The Economic Impact of Cystic Echinococcosis in Rio Negro Province, Argentina

Glenda M. Bingham,* Edmundo Larrieu, Leonardo Uchiumi, Carlos Mercapide, Guillermo Mujica, Mario Del Carpio,
Eduardo Hererro, Juan Carlos Salvitti, Bo Norby, and Christine M. Budke

*Department of Veterinary Integrative Biosciences, College of Veterinary Medicine and Biomedical Sciences, Texas A&M University, College Station,
Texas; Ministry of Health, Viedma, Rio Negro Province, Argentina; National University of La Pampa, General Pico, La Pampa Province,
Argentina; Artemides Zatti Hospital, Viedma, Rio Negro Province, Argentina; Rogelio Cortizo Hospital, Ingeniero Jacobacci, Rio Negro Province,
Argentina; Ramon Carrillo Hospital, Bariloche, Rio Negro Province, Argentina; Department of Large Animal Clinical Sciences,
College of Veterinary Medicine, Michigan State University, East Lansing, Michigan*

Abstract. Cystic echinococcosis (CE), a parasitic zoonosis with substantial human health and economic consequences, is highly endemic in Rio Negro Province, Argentina. The objective of this study was to estimate the direct and indirect human and livestock-associated monetary losses attributable to CE, in Rio Negro Province, for the year 2010. Human costs were estimated using data obtained from hospital chart reviews, patient interviews, and government reports. Livestock-associated losses were estimated using data from government reports and scientific publications. Spreadsheet models were developed utilizing Latin Hypercube sampling to account for uncertainty in the input parameters. In 2010, the estimated total cost of CE, in Rio Negro Province, ranged from US$4,234,000 (95% credible interval [CI]: US$2,709,000–US$6,226,000) to US$5,897,000 (95% CI: US$3,452,000–US$9,105,000), with livestock-associated losses representing between 80% and 94% of the total losses, depending on whether non-healthcare-seeking human cases were included and if livestock slaughter values were adjusted to account for underreporting. These estimates suggest that CE is responsible for considerable human and livestock-associated monetary losses in Rio Negro Province. Stakeholders and policymakers can use these data to better allocate public health and agricultural resources for this region.

INTRODUCTION

Cystic echinococcosis (CE), caused by the larval stage of the taeniid tapeworm *Echinococcus granulosus*, represents a public health challenge in many parts of the world. The adult parasite is maintained in the small intestine of the dog definitive host, and *E. granulosus* eggs are shed into the environment in the dog's feces. Livestock and humans become infected through the ingestion of these eggs. Infection leads to the development of cysts in the liver, lungs, or other organs.[1] In humans, CE remains asymptomatic until the cyst either ruptures or becomes large enough to exert pressure on the surrounding tissues. Although the clinical presentation of CE is variable and depends on the size and location of the cyst, symptoms often resemble those of a space-occupying mass.[2,3] Livestock do not typically exhibit overt clinical signs of disease. However, livestock infection can have substantial economic consequences, as a result of condemnation of infected offal and production losses.[4,5]

Echinococcus granulosus is endemic throughout much of South America, with the highest reported prevalences occurring in portions of Argentina, Peru, Uruguay, Chile, and Brazil.[4,6] The Patagonia region of Argentina, which includes Rio Negro Province, is one of the most substantially affected regions in South America.[6,7] Due to the climate and geography of Rio Negro Province, one of the principal economic activities in this area is extensive livestock rearing.[8] Much of the population lives in close association with dogs and sheep or other livestock, which has been shown to increase the risk for human CE infection.[7–10]

In 1980, Rio Negro Province implemented a control program to reduce *E. granulosus* infection rates in the local human and animal populations. Prior to initiating the program, the estimated canine and ovine infection prevalences were 41.5% and 61%, respectively, while the annual incidence of newly identified human cases was estimated to be 73 cases per 100,000 members of the population. In 1997, the estimated prevalences of canine and ovine infection were 2.3% and 18%, respectively, while the annual incidence of newly identified human cases was estimated to be 29 cases per 100,000 members of the population.[8,10] The CE control program, which had an estimated annual operational cost of US$457,000 in 1997, has provided education to the public, tested and dewormed dogs, and screened children for CE using abdominal ultrasound examination and serological testing.[11] Although this program appears to have greatly reduced both human cases and animal infections, CE is still an important agricultural and public health problem in this region of Argentina.[12–15]

In regions of the world where CE is highly endemic, the disease has been shown to be a substantial financial burden for affected individuals, families, and communities. Since CE affects both human and livestock health and productivity, it is important for a comprehensive economic analysis to include both the human-associated and livestock-associated economic losses.[5,16] The human-associated economic losses include both direct and indirect costs. Direct costs include costs associated with diagnostics, treatment, and follow-up care. Indirect costs include costs associated with treatment-related travel expenses, lost wages, and decreased productivity due to CE-related morbidity and mortality. Similarly, livestock-associated economic losses include direct costs, resulting from the condemnation of infected viscera, as well as indirect costs due to production losses.[5,16] The objective of this study was to estimate the economic losses associated with CE in humans and livestock in Rio Negro Province, Argentina in 2010. Although the costs associated with CE have been examined in other regions of the world, this is the first study to estimate the combined economic impact of human and livestock CE in Rio Negro Province, Argentina.[17–23]

* Address correspondence to Glenda M. Bingham, Department of Veterinary Integrative Biosciences, College of Veterinary Medicine and Biomedical Sciences, Texas A&M University, College Station, TX 77843-4458. E-mail: GBingham@tamu.edu

METHODS

Study area. Rio Negro Province is located in the northern Patagonia region of southern Argentina. In 2010, there were 638,645 inhabitants in the province, approximately 15% of whom lived in rural areas.[24] The province has a population density of approximately 3.1 inhabitants per km[2], which is one of the lowest in the country.[24] The economy in this region relies heavily on extensively raised livestock, with sheep being the most economically important species, followed by cattle and goats. Rio Negro Province has a sheep population of over 1.8 million, which represents approximately 12% of the national sheep population.[25]

Human epidemiological data. *Population characteristics.* Population data for Rio Negro Province, including the size and age structure of the population, were obtained from the 2010 Argentina national population census.[24] The reported annual incidence of human CE for the population of Rio Negro Province, as well as the annual mortality attributable to human CE, among cases treated surgically in Rio Negro Province, were obtained from official government sources.[26] These values are presented in Table 1.

