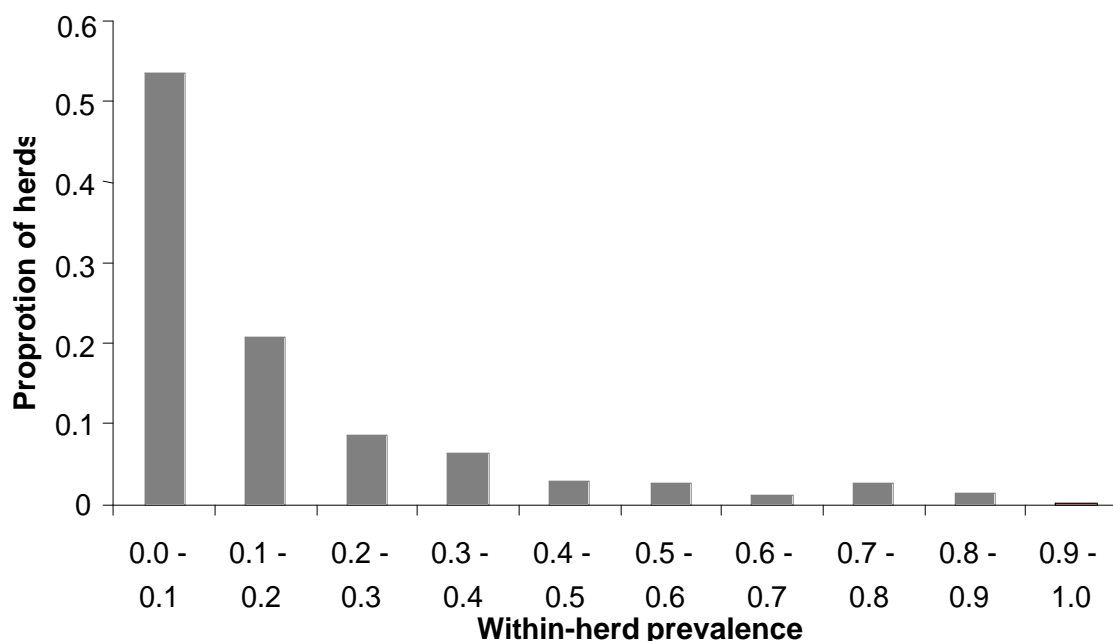


Fig. 1. Assumed starting distribution of within-herd true prevalence in infected herds.

Table 1. Assumptions on losses caused by infection with MAP. Losses did not include effects of a potential reduction in milk consumption due to consumer concerns.

Category		Costs (Euro)
Milk production	Reduction depends on infection state: 5% (early) to 20% (clinical)	0.08 / kg
Treatment	Treatment of clinical case	30
Reduced slaughter value	Standard slaughter value (per cow)	448.75
	Reduction depends on infection state (early 5%, infectious 10%, clinical 100%)	
Missed future income	Retention Pay Off (depending on parity, month in lactation and production level assuming no alternative use of production factors)	- 111.63 to 1431.23

Table 2. Variable costs (Euro) of participation in the bulk milk quality assurance programme. Subscription costs were 90 Euro per year. Costs do not include Value Added Tax (VAT for subscription and laboratory tests = 6%; VAT on other costs 19%).

Test / action	Costs : veterinarian	Transport	Lab / submission	Lab / test
Veterinarians' visit	22 per visit			
IFC	2.75 per animal	10	7.80	30.00 per animal
ELISA	2.75 per animal	10	7.80	6.15 per animal

Table 3. Assumed costs (Euro) of preventive management measures (including labour at 18.21 Euro per hour). Fifty percent of the costs of additional preventive management measures imposed on the 'background' management (Groenendaal et al. 2002) were attributed to the control of paratuberculosis.

Category		Loss or costs
Calving	Costs of cleaning per year	€ 100 per year
	Extra labour (hygiene, milking own dam) per calving	Own dam colostrum of €9.11
Milk replacer	280 litres of artificial milk, 8 litre of milk replacer per kg milkpowder, costs of milkpowder € 1.30 per kg, value of bulkmilk €0.20 per litre.	42 litre vs. rest milk = €6.83 238 litre vs. bulkmilk = - €9.11 Total = - €2.28
Hygiene barrier	Between adult stock and young stock	€ 726.71 per year (including labour)
Roughage	Better quality roughage, straw during housing in summer season only.	€ 39.03 for calves 0 – 6 months
Housing	Separate housing of animals 0 – 70 days (initially 5 animals)	€ 487.5 per year; 5% increment per year
	Separate housing of animals 70 – 180 days (initially 7 animals)	€ 682.5 per year; 5% increment per year
	Separate housing of animals 180 – 360 days (initially 9 animals)	€ 877.5 per year; 5% increment per year

Table 4. Assumptions on sensitivity (Se) and specificity (Sp) of individual faecal culture (IFC) and serum ELISA.

	Stage of infection	IFC	ELISA
Se	Early, minimal shedding	0	0.01
	Low level shedding	0.40	0.10
	Heavy shedding	0.95	0.60
	Clinical disease	0.90	0.80
Sp	Not infected	1 ^(a)	0.997 ^(b)

^(a) Reinders (1963); ^(b) van Maanen et al. (2002).

