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Break-even analysis of costs for controlling *Toxoplasma gondii* infections in slaughter pigs via a serological surveillance program in the Netherlands

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ABSTRACT

Toxoplasma gondii (*T. gondii*) is a food safety hazard which causes a substantial human disease burden and cost-of-illness. Infected pig meat is a common source of toxoplasmosis. A break-even analysis was conducted to estimate the point for which the intervention cost at fattening pig farms equaled the cost of averted human disease burden and cost-of-illness minus the costs of a *T. gondii* surveillance program. The surveillance program comprised serological testing of blood samples taken at slaughter. Break-even points were determined given alternative levels of the effectiveness of the intervention program (10% up to 90% in steps of 10%), the value of an averted DALY (20,000, 50,000 and 80,000 Euro), and threshold of sample prevalence for a farm to be under intervention (5% up to 50% out of 20 samples in steps of 5%). Since test characteristics are a determining factor in the break-even analysis, and literature is inconclusive concerning sensitivity (se) and specificity (sp) of the serological test kit used, two alternative sets of assumptions were analysed. The estimated maximum costs of an intervention if only benefits for domestic consumers were accounted amounted approximately 2981 Euro (se = 98.9% and sp = 92.7%) versus 4389 Euro (se = 65.2% and sp = 97.4%) per year per fattening pig farm under intervention assuming an effectiveness of 50%, 50,000 Euro per averted DALY and threshold *T. gondii* sample prevalence of 5% for a farm to be under intervention. Since almost 80% of the gross domestic production is exported corresponding break-even values increased up to 12,034 Euro and 18,366 Euro if benefits for consumers abroad were included as well. Empirical research to strengthen the knowledge about the efficacy of a farm intervention measures is recommended.

1. Introduction

Toxoplasma gondii (*T. gondii*) is the causative agent of toxoplasmosis and is one of the most successful parasites worldwide. *T. gondii* is able to infect virtually all warm-blooded vertebrates. It is estimated that approximately one-third of the world's population is infected with *T. gondii* (Verma and Khanna, 2013). The integrated public health impact defined as disease burden expressed in Disability Adjusted Life Years (DALYs) is globally considered to be very high (Torgerson and Mastroiacovo, 2013). In the USA, *T. gondii* ranked third out of 14 foodborne pathogens (Batz et al., 2012), and in the Netherlands, the total burden of toxoplasmosis was estimated to be 3620 DALYs ranking *T. gondii* as the first among 14 enteral pathogens examined (Havelaar et al., 2010). It is therefore essential to develop and implement effective and economically efficient intervention strategies to reduce the burden of human *T. gondii* infections.

Cats are the definitive host of *T. gondii* (Dubey, 2010). Cats become infected by feeding on infected tissues of intermediate hosts (e.g. rodents and birds). This results in an enteroepithelial sexual cycle that leads to the shedding of millions of oocysts into the environment (Dubey, 2010). Pigs and other livestock species can become infected by oral uptake of oocysts from the environment and develop the tissue cyst stage in striated muscles and other organs (Kijlstra and Jongert, 2008). Moreover, pigs can also become infected by the consumption of infected rodents entering the stables (Meerburg et al., 2006b).

The major source of human infection is food, causing 30% to 63% of the infections (Cook et al., 2000). Within food, pig meat is an important source causing 50% of the infections (Havelaar et al., 2012). Viable *T. gondii* tissue cysts have been isolated from

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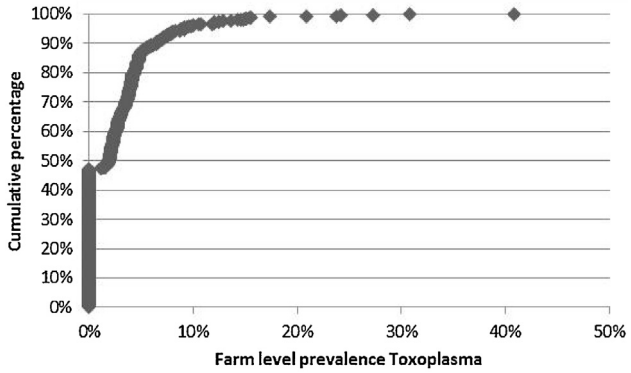

Fig. 1. Cumulative probability distribution of farm level prevalence for *T. gondii*.

tissues and meat of pigs naturally and experimentally infected with *T. gondii* (Dubey, 2009). These tissue cysts can infect humans.

Prevalence of *T. gondii* infections in pigs is related to farm management (Kijlstra et al., 2004; Van der Giessen et al., 2007). The number of pigs with antibodies against *T. gondii* on free-range farms is higher than on farms where pigs are kept indoors only (Kijlstra et al., 2004). The risk of *T. gondii* infections in pigs on a farm has also been associated with the presence of cats and rodents on the farm, the degree of cleaning and disinfection, and the use of water from private sources, especially wells (Kijlstra et al., 2004). A change of farm management aiming to control such risk factors may contribute to the reduction of *T. gondii* infections in pigs. Potential on-farm interventions to control *T. gondii* include vaccination of livestock, vaccination of farm cats and stringent on-farm bio-security measures (Kijlstra and Jongert, 2008).

The European Food Safety Authority (EFSA) included *T. gondii* as one of the public health hazards in pigs to be assessed within meat inspection (EFSA, 2011). To control *T. gondii* infections in pigs, EFSA proposed to develop a risk based surveillance system and for that purpose EFSA has proposed epidemiological indicators (EFSA, 2011). Therefore, in the Netherlands a research program was started to translate the epidemiological indicators into a practical risk based surveillance program. This surveillance program targets at identification of, and intervention at, Dutch fattening pig farms with high farm prevalence of *T. gondii* infection (i.e. risk-based intervention) using serological testing of blood samples taken at slaughter. However, the efficacy and cost-effectiveness of this risk based surveillance program is not clear yet. As part of the development of the surveillance program we calculated the break-even point for which the intervention cost at fattening pig farms equal averted human disease burden and averted cost-of-illness minus cost of the surveillance program.

2. Material and methods

2.1. Farm prevalence of T. gondii

Actual farm prevalence data of *T. gondii* from the Netherlands was used as key input in this study. For determining the farm prevalence of *T. gondii*, blood samples were collected from fattening pigs at slaughter in five slaughterhouses of the VION Food Group in the Netherlands. Sera were tested in the PrioCHECK® Toxoplasma Ab porcine ELISA (Thermo Fisher Scientific Prionics Lelystad B.V.). Farm prevalence was derived from 642 fattening pig farms from which at least 20 samples were sampled in the year 2014 (Fig. 1). This number was chosen arbitrarily to reflect the trade-off between number of farms to determine heterogeneity of prevalence and accuracy of the prevalence (low number of samples complicate an accurate estimation of a low prevalence). Details of collection of sera and the epidemiological analysis of the serological results are described by Swanenburg et al. (2015).

2.2. Modelling approach

To estimate the break-even point for which the intervention cost at fattening pig farms equal the cost of averted human disease burden and averted cost-of-illness minus the surveillance program costs, we developed a mathematical model. The model was based on the cost-utility approach proposed by Mangen et al. (2007). Interventions are implemented risk-based, only at fattening pig farms with a high risk of *T. gondii* infections. Let σ be the proportion of *T. gondii* infected fattening pigs under intervention, i.e. number of fattening pigs on high risk farms where the intervention is implemented compared to the total infected population of fattening pigs in a country. Whether a farm is a high risk farm, is classified by the prevalence threshold *pt* of positive test results in the total sample, i.e. a threshold for the number of positive samples in the total number of samples taken in a year. Each individual sample is tested by a serological test with sensitivity *se* and specificity *sp*. Thus the proportion of fattening pigs under intervention σ depends on the prevalence threshold *pt* and the characteristics *se* and *sp* of the serological test. The function of σ is in the current study derived from observed data.

For *i* being the annual incidence of human toxoplasmosis cases attributable to consumption of pig meat, the efficacy of an intervention is modelled with κ $(0 \leq \kappa \leq 1)$, the relative risk of the intervention. This is defined by the relative probability of a human acquiring toxoplasmosis after implementation of the intervention on all fattening pig farms compared to the probability before its implementation. In this study, incidence and disease burden of toxoplasmosis attributable to pig meat consumption is a combination of acquired and congenital toxoplasma infections. It was assumed that the number of human cases of toxoplasmosis caused by the consumption of meat of pigs from a herd, is proportional to the *T. gondii* prevalence in that herd. Thus, the reduction in number of infected pigs after implementation of an intervention is proportional to the reduction in human cases. Then, the number of averted human cases of toxoplasmosis per year ($\Delta i(\kappa,pt,se,sp)$) depends on the efficacy κ of the intervention, and is:

$$\Delta i(\kappa, pt, se, sp) = \kappa \cdot \sigma(pt, se, sp) \cdot i$$

We assumed that a reduction in the incidence of toxoplasmosis cases would cause a proportional reduction of cost-of-illness and disease burden. The total annual cost-of-illness of toxoplasmosis attributable to consumption of pig meat (m) includes direct healthcare costs, direct non-healthcare costs, and indirect non-healthcare costs (Mangen et al., 2013). The averted cost-of-illness in Euro per year ($\Delta m(\kappa,pt,se,sp)$) depends on the efficacy κ of the intervention and the proportion σ of infected pigs under intervention, and is:

$$\Delta m(\kappa, pt, se, sp) = \kappa \cdot \sigma(pt, se, sp) \cdot m$$

The annual human disease burden of toxoplasmosis infections attributable to consumption of pig meat *d* was quantified in DALY. A DALY quantifies the impact of premature death and disability on a population by combining them into a single, comparable measure (Murray, 1994; Murray and Lopez, 1994; Murray et al., 1994). One DALY is equal to one year of healthy life lost (Peabody et al., 2005). Ultimately, averted DALY's quantify non-monetary benefits for the society as a whole (Mangen et al., 2013). (Murray et al., 1994). The averted disease burden ($\Delta d(\kappa,pt,se,sp)$) in averted DALY per year depends on the efficacy κ of the intervention and the proportion σ of infected pigs under intervention, and is:

$$\Delta d(\kappa, pt, se, sp) = \kappa \cdot \sigma(pt, se, sp) \cdot d$$