Hospital chart reviews. To estimate the medical costs associated with the diagnosis and treatment of CE in Rio Negro Province, hospital chart reviews were conducted in three public hospitals, beginning in June 2010. The hospitals were located in the cities of Bariloche, Viedma, and Ingeniero Jacobacci, with population sizes of 130,000, 47,000, and 8,000, respectively. The hospitals located in Bariloche and Viedma were classified as tertiary care facilities, whereas the hospital located in Ingeniero Jacobacci was classified as a rural hospital.[27] Besides the hospitals included in this study, Rio Negro Province has one additional tertiary care public hospital and nine additional rural public hospitals. However, the hospitals included in this study were selected because they had CE specialists on staff, and represented both local and regional healthcare facilities. The participating hospitals provided access to the medical records of CE patients, whose diagnosis had been confirmed using imaging techniques.

Medical charts were requested for all patients who presented to one of the three participating hospitals between January 1, 2000 and May 31, 2010, for the diagnosis, treatment, or follow-up of CE or CE-associated complications. The costs, which were evaluated, included those associated with diagnostic procedures, surgery, postoperative treatment, hospital stay (cost/day), prescribed medication, and outpatient follow-up care. The procedures performed and medications prescribed for each patient were recorded using a set of standardized forms, which had been developed specifically for this study. To quantify the total number of times that each patient was seen over the course of his or her treatment, separate forms were used for each hospital admission and outpatient visit. The collected information was used to estimate the number of days, annually, that CE patients were unable to work as a result of seeking treatment. In Rio Negro Province, all public hospitals use the same official patient fee schedule. Therefore, since all three of the participating hospitals were public hospitals, all patient fees were based on this document.

Patient interviews. Patient interviews were conducted to collect indirect cost information, which could not be obtained from the hospital chart reviews. During June 2010, study personnel attempted to contact all CE patients who presented to a study hospital for diagnosis, treatment, or follow-up care between June 1, 2009 and May 31, 2010. The patients who could be reached, and agreed to participate, were interviewed at their homes by study personnel. If the patient was a child, a parent was asked to complete the interview, based on the child's illness. The interview questions examined the duration of the convalescent period, as well as the number of days that patients were unable to work or attend to their usual daily activities due to CE-associated illness during the previous year. Patients were also asked about the distance between their home and the hospital, from which they received treatment, and the primary mode of transportation used when traveling to obtain treatment.

Treatment-seeking cases. It was assumed that the patients, whose charts were reviewed, were representative of all treatment-seeking CE patients in Rio Negro Province with respect to age and sex distribution, treatment method (surgical versus nonsurgical), and average duration of treatment. The number of CE cases under care in Rio Negro Province, during 2010, was estimated by multiplying the average duration

TABLE 1
Epidemiological parameters used to estimate the costs associated with human CE in Rio Negro Province, Argentina in 2010

Parameter	Value	Units	Reference
Population of Rio Negro Province, 2010	638,645	Individuals	[24]
Reported annual incidence of CE	6.43	Individuals/10^5	[26]
Annual CE-attributable mortality*	0.5	Individuals/10^5	[26]
Proportion of CE cases treated surgically	46.8	Percent	Patient data
Distribution of CE cases by sex			
Male	48.4	Percent	Patient data
Female	51.6	Percent	Patient data
Distribution of CE cases by age			
0–17	21.3	Percent	Patient data
18–29	14.9	Percent	Patient data
30–39	18.1	Percent	Patient data
40–49	14.4	Percent	Patient data
50–59	15.4	Percent	Patient data
≥ 60	16.0	Percent	Patient data
Location of CE cysts			
Liver	76.6	Percent	Patient data
Lung	9.6	Percent	Patient data
Liver and lung	6.4	Percent	Patient data
Other	7.4	Percent	Patient data

*Among cases treated surgically.

of treatment, for CE cases whose charts were reviewed, by the officially reported 2010 incidence of CE in the province.

Undiagnosed/non-healthcare-seeking cases. There is evidence that individuals with CE begin to experience productivity losses, before the time in which they seek medical care.[28] However, for Rio Negro Province, information regarding the number of CE cases who do not seek care was not readily available. Therefore, in order to estimate the economic losses experienced by undiagnosed or non-healthcare-seeking individuals, the number of undiagnosed individuals in the population first needed to be estimated. Due to the degree of uncertainty in this estimate, a uniform distribution (0.4–2.07%) was used for the prevalence of undiagnosed CE in the population of Rio Negro Province. The minimum value, for the uniform distribution, was selected based on the results of a study that examined schoolchildren, between 6 and 14 years of age, throughout Rio Negro Province over a nine-year period (2000–2008).[29] The study reported that 0.4% of asymptomatic/non-healthcare-seeking children had CE, based on abdominal ultrasound.[29] The maximum value for the uniform distribution was calculated by incorporating data obtained from the study of schoolchildren with data from a community-based CE screening study, conducted in a highly endemic area of Rio Negro Province in 2009.[12,29] In the community-based study, the prevalence of undiagnosed CE among adults (10%) was 6.25 times the prevalence of undiagnosed CE among children (1.6%).[12] A child to adult prevalence ratio of 1:6.25 was applied to the age distribution of the population of Rio Negro Province, using the prevalence data from the region-wide school study.[29] The resulting value was subsequently adjusted to account for the fact that abdominal ultrasound is unable to detect pulmonary cases, which have represented 11–13.5% of all undiagnosed cases in other studies.[30,31] This adjustment resulted in an estimated CE prevalence of 2.07%, the maximum value in the uniform distribution used to estimate the prevalence of undiagnosed CE in Rio Negro Province.