Shedding of MAP in milk. The assumptions made on shedding of MAP in milk depended on the stage of infection are shown in Table 5. These assumptions were based on the available quantitative data on direct shedding of MAP in milk, faecal contamination of milk and shedding of MAP in faeces (Chiodini et al 1984, Stadhouders and Jørgensen 1990, van der Giessen et al. 1992, Sweeney et al. 1992a & b, Streeter et al. 1995, Millar 1996, Rossiter and Burhans 1996, Nauta and van der Giessen 1998, Giese and Ahrens 2000, Pearce et al. 2001, Corti and Stephan 2002, MacDonald et al. 2002, Grant et al 2002a, Grant et al. 2002b, Pillai and Jayaro 2002, Sevilla et al 2002, Rademaker (NIZO food research, the Netherlands), personal communication 2004, Stehman (Cornell University, USA), personal communication, 2004).

Acceptable concentration of MAP-organisms in milk. The concentration of MAP organisms in on-farm bulk milk that can be considered acceptable for eventual human consumption after pasteurization is unknown. Firstly, no quantitative data on exposure to MAP (either alive or dead organisms) are available and the probability of human disease is unknown. In the present study, we assumed that no viable MAP organisms should be present after commercial pasteurisation. Secondly, the results of pasteurisation studies seem to be inconsistent. Stabel et al. (1997) found pasteurisation in a test tube to be ineffective, but found complete killing using spiked milk samples with a lab-scale pasteuriser with a turbulent flow of milk during pasteurisation. Similarly, MAP cells could not be recovered in milk samples that were spiked with approximately 10^6 MAP cells, after disruption of cell clumps, if high-temperature short-time (HTST) pasteurisation was performed at 72°C with holding times 10 s (Rademaker et al, 2002). HTST pasteurisation is expected to give a 5 to 6 \log_{10} reduction in numbers of viable MAP in milk (Grant et al. 1996, Grant et al. 1999, Gao et al. 2002). However, surviving MAP cells were detected in 19 of 33 (55%) spiked milk samples pasteurised by HTST when MAP was initially present in a concentration of 10^4 CFU per ml (Grant et al 1996). Furthermore, MAP was found to survive HTST pasteurisation in milk from 2 infected herds (Grant et al 2002a). Sung and Collins (1998) concluded that MAP may survive HTST pasteurisation when the initial organism concentration is greater than 10^3 cells per litre. Therefore, in the present study, we considered a concentration of MAP organisms in milk less than 10^3 per litre acceptable.

Table 5. Assumed concentration of MAP in milk for each stage of the infection in adult cattle (Total MAP in milk = direct shedding + faecal contamination * MAP in faeces).

Stage	Proportion of animals by stage	Direct shedding of MAP in milk (organisms/L)	Faecal contamination of milk (g/L)	MAP in faeces (organisms per gram)	Total MAP in milk (organisms per litre)
Early stage infection	0	0	0.04	0	0
Low shedder	0.8	0	0.04	0	0
	0.2	0	0.04	10^2	4
Heavy shedder	0.6	10^2	0.04	10^2	10^2
	0.24	10^2	0.04	10^4	$5 \cdot 10^2$
	0.16	10^2	0.04	10^7	$4 \cdot 10^5$
Clinical disease	0	10^4	0.04	10^9	$4 \cdot 10^7$

Bulk milk quality assurance programmes. In our simulations, certified 'low-MAP bulk milk' dairy herds were assigned a status 'green', while other dairy herds were assigned a status 'red'. Thus, 'green' herds were herds with a high probability that the concentration of MAP in bulk milk was $<10^3$ per litre. The intake procedure was done two years after the start of the simulations. Initial assignment of a status to a herd was based on the results of the intake: test negative herds were classified as 'green' and test-positive herds as 'red'. Thereafter, 'green' herds were regularly monitored in a surveillance scheme; if a herd converted to a

test-positive status, it was moved to the pool of 'red' herds. An infection control scheme was applied to 'red' herds. Test-positive cattle and their last-born offspring were culled.

Various alternative test schemes for intake (i), surveillance (s) and control (c) were simulated (Table 6). The number of negative herd examinations required for a 'red' herd to move to the pool of 'green' herds was determined by the probability that the concentration of MAP in bulk milk was $<10^3$ per litre. A test-negative 'red' herd became 'green' if this probability was equal to, or higher than, the probability for a 'green' herd to have $<10^3$ MAP per litre immediately after the intake procedure.

All programmes were simulated with and without additional preventive management measures imposed by all participating herds on their 'background' management. When applied, the preventive measures were: improved hygiene around birth, colostrum from own dam only, feeding of artificial milk replacer only, and effective separation of young stock from adult cows from birth to the end of the first year.

Model output. In the present study, relevant herd-level outcomes over time were the within-herd true prevalence, test prevalence, concentration of MAP in bulk milk, and costs spent on the quality assurance programme. Relevant aggregate level outcomes over time included the proportion of herds initially categorized as 'green', the average concentration of MAP in bulk milk from 'green' herds, the proportion of 'green' herds with $<10^3$ MAP organisms per litre of bulk milk and costs spent on the bulk milk quality assurance programme (including herd examinations, subscription costs, preventive measures and cull of infected animals).

Table 6. Simulated test schemes for intake (i), surveillance (s) and control (c) for cattle. In the intake and surveillance procedure, a positive ELISA result was confirmed by individual faecal culture (IFC); IFC positive cattle and their lastborn calf were culled. In the control procedure, all ELISA or IFC positive cattle were culled.

