Human health benefits from livestock vaccination for brucellosis: case study

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Objective To estimate the economic benefit, cost-effectiveness, and distribution of benefit of improving human health in Mongolia through the control of brucellosis by mass vaccination of livestock.

Methods Cost-effectiveness and economic benefit for human society and the agricultural sector of mass vaccination against brucellosis was modelled. The intervention consisted of a planned 10-year livestock mass vaccination campaign using Rev-1 livestock vaccine for small ruminants and S19 livestock vaccine for cattle. Cost-effectiveness, expressed as cost per disability-adjusted life year (DALY) averted, was the primary outcome.

Findings In a scenario of 52% reduction of brucellosis transmission between animals achieved by mass vaccination, a total of 49 027 DALYs could be averted. Estimated intervention costs were US$ 8.3 million, and the overall benefit was US$ 26.6 million. This results in a net present value of US$ 18.3 million and an average benefit–cost ratio for society of 3.2 (2.27–4.37). If the costs of the intervention were shared between the sectors in proportion to the benefit to each, the public health sector would contribute 11%, which gives a cost-effectiveness of US$ 19.1 per DALY averted (95% confidence interval 5.3–486.8). If private economic gain because of improved human health was included, the health sector should contribute 42% to the intervention costs and the cost-effectiveness would decrease to US$ 71.4 per DALY averted.

Conclusion If the costs of vaccination of livestock against brucellosis were allocated to all sectors in proportion to the benefits, the intervention might be profitable and cost effective for the agricultural and health sectors.

Keywords Brucellosis/veterinary/prevention and control/transmission; Brucellosis, Bovine/prevention and control/transmission; Cattle/immunology; Sheep/immunology; Mass immunization/economics, Human; Cost of illness; Disability evaluation; Intersectoral cooperation; Cost allocation; Cost-benefit analysis; Mongolia (*source: MeSH, NLM*).

Mots clés Brucellose/médecine vétérinaire/prévention et contrôle/transmission; Brucellose bovine/prévention et contrôle/transmission; Bovin/immunologie; Mouton/immunologie; Immunisation de masse/économie; Humain; Coût maladie; Evaluation incapacité; Coopération intersectorielle; Affectation coûts; Analyse coût-bénéfice; Mongolie (*source: MeSH, INSERM*).

Palabras clave Brucelosis/veterinaria/prevención y control/transmisión; Brucelosis bovina/prevención y control/transmisión; Bovinos/inmunología; Ovinos/inmunología; Inmunización masiva/economía; Humano; Costo de la enfermedad; Evaluación de la incapacidad; Cooperación intersectorial; Asignación de costos; Análisis de costo-beneficio; Mongolia (*fuente: DeCS, BIREME*).

الكلمات المفتاحية: داء البروسيلات، داء البروسيلات البيطري، الوقاية من داء البروسيلات ومكافحته، سراية داء البروسيلات، داء البروسيلات البقري، الوقاية من داء البروسيلات البقري ومكافحته، سراية داء البروسيلات البقري، المواشي، مناعيات المواشي، الأغنام، مناعة الأغنام، التمنيع الجموعي، اقتصاديات التمنيع الجموعي، بشري، تكاليف المرض، تقييم العجز، التعاون بين القطاعات، توزيع التكالبف، تحليل التكاليف والمنافع، منغوليا. **(المصدر: رؤوس الموضوعات الطبية– المكتب الإقليمي لشرق المتوسط).**

Bulletin of the World Health Organization 2003;81:867-876

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يمكن الاطلاع على الملخص بالعربية في صفحة 875

Introduction

Brucellosis is one of the world's major zoonoses, alongside bovine tuberculosis and rabies (*1*). Brucella infection is endemic in humans and livestock in Mediterranean countries (*2*, *3*). It is also present in Asia, sub-Saharan Africa, and Latin America (*4*–*6*). The importance of brucellosis is not known precisely, but it can have a considerable impact on human and animal health, as well as wide socioeconomic impacts, especially in countries in which rural income relies largely on livestock breeding and dairy products. Human brucellosis is caused by exposure to livestock and livestock products. The most important causative bacteria in decreasing order are: *Brucella melitensis* (small ruminants), *B. abortus* (cattle), *B. suis* (pigs), and *B. canis* (dogs). Infection can result from direct contact with infected animals and can be transmitted to consumers through raw milk and milk products. Human-to-human transmission of the infection does not occur (*7*).

In humans, the symptoms of disease are extreme weakness, joint and muscle pain, headache, undulant fever, hepatomegaly, splenomegaly, and night sweats (*8*). Mortality is reported to be negligible, but the illness can last for several years. In animals, brucellosis mainly affects reproduction and fertility, reduces survival of newborns, and reduces milk yield. Mortality of adult animals is insignificant (*9*).

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Ref. No. **02-0434**

Control strategies available to prevent human infection are pasteurization of milk, livestock vaccination, and elimination of infected animals. In Mongolia, livestock rearing and milk production are important branches of the economy, employing approximately 50% of the population. In the 1970s, mass vaccination of livestock successfully reduced the annual incidence in humans to less than one case per 10 000 (J Kolar, personal communication, 1999, J Kolar, personal communication, 2000). After democratic reform, and the shift away from dependence on the former Soviet Union in 1990, human brucellosis re-emerged as a major, but preventable, source of illness. A large survey conducted during 1990–95 among herdsmen and other people who work with animals showed that 16% of the examined population were infected (*10*). Transmission mainly seems to be an occupational hazard. In contrast, in Saudi Arabia, where consumption of raw milk is important, 30% of the people reported as having brucellosis were aged <15 years (*8*).

The Mongolian authorities suspect that the high incidence of brucellosis causes significant economic losses. On the basis of recommendations made to WHO (*11*), a whole-herd vaccination strategy covering 10 years was developed to start in 2000 (*12*). Very little is known about the economic implications of brucellosis and brucellosis control for human health in any country (*13*). The particular zoonotic nature of brucellosis needs a multisectoral assessment, including human health, the socioeconomic situation of the concerned population groups, and livestock production.

The main objective of this study was to estimate the cost-effectiveness to human health and the potential net economic benefits of a nationwide mass vaccination programme for livestock over a period of 10 years. In order to present cost-effectiveness and cost-benefit ratios from different perspectives (health sector, agricultural sector, households, and society), a tool was developed that attributed costs and benefits to these different perspectives.

Material and methods

Selection of alternatives

From 1990, Mongolia has practised low-level surveillance, with occasional testing of livestock herds, followed by voluntary slaughter of infected animals. No state compensation is given for slaughtered animals.

Our analysis of the potential benefit of livestock vaccination is based on the vaccination scheme proposed in the Mongolian budget in 2000 for whole-herd vaccination (Appendix A, web version only, available at: http://www.who.int/bulletin) within the first six years, this scheme aims to vaccinate all adult animals twice (one-third of the total adult population per year). All animals born during the 10 years of the plan will be vaccinated once (at age <1 year). For the selection of vaccination scenarios, we assumed the reported efficacy for reduction of transmission as the prevented fraction (1 – R), where R is the relative risk of disease in those who receive the intervention compared to those who do not (*14*), and that the vaccines to be used in cattle (strain B19, *Brucella abortus*) and small ruminants (Rev-1, *B. melitensis*) should reduce transmission by at least 65% (*15*). In addition, a hypothetical efficacy of vaccine of 100% was also tested. Vaccine coverages were assumed to be 50% and 80%, respectively, to allow for frequent problems with cold chains.

