THE EPIDEMIOLOGY AND IMPACT OF DOG-ASSOCIATED ZOONOSES IN DEVELOPED AND DEVELOPING COUNTRIES

A Dissertation

by

GLENDA MARIE BINGHAM

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Chair of Committee,	Christine M. Budke
Committee Members,	Thomas M. Craig
	Bo Norby
	Margaret R. Slater
Head of Department,	Evelyn Tiffany-Castiglioni

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ABSTRACT

Dogs are an important part of human societies throughout the world. Although people derive many economic and health benefits from their relationships with dogs, these relationships are not without risk. Interaction with dogs can lead to an increased risk for zoonotic diseases, if the appropriate precautions are not taken. While dogs contribute to the transmission of a variety of zoonoses, only a few of these diseases, such as rabies and cystic echinococcosis, are recognized as having widespread economic and public health implications.

In order to assess the knowledge and perceptions of dog-associated zoonoses in Brazos County, Texas, random digit dialing was used to select households for participation in a cross-sectional telephone survey. Of the 1691 households, which were contacted, 922 (55%) completed the interview. Dog owners accounted for 56% of the study participants. Eighty-six percent of the respondents indicated they would report being bitten by a dog that they did not own. Factors that were shown to be significantly associated with bite reporting included, age, sex, urbanicity, and rabies knowledge. Many of the respondents lacked knowledge about dog-associated zoonoses, which could seriously affect their health.

Cystic echinococcosis (CE) is known to be endemic in Rio Negro Province, Argentina. However, current epidemiological data were not available for this region. A community-based CE screening study, which incorporated diagnostic imaging and a questionnaire, was conducted to evaluate the prevalence of human CE and identify locally relevant risk factors in the study population. The overall CE prevalence among the community volunteers was 7.1%, with 1.6% of children, and 10% of adults diagnosed as CE-positive. Age, level of education, dog ownership, and contact with sheep were found to be significantly associated with CE status.

In regions of the world where CE is highly endemic, it has been shown to be a substantial financial burden for those who are affected. When the costs associated with human CE, obtained from hospital chart reviews and patient interviews, were combined with livestock-associated costs obtained from government reports and scientific publications, the estimated total annual cost of CE in Rio Negro Province was $5,100,373 (95% CI: $2,852,345–$8,004,122).

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CHAPTER I

INTRODUCTION AND LITERATURE REVIEW

1.1. THE ROLES OF DOGS IN SOCIETY

Since being domesticated by humans, approximately 13,000–15,000 years ago, dogs have been an important part of human societies throughout the world (Driscoll et al., 2009). They are present on every continent and most islands that are settled by people, with the total worldwide dog population estimated to be in excess of 700 million (Hughes and Macdonald, 2013). Domestic dogs have been trained to perform a variety of tasks in human societies, including hunting, livestock herding, guarding people, livestock and property, and assisting police and military personnel with their duties. Working dogs can provide sizeable economic benefits to their owners, particularly those residing in rural regions of the developing world, whose livelihoods depend heavily on animal agriculture (Marker et al., 2005). In addition, dogs frequently assist individuals with physical and mental disabilities, and are kept as pets throughout much of the world (Fine, 2010). The companionship of a dog has been shown to improve human physical health and psychological wellbeing, leading to an enhanced quality of life, particularly for children, the elderly, and members of the population who are socially isolated due a serious illness or disability (Dvorak et al., 2008; Mani and Maguire, 2009; Wisdom et al., 2009).

Although people derive many economic and health benefits from their relationships with dogs, these relationships are not without risk. Interaction with dogs can lead to an increased risk for zoonotic diseases if the appropriate precautions are not taken. Zoonotic diseases, or zoonoses, are diseases that are transmissible under natural conditions between animals and humans. While zoonoses are known to occur throughout the world in association with many animal species, domestic dogs pose additional risks because of their close physical contact with the human population (Macpherson, 2005; Dvorak et al., 2008). The specific disease agents, frequency of transmission, and resulting public health and economic impacts of dog-associated zoonoses vary by region. They are influenced by a variety of factors, including climate, socioeconomic conditions, and level of interaction between people and dogs (Stehr-Green and Schantz, 1987; Beck, 2013).

The roles of dogs, in a particular community, are heavily dependent upon the local residents' economic activities as well as their attitudes toward dogs. These attitudes are often based on the religious, cultural, and socioeconomic backgrounds of the population. While some groups do not keep dogs as pets because they consider dogs to be "unclean" or "impure", these same groups may still use dogs for protection, herding, or hunting (Dowling et al., 2000; Macpherson and Torgerson, 2013). Many people consider their dogs to be important members of the family, allowing them to live inside of their homes and sleep in their beds (McNicholas et al., 2005; Chomel and Sun, 2011). Local attitudes and cultural values regarding dogs directly influence whether owned dogs are confined or allowed to roam freely, and whether ownerless dogs are tolerated by the community (OIE, 2013). Cultural norms may also influence vaccination coverage in the local dog population as well as the level of physical contact between the human and dog populations (Macpherson, 2005; OIE, 2013). Management practices, such as these, can have important implications for zoonotic disease transmission, control, and prevention.

Dog management practices may also be affected by laws or ordinances imposed by state and local governments. In most developed countries, people are obligated to properly care for their dogs by providing them with food, water, shelter, and specific vaccinations. Dog owners are also expected to take precautions to ensure that their dogs do not bite people or other domestic animals, or defecate on public property. In these countries, dog owners can be held legally liable for injuries or property damage caused by their dogs. However, in many developing countries, dog owners may have very little, if any, government-mandated responsibility for the care and actions of their dogs. In addition, while most developed countries have strategies for controlling the free-roaming dog population, these programs often do not exist in the developing world and their implementation is frequently met with resistance from the local population (Wandeler et al., 1993; OIE, 2013). Differences in dog management policies could help to explain why dog-associated zoonoses differ dramatically, in both number and magnitude, between the developed and developing world.

1.2. KNOWLEDGE OF DOG-ASSOCIATED ZOONOSES

In order to prevent or reduce the transmission of zoonotic diseases from dogs to humans, it is essential for people to be aware of the existence of these diseases. In addition, it is important for people to understand how such diseases are transmitted, in order to reduce their risk of infection. Dog owners as well as individuals who do not own dogs need to understand the importance of these diseases because both groups have the potential to be infected, if proper precautions are not taken. However, very few published studies have evaluated local knowledge of dog-associated zoonoses. Fontaine and Schantz (1989) reported that individuals from De Kalb County, Georgia lacked information about the zoonotic disease risks associated with pets. They found that only 63% of their study participants were aware that diseases could be transmitted from pets to humans. A Canadian study, conducted in 2010, concluded that pet owners were more knowledgeable than individuals who did not own pets about zoonotic diseases, which could be transmitted by pets (Stull et al., 2012). Their results were based on a “knowledge score” which was determined using participants’ responses to a question regarding whether a variety of diseases could be transmitted from pets to people. However, of the 11 diseases or pathogens included in the questionnaire, the only ones that pet owners were found to be significantly more knowledgeable about were *Giardia* and *Salmonella*. In addition, the descriptions of some of the diseases that were classified as “transmitted by pets” were somewhat vague, which could have biased their results. For example, one of the questions asked if “infectious diarrhea” could be transmitted from pets to people. Both of the previously mentioned studies focused on zoonotic diseases associated with pets, and not specifically those associated with dogs or dog ownership (Fontaine and Schantz, 1989; Stull et al., 2012).

1.3. DOG-ASSOCIATED ZOONOSES OF GLOBAL SIGNIFICANCE

Of the 1407 species of recognized human pathogens, almost 60% are known to be zoonotic (Woolhouse and Gowtage-Sequeria, 2005). Domestic dogs have been shown to play an important role in the transmission of approximately 60 zoonoses, including a variety of parasitic, viral, and bacterial diseases (Matter and Daniels, 2000; Dvorak et al., 2008). Although a number of these diseases may affect human health in specific regions of the world, only a few of them are recognized as having widespread economic and public health implications. Rabies, cystic echinococcosis, leishmaniasis, and Chagas disease are examples of dog-associated zoonoses, with substantial human health and economic consequences. As an indication of the significance of these diseases, in 2007, the World Health Organization included them as four of the neglected tropical diseases, which would be targeted by the Global Plan to Combat Neglected Tropical Diseases 2008–2015 (WHO, 2007). Since that time, the WHO has published their first two major reports on neglected tropical diseases, both of which have emphasized the importance of these four dog-associated zoonoses (WHO, 2010b, 2013). In 2011, representatives from the FAO, the OIE, and the WHO held an interagency meeting to develop a prioritized portfolio of neglected zoonotic diseases (WHO, 2011). Three of the diseases, which were included in the portfolio, rabies, cystic echinococcosis, and *T. solium* cysticercosis, were classified as being neglected zoonotic diseases of global importance (WHO, 2011, 2013).

Although these dog-associated zoonoses are responsible for substantial morbidity, mortality, and economic losses, they are not new diseases. In fact, most of them have been present for centuries, affecting primarily poor marginalized populations in the developing world. While cost-effective control options may be available for many of these diseases, they are greatly under-diagnosed and underreported (Knobel et al., 2005; Budke et al., 2006; Craig and Larrieu, 2006; WHO, 2006). As a result, they are classified as "neglected" zoonotic diseases because they are often unable to attract the attention of public health decision-makers, researchers, and funding agencies, which is necessary to effectively control them (WHO, 2006, 2011, 2013).

1.4. CYSTIC ECHINOCOCCOSIS

1.4.1. Transmission

Cystic echinococcosis (CE) is a parasitic zoonosis caused by the larval stage of *Echinococcus granulosus*, a taeniid cestode. *E. granulosus*, the most common *Echinococcus* species, has a cosmopolitan distribution, with endemic regions on all continents except Antarctica (Eckert et al., 2001; Moro and Schantz, 2009). Like other *Echinococcus* species, *E. granulosus* requires two mammalian hosts to complete its life cycle. A sylvatic transmission cycle, involving wild carnivores and ungulates, exists in some regions of the world. However, the most common transmission cycle is the domestic cycle, with domestic dogs serving as the definitive hosts and domestic livestock as the intermediate hosts (Eckert et al., 2001; Torgerson and Budke, 2003). The domestic *E. granulosus* transmission cycle poses the greatest risk to human health due to the close association between humans and their dogs (Macpherson, 2005; Craig et al., 2007a).

The adult parasites develop in the small intestine of the dog definitive host. *E. granulosus* eggs are released into the environment in the feces of infected dogs. The eggs contaminate the surrounding water, soil, pastures, and other vegetation. Intermediate hosts become infected when they ingest these eggs.

Livestock, which serve as the natural intermediate hosts, become infected when they ingest the eggs while grazing on contaminated pastures. Humans (accidental intermediate hosts) can also become infected through the ingestion of *E. granulosus* eggs, as a result of consuming contaminated food or water, or handling infected dogs, infected feces, contaminated plants, or contaminated soil, followed by direct hand-to-mouth transfer (Eckert and Deplazes, 2004). Once ingested by a suitable intermediate host, the eggs hatch in the small intestine, releasing oncosphere larvae. The larvae penetrate the intestinal wall and are transported, via the circulatory system, to the organs where cyst development occurs (McManus et al., 2003; Moro and Schantz, 2009). While the cysts most frequently develop in the liver or lungs, it is also possible for them to develop in other areas of the body. The *E. granulosus* transmission cycle is complete when a dog definitive host becomes infected through the ingestion of cyst-containing viscera from an infected livestock intermediate host (Eckert and Deplazes, 2004).

1.4.2. Clinical manifestations

In humans, CE is characterized by slow growing, unilocular cysts which may not be detected for months or years after the initial infection has occurred. These cysts are most frequently located in the liver or the lungs, but can also occur in other organs or tissues (Eckert et al., 2001). On average, approximately 70% of symptomatic CE cases have liver cysts, 20% of CE cases have lung cysts, and the remaining 10% of cases have cysts in other organs or tissues (Eckert and Deplazes, 2004). A review, which combined 9770 surgical patients, from 11 studies, reported a liver CE to lung CE ratio of 2.5:1 (Larrieu and Frider, 2001). However, the ratio of liver cases to lung cases has been found to differ between symptomatic patients and apparently healthy individuals, who were diagnosed incidentally or through a screening study. Individuals who are apparently healthy have been shown to have a higher liver CE to lung CE ratio than symptomatic patients. One screening study, which examined 577 apparently healthy people, in Rio Negro Province, Argentina, found a liver CE to lung CE ratio of 12:1. A screening study, conducted in Uruguay, which examined 9481 apparently healthy people, reported a liver CE to lung CE ratio of 8:1 (Perdomo et al., 1997). A more recent screening study, conducted in Peru reported a liver CE to lung CE ratio of 5:1 (Gavidia et al., 2008). However, the Peruvian study's authors did not specify whether all of the participants were asymptomatic. Therefore, it is not clear if the results can be directly compared to those of the other studies. Very few recent screening studies have estimated the prevalence of pulmonary CE in the general population, due to the ethical concerns associated with exposing healthy people to the radiation associated with thoracic radiography. A retrospective study, which examined the hospital records of surgical patients, over a 25-year period, reported that 67% of the patients had hepatic CE, while the remaining 33% of the patients had cysts located in other organs (Cubas-Castillo et al., 2011). However, because the study was focused specifically on hepatic cases, the proportion of cases with pulmonary cysts was not reported.

Early in the course of infection, *E. granulosus* cysts tend to be small, well encapsulated, and not typically associated with morbidity. Due to the slow-growing nature of the cysts, infected individuals may remain asymptomatic for months, years, or indefinitely (McManus et al., 2003; Eckert and Deplazes, 2004). CE remains asymptomatic until the cyst grows large enough to exert pressure on neighboring organs or other tissues, ruptures, or develops complications such as secondary infection. Although the clinical presentation of CE is highly variable, and depends on a variety of factors, including the size and location of the cyst, symptoms often resemble those of a space-occupying lesion (McManus et al., 2003; Eckert and Deplazes, 2004; Moro and Schantz, 2009). The most commonly reported signs and symptoms associated with hepatic CE include abdominal pain, a palpable mass in the right upper quadrant, nausea, and vomiting (Moro and Schantz, 2009; Cubas-Castillo et al., 2011). For pulmonary CE cases, the most commonly reported clinical manifestations include chronic cough, chest pain, dyspnea, and hemoptysis (Arinc et al., 2009; Santivanez and Garcia, 2010). Fever and pain typically occur in conjunction with secondary bacterial infection. If the cyst ruptures, due to pressure or trauma, the sudden release of cyst fluid can cause a potentially fatal anaphylactic reaction (Eckert and Deplazes, 2004; Moro and Schantz, 2009). In addition, when a cyst ruptures, protoscolices contained in the cyst fluid may disseminate, leading to the development of secondary cysts in the adjacent tissues (Eckert et al., 2001; McManus et al., 2003; Santivanez and Garcia, 2010).

In the dog definitive host, adult *E. granulosus* penetrate deeply between the villi of the small intestine. However, there do not appear to be major pathogenic effects, even in the presence of very heavy infections. As a result, dogs are considered asymptomatic carriers (Eckert and Deplazes, 2004).

In livestock intermediate hosts, infection with *E. granulosus* cysts is typically asymptomatic because the time that it takes for the cysts to grow to a size, which is large enough to cause clinical manifestations, is likely to exceed the lifespan of the animal. However, it has been suggested that CE may substantially affect livestock health, but the effects of the disease are overlooked (Eckert et al., 2001). Although there have been very few controlled studies, some researchers have suggested that CE affects livestock productivity, leading to decreased weight gain, fertility, milk yield, and wool values (Torgerson, 2003).

1.4.3. Diagnosis

Human CE is typically diagnosed using imaging techniques, such as ultrasonography, conventional radiography, computed tomography, and magnetic resonance imaging (Eckert and Deplazes, 2004; Brunetti et al., 2010). Ultrasound examination is the preferred method for diagnosing CE in abdominal locations (Brunetti et al., 2010). The World Health Organization Informal Working Group on Echinococcosis (WHO-IWGE) has developed a standardized ultrasound classification system for CE, which classifies cysts as active (CE1 and CE2), transitional (CE3), or inactive (CE4 and CE5) based on their appearance (WHO, 2003; Brunetti et al., 2010). Ultrasonography is considered a safe, reliable, and cost-effective method for diagnosing CE, which can be used in healthcare settings as well as for population-based CE screening studies (Macpherson et al., 2003; Macpherson and Milner, 2003; Eckert and Deplazes, 2004; Brunetti et al., 2010). Studies have reported that, for abdominal cysts, ultrasound has a diagnostic sensitivity of 88-98% and a specificity of 93-100% (Caremani et al., 1997; Del Carpio et al., 2000). However, ultrasound is unable to detect pulmonary cysts. Therefore, conventional radiography is typically used to diagnose pulmonary CE (Brunetti et al., 2010).

Although serologic techniques are also available, to aid in diagnosing CE, the diagnostic accuracy of these tests has been shown to be much lower than that of imaging techniques. Most current serological tests, used to diagnose human CE, are based on the detection of IgG antibodies to antigen from CE cyst fluid, using primarily enzyme-linked immunosorbent assay (ELISA) and immunoblotting techniques. Some studies have reported that these tests perform relatively well when using sera from clinically confirmed cases of CE, with sensitivities and specificities ranging from 80 and 95% for liver cysts (Verastegui et al., 1992; Li et al., 2003). However, when they were used for screening human populations in community-based studies they have performed very poorly, with diagnostic sensitivities near or below 50%, when abdominal ultrasound was used as the gold standard (Moro et al., 2005; Gavidia et al., 2008; Harandi et al., 2011).

In a 2005 community-based study, conducted in Peru, 389 individuals were screened for CE using both abdominal ultrasound and the enzyme-linked immunoelectrotransfer blot (EITB) assay (Moro et al., 2005). The authors reported that the prevalence of CE was 4.9% (19/387) based on abdominal ultrasound, and 2.6% (10/389) based on EITB. However, there were two additional ultrasound-positive participants who were not included in the ultrasound-based prevalence because they refused to provide a blood sample. If these individuals had been included, the ultrasound-based prevalence would have greatly increased, to 5.4%. Their EITB-based prevalence included only those individuals who were positive on both tests (ultrasound and EITB). However, they indicated that 17/389 individuals were actually EITB-positive. If that were the case, the EITB-based prevalence would have increased to 4.4%. In addition, while two ultrasound-positive participants were excluded from the ultrasound-based prevalence calculation because their refusal to provide a blood sample, all 389 participants were included in the EITB-based prevalence calculation. The authors did not indicate if additional individuals declined to provide blood samples. However, if we assume that 387 individuals were examined using both screening methods and that the ultrasound-positive individuals were all truly CE positive, the resulting sensitivity and specificity of EITB would be 52.6% and 98.1%, respectively. The positive and negative predictive values of EITB would be 58.8% and 97.6%, respectively.

A cross-sectional study, which was conducted in Iran between 2006 and 2008, screened 1140 people for CE (Harandi et al., 2011). The study incorporated both abdominal ultrasound and an ELISA test. While all 1140 individuals were examined using abdominal ultrasound, only 1062 agreed to provide a blood sample. The authors reported that the prevalence of CE was 0.2% (2/1140) based on abdominal ultrasound, and 7.3% (77/1062) based on the ELISA. If 1062 individuals were examined using both screening methods and the two ultrasound-positive individuals were both truly CE positive, the resulting sensitivity and specificity of the ELISA would be 50% and 92.8%, respectively. The positive and negative predictive values of the ELISA would be 1.3% and 99.8%, respectively. In this case, because the prevalence of CE in this population is very low, and the ELISA greatly overestimates the true prevalence of CE, a CE positive diagnosis based on the ELISA used in this study is of very little value.

It should be noted that these studies did not incorporate thoracic radiography, for the purpose of diagnosing pulmonary CE. In addition, the diagnostic sensitivity of abdominal ultrasound is not 100% for CE. However, neither of those factors is likely to account for the differences between the ultrasound-based prevalence and serology-based prevalence seen in the studies mentioned above because the number of pulmonary cases is typically substantially lower than the number of hepatic cases in community-based CE screening studies (Gavidia et al., 2008). Due to their demonstrated inability to accurately diagnose CE in community-based studies, if serological tests are to be incorporated into such studies, they should only be used in conjunction with imaging techniques.