Scheme	Intake		Surveillance			Control		
	Test (once)	Animals	Test	Interval	Animals	Test	Interval	Animals
i1-s1-c1	ELISA	All, ≥ 3 yr	ELISA	1 yr	All, ≥ 3 yr	ELISA	1 yr	All, ≥ 3 yr
i1-s1-c7	ELISA	All, ≥ 3 yr	ELISA	1 yr	All, ≥ 3 yr	IFC	2 yr	All, ≥ 2 yr
i1-s2-c1	ELISA	All, ≥ 3 yr	ELISA	2 yr	All, ≥ 3 yr	ELISA	1 yr	All, ≥ 3 yr
i1-s2-c7	ELISA	All, ≥ 3 yr	ELISA	2 yr	All, ≥ 3 yr	IFC	2 yr	All, ≥ 2 yr

Sensitivity analyses. The influence of various input parameters on the study results was analysed by changing one parameter at the time. These sensitivity analyses were performed with test scheme i1_s1_c1, with or without additional preventive management measures taken in the herds. Two possible values were assessed for each of four scenarios: (1) The default numbers of MAP bacteria in milk (Table 5, last column) were multiplied by 10^4 and 10^6 respectively to study the effect of altering the value of this uncertain parameter. (2) The model's default effect of preventive management measures was to reduce the probability of infection through the environment by 90%. An alternative assumption was tested whereby the reduction was only 50%. (3) By default, the initial herd-level true prevalence was 0.30. Alternatively, a prevalence of 0.56 was simulated. (4) By default, multiple negative herd-examinations were required for a 'red' herd to become 'green' (based on the probability for such herd to have $<10^3$ MAP per litre of bulk milk). The effects on the model of requiring only one negative herd-examination to receive a 'green' status was tested.

RESULTS

Simulated bulk milk quality assurance programmes. At intake (scheme i1: ELISA, all cattle ≥ 3 yr, ELISA positive confirmed by IFC), 90% of all herds were test-negative and classified as 'green'. The remaining 10% of herds were test-positive (i.e. $\sim 35\%$ of the infected herds at that time, and none of the non-infected herds) and therefore classified as 'red'. The assumed within-herd prevalence of adult cattle in 'green' and 'red' herds at the intake is shown in Fig. 2A. The concomitant distribution of the concentration of MAP in bulk milk is shown in Fig. 2B. Immediately after the intake procedure (with scheme i1), 98% of 'green' herds had a concentration of MAP in bulk milk $<10^3$ per litre. During control in 'red' herds, two consecutive negative herd-examinations by IFC or six consecutive negative herd-examinations by ELISA were required to reach the same probability of having $<10^3$ MAP per litre milk. Therefore, by default, 'red' herds were re-

classified as ‘green’ only after two consecutive negative herd-examinations by IFC, or six consecutive negative herd-examinations by ELISA.