These assumptions produced three alternative vaccination scenarios, with percentages for protection from transmission of 32% (65% efficacy × 50% coverage), 52% (65% efficacy × 80% coverage), and 80% (100% efficacy × 80% coverage). We assumed that different vaccination coverages would not affect the budget for the intervention because the costs of personnel, transport, and vaccine costs would remain very much the same irrespective of whether the farmers and their animals were present or absent when the mobile teams visited.

Form of evaluation

We performed an incremental cost-effectiveness analysis to compare the cost and health effects of the vaccination programme for the human population with the cost and health effects of current practice. The burden of brucellosis on the human population was estimated for different age groups and sexes from data on morbidity and mortality and on the duration of the disease (case–fatality and remission rates). The benefit-cost analysis focused on the net monetary gain associated with different vaccination strategies (current practice vs 32%, 52%, and 80% protection from transmission) for brucellosis prevention and control. The net present value is used as a key evaluation criterion.

Data collection

We developed a conceptual framework to consider human health and livelihood, and animal production and health perspectives. Baseline disease data on reported cumulative incidence of human brucellosis listed by Aimag province for 1990–99 were provided by the Infectious Disease Research Institute in Ulaanbaatar, Mongolia. The Ministry of Agriculture Survey provided data on prevalence of animal brucellosis at the provincial level for cattle, sheep, and goats for 1990–99. The quality of data could not be checked, but ongoing studies on brucellosis in livestock indicate that reported prevalence is underestimated. Our analysis thus is rather conservative.

A household survey was undertaken of 240 patients clinically diagnosed with brucellosis who attended public health facilities between May and August 2000. To complete and compare the data, a Delphi study was organized with two panels: one consisted of 17 specialists in human brucellosis, the other of 16 national experts on animal brucellosis.

Benefit measurement and valuation

Disability-adjusted life year (DALY) is used as a measure of health outcome. An estimate of the burden of disease for brucellosis is not readily available (*16*), so we therefore estimated the DALYs lost as a result of the disease by assuming that brucellosis is associated with a class II (0.2) disability weight, as the disease is perceived as very painful and affects occupational ability even during periods of remission (*17, 18*). Average age at onset was calculated for every age group. For the duration of illness, we considered data by Beklemischew on the duration of clinical cure of 1000 patients with brucellosis in the Russian Federation (*19*). The frequency distribution of clinical disease duration fits best with an exponential function for an average duration of 4.5 years. For duration of disease, we used @Risk expon function, with $\beta = 4.5$ years. For cost effectiveness, we used the median of the cumulated discounted DALYs, which corresponds to a median duration of brucellosis of 3.11 years.

The economic evaluation included the impact on human health costs and income loss, coping costs, and impact on livestock production. Benefits in monetary terms were computed for three different sectors. For the agricultural sector, we considered the benefit of avoidance of losses in animals and animal products; for the public health sector, we considered the benefit of avoiding costs and for private households with patients suffering from brucellosis, we considered the benefit resulting from avoidance of out-of-pocket payments for treatment, loss of income (opportunity costs), and costs of coping.

The sum of all three mentioned benefits was considered a benefit for society as a whole and represents a monetary valuation of the health benefit. The method avoided double counting of common costs between the public health sector and payments for treatments made by patients. For every sector, the net present value and benefit–cost ratio were computed. The Mongolian Ministry of Agriculture, which started implementation of the vaccination campaign in 2000, established a budget calculation for the whole 10-year campaign of about 11 334 million Mongolian Tugrik (MNT) (equivalent to about US$ 10.5 million on the basis of an exchange rate of MNT 1080 = US$ 1 in October 2000) (Appendix A).

Costing

A societal perspective was used to conduct the costing part of the analysis (*20*). The costing is based on the budget of the Mongolian Ministry of Agriculture for the 10-year vaccination campaign against brucellosis (Appendix A). This budget considers the number of animals to be vaccinated; cost of vaccines (*B. melitensis* Rev-1 and *B. abortus* S19); service costs of vaccination (transportation, cold chain, and veterinary fees); costs related to ear tagging; service costs for surveillance and diagnostic tests; and costs of health education, training, and advocacy for herders. The overhead costs of national and local government authorities that administered the programme were not considered in the calculations, as the marginal cost for adding this brucellosis control programme were expected to be negligible. As all breeders' activities are shared within the family, marginal product lost because of their involvement in the campaign was very low to zero: we assumed that the time a farmer spent on the campaign did not make him lose money from an activity he could have pursued instead. Consequently, the opportunity cost of breeders' time was given a value of zero (*21*).

Quantities and unit costs for animals and animal products were obtained from the household survey, Delphi panels, and business publications (*22*). Livestock production was calculated from herd structures and productivity parameters with the *Livestock development planning system* (LDPS2) (*23, 24*). Quantities and unit costs for the human health sector and opportunity costs of human brucellosis infection were generated by the Delphi panel, patient-based household survey, and Mongolian Ministry of Health. All model calculations were in MNT, with prices from the year 2000 (MNT 1080 = US$ 1).

Sharing costs among sectors

As the vaccination campaign improves human health through interventions in the veterinary sector, the allocation of costs of the intervention among different sectors had to be decided. Although the benefit side can be assigned easily to the breeders (benefits from livestock production), patients (reduced out-of-pocket expense and coping costs), and public health sector (avoidance of hospitalization and drugs), the costs cannot be assigned wholly to the agricultural sector or to the health sector.

In order to attribute the cost to the different sectors, we applied basic elements of the technique for joint cost allocation in multipurpose projects, known as the "separable costs–remaining benefits" method (*25*). In the vaccination campaign against brucellosis, all expenditure was associated with animal health, while human health benefit was produced without separable costs. We therefore used an adaptation of the method, in which we regarded all costs as joint costs and allocated the costs proportionally to the benefit. Out of this allocation, the cost-effectiveness of the intervention for human health could be derived, as could measures for economic benefit.

Modelling

To assess the reduction of the effects of brucellosis in humans and animals by its control through vaccination in livestock, we modified and extended the susceptible–infected–recovered models of brucellosis transmission used by Gonzalez-Guzman & Naulin (*26*) to include animal-to-human transmission (Fig. 1). Poisson regression analyses of existing data on the provincial level showed a significant ecological relation between seroprevalence of brucellosis in cattle and sheep and cumulative incidence of reported human cases. The coefficients from such analyses were used as initial parameter estimates for the fitting of deterministic equations (Vensim; Ventana Systems Inc., Harvard, Massachusetts, USA). The model was validated with human and livestock demographic and disease data from 1991 to 1999 (before the start of the vaccination campaign by steps of one year). The validation of the vaccination intervention used data from the first three years of the ongoing brucellosis mass vaccination campaign in Mongolia (2000–02). The detailed model will be published elsewhere.

