Reichel, Michael Philipp; Ayanegui-Alcerreca, M. Alejandra; Gondim, Luis Fernando Pita; Ellis, John T.

What is the global economic impact of Neospora caninum in cattle - the billion dollar question

International Journal for Parasitology, 2013; 43(2):133-142

Graphical Abstract (for review)
Click here to download high resolution image

***Highlights (for review)**

Bullet points

- A systematic review of literature conducted after Pubmed search for *Neospora* and *cattle*
- Modelling after review suggests that the cost of *N caninum* globally exceeds one billion dollars
- Approximately two thirds of the costs of *N caninum* are incurred by dairy industries world-wide
- Analysis of the regional distribution of global costs of *N caninum* highlights the cattle industries of the North American as incurring two thirds of the overall global cost
- At the farm level, costs only exceed US$ 2,000 in four countries

Invited review

What is the global economic impact of *Neospora caninum* in cattle – the billion dollar question

Michael P Reichel[*, a, b], M. Alejandra Ayanegui-Alcérreca[c], Luís F P Gondim[d], and John T Ellis [b, e]

[a] School of Animal and Veterinary Sciences, University of Adelaide, Roseworthy Campus, Roseworthy SA 5371, Australia

[b] School of Medical and Molecular Biosciences, University of Technology, Sydney, PO Box 123, Broadway, NSW 2007, Australia

[c] Medtronic México, S de R.L de C.V. Paseo de Cucapah 10510, El Lago, CP22210, Tijuana, Baja California Norte, Mexico; alejandra.ayanegui@medtronic.com

[d] Departamento de Patologia e Clínicas, Escola de Medicina Veterinária, Universidade Federal da Bahia, Salvador, Bahia, Brazil; pitagondim@gmail.com

[e] i3 Institute, University of Technology Sydney, Broadway, Australia; john.ellis@uts.edu.au

[*] Email: michael.reichel@adelaide.edu.au, ph: +61-8-8303 7882, fax: +61-8-8313 7956

Abstract

Neospora caninum is regarded as one of the most important infectious causes of abortions in cattle world-wide, yet the global economic impact of the infection has not been established. A systematic review of the economic impact of *N caninum* infections/abortions was conducted, searching PubMed with the terms *cattle* and *Neospora*. This yielded 769 publications whose abstracts were screened for economically relevant information (e.g. abortion prevalence and risk, serological prevalence). Further analysis was restricted to countries with at least 5 relevant publications. In total, 99 studies (12.9%) from ten countries contained data from the beef industry (25 papers (25.3%)) and 72 papers (72.8%) from the dairy industry (with the remainder two papers (2.0%) describing general abortion statistics). The total annual cost of *N caninum* infections/abortions was estimated to range from a median US $1.1 million in the New Zealand beef industry to an estimated median total of US$ 546.3 million impact *per annum* in the US dairy population. The estimate for the total median *N caninum*-related losses exceeded US$ 1.298 billion *per annum*, ranging as high as US$ 2.380 billion. Nearly two thirds of the losses were incurred by the dairy industry (US$ 842.9 million). Annual losses on individual dairy farms were estimated to reach a median of US$ 1,600.00, while on beef farms these costs amounted to just US$ 150.00. Pregnant cows and heifers were estimated to incur, on average, a loss due to *N caninum* of less than US$20.00 for dairy, and less than US$ 5.00 for beef. These loss estimates, however rose to ~US$ 110.00 and US$ 40.00, respectively for *N caninum*-infected pregnant dairy and beef cows. This estimate of global losses due to *N caninum*, with the identification of clear target markets (countries, as well as cattle industries), should provide incentive to develop treatment options and/or vaccines.

Keywords: *Neospora caninum*, abortion, cattle, costs, economics, dairy, beef

1. Introduction

Neospora caninum is recognised world-wide as an important infectious cause of abortion in primarily cattle, and of clinical disease in dogs (Dubey and Schares, 2011).

Infection with *N caninum* is frequent in canid populations (Barber et al., 1997; Reichel, 1998); also recently reviewed by Al-Qassab et al. (2010)) yet clinical cases in dogs are rarely reported (Barber and Trees, 1996; Gasser et al., 1993; McInnes et al., 2006; Munday et al., 1990; Patitucci et al., 1997; Reichel et al., 1998; Ruehlmann et al., 1995). Clinical cases of neosporosis in dogs can be treated, although often with limited success (Reichel et al., 2007). Although there is a cost to that treatment which has to be borne by the owner, these canine cases tend to be mostly singular in nature and thus costs are usually contained.

In cattle, *N caninum* is generally viewed as primarily an abortifacient, and abortions follow three main patterns (sporadic, endemic and epidemic abortions). The epidemic, "storm-like" pattern is the most devastating, and costly, with a large proportion (>10%) of at risk ("in-calf") cows aborting over a short period of time (Dubey et al., 2007). These abortion storms are generally viewed as very costly (and sometimes devastating in the extreme) to the primary producer. Endemic abortions, however, can also be costly (Hall et al., 2005). There have also been reports of *N caninum* infection effects on milk production; in some publications the infection with *N caninum* is shown to be associated with a decrease in milk production (Thurmond and Hietala, 1997b), in other reports, however, milk production increases in sero-positive cows (Hall et al., 2005; Pfeiffer et al., 2002). A reduction in neonatal mortality in congenitally *N caninum*-infected calves has also been reported and may be a potential benefit (Paré et al., 1996). Earlier culling of sero-positive cattle has been reported (Thurmond and Hietala, 1996), as have increased costs of veterinary medical treatment (Barling et al., 2000) and a reduction in growth rates (Barling et al., 2001a; Barling et al., 2000). Thus, while some of the above reported effects of *N caninum* infection cost primary producers money, some of the information is equivocal; the majority of reports however describe abortions as the main impact of infection, and this will be the focus of this review.

Control options for *N caninum* infection in cattle have been discussed previously (Reichel and Ellis, 2002). The costs of these control options have also been modelled, and threshold levels of *N caninum* infection that make intervention economically preferable over living with the disease, defined (Reichel and Ellis, 2006). The treatment option (with toltrazuril (Kritzner et al., 2002)) has been identified as expensive in cattle and is potentially fraught with issues of milk and meat residues. Vaccines appear to be the favoured control option and the subject of a considerable body of research (Liddell et al., 1999; Miller et al., 2005). The different approaches to *N caninum* vaccines have recently been comprehensively reviewed (Reichel and Ellis, 2009). However, after the withdrawal from world-wide sales of the only commercial *N caninum* vaccine (Neoguard®), a vaccine which had demonstrated little more than 60% efficacy at best, and whose efficacy may have been as low as 25% (Weston et al., 2012), there are now only few management options available.

One option available, apart from living with the disease, is to test, and then cull *N caninum*-infected cattle from the herd. This approach has been found to be quite efficacious (Hall et al., 2005), but is also costly, and the cost of this approach needs to be put into the perspective of the cost of the disease. Variations to this option might include selective breeding from only sero-negative cows, breeding of sero-positives only to beef, and the culling of those cows that have actually aborted. Herds with reduced, or reducing sero-prevalence of *N caninum* infection also need to be protected from subsequent infection (although, in general, the published literature reports very low post-natal infection rates (Davison et al., 1999b; Paré et al., 1996; Thurmond and Hietala, 1997a)), thus enhanced biosecurity measures (fencing, the exclusion of canine faeces from feed and water, and prevention of access for canids to bovine material (carcasses, placentas, aborted foetuses) would need to be instituted, at some cost.

"Test-and-cull" would essentially incur the cost of testing all cattle, additionally incur the cost of culling all infected cattle (i.e. the replacement cost with non-infected, tested cattle) against the long-term benefit of the reduced cost of abortions. The cost of *N caninum* abortions at farm, industry, national and world-wide level are hitherto ill-defined and the present review is aimed at establishing these costs based on the published literature.

2. Materials and methods

2.1. Cost of an abortion in cattle

In order for the specific contribution and cost of *N caninum* to abortions to be measured, the baseline rate of abortions (those that are not caused by *N caninum*) needs to be established. Thereafter, the relative (increased) risk of abortion caused specifically by *N caninum* needs to be established.

Female *N caninum*-infected and pregnant cattle (generally, annual pregnancy rates of 90% of all breeding-age dairy female cattle and 75% of all breeding-age female beef cattle were assumed, unless country-specific data were available) are at risk of aborting, thus sero-prevalence data for *N caninum* for pregnant cattle (see above), multiplied by the specific *N caninum* risk of abortion, will result in the average expected number of *N caninum* abortions to be calculated.

N caninum abortions usually occur between 5-7 months of gestation (Dubey et al., 2006), and aborted cows can be expected to miss one lactation, thus the cost of a *N caninum* abortion (in dairy cattle) is essentially the cost of replacing that cow with an identical, similar stage of lactation cow that will go on to produce a calf and milk. In beef cattle, the cost of *N caninum* abortions is the cost of a replacement calf.