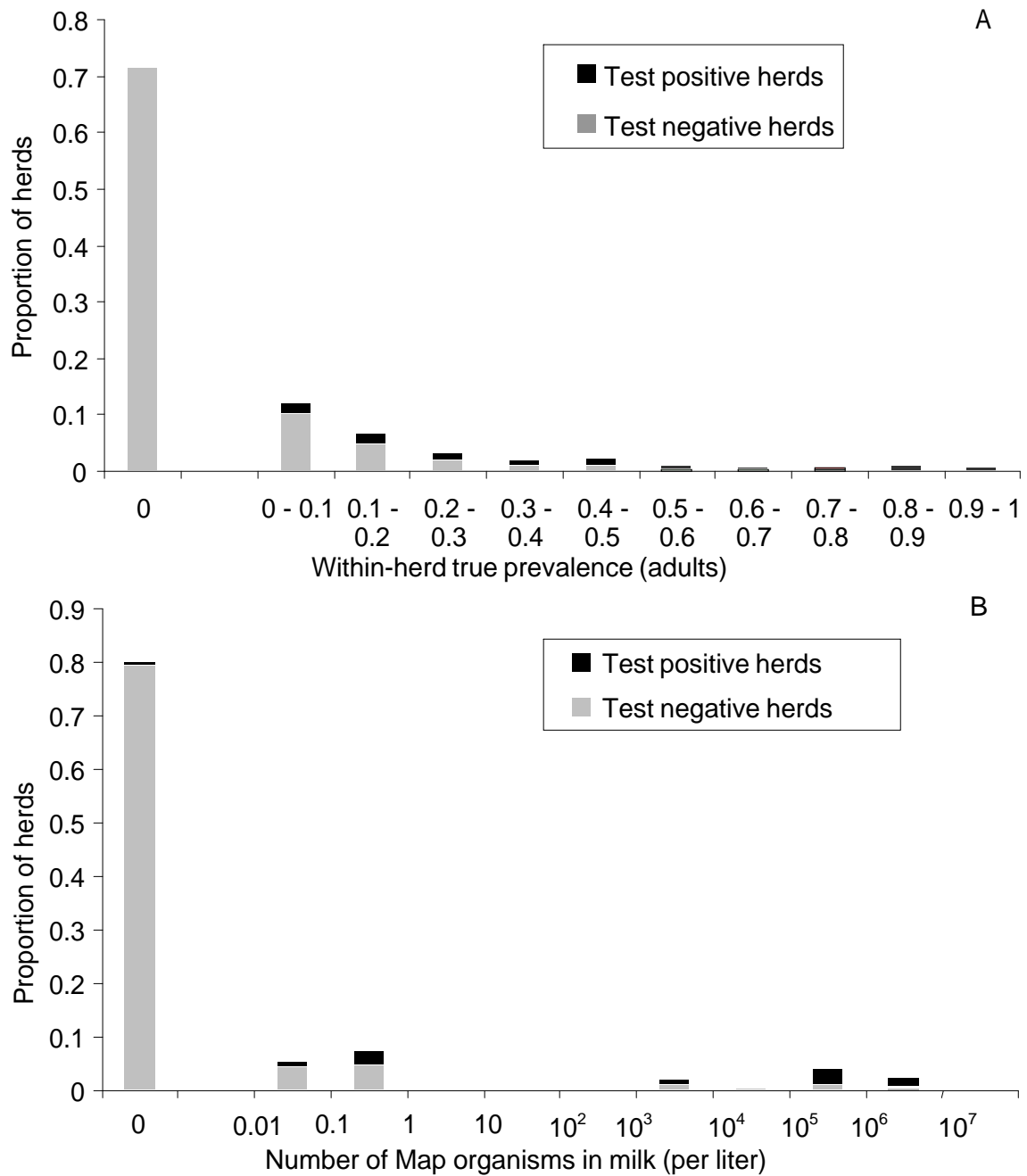


Fig. 2. Estimated within-herd prevalence in adult cattle (A) and estimated number of MAP organisms per litre of bulk milk (B) immediately after intake in simulated herds that were test-positive (‘red’) and test-negative (‘green’) at intake, using intake scheme i1 (ELISA, all cattle ≥3 yr).

The proportion of herds classified as ‘green’ decreased over time if no preventive measures were taken (Fig. 3A). However, if preventive management measures were taken, this proportion first decreased, but, thereafter, increased towards 86% - 99%, depending on the test scheme used (Fig. 3B). Preventive measures were pivotal for ‘red’ herds to become ‘green’. Furthermore, these measures reduced the proportion of ‘green’ herds that lost their status. If preventive measures were taken, culling based on IFC was more effective than culling based on ELISA.

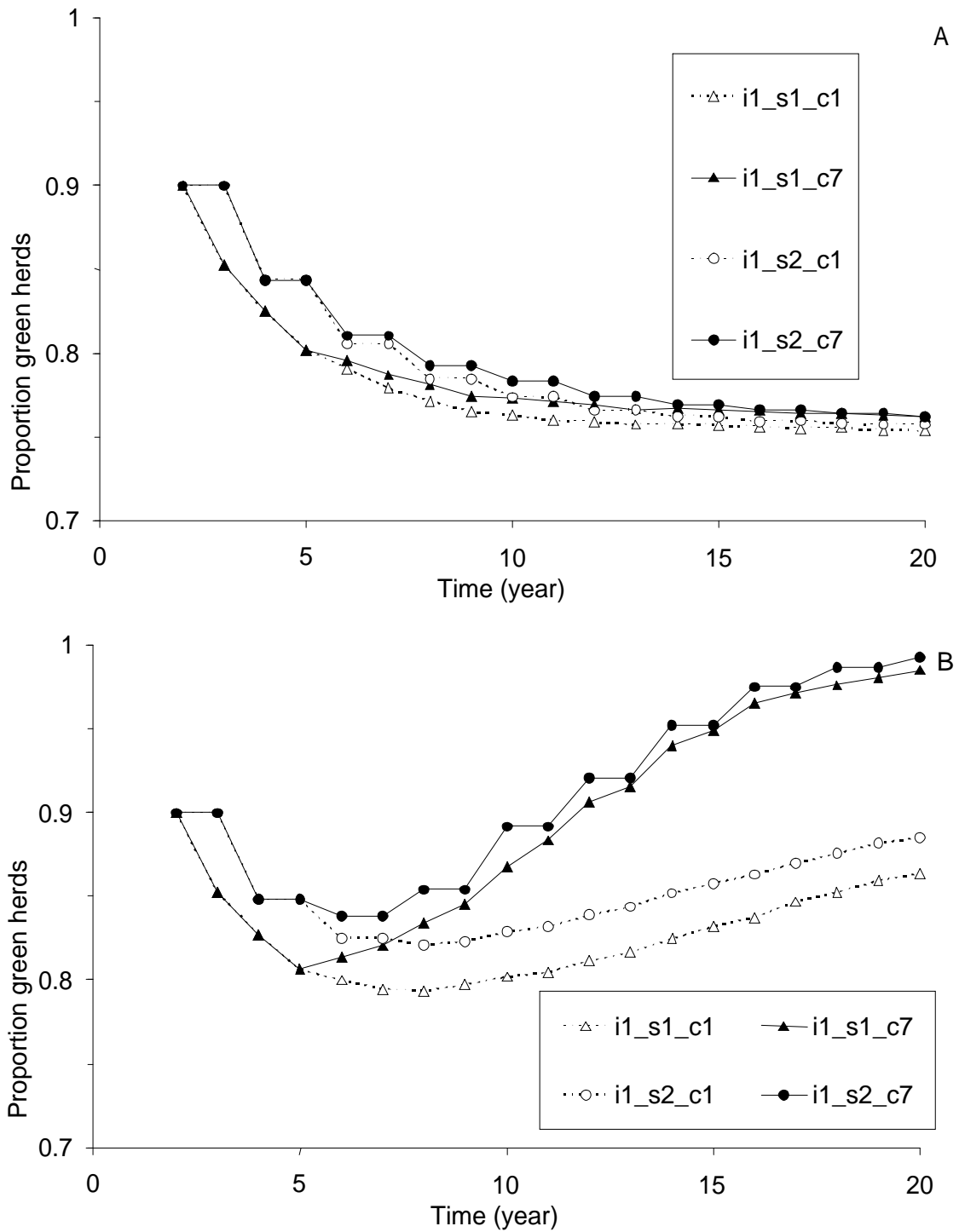


Fig. 3. Proportion of herds that are classified as ‘green’ over time, assuming a population of closed herds with an initial herd-level true prevalence of 30%. (A) Without additional preventive measures, (B) with additional preventive measures. Test schemes are defined in Table 4.