Fig. 1 shows the model framework, which is composed of compartments for susceptible sheep and cattle (serologically negative by the Rose Bengal test). We omitted transmission from goats because of the lack of data, but the productivity of goats was considered in the economic analysis by using disease data from sheep. Susceptible sheep and cattle become infected and move to the compartments of seropositive sheep and cattle (Rose Bengal test). We did not consider a compartment of "recovered", because data on seroprevalence were available for validation of the model only. The compartment of seropositive animals is composed of an unknown proportion of infected animals capable of infecting other animals and humans. The transmission (infected sheep and cattle in Fig. 1) is shown in the example of cattle in equation (1), in which γ is the proportion of infectious animals, expressed as a uniform probability distribution, β is the contact rate, X are susceptible cattle, and Y are seropositive cattle.

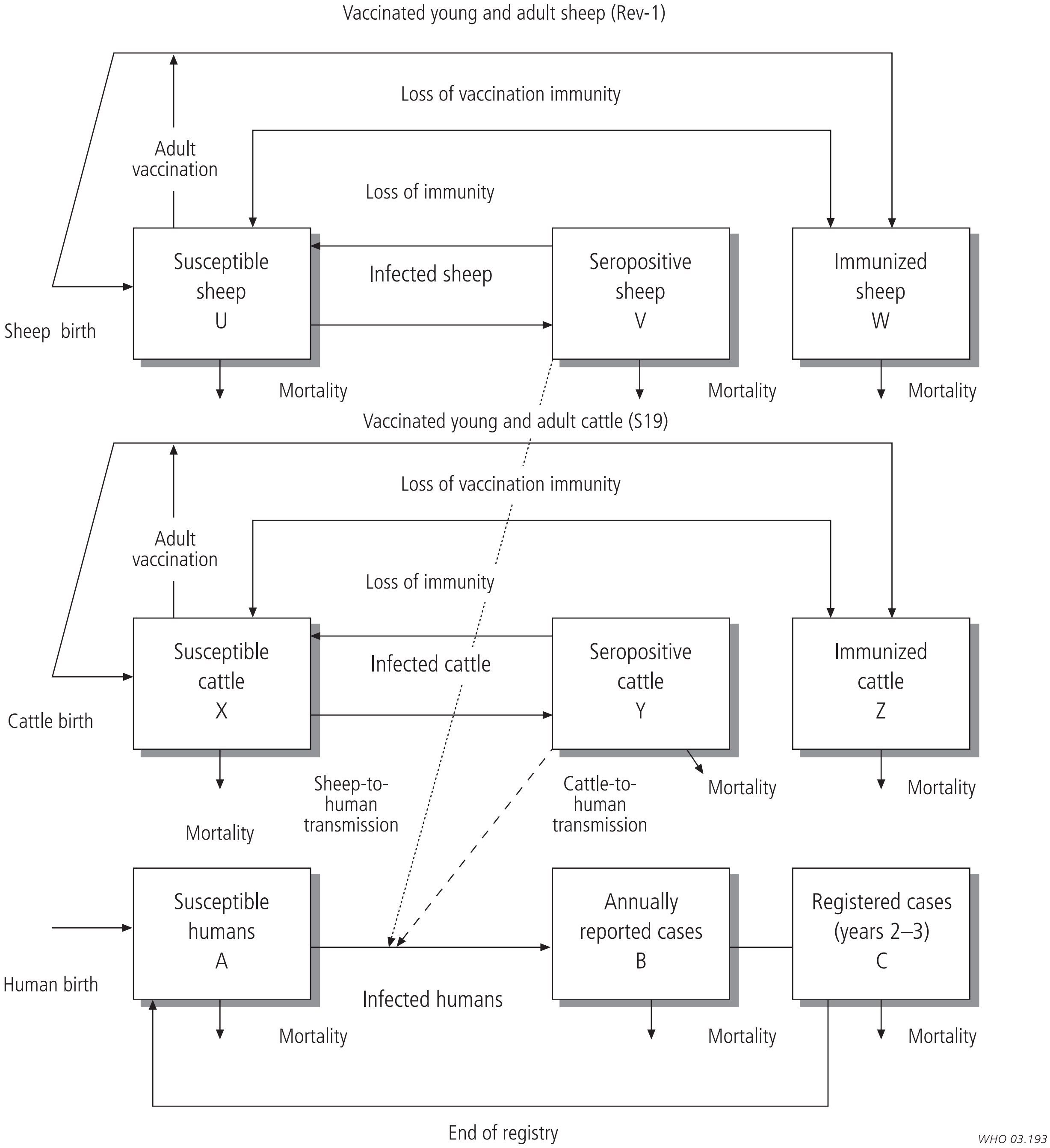
$$\gamma\beta XY \qquad (1)$$

Seropositive animals may convert to seronegative animals (loss of immunity). For the fitting of between-animal transmission, the boundaries of the proportion of infective animals were varied to identify the best fit. Transmission to humans is expressed as the additive contributions of transmission from sheep and cattle to humans (sheep-to-human transmission and cattle-to-human transmission in Fig. 1) in equation (2), in which A is the susceptible human population.

$$(\gamma_{cattle}\,\beta_{cattle}\,XA) + (\gamma_{sheep}\,\beta_{sheep}\,UA) \qquad (2)$$

Compartment A represents the whole Mongolian population, as precise estimates of the population at risk are not available. Compartment B represents the annual number of patients newly registered as having brucellosis. The economic analysis was based

Fig. 1. **Model for joint human–animal brucellosis transmission in Mongolia** (for an explanation of symbols, see text)



on this compartment and accounted for the whole treatment cost, including treatment of chronic cases in the same year. The annual rate of outflow (registry in Fig. 1) of compartment B = 1 by definition. Compartment C represents the patients registered as having brucellosis between year 2 and 3 of state registration (end of registry = 0.5 by definition), after which they are no longer considered as registered brucellosis patients. The model takes Mongolian health policy into account, as it is important to adapt assessments to local health policy decision pathways (*27*). The estimation of DALYs is also made on compartment B, but by using the duration of untreated brucellosis. The different vaccination scenarios were expressed as the proportions (32%, 52%, and 80%) of vaccinated young and adult sheep and cattle protected from transmission.

Estimates of the transmission parameters obtained by fitting this model were used to simulate various scenarios for 10 years with and without interventions (Appendix B, web version only, available at: http//www.who.int/bulletin). Outcomes of the simulations were prevalence in animals and annual cumulative incidence in humans. As inputs into the economic assessment, these were expressed as normal probability functions, with means and standard deviations provided from Monte Carlo sensitivity analysis on the fitted parameters in Vensim, and were linked to human health and livestock productivity (Appendix C, web version only, available at: http://www.who.int/bulletin). Links to prevalence of animal disease were expressed as probability distributions for the decrease in fertility (annual calving or kidding rates) and milk production (Appendix C, ref. *13*).

Human health parameters, such as duration of treatment and hospital and outpatient treatment, were derived from the household survey. Human age and sex distributions were obtained from the cases reported in 1999 (Appendix D, web version only, available at http://www.who.int/bulletin).

Human health parameters and livestock productivity parameters linked to outcomes of the transmission model and human and livestock demographic population structures (*28*) were then introduced into a new human and animal health economic model (ECOZOO) developed for this study (Appendices D–G, web version only, available at: http://www.who.int/bulletin) (*29*). ECOZOO is composed of a spreadsheet backbone in Microsoft Excel, which is linked to @Risk stochastic simulation capability and LDPS2. ECOZOO simultaneously computes human and animal effectiveness and economic assessments of health interventions.