Estimation of costs associated with human CE. *Direct costs.* When determining the economic losses associated with human CE in Rio Negro Province, the costs were separated into direct costs and indirect costs. The direct costs included all of the diagnostic and treatment costs, including fees for diagnostic procedures, surgical treatment, postoperative care, hospital stays, outpatient visits, and prescribed medication. Drug prices, for the country of Argentina, were obtained from an online pharmaceutical database.[32] For all other items, fees were obtained from the official patient fee schedule used by all public hospitals in Rio Negro Province. The costs associated with tests and procedures are presented in Table 2. Laboratory tests were grouped based on fee category. All direct costs were calculated based on individual patient care data. Patients were categorized into treatment groups based on whether they were treated surgically or nonsurgically, with separate cost estimates calculated for each group. Since percutaneous treatment with the puncture, aspiration, injection, re-aspiration (PAIR) technique is not routinely performed in this region of Argentina, treatment costs for nonsurgical patients were calculated based on the cost of chemotherapeutic treatment. The average cost per patient was then applied to the estimated number of patients under care in each treatment group during 2010. Costs were converted from Argentine pesos (ARS) to U.S.

TABLE 2
Procedure costs used to estimate the direct costs associated with human CE in Rio Negro Province, Argentina in 2010

Procedure	Cost/procedure (US$)	Mean frequency/ patient¶
Outpatient consultation	3.85	2.60
Laboratory tests		
Category 1*	0.64	5.04
Category 2†	1.60	0.80
Category 3‡	2.56	0.32
Category 4§	4.81	1.16
Diagnostic imaging		
Thoracic radiography	6.67	0.29
Ultrasonography	8.97	1.47
Computed tomography	22.44	0.22
Magnetic resonance imaging	44.87	0.01
Other		
Electrocardiogram	6.67	0.18
Pulmonary function test	57.69	0.07

CE = cystic echinococcosis; ELISA = enzyme-linked immunosorbent assay; US$ = U.S. dollar.
*Category 1: Complete blood count, blood glucose, blood creatinine, blood urea nitrogen, coagulation time, or urinalysis.
†Category 2: Electrolyte panel or partial thromboplastin time.
‡Category 3: Arterial blood gas analysis, pleural fluid analysis, sputum culture, or ELISA.
§Category 4: Hepatic function panel.
¶The average number of procedures per patient, per year.

dollars (US$) using the official exchange rate for 2010, of 3.91 ARS to US$1.[33]

Indirect costs. For both surgical and nonsurgical patients, CE-associated indirect costs included wages lost during treatment times, lost wages for days that patients were unable to work or attend to their usual daily activities due to CE-associated illness, and costs incurred for travel to obtain treatment. In addition, for surgical patients, CE-associated indirect costs also included wages lost during convalescence, and wage losses resulting from CE-associated mortality. For purposes of calculating lost wages, treatment time was defined as the number of days per year, that the patient was unable to work, attend school, or complete their daily tasks, as a direct result of seeking diagnostic, treatment, or follow-up care for CE. Convalescence was defined as the number of days, during which the patient was unable to work, attend school, or complete their daily tasks after returning home following surgical treatment of CE.

The average monthly wage for citizens of Rio Negro Province, stratified by sex and age, was calculated using data obtained from the Annual Survey of Urban Households for the fourth quarter of 2010.[34] Activity and employment rates, stratified by sex and age, were also obtained from this survey.[34] For adults with full-time employment, a 100% loss of daily wages was assumed during times of treatment and convalescence, as well as for days that patients were unable to work or attend to their usual daily activities due to CE-associated illness. It was assumed that because someone must care for a sick child throughout the child's illness, a parent would incur income losses when the CE patient was a child. Therefore, for patients under 18 years of age, wage losses equivalent to those of a female, between 30 and 39 years of age were assumed during times of treatment and convalescence, as well as for days when the child was unable to attend school or participate in their usual daily activities due to CE-associated illness.

When estimating wage losses resulting from CE-associated mortality, a 100% loss of daily wages was assumed for the portion of the year remaining after death, for all fatal cases.

To account for the fact that death could occur at any point during the year, for each fatal case, a uniform distribution (1–364 days) was used to represent the number of days that were lost due to CE-associated mortality in 2010.

Using methods that are consistent with those used in previous studies, an income loss equal to 30% of the daily wage of employed individuals, of the same age and sex, was assumed for all individuals who were classified as "inactive."[19,20] The inactive sector of the population included primarily individuals who identified themselves as either homemakers or full-time students. Wage losses were not included for members of the population who were classified as "unemployed" because those individuals received government benefits, which were assumed to be unaffected by their illness. The employment and wage data used to estimate the indirect costs associated with human CE are presented in Table 3. Based on the estimates used in other studies, all undiagnosed cases of CE were assumed to experience a 0–5% reduction in annual productivity.[17,22,35]

Patient travel costs were estimated based on the mode of transportation that each patient reported using for the majority of their treatment-related travel, the distance between the patient's home and the hospital from which they received treatment, and the number of annual treatment visits. Costs were estimated for three modes of transportation (public transportation, private car, and ambulance), based on the cost per kilometer for each type of transportation. For patients who reported using public transportation as their primary mode of transportation for treatment-related travel, bus fares were used to estimate travel costs.[36] Fuel costs were used to estimate travel costs for patients who traveled primarily by private car to obtain treatment.[37] For patients who reported being transported to the hospital by ambulance, the hospital fee schedule was used to estimate travel costs. When estimating the travel costs for these patients, it was assumed that they traveled by ambulance to the hospital and used public transportation to return home.

