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RESEARCH

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Profitability and cost-effectiveness analysis of brucellosis control in Armenia: A One Health approach

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Abstract

Brucellosis is endemic in the Republic of Armenia and constitutes a financial and public health burden on the nation. Control of the disease is currently using the test-and-slaughter strategy, reportedly at a coverage level deemed insufficient to interrupt transmission by the authorities responsible for disease control. A key aspect of this control strategy is the shared costs between the agricultural and public health sectors. An earlier study conducted by the Advanced One Health Class at the Swiss Tropical and Public Health Institute developed a mathematical-compartmental transmission model to represent the transmission of *Brucella* between cattle, sheep, and humans. The study simulated the performance of the existing control strategy and three other upgraded scenarios over a decade, giving the cumulative incidence of human and livestock prevalence (2022–2031). Based on the cumulative incidence of human and livestock prevalence from 10-year simulations, this study evaluates Armenia's current brucellosis control program's profitability, cost-effectiveness, and cost distribution for the existing test-and-slaughter level and three proposed upgraded scenarios in cattle and sheep. In these scenarios, the percentages represent the proportion of animals that were culled when they tested positive for brucellosis: Scenario 1 – 86% of cattle and 65% of sheep; Scenario 2 – 88% of cattle and 70% of sheep; Scenario 3 – 90% of cattle and 75% of sheep. Further estimations were made on public and private health costs, and income loss of human brucellosis patients averted through the different livestock-level interventions. The incremental livestock production and the averted human health cost were summed up as societal benefits of brucellosis interventions. From a societal perspective, the most profitable scenario is estimated to have a net present value of US$ 41.82 million, from an overall cost of US$ 48.27 million and a benefit of US$ 6.45 million, resulting in a benefit-cost ratio of 0.133 at 80% compensation for farmers' losses and discounted at 5%. From a public health perspective, the cost-effectiveness ratio for the same intervention scenario is US$ 1587 per DALY averted (95% CI: US$ 1268–US$ 2009). When private costs, which are the private income loss and out-of-pocket costs of patients, are added to the public health costs, the cost-effectiveness decreases to US$ 6727 per DALY averted at a 5% discount rate (95% CI: US$ 5371–US$ 8504). These cost-effectiveness and benefit-cost ratios highlight the remarkable disparity in the cost of the test-and-slaughter strategy across the agriculture and public health sectors. Our study highlights the need to reassess the cost-effectiveness of the test-and-slaughter strategy for brucellosis control in Armenia and consider an equitable distribution of the cost of the test-and-slaughter strategy among the sectors as this could facilitate better disease control and cost-effectiveness of the strategy. Armenia should view brucellosis elimination as a public good, justifying public spending for compensation. As seen in other countries, its elimination could boost the economy by lowering trade barriers, making brucellosis-free status a societal benefit.

One Health impact statement

Our study focuses on controlling brucellosis in Armenia using an integrated approach called One Health, which seeks to demonstrate the incremental benefit of closer cooperation between human and animal health and other sectors. We evaluate how profitable and cost-effective test-and-slaughter interventions are in improving the health of both humans and animals while also considering the costs for farmers and the state. Using a One Health approach, we can better understand the cross-sector expenses related to the disease and develop more efficient strategies to interrupt transmission and eventually eliminate the disease. The result is improved animal and human health outcomes, enhanced livelihoods, and a positive contribution to the economy's overall growth (Narrod *et al*., 2012). To carry out this study, we collaborated closely with non-academic partners from the Food Safety and Inspectorate Body (FSIB) and the National Centre for Disease Control in Armenia (NCDC). This collaboration resulted in the creation of valuable knowledge and practical solutions, underscoring the importance of working together across different sectors, including indigenous communities, academia, and non-academic organizations.

Keywords: brucellosis, Armenia, One Health approach, cost-effectiveness, profitability, test-and-slaughter strategy, livestock productivity, public health, compensation level, society

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Introduction

Brucellosis is a transmittable disease caused by *Brucella* spp. that affects animals, humans, and wildlife (Musallam *et al*., 2015). The bacterium *Brucella* has six species known to cause brucellosis in livestock (Li *et al*., 2017); four of these species with the livestock they affect are *B. melitensis* in small ruminants such as sheep and goats, *B. abortus,* primarily seen on cattle, *B. suis* in pigs, and *B. canis* in dogs. Additionally, the *B. melitensis*, *B. abortus, B. suis,* and *B. canis* species are zoonotic and known to be harmful to humans (Glowacka *et al*., 2018), with *B. melitensis* being the main causative *Brucella* species for human brucellosis globally (Corbel, 2006; Li *et al*., 2017). Brucellosis infection in humans occurs through consuming unpasteurized dairy, undercooked meat, and direct contact with infected animal tissues. Animals can acquire the disease directly from infected animals or indirectly from contaminated food sources. Brucellosis presents as a severe illness with fluctuating fever in humans. At the same time, domestic ruminants primarily manifest reproductive issues such as abortions, infertility, and retained placenta (Muema *et al*., 2022), accompanied by reduced milk production (Khan and Zahoor, 2018). A growing body of literature recognizes the elimination of brucellosis in some advanced countries, including New Zealand, Australia, Japan, Canada, and many European nations (Khan and Zahoor, 2018).

Contrarily, each year, approximately 500,000 cases of human brucellosis are reported worldwide (Glowacka *et al*., 2018). These cases are predominantly found in regions where animal brucellosis is widespread, such as South America, Africa, Western Asia, the Middle East, and the Mediterranean region (Li *et al*., 2017). However, these statistics are questionable as cases are missed as other health conditions and inadequately reported (Li *et al*., 2017). Brucellosis poses significant challenges to human health and the economy, disrupting daily activities and impairing livestock production, necessitating effective measures for control (Ghanbari *et al*., 2020). Hence, the World Health Organization (WHO) emphasizes that eliminating animal infection is the best way to prevent brucellosis (WHO, 2020). This stance is also supported by the World Organization for Animal Health (OIE) (OIE, 2023). Vaccinating cattle, goats, and sheep, a strategy promoted by both the Food and Agriculture Organization of the United Nations (FAO) (FAO, 2014) and the OIE (OIE, 2023), is recommended in areas where the disease is prevalent. In regions with low prevalence, effective measures such as serological or other testing and culling infected animals are endorsed by the WHO (WHO, 2020), FAO (FAO, 2014), and OIE (OIE, 2023). Studies assessing the economics of brucellosis interventions have yielded diverse outcomes. Positive benefit-cost ratios (BCRs) were observed in selected populations when only vaccination was implemented (Roth *et al*., 2003; Singh *et al*., 2018; Zeng *et al*., 2019; Al Hamada *et al*., 2021); conversely, employing only the test-and-slaughter strategy resulted in negative BCRs (Oseguera Montiel *et al*., 2015; Zeng *et al*., 2019). However, a combination of vaccination and test-and-slaughter yielded varied results (Oseguera Montiel *et al*., 2015; Singh *et al*., 2018; Zeng *et al*., 2019).