Adjustment for timing of costs and benefit

Our economic evaluation was based on the 10-year period of the vaccination programme planned for 2000–09 (base year 1999) by the Mongolian authorities. Limitation of the period of analysis was arbitrary and biased the estimated net benefit of the vaccination campaign downwards. The transmission model therefore was also run for 30 years to estimate time to eradication of the disease, on the assumption that vaccination of young animals would continue in the same way. For consistency reasons, the monetary benefits, costs, and health benefits were discounted at the same rate. A discount rate of 5% was used (*30*), with a rate of 3% used in the sensitivity analysis.

Allowance for uncertainty

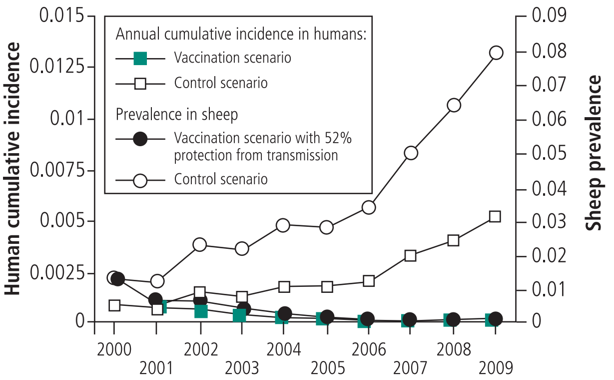
The uncertainty of disease frequency outputs of the deterministic models, health care unit costs, health care units, livestock numbers, livestock product prices, and livestock production parameters was expressed as probability distribution functions using @Risk. Distributions of the societal benefit–cost ratios were then calculated for the different sectors with a latin hypercube sampling type, with 500 iterations on 180 different variables specified as @Risk functions. The relative contribution of the different variables was explored in an automatic sensitivity analysis in @Risk. Sensitivities were expressed as dimensionless, normalized regression coefficients (R-square). Manual sensitivity analyses were done at the level of the economic model by varying selected input parameters (scenarios of 32%, 52%, and 80% protection and 3% and 5% discount rates).

Results

Incremental analysis to compare relevant alternatives

The protection achieved depends on the efficacy of the available vaccines and the vaccine coverage. We assumed that different vaccination coverages do not affect the budget for the intervention for comparisons of annual cumulative incidence of brucellosis in humans between different protection scenarios. When the scenario of 32% protection from transmission was considered, the incidence dropped from six cases per 10 000 at the beginning of the programme to five cases at the end of the programme, whereas with the scenario of 52% protection from transmission it dropped to one case per 10 000 with the same costs involved (Fig. 2). The scenario of 52% protection considered the observed efficacy of S19 (*15*) and Rev-1 vaccines and a feasible level of coverage (Mikolon A, personal communication, 2000).

Fig. 2. **Effect of livestock brucellosis vaccination on humans. Prevalence and cumulative incidences are given as straight proportions**



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Major outcomes

Table 1 presents the major economic outcomes by scenario. When the scenario of 52% protection and 5% discount rate was considered, an average number of 61 070 (median 49 027) DALYs could be averted through use of the intervention. The same scenario showed discounted intervention costs of MNT 8957 million (about US$ 8.3 million) and an overall discounted benefit of MNT 28 753 million (about US$ 26.6 million). This results in a net profit value of MNT 19 796 million (about US$ 18.3 million) and a benefit–cost ratio for society of 3.2 (range 2.27–4.37).

Cost-sharing scenario

We developed a cost-sharing scenario to take into consideration the multisectoral effects of the intervention (Table 2). This derived a realistic ratio for cost-effectiveness and profitability of the intervention. If costs of the intervention were shared in proportion to the benefit of each sector, the public health sector would contribute 11% to the intervention costs, giving a cost-effectiveness of US$ 19.1 (95% confidence interval 5.3–486.8) per DALY averted (Table 3). If private economic gain because of improved human health was included, the health sector would contribute 42% to the intervention costs and the cost-effectiveness would decrease to US$ 71.4 (19.7–1824.1) per DALY averted.

Sensitivity analysis of benefit–cost ratio and DALYs

A sensitivity analysis of the benefit–cost ratio was done by Monte Carlo simulation in @Risk, with 180 variables expressed as probability distributions (*31*). The most sensitive parameters were hospital cost (sensitivity 0.69), transport cost (0.36), meat price (0.25), human cumulative incidence (0.2), cashmere price (0.19), unit doctor's fee (0.14), and unit cost of hospital food (0.13). All other variables had sensitivities <0.1. The DALY estimate was highly sensitive to the duration of disease (sensitivity = 0.96) and disease incidence (0.15).

Discussion

At present, the health sector has to bear the cost of human brucellosis at a level of nearly 60 cases per 100 000 per year because of the lack of an effective control programme in the livestock sector. As human brucellosis originates essentially from livestock and livestock products, the health sector is expected to profit if brucellosis in livestock is controlled. Although it would not be cost effective for the health sector to cover the full cost of the programme, it could be asked to contribute a share (such as the share suggested by our cost allocation model) that would make the programme cost effective from the health sector perspective.

Table 2 shows that with the cost-sharing scenario, the intervention could be profitable for the health and agricultural sectors. The Ministry of Agriculture could meet its share of the project costs, possibly with donor support. As livestock breeders are likely to be the most favoured beneficiaries of the vaccination campaign (economically), they might be willing to contribute to the campaign, and clearly there is some interest from the public sector in attaining a higher degree of cost recovery from this group.

The patients are the second group of beneficiaries. As patients would have contracted brucellosis if there had been no intervention, they avoid out-of-pocket expenses and income loss. As there is no way of identifying people who might have avoided infection, no mechanism would allow their contribution to the intervention costs to be obtained. As shown in Table 2, however, the campaign would still be profitable to the public health sector, if less than 85.6% (3240/3782) of the costs are attributed to this sector. The case for attribution of private costs that result from disease to the public health sector can be strengthened through the argument of poverty reduction. When a patient is ill from brucellosis, this has a strong impact on the household economy in terms of out-of-pocket contributions to health costs and change in income. Brucellosis mass vaccination for livestock may thus contribute towards alleviating poverty in households.

Health expenditure for Mongolia in 1998 amounted to US$ 33.2 million, and international donor support to the Mongolian health sector was US$ 4 million (12%) (*32*). Given this background, the intervention costs for the vaccination programme (US$ 10.5 million over 10 years) are very significant. With the cost-sharing scenario, the multisectoral character of interventions to control zoonotic diseases is taken into consideration. When we computed the cost-effectiveness ratio from the Ministry of Health's point of view, US$ 19.1 per DALY would be averted, which falls into WHO's range of highly cost-effective programmes (<US$ 25 per DALY averted) (*33*). When we included the incremental costs of patients in the total incremental costs, US$ 71.4 per DALY would be averted, which is still in the next band of cost effective (<US$ 150 per DALY averted). In our context, the cost-effectiveness result of US$ 19.1–71.4 (costs allocated to patients plus public health sector costs) per avoided DALY represents 5.7–21.5% of the gross domestic product per capita (US$ 333 in 1999 (*34*)) and therefore also can be rated as attractive from this point of view.