TABLE 3

Employment and wage parameters used to estimate the indirect costs associated with human CE in Rio Negro Province, Argentina in 2010

Parameter	Value	Units	Reference
Employment status of the adult male population			
Employed	72.3	Percent	34
Unemployed	5.1	Percent	34
Inactive	22.6	Percent	34
Employment status of the adult female population			
Employed	44.9	Percent	34
Unemployed	6.0	Percent	34
Inactive	49.1	Percent	34
Mean monthly wage for employed males, by age (years)			
18–29	416	US$/month	34
30–39	658	US$/month	34
40–49	674	US$/month	34
50–59	568	US$/month	34
≥ 60	570	US$/month	34
Mean monthly wage for employed females, by age (years)			
18–29	358	US$/month	34
30–39	534	US$/month	34
40–49	575	US$/month	34
50–59	599	US$/month	34
≥ 60	371	US$/month	34

CE = cystic echinococcosis; US$ = U.S. dollar.

Livestock epidemiological data. In Rio Negro Province, sheep, cattle, and goats are the most economically important livestock species. Therefore, this analysis focused on losses incurred due to CE in these three species. For each livestock species, data related to the size and age distribution of the population and the numbers of animals slaughtered each year were obtained from official government reports.[25] The prevalence of CE, at slaughter, was also obtained from officially reported values.[38] Although prevalence values were available for sheep and cattle, values were not reported for goats. Therefore, the reported prevalence of CE for sheep was also used for goats. The CE prevalence values provided in the government reports did not differentiate between young animals and older animals. Therefore, literature-based values were used, when available, to account for the fact that the prevalence of CE is often higher in older animals. To estimate the total number of infected animals, the CE prevalence value was extrapolated to the total population of each livestock species in Rio Negro Province. Meat, milk, and fiber production values were obtained from government reports. The epidemiological parameters used to estimate the costs associated with CE in livestock are presented in Tables 4–6.

Estimation of costs associated with livestock CE. Both direct and indirect costs associated with CE in livestock species were evaluated. The direct costs included those losses, which resulted from the condemnation of infected offal at slaughter. In Argentina, if any portion of an organ is infected, the entire organ must be condemned. Based on the results of an abattoir study, conducted in Rio Negro Province, it was assumed that the liver, lungs, and both the liver and lungs would be condemned for 50%, 20.6%, and 29.4% of infected livestock, respectively.[39] The indirect costs associated with CE-infected livestock included the production losses that have been reported in a number of other studies, with uniform distributions used to represent the uncertainty in the estimates.[17,22,35,40] These losses included decreased carcass weights at the time of slaughter (2.5–10%) and decreased fecundity (0–10%) for sheep, cattle, and goats. Losses associated with a decrease in milk production (0–10% per year) were included for cattle, and losses associated with decreased fiber value (10–20% per year) were included for sheep and goats. Monetary values for all livestock products were estimated based on local market values or extrapolated from other studies. These values are presented in Table 7.

Due to the low numbers of sheep and goats, which were officially reported to have been slaughtered during 2010, annual monetary losses associated with livestock CE were calculated using two different scenarios. In scenario 1, annual livestock losses were calculated using government-reported slaughter statistics. In scenario 2, annual livestock losses were calculated using values, which had been adjusted to account for underreporting of the numbers of sheep and goats slaughtered during 2010. For each livestock species, the adjusted slaughter value was estimated using the following equation:

$$\text{Adjusted slaughter value} = P_2 - (P_1 + [F \times R])$$

In this equation, P_2 is the number of animals in the population in 2011, P_1 is the number of animals in the population

TABLE 4
Epidemiological parameters used to estimate the costs associated with sheep CE in Rio Negro Province, Argentina in 2010

Parameter	Distribution	Value	Units	Reference
Total population	Fixed	1,861,270	Animals	[25]
Adults	Fixed	1,567,189	Animals	[25]
Lambs	Fixed	294,081	Animals	[25]
Number slaughtered*	Fixed	79,242	Animals	[25]
Adults	Fixed	22,644	Animals	[25]
Lambs	Fixed	56,598	Animals	[25]
Number slaughtered†	Fixed	723,295	Animals	Estimated
Adults	Fixed	206,687	Animals	Estimated
Lambs	Fixed	516,608	Animals	Estimated
Prevalence of CE at inspection				
Adults	Uniform	21.9–33.6	Percent infected	[38,42]
Lambs	Uniform	5.3–21.9	Percent infected	[38,39]
Carcass weight				
Adults	Fixed	20.3	kg	[25]
Lambs	Fixed	11.9	kg	[25]
Liver weight				
Adults	Uniform	0.82–0.85	kg	Estimated from[43,44]
Lambs	Uniform	0.48–0.5	kg	Estimated from[43,44]
Lung weight				
Adults	Uniform	0.66–0.7	kg	Estimated from[43,44]
Lambs	Uniform	0.39–0.41	kg	Estimated from[43,44]
Number of lambs, per year	Uniform	0.6–0.8	Lambs per ewe	[45]
Annual wool production, per sheep	Fixed	4.225	kg	[45]

CE = cystic echinococcosis; kg = kilogram.
*Officially reported values.
†Values adjusted to account for underreporting.

in 2010, F is the number of adult females in the population in 2010, and R is the rate of reproduction for the species. This adjustment greatly increased the numbers of sheep and goats slaughtered during 2010. However, for cattle, the adjustment yielded a value that was lower than the officially reported value. Therefore, the adjusted values were used for sheep and goats in scenario 2, while the officially reported cattle slaughter numbers were used in both scenarios.