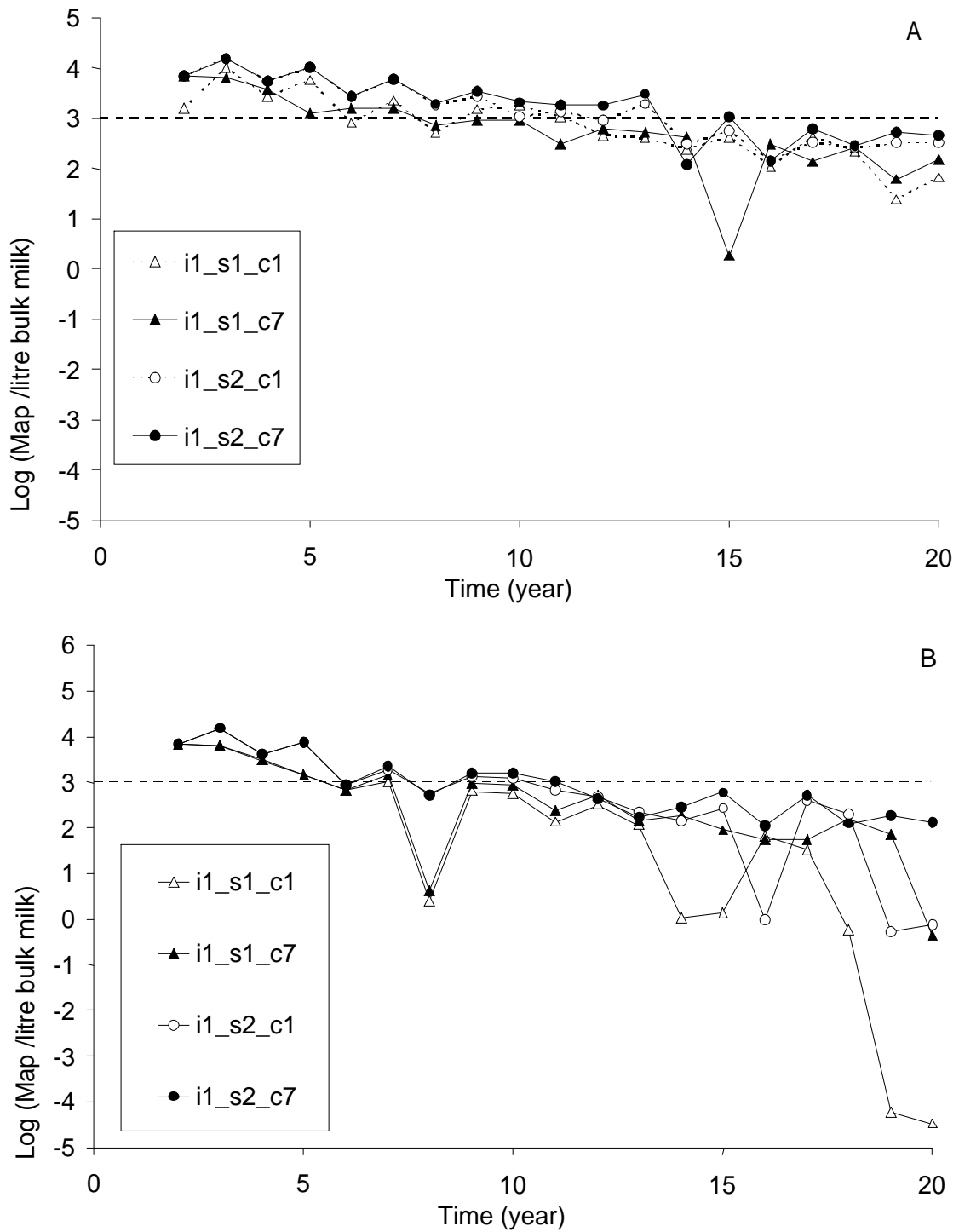


Figure 4. Logarithm (\log_{10}) of the average number of MAP bacteria per litre of bulk milk from ‘green’ herds (A) without preventive management measures, (B) with preventive measures. Test schemes are defined in table 4. The dashed horizontal line indicates the threshold of 10^3 MAP bacteria per litre of bulk milk. Test schemes are defined in Table 4.