Our assessment is based on a disability weight of 0.2. More research is needed to establish the disability weight of human brucellosis. The median duration of disease (3.11 years) we used (on the basis of on data from Beklemischew (*20*)) tallies

Table 1. **Summary results of a 10-year brucellosis vaccination campaign in Mongolia**

Variable	Protection					
	80%		52%		32%	
	Discounted rate		Discounted rate		Discounted rate	
	3%	5%	3%	5%	3%	5%
Scenario						
Vaccine efficacy (%)	100		65		65	
Vaccine coverage (%)	80		80		50	
Protected animals (%)	80		52		32.5	
Health benefits						
Discounted cumulated median DALYs[a]						
Disability class weight I	Not done	Not done	Not done	24 530	Not done	Not done
Disability class weight II	63 217	52 618	58 675	49 027	52 618	42 394
Intervention costs (MNT million)[b,c]	9 806.2	8 957.3	9 806.2	8 957.3	9 806.2	8 957.3
Benefits in monetary terms (MNT million)						
A Agriculture sector[d]	21 702.5	18 850.0	19 133.8	16 611.6	13 630.5	11 816.8
B Public health system[e]	4 062.7	3 513.1	3 760.9	3 240.3	3 237.7	2 779.9
C Out of pocket contributed for health care[f]	6 718.6	5 809.8	6 219.6	5 358.7	5 354.3	4 597.3
D Private income[g]	4 441.8	3 841.0	4 111.9	3 542.8	3 539.8	3 039.4
B+C[h]	10 781.3	9 322.9	22 894.7	8 599.0	8 592.0	7 377.2
A+C+D[i]	32 862.9	28 500.8	29 465.3	25 513.1	22 524.6	19 463.5
A+B+C+D[j]	36 925.6	32 013.9	33 226.2	28 753.4	25 762.3	22 233.4

[a] DALY = disability-adjusted life year.
[b] Budget of Ministry of Agriculture.
[c] MNT = Mongolian Tugrik.
[d] Discounted net incremental profit to the breeder.
[e] Discounted reduction of costs in public health sector.
[f] Discounted reduction of heath costs to patient.
[g] Discounted reduction of income loss to patient.
[h] Discounted total benefit to overall health sector.
[i] Discounted total benefit to private society.
[j] Discounted total benefit to society.

if interventions costs were shared between the different beneficiaries on the basis of an intersectoral economic assessment. The presented trans-sectoral analysis is applicable to other zoonoses and environmental threats to public health and contributes to the perception that human interventions in the livestock sector can control disease transmission to humans (*36*). ■

Acknowledgements
We thank Ms Oyunaa Tsendendorji (and collaborators at the Ministry of Health in Ulaan Baatar) for helping throughout our stay in Mongolia, arranging the timetable and logistical support, organizing the studies, entering the data, and serving as competent interpreter and friendly guide. We also thank the collaborators at the Ministry of Agriculture and Industry and Ministry of Health for their hospitality and sound introduction to the complex topic of brucellosis in Mongolia. Data was provided by D. Bat-Ochir and D. Idesh (National Centre of Infectious Diseases, Ministry of Health), D. Nyamkhorol (Statistical Information Department, Directorate of Medical Services). P. Dorjsuren and P. Bolortuya (State Veterinary And Animal Breeding Department), and A. Yondondorj (Veterinary Research Institute), all based in Ulaan Baatar, Mongolia. Tumurkhuu Gantsetseg provided information on clinical aspects of brucellosis in Mongolia. M. Nansalmaa, international project coordinator at the Mongolian Academy of Sciences in Ulaan Baatar, is acknowledged for the data collection of the vaccination campaigns. We thank the staff of WHO in Mongolia for their hospitality, especially R. Salmela for introducing us to the health system in Mongolia. M. Dubach is acknowledged for providing background information. J. Jenkins and C. Lengeler are thanked for critical review of the manuscript. I. Packer and D. Pfeiffer contributed to the initial design of the study. E. Schelling entered the data of the Delphi studies. K. Wyss contributed to the development of the economic model. A. Mikolon gave substantial technical input to brucellosis control strategies and intervention budgets. P. Vounatsou gave support to the development of the deterministic transmission model. J. Kolar contributed to the conception of the study and appraisal of the intervention budget from his experience in running mass vaccination campaigns against brucellosis in Mongolia. Many thanks also to patients who were willing to be interviewed, interrogators who carried out these interviews, and experts in the Delphi panels who took time to answer the questionnaires and gave us an insight into brucellosis in Mongolia. This work was supported by the National Centre for Competence in Research North-South "Mitigating syndromes of global change", Individual Project 4 "Health and wellbeing".

Funding: World Health Organization, Food and Agriculture Organization, Swiss Tropical Institute, Swiss National Science Foundation, and Swiss Agency for Development and Cooperation.

Conflicts of interest: none declared.

Résumé

Avantages pour l'homme de la vaccination du cheptel contre la brucellose : étude de cas

Objectif Estimer l'intérêt économique et le rapport coût/efficacité – répartition comprise des avantages économiques – des progrès sanitaires obtenus en Mongolie en procédant à la vaccination de masse du cheptel contre la brucellose.

Méthodes Le rapport coût/efficacité et l'intérêt économique de la vaccination de masse contre la brucellose pour la société humaine et le secteur agricole ont été modélisés. L'intervention a consisté à planifier sur 10 ans la vaccination de masse du cheptel par la souche Rev-1 pour les petits ruminants et S19 pour les bovins. Le principal résultat obtenu a été le rapport coût/efficacité, soit le coût par années de vie ajustées sur l'incapacité (DALY) évitées.

Résultats Dans l'hypothèse d'une diminution de 52 % de la transmission de la brucellose chez l'animal grâce à la vaccination, on peut éviter 49 027 DALY. On estime le coût de cette intervention à US $8,3 millions et le gain brut à US $26,6 millions. Le bénéfice net s'établit donc à US $18,3 millions, avec un rapport moyen coût/avantages pour la société de 3,2 (2,27–4,37). Si l'on répartissait les coûts de cette intervention entre les secteurs en fonction des bénéfices qu'ils en retirent, la santé publique devrait contribuer à hauteur de 11 % et obtiendrait un rapport coût/efficacité de US $19,1 par DALY évitée (intervalle de confiance 95 % : 5,3–486,8). En revanche, si l'on inclut dans le calcul les bénéfices privés dus à l'amélioration de la santé humaine, le secteur de la santé devrait alors contribuer à hauteur de 42 % des coûts de l'intervention, ce qui ramène le rapport coût/efficacité à US $74,1 par DALY évitée.

Conclusion Si l'on répartit les coûts de la vaccination du cheptel contre la brucellose en fonction des bénéfices que retire chaque secteur de cette intervention, celle-ci pourrait s'avérer profitable et rentable pour la santé et l'agriculture.

Resumen

Beneficios para la salud humana de la vacunación del ganado contra la brucelosis: estudio de casos

Objetivo Estimar el beneficio económico, la relación costo-eficacia y la distribución de los beneficios para la salud humana reportados por la vacunación masiva del ganado contra la brucelosis en Mongolia.