1.4.4. Treatment

Human CE is a chronic disease, which causes substantial morbidity and has the potential to be fatal without adequate treatment (Ammann and Eckert, 1996; Eckert and Deplazes, 2004). There are four basic treatment options for CE, including surgical resection, antiparasitic drug treatment using benzimidazoles, the PAIR technique (percutaneous puncture of cysts, aspiration of fluid, injection of protoscolicidal agent, and reaspiration of fluid), and a "watch and wait" approach (Brunetti et al., 2010). Treatment decisions are made based on the number, size, location, and stage (based on the WHO-IWGE ultrasound classification system) of cysts. Other factors to consider include whether there are complications, the overall health of the patient, and proximity to a surgical facility (Eckert and Deplazes, 2004; Craig et al., 2007b; Brunetti et al., 2010).

1.4.5. Global distribution

Cystic echinococcosis has a worldwide geographic distribution. The most highly endemic areas include the eastern Mediterranean region, southern and Eastern Europe, Russia, central Asia, western China, northern and eastern Africa, and the southern portion of South America (Chile, Peru, Uruguay, and Argentina) (Craig and Larrieu, 2006; Moro and Schantz, 2009; WHO, 2013). In some regions of the world, the disease may be emerging or reemerging. One point of particular concern is that increasing numbers of pediatric CE cases are being reported in some areas, indicating that transmission is ongoing in those areas (WHO, 2010b). There are a number of reasons for the re-emergence of CE being seen in some countries. The number of human cases in a particular region is usually reported using one of three values: prevalence, reported incidence, and surgical incidence.

Incidence values are typically obtained from government databases or hospital records. While the incidence of CE has been shown to very high in many developing countries, particularly in the most economically disadvantaged communities, the disease is frequently underreported, even in regions in which it is considered a reportable disease (WHO, 2006). CE is likely to be underreported for a number of reasons. The disease is difficult to diagnose, typically requiring diagnostic imaging which may not be readily available to those who live in endemic communities (Moro and Schantz, 2009; Brunetti et al., 2010). In addition, treatment for CE can be difficult and expensive, frequently requiring access to surgical facilities (Eckert and Deplazes, 2004; Brunetti et al., 2010). Also, the frequency with which CE occurs is likely to be underestimated because the infection can remain asymptomatic for a number of years before clinical signs become apparent (Eckert and Deplazes, 2004; Craig et al., 2007b; Brunetti et al., 2010). Even the cases who are properly diagnosed, may not be reported if the diagnostic facility does not regularly report new cases.

In contrast to incidence values, prevalence values for CE have a tendency to overestimate the true prevalence of CE in a particular region because these values are usually obtained from studies, which were conducted in highly endemic communities (Moro et al., 2005; Gavidia et al., 2008; Harandi et al., 2011). The most accurate estimate of the disease burden in a particular region would be one, which combined the reported incidence of CE with prevalence values obtained from multiple community-based studies from the region into one comprehensive estimate. However, such estimates are rarely available.

1.4.6. Risk factors

In order to begin to control the disease in a particular region, it is important to understand the epidemiological risk factors, which are potentially facilitating the transmission of *E. granulosus* to humans. A number of factors have been found to be associated with an increased risk for human CE. These factors include: owning large numbers of dogs, owning dogs for a long period of time, close contact with dogs (particularly during childhood), having large numbers of free roaming (stray) dogs in the area, allowing owned dogs to roam, allowing dogs to enter the home, and allowing dogs to eat raw viscera, as well as gender, level of education, and household income (Carmona et al., 1998; Campos-Bueno et al., 2000; Dowling et al., 2000; Dowling and Torgerson, 2000; Larrieu et al., 2002; McManus et al., 2003; Moro et al., 2008). However, the findings have not been consistent between studies because each study evaluated a different group of variables using different statistical techniques.

A case-control study, which was conducted in Peru in 2005, reported that people who owned a large number of dogs (≥ 10 dogs) and those who raised sheep had a significantly greater risk for developing CE (Moro et al., 2008). The authors reported that individuals who worked with goats and those who believed that CE could be transmitted through food had a significantly lower risk for developing CE. However, it was a small study that included only 32 surgical cases and 64 controls. Therefore, it may not be representative of the entire population of CE cases in the study location. In addition, while the controls who were selected did not have a history of CE, they did not appear to have undergone any diagnostic testing to confirm that they were CE-negative.

Factors which were shown to be significantly associated with an increased risk for human CE, in Uruguay, included having a personal history of previously treated CE, feeding viscera (raw or cooked) to dogs, improper disposal of offal, having an enclosed vegetable garden, and obtaining drinking water from an open source (Carmona et al., 1998). The study was quite large, including over 9,000 participants. All potential risk factors were analyzed individually, using chi-square tests. Therefore, the potential for confounding was not taken into account.

A case-control study, which examined children attending school in a community in Rio Negro Province, Argentina found that having a father who worked in an abattoir, living in a household that owned dogs within the 10 years prior to the interview, and having other cases of CE within the household were significantly associated with an increased risk for infection (Larrieu et al., 2002). The study examined all 1,070 children who attended school in the community. A questionnaire was completed for each of the 26 cases and 66 controls, by a parent or grandparent. One problem with this study was that it only examined children. There have not been any recent studies, which have examined risk factors for adults in this region of Argentina.

1.4.7. Socioeconomic impact

Although both monetary and non-monetary methods have been used to estimate the socioeconomic impact of CE, each method has unique advantages and disadvantages, which should be considered. One of the primary advantages of using a monetary approach to estimate the losses associated with CE, is that it allows both human-associated and livestock-associated losses to be incorporated into the same estimate. It is particularly important for burden of disease estimates to include the livestock-associated economic losses attributable to CE, in low-income countries, where livestock production represents a substantial proportion of rural income (Carabin et al., 2005). In addition, including livestock-associated losses when estimating the socioeconomic impact of CE has the potential to greatly improve the cost-effectiveness of disease control programs, especially if costs are shared between the agricultural and public health sectors (Roth et al., 2003). The disadvantage of using only a monetary approach to estimate the burden associated with CE, is that it has been shown to underestimate the impact of the disease in very poor regions, due to having lower incomes and livestock values than those of wealthier regions (Budke et al., 2006).

The economic losses associated with human CE include both direct and indirect costs. The direct costs include all expenses associated with the diagnosis and treatment of CE, while the indirect costs typically include costs associated lost wages, and decreased productivity due to CE-related morbidity and mortality. One of the best methods of estimating the human treatment costs is to calculate the cost per patient from a representative sample of CE patient medical records for the time-period of interest. This method has been used in studies, which have estimated the economic impact of CE in Uruguay, Jordan, and the UK (Torgerson et al., 2000; Torgerson and Dowling, 2001; Torgerson et al., 2001). However, it should be noted that the UK study included records for only 8 patients, which may have biased the results if even a few of the patients differed substantially from the typical patient. Human indirect losses are usually calculated using either wage data or per capita GDP, with wage data providing a better estimate of the impact of CE on infected individuals and their families.

Livestock-associated economic losses include direct costs, resulting from the condemnation of infected offal, as well as indirect costs due to decreased productivity (Eckert et al., 2001; Torgerson, 2003). The direct costs can be calculated using market values for the condemned organs (Torgerson et al., 2001; Benner et al., 2010; Harandi et al., 2012). However, livestock productivity losses can be difficult to accurately estimate due to the extremely limited number of controlled studies (Torgerson, 2003).

The monetary burden of CE has been estimated globally as well as at the country-level for several locations. Based on an estimate of the global burden of CE, the monetary losses attributable to human CE were estimated to be $193 million, and increased to $764 million when adjusted for underreporting (Budke et al., 2006). The livestock-associated monetary losses were estimated to be $142 million when only direct costs attributable to liver condemnation were included (Budke et al., 2006). However, the livestock-associated monetary losses increased to approximately $2.2 billion when productivity losses were included and the estimate was adjusted to account for underreporting. The authors of this study had to account for a substantial amount of missing data in order to obtain their estimate of the total global monetary losses attributable to CE. In addition to the previously mentioned lack of available data regarding the degree to which CE affects human and livestock productivity, reliable estimates of human disease incidence and livestock prevalence are rarely available, particularly for developing countries. Monte Carlo techniques were used to model uncertainty in the parameter estimates. However, due to the degree of uncertainty in their estimates, the authors presented their results as a preliminary estimate of the global monetary burden of CE. The study demonstrated that CE is responsible for substantial monetary losses throughout much of the world.

Although the CE-associated economic losses have been estimated for several countries, it is difficult to directly compare the monetary burden estimates from different studies because there are no standardized methods for conducting these analyses. As a result, the types of costs that are included in the overall total may vary greatly between studies. While a few studies have estimated only livestock-associated costs, most studies have incorporated both human-associated and livestock-associated costs into their estimates (Torgerson et al., 2000; Torgerson et al., 2001; Budke et al., 2005; Majorowski et al., 2005; Sariozkan and Yalcin, 2009; Benner et al., 2010; Ahmadi and Meshkehkar, 2011; Moro et al., 2011; Harandi et al., 2012). Depending on the purpose of the study, and the availability of data, each study has estimated the costs associated with a different set of variables, with some studies estimating only direct costs and others incorporating both direct and indirect costs. In addition, the total monetary losses associated with CE vary depending on a number of factors, including the human and livestock population sizes, the human incidence and livestock prevalence of CE, the availability of medical care, and the socioeconomic status of the region (Torgerson et al., 2000; Torgerson et al., 2001; Budke et al., 2005; Benner et al., 2010; Moro et al., 2011; Harandi et al., 2012).

Very few studies have been conducted to estimate the non-monetary burden of CE in specific regions (Budke et al., 2004; Moro et al., 2011). However, the global socioeconomic impact of CE was evaluated in a study, which estimated both the human-associated and livestock-associated monetary losses, as well as the non-monetary losses attributable to CE (Budke et al., 2006). The study used disability adjusted life years (DALYs) to measure the global non-monetary burden of CE. The DALY is a summary measure of population health, which incorporates morbidity and mortality information into a single unit, with each DALY representing the loss of one year of healthy life (Murray et al., 2012). Without adjusting for underreporting, an estimated 285,400 DALYs were lost to CE. However, after the value was adjusted for underreporting, the estimate increased to more than 1 million DALYs lost, suggesting that the global burden of CE is similar to, or greater than, that of other important neglected diseases such as Chagas disease, dengue, and onchocerciasis (Budke et al., 2006). These results indicate that CE represents a substantial burden for individuals and public health systems, increasing poverty and poor health in endemic regions of the world. Non-monetary measures of disease burden are beneficial because they allow diseases to be compared based on state of health, instead of using monetary estimates. However, non-monetary measures of burden of disease completely exclude the importance of livestock-associated losses. Therefore, for zoonotic diseases, which are believed to affect livestock health and productivity, monetary and non-monetary approaches should be used together, whenever possible.

CHAPTER II

OBJECTIVES AND STUDY LOCATIONS

2.1. STUDY LOCATION 1: BRAZOS COUNTY, TEXAS, USA

The primary objective of this portion of the study was to examine the knowledge and perceived local impact of dog-associated zoonoses in a community, within a developed country, in order to begin assessing the threat posed by these diseases in an industrialized setting. Data were obtained from questionnaires, which were administered via telephone, in order to address three specific aims:

1. Evaluate the level of knowledge regarding dog-associated zoonotic diseases, held by Brazos County, Texas residents.

2. Evaluate the perceived threat of dog-associated zoonotic diseases to the local population, among Brazos County, Texas residents.

3. Evaluate the willingness, of Brazos County, Texas, residents to take the actions necessary to prevent dog-associated zoonotic diseases.

2.2. STUDY LOCATION 2: RIO NEGRO PROVINCE, ARGENTINA

Rio Negro Province is located in the northern Patagonia region of southern Argentina. Although human cystic echinococcosis (CE) is known to be highly endemic in this region, current epidemiologic data are scarce (Larrieu et al., 2000b). In addition, to the author's knowledge, the economic impact of CE has never been estimated for Rio Negro Province. Therefore, the primary objectives of this portion of the project were to evaluate the epidemiology and socioeconomic impact of CE in Rio Negro Province. In order to accomplish these tasks, we focused on three specific aims:

1. Estimate the prevalence of CE among community volunteers in a highly endemic region of Rio Negro Province, Argentina.

2. Identify locally relevant risk factors for human CE in the study population, using data obtained from questionnaires, which were administered to individuals who participated in a community-based abdominal ultrasound screening survey in Rio Negro Province.

3. Estimate the economic impact of CE in Rio Negro Province, Argentina.
    a. Calculate both the direct and indirect costs associated with human CE in Rio Negro Province, using data obtained from hospital chart reviews and interviews with CE patients.

b. Calculate the CE-attributable economic losses to the livestock industry in Rio Negro Province, using information obtained from scientific publications, government reports, and meetings with local experts.

CHAPTER III

KNOWLEDGE AND PERCEPTIONS OF DOG-ASSOCIATED ZOONOSES: BRAZOS COUNTY, TEXAS, USA*

3.1. INTRODUCTION

More than 60% of United States households own pets (AVMA, 2007) accounting for more than 140 million cats and dogs. The number of pet owning households (68.7 million in 2006) has increased by approximately 12% over the past 5 years. In Texas, 45% of households own at least one dog, which is substantially higher than the national average of 37% (AVMA, 2007). Greater than 50% of families in the United States that have a dog also have children at home (Macpherson, 2005), with pet ownership shown to increase with family size and income (AVMA, 2007). Fifty-three percent of U.S. dog owners consider their dog to be a member of the family (AVMA, 2007). Because of this, increasing numbers of dogs live inside the home with their owners, often sleeping in their beds. While dogs can be a beneficial addition to a family, the risk of disease transmission from dogs to humans should be an important consideration.

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Dogs have roles that range from treasured family member to working dog to stray dog. The role of a dog in society makes a substantial difference in the role that it plays in zoonotic disease transmission and our ability to prevent those diseases from occurring. In locations such as the United States, in which feral and stray dog control programs are in place and functioning, pet dogs become an important target for zoonotic disease prevention (Macpherson, 2005). The primary dog-associated zoonoses of concern in the U.S. are bite-associated bacterial infections, rabies and zoonotic helminthes.

A recent study indicated that dog bites account for approximately 80% of the animal bites that occur in the U.S. (Patronek and Slavinski, 2009). Of the 4.7 million people who are bitten by dogs each year, approximately 800,000 of those people seek medical treatment (Dvorak et al., 2008). Children are the most common victims of dog bites and tend to have the most severe injuries. In Texas, there are 400,000 dog bites reported each year with over 40% of severe bite victims being children under 11 years of age (TDSHS, 2009a). Steele et al. (2007) reported that 87% of animal exposures requiring emergency department treatment in children were dog-associated, with 76% of those occurring inside the home or a private yard. Unless they become infected, many bites are never reported to a physician. Three to 18% of dog bites will become infected. *Pasturella* spp. are commonly isolated from infected bite wounds, with *Pasturella canis* being the most common isolate from dog bite wounds (Talan et al., 1999;

Chomel and Arzt, 2000; Patronek and Slavinski, 2009). Other examples of bacteria that commonly lead to bite wound infection are aerobic bacteria such as *Staphylococcus* spp. and *Streptococcus* spp. in addition to anaerobes such as *Fusobacterium* and *Bacteriodes* (Tan, 1997; Talan et al., 1999; Patronek and Slavinski, 2009).

Rabies is the most severe zoonotic disease commonly associated with dog bites. While human cases of rabies in the United States are rare, the disease is almost always fatal without treatment. Postexposure treatment in humans has been found to be very effective if it begins soon after exposure (Jackson et al., 2003; Manning et al., 2008). However, postexposure treatment can be very expensive, with an average cost of $2315 for biologics alone (Dhankhar et al., 2008). On average, there are less than 3 human rabies deaths reported each year in the U.S. This is likely due to well established dog and cat vaccination laws and the widespread use of human post exposure treatment, with over 40,000 treatments administered each year (Dhankhar et al., 2008). Large-scale control programs have been implemented for rabies with a great deal of success, including extensive dog and cat vaccination campaigns during the 1940s and 1950s. Due to these programs, domestic animals accounted for less than 7% of all rabid animals reported in the United States during 2007. In 2007, there were 93 confirmed cases of rabies in dogs in the U.S., with 12 cases in Texas (Blanton et al., 2008). Vaccinating pets is the most convenient and effective method of reducing the incidence of human infection because it prevents the vast majority of human exposure to the rabies virus (Hanlon et al., 1999).

In addition to bite-associated zoonoses, zoonotic helminthes can cause important dog-associated zoonoses. The most common parasitic zoonoses associated with dogs in the United States are due to *Ancylostoma* spp. and *Toxocara canis* (Schantz, 1989; Hendrix et al., 1996; Overgaauw and Nederland, 1997). *Toxocara* infections occur commonly in small children who ingest soil contaminated with *Toxocara* eggs (Schantz, 1989). However, *Toxocara* can also be transmitted through unwashed hands and contaminated food. Hookworm (*Ancylosoma* spp.) infections occur when infective larvae penetrate the skin of humans who are in contact with contaminated soil.

Very little research into the knowledge and perceptions of dog-associated zoonotic diseases, in the United States, has been reported in the literature. In a study conducted in DeKalb County, Georgia, Fontaine and Schantz (1989) found that respondents were not adequately informed about the health hazards associated with pets. They determined that only 63% of the studied household heads were aware that diseases could be transmitted from pets to humans and very few could recognize signs of specific zoonotic infections, with the exception of rabies. To the authors' knowledge, aside from the previously mentioned study, there have been no other studies with this primary focus. The objective of the study presented here was to update and broaden the amount of information with regards to the general public's knowledge and perceptions of dog-associated zoonoses. Increased information about any deficiencies that exist could lead to improved educational programs that could positively impact public health.

3.2. MATERIALS AND METHODS

3.2.1. Sample selection

The site chosen for this study was Brazos County, Texas. Data from the United States Census Bureau (2008) reported that there were 170,954 residents and 61,905 households in Brazos County in 2007. The racial/ethnic composition of the population of Brazos County was very similar to that of the United States. The racial/ethnic breakdown of the county was as follows: White (76%), Black/African American (11%), Asian (5%), and all other groups (8%). Hispanics/Latinos of any race made up 20% of the population. According to the United States Census Bureau (2008), for 84% of the Brazos County population, English was the only language spoken at home. The United States Census Bureau also reported that while Spanish was the primary language spoken in 11% of Brazos County homes, only 5% of the Brazos County population spoke English "less than very well." The median household income was $37,783 with

24% of the population living below the poverty level (United States Census Bureau, 2008).

A countywide telephone survey of adults, 18 years of age and older, from Brazos County households was conducted to evaluate the knowledge and perceptions of dog-associated zoonoses. The sample was selected from a random digit dialing (RDD) sampling frame which included listed and unlisted landline telephone numbers in the study area provided by Survey Sampling International (Shelton, CT). This study sought to compare dog owners' knowledge and perceptions of dog-associated zoonoses with that of people who did not own dogs. Because this comparison had not been previously reported in the literature, a minimum target sample size of 385 was calculated for a proportion of 0.5 using a 95% confidence level and a 5% error rate.

The Public Policy Research Institute (PPRI) at Texas A&M University conducted the survey at their onsite internet computer-assisted telephone interview (iCATI) facility. The iCATI system displays questions for the interviewer and electronically records responses. This system prevents most mistakes by guiding the interviewer through the questionnaire and automatically skipping questions as appropriate, based on the respondent's answers. Adults in a household were selected to participate in the study based on which member of the household had had the most recent birthday. Interviews were conducted from Monday through Friday between 8:00 a.m. and 9:30 p.m., on Saturdays between 10:00 a.m. and 6:00 p.m., and on Sundays between 1:00 p.m. and 9:30 p.m. These times were employed in order to reach respondents with varying schedules. However, the majority of the interviews took place during the late afternoon and evening hours. Five attempts were made to contact each of the selected respondents. Phone numbers that had been disconnected were tried twice in order to confirm that they were disconnected and then replaced. Interviewers were trained and monitored during every shift by 1 to 3 shift supervisors, with more supervisors being assigned to the busier evening and weekend shifts.

3.2.2. Questionnaire design

A confidential questionnaire was designed with guidance from epidemiologists, veterinarians and survey research experts. The questionnaire was pretested by calling 15 households in the survey area and revised accordingly (word selection, question sequence, etc.) incorporating advice from the above experts. The questionnaire was translated into Spanish and back-translated into English by native Spanish speakers at the Public Policy Research Institute so that a version was available for native Spanish-speaking participants.