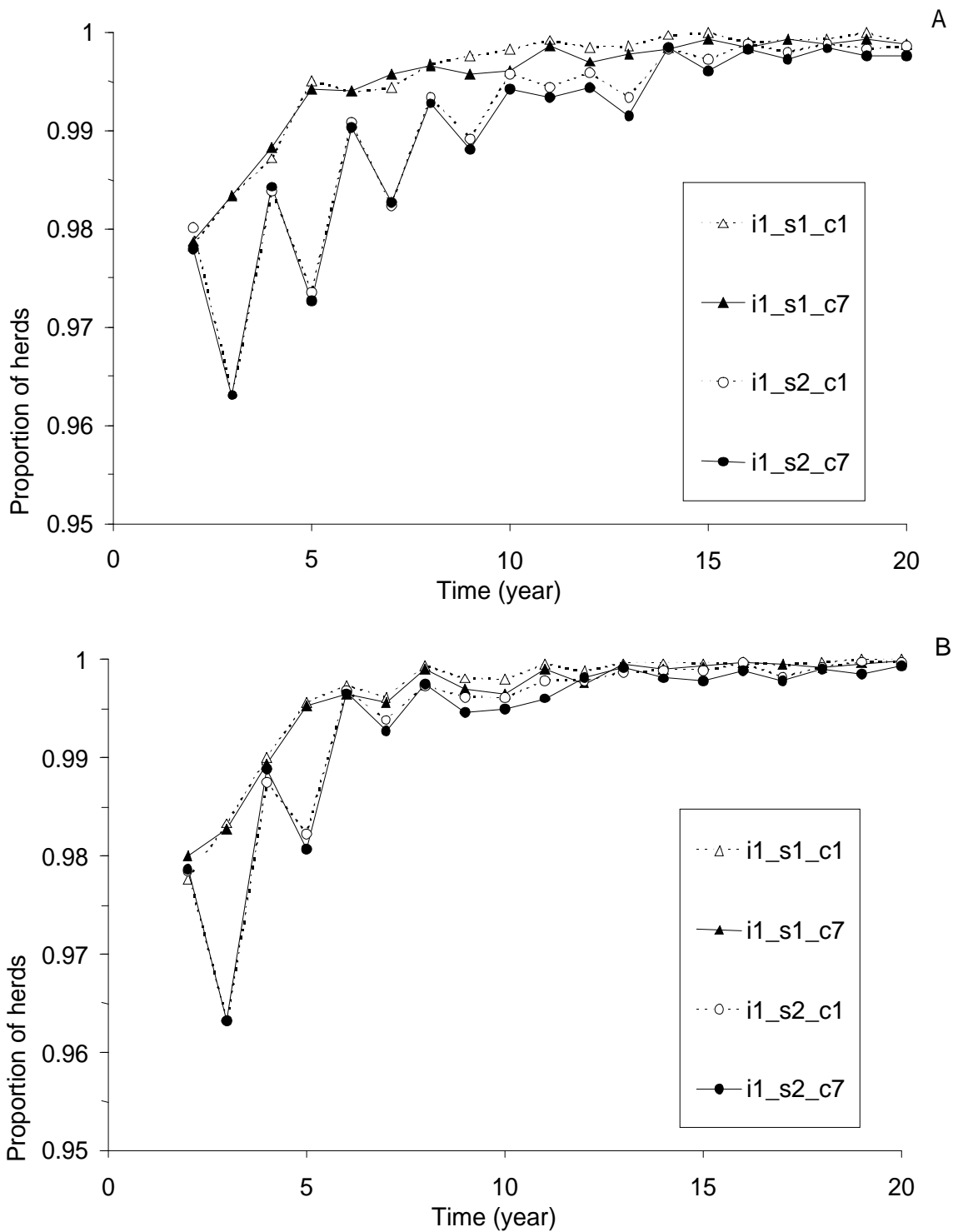


Fig. 5. Proportion of 'green' herds with $<10^3$ MAP per litre of bulk milk (A) without additional preventive measures. (B) with additional preventive measures. Test schemes are defined in Table 4.

Depending on the scheme used and whether or not additional preventive measures were taken, the estimated average concentration of MAP bacteria per litre of bulk milk in 'green' herds did not decrease below 10^3 before year 8 to 15 (Fig. 4). The proportion of 'green' herds with $<10^3$ MAP per litre of bulk milk increased towards 100% in year 20 (Fig. 5).

The median cumulative discounted costs during the 20 simulated years for schemes without additional preventive measures ranged from 6,000 to 10,000 Euro (Fig 6). For schemes with additional preventive measures these costs were higher, ranging from 40,000 to 44,000 Euro. However, the 90% range of costs

was much broader if no preventive measures were taken; therefore, for some schemes, the 95% percentile of costs were higher if no preventive measures were taken than if preventive measures were taken.