Métodos Se modelizaron la relación costo-eficacia y el beneficio económico para la sociedad y el sector agrícola de la vacunación masiva contra la brucelosis. La intervención consistió en una campaña de 10 años de vacunación masiva del ganado, basada en la administración de la vacuna Rev-1 para pequeños rumiantes y la vacuna S19 para el ganado bovino. Como variable de evaluación se utilizó la relación costo-eficacia, expresada como costo por año de vida ajustado en función de la discapacidad (AVAD) evitado.

Resultados En un escenario de reducción del 52% de la transmisión de brucelosis entre los animales, gracias a la vacunación masiva, se pudo evitar un total de 49 027 AVAD. El costo estimado de la intervención ascendió a US$ 8,3 millones, y el beneficio global a US$ 26,6 millones. Ello se traduce en un valor neto de US$ 18,3 millones y una relación beneficio-costo media para la sociedad de 3,2 (2,27–4,37). Si los distintos sectores compartieran los costos de la intervención en proporción al beneficio de cada uno, el sector de salud pública contribuiría con un 11%, lo que arroja una relación costo-eficacia de US$ 19,1 por AVAD evitado (intervalo de confianza del 95%: 5,3–486,8). Incluyendo el beneficio económico privado resultante de la mejora de la salud humana, el sector de la salud debería contribuir con el 42% a los costos de intervención, y la relación costo-eficacia aumentaría a US$ 71,4 por AVAD evitado.

Conclusión Si los costos de la vacunación del ganado contra la brucelosis se asignaran a todos los sectores proporcionalmente a los beneficios, la intervención podría ser rentable y costoeficaz para los sectores agrícola y sanitario.

ملخص

المنافع الصحية التي تعود على الناس من تلقيح المواشي ضد داء البروسيلات: دراسة حالة

الهدف: تقدير المنافع الإقتصادية و المردودية و توزيع المنافع الناجمة عن تحسن صحة الناس بسبب مكافحة داء البروسيلات بتلقيح المواشي جموعيا في منغوليا.

الطريقة: وضع نموذج لتقدير المردودية و المنافع الاقتصادية التي تعود على الناس و القطاع الزراعي نتيجة التلقيح الجموعي للمواشي ضد داء البروسيلات. و تضمن التدخل حملة تلقيح جموعي للمواشي خطط لها لتستمر عشر سنوات باستخدام لقاح (Rev-1) للمجترات و لقاح (S19) للأبقار. وقد عبر عن المردودية باعتبارها الحصيلة الأولية بتكلفة توفير سنة من سنوات العمر المصححة باحتساب مدد العجز.

الموجودات: في إحدى السيناريوهات التي تحقق فيها ٥٢٪ من النقص في سراية داء البروسيلات بين الحيوانات نتيجة التلقيح، أمكن توفير ما مجموعه ٤٩،٠٢٧ سنة من سنوات العمر المصححة باحتساب مدد العجز, فيما كانت التكلفة المقدرة ٨،٣ مليون دولاراً أمريكياً، و كان متوسط نسبة التكاليف إلى المنافع التي يجنيها المجتمع ٣,٢ (وتتراوح بين ٢,٢٧ و ٤,٣٧)، وإذا ما تشاركت القطاعات في تحمل التكاليف وبمقادير تتناسب مع المنافع التي تعود على كل منها فإن القطاع الصحي العام سيساهم في ١١٪، وهذا يعطي مردودية تعادل ١٩,١ دولاراً أمريكياً لكل سنة يتم توفيرها من سنوات العجز المصححة باحتساب مدد العجز (وذلك بفاصلة ثقة ٩٥٪ وتتراوح بين ٥,٣ و٤٨٦,٨) ، وإذا ما أدمجت المرابح الاقتصادية الخاصة الناجمة عن تحسن صحة الناس، فإن القطاع الصحي سيساهم بمقدار ٤٢٪ من تكاليف التدخلات، وستن قص المردودية لتصل إلى ٧١,٤ دولاراً أمريكياً مقابل توفير سنة من سنوات العمر المصححة باحتساب مدد العجز.

النتيجة: عند توزيع تكاليف تلقيح المواشي ضد داء البروسيلات على جميع القطاعات وبمقادير تتناسب مع المنافع التي تعود على كل قطاع منها، فإن هذا التدخل سيكون مربحاً وسيكون له مردرد مرتفع في كل من القطاعين الصحي والزراعي.

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This article has received corrections in agreement with the ERRATUM published in Volume 82 Number 1.

Appendix A. **Budget and vaccination scheme of the Mongolian Ministry of Agriculture for a whole-herd vaccination programme of brucellosis in cattle and small ruminants in Mongolia[a] (MNT millions[b])**

Intervention cost per year	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009
Testing	87.56									
Vaccination of adult sheep and goats[c]	382.84	266.05	244.14							
Second vaccination of adult sheep and goats[d]				382.84	266.05	244.14				
Vaccination of cows[c]	119.85	72.75	48.60							
Second vaccination of cows[d]				119.85	72.75	48.60				
Vaccination of bulls	7.09	7.09	7.09	7.09	7.09	7.09	7.09	7.09	7.09	7.09
Vaccination of newborn sheep and goats[e]	428.70	428.70	428.70	428.70	428.70	428.70	428.70	428.70	428.70	428.70
Vaccination of newborn calves[e]	129.43	129.43	129.43	129.43	129.43	129.43	129.43	129.43	129.43	129.43
Cost of testing							8.52	6.68	8.41	
Ear tags	325.28	325.28	325.28	325.28	325.28	325.28	325.28	325.28	325.28	325.28
Training		50.00								
Annual intervention costs	1 480.74	1 279.29	1 183.23	1 393.18	1 229.29	1 183.23	899.02	897.17	898.90	890.49
Cumulative intervention costs 10 years										11 334.54
Discounted cumulative annual intervention costs at end of year										
5%	1 410.23	2 570.58	3 592.70	4 738.87	5 702.05	6 585.00	7 223.91	7 831.15	8 410.59	8 957.28
3%	1 437.61	2 643.46	3 726.29	4 964.11	6 024.50	7 015.44	7 746.42	8 454.66	9 143.59	9 806.20

[a] Budget assumes stable livestock population and considers number of animals to be vaccinated; cost of vaccines (*B. melitensis* (Rev-1) and *B. abortus* (S19)); service costs of vaccination (transportation, cold chain, and veterinary fees); costs related to ear tagging; service costs for surveillance and diagnostic tests; and costs of health education, training, and advocacy for herders.

[b] Reference for cost is year 2000.

[c] Adult animals (first vaccination).

[d] Adult animals (second vaccination).

[e] Young animals (less than one year old).