Data analysis. Separate spreadsheet models were developed to estimate the costs associated with CE, in the human and livestock populations, in Rio Negro Province. All data were entered into Excel (Microsoft Corp., Redmond, WA) spreadsheets. The monetary losses were estimated using @Risk Version 6 software (Palisades Corp., Ithaca, NY), as an add-in to Excel. To account for the uncertainty in some of the parameter estimates, a distribution was assigned to each

TABLE 5
Epidemiological parameters used to estimate the costs associated with goat CE in Rio Negro Province, Argentina in 2010

Parameter	Distribution	Value	Units	Reference
Total population	Fixed	217,012	Animals	[25]
Adults	Fixed	193,877	Animals	[25]
Kids	Fixed	23,135	Animals	[25]
Number slaughtered*	Fixed	810	Animals	[25]
Adults	Fixed	690	Animals	[25]
Kids	Fixed	120	Animals	[25]
Number slaughtered†	Fixed	113,558	Animals	Estimated
Adults	Fixed	96,740	Animals	Estimated
Kids	Fixed	16,818	Animals	Estimated
Prevalence of CE at inspection				
Adults	Uniform	21.9–33.6	Percent infected	[38,42]
Kids	Uniform	5.3–21.9	Percent infected	[38,39]
Carcass weight				
Adults	Fixed	13.2	kg	[25]
Kids	Fixed	7.45	kg	[25]
Liver weight				
Adults	Fixed	0.66	kg	[46]
Kids	Fixed	0.65	kg	[46]
Lung weight				
Adults	Fixed	0.462	kg	[46]
Kids	Fixed	0.46	kg	[46]
Number of kids, per year	Uniform	1–1.4	Kids per nanny	[47]
Annual mohair production, per goat	Fixed	3	kg	[48]

CE = cystic echinococcosis; kg = kilogram.
*Officially reported values.
†Values adjusted to account for underreporting.

TABLE 6
Epidemiological parameters used to estimate the costs associated with cattle CE in Rio Negro Province, Argentina in 2010

Parameter	Distribution	Value	Units	Reference
Total population	Fixed	431,855	Animals	25
Adults	Fixed	335,512	Animals	25
Calves	Fixed	96,343	Animals	25
Number slaughtered*	Fixed	93,352	Animals	25
Adults	Fixed	70,929	Animals	25
Calves	Fixed	22,423	Animals	25
Prevalence of CE at inspection	Fixed	19.1	Percent infected	38
Carcass weight				
Adults	Fixed	238.55	kg	25
Calves	Fixed	170.96	kg	25
Liver weight				
Adults	Uniform	4.5–6	kg	49
Calves	Uniform	3–4.5	kg	49
Lung weight				
Adults	Uniform	5.5–7	kg	49
Calves	Uniform	4–5.5	kg	49
Number of calves, per year	Uniform	0.4–0.6	Calves per cow	50
Number of dairy cattle	Fixed	2,066	Animals	25
Annual milk yield, per cow	Fixed	4,346	Liters	25

CE = cystic echinococcosis; kg = kilogram.
* Officially reported values.

of the parameters based on a likely range of values for the parameter. Uniform distributions were used for all uncertain variables, unless otherwise noted. The mean and 95% credible intervals (CIs) were calculated for each output variable. Values for each cost category were summed to calculate the total costs associated with CE in Rio Negro Province, Argentina. For each model, 20,000 iterations were generated using Latin Hypercube sampling to account for uncertainty in the input parameter estimates. Stepwise linear regression sensitivity analyses were conducted to examine the impact of each input parameter on the overall cost estimate.

Ethical considerations. To maintain patient confidentiality, a unique identification number was assigned to each patient who was either interviewed or whose records were examined for this study. This number was subsequently used on all data collection forms associated with the patient. This study

TABLE 7
Economic parameters used to estimate the costs associated with livestock CE in Rio Negro Province, Argentina in 2010

Parameter	Value/kg	Units	Reference
Sheep			
Liver	1.64	US$	25
Lung	0.87	US$	25
Sheep carcass	3.34	US$	25
Lamb carcass	6.22	US$	25
Wool	5.02	US$	48
Goats			
Liver	1.64	US$	25
Lung	0.87	US$	25
Goat carcass	3.34	US$	25
Kid carcass	6.22	US$	25
Mohair	4.33	US$	48
Cattle			
Liver	1.32	US$	25
Lung	0.70	US$	25
Adult carcass	2.86	US$	25
Calf carcass	3.35	US$	25
Milk*	0.35	US$	25

CE = cystic echinococcosis; US$ = U.S. dollar; kg = kilogram.
* Milk prices in US$/liter.

was reviewed and approved by the Medical Committee of the Hydatidosis Control Program in Rio Negro Province, Argentina, as well as the Institutional Review Board at Texas A&M University.

RESULTS

The three participating hospitals provided access to medical records for a combined total of 188 CE patients. Overall, 51.6% (97) of the patients were female and 21.3% (40) of the patients were children less than 18 years of age. Most of the CE patients (144; 76.6%), who were treated at the participating hospitals, had only hepatic lesions. Additional information regarding the patients' ages, as well as cyst locations, is presented in Table 1. Of the 188 patients, whose records were reviewed, 79 (42%) were treated at the hospital in Viedma, 55 (29.3%) received treatment from the hospital in Ingeniero Jacobacci, and the remaining 54 (28.7%) were treated at the Bariloche hospital. Surgical patients accounted for 46.8% (88) of the patients. While 83.3% of the patients who were treated in Bariloche, and 50.6% of the Viedma patients received surgical treatment, only 5.5% of the Ingeniero Jacobacci patients were treated surgically.

A total of 72 CE patients were eligible to participate in the interview portion of this study. Study personnel were able to contact 34 patients, all of whom agreed to be interviewed. Of the 34 CE patients who were interviewed, 21 (61.8%) received treatment at the Bariloche hospital, 7 (20.6%) were treated in Viedma, and the remaining 6 (17.6%) were treated in Ingeniero Jacobacci. Sixteen (47.1%) of those who were interviewed were female. The interviewed patients ranged in age from 4 to 92 years, with an average age of 38 years. Although most of the patients were adults (25; 73.5%), a parent completed the interview for the nine (26.5%) patients who were children. Surgical patients accounted for 64.7% (22) of the patients who completed the interview.