ARMENIA

Brucellosis is prevalent in Armenia and strains the national economy (Asoyan *et al*., 2018). In 2005, the Food Safety & State Veterinary Inspectorate (FS&SVI) started a test-and-slaughter brucellosis control scheme using the Rose Bengal test (RBT). However, the program was inefficient due to functional and organizational inadequacies such as the absence of permanent individual animal identification, inadequate funding, lack of compensation for farmers, and variations in the use and interpretation of the Rose Bengal plate agglutination test among regional laboratories (Porphyre *et al*., 2010). By 2010, Armenia had a higher incidence rate of human brucellosis cases than Azerbaijan and Georgia. The incidence rate grew from 5.1 per 100,000 people in 1990 to approximately 9.2 per 100,000 in 2016. The economic losses caused by human brucellosis in Armenia were estimated to be around 36 million Armenian Dram (AMD) per year for the Nork Republican Infectious Disease Referral Hospital in Yerevan, equivalent to roughly US$ 74,000 (Sargsyan *et al*., 2019). However, no research is available on the economic losses caused by brucellosis in the Armenian human population or livestock.

ONE HEALTH AND ITS APPLICATION TO BRUCELLOSIS CONTROL

Understanding techniques for diagnosing, controlling, preventing, and predicting infectious diseases is crucial for public health (Ghanbari *et al*., 2020). The One Health theory recognizes the interconnectedness of humans, animals, and the environment, emphasizing interdisciplinary cooperation to achieve sustainable development (Schneider *et al*., 2019; Ghanbari *et al*., 2020). This approach aims to improve global health equity and promote sustainable development by integrating human, animal, and ecosystem health (Ghanbari *et al*., 2020).

Given the zoonotic nature of brucellosis and its impact on both human health and livestock production, a key aspect of effective control measures is the fair distribution of costs between the agricultural and public health sectors. This is particularly relevant when implementing strategies, such as test-and-slaughter, which can impose significant costs on farmers due to the loss of livestock without compensations. On the other hand, the public health sector benefits from reduced disease transmission to humans. Therefore, it is crucial that these costs are shared in a manner that is proportionate to the benefits accrued by each sector. This approach, which aligns with the principles of One Health, not only ensures the sustainability of control measures but also promotes equity and cooperation between different sectors. As shown in the study on brucellosis control in Mongolia (Roth *et al*., 2003), the health sector is expected to profit if brucellosis in livestock is controlled, suggesting that it could contribute a share that would make the program cost-effective from the health sector perspective. The study also identified livestock breeders and patients as the main beneficiaries of the intervention. It suggested that breeders might be willing to contribute to the campaign, and patients avoid out-of-pocket expenses and income loss.

Schelling *et al*. (2020) support the One Health approach for brucellosis control, which involves a comprehensive survey and surveillance program covering all animal and human species. Bio-molecular and biological research is crucial for identifying transmission links (Schelling *et al*., 2020). The approach utilizes models to study the impact of brucellosis and interventions on transmission between animals and humans, as seen in the Mongolian study (Zinsstag *et al*., 2005). The study's cost-effectiveness analysis demonstrated the health benefits of implementing brucellosis control measures in livestock. Incorporating public health and animal production sectors in the economic analysis showed incremental benefits and cost-effectiveness for public health (Roth *et al*., 2003; Zinsstag *et al*., 2005). Coordination between animal and human health sectors is essential within the One Health framework (Schelling *et al*., 2020).

PREPARATORY WORK BY THE ADVANCED ONE HEALTH COURSE TEAM

The Advanced One Health class participants at the Swiss Tropical and Public Health Institute in Basel have developed a model for animal-human transmission with the test-and-slaughter control strategy for brucellosis in Armenia. The model depicts brucellosis transmission between sheep, cattle, and humans. The method section highlights some details of the model in Fig. 1, from which prevalence projections on the baseline impact of the current test-and-slaughter for specified species in Armenia were simulated, along with three optimized scenarios for the next 10 years (2022–2031).

Using predictions and additional data, we examined the profitability and cost-effectiveness analysis of brucellosis control in Armenia

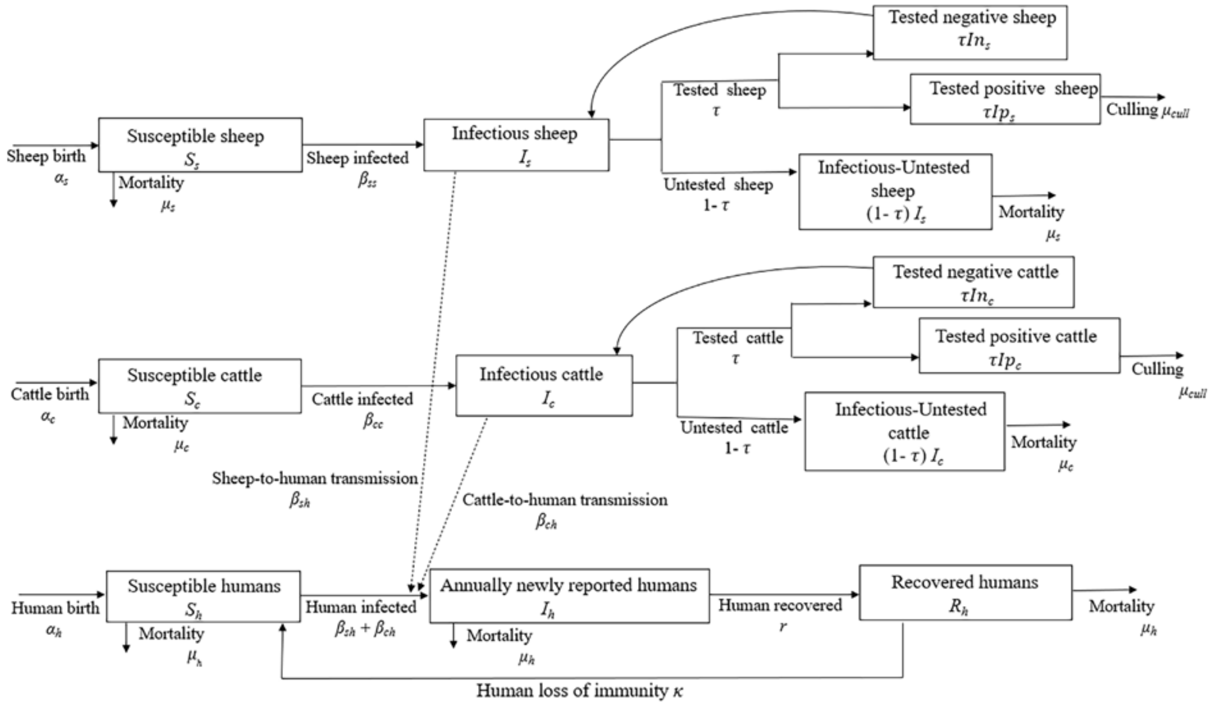

Fig. 1. Livestock-human brucellosis model from 2022 advanced One Health class at Swiss Tropical and Public Health Institute.

with a One Health approach, considering different scenarios (coverage levels) of the test-and-slaughter control strategy for public health and animal production. Our hypothesis proposes that while mass vaccination of livestock against brucellosis is demonstrated to be profitable from both an agricultural and societal perspective, test-and-slaughter strategies may not be profitable from a societal perspective. However, properly compensating farmers and an equitable distribution of the cost of the disease across the agriculture and public health sectors could eliminate the disease with this strategy.