Appendix B. **Compartments, fitted parameters, and differential equations in 1999 to 2009 by one-year steps**

Variable	Value
Compartments size in 1999	
Sheep	
Susceptible (U)	15 069 770
Seropositive (V)	121 530
Cattle	
Susceptible (X)	3 776 780
Seropositive (Y)	48 018
Humans	
Susceptible (A)	2446400
Newly reported cases annually (B)	1482
Registered cases between years 2 and 3 of registration (C)	2066
Parameter estimates	
Proportion of infectious seropositive cattle (V) (γ_s)	Random uniform (0.2, 0.7)
Immunity loss constant sheep (ε_s)	0
Sheep–human contact rate (β_{sh})	1.12738e-008
Mortality rate of sheep (μ_s)	0.79[a]
Birth rate of sheep (α_s)	0.83
Sheep contact rate (β_s)	1.56082e–007
Decrease of fertility (η)	Random uniform (0.15, 0.5) (*C1*)
Proportion of infectious seropositive cattle (Y) (γ_c)	Random uniform (0.1, 0.7)
End of registry constant (λ)	0.5 (Def [b])
Registry change (κ)	1 (Def)

Appendix B. **Compartments, fitted parameters, and differential equations in 1999 to 2009 by one-year steps**

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Compartments size in 1999	
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Birth rate of sheep (α_s)	0.83
Sheep contact rate (β_s)	1.56082e–007
Decrease of fertility (η)	Random uniform (0.15, 0.5) (*C1*)
Proportion of infectious seropositive cattle (Y) (γ_c)	Random uniform (0.1, 0.7)
End of registry constant (λ)	0.5 (Def [b])
Registry change (κ)	1 (Def)
Cattle animal contact rate (β_c)	3.49736e-007
Cattle animal human contact rate (β_{ch})	2.11247e-009
Cattle birth rate (α_c)	0.28
Human birth rate (α_h)	0.018159
Human mortality rate (μ_h)	0.00333868
Cattle immunity loss constant (ε_s)	0
Cattle mortality rate (μ_c)	0.23[c]
Vaccine efficacy of Rev 1 (ν_{Rev-1})	0.65[d]
Vaccine efficacy of S19 (ν_{S19})	0.65[e]
Inverse duration vaccination protection S19 (τ_{S19})	Random uniform (0.125, 0.142)
Inverse duration vaccination protection Rev-1 (τ_{Rev-1})	Random uniform (0.2, 0.25)
Vaccination coverage (adult) sheep (c_{as})	
No vaccination	0
Scenario 5065[f]	0.5
Scenario 8065[g]	0.8
Scenario 80100[h]	0.8
Proportion of young sheep vaccinated (c_{ys})	
No vaccination	0
Scenario 5065	0.5
Scenario 8065	0.8
Scenario 80100	0.8
Vaccination coverage (adult) cattle (c_{ac})	
No vaccination	0
Scenario 5065	0.5
Scenario 8065	0.8
Scenario 80100	0.8
Proportion of young cattle vaccinated (c_{yc})	
No vaccination	0
Scenario 5065	0.5
Scenario 8065	0.8
Scenario 80100	0.8

(Appendix B, cont.)

Variable	Value
Differential equations for the fitting and simulation of vaccination	
$\frac{dU}{dt} = \varepsilon_s V + \tau_{\text{Rev1}} W + (\alpha_s (U+V+W)(1-(\eta(\frac{V}{(U+V+W)})))(1-(c_{ys}\nu_{\text{Rev1}})) - \mu_s U - \gamma_s \beta_s UV - c_{as}\nu_{\text{Rev1}}(0.333)U$	
$\frac{dV}{dt} = \gamma_s \beta_s UV - \varepsilon_s V - \mu_s V$	
$\frac{dW}{dt} = c_{as}\nu_{\text{Rev1}}(0.333)U + (\alpha_s (U+V+W)(1-(\eta(\frac{V}{(U+V+W)})))(c_{ys}\nu_{\text{Rev1}}) - \mu W - \tau_{\text{Rev1}} W$	
$\frac{dX}{dt} = \varepsilon_c Y + (\alpha_c (X+Y+Z)(1-(\eta(\frac{Y}{(X+Y+Z)})))(1-(c_{yc}\nu_{S19})) - \mu_c X - \gamma_c \beta_c XY - c_{ac}\nu_{S19}(0.333)X + \tau_{S19} Z$	
$\frac{dY}{dt} = \gamma_c \beta_c XY - \varepsilon_c Y - \mu_c X$	
$\frac{dZ}{dt} = c_{ac}\nu_{S19}(0.333)X + (\alpha_c (X+Y+Z)(1-(\eta(\frac{Y}{(X+Y+Z)})))(c_{yc}\nu_{S19}) - \mu_c Z - \tau_{S19} Z$	
$\frac{dA}{dt} = \alpha_h (A+B+C) + \lambda C - ((\beta_{ch}\gamma_c AY) + (\beta_{sh}\gamma_s AV)) - \mu_h A$	
$\frac{dB}{dt} = ((\beta_{ch}\gamma_c AY) + (\beta_{sh}\gamma_s AV)) - \mu_h B - \kappa B$	
$\frac{dC}{dt} = \kappa B - \mu_h C - \lambda C$	

[a] 0.83 during vaccination campaign, accounts for stable sheep population assumption.

[b] Def = definition.

[c] 0.28 during vaccination campaign accounts for stable cattle population assumption.

[d] Also accounts for loss of efficacy in field.

[e] Also accounts for loss of efficacy in field (*C2*).

[f] 5065 = scenario with 50% coverage and 65% efficacy.

[g] 8065 = scenario with 80% coverage and 65% efficacy.

[h] 80100 = scenario with 80% coverage and 100% efficacy.

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Appendix C. **Key functions used to link disease outcome to human health and livestock productivity**

Area	Definition
Human health	
Number of cases	= (Population/proportion of age and sex class)[a] exposure constant[b]
Livestock productivity	
Fertility	= Annual number of offspring per breeding female
	= Baseline fertility[c] × (1 – (Beta-Pert (10%; 15%; 50%)[d] × prevalence))
Cattle milk production	= Annual milk production per lactating female[e]
	= Baseline milk production[e] × (1 – (Beta-Pert (10%; 15%; 25%)[f] × prevalence))

[a] Cumulative incidence.

[b] Age- and sex-specific exposure constant, derived from the proportion of the respective age or sex group among those with disease to their respective proportion in the total population (*D1*) based on the reported brucellosis cases in 1999 (Appendix B).

[c] Baseline proportion of annual number of offspring per breeding female in cattle, sheep, and goats.

[d] Beta-Pert Distribution (*D2*) with minimum, most likely and maximum decrease of fertility among diseased (considers abortions, sterility, and mortality of newborn) (Appendix C) (*D3*).

[e] Baseline annual milk production per breeding female.

[f] Reduction of milk production among seropositive adult female animals (Appendix C) (*D3*).

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Appendix D. **Calculation of exposure constants[a]**

Population	Human population of Mongolia in 1999	Proportion of total population (*a*)	Reported human brucellosis cases in 1999	Proportion of all brucellosis cases (*b*)	Exposure constant (*e*)
Children					
Aged <5 years	193 900	0.08	15	0.01	0.0008
Aged 5–15 years	604 500	0.25	152	0.10	0.0250
Women	834 900	0.34	611	0.41	0.1394
Men	813 100	0.33	704	0.48	0.1584
Total	2 446 400		1482		

[a] Exposure constants, $e = a \times b$, calculated based on 1999 population and reported brucellosis data (*23*, Ministry of Health, personal communication).