Individual patient costs. The average total annual cost per patient was US$4,605, for surgical patients, and US$251, for nonsurgical patients. Direct costs accounted for 19% of the

total annual costs, for surgical patients, and 29% of the total annual costs, for nonsurgical patients. For surgical patients, the annual direct cost per patient was US$952 in Bariloche, US$838 in Viedma, and US$592 in Ingeniero Jacobacci. The annual direct cost per patient, for nonsurgical patients, was US$126 for patients treated in Bariloche, US$82 for Ingeniero Jacobacci patients, and US$48 for individuals treated in Viedma.

The median duration of time under care, for all surgical patients, was 1.21 years (range: 0.025–10.42 years). Surgical patients were under a physician's care for a median of 2.56 years (range: 1.77–3.05 years) in Ingeniero Jacobacci, 1.24 years (range: 0.025–7.22 years) in Bariloche, and 0.88 years (range: 0.027–10.42 years) in Viedma. Overall, nonsurgical patients were under a physician's care for a median of 1.21 years (range: 0.003–11.22 years). In Bariloche, nonsurgical patients were under a physician's care for a median of 1.69 years (range: 0.047–7.56 years), while physicians monitored non-surgical patients in Viedma and Ingeniero Jacobacci for 1.61 years (range: 0.003–11.22 years) and 0.91 years (range: 0.003–9.14 years), respectively.

Surgical patients were unable to work or attend to their usual daily activities for an average of 39.5 days, per year. Of those days, 14.8 were directly associated with treatment, while 24.7 days were missed as result of CE-associated illness. Nonsurgical patients were unable to work or attend to their usual daily activities for an average of 10.25 days per year. Approximately half of those days (4.8 days) were missed as result of treatment, while the remaining 5.45 days were missed due to CE-associated illness.

Total human costs. The estimated total annual direct and indirect costs associated with human CE, among surgical, nonsurgical, and non-healthcare-seeking cases are presented in Table 8. When productivity losses attributed to non-healthcare-seeking cases were included, the total cost of human CE, in Rio Negro Province, for 2010 was estimated to be US$1,194,000 (95% CI: US$218,000–US$2,813,000). The total costs associated with human CE were estimated to be US$272,000 (95% CI: US$91,000–US$814,000), when losses associated with non-healthcare-seeking individuals were excluded from the analysis. Indirect costs accounted for approximately 95.5% of the estimated total annual economic losses attributable to human CE, when productivity losses

TABLE 8
Annual costs associated with human CE in Rio Negro Province, Argentina in 2010

Category	Mean cost (US$)	95% CI (US$)
Surgical cases		
Direct costs	49,000	18,000–146,000
Indirect costs*	207,000	64,000–621,000
Total costs	256,000	84,000–764,000
Nonsurgical cases		
Direct costs	4,600	1,700–13,600
Indirect costs	11,300	4,100–33,400
Total costs	15,900	5,800–46,900
Non-healthcare-seeking cases		
Indirect costs	922,000	37,000–2,491,000
Total direct costs of human CE	54,000	20,000–160,000
Total indirect costs of human CE	1,140,000	187,000–2,747,000
Total costs of human CE	1,194,000	218,000–2,813,000
Total costs of human CE†	272,000	91,000–814,000

CE = cystic echinococcosis; CI = credible interval; US$ = U.S. dollar.
* Includes the costs attributable to CE-associated mortality (US$7,300).
† Excluding productivity losses associated with non-healthcare-seeking cases.

associated with non-healthcare-seeking cases were included. When losses associated with non-healthcare-seeking cases were excluded, indirect costs represented 80.2% of the total cost of human CE, for 2010.

The sensitivity analysis indicated that the uncertain parameter with the greatest impact on the total estimated losses associated with human CE, was the percentage decrease in productivity for non-healthcare-seeking cases (standardized regression coefficient = 0.75). Other parameters, which were shown to influence the total estimated costs associated with human CE, included the number of non-healthcare-seeking cases and the duration of time in treatment, with standardized regression coefficients of 0.51 and 0.28, respectively. The standardized regression coefficients for all other parameters were between 0 and 0.1.

When non-healthcare-seeking cases were excluded, the parameters with the greatest influence on the total estimated losses for human CE were the duration of time in treatment (standardized regression coefficient = 0.95) and the duration of the convalescent period (standardized regression coefficient = 0.25). For all other parameters, the standardized regression coefficients were between 0 and 0.1.

Livestock costs. When annual livestock losses were calculated using government-reported slaughter statistics (scenario 1), the total cost of livestock CE, in Rio Negro Province, for 2010 was estimated to be US$3,962,000 (95% CI: US$2,619,000–US$5,412,000). However, the estimated total annual cost of livestock CE was US$4,703,000 (95% CI: US$3,234,000–US$6,293,000), when livestock losses were calculated using values, which had been adjusted to account for underreporting (scenario 2). Indirect costs represented 96.4% of the total annual livestock-associated losses, when government-reported slaughter statistics were used, and 93.7% of the total annual livestock-associated losses, when values were adjusted for underreporting. In both scenarios, the majority of the livestock-associated losses were attributable to sheep, with sheep contributing 57.4% and 61.7% of the total livestock-associated losses in scenarios 1 and 2, respectively. The total annual direct and indirect costs associated with livestock CE, in Rio Negro Province, for the year 2010, are presented in Table 9.

Using scenario 1, the uncertain parameters, which had the greatest impact on the total estimated losses associated with livestock CE, included decreases in sheep fecundity and cattle fecundity with standardized regression coefficients of 0.55 and 0.50, respectively, and decrease in wool value (standardized regression coefficient = 0.40). Other parameters, which were shown to influence the total estimated costs associated with livestock CE, included the CE prevalence for adult sheep and decrease in cattle carcass weight, with standardized regression coefficients of 0.36 and 0.35, respectively. When livestock production losses were excluded, the most influential parameter was the liver weight for adult cattle (standardized regression coefficient = 0.85).