The questionnaire began with an introduction explaining the purpose of the study in addition to the assurance that the respondent's answers and personal information would remain confidential. The initial questions asked about the type and number, if any, of pets owned by the household. Respondents who owned dogs were asked a series of questions about where the dog(s) were kept, whether they had identification, and if they were allowed to roam freely. In addition, they were asked questions regarding veterinary care including vaccination (rabies) and deworming history. All respondents were asked questions about their knowledge of dog-associated zoonotic diseases, with particular emphasis placed on rabies and zoonotic helminthes. Respondents were then asked where they receive their information about zoonotic diseases including the causes, treatment, and prevention of these diseases. To assess the respondents' perception of zoonotic diseases and what actions they might take to avoid them, respondents were asked a series of hypothetical questions regarding reporting animal bites to authorities. The final section of the questionnaire included demographic questions about the respondent and the household.

Closed-ended questions were used whenever possible in order to streamline the data analysis. However, some questions were partially closed-ended in order to give the respondents the ability to give the answer they felt was most correct using an "other" category (Dillman, 2007). In order to give the respondent the opportunity to provide an answer for every question that they were asked, all questions included options for "do not know" and "refused." Approval for this study was obtained from the Institutional Review Board at Texas A&M University.

3.2.3. Data analysis

All analyses were carried out using Intercooled Stata version 10.0 (Stata Corp., College Station, TX, USA). Descriptive statistics were calculated for each variable of interest and stratified on dog ownership status. Age was normally distributed but not linearly associated with any of the outcomes of interest (outcomes were: would dog owners report their dog being bitten by a dog they did not own; would respondents report being bitten by a dog they did not own; would respondents report being bitten by a wild animal; dog ownership). Linearity was assessed by dividing age into quartiles in addition to dividing age into categories based on age decades. Ultimately, age was categorized hierarchically (based on decades) and categories were collapsed into two groups (60 years and below; greater than 60 years of age). The groups were collapsed in this way because there appeared to be a clear threshold in the data that occurred at the age of 60, which was not present with any of the other age categories.

Logistic regression was used to assess each variable for inclusion in the multivariable models. The "don't know" responses were included as a separate category in all analyses. All potential independent variables, which were considered in the univariable analyses for each of the models, can be found in Tables 3.1 and 3.2. While the variables listed in Table 3.1 were assessed for all models, the variables included in Table 3.2 were assessed only for the models that required dog ownership (dog ownership; reporting their dog being bitten by a dog they did not own). Those variables with a *p*-value of less than 0.25 (Hosmer and Lemeshow, 2000) were put forward for evaluation in the multivariable models. These variables are listed in Table 3.3.

Multivariable logistic regression models were developed using backward stepwise variable selection, assessing the statistical significance of the exclusion of each variable using likelihood ratio tests ($p < 0.05$). Each model was tested for interactions between pair-wise combinations of all variables that remained in the model. The fit of each model was assessed using the Hosmer–Lemeshow goodness-of-fit test. The standardized Pearson residuals, deviance residuals and deviance χ^2 were used to assess the models for outliers. Leverage and delta–betas were calculated to determine if there were covariate patterns that had values high enough to cause concern (Dohoo et al., 2003).

Table 3.1
Descriptive statistics and bivariate Chi-square analyses for demographic and zoonoses questions categorized on the basis of dog ownership for a study of dog-associated zoonoses in Brazos County, Texas, USA (N = 922, yes = 516, 56%)

Variables	Dog Owner		*P*-value (χ^2)
	Yes, *N* (%)	**No, *N* (%)**	
Gender			0.40
Male	157 (30)	134 (33)	
Female	359 (70)	272 (67)	
Age			0.001*
Mean	47.6	52.6	
Median	47	53	
Min-max	18-90	18-99	
Education			0.006
Less than high school	12 (2)	22 (5)	
High school/GED	88 (17)	102 (25)	
Some college	136 (26)	93 (23)	
Completed college	149 (29)	93 (23)	
Advanced degree	127 (25)	94 (23)	
Don't know/Refused	4 (1)	2 (1)	
Race/Ethnicity			<0.0001
White	441 (86)	280 (69)	
African American	25 (5)	39 (10)	
Hispanic	31 (6)	55 (14)	
Other	13 (3)	23 (6)	
Don't know/Refused	6 (1)	9 (2)	
Household Income Range			<0.0001
Less than $25,000	27 (5)	60 (15)	
$25,000-$49,999	83 (16)	70 (17)	
$50,000-$74,999	82 (15)	55 (14)	
$75,000-$99,999	83 (16)	36 (9)	
$100,000 or more	124 (24)	55 (14)	
Don't know/Refused	117 (23)	130 (32)	
Live in city limits			<0.0001
Yes	366 (71)	341 (84)	
No	148 (29)	64 (16)	
Don't know/Refused	2 (0.4)	1 (0.2)	

Table 3.1 (Continued)

Variables	Dog Owner		P-value (χ^2)
	Yes, N (%)	**No, N (%)**	
No. of people in household			<0.0001
1	56 (11)	91 (22)	
2	199 (39)	149 (37)	
3	90 (17)	54 (13)	
4	105 (20)	50 (12)	
5	34 (7)	31 (8)	
6 or more	23 (4)	21 (5)	
Don't know/refused	9 (2)	10 (3)	
No. of children in household			0.001
0	288 (56)	265 (65)	
1	91 (18)	42 (10)	
2	85 (17)	46 (11)	
3 or more	43 (8)	45 (11)	
Don't know/refused	9 (2)	8 (2)	
Most important source of information about zoonotic diseases			<0.0001
Veterinarian	260 (50)	63 (16)	
TV or newspaper	103 (20)	176 (43)	
Internet	60 (12)	62 (15)	
Combination of media	31 (6)	15 (4)	
Doctor	29 (6)	26 (6)	
Family or friend	16 (3)	22 (5)	
Don't know/Refused	10 (2)	32 (8)	
Other	7 (1)	10 (3)	
Would report being bitten by a dog they do not own to someone of authority			0.09
Yes	447 (87)	353 (87)	
No	42 (8)	42 (10)	
Don't know	27 (5)	11 (3)	
Would report being bitten by a wild animal to someone of authority			0.32
Yes	495 (96)	386 (95)	
No	14 (3)	17 (4)	
Don't know	7 (1)	3 (1)	

Table 3.1 (Continued)

Variables	Dog Owner		*P*-value (χ^2)
	Yes, *N* (%)	**No, *N* (%)**	
Believe that people can get intestinal helminthes from dogs			0.06
Yes	288 (56)	206 (51)	
No	90 (17)	62 (15)	
Don't know	138 (26)	138 (34)	
Have heard of rabies			0.026
Yes	511 (99)	394 (97)	
No	5 (1)	12 (3)	
Perceived consequences of exposure to rabies without treatment			0.81
Mild illness	3 (1)	4 (1)	
Skin infection	7 (1)	7 (2)	
Serious illness/hospitalization	147 (29)	123 (31)	
Death	312 (61)	227 (58)	
Other	21 (4)	17 (4)	
Don't know/Refused	21 (4)	16 (4)	
Not applicable	5	12	
Believe that if a person thinks that they may have been exposed to rabies, they should:			0.12
Make appointment with M.D.	74 (15)	45 (11)	
Seek emergency treatment	429 (84)	337 (86)	
Other	7 (1)	7 (2)	
Don't know	1 (0.2)	5 (1)	
Not applicable	5	12	
Believe that if they see an animal that may be rabid, they should:			0.076
Contact someone of authority	429 (84)	346 (88)	
Kill the animal	62 (12)	31 (8)	
Other	13 (3)	15 (4)	
Don't know	7 (1)	2 (1)	
Not applicable	5	12	

Table 3.1 (Continued)

Variables	Dog Owner		P-value (χ^2)
	Yes, *N* (%)	**No, *N* (%)**	
Believe that rabies is present in Texas			0.001
Yes	496 (97)	360 (91)	
No	5 (1)	8 (2)	
Don't know	10 (2)	26 (7)	
Not applicable	5	12	
Believe that people can get rabies			0.49
Yes	498 (98)	386 (98)	
No	1 (0.2)	2 (1)	
Don't know	12 (2)	6 (2)	
Not applicable	5	12	
Believe that it is possible to get rabies from a dog			0.24
Yes	491 (99)	377 (98)	
No	0 (0)	2 (1)	
Don't know	7 (1)	7 (2)	
Not applicable	18	20	
Believe that it is possible to get rabies from a cat			<0.0001
Yes	427 (86)	292 (76)	
No	10 (2)	22 (6)	
Don't know	61 (12)	72 (19)	
Believe that it is possible to get rabies from a skunk			<0.0001
Yes	489 (98)	348 (90)	
No	2 (0.4)	12 (3)	
Don't know	7 (1)	26 (7)	
Believe that it is possible to get rabies from a raccoon			<0.0001
Yes	483 (97)	345 (89)	
No	2 (0.4)	11 (3)	
Don't know	13 (3)	30 (8)	

Table 3.1 (Continued)

Variables	Dog Owner		P-value (χ^2)
	Yes, *N* (%)	**No, *N* (%)**	
Believe that it is possible to get rabies from a bat			<0.0001
Yes	480 (96)	343 (89)	
No	4 (1)	9 (2)	
Don't know	14 (3)	34 (9)	
Not applicable	18	20	
Perceived as the most common way people get rabies in Texas (among those who believe that rabies is present in Texas and people can be infected)			0.002
Wild animal bite	288 (59)	161 (45)	
Dog bite	147 (30)	139 (39)	
Cat bite	5 (1)	8 (2)	
Contact with infected person	1 (0.2)	0 (0)	
Other	27 (6)	24 (7)	
Don't know	18 (4)	24 (7)	
Not applicable	30	50	

**P*-value for age as a continuous variable, Mann-Whitney rank sum test.

Table 3.2
Descriptive statistics for all questions asked solely of dog owners for a study of dog-associated zoonoses in Brazos County, Texas, USA (N = 516)

Dogs have identification	
Yes	469 (91)
No	44 (9)
Missing	3
Dogs are allowed indoors	
Yes	437 (85)
No	76 (15)
Missing	3
Dogs are usually fenced/tied when outdoors, unsupervised	
Yes	431 (84)
No	76 (15)
Don't know/Refused	9 (2)
Most recent time any of their dogs was seen by a vet	
<1 year ago	470 (94)
1-2 years ago	24 (4)
3 or more years ago	4 (1)
Don't know	4 (1)
Not applicable	14
Amount spent last year for annual exam, vaccinations, etc. for one of their dogs	
None	7 (1)
<$100	89 (18)
$101-$200	196 (39)
$201-$300	93 (19)
>$300	83 (17)
Don't know	34 (7)
Not applicable	14
At least one of their dogs has been vaccinated for rabies	
Yes	492 (96)
No	16 (3)
Don't know	7 (1)
Missing	1

Table 3.2 (Continued)

Most recent rabies vaccine for any of their dogs	
<1 year ago	373 (76)
1-3 years ago	102 (21)
4-6 years ago	4 (1)
Don't know	13 (3)
Not applicable	24
At least one of their dogs has been dewormed	
Yes	339 (66)
No	146 (28)
Don't know	30 (6)
Missing	1
Most recent deworming for any of their dogs	
<1 month ago	125 (37)
<1 year ago	119 (35)
1-2 years ago	38 (11)
3-5 years ago	22 (7)
>5 years ago	22 (7)
Don't know	13 (4)
Not applicable	177
Would report their dog being bitten by another dog	
Yes	407 (79)
No	85 (17)
Don't know	24 (5)
Would report being bitten by their own dog	
Yes	233 (45)
No	256 (50)
Don't know/Refused	27 (5)

Table 3.3
Variables which were found to be significant ($p < 0.25$) in univariable analyses and were further evaluated for inclusion in the multivariable models for a study of dog-associated zoonoses in Brazos County, Texas, USA

Model	Variable name
Dog Ownership	age, race/ethnicity, income, education, live in city limits, number of people in the household, number of children in the household, believe that it is possible to get rabies from a cat, believe that it is possible to get rabies from a skunk, believe that it is possible to get rabies from a raccoon, believe that it is possible to get rabies from a bat, believe that people can get zoonotic helminthes from dogs, would report being bitten by a dog they do not own to someone of authority, would report being bitten by a wild animal to someone of authority, believe that rabies is present in Texas
Would report their dog being bitten by another dog	gender, age, race/ethnicity, education, live in city limits, number of children in the household, dogs have identification, dogs are usually fenced/tied when outdoors unsupervised, at least one of their dogs has been dewormed, most important source of information about zoonotic diseases, believe that if a person thinks they may have been exposed to rabies they should seek emergency treatment
Would report being bitten by a dog they did not own	gender, age, race/ethnicity, level of education, live in city limits, number of people in the household, most important source of information about zoonotic diseases, believe that it is possible to get rabies from a dog, believe that it is possible to get rabies from a cat, believe that it is possible to get rabies from a skunk, believe that it is possible to get rabies from a raccoon, believe that it is possible to get rabies from a bat, believe that if a person believes they may have been exposed to rabies they should seek emergency treatment
Would report being bitten by a wild animal	gender, age, live in city limits, number of children in the household, believe that it is possible to get rabies from a raccoon, believe that it is possible to get rabies from a bat, believe that if a person thinks they may have been exposed to rabies they should seek emergency treatment

3.3. RESULTS

3.3.1. Descriptive statistics

The study took place between June 3 and June 15, 2008. Of the 1,691 households, which were contacted, 946 agreed to participate in the study and 922 completed the interview (55% response rate), exceeding the minimum sample size required for this study. Of the 922 interviews, which were conducted, 899 (97.5%) were conducted in English and the remaining 23 (2.5%) were conducted in Spanish. Fifty-six percent of the respondents who completed the questionnaire were dog owners.

Tables 3.1 and 3.2 include the descriptive statistics from select questions that were included in the questionnaire. Table 3.1 includes the descriptive statistics and bivariate analyses for questions, which were answered by all study participants. Table 3.2 includes the descriptive statistics for questions that pertained only to dog owners.

Table 3.4
Final multivariable logistic regression model of factors associated with dog ownership (no/yes) for a study of dog-associated zoonoses in Brazos County, Texas, USA

Variable	Odds ratio	95% CI	*P*-value of category
Live in city limits			
No	1.0 (Ref.)		
Yes	0.5	0.4-0.8	0.001
Age			
< 60 years	1.0 (Ref.)		
≥ 60 years	0.5	0.4-0.7	< 0.0001
Race			
White	1.0 (Ref.)		
African American	0.5	0.3-0.9	0.01
Hispanic	0.3	0.1-0.5	< 0.0001
Other	0.4	0.2-0.9	0.04
Annual household income			
< $25,000	1.0 (Ref.)		
$25,000-49,999	1.7	0.9-3.2	0.08
$50,000-74,999	1.8	0.9-3.3	0.09
$75,000-99,999	2.6	1.3-5.2	0.005
$100,000+	2.3	1.2-4.3	0.01
Number of people in household			
1	1.0 (Ref.)		
2	1.7	1.1-2.7	0.02
3	2.5	1.4-4.4	0.001
4	2.9	1.6-5.0	< 0.0001
5	1.5	0.7-3.0	0.28
6+	1.7	0.8-4.0	0.2
Believe that it is possible for humans to get rabies from cats			
No	1.0 (Ref.)		
Yes	3.3	1.4-7.7	0.006
Don't know	2.2	0.9-5.4	0.09
Believe that it is possible for humans to get worms from dogs			
No	1.0 (Ref.)		
Yes	0.7	0.4-1.1	0.09
Don't know	0.5	0.3-0.9	0.01
Person would report being bitten by a dog they do not own			
No	1.0 (Ref.)		
Yes	1.5	0.9-2.7	0.11
Don't know	4.8	1.7-13.4	0.003

No or yes. $N = 853$ observations, likelihood ratio chi-square = 155.2, $p < 0.0001$; Hosmer-Lemeshow goodness-of-fit test $p = 0.2$.

3.3.2. Multivariable logistic regression

As shown in Table 3.4, dog ownership was associated with the respondent's age, race, annual household income, number of people in the household and whether they lived in the city limits. Dog ownership was also associated with whether the respondent believed that it was possible for humans to get rabies from cats, whether they believed that humans could get zoonotic helminthes from dogs, and whether they would report being bitten by a dog that they did not own. No interaction terms were significant ($p < 0.05$).

When asked if they would report their dog being bitten by an apparently healthy dog that they did not own to someone of authority such as a veterinarian, police, sheriff or animal control, 79% of dog owners indicated that they would. As can be seen in Table 3.5, this could be predicted by the gender, age, and education of the respondent in addition to whether or not they lived in the city limits. No interaction terms were significant ($p < 0.05$).

When asked if they would report being bitten by an apparently healthy dog that they did not own to some one of authority such as a veterinarian, police, sheriff or animal control, 87% of respondents indicated that they would. As shown in Table 3.5, this could be predicted by whether or not they believed being bitten by a bat could cause rabies, whether or not they would seek emergency treatment if they believed that they had been exposed to rabies, whether or not they were over 60 years of age, their gender, and whether or not they lived in the city limits. None of the interaction terms were significant ($p < 0.05$).

When asked if they would report being bitten by a wild animal to someone of authority such as a veterinarian, police, sheriff or animal control, 95% of respondents indicated that they would. As shown in Table 3.5, this could be predicted by the gender of the respondent and whether or not they were over 60 years of age. None of the interaction terms were significant ($p < 0.05$).

When the models were tested for interactions between pair-wise combinations of all variables that were included, there was not substantial correlation in the data that needed to be accounted for in the models. There were no covariate patterns that had values high enough to cause concern, indicating that there were not any individual covariate patterns that had excessive influence on the models.

Table 3.5
Final logistic regression models of factors associated with bite reporting for a study of dog-associated zoonoses in Brazos County, Texas, USA

Variable	Dog bitten by dog[a]	Human bitten by dog[b]	Human bitten by wild animal[c]
	OR (95% CI)	OR (95% CI)	OR (95% CI)
Gender			
Male	1.0 (Ref.)	1.0 (Ref.)	1.0 (Ref.)
Female	2.0 (1.2-3.5)	2.3 (1.4-3.7)	10.6 (4.0-28.5)
Age			
< 60 years	1.0 (Ref.)	1.0 (Ref.)	1.0 (Ref.)
≥ 60 years	2.1 (1.1-4.1)	2.3 (1.2-4.4)	3.7 (1.1-12.4)
Live in city limits			
No	1.0 (Ref.)	1.0 (Ref.)	-
Yes	2.4 (1.4-4.1)	2.3 (1.4-3.9)	-
Education			
<High school	1.0 (Ref.)	-	-
High school	8.3 (1.8-38.2)	-	-
Some college	10.5 (2.3-47.6)	-	-
Completed college	12.5 (2.7-57.1)	-	-
Advanced degree	9.0 (2.0-40.6)	-	-
Would seek emergency treatment if they believed they had been exposed to rabies			
No	-	1.0 (Ref.)	-
Yes	-	3.1 (1.8-5.4)	-
Believe that humans can get rabies from bat bite			
No	-	1.0 (Ref.)	-
Yes	-	5.5 (1.6-18.6)	-
Don't know	-	3.3 (0.7-16.4)	-

[a] No or yes. *N* = 452 observations, likelihood ratio chi-square = 29.32, *p* = 0.0001; Hosmer-Lemeshow goodness-of-fit test *p* = 0.3.

[b] No or yes. *N* = 826 observations, likelihood ratio chi-square = 52.15, p < 0.0001; Hosmer-Lemeshow goodness-of-fit test *p* = 0.5.

[c] No or yes. *N* = 861 observations, likelihood ratio chi-square = 36.75, p < 0.0001; Hosmer-Lemeshow goodness-of-fit test *p* = 0.5.

3.4. DISCUSSION

While this study provided valuable information with regards to citizens' knowledge of dog-associated zoonoses, there were some study limitations which should be noted. Due to the data collection procedures used in this study, information regarding non-responders was not collected by the survey company; therefore, it was not possible to characterize non-responders. Consequently, the impact of non-response bias could not be assessed. In addition, the study was conducted in only one county in Texas. One primary difference between the populations of Brazos County and Texas is the proportion of the population that identifies themselves as Hispanic/Latino. While 35% of the Texas population is Hispanic/Latino, only 20% of the Brazos County population is Hispanic/Latino. Therefore, cultural differences are likely to have less of an impact on knowledge in Brazos County than in other regions of Texas. An additional aspect, which makes Brazos County unique, is that Brazos County is home to a large university with a veterinary college. Therefore, the level of educational attainment in the Brazos County population greatly exceeds that of the general populations of both Texas and United States. In Brazos County, 40% of the population holds a bachelor's degree or higher with 18% of the population holding a graduate or professional degree (United States Census Bureau, 2008). Because of the high level of educational attainment and the presence of the veterinary college in the county in which this study was conducted, deficiencies in knowledge, which were identified by this study, are likely to be amplified in regions with lower levels of education.

Demographic questions were asked for a variety of reasons, one of which was to determine if those people who participated in the project were representative of the population being studied (Brazos County, TX). The proportion of respondents who had attained at least a high school diploma (96%) was higher than that of the Brazos County population as a whole (85%). In addition, the proportion of respondents who had attained at least a bachelor's degree (50%) was higher than that reported by the 2007 U.S. Census estimates (40%) for Brazos County. The income of participants in this study was higher than that reported by the 2007 U.S. Census estimates. However, this measure may not be reliable because 27% of study respondents either did not know or refused to report their income. Approximately 67% of the respondents to our study were females. This could be of concern because gender was important in all models used to predict reporting of animal bites. The racial/ethnic composition of the study respondents was similar to that of the entire Brazos County population as reported by the 2007 U.S. Census estimates. However, neither the race nor the ethnicity of the respondents was significantly associated with the knowledge questions or bite-reporting models presented in this study.

In this study, there were some notable differences between dog owners and those who did not own dogs. The dog owners tended to be younger and more highly educated than those who did not own dogs. Dog owners were more likely to be white, have a higher income and more children than those who did not own dogs. Dog owners were also more likely to live outside the city limits. The largest percentage of dog owners listed a veterinarian as their most common source of information about zoonotic diseases while those who did not own dogs most commonly obtained this type of information from the media (television, newspaper and the internet). Significantly more dog owners were aware that rabies was present in Texas. The primary reason for this difference could be that dog owners are required by the state of Texas to vaccinate their dogs for rabies. The majority of dog owners correctly believed that wild animal bites were the most common source of rabies in Texas while those respondents who did not own dogs were evenly split between dog bites and wild animal bites as the most common source. The dog owners, in the study, were significantly more aware that people could get rabies from cats and wild animals such as raccoons, skunks, and bats than respondents who did not own dogs. This increased awareness could be due to the dog owners in this study being more likely to live in rural areas (outside the city limits) which may lead to increased contact with wild animals and/or increased education concerning the rabies risk that these animals pose.

While the veterinary profession is one of the best sources of zoonotic disease information, it appears that many veterinarians are still not discussing the potential for these diseases with their clients. Although 94% of dog owners in this study had seen a veterinarian within the previous year, only 50% reported getting the majority of their information about zoonoses from their veterinarian. This result is very similar to that obtained by a study conducted 20 years ago in DeKalb County, GA which found that 55% of pet owning respondents received some of their information about diseases transmitted from pets to people from their veterinarian (Fontaine and Schantz, 1989).

In the present study, 98% of respondents had heard of rabies and knew that it could be transmitted by dogs while only 54% of respondents knew that zoonotic helminthes could be transmitted from dogs to people. It is possible that a veterinarian provided this type of information to the respondents and they simply did not remember receiving it. However, there may be numerous reasons why people are not receiving a great deal of information about dog-associated zoonoses from their veterinarians. Because veterinarians often have a very busy schedule, discussion of these diseases may be omitted due to time constraints. They may not believe that some diseases (such as zoonotic helminthes) pose a significant threat to the health of the client; therefore, they may feel that discussing such diseases would lead the client to worry needlessly. In addition, the veterinarian may incorrectly assume that the client is informed of the important facts about these diseases and is taking proper precautions to avoid them. Finally, veterinary schools may not be adequately training veterinarians to effectively communicate the risks that dog-associated zoonoses pose to their clients.

It is important for veterinarians to understand the vital roles that they play in educating the public and preventing the spread of dog-associated zoonoses. One approach to increasing the likelihood of veterinarians discussing these important diseases with their clients may be for veterinary education programs to place greater emphasis on the communication of disease risk. This could be accomplished during veterinary school as well as through continuing education courses. Another method might be to encourage veterinarians to have simple informational displays and pamphlets, which focus on the primary dog-associated diseases for that particular region, in the waiting areas of their clinics. Including this type of information in the "welcome packs" that are often provided when new puppies or kittens present for their first round of vaccinations would also be a convenient way for veterinarians to educate their clients. In addition, while it may be difficult for veterinarians to spend a great deal of time on client education, veterinary technicians could be trained to play an important role in providing zoonotic disease information to clients. These simple techniques could be used by veterinarians to provide education and initiate discussion concerning this very important topic without requiring them to commit an excessive amount of time or resources.

With respect to public health, the results of this study present some cause for concern. For example, while 95% of people would report being bitten by a wild animal, only 86% of the respondents would report being bitten by a dog that they did not own. Those who would not report such a bite could be putting their health at risk. Only 59% of respondents were aware that exposure to rabies without treatment could lead to death and only 85% of respondents stated that they would seek emergency treatment if they believed that they may have been exposed to rabies. The most likely reason for this deficiency in knowledge and willingness to take action is societal complacency. There are very few human cases of rabies in Texas and the United States each year (TDSHS, 2009b). Therefore, people may be less vigilant about protecting themselves against this deadly disease than they would have been before the problem was controlled by pet vaccination programs.

Gender and age were important factors in all three bite-reporting models, with female and elderly respondents being more likely to report bites. This is not surprising because these groups have been shown to be more likely to seek healthcare, in general (Bernstein et al., 2003; Galdas et al., 2005). Respondents who lived in the city limits were more likely to report dog bites. This could be because they have less contact with dogs, which they do not own, than their rural counterparts. This study also found that respondents who believed that humans can contract rabies from a bat bite were more likely to report being bitten by a dog. While this relationship has not been reported in other studies, it is likely that these respondents are more knowledgeable about rabies. In the United States, the majority of recent human rabies cases have been attributed to bat bites and have received considerable media attention.

The findings of this study could be used to develop educational programs which place particular emphasis on those who were found to be less likely to report animal bites including young, male, and rural populations. The public needs to be made aware of how rabies is transmitted and what constitutes a possible exposure to rabies. Veterinarians can take the steps mentioned previously to educate their clients. In order to reach members of the population who do not have pets or do not visit a veterinarian regularly, educational campaigns incorporating short television commercials and newspaper advertisements can be used. These materials should provide a brief description of the disease as well as the precautions that should be taken in order to prevent it, in a simple, easy to understand format, without the use of confusing terminology. In addition, because the internet is an important source of information for many people, these messages could be placed on websites for cities, counties, parks and animal shelters. Informational fliers could also be mailed to citizens residing in high-risk areas, such as near a location with a recently confirmed case of animal rabies. Based on the results of this study, when educational programs are developed, more emphasis needs to be placed on what to do in the event of a possible exposure to rabies and the deadly consequences of not seeking appropriate treatment. In addition to providing information about rabies, veterinarians, physicians and public health authorities must take an active role in educating the public about the risks that zoonotic helminthes pose to human health because this study found that only half of respondents were aware of these diseases. In addition to physicians and veterinarians discussing these risks with their clientele, these goals could be accomplished by posting informational posters at parks and other places where humans could have contact with dog feces. These posters should include a brief description of the diseases as well as the precautions that should be taken in order to prevent them. Children are most commonly affected by dog-associated zoonotic helminthes (Overgaauw and van Knapen, 2000). Therefore, particular emphasis should be placed on educating the parents of small children.

3.5. CONCLUSIONS

This cross-sectional study suggests that there are several factors which could affect the likelihood of reporting animal bite incidents to authorities. These factors include living inside the boundaries of a city or town, being female and over 60 years of age as well as being aware that exposure to rabies constitutes an emergency. Many people in this study lacked knowledge about zoonotic diseases, which could seriously impact their health and the health of their families. It is important to find effective methods of providing information to the public in order to correct this deficiency in knowledge. By discussing rabies and other pet-associated zoonoses with their clients, physicians, veterinarians and other public health officials could begin to bridge this gap.

CHAPTER IV

A COMMUNITY-BASED STUDY TO EXAMINE THE EPIDEMIOLOGY OF HUMAN CYSTIC ECHINOCOCCOSIS IN RIO NEGRO PROVINCE, ARGENTINA[*]

4.1. INTRODUCTION

Cystic echinococcosis (CE) is a zoonotic disease caused by the larval stage of *Echinococcus granulosus*, a taeniid cestode with a worldwide geographical distribution (Eckert et al., 2001). *E. granulosus* is usually transmitted in a cycle between dog definitive hosts and livestock (sheep, goats, cattle and swine) intermediate hosts. Although there are multiple *E. granulosus* transmission cycles, the cycle between domestic dogs and sheep has been shown to have the greatest global public health significance (Craig et al., 2007; Eckert and Deplazes, 2004; McManus et al., 2003). Dogs acquire the infection through the ingestion of cyst-containing offal from infected livestock. *E. granulosus* eggs are shed into the environment with the dogs' feces, contaminating the surrounding soil, water, and pastures. Livestock become infected when they ingest the eggs

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[*]Reprinted with permission from "A community-based study to examine the epidemiology of human cystic echinococcosis in Rio Negro Province, Argentina" by Bingham, G.M., Budke, C.M., Larrieu, E., Del Carpio, M., Mujica, G., Slater, M.R., Moguillansky, S., 2014. *Acta Tropica,* 136, 81-88, Copyright [2014] by Elsevier B.V.

while grazing on contaminated pastures. Human infection typically occurs as a result of consuming contaminated food or water. Other routes of infection include handling infected dogs, feces from infected dogs, contaminated vegetation, or contaminated soil, followed by direct hand-to-mouth transfer. Once ingested by an intermediate host, *E. granulosus* eggs hatch in the small intestine, releasing oncospheres, which penetrate the intestinal wall, and are subsequently transported via the circulatory system to the organs, where cyst development occurs (Craig and Larrieu, 2006; Eckert and Deplazes, 2004; Moro and Schantz, 2009).

Human CE is typically characterized by slow growing, unilocular cysts which are most commonly located in the liver (~70%), or the lungs (~20%), but can also occur in other organs and tissues (Eckert et al., 2001; McManus et al., 2003). During the initial phase of infection, *E. granulosus* cysts are small, well encapsulated, and not associated with morbidity. Due to the slow-growing nature of the cysts, infected individuals may remain asymptomatic for months, years, or even permanently (Eckert and Deplazes, 2004; McManus et al., 2003). CE typically remains asymptomatic until the cyst grows large enough to exert pressure on neighboring organs or other tissues, ruptures, or develops complications such as secondary infection. The clinical presentation of CE is highly variable, and depends on the size and location of the cyst. While symptoms often resemble those of a space-occupying lesion, anaphylaxis may occur if a cyst ruptures, and fever and pain typically occur in conjunction with secondary bacterial infection (Eckert et al., 2001; McManus et al., 2003; Moro and Schantz, 2009).

In humans, CE is diagnosed primarily based on imaging techniques, such as ultrasound, conventional radiography, computed tomography, and magnetic resonance imaging (Brunetti et al., 2010; Eckert and Deplazes, 2004). Ultrasound examination is one of the preferred methods for diagnosing CE in abdominal locations, while conventional radiography is typically used to diagnose pulmonary CE (Brunetti et al., 2010). Ultrasonography is considered a safe, reliable, and cost-effective method for diagnosing the disease at both the individual and community levels (Brunetti et al., 2010; Eckert and Deplazes, 2004; Macpherson et al., 2003).

Cystic echinococcosis is an important public health and economic concern in many areas throughout the world, with the greatest impact occurring in agricultural and pastoral regions (Eckert and Deplazes, 2004; Moro and Schantz, 2009). As is the case in other South American countries, including Brazil, Chile, Peru, and Uruguay, CE is endemic in Argentina (Craig and Larrieu, 2006; Moro and Schantz, 2006; Moro and Schantz, 2009). Rio Negro Province is in the Patagonia region of southern Argentina, which is one of the most severely impacted areas in South America (Larrieu et al., 2004a; Moro and

Schantz, 2006; Pierangeli et al., 2007). Due to the climate and geography of Rio Negro Province, extensive livestock production is an important sector of the provincial economy.

In Argentina, healthcare providers are required to report all newly diagnosed human CE cases to the Ministry of Health (Ministerio de Salud, 2009). In Rio Negro Province, the provincial CE control program screens schoolchildren between 6 and 14 years of age for the presence of CE (Del Carpio et al., 2009). However, adults are not routinely screened for the disease, and there are no recently published community-based studies for Rio Negro Province. As a result, the current prevalence of CE and the risk factors associated with the disease, particularly among the adult population, in Rio Negro Province, are not known. Therefore, a community-based screening survey was conducted in a highly endemic region of Rio Negro Province in order to obtain current data, which can be used by program coordinators to evaluate, and potentially improve the present CE control program in this region of the province.

Abdominal ultrasonography was used to evaluate the prevalence of human CE, and a questionnaire was incorporated to identify locally relevant risk factors for human infection in this population. While both children and adults were included in the abdominal ultrasound portion of the study, the questionnaire was designed to focus on adults due to the overall lack of available risk factor data for this demographic.

4.2. MATERIALS AND METHODS

4.2.1. Study area

The study was conducted in Ingeniero Jacobacci, in southern Rio Negro Province, Argentina. Ingeniero Jacobacci is a small town with a population of approximately 8,000 individuals. Extensive livestock production is the primary agricultural activity, in this area, with sheep and goats being the most common livestock species. Other important economic activities, in the region, include the meat processing and mining industries. Ingeniero Jacobacci has one hospital, tasked with serving people in a catchment area of approximately 15,520 km2, and 6 healthcare outposts. Nurses, paramedics, and other clinical officers, who staff the healthcare outposts, provide basic primary care to residents (Del Carpio et al., 2012). The climate and geography of the area can make travel difficult, as many of the roads are unpaved and winters can be very harsh. Therefore, the healthcare outposts are set up to make healthcare more accessible to residents of Ingeniero Jacobacci.

4.2.2. Study design

In October 2009, all residents of Ingeniero Jacobacci were invited to participate in a community-based cross sectional CE screening survey, which incorporated abdominal ultrasonography, thoracic radiography, and a questionnaire. In order for the screening survey to be accessible to a greater proportion of the population, the study was conducted in 4 locations in Ingeniero Jacobacci, including the hospital and 3 healthcare outposts.

All study participants were examined via abdominal ultrasound for the presence of cysts compatible with a diagnosis of CE. Study participants who received a CE-positive diagnosis, based on the abdominal ultrasound examination, were also examined using thoracic radiography. All study participants who were found to be positive for CE, based on diagnostic imaging, were referred to a physician for follow-up and treatment, in accordance with the guidelines set by the Ministry of Health for Rio Negro Province (Del Carpio et al., 2009). All adults (≥ 18 years of age), who participated in the study, were asked to complete an epidemiological questionnaire before their abdominal ultrasound examination. The adult study participants who were found to be CE-positive, and completed the questionnaire, formed the “CE-positive” group, while the CE-negative adults who completed the questionnaire, were included in the “CE-negative” group.

4.2.3. Diagnostic imaging

All abdominal ultrasound examinations were performed by experienced physicians using two SonoSite Titan portable ultrasound machines with 2-5 MHz curved array transducers (SonoSite, Bothell, WA, USA). With participants in the supine position, the entire abdominal cavity was scanned in four basic planes, as described by Del Carpio et al. (2012). Ultrasonographic evidence of cysts was categorized based on the World Health Organization Informal Working Group on Echinococcosis (WHO-IWGE) recommended ultrasound classification system for CE, which classifies cysts as active (CE1 and CE2), transitional (CE3), or inactive (CE4 and CE5) based on their appearance (Brunetti et al., 2010; WHO, 2003). In addition, because the guidelines used for treating asymptomatic cases of CE, set forth by the Ministry of Health, are based on the diameter of the cyst, the diameter of each cyst was recorded (Ministerio de Salud, 2009). Anteroposterior and lateral thoracic radiographs were obtained using Dinan 500/125 radiographic imaging equipment (Rayos X Dinan, Buenos Aires, Argentina). A radiologist examined all radiographic images for the presence of pulmonary cysts compatible with a diagnosis of CE.

4.2.4. Questionnaire

A structured questionnaire was designed with guidance from physicians, veterinarians, epidemiologists, and local public health experts. The questionnaire was administered in Spanish, after being translated from English into Spanish and then back-translated into English by native Spanish speakers in the study region. A trained interviewer administered the questionnaire, verbally, to all adult (≥ 18 years of age) study participants, in order to reduce issues associated with the inability to read or comprehend the content of the questions.

The first section of the questionnaire was used to obtain basic demographic information about the survey participants, including age, sex, level of education, and employment status. To further examine socioeconomic status, questions regarding whether participants had health insurance, and if they received government financial assistance were also included.

The second group of questions examined the participants' exposure to potential risk factors for CE. Survey participants were asked questions pertaining to current and childhood dog ownership, including whether they owned dogs and the number of dogs owned. Individuals who reported owning one or more dogs at the time in which the study took place were asked if the dogs ever visited agricultural areas and if the dogs were allowed to consume raw livestock viscera. Participants were also asked if they had ever lived in an agricultural area, if they currently lived in an agricultural area, and if they visited agricultural areas. All participating individuals were asked about their primary water source at the time of the study, as well as during childhood, whether they owned or worked with sheep, and if they participated in home or field livestock slaughter practices. Finally, participants were asked if there was a history of CE among members of their family. All questionnaires were administered prior to ultrasound diagnosis. As a result, the study participant's CE status was not known at the time in which the questionnaire was administered, helping to limit bias.

4.2.5. Ethical considerations

Informed consent was obtained from all adult survey participants and from a parent for each participating child, prior to their participation in the study. Each study participant was assigned a unique identification number, which was used to maintain participant confidentiality. Study participation was voluntary and participants could decline to participate in any portion of the study. This study was reviewed and approved by the Medical Committee of the Hydatidosis Control Program in Rio Negro Province and the Texas A&M University Institutional Review Board.

4.2.6. Data analysis

All diagnostic imaging and questionnaire results were entered into Excel spreadsheets (Microsoft Corp., Redmond, WA). Data analyses were performed using Stata version 12.1 (Stata Corp., College Station, TX, USA). Diagnostic imaging results were used to compare the CE prevalence of the children, living in the study area, with the CE prevalence of the adult population.

Descriptive statistics were calculated for each of the demographic and risk factor variables examined in the questionnaire. Variables were stratified based on CE status and bivariate analyses were conducted using chi-square ($\chi 2$) and Fisher's exact tests, as appropriate. The "don't know/refused" responses were included as a separate category in all analyses. Those variables with a *p*-value of less than 0.25 were put forward for inclusion in a multivariable model (Hosmer and Lemeshow, 2000). For the multivariable model, level of education was collapsed into two groups (less than completed primary; completed primary or higher) because the data indicated that there was a significant difference between these groups.

The multivariable logistic regression model was developed using forward stepwise variable selection, assessing the statistical significance of the inclusion of each variable using likelihood ratio tests ($p < 0.05$). The model was tested for interactions between pair-wise combinations of all variables that remained in the model. The fit of the final model was assessed using the Hosmer–Lemeshow goodness-of-fit test. The standardized Pearson residuals, deviance residuals and deviance $\chi 2$ were used to assess the model for outliers, while leverage and delta-betas were calculated to determine if there were any covariate patterns with values high enough to cause concern (Dohoo et al., 2009).

4.3. RESULTS

4.3.1. Descriptive statistics

A total of 560 individuals volunteered to participate in the study. None of the study participants indicated that they had previously sought care for symptoms, which may be associated with CE. All study participants were examined using abdominal ultrasound scanning. During the ultrasound examination, 7.1% (40/560) of the study participants were found to be CE-positive. Those who were diagnosed as CE-positive, based on the ultrasound examination, were subsequently examined using thoracic radiography. Evidence of pulmonary CE was detected for 5% (2/40) of these individuals. While 1.6% (3/189) of the children who participated in the study were diagnosed as CE-positive, the prevalence of CE among adult study participants was found to be even greater, at 10% (37/371). Therefore, the odds of receiving a CE-positive diagnosis were 6.87 times greater for adults than for children ($p < 0.001$). Of the 371 adults who participated in the study, 340 (91.6%) completed the questionnaire. All subsequent demographic and risk factor data refer to these 340 individuals.

Diagnostic imaging characteristics for each of the CE-positive individuals are presented in Table 4.1. The number of cysts, per CE-positive individual, ranged from 1 to 3, with a mean of 1.33 cysts, and a median of 1 cyst per person. Although the vast majority (94.3%) of identified cysts were located in the liver, two study participants had cysts in both the liver and lungs, and one individual had a single kidney cyst. Based on the WHO-IWGE ultrasound classification system for CE, 25.5% of abdominal cysts were classified as active (CE1 or CE2), 5.9% were considered transitional (CE3), and 68.6% were classified as inactive (CE4 or CE5). The average diameter of abdominal cysts was 3.6 cm (range 0.9 – 9.9 cm).

Descriptive statistics and bivariate analyses for each of the independent variables, which were examined in this study, are presented in Table 4.2. The variables which met the previously mentioned criteria ($p < 0.25$) to be further evaluated for inclusion in the multivariable model included the following: sex, age, level of education, employment status, currently living in a livestock farming area, visiting livestock farming areas, owning dogs during childhood, currently owning dogs, number of dogs currently owned, owning or working with sheep, participating in home or field slaughter of livestock, primary water source during childhood, and having health insurance.

Table 4.1
Diagnostic imaging characteristics of human cystic echinococcosis cases detected in a screening survey in Rio Negro Province, Argentina, 2009

Case Number	Age (years)	Sex	No. of Cysts	Cyst Location[a]	Size (cm)	WHO-IWGE Classification[b]
1	9	Female	1	Liver	3.9	CE1
2	14	Male	1	Liver	1.5	CE5
3	14	Male	1	Liver	3	CE4
4	19	Female	1	Liver	2.4	CE4
5	28	Female	1	Liver	4.1	CE4
6	30	Female	2	Liver	−	CE5
				Liver	−	CE4
7	32	Female	1	Liver	2.8	CE2
8	32	Male	3	Liver	−	CE5
				Liver	−	CE4
				Lung	−	−
9	34	Female	2	Liver	6	CE2
				Liver	−	CE2
10	36	Female	1	Liver	−	CE4
11	36	Female	1	Liver	5	CE1
12	37	Male	1	Kidney	4.6	CE4
13	40	Male	1	Liver	5	CE3
14	41	Female	1	Liver	2.8	CE5
15	41	Female	2	Liver	4.3	CE4
				Liver	4	CE4
16	41	Female	1	Liver	2	CE1
17	41	Male	1	Liver	9.9	CE4
18	43	Female	1	Liver	3.8	CE5
19	46	Male	1	Liver	−	CE5
20	48	Male	1	Liver	1.2	CE1
21	49	Male	1	Liver	3.9	CE3
22	49	Female	2	Liver	3	CE2
				Liver	−	CE3
23	49	Female	1	Liver	1.4	CE5
24	50	Female	1	Liver	−	CE1
25	55	Female	2	Liver	3	CE4
				Liver	6	CE5
26	58	Male	1	Liver	2.4	CE5
27	65	Female	1	Liver	3.5	CE5
28	66	Female	1	Liver	4.3	CE5
29	66	Female	2	Liver	3.5	CE4
				Liver	−	CE4

Table 4.1 (Continued)

Case Number	Age (years)	Sex	No. of Cysts	Cyst Location[a]	Size (cm)	WHO-IWGE Classification[b]
30	68	Female	1	Liver	3.9	CE4
31	68	Female	2	Liver	4.6	CE5
				Liver	4	CE5
32	70	Male	1	Liver	6	CE1
33	71	Male	1	Liver	5.4	CE4
34	72	Female	2	Liver	4.2	CE4
				Liver	1.4	CE4
35	73	Female	1	Liver	−	CE4
36	75	Female	1	Liver	4.5	CE5
37	76	Female	2	Liver	3.7	CE4
				Lung	−	−
38	79	Male	1	Liver	−	CE5
39	84	Female	1	Liver	1.6	CE5
40	87	Male	3	Liver	1.4	CE1
				Liver	0.9	CE1
				Liver	1	CE1
Mean	49.8		1.3		3.6	
Median	48.5		1		3.8	
Range	9−87		1−3		0.9−9.9	

[a] Liver and kidney cysts detected using abdominal ultrasound imaging. Lung cysts detected using conventional thoracic radiography among participants with a CE-positive diagnosis, based on abdominal ultrasound imaging.
[b] WHO-IWGE classification system for cysts detected via abdominal ultrasound imaging.
[−] Value not recorded

Table 4.2
Descriptive statistics for demographic and risk factor variables categorized on the basis of CE status for 340 adult participants in an abdominal ultrasound screening survey in Rio Negro Province, Argentina, 2009

Variable	CE Status[a]		*P*-value[b]
	Negative, *n* (%)	Positive, *n* (%)	
Sex			0.12
Male	66 (21.5)	11 (33.3)	
Female	241 (78.5)	22 (66.7)	
Age group			0.001
18-29 years	74 (24.1)	2 (6.1)	
30-39 years	78 (25.4)	5 (5.2)	
40-49 years	61 (19.9)	9 (27.3)	
50-59 years	43 (14)	3 (9.1)	
60-89 years	41 (13.4)	14 (42.4)	
Don't know/Refused	10 (3.3)	0 (0)	
Education			< 0.0001
None	35 (11.4)	6 (18.2)	
Primary (incomplete)	54 (17.6)	16 (48.5)	
Primary (complete)	114 (37.1)	8 (24.2)	
≥ High school	86 (28)	1 (3)	
Don't know/Refused	18 (5.9)	2 (6.1)	
Employed			0.23
No	177 (57.7)	24 (72.7)	
Yes	119 (38.8)	8 (24.2)	
Don’t know/Refused	11 (3.6)	1 (3)	
Family history of CE			0.27
No	228 (74.3)	21 (63.6)	
Yes	69 (22.5)	10 (30.3)	
Don't know/Refused	10 (3.3)	2 (6.1)	
Has ever lived in livestock farming area			0.34
No	110 (35.8)	8 (24.2)	
Yes	179 (58.3)	22 (66.7)	
Don't know/Refused	18 (5.9)	3 (9.1)	
Currently lives in livestock farming area			0.17
No	258 (84)	24 (72.7)	
Yes	17 (5.5)	3 (9.1)	
Don't know/Refused	32 (10.4)	6 (11.2)	
Visits livestock farming area			0.14
No	131 (42.7)	18 (54.6)	
Yes	146 (47.6)	10 (30.3)	
Don't know/Refused	30 (9.8)	5 (15.2)	
Owned dogs during childhood			0.18
No	33 (10.8)	7 (21.2)	
Yes	153 (49.8)	13 (39.4)	
Don't know/Refused	121 (39.4)	13 (39.4)	

Table 4.2 (Continued)

Variable	CE Status[a]		*P*-value[b]
	Negative, *n* (%)	Positive, *n* (%)	
Number of dogs owned during childhood			0.36
0	33 (10.7)	7 (21.2)	
1	30 (9.8)	2 (6.1)	
2 or more	123 (40.1)	11 (33.3)	
Don't know/Refused	121 (39.4)	13 (39.4)	
Currently owns dogs			0.05
No	60 (19.5)	9 (27.3)	
Yes	210 (68.4)	16 (48.5)	
Don't know/Refused	37 (12.1)	8 (24.2)	
Number of dogs currently owned			0.003
0	60 (19.5)	9 (27.3)	
1	95 (30.9)	13 (39.4)	
2 or more	115 (37.5)	3 (9.1)	
Don't know/Refused	37 (12.1)	8 (24.2)	
Currently owned dogs visit farming area			0.78
No	144 (68.6)	10 (62.5)	
Yes	43 (20.5)	4 (25)	
Don't know/Refused	23 (10.9)	2 (12.5)	
Not applicableC	97	17	
Feeds raw offal to currently owned dogs			0.99
No	127 (60.5)	10 (62.5)	
Yes	65 (30.9)	5 (31.3)	
Don't know/Refused	18 (8.6)	1 (6.3)	
Not applicableC	97	17	
Owns or works with sheep			0.004
No	166 (54.1)	17 (51.5)	
Yes	123 (40.1)	9 (27.3)	
Don't know/Refused	18 (5.9)	7 (21.2)	
Participates in home slaughter of livestock			0.04
No	131 (42.7)	14 (42.4)	
Yes	151 (49.2)	12 (36.4)	
Don't know/Refused	25 (8.1)	7 (21.2)	

Table 4.2 (Continued)

Variable	CE Status[a]		*P*-value[b]
	Negative, *n* (%)	Positive, *n* (%)	
Current primary water source			0.54
Tap	259 (84.4)	28 (84.9)	
Well	23 (7.5)	1 (3)	
Surface	11 (3.6)	1 (3)	
Don't know/Refused	14 (4.6)	3 (9.1)	
Primary water source during childhood			0.21
Tap	85 (27.7)	4 (12.1)	
Well	120 (39.1)	15 (45.5)	
Surface	30 (9.7)	3 (9.1)	
Don't know/Refused	72 (23.5)	11 (33.3)	
Receives government financial assistance			0.31
No	204 (66.5)	18 (54.6)	
Yes	97 (31.6)	14 (42.4)	
Don't know/Refused	6 (1.9)	1 (3)	
Has health insurance			0.1
No	160 (52.1)	14 (42.4)	
Yes	143 (46.6)	17 (51.5)	
Don't know/Refused	4 (1.3)	2 (6.1)	

[a] CE Status; 33/340 (9.7%) of survey participants received a CE-positive diagnosis.

[b] All *P*-values calculated using χ^2 or Fisher's exact test, as appropriate.

[c] Analysis includes only individuals who reported currently owning at least one dog.

Table 4.3
Multivariable logistic regression model of factors associated with a CE-positive diagnosis[a] among adult participants in a cystic echinococcosis screening survey in Rio Negro Province, Argentina, 2009

Variable	Odds ratio	95% CI	*P*-value of category
Age group			
18-29 years	1.0 (ref.)		
30-39 years	2.58	0.45-14.91	0.29
40-49 years	5.66	1.05-30.48	0.04
50--59 years	1.53	0.22-10.86	0.67
60-89 years	7.09	1.23-40.75	0.02
Education			
Completed primary or higher	1.0 (ref.)		
Less than completed primary	3.78	1.40-10.20	0.009
Don't know/Refused	2.27	0.34-15.05	0.39
Number of dogs currently owned			
0	1.0 (ref.)		
1	0.99	0.36-2.76	0.99
2 or more	0.15	0.04-0.66	0.01
Don't know/Refused	1.05	0.29-3.81	0.94
Owns or works with sheep			
No	1.0 (ref.)		
Yes	0.6	0.23-1.52	0.28
Don't know/Refused	4.77	1.29-17.77	0.02

[a] CE-positive or CE-negative diagnosis based on abdominal ultrasound.

[b] N = 330 observations, likelihood ratio chi-square = 50.6, $p < 0.0001$; Hosmer-Lemeshow goodness-of-fit test $p = 0.64$.

4.3.2. Multivariable logistic regression

As shown in Table 4.3, in the final multivariable model, CE status was significantly ($p < 0.05$) associated with the participant's age, level of education, the number of dogs that they owned at the time of the study, and their response to a question regarding whether or not they owned or worked with sheep. Individuals between 40 and 49 years of age, and those who were greater than 59 years of age were significantly more likely to be CE-positive than those who were in the 18-29 year age grouping. Study participants who had less than a primary school level of education were also significantly more likely to be CE-positive. In addition, those who either did not know, or refused to answer, whether or not they owned or worked with sheep were significantly more likely to be CE-positive. However, owning 2 or more dogs significantly decreased the likelihood of being CE-positive.

When the model was examined for interactions between pair-wise combinations of the included variables, there was not substantial correlation in the data that needed to be accounted for in the model. There were no covariate patterns that had values high enough to cause concern, indicating that there were not any individual covariate patterns that had excessive influence on the model.

4.4. DISCUSSION

In 1980, in an effort to reduce the rates of *E. granulosus* infection in the human and animal populations, the provincial government of Rio Negro Province implemented an echinococcosis control program. The program focused on providing health education to the public, systematically deworming dogs using praziquantel, and regulating livestock slaughter practices (Larrieu et al., 2000b). In addition, the program sought to improve the prognosis of CE patients, particularly children, through the use of screening procedures to detect the disease during its early stages. From 1980 to 1996, serological testing was the primary method of screening for CE (Larrieu et al., 2000b). Abdominal ultrasound became the Rio Negro Province echinococcosis control program's preferred screening method in 1997 (Frider et al., 2001; Larrieu et al., 2004b). Prior to initiating the program, in 1980, the prevalences of canine and ovine infection were estimated to be 41.5 and 61 percent, respectively, while the annual incidence of human cases was estimated to be 73 cases per 100,000 members of the population of Rio Negro Province (Larrieu et al., 2000a; Larrieu et al., 2000b). According to the most recently published comprehensive livestock studies from the region, in 1998, the prevalences of canine and ovine infection were estimated to be 2.3 and 18 percent, respectively (Larrieu et al., 2000a; Larrieu et al., 2000b).

In 2009, the reported annual incidence of human CE cases in Rio Negro Province was approximately 9.16 cases per 100,000 members of the population (Ministerio de Salud, 2013). However, since CE is a chronic disease with a lengthy asymptomatic period, it is likely that many cases are not detected because the individuals do not seek care for their illness. Therefore, the true incidence of CE in Rio Negro Province is likely to be much greater than that which is officially reported. In the present study, the prevalence of CE among study participants was found to be 7.1%. Although there are no recently published studies of CE prevalence in this area, which could be used for comparison, it should be noted that this study was conducted in a region of Rio Negro Province in which CE has been shown to be highly endemic. Therefore, the prevalence of CE found here is not representative of the CE prevalence for the entire province. In addition, because the study participants were volunteers from the local community, we cannot make the assumption that the CE prevalence obtained in this study reflects the true prevalence of CE in Ingeniero Jacobacci. However, it should be noted that even if the cases detected in this study were the only cases of CE in Ingeniero Jacobacci, the CE prevalence in this community would still be very high, at 0.5% (40/8000) of the population. In addition, because pulmonary cysts cannot be diagnosed via ultrasound, and it is not ethical to radiograph healthy populations, it is possible that some cases of pulmonary CE were not detected among study participants.

It should also be noted that because CE is a disease, which frequently has a lengthy duration, but is typically not fatal, the prevalence of the disease would greatly exceed its incidence in any endemic region. Although the majority (68.6%) of the cysts detected in this study were classified as inactive (CE4 or CE5) which may indicate less recent transmission, 31.4% of the cysts were classified as either active (CE1 or CE2) or transitional (CE3), based on the WHO-IWGE classification system (WHO, 2003), indicating that there is likely to be ongoing transmission of CE in the study region. This is further confirmed by the fact that 1.6% of the children who were examined were found to be CE-positive. While the prevalence of CE among children was much lower than the prevalence among adults, detecting the disease in children provides evidence of recent transmission. Therefore, while the CE control program has dramatically reduced the rates of human and animal infection, in Rio Negro Province, CE continues to be a significant problem in this region of Argentina (Craig and Larrieu, 2006; Larrieu et al., 2000a; Larrieu et al., 2000b; Larrieu et al., 2004b; Larrieu and Zanini, 2012; Ministerio de Salud, 2009; Moro and Schantz, 2006).

It is important to understand the epidemiological risk factors, which are potentially facilitating the transmission of *E. granulosus* to humans in Rio Negro Province. It has been suggested that factors such as age, gender, level of education, employment status, having a surface water supply, living in or visiting rural areas, owning dogs (particularly large numbers of dogs), owning dogs during childhood, and having a family history of CE are associated with an increased risk for human CE (Campos-Bueno et al., 2000; Carmona et al., 1998; Dowling et al., 2000; Dowling and Torgerson, 2000; Larrieu et al., 2002; McManus et al., 2003; Moro et al., 2008). However, the findings are not consistent between studies because each of the studies examined a different combination of risk factors for inclusion in their models.

Although, in the present study, sex of the participant was not found to be significantly associated with a CE-positive diagnosis, it should be mentioned that approximately 77% of the study participants were female. It is possible that fewer men were available to be examined during the working day, leading to the lower level of participation among men. As has been shown in other studies, the likelihood of being CE-positive in this population increased with age. However, there was one exception. The likelihood of receiving a CE-positive diagnosis for individuals who were between 50 and 59 years of age did not differ significantly from that of individuals in the 18-29 years age group. Although the reason for this is not clear, it may be due to the small number of people in this age group. There was also a significant association between level of education and CE status, with individuals having less than a primary school level of education being 3.8 times as likely to be CE-positive as those who had a greater level of education.

While other studies have demonstrated a connection between CE and socioeconomic factors such as employment status, none of the socioeconomic factors examined in the present study were significantly associated with CE status. There was not a significant association between CE status and current primary water source, primary water source during childhood, or visiting rural areas. In addition, in this study, neither childhood dog-ownership nor having a family history of CE significantly increased the likelihood of being CE-positive. It should be noted that the quality of the data, obtained from the questions regarding childhood exposures, is determined by the participants' ability to accurately recall these exposures. Since the participants were not aware of their CE status at the time in which they completed the questionnaire, the ability to accurately recall past exposures is not likely to differ based on CE status. Non-differential misclassification of the exposure typically decreases the strength of the association between the exposure and the disease. Therefore, the participants' inability to recall information may have resulted in an underestimation of the association between CE status and some of the childhood exposure variables examined in this study.

According to previous reports, close contact between humans, dogs, and livestock, home slaughter of adult sheep for human consumption, and feeding raw offal to dogs are widespread practices, which may help to maintain the *E. granulosus* transmission cycle in Rio Negro Province (Craig and Larrieu, 2006;

Larrieu et al., 2000a; Larrieu et al., 2000b). Although owning or working with sheep was not found to be significantly associated with CE status, individuals who refused to answer the question were significantly more likely to be CE-positive than those who did not own or work with sheep. The reason for this association is not entirely clear. However, it is possible that failure to answer this question is a confounding variable, which represents a risk factor that was not identified in this study. Thirty-one percent of the study participants, who owned dogs at the time in which the study took place, stated that they fed raw offal to their current dogs. However, CE-positive and CE-negative individuals did not differ significantly with respect to feeding raw offal to their current dogs. Since it is common for individuals to become infected years before the disease is diagnosed, it is possible that some of the study participants have changed their behavior over time so that current feeding of dogs did not indicate previous feeding of offal to dogs. Although the practice of home slaughter of livestock was significantly associated with being CE-positive in the univariable analysis, it did not remain in the multivariable model. A significant association between current dog ownership and CE status was demonstrated in this study. Although the CE status of participants who owned one dog did not differ from those who did not own dogs, individuals who owned two or more dogs were significantly less likely to be CE-positive. The reason for this association is not known. However, it is possible that the individuals who owned more dogs were taking additional precautions to prevent the disease. It could also be due to the number of participants who did not know or did not answer the dog ownership question.

4.5. CONCLUSIONS

The present study demonstrates that community-based abdominal ultrasound screening surveys can provide important information about the prevalence of CE as well as factors, which may be associated with an increased risk for the disease in endemic regions. In addition, because this is the only recent study that has examined the prevalence of CE and the risk factors associated with infection in adults, in Rio Negro Province, it adds valuable information to the existing body of knowledge about CE in this region. In Rio Negro Province, the CE control program has been able to successfully decrease the reported annual incidence of CE from 73 cases per 100,000 in 1980, to 9.16 cases per 100,000 in 2009. However, the results of this study indicate that members of the population continue to be exposed to the parasite and new cases of CE are still occurring. Therefore, it is important to continue efforts to combat the disease in this region of Argentina.

CHAPTER V

THE ECONOMIC IMPACT OF CYSTIC ECHINOCOCCOSIS IN RIO NEGRO PROVINCE, ARGENTINA

5.1. 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 (McManus et al., 2003). In humans, CE remains asymptomatic until the cyst either ruptures or becomes large enough to exert pressure on the surrounding tissues. While 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 (Eckert and Deplazes, 2004). Although livestock do not typically exhibit visible clinical signs of disease, livestock infection can have substantial economic consequences, as a result of condemnation of infected offal and decreased productivity (Torgerson, 2003).

E. granulosus is endemic throughout much of South America, with the highest reported prevalences occurring in portions of Argentina, Peru, Uruguay, Chile, and Brazil (Eckert et al., 2001; Craig and Larrieu, 2006). The Patagonia region of Argentina, which includes Rio Negro Province, is one of the most substantially affected regions in South America (Larrieu et al., 2000a; Craig and Larrieu, 2006). Due to the climate and geography of Rio Negro Province, one of the principal economic activities in this area is extensive livestock farming (Larrieu et al., 2000b). 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 (Larrieu et al., 2000a; McManus et al., 2003; Craig and Larrieu, 2006).

In 1980, the provincial government of 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 prevalences of canine and ovine infection were estimated to be 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. The program provided education to the public, tested and dewormed dogs, and screened children for CE using abdominal ultrasound examination and serological testing. In 1997, the prevalences of canine and ovine infection were estimated to be 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 (Larrieu et al., 2000a; Larrieu et al., 2000b). Although this program appears to have dramatically reduced both human cases and animal infections, CE is still a significant agricultural and public health problem in this region of Argentina (Larrieu et al., 2000a; Larrieu et al., 2000b; Frider et al., 2001; Larrieu et al., 2004b; Craig and Larrieu, 2006; Larrieu and Zanini, 2012).

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 (McManus et al., 2003; Eckert and Deplazes, 2004; Budke et al., 2006; Craig and Larrieu, 2006). 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 (Torgerson, 2003; Carabin et al., 2005).

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 decreased productivity (Eckert et al., 2001; Torgerson, 2003). 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 (Torgerson et al., 2000; Torgerson et al., 2001; Budke et al., 2005; Majorowski et al., 2005; Benner et al., 2010; Moro et al., 2011; Harandi et al., 2012), this is the first such assessment to be conducted in Rio Negro Province.

5.2. METHODS

5.2.1. 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 (Instituto Nacional de Estadística y Censos (INDEC), 2012). The province has a population density of approximately 3.1 inhabitants per km^2, which is one of the lowest in the country (Instituto Nacional de Estadística y Censos (INDEC), 2012). The economy in this region relies heavily upon extensively raised livestock, with sheep being the most 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 total (Ministerio de Agricultura Ganadería y Pesca (MAGyP), 2011).

5.2.2. Human epidemiological data

5.2.2.1. 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 (Instituto Nacional de Estadística y Censos (INDEC), 2012). The reported annual incidence of human CE for the population of Rio Negro Province, as well as the annual mortality attributable to human CE in Rio Negro Province, were obtained from official government sources (Argentina Ministerio de Salud (MSAL), 2013). These values are presented in Table 5.1.

5.2.2.2. Hospital chart reviews

In order 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, while the hospital located in Ingeniero Jacobacci was classified as a rural hospital (Del Carpio et al., 2012).

Table 5.1
Epidemiological information used to estimate the indirect costs associated with human CE in Rio Negro Province, Argentina

Parameter	Value	Units	Reference[a]
Population of Rio Negro Province, 2010	638,645	Individuals	INDEC, 2012
Reported annual incidence of CE	6.43	Individuals/10^5	MSAL, 2013
Annual CE-attributable mortality	0.5	Individuals/10^5	MSAL, 2013
Proportion 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
Modes of transportation			
Private car	28.3	Percent	Patient Data
Public transportation	54.2	Percent	Patient Data
Ambulance	17.5	Percent	Patient Data

[a] MSAL: Argentina Ministerio de Salud; INDEC: Instituto Nacional de Estadística y Censos

Although there were other healthcare facilities, such as clinics, in each of these towns, the hospitals included in this study were the primary treatment facilities for CE in each of their respective locations. The participating hospitals provided access to the medical records of their CE patients, whose diagnosis had been confirmed using imaging and/or serological techniques.

Medical charts were requested for all patients who presented to one of 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), nonsurgical treatment, 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. Separate forms were used for each hospital admission and outpatient visit, allowing us to quantify the total number of times that each patient was treated. This 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.

5.2.2.3. Patient interviews

Patient interviews were conducted in order to collect information, needed to estimate the economic burden of CE on treatment-seeking individuals, which could not be obtained from the hospital chart reviews. The information obtained from these interviews was used to estimate the indirect costs associated with illness and treatment for CE patients in Rio Negro Province. 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. Patients who could be reached, and were willing to be interviewed, were asked a series of questions related to their illness and treatment. When 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 daily activities due to CE-associated illness during the previous year. In addition, patients were asked about the distance between their home and the hospital, the mode of transportation typically used when traveling to obtain treatment, and the number of family members who typically accompany them to obtain treatment.

5.2.2.4. Treatment-seeking cases

It was assumed that the patients, who received treatment in the study hospitals, were representative of the spectrum of typical treatment-seeking CE patients in Rio Negro Province. In addition, the age and sex distribution, treatment method (surgical versus non-surgical), and average duration of treatment, for CE cases treated in the study hospitals, were used to represent those of all CE patients who received treatment in Rio Negro Province. The number of CE cases under care, annually, in Rio Negro Province was estimated by multiplying the average duration of treatment, for CE cases treated in the study hospitals, by the officially reported incidence of CE in the province.

5.2.2.5. Undiagnosed/non-healthcare seeking cases

There is evidence that individuals with CE begin to experience productivity losses, prior to the time in which they seek medical care (Budke et al., 2004). 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, we needed to first estimate the number of undiagnosed individuals in the population. Due to the degree of uncertainty in this estimate, a uniform distribution (0.4%–1.84%) was used to estimate 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 which examined schoolchildren, between 6 and 14 years of age, throughout Rio Negro Province over a nine-year period (2000-2008) (Larrieu et al., 2011). The study reported that 0.4% of asymptomatic children had CE based on an abdominal ultrasound (Larrieu et al., 2011). The maximum value for the uniform distribution was calculated by incorporating data obtained from 1) the study of schoolchildren (Larrieu et al., 2011), 2) a community-based CE screening study conducted in 2009 (Bingham et al., 2014), and 3) the age distribution of the population in Rio Negro Province (Instituto Nacional de Estadística y Censos (INDEC), 2012). 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%) (Bingham et al., 2014). The estimated prevalence of undiagnosed CE among the adult population, 2.5%, was calculated by multiplying the province-level results for children (0.4%) by 6.25. When these values were applied to the age distribution of the population of Rio Negro Province, the prevalence of undiagnosed CE was estimated to be 1.84%.

5.2.3. Estimation of costs associated with human CE

5.2.3.1. 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 medication. Medication prices were obtained from a searchable online medication database (Manual Farmacéutico, 2011). For all other items, fees were obtained from the official patient fee schedule used by all public hospitals in Rio Negro Province. These costs are presented in Table 5.2.

All direct costs were calculated based on individual patient care data. Patients were categorized into treatment groups based on the type of treatment that they received, surgical or nonsurgical. Then, separate cost estimates were calculated for each treatment group. The average annual cost per patient, in each treatment group, was then applied to the number of patients under care, annually, within each of their respective treatment groups. Costs were converted from Argentine pesos (ARS) to U.S. dollars (US$) using the official exchange rate for 2010, of 3.91 ARS to 1 US$, which is calculated as an annual average based on monthly averages (The World Bank, 2011a).

5.2.3.2. Indirect costs

The indirect costs included 1) lost wages during treatment and convalescence, 2) lost wages for days that patients were unable to work or attend to their daily activities due to CE-associated illness 3) lost wages due to CE-associated mortality, and 4) costs incurred for travel to receive treatment.

Table 5.2
Procedure costs used to estimate the direct costs associated with human CE in Rio Negro Province, Argentina

Procedure	Cost/Procedure (US$)	Mean Frequency/Patient[e]
Outpatient consultation	3.85	2.60
Laboratory procedures		
Level 1[a]	0.64	5.04
Level 2[b]	1.60	0.80
Level 3[c]	2.56	0.32
Level 4[d]	4.81	1.16
Diagnostic imaging		
Thoracic radiography	6.67	0.29
Ultrasonography	8.97	1.47
Computed tomography (CT)	22.44	0.22
Magnetic resonance imaging (MRI)	44.87	0.01
Other		
Electrocardiogram (EKG)	6.67	0.18
Pulmonary function test	57.69	0.07

[a] Level 1: Complete blood count (CBC), blood glucose, blood creatinine, blood urea nitrogen (BUN), coagulation time, or urinalysis
[b] Level 2: Electrolyte panel or partial thromboplastin time (PTT)
[c] Level 3: Arterial blood gas analysis, pleural fluid analysis, sputum culture, or ELISA
[d] Level 4: Hepatic function panel
[e] The average number of procedures per patient, per year.

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. 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 for CE. Travel costs and wage losses were calculated for the patients as well as the family members who accompanied the patients to obtain treatment.

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 (EAHU) for the 4th quarter of 2010 (Instituto Nacional de Estadística y Censos (INDEC), 2011). Activity and employment rates, stratified by sex and age, were also obtained from the EAHU (Instituto Nacional de Estadística y Censos (INDEC), 2011). A 100% loss of daily wages was assumed for the duration of the treatment and convalescent periods for all adults with full-time employment. 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 30-39 year old female were assumed for the duration of the treatment and convalescence periods.

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" (Majorowski et al., 2005; Harandi et al., 2012). The inactive sector of the population included 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 5.3. Based on the estimates used in other studies, all undiagnosed cases of CE were assumed to experience a 0-5% reduction in annual productivity (Torgerson et al., 2000; Torgerson et al., 2001; Benner et al., 2010).

Travel costs were estimated based on 1) the mode of transportation (private car, public transportation, or ambulance), 2) the proportion of patients who used each mode of transportation, 3) average distance between the patient's home and the hospital, and 4) the number of family members accompanying the patient. Costs were estimated for each mode of transportation, based on the average cost per kilometer, for that mode of transportation. Fuel costs were used to estimate costs for patients who traveled by private car (The World Bank,

Table 5.3
Employment and wage data used to estimate the indirect costs associated with human CE in Rio Negro Province, Argentina

Parameter	Value	Units	Reference[a]
Employment status of the adult male population			
Employed	72.3	Percent	INDEC, 2011
Unemployed	5.1	Percent	INDEC, 2011
Inactive	22.6	Percent	INDEC, 2011
Employment status of the adult female population			
Employed	44.9	Percent	INDEC, 2011
Unemployed	6.0	Percent	INDEC, 2011
Inactive	49.1	Percent	INDEC, 2011
Mean monthly wage for employed males, by age			
18–29	415.64	US$	INDEC, 2011
30–39	658.19	US$	INDEC, 2011
40–49	674.35	US$	INDEC, 2011
50–59	567.56	US$	INDEC, 2011
≥ 60	570.03	US$	INDEC, 2011
Total	568.62	US$	INDEC, 2011
Mean monthly wage for employed females, by age			
18–29	358.44	US$	INDEC, 2011
30–39	534.38	US$	INDEC, 2011
40–49	575.01	US$	INDEC, 2011
50–59	598.81	US$	INDEC, 2011
≥ 60	371.22	US$	INDEC, 2011
Total	502.82	US$	INDEC, 2011

[a] INDEC: Instituto Nacional de Estadística y Censos

2011b), while bus fares were used to estimate costs for patients who traveled using public transportation (Ministerio del Interior y Transporte (MIyT), 2013). The hospital fee schedule was used to estimate the travel costs for patients who were transported to the hospital by ambulance.

5.2.4. Livestock epidemiological data

In Rio Negro Province, sheep, goats, and cattle 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 size and age distribution of the population and the numbers of animals slaughtered each year were obtained from official government reports (Ministerio de Agricultura Ganadería y Pesca (MAGyP), 2011). The prevalence of CE, at slaughter, was obtained from officially reported values (Servicio Nacional de Sanidad y Calidad Agroalimentaria (SENASA), 2012). Although prevalence values were available for cattle and sheep, values were not reported for goats. Therefore, the reported prevalence of CE in sheep was also used for goats. The CE prevalence values provided in government reports did not differentiate between young animals and older animals. Therefore, literature-based values were incorporated, when available, in order to account for the fact that the prevalence of CE is often much 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 wool production values were obtained from official government reports (Ministerio de Agricultura Ganadería y Pesca (MAGyP), 2011).

5.2.5. 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. Therefore, it was assumed that for each infected animal, the liver (50%), the lungs (20.6%), or both the liver and lungs (29.4%) would be condemned (Larrieu et al., 2001). The indirect costs associated with CE infected livestock included the productivity losses that have been reported in a number of other studies, with uniform distributions used to represent the uncertainty in the estimates (Torgerson et al., 2000; Torgerson et al., 2001; Budke et al., 2006; Benner et al., 2010). These losses included decreased carcass weights at the time of slaughter (2.5-10%) and decreased fecundity (0-10%) for cattle, sheep, 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 5.4.

Table 5.4
Economic parameters used to estimate the costs associated with livestock CE in Rio Negro Province, Argentina

Parameter	Value/Kg	Units	Reference[a]
Sheep			
Liver	1.64	US$	MAGyP, 2010
Lung	0.87	US$	MAGyP, 2010
Sheep carcass	3.34	US$	MAGyP, 2010
Lamb carcass	6.22	US$	MAGyP, 2010
Wool	5.02	US$	INTA, 2011
Goats			
Liver	1.64	US$	MAGyP, 2010
Lung	0.87	US$	MAGyP, 2010
Goat carcass	3.34	US$	MAGyP, 2010
Kid carcass	6.22	US$	MAGyP, 2010
Mohair	4.33	US$	INTA, 2011
Cattle			
Liver	1.32	US$	MAGyP, 2010
Lung	0.70	US$	MAGyP, 2010
Kidney	0.98	US$	MAGyP, 2010
Adult carcass	2.86	US$	MAGyP, 2010
Calf carcass	3.35	US$	MAGyP, 2010
Milk*	0.35	US$	MAGyP, 2010

* Milk prices in US$/Liter
[a] MAGyP: Ministerio de Agricultura Ganadería y Pesca; INTA: Instituto Nacional de Tecnología Agropecuaria

5.2.6. Data analysis

Separate economic 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, USA). The monetary losses were estimated using @Risk Version 6 software (Palisades Corp., Ithaca, NY, USA), as an add-in to Excel. In order to account for the uncertainty in some of the parameter estimates, a distribution was assigned to each 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, as well as 2.5 and 97.5 percentiles (95% 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. In order to model parameter uncertainty, Latin Hypercube sampling, with 20,000 iterations, was performed. Stepwise linear regression sensitivity analysis was conducted to examine the impact of each input parameter on the overall cost estimate.

5.2.7. Ethical considerations

In order to maintain patient confidentiality, a unique identification number was assigned to each patient whose records were examined for this study. This number was subsequently used on all data collection forms associated with the patient. This study 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.

5.3. RESULTS

In total, the three participating hospitals provided access to the medical records of 188 CE patients. Overall, 51.6% (97) and 48.4% (91) of the patients were female and male, respectively. Forty (21.3%) 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 5.1. Of the 188 patients, whose records were reviewed, 79 (42%) were treated at the hospital in Viedma, 55 (29.3%) patients received treatment from the hospital in Ingeniero Jacobacci, and the remaining 54 patients (28.7%) were treated at the Bariloche hospital. Surgical patients accounted for 46.8% (88) of the 188 patients whose records were reviewed. While 83.3% (45) of the patients who were treated in Bariloche, and 50.6% (40) of the Viedma patients received surgical treatment, only 3 (5.5%) of the Ingeniero Jacobacci patients were treated surgically.

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. Eighteen (52.9%) of those who were interviewed were male, and 16 (47.1%) patients were female. The patients ranged in age from 4 to 92 years, with an average age of 38. Although most of the patients were adults (25; 73.5%), a parent completed the interview for the 9 (26.5%) patients who were children. Surgical patients accounted for 64.7% (22) of the 34 patients who completed the interview.

5.3.1. Individual patient costs

The average total annual cost per patient was $5,046, for surgical patients, and $309, for nonsurgical patients. Direct costs accounted for 17.6% of the total annual costs, for surgical patients, and 23.5% of the total annual costs, for nonsurgical patients. In Viedma, the annual direct cost per patient was $838 for surgical patients, and $48 for nonsurgical patients, while in Ingeniero Jacobacci, the annual direct costs were $592 for surgical patients, and $82 for nonsurgical patients. For the patients who were treated in Bariloche, the annual direct costs for surgical and nonsurgical patients were $952 and $126, respectively.

For all surgical patients, the average duration of time under care was 2.12 years (range: 0.025 – 10.42 years). The average duration of time under care for surgical patients was 1.99 years (range: 0.027 – 10.42 years), in Viedma, 2.46 years (range: 1.77 – 3.05 years) in Ingeniero Jacobacci, and 2.22 years (range: 0.025 – 7.22 years) in Bariloche. Nonsurgical patients were under a physician's care for an average of 2.18 years (range: 0.003 – 11.22 years). In Viedma, nonsurgical patients were under a physician's care for an average of 2.45 years (range: 0.003 – 11.22 years), while nonsurgical patients in Ingeniero Jacobacci and Bariloche were monitored by a physician for 1.89 years (range: 0.003 – 9.14 years) and 2.68 years (range: 0.047 – 7.56 years), respectively.

Surgical patients were unable to work or attend to their 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 illness. Nonsurgical patients were unable to work or attend to their regular daily activities for an average of 10.25 days per year. Approximately half of those days (4.8 days) were missed due to treatment related activities, while the remaining days were due to illness. Public transportation, used by more than half of the patients, was the most common mode of transportation for CE patients to travel to the hospital (Table 5.1).

5.3.2. 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 5.5. When productivity losses attributed to non-healthcare seeking cases were included, the total cost of human CE in Rio Negro Province, Argentina, for 2010 was estimated to be $1,138,402 (95% CI: $233,649–$2,591,826). The total costs associated with human CE were estimated to be

$300,131 (95% CI: $100,701–$903,257), when losses associated with non-healthcare seeking individuals were excluded from the analysis. Indirect costs accounted for approximately 95.3% of the estimated total annual economic losses attributable to human CE when non-healthcare seeking cases were included and 82.1% of the losses when they were not included.

Table 5.5
Annual costs associated with human CE in Rio Negro Province, Argentina

Category	Mean cost (US$)	95% CI (US$)
Surgical cases		
Direct costs	49,281	17,915–145,943
Indirect costs	231,321	73,427–701,417
Total costs	280,602	93,247–847,883
Nonsurgical cases		
Direct costs	4,588	1,668–13,586
Indirect costs	14,942	4,646–45,861
Total costs	19,529	6,419–59,129
Non-healthcare seeking cases		
Indirect costs	838,271	35,104–2,223,876
Total direct costs of human CE	*53,869*	*19,582–159,529*
Total indirect costs of human CE	*1,084,533*	*203,024–2,509,464*
Total costs of human CE	**1,138,402**	**233,649–2,591,826**
Total costs of human CE*	**300,131**	**100,701–903,257**

* Excluding productivity losses associated with non-healthcare seeking cases

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 0.48 and 0.34, 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 treatment (standardized regression coefficient = 0.96) and the duration of the convalescent period (standardized regression coefficient = 0.22). For all other parameters, the standardized regression coefficients were between 0 and 0.1.

5.3.3. Livestock costs

In Rio Negro Province, in 2010, livestock CE was responsible for an estimated \$3,961,971 (95% CI: \$2,618,696–\$5,412,296) in economic losses (Table 5.6). The vast majority (96.4%) of the livestock-associated losses were due to decreased productivity, resulting in losses of \$3,818,660 (95% CI: \$2,475,550–

Table 5.6
Annual costs associated with human CE in Rio Negro Province, Argentina

Category	Mean cost (US$)	95% CI (US$)
Sheep		
Direct costs	14,941	10,506–19,429
Indirect costs	2,259,094	1,267,456–3,432,844
Total costs	2,274,035	1,281,227–3,450,626
Goats		
Direct costs	238	191–285
Indirect costs	178,351	91,313–281,397
Total costs	178,589	91,545–281,676
Cattle		
Direct costs	128,132	115,866–140,458
Indirect costs	1,381,215	549,709–2,245,472
Total costs	1,509,347	679,698–2,373,093
Total direct costs of livestock CE	**143,311**	**130,005–156,614**
Total indirect costs of livestock CE	**3,818,660**	**2,475,550–5,265,916**
Total costs of livestock CE	**3,961,971**	**2,618,696–5,412,296**

$5,265,916). Most of the livestock losses were attributable to sheep (57.4%) and cattle (38.1%), with only 4.5% of the total livestock losses attributable to goats.

Based on the sensitivity analysis, the uncertain parameters which had the greatest impact on the overall 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. The standardized regression coefficients for the remaining parameters ranged from 0 and 0.1. When livestock production losses were excluded, the most influential parameter was liver weight for adult cattle (standardized regression coefficient = 0.851).

5.3.4. Total costs

When the human and livestock losses were combined, the estimated total annual cost of CE was $5,100,373 (95% CI: $2,852,345–$8,004,122), in Rio Negro Province in 2010. When the productivity losses associated with non-healthcare seeking human cases were included, livestock losses represented approximately 78% of the estimated total annual economic losses attributable to CE. However, when the productivity losses associated with non-healthcare seeking human cases were excluded, livestock losses accounted for 93% of the total estimated annual cost of CE.

5.4. 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 report a comprehensive estimate of the annual economic impact of CE in humans and livestock in Rio Negro Province, Argentina. Combining the costs associated with human and livestock disease into a single estimate allowed us to examine 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 was US $5.1 million, which equates to a loss of approximately 0.11% of the annual *per capita* gross domestic product (GDP) for 2010. The annual CE-associated loss of 0.11% of the *per capita* GDP, observed in the present study, is greater than the losses that have been reported by some other studies. Studies, which examined the costs associated with CE in Iran, Uruguay, and Jordan, reported annual *per capita* GDP losses of 0.03%, 0.058%, and 0.074%, respectively (Torgerson et al., 2000; Torgerson et al., 2001; Harandi et al., 2012). Conversely, 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 the present study (Budke et al., 2005). However, with the exception of the study which took place in China, the previously mentioned studies were country-level economic analyses. The country-level studies included both urban and rural areas in their estimates. While Rio Negro Province also includes 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 much lower than that of Argentina. Therefore, the losses incurred represent a greater proportion of GDP, in this region, than they would for the country of Argentina.

Although there have been several studies which have estimated the economic losses associated with CE in different countries and regions, it is very difficult to directly compare the findings of these studies. This is because there are no standardized methods for conducting these analyses. Each study estimates the costs of a different set of variables, with some studies estimating only direct costs and others incorporating both direct and indirect costs. In addition, the total costs vary depending on the human and livestock population sizes, the type and availability of medical care, CE prevalence, and numerous other factors.

Such comparisons are likely to undervalue the importance of the disease in poor communities without access to proper diagnosis and care.

Costs associated with human CE accounted for 22.3% of the total economic losses attributable to CE. Although *per capita* GDP can be useful for comparing losses between different locations, it provides very little insight into the economic impact of the disease on those who are infected. The total annual CE-related costs, for nonsurgical cases, represented 5.6% of an annual minimum wage salary of $5484 (The World Bank, 2011a). However, for surgical patients, the annual costs associated with CE were considerably greater, consuming approximately 92% of an annual minimum wage salary.

The annual direct costs for surgical patients were much lower for patients treated in Ingeniero Jacobacci, than for patients treated in the other hospitals. There are several factors, which are likely to have contributed to the cost difference. Because the hospital in Ingeniero Jacobacci is a rural hospital, complicated cases are often referred to the larger hospitals in Viedma or Bariloche. As a result, only three of the surgical patients were treated in Ingeniero Jacobacci. In addition, none of the surgical patients from the Ingeniero Jacobacci hospital received surgical treatment for pulmonary CE, which tends to be more complicated and as a result, more expensive.

Livestock associated losses accounted for 77.7% of the total monetary burden of CE in Rio Negro Province. The vast majority of sheep and goats in this region of Argentina are raised for wool and mohair. As a result, decreased production of wool and mohair were the most important productivity losses for sheep and goats. Although most (57.4%) of the total monetary losses associated CE in livestock, as well as the indirect costs (59.2%) were attributed to sheep, 89.4% of the direct costs were associated with cattle. The reason for this is that while the sheep population is much larger than the cattle population in the region, beef livers have a much higher value than sheep livers.

This study had a few limitations, which should be mentioned. First, the employment and wage data used to estimate lost wages associated with CE were based on province level data. If the affected individuals have higher or lower than average incomes, the estimates for lost wages could be an underestimate or overestimate of the true value. In addition, other studies have indicated that CE patients have higher levels of unemployment than the general population (Torgerson et al., 2000; Torgerson et al., 2001). Although the unemployment benefits for the officially unemployed sector of the population are not expected to be affected by illness, if the affected individuals are not officially classified as unemployed, but are underemployed or “inactive”, it could affect our estimates.

Next, although the number of undiagnosed individuals was estimated using the best available data, the true number of non-healthcare seeking cases may differ from our estimates. Since this value was shown to be one of the most important factor in the sensitivity analysis, it could greatly influence the total losses associated with human CE. In addition, while other studies have indicated that CE affects an individual's ability to work, the actual decrease in productivity is not known. Similarly, although CE is likely to affect livestock productivity, the degree of impact is not truly known. For the present study, we have estimated these losses using values that have been used in other studies. However, the lack of experimental data makes it extremely difficult to accurately estimate livestock production losses. Therefore, in order to account for the degree of uncertainty in the available data, wide confidence intervals were used.

In conclusion, the results of this analysis clearly indicate that CE is an important economic problem in Rio Negro Province, Argentina. However, additional research is needed to continue to refine our estimate of the economic impact of the disease in this region. As additional data become available, the confidence intervals for cost estimates will become narrower, allowing for a more precise estimate.

CHAPTER VI

SUMMARY AND CONCLUSIONS

6.1. SUMMARY

The primary objectives of this project were to evaluate the epidemiology and socioeconomic impact of selected dog-associated zoonoses in the developed and developing world. Data collection for this project took place in two locations. In order to examine community knowledge of locally relevant dog-associated zoonoses in a developed country, data were collected from Brazos County, Texas, USA residents using a telephone questionnaire. Community ultrasound, hospital chart review, and patient interview data collected in Rio Negro Province, Argentina were used to evaluate the epidemiology and socioeconomic impact of a locally relevant dog-associated zoonotic disease, cystic echinococcosis (CE), in a developing country.

Very few studies have evaluated the knowledge and perceptions of dog-associated zoonoses, in the United States. To the author's knowledge, only one other published study has focused on this subject matter. In that study, Fontaine and Schantz (1989) reported that residents of De Kalb County, Georgia were inadequately informed about the zoonotic disease risks associated with pets.

They found that only 63% of study participants were aware that diseases could be transmitted from pets to humans (Fontaine and Schantz, 1989). Since this research was conducted over 25 years ago, the study presented in Chapter 3, is the only recent study to evaluate knowledge of dog-associated zoonoses, in the United States. In addition, it was the first study to attempt to evaluate residents' willingness to take the actions necessary to prevent dog-associated zoonotic diseases.

The dog owners who participated in the Brazos County study were significantly more knowledgeable about rabies than the study participants who did not own dogs. For example, significantly more dog owners were aware that rabies was present in Texas. In addition, the dog owners in the study were significantly more likely to be aware that people could contract rabies from cats and wild animals such as raccoons, skunks, and bats. Finally, while the majority of dog owners knew that wild animal bites were the most common source of human rabies exposure in Texas, study participants who did not own dogs incorrectly believed that dog bites were the most common cause of human rabies exposure.

From a public health perspective, the results of this study present some cause for concern. First, 41% of the study participants were unaware that exposure to rabies without treatment could be fatal. Next, 14% of the study participants stated that they would not report being bitten by a dog that they did not own to someone of authority. Furthermore, 15% of the individuals who participated in the study indicated that they would not seek emergency treatment if they believed that they had been exposed to rabies. Finally, only 54% of the study participants were aware that dog-associated zoonotic helminthes could be transmitted to people. However, none of these factors differed significantly between dog owners and the individuals who did not own dogs. Based on the findings of this study, many of the study participants lacked knowledge about dog-associated zoonoses. As a result, these individuals may be failing to take the necessary precautions to protect their health and the health of their families.

Although CE is known to be highly endemic in Rio Negro Province, Argentina, current epidemiologic data are scarce, particularly for the adult population. The study presented in Chapter 4 is the only recent study to estimate the prevalence of CE for all age groups, and evaluate potential risk factors for CE among adults in this region of Argentina.

This community-based cross sectional CE screening survey, which incorporated abdominal ultrasonography, follow-up thoracic radiography, and a questionnaire, was conducted in Ingeniero Jacobacci, a small town with approximately 8000 residents. The prevalence of CE was very high in this community, with 7.1% (40/560) of the study participants receiving a CE-positive diagnosis based on the abdominal ultrasound examination. However, the CE prevalence observed in this study is not representative of the CE prevalence of the population of Rio Negro Province because the study was conducted in a highly endemic region of the province and the study participants were community volunteers.

Most of the cysts observed in this study were classified as inactive (CE4 or CE5), according to the WHO-IWGE classification system (WHO, 2003; Brunetti et al., 2010). However, approximately 31% of the cysts were classified as either active (CE1 or CE2) or transitional (CE3), indicating that there is likely to be ongoing transmission of CE in the study region. The fact that several of the children who were examined received a CE-positive diagnosis provides additional evidence of recent transmission.

The CE control program in Rio Negro Province has been one of the most successful CE control programs in South America (Craig and Larrieu, 2006). The reported annual incidence of human CE has decreased from 73 cases per 100,000, in 1980, to 9.16 cases per 100,000, in 2009. However, the findings of this study indicated that residents of Rio Negro Province continue to be exposed to *E. granulosus* and new human cases of CE are still occurring. Therefore, it is important to continue efforts to combat the disease in this region of Argentina.

Risk factors, which were found to be significantly associated with the CE status of adult study participants in Ingeniero Jacobacci, included age, level of education, dog ownership, and contact with sheep. As the only recent study to examine the prevalence of CE and the risk factors associated with infection in adults, in Rio Negro Province, this study adds valuable information to the existing body of knowledge about CE in this region. The data obtained from this study can be used by program coordinators to evaluate and potentially improve, the present CE control program in Rio Negro Province.

The costs associated with CE in humans and livestock have been estimated for a number of countries (Torgerson et al., 2000; Torgerson et al., 2001; Budke et al., 2005; Majorowski et al., 2005; Benner et al., 2010; Moro et al., 2011; Harandi et al., 2012). However, the study presented in Chapter 5 provides the first comprehensive estimate of the economic losses attributable to human and livestock CE for Rio Negro Province, Argentina. Based on the results of this study, CE was responsible for substantial economic losses to individual patients as well as the provincial economy.

The annual costs associated with CE were a considerable financial burden for CE patients. For non-surgical patients, the average annual costs attributable to CE were $309, which represented approximately 6% of an annual minimum wage salary of $5484 (The World Bank, 2011a). However, for surgical patients, the $5,046 in annual costs associated with CE were an even greater financial hardship, consuming more than 90% of an annual minimum wage salary.

When the livestock-associated and human-associated losses were combined, the estimated total annual cost of CE for Rio Negro Province was $5.1 million. The annual economic losses associated with human CE were estimated to be $1.1 million, approximately 74% of which were due to productivity losses for non-healthcare seeking cases. Livestock CE was responsible for an estimated $4 million in annual economic losses, 96% of which were due to decreased productivity.

Latin Hypercube sampling was used to account for uncertainty in the input parameter estimates. Stepwise linear regression sensitivity analyses were conducted in order to examine the impact of each input parameter on the overall cost estimate. The sensitivity analysis indicated that the input 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. The parameters that had the greatest impact on the overall estimated losses associated with livestock CE, were the productivity losses, including percentage decreases in sheep fecundity, cattle fecundity, and wool value.

While several studies have indicated that CE affects an individual's ability to work, prior to the time in which they seek treatment, the actual decrease in productivity is not known (Torgerson, 2003; Budke et al., 2004). Similarly, although CE is believed to affect livestock productivity, the degree of impact is not truly known (Torgerson, 2003). Therefore, for this study, human and livestock productivity losses were estimated using values, which have been used in other studies (Torgerson et al., 2000; Torgerson et al., 2001; Budke et al., 2006; Benner et al., 2010). Due to the lack of available experimental data, uniform distributions were used to estimate productivity losses for non-healthcare seeking human cases. For the same reason, uniform distributions were used to model all livestock productivity losses. More informative distributions can be selected as additional data become available.

The results of this economic analysis indicate that CE is responsible for considerable monetary losses to both the human health and livestock sectors of the economy in Rio Negro Province, Argentina. These findings could be used to inform cost-benefit analyses of different CE control program options in this region, as well as to potentially encourage cost sharing between the public health and livestock sectors.

6.2. CONCLUSIONS

The monetary and non-monetary costs associated with some dog-associated zoonoses, such as rabies and cystic echinococcosis, have been reported to be very high (Knobel et al., 2005; Budke et al., 2006; WHO, 2010a, 2012). For many dog-associated zoonoses, vaccinating and deworming dogs can be the most cost-effective methods for preventing human exposure and illness, especially in countries with limited resources (Cleaveland et al., 2006; Zinsstag et al., 2007; WHO, 2012, 2013). However, the economic benefit of preventing disease in dogs can be difficult to calculate because their monetary value is rarely quantified (WHO, 2006, 2011). Without direct financial benefits to be gained by treating the animal reservoir, it can be difficult to convince human and veterinary public health officials that such treatments will be beneficial to their respective sectors (WHO, 2006; Zinsstag et al., 2007). While it could greatly benefit both the human and veterinary public health sectors to share the costs associated with controlling, preventing or even potentially eliminating these diseases, this type of collaboration may be unlikely to occur, particularly in developing countries with limited resources (WHO, 2006; Zinsstag et al., 2007; WHO, 2011).

The transmission of dog-associated zoonotic diseases is facilitated by the general lack of awareness, among the population at risk, of how these diseases are transmitted and the measures that can be taken to prevent them. It can be difficult to convince dog owners, particularly those with extremely limited resources, that deworming and vaccinating their dogs can greatly benefit their health and the health of their families. In addition, in many areas where dog-associated zoonoses are endemic, dogs are allowed to roam freely, increasing their risk for infection as well as that of the human population. While it is possible to educate the population at risk about the transmission of these diseases and the importance of restricting the movement of their dogs, it can to be very difficult to change human behavior, even when such a change has the potential to protect human health and save lives. Consequently, these preventable diseases continue to affect the health and livelihoods of millions of people throughout the world. However, studies such as those presented here can provide additional information on the epidemiology, public knowledge, and burden of these diseases, which has the potential to advance control and prevention efforts in many regions of the world.

REFERENCES

Ahmadi, N.A., Meshkehkar, M., 2011. An abattoir-based study on the prevalence and economic losses due to cystic echinococcosis in slaughtered herbivores in Ahwaz, south-western Iran. J. Helminthol. 85, 33-39.

Ammann, R.W., Eckert, J., 1996. Cestodes: *Echinococcus*. Gastroenterol. Clin. North Am. 25, 655-689.

Arinc, S., Kosif, A., Ertugrul, M., Arpag, H., Alpay, L., Unal, O., Devran, O., Atasalihi, A., 2009. Evaluation of pulmonary hydatid cyst cases. International Journal of Surgery 7, 192-195.

AVMA, 2007. U.S. Pet Ownership & Demographics Sourcebook. American Veterinary Medical Association, Schaumburg, IL, USA.

Beck, A.M., 2013. The human-dog relationship: a tale of two species. CABI Pub, Wallingford, UK.

Benner, C., Carabin, H., Sanchez-Serrano, L.P., Budke, C.M., Carmena, D., 2010. Analysis of the economic impact of cystic echinococcosis in Spain. Bull. World Health Organ. 88, 49-57.

Bernstein, A.B., Hing, E., Moss, A.J., Allen, K.F., Siller, A.B., Tiggle, R.B., 2003. Health care in America: trends in utilization. National Center for Health Statistics, Hyattsville, MD, USA.

Bingham, G.M., Budke, C.M., Larrieu, E., Del Carpio, M., Mujica, G., Slater, M.R., Moguillansky, S., 2014. A community-based study to examine the epidemiology of human cystic echinococcosis in Rio Negro Province, Argentina. Acta Trop. 136, 81-88.

Blanton, J.D., Palmer, D., Christian, K.A., Rupprecht, C.E., 2008. Rabies surveillance in the United States during 2007. J. Am. Vet. Med. Assoc. 233, 884-897.

Brunetti, E., Kern, P., Vuitton, D.A., 2010. Expert consensus for the diagnosis and treatment of cystic and alveolar echinococcosis in humans. Acta Trop. 114, 1-16.

Budke, C.M., Deplazes, P., Torgerson, P.R., 2006. Global socioeconomic impact of cystic echinococcosis. Emerg. Infect. Dis. 12, 296-303.

Budke, C.M., Jiamin, Q., Qian, W., Torgerson, P.R., 2005. Economic effects of echinococcosis in a disease-endemic region of the Tibetan Plateau. Am. J. Trop. Med. Hyg. 73, 2-10.

Budke, C.M., Qiu, J.M., Zinsstag, J., Wang, Q.A., Torgerson, P.R., 2004. Use of disability adjusted life years in the estimation of the disease burden of echinococcosis for a high endemic region of the Tibetan plateau. Am. J. Trop. Med. Hyg. 71, 56-64.

Campos-Bueno, A., Lopez-Abente, G., Andres-Cercadillo, A., 2000. Risk factors for Echinococcus granulosus infection: a case-control study. Am. J. Trop. Med. Hyg. 62, 329-334.

Carabin, H., Budke, C.M., Cowan, L.D., Willingham, A.L., 3rd, Torgerson, P.R., 2005. Methods for assessing the burden of parasitic zoonoses: echinococcosis and cysticercosis. Trends Parasitol. 21, 327-333.

Caremani, M., Benci, A., Maestrini, R., Accorsi, A., Caremani, D., Lapini, L., 1997. Ultrasound imaging in cystic echinococcosis. Proposal of a new sonographic classification. Acta Trop. 67, 91-105.

Carmona, C., Perdomo, R., Carbo, A., Alvarez, C., Monti, J., Grauert, R., Stern, D., Perera, G., Lloyd, S., Bazini, R., Gemmell, M., Yarzabal, L., 1998. Risk factors associated with human cystic echinococcosis in Florida, Uruguay: results of a mass screening study using ultrasound and serology. Am. J. Trop. Med. Hyg. 58, 599-605.

Chomel, B.B., Arzt, J.J., 2000. Dogs and bacterial zoonoses. In: Macpherson, C.N.L., Meslin, F.X., Wandeler, A.I. (Eds.), Dogs, Zoonoses and Public Health. CABI Pub., New York, 91-113.

Chomel, B.B., Sun, B., 2011. Zoonoses in the Bedroom. Emerg. Infect. Dis. 17, 167-172.

Cleaveland, S., Kaare, M., Knobel, D., Laurenson, M.K., 2006. Canine vaccination--Providing broader benefits for disease control. Vet. Microbiol. 117, 43-50.

Craig, P.S., Budke, C.M., Schantz, P.M., Li, T., Qiu, J., Yang, Y., Zeyhle, E., Rogan, M.T., Ito, A., 2007a. Human echinococcosis: a neglected disease? Trop. Med. Health 35, 283-292.

Craig, P.S., Larrieu, E., 2006. Control of cystic echinococcosis/hydatidosis: 1863-2002. Adv. Parasitol. 61, 443-508.

Craig, P.S., McManus, D.P., Lightowlers, M.W., Chabalgoity, J.A., Garcia, H.H., Gavidia, C.M., Gilman, R.H., Gonzalez, A.E., Lorca, M., Naquira, C., Nieto, A., Schantz, P.M., 2007b. Prevention and control of cystic echinococcosis. The Lancet Infectious Diseases 7, 385-394.

Cubas-Castillo, R., Brain, C.O., Lopez-Guillemain, R., Ballarino, E.A., 2011. Hydatid liver disease. Our 25-year experience. Cir. Cir. 79, 306-312.

Del Carpio, M., Mercapide, C., Salvitti, J.C., Sustercic, J., Panomarenko, H., Perez, A., 2009. Normas de diagnostico y tratamiento de la hidatidosis humana. Ministerio de Salud, Provincia de Río Negro, Argentina.

Del Carpio, M., Mercapide, C.H., Salvitti, J.C., Uchiumi, L., Sustercic, J., Panomarenko, H., Moguilensky, J., Herrero, E., Talmon, G., Volpe, M., Araya, D., Mujica, G., Calabro, A., Mancini, S., Chiosso, C., Labanchi, J.L., Saad, R., Goblirsch, S., Brunetti, E., Larrieu, E., 2012. Early diagnosis, treatment and follow-up of cystic echinococcosis in remote rural areas in Patagonia: impact of ultrasound training of non-specialists. PLoS Negl. Trop. Dis. 6, e1444.

Del Carpio, M., Moguilansky, S., Costa, M., Panomarenko, H., Bianchi, G., Bendersky, S., Lazcano, M., Frider, B., Larrieu, E., 2000. Diagnosis of human hydatidosis - Predictive value of a rural ultrasonographic survey in an apparently healthy population. Medicina-Buenos Aires 60, 466-468.

Dhankhar, P., Vaidya, S.A., Fishbien, D.B., Meltzer, M.I., 2008. Cost effectiveness of rabies post exposure prophylaxis in the United States. Vaccine 26, 4251-4255.

Dillman, D.A., 2007. Mail and Internet Surveys : The Tailored Design Method, 2007 Update. John Wiley & Sons Inc. Hoboken, NJ, USA.

Dohoo, I.R., Martin, S.W., Stryhn, H., 2003. Veterinary Epidemiologic Research. AVC Inc. Charlottetown, P.E.I., Canada.

Dohoo, I.R., Martin, S.W., Stryhn, H., 2009. Veterinary Epidemiologic Research. VER Inc. Charlottetown, P.E.I., Canada.

Dowling, P.M., Abo-Shehada, M.N., Torgerson, P.R., 2000. Risk factors associated with human cystic echinococcosis in Jordan: results of a case-control study. Ann. Trop. Med. Parasitol. 94, 69-75.

Dowling, P.M., Torgerson, P.R., 2000. A cross-sectional survey to analyse the risk factors associated with human cystic echinococcosis in an endemic area of mid-Wales. Ann. Trop. Med. Parasitol. 94, 241-245.

Driscoll, C.A., Macdonald, D.W., O'Brien, S.J., 2009. From wild animals to domestic pets, an evolutionary view of domestication. Proc. Natl. Acad. Sci. U. S. A. 106, 9971-9978.

Dvorak, G., Spickler, A.R., Roth, J.A., 2008. Handbook for Zoonotic Diseases of Companion Animals. The Center for Food Security and Public Health, Iowa State University, College of Veterinary Medicine Ames, Iowa.

Eckert, J., Deplazes, P., 2004. Biological, epidemiological, and clinical aspects of echinococcosis, a zoonosis of increasing concern. Clin. Microbiol. Rev. 17, 107-135.

Eckert, J., Gemmell, M.A., Meslin, F.X., Pawlowski, Z.S. (Eds.), 2001. WHO/OIE Manual on Echinococcosis in Humans and Animals: a Public Health Problem of Global Concern. World Organization for Animal Health, Paris.

Fine, A.H., 2010. Handbook on animal-assisted therapy theoretical foundations and guidelines for practice. London : Academic London.

Fontaine, R.E., Schantz, P.M., 1989. Pet ownership and knowledge of zoonotic diseases in DeKalb County, Georgia. Anthrozoos 3, 45-49.

Frider, B., Moguilensky, J., Salvitti, J.C., Odriozola, M., Cantoni, G., Larrieu, E., 2001. Epidemiological surveillance of human hydatidosis by means of ultrasonography: its contribution to the evaluation of control programs. Acta Trop. 79, 219-223.

Galdas, P.M., Cheater, F., Marshall, P., 2005. Men and health help-seeking behaviour: literature review. J. Adv. Nurs. 49, 616-623.

Gavidia, C.M., Gonzalez, A.E., Zhang, W., McManus, D.P., Lopera, L., Ninaquispe, B., Garcia, H.H., Rodriguez, S., Verastegui, M., Calderon, C., Pan, W.K., Gilman, R.H., 2008. Diagnosis of cystic echinococcosis, central Peruvian Highlands. Emerg. Infect. Dis. 14, 260-266.

Hanlon, C.A., Olson, J.G., Clark, C.J., 1999. Prevention and education regarding rabies in human beings. J. Am. Vet. Med. Assoc. 215, 1276-1280.

Harandi, M.F., Budke, C.M., Rostami, S., 2012. The monetary burden of cystic echinococcosis in Iran. PLoS Negl. Trop. Dis. 6, e1915.

Harandi, M.F., Moazezi, S.S., Saba, M., Grimm, F., Kamyabi, H., Sheikhzadeh, F., Sharifi, I., Deplazes, P., 2011. Sonographical and Serological Survey of Human Cystic Echinococcosis and Analysis of Risk Factors Associated with Seroconversion in Rural Communities of Kerman, Iran. Zoonoses and Public Health 58, 582-588.

Hendrix, C.M., Bruce, H.S., Kellman, N.J., Harrelson, G., Bruhn, B.F., 1996. Cutaneous larva migrans and enteric hookworm infections. J. Am. Vet. Med. Assoc. 209, 1763-1767.

Hosmer, D.W., Lemeshow, S., 2000. Applied Logistic Regression. John Wiley & Sons New York, NY, USA.

Hughes, J., Macdonald, D.W., 2013. A review of the interactions between free-roaming domestic dogs and wildlife. Biol. Conserv. 157, 341-351.

Instituto Nacional de Estadística y Censos (INDEC), 2011. Encuesta Anual de Hogares Urbanos (EAHU), 2010. Available: http://www.indec.mecon.ar/principal.asp?id_tema=1105. Accessed February 9, 2013.

Instituto Nacional de Estadística y Censos (INDEC), 2012. Censo Nacional de Población, Hogares y Vivienda, 2010. Available: http://www.censo2010/indec.gov.ar. Accessed September 14, 2013.

Jackson, A.C., Warrell, M.J., Rupprecht, C.E., Ertl, H.C.J., Dietzschold, B., O'Reilly, M., Leach, R.P., Fu, Z.F., Wunner, W.H., Bleck, T.P., Wilde, H., 2003. Management of rabies in humans. Clin. Infect. Dis. 36, 60-63.

Knobel, D.L., Cleaveland, S., Coleman, P.G., Fevre, E.M., Meltzer, M.I., Miranda, M.E., Shaw, A., Zinsstag, J., Meslin, F.X., 2005. Re-evaluating the burden of rabies in Africa and Asia. Bull. World Health Organ. 83, 360-368.

Larrieu, E., Belloto, A., Arambulo, P., Tamayo, H., 2004a. Cystic echinococcosis: epidemiology and control in South America. Parasitologia Latinoamericana 59, 82-89.

Larrieu, E., Costa, M.T., Cantoni, G., Alvarez, R., Cavagion, L., Labanchi, J.L., Bigatti, R., Araya, D., Herrero, E., Alvarez, E., Mancini, S., Cabrera, P., 2001. Ovine Echinococcus granulosus transmission dynamics in the province of Rio Negro, Argentina, 1980-1999. Vet. Parasitol. 98, 263-272.

Larrieu, E., Costa, M.T., Cantoni, G., Labanchi, J.L., Bigatti, R., Aquino, A., Araya, D., Herrero, E., Iglesias, L., Mancini, S., Thakur, A.S., 2000a. Rate of infection and of reinfection by Echinococcus granulosus in rural dogs of the province of Rio Negro, Argentina. Vet. Parasitol. 87, 281-286.

Larrieu, E., Costa, M.T., Cantoni, G., Labanchi, J.L., Bigatti, R., Perez, A., Araya, D., Mancini, S., Herrero, E., Talmon, G., Romeo, S., Thakur, A., 2000b. Control program of hydatid disease in the province of Rio Negro Argentina. 1980-1997. Bol. Chil. Parasitol. 55, 49-53.

Larrieu, E., Del Carpio, M., Mercapide, C.H., Salvitti, J.C., Sustercic, J., Moguilensky, J., Panomarenko, H., Uchiumi, L., Herrero, E., Talmon, G., Volpe, M., Araya, D., Mujica, G., Mancini, S., Labanchi, J.L., Odriozola, M., 2011. Programme for ultrasound diagnoses and treatment with albendazole of cystic echinococcosis in asymptomatic carriers: 10 years of follow-up of cases. Acta Trop. 117, 1-5.

Larrieu, E., Del Carpio, M., Salvitti, J.C., Mercapide, C., Sustersic, J., Panomarenko, H., Costa, M., Bigatti, R., Labanchi, J., Herrero, E., Cantoni, G., Perez, A., Odriozola, M., 2004b. Ultrasonographic diagnosis and medical treatment of human cystic echinococcosis in asymptomatic school age carriers: 5 years of follow-up. Acta Trop. 91, 5-13.

Larrieu, E., Zanini, F., 2012. Critical analysis of cystic echinococcosis control programs and praziquantel use in South America, 1974-2010. Rev. Panam. Salud Publica 31, 81-87.

Larrieu, E.J., Costa, M.T., del Carpio, M., Moguillansky, S., Bianchi, G., Yadon, Z.E., 2002. A case-control study of the risk factors for cystic echinococcosis among the children of Rio Negro province, Argentina. Ann. Trop. Med. Parasitol. 96, 43-52.

Larrieu, E.J., Frider, B., 2001. Human cystic echinococcosis: contributions to the natural history of the disease. Ann. Trop. Med. Parasitol. 95, 679-687.

Li, J., Zhang, W.B., Wilson, M., Ito, A., McManus, D.P., 2003. A novel recombinant antigen for immunodiagnosis of human cystic echinococcosis. J. Infect. Dis. 188, 1951-1960.

Macpherson, C.N.L., 2005. Human behaviour and the epidemiology of parasitic zoonoses. Int. J. Parasitol. 35, 1319-1331.

Macpherson, C.N.L., Bartholomot, B., Frider, B., 2003. Application of ultrasound in diagnosis, treatment, epidemiology, public health and control of *Echinococcus granulosus* and *E. multilocularis*. Parasitology 127, S21-S35.

Macpherson, C.N.L., Milner, R., 2003. Performance characteristics and quality control of community based ultrasound surveys for cystic and alveolar echinococcosis. Acta Trop. 85, 203-209.

Macpherson, C.N.L., Torgerson, P.R., 2013. Dogs and cestode zoonoses. CABI Pub, Wallingford, UK.

Majorowski, M.M., Carabin, H., Kilani, M., Bensalah, A., 2005. Echinococcosis in Tunisia: a cost analysis. Trans. R. Soc. Trop. Med. Hyg. 99, 268-278.

Mani, I., Maguire, J.H., 2009. Small animal zoonoses and immuncompromised pet owners. Top. Companion Anim. Med. 24, 164-174.

Manning, S.E., Rupprecht, C.E., Fishbein, D., Hanlon, C.A., Lumlertdacha, B., Guerra, M., Meltzer, M.I., Dhankhar, P., Vaidya, S.A., Jenkins, S.R., Sun, B., Hull, H.F., 2008. Human rabies prevention − United States, 2008:

recommendations of the Advisory Committee on Immunization Practices. Morb. Mortal. Weekly Rep. 57, 1-28.

Manual Farmacéutico, 2011. Available: http://www.alfabeta.net. Accessed February 19, 2013.

Marker, L.L., Dickman, A.J., Macdonald, D.W., 2005. Perceived effectiveness of livestock-guarding dogs placed on Namibian farms. Rangeland Ecol. Manage. 58, 329-336.

Matter, H.C., Daniels, T.J., 2000. Dog ecology and population biology. In: Macpherson, C.N.L., Meslin, F.X., Wandeler, A.I. (Eds.), Dogs, Zoonoses and Public Health. CABI Pub., New York, 17-62.

McManus, D.P., Zhang, W., Li, J., Bartley, P.B., 2003. Echinococcosis. The Lancet 362, 1295-1304.

McNicholas, J., Gilbey, A., Rennie, A., Ahmedzai, S., Dono, J.A., Ormerod, E., 2005. Pet ownership and human health: a brief review of evidence and issues. Br. Med. J. 331, 1252-1254.

Ministerio de Agricultura Ganadería y Pesca (MAGyP), 2011. Anuario 2010: Ganados y carnes. Ministerio de Agricultura, Ganadería y Pesca de la Nación, Argentina, Buenos Aires.

Ministerio de Salud (MSAL), 2013. Enfermedades infecciosas. Available: http://www.msal.gov.ar. Accessed September 5, 2013.

Ministerio de Salud, 2009. Norma técnica y manual de procedimientos para el control de la hidatidosis en la República Argentina. Ministerio de Salud de la Nación, Buenos Aires, Argentina.

Ministerio del Interior y Transporte (MIyT), 2013. Available: http://www.mininterior.gob.ar. Accessed October 19, 2013.

Moro, P.L., Budke, C.M., Schantz, P.M., Vasquez, J., Santivanez, S.J., Villavicencio, J., 2011. Economic impact of cystic echinococcosis in peru. PLoS Negl. Trop. Dis. 5, e1179.

Moro, P.L., Cavero, C.A., Tambini, M., Briceno, Y., Jimenez, R., Cabrera, L., 2008. Identification of risk factors for cystic echinococcosis in a peri-urban population of Peru. Trans. R. Soc. Trop. Med. Hyg. 102, 75-78.

Moro, P.L., Garcia, H.H., Gonzales, A.E., Bonilla, J.J., Verastegui, M., Gilman, R.H., 2005. Screening for cystic echinococcosis in an endemic region of Peru using portable ultrasonography and the enzyme-linked immunoelectrotransfer blot (EITB) assay. Parasitol. Res. 96, 242-246.

Moro, P.L., Schantz, P.M., 2006. Cystic echinococcosis in the Americas. Parasitol. Int. 55 Suppl, S181-186.

Moro, P.L., Schantz, P.M., 2009. Echinococcosis: a review. Int. J. Infect. Dis. 13, 125-133.

Murray, C.J.L., Vos, T., Lozano, R., Naghavi, M., Flaxman, A.D., Michaud, C., Ezzati, M., Shibuya, K., Salomon, J.A., Lopez, A.D., et al., 2012. Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet 380, 2197-2223.

OIE, 2013. Terrestrial animal health code. Volume I: general provisions. OIE (World Organisation for Animal Health) Paris.

Overgaauw, P.A.M., Nederland, V., 1997. Aspects of *Toxocara* epidemiology: human toxocarosis. Crit. Rev. Microbiol. 23, 215-231.

Overgaauw, P.A.M., van Knapen, F., 2000. Dogs and nematode zoonoses. In: Macpherson, C.N.L., Meslin, F.X., Wandeler, A.I. (Eds.), Dogs, Zoonoses and Public Health. CABI Pub., New York, 213-256.

Patronek, G.J., Slavinski, S.A., 2009. Animal bites. J. Am. Vet. Med. Assoc. 234, 336-345.

Perdomo, R., Alvarez, C., Monti, J., Ferreira, C., Chiesa, A., Carbo, A., Alvez, R., Grauert, R., Stern, D., Carmona, C., Yarzabal, L., 1997. Principles of the surgical approach in human liver cystic echinococcosis. Acta Trop. 64, 109-122.

Pierangeli, N.B., Soriano, S.V., Roccia, I., Gimenez, J., Lazzarini, L.E., Grenovero, M.S., Menestrina, C., Basualdo, J.A., 2007. Heterogeneous distribution of human cystic echinococcosis after a long-term control program in Neuquen, Patagonia Argentina. Parasitol. Int. 56, 149-155.

Roth, F., Zinsstag, J., Orkhon, D., Chimed-Ochir, G., Hutton, G., Cosivi, O., Carrin, G., Otte, J., 2003. Human health benefits from livestock vaccination for brucellosis: case study. Bull. World Health Organ. 81, 867-876.

Santivanez, S., Garcia, H.H., 2010. Pulmonary cystic echinococcosis. Curr. Opin. Pulm. Med. 16, 257-261.

Sariozkan, S., Yalcin, C., 2009. Estimating the production losses due to cystic echinococcosis in ruminants in Turkey. Vet. Parasitol. 163, 330-334.

Schantz, P.M., 1989. Toxocara larva migrans now. Am. J. Trop. Med. Hyg. 41, 21-34.

Servicio Nacional de Sanidad y Calidad Agroalimentaria (SENASA), 2012. Sistema de vigilancia epidemiologica de la hidatidosis animal, en establecimientos con bovinos, ovinos o porcinos, por medio de la faena en la republica Argentina. Ministerio de Agricultura, Ganadería y Pesca de la Nación, Republica Argentina.

Steele, M.T., Ma, O.J., Nakase, J., Moran, G.J., Mower, W.R., Ong, S., Krishnadasan, A., Talan, D.A., 2007. Epidemiology of animal exposures presenting to emergency departments. Acad. Emerg. Med. 14, 398-403.

Stehr-Green, J.K., Schantz, P.M., 1987. The impact of zoonotic diseases transmitted by pets on human health and the economy. Veterinary Clinics of North America Small Animal Practice 17, 1-15.

Stull, J.W., Peregrine, A.S., Sargeant, J.M., Weese, J.S., 2012. Household knowledge, attitudes and practices related to pet contact and associated zoonoses in Ontario, Canada. BMC Public Health 12, 553.

Talan, D.A., Citron, D.M., Abrahamian, F.M., Moran, G.J., Goldstein, E.J.C., 1999. Bacteriologic analysis of infected dog and cat bites. N. Engl. J. Med. 340, 85-92.

Tan, J.S., 1997. Human zoonotic infections transmitted by dogs and cats. Arch. Intern. Med. 157, 1933-1943.

Texas Department of State Health Services (TDSHS), 2009a. Dog bite facts. Available:http://www.dshs.state.tx.us/idcu/health/zoonosis/animal/bites/information/facts. Accessed February, 2009.

Texas Department of State Health Services (TDSHS), 2009b. Rabies in humans in the USA: 1950 – present. Available: http://www.dshs.state.tx.us/idcu/disease/rabies/cases/statistics/reports/us.pdf. Accessed August, 2009.

The World Bank, 2011a. World Development Indicators, 2010. Available: http://data.worldbank.org/indicator/PA.NUS.FCRF. Accessed January 30, 2014.

The World Bank, 2011b. World Development Indicators, 2010. Available: http://data.worldbank.org/indicator/EP.PMP.SGAS. Accessed February 6, 2014.

Torgerson, P.R., 2003. Economic effects of echinococcosis. Acta Trop. 85, 113-118.

Torgerson, P.R., Budke, C.M., 2003. Echinococcosis - an international public health challenge. Res. Vet. Sci. 74, 191-202.

Torgerson, P.R., Carmona, C., Bonifacino, R., 2000. Estimating the economic effects of cystic echinococcosis: Uruguay, a developing country with upper-middle income. Ann. Trop. Med. Parasitol. 94, 703-713.

Torgerson, P.R., Dowling, P.M., 2001. Estimating the economic effects of cystic echinococcosis. Part 2: an endemic region in the United Kingdom, a wealthy, industrialized economy. Ann. Trop. Med. Parasitol. 95, 177-185.

Torgerson, P.R., Dowling, P.M., Abo-Shehada, M.N., 2001. Estimating the economic effects of cystic echinococcosis. Part 3: Jordan, a developing country with lower-middle income. Ann. Trop. Med. Parasitol. 95, 595-603.

United States Census Bureau, 2008. 2007 American community survey. Available: http://www.factfinder.census.gov. Accessed October, 2008.

Verastegui, M., Moro, P., Guevara, A., Rodriguez, T., Miranda, E., Gilman, R.H., 1992. Enzyme-linked immunoelectrotransfer blot test for diagnosis of human hydatid-disease. J. Clin. Microbiol. 30, 1557-1561.

Wandeler, A.I., Matter, H.C., Kappeler, A., Budde, A., 1993. The ecology of dogs and canine rabies: a selective review. Revue Scientifique et Technique Office International des Epizooties 12, 51-71.

WHO, 2003. International classification of ultrasound images in cystic echinococcosis for application in clinical and field epidemiological settings. Acta Trop. 85, 253-261.

WHO, 2006. The control of neglected zoonotic diseases: a route to poverty alleviation: report of a joint WHO/DFID-AHP meeting, 20 and 21 September 2005, Geneva, Switzerland. World Health Organization, Geneva.

WHO, 2007. Global plan to combat neglected tropical diseases 2008-2015. World Health Organization, Geneva.

WHO, 2010a. Human and dog rabies prevention and control: report of the WHO/Bill and Melinda Gates Foundation Consultation. World Health Organization Geneva.

WHO, 2010b. Working to overcome the global impact of neglected tropical diseases. World Health Organization, Geneva.

WHO, 2011. Interagency meeting on planning the prevention and control of neglected zoonotic diseases. World Health Organization, Geneva.

WHO, 2012. Research priorities for zoonoses and marginalized infections: Technical report of the TDR Disease Reference Group on Zoonoses and Marginalized Infectious Diseases of Poverty. World Health Organization, Geneva.

WHO, 2013. Sustaining the drive to overcome the global impact of neglected tropical diseases: second WHO report on neglected diseases. World Health Organization, Geneva.

Wisdom, J.P., Saedi, G.A., Green, C.A., 2009. Another breed of "service" animals: STARS study findings about pet ownership and recovery from serious mental illness. Am. J. Orthopsychiatry 79, 430-436.

Woolhouse, M.E.J., Gowtage-Sequeria, S., 2005. Host range and emerging and reemerging pathogens. Emerg. Infect. Dis. 11, 1842-1847.

Zinsstag, J., Schelling, E., Roth, F., Bonfoh, B., de Savigny, D., Tanner, M., 2007. Human benefits of animal interventions for zoonosis control. Emerg. Infect. Dis. 13, 527-531.