2.2. Database search

A search was conducted on PubMed, using *cattle* and *Neospora* as search terms. As of January 31, 2012, this search yielded 769 publications whose abstracts were screened individually initially for the reporting of economic relevant information (abortion incidence, prevalence and risk, serological data, impact on milk production and reproductive parameters) (Figure 1).

Published papers with relevant information originated from just nine countries (Australia and New Zealand, the US and Canada, Argentina, Brazil, Mexico, Spain and the United Kingdom) were then subjected to further analysis, once countries with fewer than five publications with economically relevant data were excluded to allow for a more robust data range for individual countries.

2.3. Baseline data for abortions

Abortions occur frequently in cattle, for a variety of reasons, and not all of them are caused by infectious agents, however baseline data (i.e. the prevalence of those abortion that are not caused by *N caninum*) are difficult to obtain. In New Zealand, the overall loss rate has been estimated to be 6.4% of pregnancies in one publication (McDougall et al., 2005), in others however as high as 25% (Thornton et al., 1994), with the median value for abortion losses being 2.9%. In Australia, the median value for abortions is 2.5% (ranging from 2.4% to 21.3% in some reports (Atkinson et al., 2000; Hall et al., 2005; Quinn et al., 2004)) (further details, see Table 1). Where baseline data for a specific cattle industry were unobtainable, a baseline figure of 3% of pregnant cattle aborting was assumed.

2.4. Cost of abortion

The cost of abortion in each country that qualified for further economic evaluation (i.e. where at least five peer-reviewed publications with economically relevant data was available) was calculated from the relative risk of abortion, specific to *N caninum* multiplied by the sero-prevalence (where reported) of *N caninum* in the cattle population times the loss/cost incurred by that abortion, in large parts as previously described (Reichel and Ellis, 2006).

As an example, the cost of *N caninum* in Argentina was calculated as the cost of a replacement pregnant dairy cow (USS 2,400.00) from which the slaughter (salvage) value of an empty cow (US$ 900.00) was subtracted to arrive at an estimate of the loss from one abortion (US $1,500.00). In beef cattle, the cost was calculated as the loss of a calf and the differential between replacement and slaughter value (US $ 830.00). These respective values were multiplied by the number of cows and heifers at risk of abortion (total number of beef (75%) cows and dairy (80%) cows pregnant, times the overall risk of abortion (4.5%, or 8%, respectively) multiplied by the specific median contribution of *N caninum* to abortions in Argentina from available abortion statistics (Table 1).

Where sero-prevalence, and *N caninum*-specific risk (odds or relative risk) of abortion data were available, the cost of *N caninum* abortions was calculated as follows: total number of cows at risk (as above), times the specific median sero-prevalence for *N caninum*, multiplied by *N caninum*-specific abortion risk (or “background” abortion risk times the odds increased by *N caninum* infection), as in the case of the calculation for the New Zealand dairy situation (Table 1), multiplied by the cost of an abortion.

Cattle population statistics and values for cattle in the respective countries were procured from publicly available databases and sources. Results were converted to US dollars at the prevailing exchange rates in early May 2012 (www.xe.com).

3. Results

3.1. Literature cited

In total, 99 studies (12.9%) contributed to this review, containing data that pertained to a total of 221,713 head of cattle, of which 45,863 (20.7%) resided in the beef industry (25 papers (25.3%) and 175,850 (79.3%) in the dairy industry (72 papers (72.8%)) with the remainder two papers (2.0%) describing general abortion statistics.

3.2 Sero-prevalence and N caninum abortion risk

An overview of the sero-prevalence data for the ten countries and their industries, i.e. where the numbers of peer-reviewed publications reached the threshold, suggests that the level of *N caninum* infection generally is about 50% higher in dairy cattle (median sero-prevalence 16.1%) than in beef cattle (median sero-prevalence 11.5%). The *N caninum* specific abortion risk in dairy cattle reached a median of 14.3% across all nine countries, with a wide range from 0.6% to 39.4% being reported. The increase in risk of *N caninum* causing abortions reached a median value of 3.5 (ranging from 1.3 to 40.0) in dairy cattle, while in beef cattle the median value was 9.0 (5.7 to 23.3) (which however could only be calculated from two countries).

3.3. Country-specific literature search statistics

3.3.1. Argentina

The Pubmed search, and subsequent evaluation revealed that there were five publications from Argentina with economically relevant information, three covering the dairy (Moore et al., 2002; Moore et al., 2009; Venturini et al., 1999) reporting on studies that included in excess of 4,000 cattle (n=4,280) and three from the beef industry (Moore et al., 2003; Moore et al., 2002; Moore et al., 2009) (n=3,241), with one publication reporting on abortion statistics with specific reference to *N caninum* (Moore et al., 2008) (n=666).

3.3.2. Australia

The database search recovered eight relevant publications for Australia, with six describing the dairy situation in relation to *N caninum* (Atkinson et al., 2000; Boulton et al., 1995; Hall et al., 2005, 2006; Nasir et al., 2012; Obendorf et al., 1995; Quinn et al., 2004) (n= 1,246) and only two the beef situation (Nasir et al., 2012; Stoessel et al., 2003) (n= 2,483).

3.3.3. Brazil

In Brazil, six publications contained relevant data on *N caninum* in the dairy industry (Aguiar et al., 2006; Corbellini et al., 2006; Gondim et al., 1999; Guimaraes et al., 2004; Locatelli-Dittrich et al., 2001; Minervino et al., 2008) (n=3,842), three in the beef industry (Aguiar et al., 2006; Marques et al., 2011; Minervino et al., 2008) (n= 863), and one abortion statistics in general (Pescador 2007) (n=258).

3.3.4. Canada

From Canada, 11 publications described mostly sero-prevalence data from 36,072 dairy cattle (Bildfell et al., 1994; Chi et al., 2002; Cramer et al., 2002; Hobson et al., 2005; Keefe and VanLeeuwen, 2000; Pan et al., 2004; Paré et al., 1998; Peregrine et al., 2006; Tiwari et al., 2009; VanLeeuwen et al., 2005; Wapenaar et al., 2007) and in five publications studies data from beef cattle (Waldner et al., 2004; Waldner, 2005; Waldner et al., 2001; Waldner et al., 1999; Waldner et al., 1998) (n=7,324).

3.3.5. Mexico

Three publications described *N canimum* in dairy cattle (Garcia-Vazquez et al., 2002; Garcia-Vazquez et al., 2005; Morales et al., 2001b) (n=2,003) and one study the beef situation (Garcia-Vazquez et al., 2008) (n=596), as well as one study that described abortion statistics in the dairy industry (Morales et al., 2001a) (n=211).

3.3.6. Netherlands

Five publications from the Netherlands described the impact in dairy cattle (n=11,767) (Bartels et al., 2006a; Bartels et al., 2006b; Dijkstra et al., 2003; Moen et al., 1998; Wouda et al., 1998)

3.3.7 New Zealand

For New Zealand, reports with relevant information were able to be obtained from 12 publications, 11 for dairy cattle (Cox et al., 1998; Faria et al., 2010; Patitucci et al., 1999; Pfeiffer et al., 2002; Reichel, 1998; Reichel and Pfeiffer, 2002; Schares et al., 1999; Thobokwe and Heuer, 2004; Thornton et al., 1994; Thornton et al., 1991; Weston et al., 2005) (n= 6,636) and one for the beef industry (Tennent-Brown et al., 2000) (n=499).

3.3.8. Spain

From Spain there were six publications describing the situation in the dairy industry (Bartels et al., 2006a; Eiras et al., 2011; Gonzalez-Warleta et al., 2008; Gonzalez-Warleta et al., 2011; Mainar-Jaime et al., 1999; Quintanilla-Gozalo et al., 1999) (n=48,790) and four publications describing the contribution of *N caninum* to economic losses in in the beef industry (Armengol et al., 2007; Bartels et al., 2006a; Eiras et al., 2011; Quintanilla-Gozalo et al., 1999) (n=26,083).

3.3.9. United Kingdom

Seven studies from the British dairy industry reported *N caninum* related information (Brickell et al., 2010; Crawshaw and Brocklehurst, 2003; Davison et al., 1999a; Davison et al., 1999c; Trees et al., 1994; Williams et al., 1999; Woodbine et al., 2008) (n= 23,007).

3.3.10. United States of America

For the US, eleven published papers described the situation in the dairy industry (Anderson et al., 1995; Dubey et al., 1997; Dyer et al., 2000; Hernandez et al., 2002; Hietala and Thurmond, 1999; Jenkins et al., 2000; McAllister et al., 1996; Paré et al., 1997; Rodriguez et al., 2002; Thurmond and Hietala, 1997a; Thurmond et al., 1997) (n=38,207) and five papers the impact of *N caninum* in beef cattle (Barling et al., 2001b; Barling et al., 2000; McAllister et al., 2000; Sanderson et al., 2000; Thurmond et al., 1997) (n=4,774).