When scenario 2 was used, the uncertain parameters with the greatest influence on the total annual livestock-associated losses included decreases in fecundity for sheep and cattle, with standardized regression coefficients of 0.55 and 0.46, respectively, followed by the CE prevalence for adult sheep and decrease in wool value, both with standardized regression coefficients of 0.37. Other parameters, which impacted the estimated livestock-associated costs, included

Category	Scenario 1*		Scenario 2†	
	Mean (US$)	95% CI (US$)	Mean (US$)	95% CI (US$)
Sheep				
Direct costs	15,000	11,000–19,000	136,000	96,000–177,000
Indirect costs	2,259,000	1,267,000–3,433,000	2,765,000	1,647,000–4,067,000
Total costs	2,274,000	1,281,000–3,451,000	2,901,000	1,763,000–4,224,000
Goats				
Direct costs	240	190–290	33,000	27,000–40,000
Indirect costs	178,000	91,000–281,000	258,000	150,000–384,000
Total costs	179,000	92,000–282,000	291,000	180,000–422,000
Cattle				
Direct costs	128,000	116,000–140,000	128,000	116,000–140,000
Indirect costs	1,381,000	550,000–2,245,000	1,382,000	549,000–2,243,000
Total costs	1,509,000	680,000–2,373,000	1,510,000	679,000–2,372,000
Total direct costs of livestock CE	143,000	130,000–157,000	298,000	254,000–342,000
Total indirect costs of livestock CE	3,819,000	2,476,000–5,266,000	4,405,000	2,951,000–5,973,000
Total costs of livestock CE	3,962,000	2,619,000–5,412,000	4,703,000	3,234,000–6,293,000

CE = cystic echinococcosis; CI = credible interval; US$ = U.S. dollar.
*Costs calculated using officially reported slaughter values
†Costs calculated using slaughter values, which had been adjusted to account for underreporting for sheep and goats, and officially reported slaughter values for cattle

decreases in cattle and sheep carcass weight, with standardized regression coefficients of 0.32 and 0.25, respectively, and the CE prevalence for lambs (standardized regression coefficient = 0.23). When livestock production losses were excluded, the most influential parameters included the CE prevalence for lambs and adult sheep, with standardized regression coefficients of 0.85 and 0.41, respectively. Other influential parameters included the liver weight for adult cattle and the CE prevalence for adult goats, with standardized regression coefficients of 0.26 and 0.16, respectively.

Total costs. When the human and livestock losses were combined, the estimated total annual cost of CE, in Rio Negro Province in 2010, ranged from US$4,234,000 (95% CI: US$2,709,000–US$6,226,000), when non-healthcare-seeking human cases were excluded and government-reported livestock slaughter statistics were used, to US$5,897,000 (95% CI: US$3,452,000–US$9,105,000), when non-healthcare-seeking human cases were included and livestock slaughter values were adjusted to account for underreporting. When non-healthcare-seeking human cases were excluded and government-reported livestock slaughter statistics were used, livestock-associated losses represented 94% of the estimated total annual economic losses attributable to CE. However, when non-healthcare-seeking human cases were included and livestock slaughter values were adjusted to account for underreporting, livestock losses accounted for 80% of the total estimated annual cost of CE.

DISCUSSION

As a zoonotic disease, which affects both humans and livestock, CE is responsible for monetary losses to both the public health and agricultural sectors of the economy. This is the first study to estimate the annual economic impact of CE in humans and livestock in Rio Negro Province, Argentina. By estimating the costs associated with both human and livestock disease in this study, we were able to obtain a more complete estimate of the overall economic impact of CE in this region of Argentina. Our findings indicated that CE is responsible for substantial economic losses in Rio Negro Province.

The total estimated annual cost associated with CE in Rio Negro Province was US$5.9 million, which equates to a loss of approximately 0.08% of the annual per capita gross domestic product (GDP), based on Argentina's per capita GDP for the year 2010. A 0.08% loss of annual per capita GDP is greater than the annual GDP losses of 0.03%, 0.058%, and 0.074% reported in studies, which estimated the costs associated with CE in Iran, Uruguay, and Jordan, respectively.[19,22,35] However, the monetary losses attributable to CE in an endemic region of western China were estimated to be 1.4% of the annual per capita GDP for that region, a value which is substantially greater than the GDP losses seen in this study.[18] With the exception of the study that took place in China, the previously mentioned studies were country-level economic analyses, which included both urban and rural areas in their estimates. While Rio Negro Province includes a few urban areas, the population density of Rio Negro Province is much lower than that of Argentina, as a whole, with many people working in rural agricultural jobs. As a result, the per capita GDP in Rio Negro Province is likely to be less than that of Argentina. Therefore, the losses incurred are likely to represent a greater proportion of GDP, in this region, than they would for the country as a whole.

Although presenting the costs associated with CE, as a proportion of per capita GDP, can be useful when evaluating the economic impact of the disease in a particular region, it provides minimal insight into the monetary burden of CE on those who are infected. The total annual CE-related costs, for nonsurgical cases, represented 4.6% of Argentina's annual minimum wage salary, for the year 2010, of US$5,484.[41] However, for surgical patients, the annual costs associated with CE were considerably greater, representing 84% of an annual minimum wage salary. Although indirect costs represented the majority of the total annual costs for both surgical and nonsurgical patients, these costs represented a larger proportion of the total annual costs for surgical patients than for nonsurgical patients. The primary reason for this difference is that the number of days that surgical patients were unable to work due to CE was much greater than the number of days, per year, that nonsurgical patients were unable to work because of CE. As a result, the CE-associated wage losses

for surgical patients were substantially greater than the CE-associated wage losses for nonsurgical patients.