Appendix E. **List of input variables used as @Risk functions**

Name	@Risk function
Disease data from the transmission model[a]	
Prevalence (p)	
In unvaccinated animals (sheep and cattle) for years 1 to 10	Normal (mean, Standard deviation)
In vaccinated animals (sheep and cattle) for years 1 to 10	Normal (mean, Standard deviation)
Cumulative incidence (c)	
In humans if animals unvaccinated for years 1 to 10	Normal (mean, Standard deviation)
In humans if animals vaccinated for years 1 to 10	Normal (mean, Standard deviation)
Livestock prices (MNT) (*E1*)	
Sheep	
Meat off farm (/kg)	Normal (754;311)
Hides off farm (/hide)	Normal (3617;1322)
Goats	
Cashmere (/kg)	Normal (34583;5485)
Meat off farm (/kg)	Normal (754;311)
Hides off farm (/hide)	Normal (7083;4875)
Cattle	
Meat off farm (/kg)	Normal (692;248)
Hides off farm (/hide)	Normal (14083;2476)
Decrease in livestock production (*E2*)	
Fertility (sheep, goats, cattle)	(Beta-Pert (10%; 15%, 50%)
Milk production (cattle)	(Beta-Pert (10%; 15%; 25%)[5])
Human health cost (MNT)	
Hospital costs per day (for Ministry of Health) (*E3*)	Normal (8646;5194)
Outpatient visits (*E4*)	Normal (4;2)
Unit cost (out of pocket)	
Current transport (*E4*)	Pert (0;3200;80000)
Hospital hotel (*E4*)	Pert (0;2000;25000)
Hospital food (*E4*)	Pert (0;3000;85000)
Hospital drug (*E4*)	Pert (0;1500;65000)
Doctor fee (*E4*)	Pert (0;500;30000)
Loss of income per case (*E4*)	Pert (9000;30000;500000)

[a] Data used were outputs of Vensim Monte Carlo sensitivity analysis.

References

E1. Average 12 month in Ulaan Bataar. *Gobi Business News,* 2000. Available from: URL: http://www.gbn.mn

E2. Bernues A, Manrique E, Maza MT. Economic evaluation of bovine brucellosis and tuberculosis eradication programmes in a mountain area of Spain. *Preventive Veterinary Medicine* 1997;30:137-49.

E3. Orkhon D, personal communication, 2000.

E4. Roth F, Zinsstag J. *Economic analysis of the brucellosis control in Mongolia*. Geneva: World Health Organization; 2001. p. 225.

Appendix F. **Herd composition and productivity parameters in 1999**

Variable	Value	Source or basis of calculation or estimate
Cattle		
Total population	3 824 700	(*F1*)
Female breeders in base year	1 449 800	(*F1*)
Male breeders in base year	72 490	Estimate a ratio of 1/20 for breeding male to female
Female replacement in base year	391 446	Female calves´ survival rate
Male replacement in base year	144 980	Estimate ratio of 1/20 for preselection of breeding male to female
Other stock in base year	678 634	Total animals — all other categories (animals for offtake)
Female young in base year	543 675	(*F1*)
Male young in base year	543 675	(*F1*)
Annual calving rate	0.75	(*F1*)
Survival rate of replacement	0.72	(*F1*)
Sheep		
Total population	15 191 300	(*F1*)
Female breeders in base year	6 846 500	(*F1*)
Male breeders in base year	136 930	Estimate ratio of 1/50 for breeding male to female
Female replacement in base year	2 244 625	Female lambs´ survival rate
Male replacement in base year	273 860	1/25 for preselection of breeding male to female
Other stock in base year	6 790	Total animals — all other categories (animals for offtake)
Female young in base year	2 841 298	(*F1*)
Male young in base year	2 841 298	(*F1*)
Annual lambing rate	0.83	(*F1*)
Survival rate of replacement	0.79	(*F1*)
Goats		
Total population	11 033 900	(*F1*)
Female breeders in base year	4 835 200	(*F1*)
Male breeders in base year	96 704	Estimate ratio of 1/50 for breeding male to female
Female replacement in base year	1 585 220	Female lambs´ survival rate
Male replacement in base year	193 408	1/25 for preselection of breeding male to female
Other stock in base year	310 152	Total animals — all other categories (animals for offtake)
Female young in base year	2 006 608	(*F1*)
Male young in base year	2 006 608	(*F1*)
Annual lambing rate	0.83	(*F1*)
Survival rate of replacement	0.79	(*F1*)

References

F1. Agriculture. In: Bajiikhuu K, Tegshjargal T, Orso G, editors. *Mongolian statistical yearbook*. Ulaan Baatar: National Statistical Office; 1999.

Appendix G. **Human health input variables from household survey and Delphi panel**

Disease characteristic	Value	Source or basis of calculation or estimate
Proportion of chronic cases	0.66	(*G1*)
Duration of illness (years)	4.5	Data on duration of clinical cure of 1000 brucellosis patients in Russia (*G2*).[a]
Proportion of inpatient in chronic cases	0.40	(*G1*)
Average age at onset (for DALYs) (years)		
Women	37.00	(*G3*)
Men	37.00	(*G3*)
Children		
Aged 5–15	10.50	(*G3*)
Aged <5	3.20	(*G3*)
Inpatient days		
Women	21.00	(*G1*)
Men	21.00	(*G1*)
Children		
Aged 5–15	21.00	(*G4*)
Aged <5	21.00	(*G4*)
Proportion of hospitalization	0.50	(*G1*)
Rate of non-formal treatment	0.45	(*G1*)
Proportion of cases reporting loss of income	0.42	(*G1*)
Coping cost per case (MNT)	10.00	As we assume that relatives replace for the routine work of the patients and not extra persons have to be engaged; only a symbolic figure has been considered.
Disability-adjusted live years		
Disability weight (D)	0.20	No reference was found so far. A class 0,2 has been chosen since the disease is perceived as very painful. Sensitivity analysis for 0,1 has been done.
Discount rate (r)	0.05	Discount rate 5% with sensitivity analysis 3% based on the interest rate for savings in USD in Mongolia: 5.4% (November 2000) and real growing rate of the Mongolian economy: 3.3% in the last few years.
Age weighing (C)	0.16	(*G5*)
Parameter of age weighting (beta)	0.04	(*G5*)
Duration of disability in years (L) (median)	3.11	Data on duration of clinical cure of 1000 brucellosis patients in the Russian Federation (*G2*).[a]

[a] The frequency distribution of clinical disease duration fits best with an exponential function for an average duration of 4.5 years. For duration of disease, we used @Risk expon function with beta = 4.5 years. For cost effectiveness, we used the median of the cumulated discounted DALYs, which corresponds to a median duration of brucellosis of 3.11 years

References

G1. Roth F, Zinsstag J. *Economic analysis of the brucellosis control in Mongolia*. Geneva: World Health Organization; 2001. p. 225.

G2. Beklemischew cited by Wundt W. Krankheiten durch Brucellen. engl. Diseases from Brucella. In: Gsell O, Mohr W. *Infektionskrankheiten*. [*Infectious diseases.*] Berlin: Springer Verlag; 1968. p. 483-542. In German.

G3. Agriculture. In: Bajiikhuu K, Tegshjargal T, Orso G, editors. *Mongolian statistical yearbook*. Ulaan Baatar: National Statistical Office; 1999. p. 26.

G4. Ministry of Health, Personal communication, 2000.

G5. Murray CJL, Lopez AD. *Global comparative assessments in the health sector*. Geneva: World Health Organization; 1994. p. 196.