This study aimed to estimate current costs and sector-wise cost distribution in upgraded test-and-slaughter control programs in Armenia, to assess the losses in livestock productivity and the public health sectors due to brucellosis, and to evaluate the potential economic benefits, cost-effectiveness, and averted disability-adjusted life years (DALYs) of different upgraded brucellosis control scenarios.

Methods

STUDY DESIGN

This study on cost-effectiveness analysis employs a livestock-human brucellosis transmission model implemented from the 2022 Advanced One Health Class at Swiss Tropical and Public Health, based on previous research by Zinsstag *et al*. conducted in Mongolia (Zinsstag *et al*., 2005). The model was designed using data from 2019 to 2021 in Armenia and takes into account susceptible populations of sheep and cattle represented by S_s and S_c respectively, which are subject to the birth rate α_s and α_c and subsequent infection rates β_{ss} and β_{cc}. Mortality rates μ are considered for susceptible and seropositive partitions, while infectious animals are in the I_s and I_c partitions. These infected partitions transmit the disease to humans through $\beta_{sh} + \beta_{ch}$. The model also accounts for the human susceptible population S_h, representing the entire Armenian population, which becomes infected with $\beta_{sh} + \beta_{ch}$ and results in annual human infections I_h that recover and return to the susceptible state S_h. Figure 1 shows the partitions and their respective transmission/recovery flows based on a positive brucellosis status determined using the RBT, which guides the culling of infected animals.

In Armenia, the annual testing rates for cattle and sheep are 85% and 60%, respectively, with a 100% culling rate for both species. These rates were determined through random sampling tests using the Rose Bengal Test (RBT), as per personal communications. From 2019–2021, a prevalence of 0.84% to 2.15% in cattle and 0.44% to 0.55% in sheep was recorded (Supplementary Materials: Appendix S8). These low prevalence rates, which are based on the aforementioned testing rates, justify the Armenian authorities' choice of the test-and-slaughter strategy which aligns with the WHO's recommendation that eliminating the infection in animals stands as the most potent strategy to prevent brucellosis, while in regions with low prevalence, serological testing, and culling have shown to be effective (WHO, 2020). Over 10 years, the model simulated various test-and-slaughter scenarios for cattle and sheep in Armenia. The baseline scenario used the current test-and-slaughter levels of 85% for cattle and 60% for sheep and their effect on human brucellosis incidence. The model also considered upgraded scenarios with higher test-and-slaughter rates (coverage levels) for both cattle and sheep: Scenario 1 with 86% cattle and 65% sheep, Scenario 2 with 88% cattle and 70% sheep, and Scenario 3 with 90% cattle and 75% sheep. These scenarios were designed to study the effect of higher coverage levels on brucellosis prevalence in livestock and humans. The parameters used in the model are listed in Supplementary Materials: Appendix S1.

STUDY POPULATION

This study develops a population matrix model (PMM) to compute livestock productivity and intervention costs based on prevalence-dependent transition factors. The PMM, similar to the one used in the control of bovine tuberculosis in Ethiopia (Tschopp *et al*., 2022), is represented by Eqns 1 and 2. The model includes a projection matrix with yearly survival, fertility, constancy, and discharge rates. The population vector (Vt) comprises male and female calves, lambs, mature cows, and sheep. We categorized the resulting data by gender and stage based on class gender ratios applied (Tschopp *et al*., 2022). As we did not have these transition parameters in the matrix provided in the actual data, we optimized the matrix components against the livestock population data from the animal-human transmission model predicted for 2019–2021, considering cattle and sheep of different ages, genders, and biological population uniqueness.

OPTIMIZATION OF PARAMETERS

The parameters in the transition matrix are a_{13} for birthrate; a_{21} for the survival rate in young animals; a_{32} for survival rate in sub-adults and; a_{33} for persistence rate adults. In the matrix, we set the sub-adult persistence rate at a constant value of 0.5, and we set the adult population persistence a_{33} at 0.65 and 0.7 for cattle and sheep, respectively. For cattle, we capped the birthrate a_{13}, at 0.65, and 0.7 for sheep. We illustrate the matrix model for cattle in the Eqn 1 and sheep in the Eqn 2.

$$\begin{pmatrix} J_c \\ sA_c \\ A_c \end{pmatrix}_{T+1} = \overbrace{\begin{pmatrix} 0 & 0 & a_{13,c} \\ a_{21,c} & 0.5 & 0 \\ 0 & a_{32,c} & 0.65 \end{pmatrix}}^{\text{Matrix model for cattle}} \begin{pmatrix} J_c \\ sA_c \\ A_c \end{pmatrix}_{T} \quad (1)$$

$$\begin{pmatrix} J_s \\ sA_s \\ A_s \end{pmatrix}_{T+1} = \overbrace{\begin{pmatrix} 0 & 0 & a_{13,s} \\ a_{21,s} & 0.5 & 0 \\ 0 & a_{32,s} & 0.7 \end{pmatrix}}^{\text{Matrix model for sheep}} \begin{pmatrix} J_s \\ sA_s \\ A_s \end{pmatrix}_{T} \quad (2)$$

We developed a custom R function to optimize input parameters by computing the root mean square error (RMSE) (Hodson, 2022) between an input matrix model and data. This function transforms parameters into a matrix model and compares projected populations to the input data. We applied the R function *optim* with the L-BFGS-B method (Zhu *et al*., 1997) for optimization. These functions were used to calculate the best-fit matrix model for RMSE in cattle and to define constraints using simulated data from the animal-human brucellosis transmission model for the period 2016–2021. We selected this period as it represents a more homogeneous population trend. Similarly, we applied the same functions for sheep using data from the same period and we presented the data used in Supplementary Materials: Appendix S2.

POPULATION PROJECTIONS

To estimate and consider the impact of brucellosis on the birth rate, we used the general PMM for 2016–2021. For specific assessment, we created annual PMMs for 2019–2021 by fixing all parameters except the birth rate. To achieve this, we calculated the observed birth rate as the weighted mean of healthy animals and animals infected by brucellosis, with the prevalence serving as the weight.