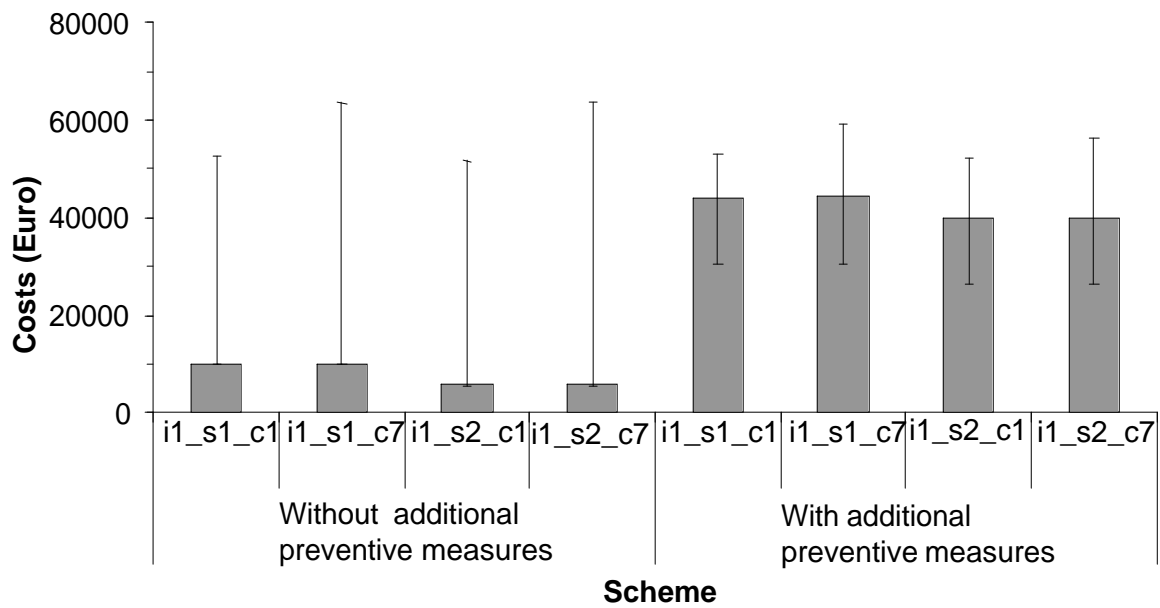


Fig. 6. Median cumulative discounted costs per herd up to year 20 (averaged over all ‘green’ and ‘red’ herds). Error bars indicate the 5% to 95% range. Test schemes are defined in Table 4.

Sensitivity analyses. When control of environmental transmission through preventive measures was assumed to be 50% vs. 90% effective, the number of “green” herds after 8 years was increased by only 5% (81% vs. 86%). If no preventive measures were taken, the number of herds certified as “green” dropped to 75%. Changing the value of the environmental contamination control variable in the model had no effect on the proportion of ‘green’ herds with $<10^3$ MAP per litre bulk milk.

If the default level of contamination of milk with MAP was multiplied by 10^4 or 10^6 , the proportion of ‘green’ herds with $<10^3$ MAP per litre bulk milk was reduced by up to 10% during the first years after intake. However, beyond approximately year 10 (i.e. 8 years after intake), this effect was very small (Fig. 7).

If a higher initial herd-level prevalence was assumed (0.56 instead of 0.30), the proportion of ‘green’ herds in year 20 was reduced by 21% (54% instead of 75% without additional preventive management measures; 75% instead of 86% with additional preventive measures). The proportion of ‘green’ herds with $<10^3$ MAP per litre of bulk milk during the first years of the simulations was decreased by up to 2%, but this decrease was small beyond year 10. Effects on the cumulative discounted costs up to year 20 were negligible.

Changing the assumption about the number of negative herd examinations by ELISA that were required for a ‘red’ herd to be re-classified as ‘green’ has a strong effect. When the model assumed that only one, vs. six, negative tests were required, over 99% of herds were classified as ‘green’ in year 20 (instead of 86%), if additional preventive management measures were taken. The reason is, of course, that ‘red’ herds move to the pool of ‘green’ herds sooner. If no additional preventive measures were taken, there was only a minor effect on the proportion of ‘green’ herds. However, the bulk milk ‘quality’ of these ‘green’ herds was lower: the proportion of ‘green’ herds with $<10^3$ MAP/l was reduced by up to 2% if only one negative herd examination by ELISA was required instead of six.