3.4. Economic impact calculation

Once the specific contribution of *N caninum* to abortion in these nine countries had been ascertained (i.e. the number of abortions that were likely to be caused by *N caninum* calculated for each country), the cost of abortion could be calculated per industry and country (Table 2). Where several publications reported differing figures for *N caninum* abortion risk or sero-prevalence, median values were calculated, and the estimates ranged through the lowest and highest estimate for either or both (risk or prevalence, as available).

3.5. Global economic impact assessment

Globally, the estimated median losses due to *N caninum*-induced abortions were estimated to be in excess of US$ 1,298.3 million (range US$ 633.4 million to US$ 2,380.1 million), with approximately two thirds of the losses, US$ 842.9 million (range US$ 341.1 million to US$ 1,739.3 million) losses incurred by the national dairy industries in the ten countries included, and over a one third at US$ 455,4 million (range US$ 292.3 million to US$ 640.8 million) in the respective eight beef industries (summarised in Table 2). Close to two thirds of the global costs of US$ 1,298 million *per annum* are estimated to occur in North America (US$ 852.4 million (65.7%)), followed by South America (US$ 239.7 million (18.5%)) and Australasia, which incurs 10.6% of the global losses at a median value of US$ 137.5 million annually. Losses due to *N caninum* abortions in Europe only accounted for 5.3% of the global losses or an estimated US$ 68.7 million.

As 46.4 million cows were at annual risk of abortion (i.e. pregnant) in the ten countries included in the calculation for the dairy cattle industry, the cost per individual cow can be estimated to be, on average US$ 18.16 (range US$ 7.35 to US$ 37.48). For the 102.2 million beef cattle at risk (i.e. pregnant) in eight countries the average loss per cow was estimated to be just US$ 4.46 (ranging from US$ 2.86 to US$ 6.27).

At the farm level, the median loss per farm was estimated to be US$1,600.00 (range <US$100 to US$ 68,000.00) in the dairy industry, and just US$ 150.00 (range <US$100 to US$2,800.00)

3.6. Country and industry-specific economic impact assessment

3.6.1. Argentina

In Argentina, the economic impact for the whole country was estimated to be a US$ 87.4 million *per annum*, with US$38.5 million incurred by the dairy industry (ranging in estimates from US$ 29.2 million to US$ 85.3 million) and US$ 48.9 million (range US$ 22.6 million to US$57.6 million) by the beef industry. At the farm level, dairy farmers were likely to incur a median *N caninum* loss of close to US$ 4,000 (ranging from close to US$ 2,993.41 to US$ 8,740.75) and beef farmers of approximately US$ 550.00 (ranging from US$ 256.66 to US$ 654.06).

3.6.2. Australia

Australian dairy farmers were calculated to incur a median annual loss of US$ 26.6 million (range US$ 7.1 million to US$ 54.0 million) at the national level, and US$ 9,300 (range US$ 2,500 to US$ 18,800) at the herd level. The beef industry was estimated to lose an annual median US$ 74.1 million (range US$ 27.7 million to US$ 139.5 million), with the losses at the herd level amounting to a median US$ 1,500 (range US$ 600 to US$ 2,800).

3.6.3. Brazil

In Brazil, dairy farmers were estimated to incur N caninum-associated losses at the national level of US$ 51.3 million per annum (ranging in estimates from US$ 35.8 million to US$ 111.3 million), while the losses at the farm level where less than US$ 100.00. In the Brazilian beef industry *N caninum* losses amounted to nationally, US$ 101.0 million (ranging from US$ 63.6 million to US$ 111.7 million), while at the average dairy farm level they didn't exceed US$ 100.00.

3.6.4. Canada

In Canada, the dairy industry was estimated to experience losses related to *N caninum* at the national level amounting to a median US$ 17.1 million (ranging from US$ 10.0 to US$ 32.1 million), while losses at the individual, average farm where estimated to be median US$ 1,300 (range US$ 800 to US$ 2,500). In the beef industry, losses were estimated to amount to a median annual US$ 14.3 million (range (US$ 13.6 million to US$ 14.8 million). At the farm level, beef losses were estimated to reach an annual US 200 only.

3.6.5. Mexico

The Mexican dairy industry was expected to incur losses due to *N caninum* infection/abortion of approaching US$ 68.5 million (ranging from US$ 52.4 million to US$ 403.2 million). Annual losses in the beef industry in Mexico were estimated to be US$ 94.8 million. At the average farm level, the losses did not exceed US$ 100.00 for both, beef and dairy farms.

3.6.6. Netherlands

The Dutch dairy industry was estimated to incur annual median losses due to *N caninum* infection/abortion of US$ 12.1 million (ranging from US$ 8.3 million to US$ 20.2 million). At the dairy farm level, losses were estimated to attain a median of US$ 700.00 (range from US$ 480.00 to US$ 950.00).

3.6.7. New Zealand

New Zealand dairy farmers were estimated to incur *N caninum*-related median annual losses of US $35.7 million nationally (range US$ 14.5 to US$ 221 million), while the average dairy farm was expected to incur losses of US$ 11,000 (range US$ 4,500 to USS 68,000). The national beef industry was thought to lose a median US$ 1.1 million only, with the average farm incurring losses of just US$ 100 annually.

3.6.8. Spain

The Spanish dairy industry nationally, was estimated to incur losses specific to *N caninum* of a median US$ 19.8 million (range US$ 7.2 million to US$ 57.9 million), with individual farms incurring annual losses of US$ 500 (range US$ 200 to US$ 1,600). The beef industry was expected to incur losses amounting to a median annual figure of US$ 9.8 million (range US$ 4.6 million to US$ 15.6 million), while individual farmers might incur costs of a median of US$ 200 (range US$ 100 to US$ 200).

3.6.9. United Kingdom

In the UK, figures were only available for the dairy industry. Nationally, *N caninum* abortions were estimated to cost an annual median of US$ 27 million (range US$ 10.8 million to US$ 32.4 million), which translated into annual median cost to the average farm of US$ 1,800 (range US$ 700 to US$ 2,100).

3.6.10. United States

In the US, annual median losses due to *N caninum* were estimated to be around US$ 546.3 million in the dairy industry (range US$ 165.8 million to US$ 721.9 million), while on the average farm the costs were US$ 12,200 (range US$ 3,700 to US$ 16,100). In the beef industry, annual median losses were estimated to be US$ 111.4 million (range (US$ 64.3 million to US$ 205.7 million) nationally, with US$ 100 only (range US$ 100 to US$ 300) being incurred by the individual average farm.

4. Discussion

The review of the peer-reviewed literature related to *N caninum*-associated abortions in cattle suggests that the median specific risk of abortion due to *N caninum* infection is higher in dairy cattle at 14.3% (range: 0.6% to 39.4%) than it is in beef cattle at 9.1%. Also, the median seroprevalence of *N caninum* world-wide, at 16.1% (range 3.8% to 89.2%) was higher in dairy cattle compared to that prevailing in the beef industries, at 11.5% (range 2.5% to 81.7%). The odds of aborting in *N caninum*-infected animals, however, were almost triple (at 9.0 times) in the beef industry than in the dairy industries (3.5 times higher). The figures give a first global assessment of the risk of infection and abortion of *N caninum*. The background level of abortions that are not *N caninum*-associated appears to be higher in dairy cattle at 2.5%, compared to beef cattle at 1.2%.

The total losses in the cattle industries of the ten countries surveyed, exceeded US$ 1,298 million *per annum*, with approximately two thirds of these losses incurred by dairy industries (US$ 842.9 million; 64.9%) and one third by the beef industries (US$ 455.4 million; 35.1%). The higher assumption for abortion risk for the total cattle industries for abortion risk and sero-prevalence, had the annual global loss to *N caninum* abortions amount to at least US$ 2,380 million (US$ 1,739 million in the dairy industries and US$ 641 million in the beef industries, respectively), while the lower estimates suggested that costs are approaching US$ 633 million in the combined cattle industries (with a minimum of US$ 341.1 million (53.9%) incurred by the dairy industries, and US$ 292.3 (46.1%) incurred by the beef industries). As the estimate of losses was restricted to the ten countries that contributed more than five relevant publications each to the analysis, this estimate is likely to be at the lower end of the total global losses caused by *N caninum* infection in cattle.

Two thirds of the global costs of US$ 1,298 million *per annum* are estimated to be incurred in North America (US$ 852.4 million (65.7%)), followed by South America (US$ 239.7 million (18.5%)) and Australasia US$ 137.5 million (10.6%). Losses in the three countries from Europe included in the analysis only accounted for 5.3% of the global losses or US$ 68.7 million.