Although the duration of time under care ranged from 0.025 to 10.42 years for surgical patients and 0.003 to 11.22 years for nonsurgical patients, the median duration of time under care for both surgical and nonsurgical patients was 1.21 years. Given that CE is a chronic disease, which should ideally be followed by a physician for an extended period of time, the duration of time under care for some patients was very short. It is possible that some of these patients received long-term follow-up care from other healthcare facilities due to the distance between their homes and the treatment hospitals. Other patients could have discontinued follow-up care prematurely due to being unable to miss work, difficulty obtaining transportation, or a lack of available childcare.

Since two of three study hospitals were tertiary care facilities, approximately 70% of the 188 patients, whose records were reviewed for this study, were treated at tertiary care hospitals. In Rio Negro Province, CE patients are frequently referred to hospitals with CE specialists, for diagnostic confirmation and treatment. In addition, the hospitals whose patient records were included in this study were the principal CE treatment hospitals, in each location. However, if the actual proportion of treatment-seeking CE patients who were treated at tertiary care hospitals, in Rio Negro Province, was substantially less than the 70% assumed in the present study, this could result in an overestimation of costs.

The estimated annual direct costs for nonsurgical patients treated in the rural hospital, in Ingeniero Jacobacci, were similar to the direct costs for nonsurgical patients treated in the tertiary care hospitals, in Viedma and Bariloche. However, the estimated annual direct costs for the surgical patients, who were treated in Ingeniero Jacobacci, were much lower than the direct costs for surgical patients treated at the other hospitals. Although a number of factors could have contributed to the cost difference for surgical patients, the primary reason for the difference is likely to be that complicated cases from rural hospitals, such as the hospital in Ingeniero Jacobacci, are often referred to larger hospitals for treatment. As a result, none of the surgical patients, from the Ingeniero Jacobacci hospital, were treated surgically for pulmonary CE, which tends to be more complicated and consequently, more expensive to treat than hepatic CE.

The costs associated with human CE represented approximately 20% of the total economic losses attributable to CE in Rio Negro Province, in 2010. Approximately 77% of the estimated US$1.2 million in human-associated costs were attributed to productivity losses for undiagnosed/non-healthcare-seeking CE cases. Therefore, the parameters that were shown to have the greatest influence on human CE costs were the reduction in productivity for undiagnosed/non-healthcare-seeking cases, and the prevalence of these cases in the Rio Negro Province population. Although other studies have indicated that CE can affect an individual's ability to work, prior to the time in which they seek diagnosis or treatment, the actual percentage that productivity is decreased is unknown. However, this value is likely to vary greatly between individuals and depend on factors such as disease progression and occupation, with individuals with advanced disease and those with physically demanding occupations expected to experience the greatest productivity losses.

Although the prevalence of undiagnosed CE was estimated using the best available data, including two recent studies from Rio Negro Province, the true number of undiagnosed or non-healthcare-seeking cases is not known. In Rio Negro Province, schoolchildren between 6 and 14 years of age are screened for CE. However, adults are not routinely screened for the disease, and the only recently published community-based CE screening study was conducted in a highly endemic region of the province.[12] Therefore, more studies are needed to evaluate the prevalence of undiagnosed CE and its effect on productivity, in Rio Negro Province. It would be particularly helpful to conduct additional population-based abdominal ultrasound screening studies, which examine both adults and children living in the same communities. Although this type of study can be costly and labor intensive, such studies provide a much better estimate of the prevalence of CE, in a particular community, than studies that examine only children.

With estimated losses of approximately US$4.7 million, in 2010, livestock-associated losses represented 80% of the total monetary burden of CE in Rio Negro Province. Livestock production losses were responsible for approximately 94% of the annual costs associated with livestock CE, and 75% of the total economic losses attributable to CE in Rio Negro Province. Although a number of studies have suggested that CE is responsible for livestock production losses, these losses are difficult to accurately estimate due to the lack of available experimental data. The controlled studies, which would be required to obtain the data needed to improve the accuracy of these estimates, require a substantial amount of time to complete and can be cost-prohibitive. However, data obtained from controlled studies would greatly improve monetary burden estimates for livestock-associated CE.

The results of this study demonstrate that CE is an important economic problem in Rio Negro Province, Argentina. In addition, because this is the first study to examine the monetary burden of CE, in Rio Negro Province, it adds valuable information to the existing body of knowledge about CE in this region. CE is responsible for considerable monetary losses to both the human health and livestock sectors in Rio Negro Province. Therefore, it is important to continue efforts to combat CE in this region of Argentina. These findings can be used to inform cost-benefit analyses of different regional CE control program options, as well as to potentially encourage cost sharing between the public health and livestock sectors.

Authors' addresses: Glenda M. Bingham and Christine M. Budke, Department of Veterinary Integrative Biosciences, College of Veterinary Medicine and Biomedical Sciences, Texas A&M University, College Station, TX, E-mails: gbingham@tamu.edu and cbudke@cvm.tamu.edu. Edmundo Larrieu and Eduardo Hererro, Ministry of Health, Rio Negro Province Government, Viedma, Rio Negro Province, Argentina, E-mails: elarrieu@salud.rionegro.gov.ar and ehererro@salud.rionegro.gov.ar. Leonardo Uchiumi and Carlos Mercapide, Artemides Zatti Hospital, Viedma, Rio Negro Province, Argentina, E-mails: luchiumi@gmail.com and chmercapide@salud.rionegro.gov.ar. Guillermo Mujica and Mario Del Carpio, Rogelio Cortizo Hospital, Ingeniero Jacobacci, Rio Negro Province, Argentina, E-mails: mdelcarpio@yahoo.com.ar and jcsalvitti@yahoo.com.ar. Juan Carlos Salvitti, Ramon Carrillo Hospital, Bariloche, Rio Negro Province, Argentina, E-mail: jcsalvitti@

yahoo.com.ar. Bo Norby, College of Veterinary Medicine, Michigan State University, East Lansing, MI, E-mail: bnorby@cvm.msu.edu.

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