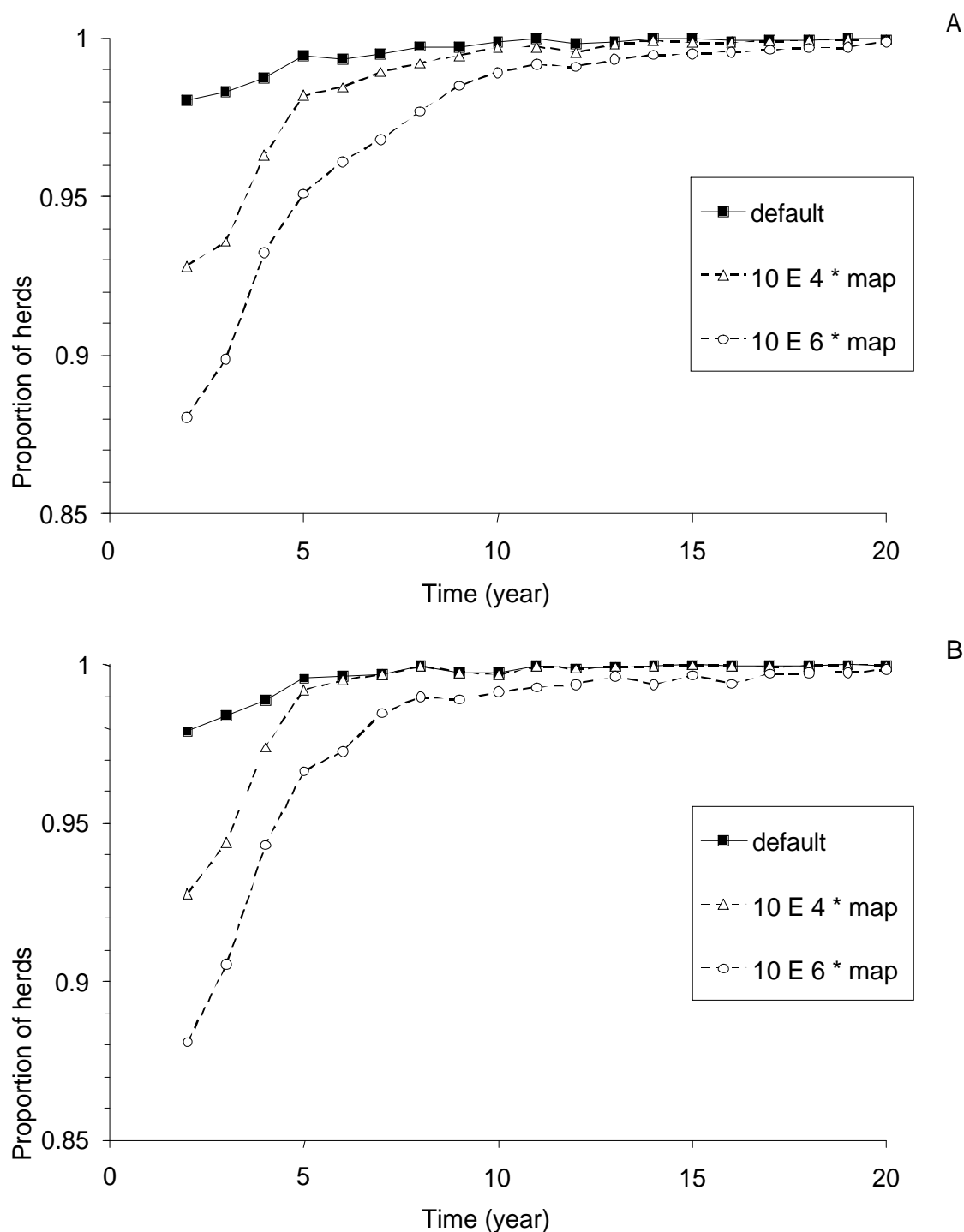


Fig. 7. Sensitivity analysis for the effect of contamination of milk with MAP, using scheme i1_s1_c1. Default concentrations of MAP bacteria in milk are given in Table 5. Alternatively, these concentrations were multiplied by 10^4 and 10^6 . Proportion of 'green' herds with $<10^3$ MAP per litre of bulkmilk, (A) without additional preventive measures, (B) with additional preventive measures being taken.

DISCUSSION

To our knowledge, this is the first modelling study of a bulk milk quality assurance programme for paratuberculosis in dairy herds. By aiming to reduce MAP concentration in the bulk tank, a milk quality assurance programme can be run at considerably lower costs than certification, surveillance and control programmes that attempt to establish low infection risk trade of cattle and eliminate MAP at the herd-level.

Key elements in a successful bulk milk MAP quality assurance programme are (1) preventive measures to reduce the risk of introduction of MAP in participating herds (including trade restrictions), (2) preventive management measures to reduce the risk of within-herd spread of MAP, and (3) effective intake, surveillance, and control procedures. The present study was restricted to closed herds. Effects of animal trade were analysed separately using a mathematical model (van Roermund et al. 2005). In the present study, additional preventive management measures beyond test-and-cull to reduce within-herd spread of MAP were found to have a major effect on the proportion of herds that can be certified as 'low-MAP bulk milk' (i.e. 'green' in this study). These management measures were pivotal for test-positive ('red') herds to move to certification as 'low-map bulk milk' ('green'). However, these measures only had a minor effect on the actual bulk milk quality of 'low-MAP bulk Milk' herds ('green').

It would be optimal to base the intake, surveillance and control procedures on accurate measurement of the concentration of MAP organisms in bulk milk. However, to our knowledge, techniques to routinely quantify MAP in large numbers of bulk milk samples are not yet available. Therefore, we simulated intake, surveillance and control procedures based on tests at the animal-level (ELISA, faecal culture). The results showed that herd examinations by ELISA for intake and surveillance effectively ensure the quality of 'low-MAP bulk milk': >96% of simulated certified herds (increasing to >99% after 10 years) were below the $<10^3$ MAP/l. However, culling of test-positive animals and their last-born offspring based on biennial faecal culture was more effective than culling based on annual ELISA.

While fundamental assumptions were made in the present study, the impact of those considered to be most critical were evaluated through our sensitivity analyses. Due to deficiencies in the current methodology, it has so far been impossible to accurately quantify MAP organisms in milk from a dairy herd with paratuberculosis (Dundee et al, 2001; Grant et al, 2002a). For instance, colony forming units can not simply be translated to concentrations of MAP organisms, because of clumping of MAP in specimens and insensitivity of culture, while quantitative PCR results are estimates only of the total number of both viable and dead MAP organisms. Our sensitivity analyses showed that a 10^6 fold increase in the assumed concentration of MAP in milk from infected animals would initially decrease by 10% the number of certified 'low-MAP bulk milk' ('green') herds with $<10^3$ MAP per litre. However, such high concentrations of MAP in milk are probably not biologically plausible (for example, a clinical animal would have to be shedding $4 \cdot 10^{12}$ MAP/litre of milk). Even if this occurred, the effects of such an increase in MAP in milk from infected animals on the bulk milk quality of 'green' herds were very small beyond year 10 (i.e. 8 years after the intake procedure).

It is concluded that a bulk milk quality assurance programme for paratuberculosis in closed dairy herds is feasible. Preventive management measures should be recommended to participants given that they considerably increase the probability of obtaining and keeping a 'low-MAP bulk milk' status in the long term. Serology is sufficient for intake and surveillance in the programme. However, for control in test-positive herds, culling based on faecal culture results is more effective than culling based on ELISA results. The present study provided decision-makers with information on the cost-effectiveness of different programmes.

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