At the national level, the total annual costs of *N caninum* abortions for the cattle industries exceeded US$ 100 million *per annum* in Australia, Brazil, Mexico and the United States, which hence appear primary target markets for any control or vaccination effort. In addition, as the individual farm losses on Argentinian and New Zealand farms reach an estimated median of US$ 4,000 and US$ 11,000, respectively, these two countries seem also potential target markets for control methods. At the individual farm level, losses in both, beef and dairy sector rarely exceeded the US$ 2,000 mark. Only on the average dairy farm in Argentina, Australia, New Zealand and in the Unites States, did the losses exceed an annual estimate of US$ 2,000 and only in the case of the latter two did the estimate, per farm, exceed US$ 10,000 *per annum*. On the average beef farm, only in Argentina (US$ 600) and Australia (US$ 1,500) did the annual, *N caninum*-associated losses exceed US$ 500.00. The median global loss incurred at the farm was only US$1,800 for dairy, and US$ 150.00 for the beef industry.

In the ten countries included in the calculation for the dairy cattle industry, the cost per individual cow was estimated to be less than US$ 20.00 (US$ 18.16 (range US$ 7.35 to US$ 37.48)). In the 102.2 million beef cattle at risk (i.e. pregnant) in eight countries the average loss per cow was estimated to be just less than under US$ 5.00 (US$ 4.46 (ranging from US$ 2.86 to US$ 6.27)).

The losses at the individual cow, and farm level for both beef and dairy cattle seem to be quite low, however they are averaged over all pregnant cows. As globally only 16.1% of dairy cows and 11.5% of beef cows are estimated to be infected with *N caninum*, the losses incurred by *N caninum*-infected cows can be expected to be approximately 6 (dairy) or 9 (beef) times higher at ~ US$ 110.00 and ~ US$ 40.00 per animal. These estimates are not dissimilar to estimates for the impact of bovine viral diarrhoea (BVD) virus on cattle farms, which also range from US$10 to US$80 per pregnant cow (Heuer et al., 2007; Houe, 2003). BVD control and country-wide eradication receives a lot of attention, with Germany very recently commencing a BVD control campaign, and Switzerland essentially having just having completed its own eradication effort (Presi et al., 2011). In order to be able to offer a benefit to farmers with control or vaccination strategies (which might be difficult to demonstrate at an "all-cow" level), it would be important to cost-effectively identify infected properties and individual animals and target those specifically. As diagnostic assays are well developed and validated (Ellis, 1998; Pare et al., 1995; Paré et al., 1995; Reichel and Pfeiffer, 2002) the targeted delivery of vaccines or treatment to just infected animals might not pose the problems it might have in the past, and will deliver the benefit-to-cost ratios primary producers desire.

While the global losses incurred by *N caninum* in the cattle industries of ten countries are estimated to be in excess of a billion dollars annually, it is individual farmers that need to appreciate that the parasite poses a problem and is affecting their profitability. Median losses on farms are estimated to have the potential to range as high as US$ 68,000, but, in most countries individual farm losses may appear to be low to primary producers. Losses are only likely to exceed $2,000 per each farm/year on dairy farms in four of the countries (Argentina, Australia, New Zealand and the USA) included in the present review. This will continue to present a challenge to vaccine developers and marketers, as producers may choose to "live" with the disease (Reichel and Ellis, 2006). On the other hand, this analysis may provide a starting point, and targets countries where the initial commercialisation of an efficacious vaccine for the prevention of *N caninum* infections and/or abortions would be beneficial (Reichel and Ellis, 2009).

The only previously marketed commercial vaccine against *N caninum* abortions showed low efficacy, likely because it was unable to demonstrate sufficient protection in already infected cattle (Weston et al., 2012). Protecting naïve, uninfected cows might not need to be a priority for vaccination if post-natal infection rates are generally as low as they have been reported in the literature (Davison et al., 1999b; Hall et al., 2005; Paré et al., 1996; Thurmond and Hietala, 1997a), although others have reported post-natal transmission rates as high as 22% annually (Björkman et al., 2003). Here the benefit to cost ratio is also low, as the large majority of animals would have to be inoculated as part of an insurance policy against infection, when actual risk of infection/abortion is low. Preventing vertical transmission and/or abortions would provide far greater benefit/cost ratios as these animals are at demonstrable higher risk of abortion (being already infected). Expected losses at ~ US$ 130.00 a cow are higher and more likely to occur. An alternative might be to have two vaccines, one for a naïve population as an insurance policy against primary infection (Innes, 2007; Williams and Trees, 2006). This vaccine would need to be very cheap to give primary producers an incentive to use it with the low average cost of *N caninum* infection in that proportion of the cattle population. Another vaccine should be able to prevent the

References

Aguiar, D.M., Cavalcante, G.T., Rodrigues, A.A., Labruna, M.B., Camargo, L.M., Camargo, E.P., Gennari, S.M., 2006. Prevalence of anti-*Neospora caninum* antibodies in cattle and dogs from Western Amazon, Brazil, in association with some possible risk factors. Vet Parasitol.

Al-Qassab, S., Reichel, M.P., Ellis, J., 2010. A second generation multiplex PCR for typing strains of *Neospora caninum* using six DNA targets. Mol Cell Probes 24, 20-26.

Anderson, M.L., Palmer, C.W., Thurmond, M.C., Picanso, J.P., Blanchard, P.C., Breitmeyer, R.E., Layton, A.W., McAllister, M., Daft, B., Kinde, H., Read, D.H., Dubey, J.P., Conrad, P.A., Barr, B.C., 1995. Evaluation of abortions in cattle attributable to neosporosis in selected dairy herds in California. J Am Vet Med Assoc 207, 1206-1210.

Armengol, R., Pabon, M., Santolaria, P., Cabezon, O., Adelantado, C., Yaniz, J., Lopez-Gatius, F., Almeria, S., 2007. Low seroprevalence of *Neospora caninum* infection associated with the limousin breed in cow-calf herds in Andorra, Europe. J Parasitol 93, 1029-1032.

Atkinson, R.A., Cook, R.W., Reddacliff, L.A., Rothwell, J., Broady, K.W., Harper, P., Ellis, J.T., 2000. Seroprevalence of *Neospora caninum* infection following an abortion outbreak in a dairy cattle herd. Aust Vet J 78, 262-266.

Barber, J.S., Gasser, R.B., Ellis, J., Reichel, M.P., McMillan, D., Trees, A.J., 1997. Prevalence of antibodies to *Neospora caninum* in different canid populations. J Parasitol 83, 1056-1058.

recrudescence of *N caninum* and abortion in already infected animals (Trees and Williams, 2005; Williams et al., 2003). Such a vaccine could be more expensive, as *N caninum*-associated costs in that proportion of the cattle population are estimated to be higher also. Vaccines that confer long-lasting immunity and protection could arguably be more expensive, as the economic losses presented here per cow are annual costs. A once-only applied vaccine that confers long lasting immunity may still be a better benefit-to-cost proposition in either of the above scenarios than a more traditional vaccine that requires an annual booster. Economic consideration may be just as important as drivers for research into efficacious vaccines against *N caninum* as technical feasibility and efficacy (Reichel and Ellis, 2009).

5. Acknowledgments

We thank A/Prof Milton McAllister, Adelaide and Dr Fraser Hill, Gribbles Veterinary, New Zealand for fruitful discussions and comments on drafts of the manuscript.

Barber, J.S., Trees, A.J., 1996. Clinical aspects of 27 cases of neosporosis in dogs. Vet Rec 139, 439-443.

Barling, K.S., Lunt, D.K., Snowden, K.F., Thompson, J.A., 2001a. Association of serologic status for *Neospora caninum* and postweaning feed efficiency in beef steers. J Am Vet Med Assoc 219, 1259-1262.

Barling, K.S., McNeill, J.W., Paschal, J.C., McCollum, F.T., Craig, T.M., Adams, L.G., Thompson, J.A., 2001b. Ranch-management factors associated with antibody seropositivity for *Neospora caninum* in consignments of beef calves in Texas, USA. Prev Vet Med 52, 53-61.

Barling, K.S., McNeill, J.W., Thompson, J.A., Paschal, J.C., McCollum, F.T., Craig, T.M., Adams, L.G., 2000. Association of serologic status for *Neospora caninum* with postweaning weight gain and carcass measurements in beef calves. J Am Vet Med Assoc 217, 1356-1360.

Bartels, C.J., Arnaiz-Seco, J.I., Ruiz-Santa-Quitera, A., Björkman, C., Frössling, J., von Blumroder, D., Conraths, F.J., Schares, G., van Maanen, C., Wouda, W., Ortega-Mora, L.M., 2006a. Supranational comparison of *Neospora caninum* seroprevalences in cattle in Germany, The Netherlands, Spain and Sweden. Vet Parasitol 137, 17-27.

Bartels, C.J., van Schaik, G., Veldhuisen, J.P., van den Borne, B.H., Wouda, W., Dijkstra, T., 2006b. Effect of *Neospora caninum*-serostatus on culling, reproductive performance and milk production in Dutch dairy herds with and without a history of Neospora caninum-associated abortion epidemics. Prev Vet Med 77, 186-198.