To establish the prevalence-dependent birth rate, we used the birth rates from the annual models and the actual prevalence of brucellosis for 2019–2021. We incorporated these into a linear equation, represented as Ax=b, where A is a matrix of coefficients (annual prevalence and one minus the prevalence for 2 years), x is a column vector of unknown variables (x1 and x2), and b is a column vector of constants (computed birth rates in the annual models). Solving the equation Ax=b gave us the values for the variables x1 and x2 that satisfied the given equations. The solutions from the equations for cattle and sheep are as follows:

Cattle 2020_2021:

$$\begin{cases} 0.008440935 * x_1 + 0.991559065 * x_2 = 0.748325797102403 \\ 0.01528802 * x_1 + 0.98471198 * x_2 = 0.693098211994184 \end{cases} \quad (3)$$

Sheep 2020_2021:

$$\begin{cases} 0.004463 * x_1 + 0.995537 * x_2 = 0.888516417734686 \\ 0.005208034 * x_1 + 0.994791966 * x_2 = 0.836446613902305 \end{cases} \quad (4)$$

With the prevalence-dependent birthrates established, we projected the cattle and sheep populations for 30 years from 2020. The livestock prevalence data from Supplementary Materials: Appendix S3 of the animal-human brucellosis transmission model study were integrated into the prevalence of 2020–2021 to create birthrate models for various scenarios, excluding the baseline (current scenario). Following this, we made projections similar to those in the study by (Tschopp *et al*., 2022) using the simulation results from the same animal-human brucellosis transmission model study. This study considered four different scenarios, with the implementation of upgraded interventions planned to begin in 2022. The projections for the annual population from 2022 to 2031 are available in Supplementary Materials: Appendix S4.

PRODUCTIVITY ESTIMATES

Our study employed two approaches to address the limitations of the livestock data from Armenia (2012–2021). First, we used the proportions of age and sex categories and the offtake matrix from a previous study by Tschopp *et al*. (2022), as shown in Supplementary Materials: Appendix S5. The offtake matrix represents the offtake rates for different categories of cattle and sheep. The first row shows the offtake rate for female calves and lambs, which is 0.11. The second row shows the offtake rate for heifers and ewe lambs, which is 0.28. The third row shows the offtake rate for cows and ewes, which is also 0.28. The fourth row shows the offtake rate for male calves and lambs, which is 0.71. The fifth row shows the offtake rate for bullocks and ram lambs, which is 0.5. The sixth row shows the offtake rate for bulls and rams, which is also 0.5. These age and sex proportions were multiplied by the offtake matrix to estimate the corresponding sheep and cattle populations, allowing us to determine livestock productivity for beef, mutton, and hide. For the estimation, the carcass weight proportions of culled livestock in tons in 2021 were used (Supplementary Materials: Appendix S6).

Second, we constructed matrices for the livestock products, including milk, beef, mutton, and hide for cattle and sheep. These matrices considered these factors: average annual milk yield per cow, off-farm milk price, annual carcass prices per ton, and average hide prices per ton (Table 1). By multiplying species-specific livestock products by the offtake populations, we estimated the productivity of each livestock product for the scenarios considered in this study for 2022–2031. For the estimation, the carcass weight proportions of culled livestock in tons in 2021 were used (Supplementary

Table 1. Monetary value of livestock products in Armenian Dram (AMD).

Product	Average annual yield in kilograms	Average price per ton in AMD
Cattle		
Milk	2350 (2200–2500)	300
Beef	NA	3,500
Hide	18	12,500 (10,000–15,000)
Sheep		
Mutton	NA	4,250 (4,000–4,500)
Hide	2.5	150 (100–200)

NA = Not Available; 1 US dollar = 400 Armenian Dram in 2021 (personal communication).

Materials: Appendix S6), while Supplementary Materials: Appendix S7 shows the total annual livestock productivity estimates.

DATA SOURCES

Data on animal brucellosis-seroprevalence was obtained from the Veterinary Department of FSIB for 2012–2021 in Supplementary Materials: Appendix S8. We took human brucellosis cumulative incidence estimates for 2019–2031 from the 2022 Advanced One Health Class at the Swiss Tropical and Public Health Institute study for the Disability-Adjusted Life Year (DALY) computation (Supplementary Materials: Appendix S3). The human health costs of brucellosis following diagnosis were adopted from the health care utilization cost findings (Vered *et al*., 2015) and adapted to the Armenian context, as shown in Supplementary Materials: Appendix S9, as no human health cost data is available for Armenia. The private income loss data for human brucellosis was based on the 2021 monthly minimum wage from the World Bank (World Bank, 2022). Market unit costs for live animals, animal products, and the cost of the test-and-slaughter intervention were provided by the Scientific Centre for Risk Assessment and Analysis in the Food Safety Area, Armenia (Table 1).

DATA ANALYSES

Cost of test-and-slaughter

The intervention was costed from a societal perspective, considering the costs to the agriculture sector (specifically, breeders), the public health sector, and the private health sector (including out-of-pocket expenses and the impact of the disease on private income). For the agriculture sector, we first estimated the cost of test-and-slaughter intervention in the Armenian livestock, calculating the proportions of population and prevalence based on the upgraded scenarios of the test-and-slaughter already simulated, including the baseline. The cost of testing using the RBT was derived by multiplying the annual projected population from the PMM for each scenario and species by the cost of testing each animal. Culling costs were calculated by multiplying the culled proportions from the animal-human brucellosis transmission model for each scenario and species by the cost of culling (slaughter and transportation to slaughterhouse) for each sero-positive animal. The compensation costs using 80% (personal communication) of the value of each culled livestock were calculated by multiplying the prevalence proportions for each scenario and species by the average market price for each animal. As there is currently no compensation for farmers in Armenia, the baseline scenarios for cattle and sheep did not account for any form of compensation for the farmers. We calculated the total cost of the test-and-slaughter intervention in the agriculture sector by adding the testing, culling, and compensation costs for sheep and cattle in the four-modeled scenarios for 2022–2031. In our analysis, we assigned a value of zero to the opportunity cost of the livestock producer's time as we assumed that farmers did not experience any financial losses due to the time spent on the test-and-slaughter campaign.

For the public health sector (national government), we assume that 27% of human brucellosis cases become chronic (Sargsyan *et al*., 2019). We adopted a public human brucellosis cost for a year of US$ 1327 (Vered *et al*., 2015), computing individually the cost for 6 months in chronic cases and 2 months in acute cases, which includes the medication costs, the hospital hotel and food costs, diagnostic costs, and doctors' fees. The public health cost of brucellosis was the sum of the computed costs in both chronic and acute cases by their duration multiplied by their respective cumulative incidence. The private income losses from brucellosis infection were calculated with the individual average monthly income in Armenia (World Bank, 2022) multiplied by the proportional cumulative incidence in chronic and acute cases and their corresponding duration of treatment: 6 and 2 months, respectively. The sum of these multiples is the private income losses for human brucellosis. As we have no empirical data on the personal health payments for brucellosis, we assumed that the out-of-pocket cost contribution to the cost of brucellosis in human health is 1.7 times the estimate for public health cost, and we adopted this multiplication factor from the findings in (Roth *et al*., 2003). We detail the human health cost calculation (see Supplementary Materials: Appendix S9 for more information).

Averted cost to public health and livestock production

The cost savings in human health due to the implementation of upgraded test-and-slaughter scenarios were calculated by subtracting the annual costs of brucellosis in both public and private health sectors under the upgraded scenarios from the baseline scenario. The saved costs in livestock production are derived from estimated livestock productivity improvements from adopting the upgraded scenarios. These savings represent the benefits projected for 10 years from the enhanced test-and-slaughter control measures.

Profitability of the test-and-slaughter strategies

The benefit-cost ratios (BCR) for the three upgraded scenarios were computed by dividing the benefits from the upgraded intervention scenarios by their total costs annually. We also calculated the net present value (NPV) for the upgraded intervention by discounting the total benefits and costs for the different upgraded scenarios at 5% and then subtracting the costs from the benefits annually. Similarly, before use, we discounted the components for the metrics used to assess the cost-effectiveness and cost-benefits of the intervention at 5%.

Averted burden of disease

In assessing the burden of brucellosis on public health in Armenia, we calculated the Disability-Adjusted Life Years (DALYs) and the DALYs averted. While DALYs are often measured by combining the Years of Potential Life Lost (YLL) due to premature death and the Years Lived with a Disability (YLD), we considered only YLD in our calculation. This decision was based on the observation that brucellosis in humans rarely leads to death (Zinsstag *et al*., 2005; Singh *et al*., 2018). Therefore, the impact of the disease on disability (YLD) was deemed more relevant for our analysis than the impact on premature mortality (YLL). Chronic, localized brucellosis was proposed to have a disability weight of 0.150, based on the disability weights provided in the 2004 Global Burden of Disease Study, to reflect the burden it places on individuals. The disability weight for acute brucellosis, which measures how the illness affects those with Brucella infection, is calculated to be 0.190 (Dean *et al*., 2012). Based on this, we adopted a disability weight of 0.2 and a disease duration of 4.5 years (Roth *et al*., 2003; Zinsstag *et al*., 2005) to compute the annual DALYs for all scenarios with the formulae:

$$\text{Predicted prevalence} * (DW * L) \tag{5}$$

DW is the disability weight of the disease, while *L* stands for the disease duration. DALYs averted in the upgraded scenarios for the period we computed by subtracting the upgraded scenarios individually from the baseline scenario as benefits for public health.

Cost-effectiveness of the test-and-slaughter strategies

We assessed the cost-effectiveness of the upgraded scenarios using two metrics: the cost-effectiveness ratio (CER) and the incremental cost-effectiveness ratio (ICER). These metrics were calculated cumulatively for 8 years, excluding the first 2 years (2022 and 2023) when no DALYs were averted, making estimation impossible for those years. The CER was obtained by dividing the intervention's cost by the annually averted DALY, while the ICER was derived by dividing the cost difference between the upgraded and baseline scenarios by the difference in DALYs averted between these scenarios.

Furthermore, we conducted a manual sensitivity analysis, varying the level of compensation used in the intervention costing (at 50%), livestock prevalence, human incidence, and productivity estimates (all increased by 10%), and applied a discounting rate of 3%. All analyses, including the sensitivity analysis, were performed using R version 4.1.3 from the R Development Core Team at: https://www.r-project.org/.

Results

OPTIMIZATION OF PARAMETERS

We optimized the matrix model over 10 years, resulting in one matrix model with consistent coefficients. An interesting observation was that the coefficients aligned with the prevalence data for cattle. When the prevalence was higher, the birth rate was lower; conversely, when the prevalence decreased, the birth rate increased. The birth rate experienced a slight increase in 2020 and a slight decrease in 2021. The persistence rate in adults remained constant. These optimized parameters matched the coefficients, emphasizing their significance in population dynamics. For sheep, the survival rates for young animals and sub-adults remained consistent, while the birth rate exhibited an increasing trend. The persistence rate in adults showed no significant changes. The optimized parameters corresponded with the coefficients, further underscoring their importance. The parameter variations align with population changes across the data for cattle and sheep from 2016 to 2021, and you can find the optimization results for both species in Supplementary Materials: Appendix S2.

PREVALENCE DECREASES AND POPULATION PROJECTIONS

Based on the provided prevalence data for cattle and sheep, the overall trend is that the prevalence for the baseline scenarios (85% for cattle and 60% for sheep test-and-slaughter coverage levels) remained constant. In contrast, the prevalence for the other scenarios gradually decreased over time. From 2019 to 2022, the prevalence for all categories remained constant, but from 2023 to 2031, the prevalence for scenarios (coverage levels 86%, 88%, and 90% in cattle and 65%, 70%, and 75% in sheep) decreased yearly. To ensure consistency with our study aims, we considered the data from 2021, retaining the assumption that the intervention started in 2022–2023. Figures 2 and 3 illustrate the decline in prevalence in both species, with their supporting data in the Supplementary Materials: Appendix S3. Population projections for cattle and sheep (Supplementary Materials: Appendix S4) show a gradual decrease from 2022 to 2031 in baseline scenarios (85% for cattle and 60% for sheep). In contrast, alternative scenarios show an initial increase from 2022 to 2023, followed by a steady rise until 2031.

ECONOMIC AND HEALTH IMPACT ASSESSMENT OF THE UPGRADED TEST-AND-SLAUGHTER LEVELS

General outcomes

Table 2 presents the general profitability and cost-effectiveness analysis results for the four scenarios, with the economic and health metrics. The scenarios showed varying levels of cost-effectiveness, health impact, and economic outcomes. The current test and slaughter intervention cost in Armenia is approximately

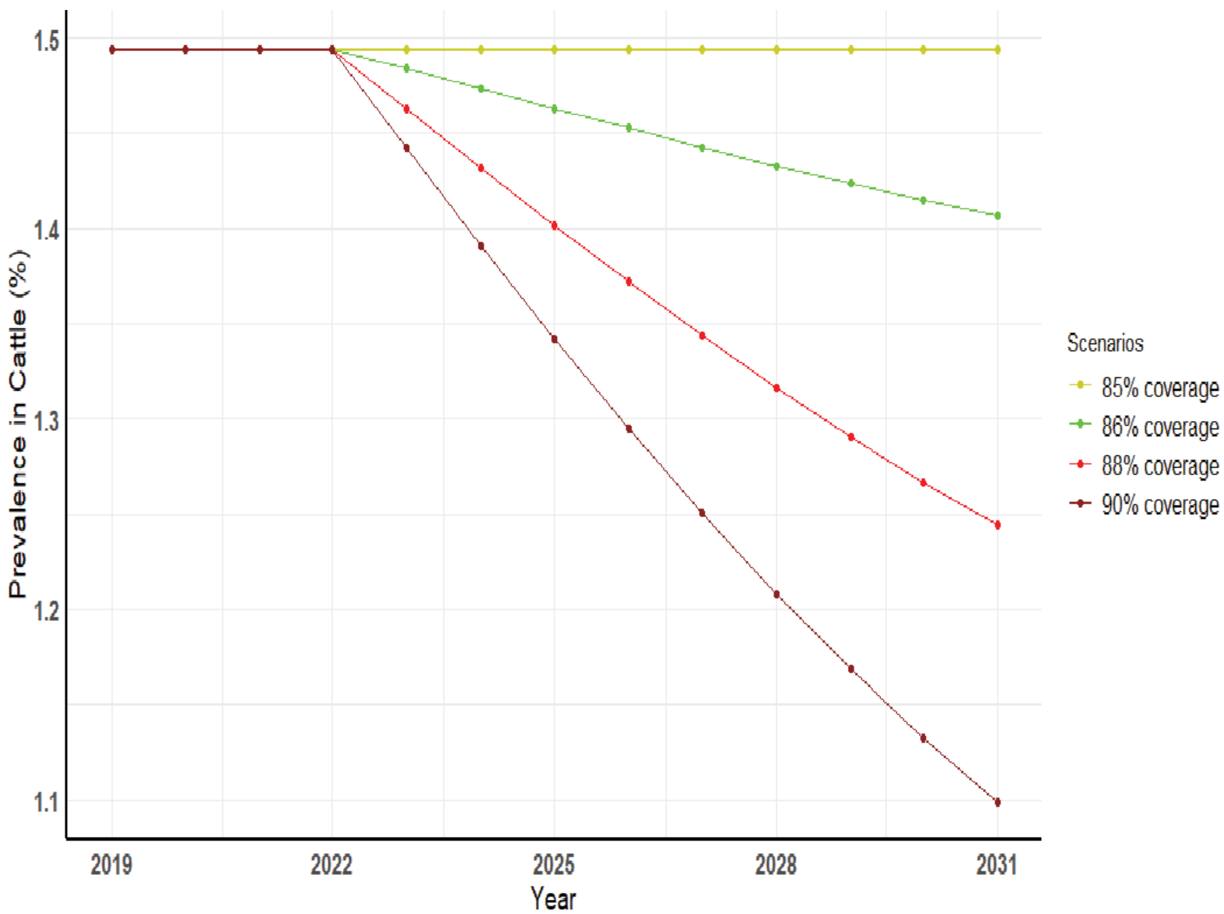

Fig. 2. Prevalence reduction in cattle across different test-and-slaughter scenarios (85%, 86%, 88%, and 90% coverage).

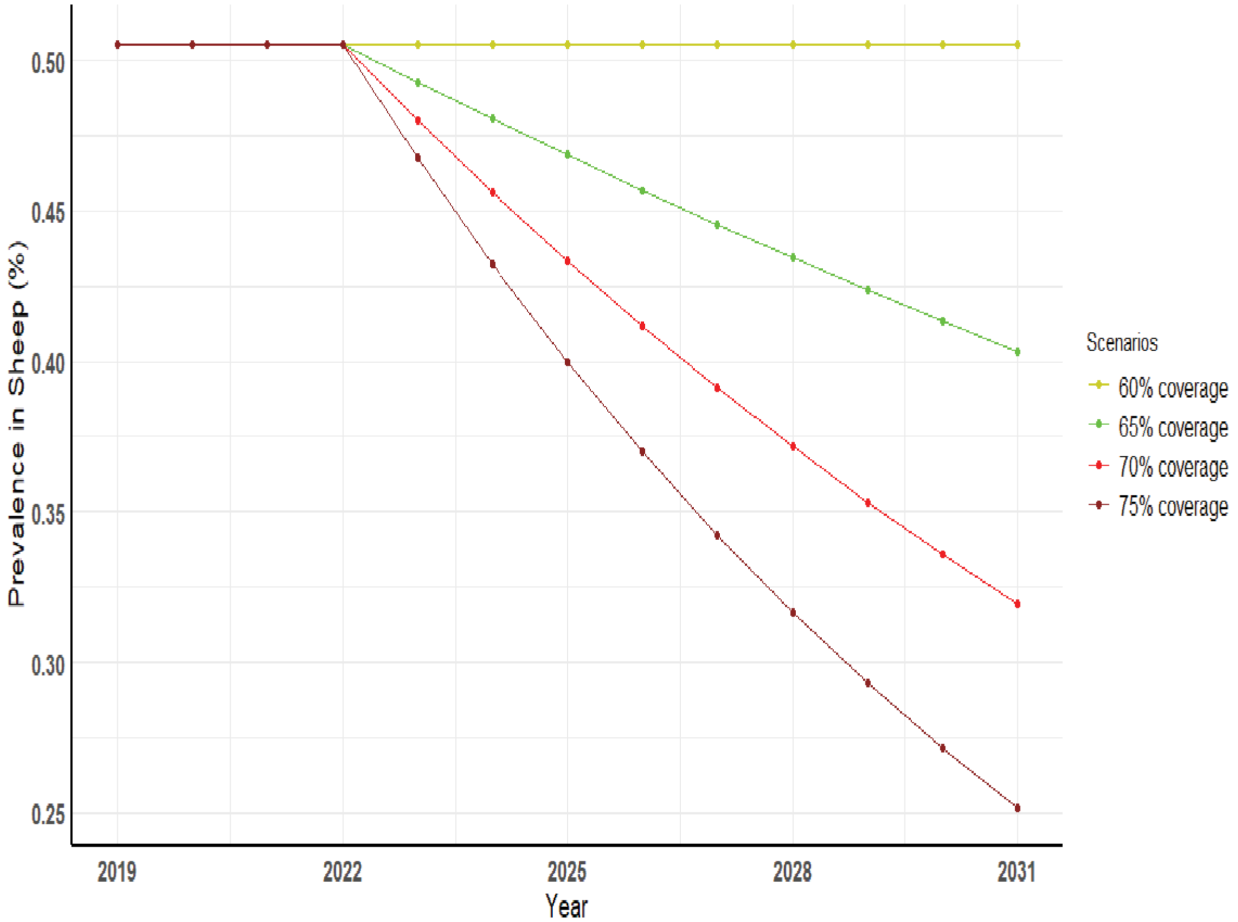

Fig. 3. Prevalence reduction in sheep across different test-and-slaughter scenarios (60%, 65%, 70%, and 75% coverage).

2.6 times lower than the average cost estimated in the upgraded scenarios, and the lack of compensation for farmers' losses using the test-and-slaughter method, which we also considered in the costing accounts for this. Scenario 3 has the lowest intervention cost among the upgraded scenarios, cumulative medical cost, DALY, ICER, and CER by 2031. However, it also has the highest medical cost savings, DALY averted, and CBR among the upgraded scenarios.

Shared-cost approach

In our analysis, we considered Scenario 3 further, as shown in Table 3. Both the agriculture and human health sectors have negative NPV and BCR of less than 1, indicating that the costs of the intervention outweigh the benefits in both sectors. Interestingly, the negative NPV is more significant in agriculture, while the BCR is slightly higher in human health. If the intervention costs were allocated based on the relative benefits accrued by each sector, the public health sector would bear approximately 1% of the intervention cost, giving a cost-effectiveness of US$ 1587 per DALY averted (Table 4). Considering the private economic and public health gains resulting from improved human health, the health sector would contribute approximately 7%. These findings highlight the significant burden of the test-and-slaughter strategy on the agricultural sector.

Sensitivity analysis

Based on the information provided in Table 5, the compensation level appears to have the most significant impact on the BCR and CER. In contrast, the variable that seems to have the highest impact on the DALY is the discount rate. Livestock prevalence and human incidence, as well as productivity estimates, have a notable effect on all three measures. The compensation level is the most sensitive variable, followed by livestock prevalence and human incidence, productivity estimates, and the discount rate.

Limitations of the study

In our analysis, we used data from secondary sources to model and estimate the costs of the intervention levels. The cost-effectiveness analysis incorporated prevalence and livestock population data derived from the brucellosis transmission model and the PMM. Based on the livestock data, we optimized the livestock PPM parameters, considering only prevalence for 2019–2021 due to irregularities. The productivity estimate relied on the offtake parameter obtained from another study conducted in a different setting. Additionally, the annual public health cost of brucellosis was acquired from another study, while the out-of-pocket contribution to the private cost was based on the proportions of our public health cost of the disease. It is important to note that this study's cumulative and annual median CER and ICER calculations spanned only 8 years, unlike other metrics used in the economic and health impact assessment. Despite these limitations, our analysis provides valuable insights into the cost of the current intervention and higher levels and their public health impacts and profitability in Armenia.

Discussion

In Armenia, where brucellosis prevalence among livestock is low, as indicated in the seroprevalence data (Supplementary Materials: Appendix S8), the test-and-slaughter control strategy has been adopted. This approach aligns with the emphasis of the WHO and OIE (WHO, 2020; OIE, 2023) on the importance of eliminating

Table 2. Cumulative profitability and cost-effectiveness analysis (10-year test-and-slaughter intervention, brucellosis, Armenia, 80% compensation, 5% discount).

	Current scenario	Scenario 1	Scenario 2	Scenario 3
Metrics	**Armenian Dram**	**Armenian Dram**	**Armenian Dram**	**Armenian Dram**
Intervention costs (livestock)				
Testing cost	6,585.73	7,096.65	7,234.85	7,420.60
Culling cost	624.32	613.88	594.94	576.49
Compensation cost	0	11,143.92	10,794.08	10,455.11
Total intervention costs (livestock)	7,210.05	18,854.45	18,623.88	18,452.20
Human health costs				
Public health cost	233.07	224.02	212.37	201.78
Private income loss	358.30	344.39	326.48	310.19
Out-of-pocket contribution to health costs	396.22	380.83	361.03	343.02
Total human health costs	987.59	949.24	899.88	854.99
Intervention benefits (livestock)	2,218.32	2,425.35	2,436.23	2,446.59
Human health benefits	—	38.35	87.71	132.60
Total societal costs	8,197.64	19,803.68	19,523.76	19,307.19
Total societal benefits	—	2,463.70	2,523.94	2,579.192
DALY	1540	1480	1403	1333
DALY averted	—	60	137	207
ICER	—	1,750.27	706.18	466.85
CER	—	3,000.35	1,221.48	816.03
BCR	—	0.124	0.129	0.134
NPV	—	−17,339.98	−16,999.82	−16,727.10

DALY = disability-adjusted life years; ICER = incremental cost-effectiveness ratio; CER = cost-effectiveness ratio; BCR = benefit-cost ratio; and NPV = net present value.
Note: All costs, benefits, ICER, CER, and NPV, are in millions of Armenian Dram (AMD). DALY, DALY Averted, and BCR are unitless. The CER and ICER calculations cover 8 years (2024–2031).

animal infection for brucellosis prevention. It involves effective measures such as serological testing and culling infected animals, as advocated by (WHO, 2020; FAO, 2014; OIE, 2023). However, brucellosis remains endemic in Armenia, posing economic and public health burdens (Asoyan *et al*., 2018). The need for a study arose to use a mathematical model under a One Health approach to predict transmissions between livestock and humans, along with their prevalence and cumulative incidence in the country's current test and slaughter scenario (baseline). Consequently, we assessed the profitability and cost-effectiveness of the three upgraded test-and-slaughter strategy scenarios, showing their performances across 2022–2031, as well as the unproportionate distribution of the cost of the strategy between the agriculture and Public Health sectors.

According to our findings from the general analysis, we expect that farmers' compensation, at 80%, will cost 19,307.19 million AMD (equivalent to US$ 48.27 million) with a benefit of 2579.19 million AMD (equivalent to US$ 6.45 million). This results in a negative NPV of 16,727.99 million AMD (US$ 41.82 million) loss and BCR of 0.133, cumulatively after 10 years discounted at 5% in the most profitable of the scenarios; scenario 3 for private breeders. The current scenario of the test-and-slaughter (livestock) in Armenia was estimated to be approximately 2.6 times lower than the cost of Scenario 3, without any compensation for farmer's losses at 7210.05 million AMD (equivalent to US$ 18.03 million) for the same period, highlighting the enormous economic burden involved with test-and-slaughter intervention considering compensation or no compensation for farmers.

From a societal point of view focusing on Scenario 3, as shown in Table 3, the total private sector cost of the intervention, which includes breeders' cost, out-of-pocket contributions to health cost, and private medical expenses, amounts to 19,105.41 million AMD (US$ 47.76 million). The scenario has a benefit of 2547.89 million AMD (US$ 6.37 million), resulting in an NPV loss of 16,557.51 million AMD (US$ 41.39 million) and a BCR of 0.133. Moreover, the cost, benefits, and NPV of all sectors (both public and private) in the intervention are roughly 1.0071% higher than that of the private sector costs alone while maintaining the same BCR.

From a public health perspective, the cost-effectiveness ratio for the intervention is US$ 1587 per DALY averted. When we added the incremental costs of patients (out-of-patient contribution and private medical costs) to the public health costs, we arrived at a cost-effectiveness of US$ 6727 per DALY averted. These cost-effectiveness ratios imply that the intervention is more cost-effective for the public health sector when compared to the intervention viewed from either the agricultural sector or societal perspective. Incorporating the cost-sharing scenario allows for a comprehensive consideration of the multi-sectoral interventions employed to combat zoonotic diseases and could be cost-effective

Table 3. Scenario 3 profitability of test-and-slaughter in Armenia (Scenario 3, 10-year cumulative, 5% discount rate).

	Intervention costs	Intervention benefits	NPV	BCR
Sector	**Armenian Dram**	**Armenian Dram**	**Armenian Dram**	
Agriculture				
Breeders	18,452.20	2,446.59	−16,005.60	0.133
Public	0	0	0	0
Total	18,452.20	2,446.59	−16,005.60	0.133
Human health				
Public health	201.78	31.29	−170.48	0.155
Ministry of Health, national government	0	0	0	0
Patients				
Out-of-pocket contribution to health cost	343.02	53.20	−289.82	0.155
Private income loss	310.19	48.11	−262.09	0.155
Total	855.99	132.60	−723.39	0.155
Total private sector	19,105.41	2,547.90	−16,557.51	0.133
Total Society	19,307.19	2,579.19	−16,728.99	0.133

NPV = net present value; and BCR = benefit-cost ratio.
1 US dollar = 400 Armenian Dram in 2021 (personal communication).
Note: All costs, benefits, ICER, CER, and NPV, are in millions of Armenian Dram (AMD).

Table 4. Cost-effectiveness of test-and-slaughter intervention in Armenia (Scenario 3, 8-year median, CI, 5% discount).

Sectors	Cost of intervention	DALY averted	Cost-effectiveness ratio
Public health sector perspective			
Armenian Dram	17.78 (14.20–22.48)	28 (16–35)	0.635 (0.51–0.80)
US Dollar	44,440 (35,502–56,196)		1,587 (1,268–2,009)
Societal perspective			
Armenian Dram	75.32 (60.17–95.25)	28 (16–35)	2.69 (2.1–3.402)
US Dollar	188,304 (150,431–238,120)		6,727 (5,371–8,504)

CI = confidence interval.
1 US dollar = 400 Armenian Dram in 2021 (personal communication).
Currency: Armenian Dram values are in millions, while U S Dollar values are presented in their exact amount.
All costs are presented from two perspectives: The public health sector and the Societal.

Table 5. Sensitivity analysis on disability-adjusted life year, benefit-cost ratio, and cost-effectiveness ratio.

Variable	DALY%	BCR%	CER%
Compensation level (50%)	0	27	−19
Livestock Prevalence and Human Incidence (10% increase)	−10	6	12
Productivity estimates (10% increase)	−10	6	12
Discount rate (3%)	8	0.3	8

for all sectors as the costs are shared. The overall non-profitability of using the test-and-slaughter alone to control brucellosis found in this study aligns with the findings in a previous study on yaks (Zeng *et al*., 2019) and goats (Oseguera Montiel *et al*., 2015).

Furthermore, the compensation of farmers for losses they bear with the use of the test-and-slaughter for brucellosis control is important as the absence of compensation discourages farmers from making the necessary contributions to the intervention, resulting in the retention of potentially infected animals (Avila-Granados *et al*., 2019). From a societal viewpoint, the compensation level is crucial in adopting the test-and-slaughter strategy for brucellosis control in Armenia. A 50% compensation level benefits the government by covering only half the value of lost animals. In comparison, an 80% compensation level shifts a greater burden of losses to the government, favoring the farmers.

When analyzing the compensation levels, from the perspectives of the most influential stakeholders, the government and farmers, a 50% compensation level benefits the government as they only reimburse half of the value of the animals lost during the control measures. Conversely, at 80% compensation, the government bears a higher percentage of the losses. The government, while bearing a higher percentage of losses compared to a 50% compensation level, still benefits from improved health outcomes, reduced costs, and better economic viability, which result from effective brucellosis control. Despite overall negative payoffs in the scenarios considered in our study, Scenario 3 (the most profitable of the scenarios) generally showed more favorable changes across the metrics, suggesting potential advantages in reduced costs, improved health outcomes, and better economic viability compared to the current scenario in Armenia from 2022 to 2031.

From a policy point of view, it is important to acknowledge that eliminating a zoonosis that affects public health and animal production comes at a cost. The freedom from brucellosis can indirectly benefit through lowered trade restrictions and improved long-term health status of the human population. However, achieving sufficient culling ratios becomes unlikely without adequate compensation for farmers' culled stock, jeopardizing disease elimination efforts. To offset some of the compensation costs, the Ministry of Agriculture and other relevant authorities in Armenia could consider implementing a system where culled animals, deemed safe after rigorous testing, are sold in the market. This approach, known as commodity-based trade, could provide a financial return that helps recover some of the costs associated with the culling process.

CONCLUSIONS AND RECOMMENDATIONS

Our study highlights the need to reassess the cost-effectiveness of the test-and-slaughter strategy for brucellosis control in Armenia. Despite its current implementation, our findings suggest that this approach may not yield significant economic benefits, even when upgraded. It is worth exploring alternative control strategies that have shown promise in other contexts to address this issue. One such strategy is combining test-and-slaughter with vaccination in higher prevalence areas. This integrated approach has economic and epidemiological advantages, making it a potentially viable option for brucellosis control in Armenia.

Moreover, considering the significant burden of the test-and-slaughter strategy on the agricultural sector, we recommend adopting a fair distribution of costs between the agricultural and public health sectors. This could facilitate better disease control and cost-effectiveness of the strategy, aligning with the principles of One Health. This approach recognizes the interconnectedness of human, animal, and environmental health and promotes collaborative efforts among different stakeholders. For further research on the profitability and cost-effectiveness of brucellosis control in Armenia, another assessment could be conducted with livestock population parameters from the Armenian livestock industry and Human health data from the responsible authorities for a more accurate prediction. It will also be beneficial to survey to assess the willingness to pay among private farmers and relevant authorities. Understanding their perspectives and potential contributions toward compensations for losses incurred in disease control can provide valuable insights for designing effective and sustainable control strategies. By exploring alternative control approaches and incorporating a One Health perspective, Armenia can enhance its brucellosis control efforts, improving economic and public health outcomes.

CONFLICT OF INTEREST

The authors state that they do not have any incompatible financial or non-financial interests related to this manuscript.

ETHICS STATEMENT

The present study relied on pre-existing research data, making it exempt from the need for ethical approval.

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AUTHORS CONTRIBUTIONS

This work was significantly shaped by the contributions of UA, AD, JZ, and FT, who were instrumental in its conception and design. UA wrote the manuscript. The task of data acquisition, organization, and interpretation was jointly undertaken by UA, AD, JZ, and TM, AD and JZ played a significant role in designing the disease transmission and livestock population models. All authors have reviewed and approved the final version of the manuscript. They have also agreed to be personally accountable for their contributions and to ensure that any questions related to the accuracy or integrity of the work are thoroughly investigated and resolved, with the resolution documented in the literature, regardless of whether they were personally involved in that part of the work.

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