Bildfell, R., Davidson, J., Dubey, J.P., 1994. Neospora-induced protozoal bovine abortion in Prince Edward Island. Can Vet J 35, 122.

Björkman, C., McAllister, M.M., Frössling, J., Naslund, K., Leung, F., Uggla, A., 2003. Application of the *Neospora caninum* IgG avidity ELISA in assessment of chronic reproductive losses after an outbreak of neosporosis in a herd of beef cattle. J Vet Diagn Invest 15, 3-7.

Boulton, J.G., Gill, P.A., Cook, R.W., Fraser, G.C., Harper, P.A., Dubey, J.P., 1995. Bovine Neospora abortion in north-eastern New South Wales. Aust Vet J 72, 119-120.

Brickell, J.S., McGowan, M.M., Wathes, D.C., 2010. Association between *Neospora caninum* seropositivity and perinatal mortality in dairy heifers at first calving. Vet Rec 167, 82-85.

Chi, J., VanLeeuwen, J.A., Weersink, A., Keefe, G.P., 2002. Management factors related to seroprevalences to bovine viral-diarrhoea virus, bovine-leukosis virus, *Mycobacterium avium* subspecies *paratuberculosis*, and *Neospora caninum* in dairy herds in the Canadian Maritimes. Prev Vet Med 55, 57-68.

Corbellini, L.G., Smith, D.R., Pescador, C.A., Schmitz, M., Correa, A., Steffen, D.J., Driemeier, D., 2006. Herd-level risk factors for *Neospora caninum* seroprevalence in dairy farms in southern Brazil. Prev Vet Med 74, 130-141.

Cox, B.T., Reichel, M.P., Griffiths, L.M., 1998. Serology of a *Neospora* abortion outbreak on a dairy farm in New Zealand: a case study. N Z Vet J 46, 28-31.

Cramer, G., Kelton, D., Duffield, T.F., Hobson, J.C., Lissemore, K., Hietala, S.K., Peregrine, A.S., 2002. *Neospora caninum* serostatus and culling of Holstein cattle. J Am Vet Med Assoc 221, 1165-1168.

Crawshaw, W.M., Brocklehurst, S., 2003. Abortion epidemic in a dairy herd associated with horizontally transmitted *Neospora caninum* infection. Vet Rec 152, 201-206.

Davison, H.C., French, N.P., Trees, A.J., 1999a. Herd-specific and age-specific seroprevalence of *Neospora caninum* in 14 British dairy herds. Vet Rec 144, 547-550.

Davison, H.C., Otter, A., Trees, A.J., 1999b. Estimation of vertical and horizontal transmission parameters of *Neospora caninum* infections in dairy cattle. Int J Parasitol 29, 1683-1689.

Davison, H.C., Otter, A., Trees, A.J., 1999c. Significance of *Neospora caninum* in British dairy cattle determined by estimation of seroprevalence in normally calving cattle and aborting cattle. Int J Parasitol 29, 1189-1194.

Dijkstra, T., Barkema, H.W., Eysker, M., Beiboer, M.L., Wouda, W., 2003. Evaluation of a single serological screening of dairy herds for *Neospora caninum* antibodies. Vet Parasitol 110, 161-169.

Dubey, J.P., Buxton, D., Wouda, W., 2006. Pathogenesis of bovine neosporosis. J Comp Pathol 134, 267-289.

Dubey, J.P., Jenkins, M.C., Adams, D.S., McAllister, M.M., Anderson-Sprecher, R., Baszler, T.V., Kwok, O.C., Lally, N.C., Björkman, C., Uggla, A., 1997. Antibody responses of cows during an outbreak of neosporosis evaluated by indirect fluorescent antibody test and different enzyme-linked immunosorbent assays. J Parasitol 83, 1063-1069.

Dubey, J.P., Schares, G., 2011. Neosporosis in animals--the last five years. Vet Parasitol 180, 90-108.

Dubey, J.P., Schares, G., Ortega-Mora, L.M., 2007. Epidemiology and control of neosporosis and *Neospora caninum*. Clin Microbiol Rev 20, 323-367.

Dyer, R.M., Jenkins, M.C., Kwok, O.C., Douglas, L.W., Dubey, J.P., 2000. Serologic survey of *Neospora caninum* infection in a closed dairy cattle herd in Maryland: risk of serologic reactivity by production groups. Vet Parasitol 90, 171-181.

Eiras, C., Arnaiz, I., Alvarez-Garcia, G., Ortega-Mora, L.M., Sanjuanl, M.L., Yus, E., Dieguez, F.J., 2011. *Neospora caninum* seroprevalence in dairy and beef cattle from the northwest region of Spain, Galicia. Prev Vet Med 98, 128-132.

Ellis, J.T., 1998. Polymerase chain reaction approaches for the detection of *Neospora caninum* and *Toxoplasma gondii*. Int J Parasitol 28, 1053-1060.

Faria, E.B., Cavalcanti, E.F., Medeiros, E.S., Pinheiro, J.W., Jr., Azevedo, S.S., Athayde, A.C., Mota, R.A., 2010. Risk factors associated with *Neospora caninum* seropositivity in sheep from the State of Alagoas, in the northeast region of Brazil. J Parasitol 96, 197-199.

Garcia-Vazquez, Z., Cruz-Vazquez, C., Medina-Espinoza, L., Garcia-Tapia, D., Chavarria-Martinez, B., 2002. Serological survey of *Neospora caninum* infection in dairy cattle herds in Aguascalientes, Mexico. Vet Parasitol 106, 115-120.

Garcia-Vazquez, Z., Rosario-Cruz, R., Mejia-Estrada, F., Rodriguez-Vivas, I., Romero-Salas, D., Fernandez-Ruvalcaba, M., Cruz-Vazquez, C., 2008. Seroprevalence of *Neospora caninum* antibodies in beef cattle in three southern states of Mexico. Trop Anim Health Prod.

Garcia-Vazquez, Z., Rosario-Cruz, R., Ramos-Aragon, A., Cruz-Vazquez, C., Mapes-Sanchez, G., 2005. *Neospora caninum* seropositivity and association with abortions in dairy cows in Mexico. Vet Parasitol 134, 61-65.

Gasser, R.B., Edwards, G., Cole, R.A., 1993. Neosporosis in a dog. Australian Veterinary Practitioner 23, 190-193.

Gondim, L.F., Sartor, I.F., Hasegawa, M., Yamane, I., 1999. Seroprevalence of *Neospora caninum* in dairy cattle in Bahia, Brazil. Vet Parasitol 86, 71-75.

Gonzalez-Warleta, M., Castro-Hermida, J.A., Carro-Corral, C., Cortizo-Mella, J., Mezo, M., 2008. Epidemiology of neosporosis in dairy cattle in Galicia (NW Spain). Parasitol Res 102, 243-249.

Gonzalez-Warleta, M., Castro-Hermida, J.A., Carro-Corral, C., Mezo, M., 2011. Anti-*Neospora caninum* antibodies in milk in relation to production losses in dairy cattle. Prev Vet Med 101, 58-64.

Guimaraes, J.S., Jr., Souza, S.L., Bergamaschi, D.P., Gennari, S.M., 2004. Prevalence of *Neospora caninum* antibodies and factors associated with their presence in dairy cattle of the north of Parana state, Brazil. Vet Parasitol 124, 1-8.

Hall, C.A., Reichel, M.P., Ellis, J.T., 2005. Neospora abortions in dairy cattle: diagnosis, mode of transmission and control. Veterinary Parasitology 128, 231-241.

Hall, C.A., Reichel, M.P., Ellis, J.T., 2006. Prevalence of *Neospora caninum* infection in Australian (NSW) dairy cattle estimated by a newly validated ELISA for milk. Vet Parasitol 142, 173-178.

Hernandez, J., Risco, C., Donovan, A., 2002. Risk of abortion associated with *Neospora caninum* during different lactations and evidence of congenital transmission in dairy cows. J Am Vet Med Assoc 221, 1742-1746.

Heuer, C., Healy, A., Zerbini, C., 2007. Economic effects of exposure to bovine viral diarrhea virus on dairy herds in New Zealand. Journal of dairy science 90, 5428-5438.

Hietala, S.K., Thurmond, M.C., 1999. Postnatal *Neospora caninum* transmission and transient serologic responses in two dairies. Int J Parasitol 29, 1669-1676.

Hobson, J.C., Duffield, T.F., Kelton, D., Lissemore, K., Hietala, S.K., Leslie, K.E., McEwen, B., Peregrine, A.S., 2005. Risk factors associated with *Neospora caninum* abortion in Ontario Holstein dairy herds. Vet Parasitol 127, 177-188.

Houe, H., 2003. Economic impact of BVDV infection in dairies. Biologicals 31, 137-143.

Innes, E.A., 2007. The host-parasite relationship in pregnant cattle infected with *Neospora caninum*. Parasitology 134, 1903-1910.

Jenkins, M.C., Caver, J.A., Björkman, C., Anderson, T.C., Romand, S., Vinyard, B., Uggla, A., Thulliez, P., Dubey, J.P., 2000. Serological investigation of an outbreak of *Neospora caninum*-associated abortion in a dairy herd in southeastern United States. Vet Parasitol 94, 17-26.

Keefe, G.P., VanLeeuwen, J.A., 2000. Neospora then and now: prevalence of *Neospora caninum* in Maritime Canada in 1979, 1989, and 1998. Can Vet J 41, 864-866.

Kritzner, S., Sager, H., Blum, J., Krebber, R., Greif, G., Gottstein, B., 2002. An explorative study to assess the efficacy of Toltrazuril-sulfone (Ponazuril) in calves experimentally infected with *Neospora caninum*. Ann Clin Microbiol Antimicrob 1, 4.

Liddell, S., Jenkins, M.C., Collica, C.M., Dubey, J.P., 1999. Prevention of vertical transfer of *Neospora caninum* in BALB/c mice by vaccination. Journal for Parasitology 85, 1072-1075.

Locatelli-Dittrich, R., Soccol, V.T., Richartz, R.R., Gasino-Joineau, M.E., Vinne, R., Pinckney, R.D., 2001. Serological diagnosis of neosporosis in a herd of dairy cattle in southern Brazil. J Parasitol 87, 1493-1494.

Mainar-Jaime, R.C., Thurmond, M.C., Berzal-Herranz, B., Hietala, S.K., 1999. Seroprevalence of *Neospora caninum* and abortion in dairy cows in northern Spain. Vet Rec 145, 72-75.

Marques, F.A., Headley, A.S., Figueredo-Pereira, V., Taroda, A., Barros, L.D., Cunha, I.A., Munhoz, K., Bugni, F.M., Zulpo, D.L., Igarashi, M., Vidotto, O., Guimaraes, J.S., Jr., Garcia, J.L., 2011. *Neospora caninum*: evaluation of vertical transmission in slaughtered beef cows (Bos indicus). Parasitol Res 108, 1015-1019.

McAllister, M.M., Björkman, C., Anderson-Sprecher, R., Rogers, D.G., 2000. Evidence of point-source exposure to *Neospora caninum* and protective immunity in a herd of beef cows. J Am Vet Med Assoc 217, 881-887.

McAllister, M.M., Huffman, E.M., Hietala, S.K., Conrad, P.A., Anderson, M.L., Salman, M.D., 1996. Evidence suggesting a point source exposure in an outbreak of bovine abortion due to neosporosis. J Vet Diagn Invest 8, 355-357.

McDougall, S., Rhodes, F.M., Verkerk, G.A., 2005. Pregnancy loss in dairy cattle in the Waikato region of New Zealand. New Zealand Veterinary Journal 53, 279-287.

McInnes, L.M., Irwin, P., Palmer, D.G., Ryan, U.M., 2006. *In vitro* isolation and characterisation of the first canine *Neospora caninum* isolate in Australia. Vet Parasitol 137, 355-363.

Miller, C., Quinn, H., Ryce, C., Reichel, M.P., Ellis, J.T., 2005. Reduction in transplacental transmission of *Neospora caninum* in outbred mice by vaccination. Int J Parasitol 35, 821-828.

Minervino, A.H., Ragozo, A.M., Monteiro, R.M., Ortolani, E.L., Gennari, S.M., 2008. Prevalence of *Neospora caninum* antibodies in cattle from Santarem, Para, Brazil. Res Vet Sci 84, 254-256.

Moen, A.R., Wouda, W., Mul, M.F., Graat, E.A., van Werven, T., 1998. Increased risk of abortion following *Neospora caninum* abortion outbreaks: a retrospective and prospective cohort study in four dairy herds. Theriogenology 49, 1301-1309.

Moore, D.P., Campero, C.M., Odeon, A.C., Chayer, R., Bianco, M.A., 2003. Reproductive losses due to *Neospora caninum* in a beef herd in Argentina. J Vet Med B Infect Dis Vet Public Health 50, 304-308.

Moore, D.P., Campero, C.M., Odeon, A.C., Posso, M.A., Cano, D., Leunda, M.R., Basso, W., Venturini, M.C., Späth, E., 2002. Seroepidemiology of beef and dairy herds and fetal study of *Neospora caninum* in Argentina. Vet Parasitol 107, 303-316.

Moore, D.P., Perez, A., Agliano, S., Brace, M., Canton, G., Cano, D., Leunda, M.R., Odeon, A.C., Odriozola, E., Campero, C.M., 2009. Risk factors associated with *Neospora caninum* infections in cattle in Argentina. Vet Parasitol 161, 122-125.

Moore, D.P., Regidor-Cerrillo, J., Morrell, E., Poso, M.A., Cano, D.B., Leunda, M.R., Linschinky, L., Odeon, A.C., Odriozola, E., Ortega-Mora, L.M., Campero, C.M., 2008. The role of *Neospora caninum* and *Toxoplasma gondii* in spontaneous bovine abortion in Argentina. Vet Parasitol 156, 163-167.

Morales, E., Trigo, F.J., Ibarra, F., Puente, E., Santacruz, M., 2001a. Neosporosis in Mexican dairy herds: lesions and immunohistochemical detection of *Neospora caninum* in fetuses. J Comp Pathol 125, 58-63.

Morales, E., Trigo, F.J., Ibarra, F., Puente, E., Santacruz, M., 2001b. Seroprevalence study of bovine neosporosis in Mexico. J Vet Diagn Invest 13, 413-415.

Munday, B.L., Dubey, J.P., Mason, R.W., 1990. *Neospora caninum* infection in dogs. Aust Vet J 67, 76-77.

Nasir, A., Lanyon, S.R., Schares, G., Anderson, M.L., Reichel, M.P., 2012. Sero-prevalence of *Neospora caninum* and *Besnoitia besnoiti* in South Australian beef and dairy cattle. Vet Parasitol 186, 480-485.

Obendorf, D.L., Murray, N., Veldhuis, G., Munday, B.L., Dubey, J.P., 1995. Abortion caused by neosporosis in cattle. Aust Vet J 72, 117-118.

Pan, Y., Jansen, G.B., Duffield, T.F., Hietala, S., Kelton, D., Lin, C.Y., Peregrine, A.S., 2004. Genetic susceptibility to *Neospora caninum* infection in Holstein cattle in Ontario. J Dairy Sci 87, 3967-3975.

Paré, J., Fecteau, G., Fortin, M., Marsolais, G., 1998. Seroepidemiologic study of *Neospora caninum* in dairy herds. J Am Vet Med Assoc 213, 1595-1598.

Pare, J., Hietala, S.K., Thurmond, M.C., 1995. Interpretation of an indirect fluorescent antibody test for diagnosis of Neospora sp. infection in cattle. J Vet Diagn Invest 7, 273-275.

Paré, J., Hietala, S.K., Thurmond, M.C., 1995. An enzyme-linked immunosorbent assay (ELISA) for serological diagnosis of *Neospora* sp. infection in cattle. J Vet Diagn Invest 7, 352-359.

Paré, J., Thurmond, M.C., Hietala, S.K., 1996. Congenital *Neospora caninum* infection in dairy cattle and associated calfhood mortality. Can J Vet Res 60, 133-139.

Paré, J., Thurmond, M.C., Hietala, S.K., 1997. *Neospora caninum* antibodies in cows during pregnancy as a predictor of congenital infection and abortion. J Parasitol 83, 82-87.

Patitucci, A.N., Alley, M.R., Jones, B.R., Charleston, W.A., 1997. Protozoal encephalomyelitis of dogs involving *Neospora caninum* and *Toxoplasma gondii* in New Zealand. N Z Vet J 45, 231-235.

Patitucci, A.N., Charleston, W.A., Alley, M.R., O'Connor, R.J., Pomroy, W.E., 1999. Serological study of a dairy herd with a recent history of *Neospora* abortion. N Z Vet J 47, 28-30.

Peregrine, A.S., Martin, S.W., Hopwood, D.A., Duffield, T.F., McEwen, B., Hobson, J.C., Hietala, S.K., 2006. *Neospora caninum* and Leptospira serovar serostatus in dairy cattle in Ontario. Can Vet J 47, 467-470.

Pfeiffer, D.U., Williamson, N.B., Reichel, M.P., Wichtel, J.J., Teague, W.R., 2002. A longitudinal study of *Neospora caninum* infection on a dairy farm in New Zealand. Prev Vet Med 54, 11-24.

Presi, P., Struchen, R., Knight-Jones, T., Scholl, S., Heim, D., 2011. Bovine viral diarrhea (BVD) eradication in Switzerland--experiences of the first two years. Preventive Veterinary Medicine 99, 112-121.

Quinn, H.E., Windsor, P.A., Kirkland, P.D., Ellis, J.T., 2004. An outbreak of abortion in a dairy herd associated with *Neospora caninum* and bovine pestivirus infection. Aust Vet J 82, 99-101.

Quintanilla-Gozalo, A., Pereira-Bueno, J., Tabares, E., Innes, E.A., Gonzalez-Paniello, R., Ortega-Mora, L.M., 1999. Seroprevalence of *Neospora caninum* infection in dairy and beef cattle in Spain. Int J Parasitol 29, 1201-1208.

Reichel, M.P., 1998. Prevalence of *Neospora* antibodies in New Zealand dairy cattle and dogs. N Z Vet J 46, 38.

Reichel, M.P., Ellis, J.T., 2002. Control options for *Neospora caninum* infections in cattle--current state of knowledge. N Z Vet J 50, 86-92.

Reichel, M.P., Ellis, J.T., 2006. If control of *Neospora caninum* infection is technically feasible does it make economic sense? Veterinary Parasitology 142, 23-34.

Reichel, M.P., Ellis, J.T., 2009. *Neospora caninum*--how close are we to development of an efficacious vaccine that prevents abortion in cattle? Int J Parasitol 39, 1173-1187.

Reichel, M.P., Ellis, J.T., Dubey, J.P., 2007. Neosporosis and hammondiosis in dogs. J Small Anim Pract 48, 308-312.

Reichel, M.P., Pfeiffer, D.U., 2002. An analysis of the performance characteristics of serological tests for the diagnosis of *Neospora caninum* infection in cattle. Veterinary Parasitology 107, 197-207.

Reichel, M.P., Thornton, R.N., Morgan, P.L., Mills, R.J., Schares, G., 1998. Neosporosis in a pup. N Z Vet J 46, 106-110.

Rodriguez, I., Choromanski, L., Rodgers, S.J., Weinstock, D., 2002. Survey of *Neospora caninum* antibodies in dairy and beef cattle from five regions of the United States. Vet Ther 3, 396-401.

Rogers, R.W., Martin, S.W., Meek, A.H., 1985. Reproductive efficiency and calf survival in Ontario beef cow-calf herds: a cross-sectional mail survey. Can J Comp Med 49, 27-33.

Ruehlmann, D., Podell, M., Oglesbee, M., Dubey, J.P., 1995. Canine neosporosis: a case report and literature review. J Am Anim Hosp Assoc 31, 174-183.

Sanderson, M.W., Gay, J.M., Baszler, T.V., 2000. *Neospora caninum* seroprevalence and associated risk factors in beef cattle in the northwestern United States. Vet Parasitol 90, 15-24.

Schares, G., Conraths, F.J., Reichel, M.P., 1999. Bovine neosporosis: comparison of serological methods using outbreak sera from a dairy herd in New Zealand. Int J Parasitol 29, 1659-1667.

Stoessel, Z., Taylor, L.F., McGowan, M.R., Coleman, G.T., Landmann, J.K., 2003. Prevalence of antibodies to *Neospora caninum* within central Queensland beef cattle. Aust Vet J 81, 165-166.

Tennent-Brown, B.S., Pomroy, W.E., Reichel, M.P., Gray, P.L., Marshall, T.S., Moffat, P.A., Rogers, M., Driscoll, V.A., Reeve, O.F., Ridler, A.L., Ritaven, S., 2000. Prevalence of *Neospora* antibodies in beef cattle in New Zealand. N Z Vet J 48, 149-150.

Thobokwe, G., Heuer, C., 2004. Incidence of abortion and association with putative causes in dairy herds in New Zealand. N Z Vet J 52, 90-94.

Thornton, R.N., Gajadhar, A., Evans, J., 1994. *Neospora* abortion epidemic in a dairy herd. New Zealand Veterinary Journal 42, 190-191.

Thornton, R.N., Thompson, E.J., Dubey, J.P., 1991. *Neospora* abortion in New Zealand cattle. New Zealand Veterinary Journal 39, 129-133.

Thurmond, M.C., Hietala, S.K., 1996. Culling associated with *Neospora caninum* infection in dairy cows. Am J Vet Res 57, 1559-1562.

Thurmond, M.C., Hietala, S.K., 1997a. Effect of congenitally acquired *Neospora caninum* infection on risk of abortion and subsequent abortions in dairy cattle. Am J Vet Res 58, 1381-1385.

Thurmond, M.C., Hietala, S.K., 1997b. Effect of *Neospora caninum* infection on milk production in first-lactation dairy cows. J Am Vet Med Assoc 210, 672-674.

Thurmond, M.C., Hietala, S.K., Blanchard, P.C., 1997. Herd-based diagnosis of *Neospora caninum*-induced endemic and epidemic abortion in cows and evidence for congenital and postnatal transmission. J Vet Diagn Invest 9, 44-49.

Tiwari, A., Vanleeuwen, J.A., Dohoo, I.R., Keefe, G.P., Haddad, J.P., Scott, H.M., Whiting, T., 2009. Risk factors associated with *Mycobacterium avium* subspecies *paratuberculosis* seropositivity in Canadian dairy cows and herds. Prev Vet Med 88, 32-41.

Trees, A.J., Guy, F., Low, J.C., Roberts, L., Buxton, D., Dubey, J.P., 1994. Serological evidence implicating *Neospora* species as a cause of abortion in British cattle. Vet Rec 134, 405-407.

Trees, A.J., Williams, D.J., 2005. Endogenous and exogenous transplacental infection in *Neospora caninum* and *Toxoplasma gondii*. Trends Parasitol 21, 558-561.

VanLeeuwen, J.A., Forsythe, L., Tiwari, A., Chartier, R., 2005. Seroprevalence of antibodies against bovine leukemia virus, bovine viral diarrhea virus, *Mycobacterium avium* subspecies *paratuberculosis*, and *Neospora caninum* in dairy cattle in Saskatchewan. Can Vet J 46, 56-58.

Venturini, M.C., Venturini, L., Bacigalupe, D., Machuca, M., Echaide, I., Basso, W., Unzaga, J.M., Di Lorenzo, C., Guglielmone, A., Jenkins, M.C., Dubey, J.P., 1999. *Neospora caninum* infections in bovine foetuses and dairy cows with abortions in Argentina. Int J Parasitol 29, 1705-1708.

Waldner, C., Wildman, B.K., Hill, B.W., Fenton, R.K., Pittman, T.J., Schunicht, O.C., Jim, G.K., Guichon, P.T., Booker, C.W., 2004. Determination of the seroprevalence of *Neospora caninum* in feedlot steers in Alberta. Can Vet J 45, 218-224.

Waldner, C.L., 2005. Serological status for *N. caninum*, bovine viral diarrhea virus, and infectious bovine rhinotracheitis virus at pregnancy testing and reproductive performance in beef herds. Anim Reprod Sci 90, 219-242.

Waldner, C.L., Henderson, J., Wu, J.T., Coupland, R., Chow, E.Y., 2001. Seroprevalence of *Neospora caninum* in beef cattle in northern Alberta. Can Vet J 42, 130-132.

Waldner, C.L., Janzen, E.D., Henderson, J., Haines, D.M., 1999. Outbreak of abortion associated with *Neospora caninum* infection in a beef herd. J Am Vet Med Assoc 215, 1485-1490, 1448-1489.

Waldner, C.L., Janzen, E.D., Ribble, C.S., 1998. Determination of the association between *Neospora caninum* infection and reproductive performance in beef herds. J Am Vet Med Assoc 213, 685-690.

Wapenaar, W., Barkema, H.W., O'Handley, R.M., Bartels, C.J., 2007. Use of an enzyme-linked immunosorbent assay in bulk milk to estimate the prevalence of *Neospora caninum* on dairy farms in Prince Edward Island, Canada. The Canadian veterinary journal. La revue veterinaire canadienne 48, 493-499.

Weston, J.F., Heuer, C., Williamson, N.B., 2012. Efficacy of a *Neospora caninum* killed tachyzoite vaccine in preventing abortion and vertical transmission in dairy cattle. Prev Vet Med 103, 136-144.

Weston, J.F., Williamson, N.B., Pomroy, W.E., 2005. Associations between pregnancy outcome and serological response to *Neospora caninum* among a group of dairy heifers. N Z Vet J 53, 142-148.

Williams, D.J., Davison, H.C., Helmick, B., McGarry, J., Guy, F., Otter, A., Trees, A.J., 1999. Evaluation of a commercial ELISA for detecting serum antibody to *Neospora caninum* in cattle. Vet Rec 145, 571-575.

Williams, D.J., Guy, C.S., Smith, R.F., Guy, F., McGarry, J.W., McKay, J.S., Trees, A.J., 2003. First demonstration of protective immunity against foetopathy in cattle with latent *Neospora caninum* infection. Int J Parasitol 33, 1059-1065.

Williams, D.J., Trees, A.J., 2006. Protecting babies: vaccine strategies to prevent foetopathy in *Neospora caninum*-infected cattle. Parasite Immunol 28, 61-67.

Woodbine, K.A., Medley, G.F., Moore, S.J., Ramirez-Villaescusa, A., Mason, S., Green, L.E., 2008. A four year longitudinal sero-epidemiology study of *Neospora caninum* in adult cattle from 114 cattle herds in south west England: associations with age, herd and dam-offspring pairs. BMC Vet Res 4, 35.

Wouda, W., Moen, A.R., Schukken, Y.H., 1998. Abortion risk in progeny of cows after a *Neospora caninum* epidemic. Theriogenology 49, 1311-1316.

Legends of Figures

Figure 1: Graphical representation of the review process for peer-reviewed literature relevant to the assessment of the economic impact of *N caninum* infections/abortions in cattle world-wide

Table(s)

Table 1: Median background and *N caninum*-specific abortion risk (and range), odds ratios (and range) and median (and range) of *N caninum* sero-prevalence in dairy and beef cattle in the cattle industries of ten countries (ND = no data)

Country		Median abortion risk in % (range)		Odds ratio	Seroprevalence in % (range)	References
		Background	*Nc*-specific abortion risk			
Argentina	Dairy	ND	ND	2.1 (1.8 – 2.4)	22.2 (16.6 – 64.5)	(Moore et al., 2002; Moore et al., 2009; Venturini et al., 1999)
	Beef	ND	ND	12.0 (6.2 – 23.3)	11.2 (4.7 – 20.3)	(Moore et al., 2003; Moore et al., 2002; Moore et al., 2009)
Australia	Dairy	2.5	9.8 (5.4 – 23.5)	6.9 (2.6 – 13.0)	10.9 (3.8 - 23.7)	(Atkinson et al., 2000; Boulton et al., 1995; Hall et al., 2005, 2006; Nasir et al., 2012; Obendorf et al., 1995; Quinn et al., 2004)
	Beef	ND	ND	ND	8.7 (2.5 – 14.9)	(Nasir et al., 2012; Stoessel et al., 2003)
Brazil	Dairy	ND	ND	ND	16.1 (14.1 – 34.8)	(Aguiar et al., 2006; Corbellini et al., 2006; Gondim et al., 1999; Guimaraes et al., 2004; Locatelli-Dittrich et al., 2001; Minervino et al., 2008)
	Beef	ND	ND	ND	15.1 (9.5 – 16.7)	(Aguiar et al., 2006; Marques et al., 2011; Minervino et al., 2008)
Canada	Dairy	2.1	15.8 (7.1 – 18.8)	ND	12.0 (5.5 – 22.5)	(Bildfell et al., 1994; Chi et al., 2002; Cramer et al., 2002; Hobson et al., 2005; Keefe and VanLeeuwen, 2000; Pan et al., 2004; Paré et al., 1998; Peregrine et al., 2006; Tiwari et al., 2009; VanLeeuwen et al., 2005)
	Beef	1.2	ND	6.0 (5.7 – 6.2)	11.3 (5.9 – 81.3)	(Rogers et al., 1985; Waldner et al., 2004; Waldner, 2005; Waldner et al., 2001; Waldner et al., 1999; Waldner et al., 1998)
Mexico	Dairy	ND	ND	1.7 (1.3 – 10)	55.9 (42.0 – 59.0)	(Garcia-Vazquez et al., 2002; Garcia-Vazquez et al., 2005; Morales et al., 2001b)
	Beef	ND	ND	ND	11.6 (11.6 – 11.6)	(Garcia-Vazquez et al., 2008)
Netherlands	Dairy	ND	ND	2.4 (1.7 – 3.1)	10.4 (9.9 – 10.8)	(Bartels et al., 2006a; Bartels et al., 2006b; Dijkstra et al., 2003; Moen et al., 1998; Wouda et al., 1998)
New Zealand	Dairy	2.9	6.4 (2.6 – 25.9)	4.2 (1.7 – 26)	30.4 (6.8 – 73.0)	(Cox et al., 1998; Faria et al., 2010; Heuer et al., 2007; McDougall et al., 2005; Patitucci et al., 1999; Pfeiffer et al., 2002; Reichel, 1998; Reichel and Pfeiffer, 2002; Schares et al., 1999; Thobokwe and Heuer, 2004; Thornton et al., 1994; Thornton et al., 1991; Weston et al., 2005)
	Beef	ND	ND	ND	2.8 (2.8 – 2.8)	(Tennent-Brown et al., 2000)
Spain	Dairy	ND	ND	6.2 (3.3 - 9.1)	19.1 (15.7 – 35.9)	(Bartels et al., 2006a; Eiras et al., 2011; Gonzalez-Warleta et al., 2008; Gonzalez-Warleta et al., 2011; Mainar-Jaime et al., 1999; Quintanilla-Gozalo et al., 1999)
	Beef	ND	ND	ND	15.8 (7.4 – 25.1)	(Armengol et al., 2007; Bartels et al., 2006a; Eiras et al., 2011; Quintanilla-Gozalo et al., 1999)
UK	Dairy	ND	14.3 (5.0 – 43.0)	3.5 (2.2 – 5.7)	15.0 (6.0 – 37.7)	(Brickell et al., 2010; Crawshaw and Brocklehurst, 2003; Davison et al., 1999a; Davison et al., 1999b, c; Trees et al., 1994; Williams et al., 1999; Woodbine et al., 2008)
USA	Dairy	ND	18.6 (0.6 – 39.4)	7.2 (1.7 – 40.0)	49.2 (16.1 – 89.2)	(Anderson et al., 1995; Dubey et al., 1997; Dyer et al., 2000; Hernandez et al., 2002; Hietala and Thurmond, 1999; Jenkins et al., 2000; McAllister et al., 1996; Paré et al., 1997; Rodriguez et al., 2002; Thurmond and Hietala, 1997a; Thurmond et al., 1997)
	Beef	ND	9.1 (9.1 – 9.1)	ND	13.0 (7.5 – 81.7)	(Barling et al., 2001b; Barling et al., 2000; McAllister et al., 2000; Sanderson et al., 2000; Thurmond et al., 1997)
TOTAL	Dairy	2.5	14.3 (0.6 – 39.4)	3.5 (1.3 – 40.0)	16.1 (3.8 – 89.2)	
	Beef	1.2	9.1 (9.1 – 9.1)	9.0 (5.7 – 23.3)	11.5 (2.5 – 81.7)	

Table 2: Number of pregnant cows and heifers at potential risk of abortion, estimated median and range of specific *N caninum* abortion costs (in USD at May 2012 exchange rates) at national and herd level in ten countries and their cattle industries

Country	Industry	Cows at risk (mill)	National cost (mill US$)	(range) mill US$	Herd cost ('000s $)	Range
Argentina	Dairy	8.8	38.5	29.2 – 85.3	4.0	3.0 – 8.7
	Beef	1.8	48.9	22.6 – 57.6	0.6	0.3 – 0.7
Australia	Dairy	1.8	26.6	7.1 – 54.0	9.3	2.5 – 18.8
	Beef	9.7	74.1	27.7 – 139.5	1.5	0.6 – 2.8
Brazil	Dairy	14.2	51.3	35.8 – 111.3	0.0	0.0 – 0.0
	Beef	29.7	101.0	63.6 – 111.7	0.0	0.0 – 0.0
Canada	Dairy	1.3	17.1	10.0 – 32.1	1.3	0.8 – 2.5
	Beef	4.3	14.3	13.6 – 14.8	0.2	0.2 – 0.2
Mexico	Dairy	2.7	68.5	52.4 – 403.2	0.1	0.1 – 0.5
	Beef	30.3	94.8	94.8 – 94.8	0.1	0.1 – 0.1
Netherlands	Dairy	1.7	12.1	8.3 – 20.2	0.7	0.5 – 0.9
New Zealand	Dairy	4.8	35.7	14.5 – 221.0	11.0	4.5 – 68.0
	Beef	1.1	1.1	1.1 – 1.1	0.1	0.1 – 0.1
Spain	Dairy	0.9	19.8	7.2 – 57.9	0.5	0.2 – 1.6
	Beef	1.7	9.8	4.6 – 15.6	0.2	0.1 – 0.2
UK	Dairy	2.0	27.0	10.8 – 32.4	1.8	0.7 – 2.1
USA	Dairy	8.2	546.3	165.8 – 721.9	12.2	3.7 – 16.1
	Beef	23.6	111.4	64.3 – 205.7	0.1	0.1 – 0.3
TOTAL per industry	Dairy	46.3	842.9	341.1 – 1739.3	1.6	0.0 – 68.0
	Beef	102.2	455.4	292.3 – 640.8	0.15	0.0 – 2.8
Total (all cattle)		148.6	1298.3	633.4 – 2380.1	0.5	0.0 – 68.0

Figure(s)

Figure 1: