A computer simulation of the prevention of the transmission of *Toxoplasma gondii* on swine farms using a feline *T. gondii* vaccine

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**Abstract**

Transmission of *Toxoplasma gondii* on swine farms was investigated using a deterministic dynamic computer simulation model. A primary focus was to evaluate a feline *T. gondii* vaccine. Animal populations (swine and cats) were compartmentalized based on the stage of *T. gondii* infection. Simulations were run under conditions of closed and equilibrium population size. Model parameters were varied in a factorial experimental design to test the following hypotheses: *T. gondii* infection in finishing pigs decreases with (1) vaccination of susceptible cats, (2) an increase in the proportion of cats captured for vaccination, (3) a decrease in the initial number of cats, (4) a decrease in the initial *T. gondii* prevalence in cats and (5) a decrease in oocyst-survival time. Seeding conditions included a total of 10, 20, 30, 40 or 50 cats, initial *T. gondii* prevalences in cats of 30, 60 or 90%, vaccination of 0, 50 or 75% of the cats and two vaccination schedules (the *field* schedule from a prior trial and a weaning-vaccination schedule). Simulations were run at oocyst-survival times of 52, 39 and 26 weeks. *T. gondii* prevalence in finishing pigs was recorded every week for 10 years. The probability of elimination of *T. gondii* from finishing pigs increased with a decrease in the number of cats and a decrease in oocyst-survival time.

The last-year average prevalence was used as the outcome in a multiple linear regression analysis. Decreased *T. gondii* prevalence in finishing pigs was the result of a decrease in the initial number of cats on the farm (squared semipartial correlation coefficient \((sr^2) = 47\%\)), decreased oocyst survival \((sr^2 = 35\%)\), using the weaning-vaccination schedule \((sr^2 = 7\%)\) and vaccination versus non-vaccination \((sr^2 = 5\%)\). Unexpectedly, the initial *T. gondii* prevalence in cats had no effect on *T. gondii* prevalence in finishing pigs. The simulation supports the field trial indicating vaccine
effectiveness. However, vaccination had less impact on decreasing \textit{T. gondii} infection in finishing pigs than a decrease in the number of farm cats.

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**Keywords:** \textit{Toxoplasma gondii}; Modeling; Vaccine-effectiveness; Deterministic; Dynamic simulation; Finishing pigs

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### 1. Introduction

Toxoplasmosis (caused by the intracellular protozoan parasite \textit{Toxoplasma gondii}) is a zoonotic disease of worldwide public-health concern (Dubey, 1980; Dubey and Beattie, 1988). Pork has been implicated as the primary meat source of \textit{T. gondii} infection for humans in the USA (Dubey, 1990). Cats are the definitive host for the parasite. \textit{T. gondii} infection of cats (particularly juveniles) is the primary factor increasing the risk of \textit{T. gondii} infection in swine (Weigel et al., 1995b). Cats shed \textit{T. gondii} oocysts in feces, which can contaminate feed, water and soil (August and Chase, 1987; Dubey and Beattie, 1988; Dubey, 1994; Dubey and Weigel, 1996).

A \textit{T. gondii} feline oral-vaccine containing live bradyzoites from a mutant strain of \textit{T. gondii} (T-263) has been developed (Frenkel et al., 1991). Eighty-four percent of vaccinated cats challenged with the wild type of \textit{T. gondii} did not shed oocysts. Two doses of the vaccine prevented oocyst shedding in 100% of the vaccinated cats (Frenkel et al., 1991; Freyre et al., 1993). The mutant strain of \textit{T. gondii} interrupts the sexual phase of the life cycle of the parasite (Choromanski et al., 1995).

In a 3-year field trial conducted on eight commercial swine farms, repeated administration of the (T-263) \textit{T. gondii} vaccine to trapped cats was associated with a decrease in \textit{T. gondii} seroprevalence in finishing pigs of 0.02–14.4% (Mateus-Pinilla et al., 1999). Because that trial had no control (unvaccinated) farms, it was not possible to separate the effects of vaccination from natural fluctuations associated with oocyst survival, number of cats on the farm and initial \textit{T. gondii} prevalence in cats. The field trial used a single, opportunistic vaccination schedule (i.e., all trapped cats were vaccinated); therefore, it was not possible to determine whether this schedule was optimal or if it could be improved.

Presented below is a dynamic computer simulation model of the transmission of \textit{T. gondii} in populations of cats and swine within the ecosystem of the swine-production unit. The model was used to evaluate the effect of vaccination of cats on the prevalence of \textit{T. gondii} in finishing pigs. Computer models have been used previously to study the spread and control of infectious diseases, the dynamics of immunity and the consequences of treatment interventions (Hethcote, 1989, 1996; Eichner et al., 1996; Blower and McLean, 1996; Medley et al., 1996; Morris, 1996). Models simulating the transmission dynamics of \textit{T. gondii} on swine farms have not been reported previously.

### 2. Methods

A dynamic compartment model (Hannon and Ruth, 1994, 1997) was constructed to represent the transmission of \textit{T. gondii} in the ecosystem of the swine-production unit and
the effect of intervention by vaccination of cats. The overall structure of the model is depicted in Fig. 1. There were two sectors representing two animal populations—cats and finishing pigs—and a sector representing the presence of *T. gondii* in the environment. Cats and finishing pigs moved between the standard epidemiologic compartments representing different states of infection and immunity (Dietz, 1982; Hethcote, 1989). Although rodents (Dubey et al., 1995) and birds (August and Chase, 1987; Dubey and Beattie, 1988) can be
involved in *T. gondii* transmission on swine farms, cats are the ultimate source of infection (Smith et al., 1992; Weigel et al., 1995b). Rodents and birds were excluded from the model because there was insufficient population data on which to base parameter estimates.

Animals moved between compartments each week, based on the values of the transition parameters. Parameter estimates were based in part on completed field studies on the transmission of *T. gondii* on swine farms (Dubey et al., 1995; Weigel et al., 1995a,b) and on a prior field trial of the effectiveness of a feline *T. gondii* vaccine, T-263 (Mateus-Pinilla et al., 1999). Simulations were deterministic in that a specified fraction of individuals moved from the source to the destination compartment (rather than simulating the probability of transition of each individual stochastically). The model was dynamic in that the values of some model parameters could vary within a simulation run to represent the changing population demographics and distribution of *T. gondii* in the ecosystem. The duration of a simulation was 10 years, which was considered sufficient to identify a steady-state condition.

2.1. Feline sector

2.1.1. Cat-population dynamics

Population size was set initially at 10, 20, 30, 40 or 50 cats. Increments and decrements to population size occurred only by birth and death. We assumed that there was no immigration or emigration (i.e., each farm was a closed population). The birth rate (*b*) was determined as follows:

\[ b_t = W_t F_t Q_t L_t \]

where *b*_\textsubscript{*t*} is the number of kittens born in week *t*, *W*_\textsubscript{*t*} the indicator variable for birth week (=1 for weeks when births occur [18, 31]; =0 for weeks with no births), *F*_\textsubscript{*t*} the number of adult females capable of giving birth in the population in week *t* [=(total number of cats in week *t* × 0.55)/2], *Q*_\textsubscript{*t*} the number of litters per adult female, for weeks when births occur=[constant = 0.8], and *L*_\textsubscript{*t*} the average litter size for females giving birth [constant = 4.4].

The justification for these estimates is as follows. For cats in temperate climates, there is a period of sexual inactivity between November and January (Pedersen, 1991). For feral cats in Illinois, most births occur from March to May (47%) and from June to August (34%), with only 11% during September–November and 8% occurring during December–February (Warner, 1985). Thus, in the simulation model, two birth waves were simulated: one in week 18 (end of April) and the second during week 31 (end of July). Estimates of birth rates for feral cats range from 1 (Voith and Borchelt, 1983) to 1.6 (Warner, 1985) litters/queen/year. The most recent estimate was used to estimate (*Q*_\textsubscript{*t*}). Mean litter size for feral cats is 4.2–4.4 (Warner, 1985); the upper value was used to estimate (*L*_\textsubscript{*t*}). Thus, during weeks 18 and 31 of each year in the simulation runs, each adult female was assigned 0.8 litters (*Q*_\textsubscript{*t*}), with a litter size (*L*_\textsubscript{*t*}) of 4.4 kittens. Based on mark-recapture data from the previous field vaccine trial (Mateus-Pinilla et al., 1999), the proportion of the population that was adult (i.e., capable of reproduction) was 55%; half of these adults were assumed to be females (*F*_\textsubscript{*t*}).

In the simulation model, only two cat-mortality estimates were used: pre-weaning and post-weaning. Weaning typically occurs at 8–9 weeks of age (Pedersen and Wasthuler, 2002).
The higher value was selected as a constant in the simulations. Estimates of pre-weaning mortality range between 14.8 and 21.6% (Pedersen, 1991); the higher value was used as an estimate in this model \( (\mu_i = 0.216) \). Thus, in this study, 78.4% of the kittens born survived to weaning. Sensitivity analysis was conducted to determine the post-weaning mortality rate needed to maintain a constant cat-population size. The equilibrium mortality rate \( (\mu_a) \) was 0.0258 per week. Birth and death rates were considered independent of chronological time. Thus, population size fluctuated around an average annual value equal to the seeding value, i.e., the farms were considered to be at an equilibrium population size.

2.1.2. Compartments in the feline sector

The feline (Fe) sector had six compartments (Fig. 1): maternally immune (Fe-MI), susceptible (Fe-S), vaccinated immune (Fe-V), infected cats shedding oocysts (Fe-I), infected cats not shedding oocysts (Fe-R), infected cats in a prepatent period (Fe-P).

2.1.2.1. Maternally immune (Fe-MI). Cats entered the compartment through birth at rate \( b_t \). At birth, cats were assumed to be immune until maternal antibodies subsided after weaning at 8 weeks of age (Pedersen, 1991). Cats left the compartment either through pre-weaning mortality \( (\mu_i) \), or through loss of immunity \( (\alpha_{Fe}) \). Because there were discrete birth periods, the transition parameter \( \alpha_{Fe} \) had two values. Nine weeks after each birth wave, all kittens \( (\alpha_{Fe} = 1 - \mu_i) \) had lost their maternally derived immunity and became susceptible moving from the Fe-MI to the Fe-S compartment. At all other times, there was no movement of cats from Fe-MI to Fe-S \( (\alpha_{Fe} = 0) \).

2.1.2.2. Susceptible (Fe-S). These cats had not been infected previously and lacked antibodies to \( T. gondii \). Cats exited this compartment through mortality \( (\mu_a) \), by becoming infected \( (i_{Fe}) \) or by developing immunity through vaccination \( (v) \).

2.1.2.2.1. Probability of infection \( (i_{Fe}) \). The probability of acquisition of \( T. gondii \) infection depended on the current environmental load of the parasite (an estimate of the existing risk of exposure to \( T. gondii \)). There are normally two sources of infection: tissue cysts from prey and oocysts in the environment (Dubey and Beattie, 1988). However, infection of prey ultimately is traced to oocyst shedding by cats. Therefore, the probability of infection \( (i_{Fe}) \) in any given week was programmed to depend on the current environmental load of oocysts. The equation for this relationship was

\[
i_{Fe} = \beta_{0_{Fe}} + \beta_{1_{Fe}} E_t
\]

This is a linear regression relationship that was fit to estimate the probability of infection of susceptible cats, which depends on the number of cats that contribute to the environmental contamination with oocysts at time \( t \) \( (E_t) \). The data used to fit Eq. (1) were from field studies conducted in 1992 and 1993 (Dubey et al., 1995; Weigel et al., 1995b). The independent variable (current environmental contamination with oocysts) was estimated from the \( T. gondii \) seroprevalence in cats on a farm. We assumed that those seroprevalences for trapped cats were unbiased estimates of the prevalence of \( T. gondii \) infection for cats
on the farm. It was apparent that not all infected cats would contribute to the present environmental load of oocysts. Some had been infected >1 year ago and not all oocysts would survive. In most cases, infected cats excrete oocysts shortly after infection, develop immunity and rarely shed oocysts again—even after challenge with *T. gondii* (Dubey and Frenkel, 1972; Frenkel and Smith, 1982).

In the absence of field data to determine the proportion of infected cats that had contributed viable oocysts to the existing environmental reservoir, we assumed that half of the seropositive cats trapped at the time of the study had shed oocysts within the last year, and that half of the seropositive cats that had died within the last year had also shed oocysts within the last year. The equation for estimating the environmental load of oocysts (*E*<sub>t</sub>) from field data was

\[ E_t = 0.5P_{Fe}N_{Fe}(1 + 52\mu_a) \]  

where *P*<sub>Fe</sub> is the *T. gondii* seroprevalence in cats on a farm and *N*<sub>Fe</sub> the number of cats trapped on a farm.

The weekly probability of infection in cats was estimated for each farm in the field study as the average of the probabilities of infection for adult and juvenile cats. The average age of trapped adult cats was assumed to be their life expectancy, estimated at 67 weeks for Illinois farm cats (Warner, 1985). For juvenile cats, the average age at capture was assumed to be 26 weeks. Thus, with the assumption that cats became susceptible after weaning at 8 weeks of age, the average adult cat captured had a maximum of 59 weeks of exposure to *T. gondii* oocysts, and the average juvenile cat had a maximum of 18 weeks of exposure. Thus, the weekly probability of infection for a given farm was estimated as

\[ i_{Fe} = 0.5\left(\frac{1}{59}P_{FeAd} + \frac{1}{18}P_{FeJuv}\right) \]  

where *P*<sub>FeAd</sub> is the *T. gondii* seroprevalence for adults cats on a farm and *P*<sub>FeJuv</sub> the *T. gondii* seroprevalence for juvenile cats on a farm.

Thus, Eq. (2) was used to estimate the risk of exposure to *T. gondii* (*E*<sub>t</sub>) based on the environmental load of *T. gondii* oocysts and Eq. (3) was used to estimate the weekly risk of *T. gondii* infection for cats (*i*<sub>Fe</sub>) for each of the 47 farms in the previous field investigations. These values were needed to fit the regression equation (1). There were 26 farms for which *T. gondii* seroprevalence estimates were available for both adult and juvenile cats. The distribution of *E*<sub>t</sub> and *i*<sub>Fe</sub> values among these farms was evaluated. The 25, 50, 75 and 90% values for each variable were selected and paired to fit the linear regression equation (1). The least-squares linear regression equation fit to these data (\(R^2 = 0.94\)) was

\[ i_{Fe} = 0.000947 + 0.00144E_t \]  

Thus, at each week in the computer simulation, Eq. (4) was used to calculate the fraction of cats that was transferred from the susceptible (Fe-S) to the infected (pre-patent) compartment (Fe-P). This required establishing the risk of exposure to *T. gondii* by determining the environmental load of *T. gondii* oocysts at that time point in the simulation run (*E*<sub>t</sub>). The simulation model tracked the number of cats that had shed oocysts (compartment Fe-I below) for each time interval. Thus, throughout the simulation, the number of cats that contributed to the environmental contamination with oocysts at any time *t* (*E*<sub>t</sub>) was the
cumulative sum of all cats that had shed in the past from a time interval (before the present) equal to the survival time of oocysts until the present:

\[ E_t = \sum_{T=t-s}^{t} N_{Fe-I_T} \]  

(5)

where \( N_{Fe-I_T} \) is the number of cats that had shed oocysts at time \( T \) in the past and \( s \) the survival time of oocysts in the environment (52, 39 or 26 weeks).

In any given week, the environmental load of oocysts was determined by including all cats that had shed oocysts prior to the current week, within a time interval equal to the survival time for oocysts. This parameter \( (E_t) \) was variable, depending upon the simulation model run, as described below.

It was straightforward to determine \( E_t \) for all time intervals where \( t > s \). However, at time 0 (when the simulation was initiated) until time \( t = s - 1 \), it was not known from the simulation which cats had excreted oocysts. For time 0, \( E_t \) was determined using Eq. (2), where \( N_{Fe} \) and \( P_{Fe} \) were the baseline values for number of cats and \( T. gondii \) prevalence in cats, respectively, with which the model was seeded. Then each week, a fraction \( (E_{t_0}/s) \) (where \( E_{t_0} \) is the baseline \( T. gondii \) environmental load) was subtracted from the environmental reservoir. This is equivalent to distributing all baseline infection evenly across the interval \( [t - s, t_0] \) and removing an equal fraction each week, until the direct contribution of oocysts to the environment from cats shedding during the simulation period could be calculated.

2.1.2.2. Vaccine-induced immunity \((v)\). Vaccination of cats with the T-263 \( T. gondii \) vaccine produces immunity, but it is not 100% effective (Frenkel et al., 1991; Freyre et al., 1993). To be vaccinated, farm cats needed to be captured. Thus, the degree of vaccine-induced immunity \((v)\) was given by

\[ v = \kappa \varepsilon \]  

(6)

where \( \kappa \) is the proportion of cats captured and vaccinated, and \( \varepsilon \) the probability of vaccine producing an immune response (i.e., vaccine efficacy).

The proportion of cats captured \((\kappa)\) was an experimental variable in the model simulations described in Section 2.3. Based on the probability of seroconversion estimated from the previous field vaccine trial (Mateus-Pinilla et al., 1999), the vaccine efficacy \((\varepsilon)\) was 48%.

2.1.2.3. Vaccinated-immune \((Fe-V)\). Successful vaccination of cats was assumed to induce lifelong immunity because vaccination consists of oral administration of live bradyzoites from a mutant strain of \( T. gondii \) (Freyre et al., 1993) and immunity associated with infection remains throughout life (Frenkel, 1990). Thus, the only exit from this compartment was via mortality \((\mu_a)\).

2.1.2.4. Infected, prepatent period \((Fe-P)\). Recently infected cats remained in this compartment from the time of initial \( T. gondii \) infection until the initiation of shedding of oocysts. The prepatent period is 5–8 days (Schmidt and Roberts, 1996). In our model, all
cats remained in the prepatent period for 1 week. Exit from the compartment also occurred through death ($\mu_d$). Thus, model parameter $\varphi$ (Fig. 1; exit alive from the pre-patent compartment (Fe-P)) was a constant with a value equal to $1 - \mu_d$ ($= 1 - 0.0258 = 0.9742$). After 1 week, all cats exited this compartment, either by death or by transfer to the shedding condition (compartment Fe-I).

2.1.2.5. Infected, shedding oocysts (Fe-I). Following the prepatent period, cats shed as many as 20 million unsporulated oocysts for about 10–15 days (August and Chase, 1987; Dubey, 1994). Cats normally go through this process only once in a lifetime. In our model, all cats shed oocysts for 2 weeks. Cats exited this compartment either by cessation of shedding ($\eta$) or via mortality ($\mu_d$). Thus, model parameter $\eta$ (Fig. 1, exit from Fe-I into the Fe-R compartment) had two values: $\eta = 0$ for cats who had been in Fe-I for 1 week and $\eta = 1 - \mu_d$ for cats who had been in Fe-I for 2 weeks.

2.1.2.6. Infected cats not shedding oocysts (Fe-R). Cats that ceased shedding oocysts remained in a lifelong chronic state of infection and could not revert to the shedding or susceptible stage (August and Chase, 1987; Frenkel, 1990; Dubey, 1994). The only exit from this compartment was via mortality ($\mu_d$).

2.2. Finishing-pig sector

Among swine, only finishing pigs were considered relevant, because they are raised for human consumption and T. gondii has been isolated from swine commercial cuts (Dubey, 1988). Thus, we believed finishing pigs to represent the greatest food-safety risk.

2.2.1. Swine population dynamics

The model for swine production used here was a farm with 200 sows. We estimated that in a swine-production unit, a sow produces 2.2 l/year with a total of 10 piglets per litter that survive to weaning, for a total of 22 pigs/sow/year (Pond and Aherne, 1996). Thus, in the simulation model, the weekly birthrate ($b_{FP}$) was 0.4231 pigs per week. In the model, we assumed that mortality of finishing pigs (FP) only was due to marketing. Age at marketing in the US is approximately 160–180 days (Pond and Aherne, 1996). In the model, all marketing (and thus, finishing-pig mortality) occurred at 26 weeks; i.e., $\mu_{FP} = 0$ for pigs <26 weeks of age and $\mu_{FP} = 1$ at 26 weeks of age.

2.2.2. Compartments in the finishing-pig sector

The finishing-pig sector contained three compartments (Fig. 1): maternally immune (FP-MI), susceptible (FP-S) and infected finishing pigs (FP-I).

2.2.2.1. Maternally immune (FP-MI). We assumed that pigs acquired T. gondii immunity shortly after birth through maternal antibodies in colostrum (Dubey and Urban, 1990). Sows have a long period of potential exposure to T. gondii and are likely to have antibodies prior to gestation. Therefore, transplacental transmission (associated with primary infection during gestation) is considered unlikely in swine (Smith et al., 1992). Finishing pigs can acquire T. gondii infection after 6 weeks of age, by which time weaning has occurred and 90% of
maternal colostral antibodies have subsided (Dubey and Urban, 1990). Thus, all births ($b_{FP}$) were into the FP-MI compartment. At 6 weeks of age, pigs lost immunity and entered the susceptible compartment (FP-S) at rate $a_{FP}$. Therefore, $a_{FP} = 0$ for pigs <6 weeks old and $a_{FP} = 1$ for pigs at 6 weeks of age.

### 2.2.2.2. Susceptible (FP-S)

These were previously unexposed finishing-pigs that could acquire *T. gondii* infection at any time after loss of maternal immunity. Exit from the FP-S compartment was either by mortality at 26 weeks ($m_{FP}$) or prior to 26 weeks, by infection with *T. gondii*. The probability of infection in finishing pigs ($i_{FP}$) was estimated in a manner similar to that for cats, i.e., the following regression function was fit:

$$i_{FP} = \beta_0_{FP} + \beta_1_{FP}E_t$$

(7)

With loss of maternally derived immunity at 6 weeks and marketing at 26 weeks, the period of potential exposure to *T. gondii* was 20 weeks. In a manner similar to the estimation of regression parameters in Eq. (1) for cats, data from a prior field study (Dubey et al., 1995) on the estimated *T. gondii* seroprevalence in market age finishing-pigs on 26 farms were used to estimate the weekly probability of infection for finishing pigs for each farm:

$$i_{FP} = \frac{1}{20}P_{FP}$$

(8)

where $P_{FP}$ is the *T. gondii* seroprevalence for market-age finishing pigs on a farm.

The weekly probability of infection for finishing pigs ($i_{FP}$) was regressed on $E_t$ (the risk of exposure to *T. gondii*). The parameter $E_t$ was based on the environmental load of *T. gondii* for a farm, as estimated from Eq. (2). Using the methods described for Eq. (4) above, the resulting regression equation ($R^2 = 0.979$) for finishing pigs was

$$i_{FP} = -0.001056 + 0.000174E_t$$

This equation was used during the simulation to estimate the probability of infection in finishing pigs from $E_t$ (the current risk of exposure to *T. gondii* based on environmental contamination with *T. gondii*) as determined from Eq. (5).

### 2.2.2.3. Infected (FP-I)

Finishing pigs that became infected with *T. gondii* remained in the IF-P compartment until marketing at the age of 26 weeks.

### 2.3. Experimental design

The outcomes of interest in the simulation were (a) the elimination of *T. gondii* in finishing pigs and (b) the prevalence of *T. gondii* in finishing pigs. The hypotheses tested were that the probability of elimination of *T. gondii* in finishing pigs increases and the *T. gondii* prevalence in finishing pigs decreases with (1) vaccination of cats, (2) an increase in the proportion of cats vaccinated (associated with an increase in the proportion of cats captured), (3) a decrease in the initial number of cats on the farm and (4) a decrease in the initial prevalence of *T. gondii* in cats. To test these hypotheses, several experimental factors were manipulated in the simulations. These variables, their definitions and initial values were the following.
2.3.1. Initial prevalence of *T. gondii* infection in cats (*P*<sub>Fe=0</sub>)

The percentage of cats infected at the onset of simulation had three values: 30, 60 and 90%. These values covered the range of values obtained from farms in the previous field studies (Dubey et al., 1995; Mateus-Pinilla et al., 1999). After initial seeding, *T. gondii* prevalence in cats was a dynamic variable that changed over the course of a simulation.

2.3.2. Initial number of cats on the farm (*N*<sub>Fe=0</sub>)

Five seeding values (10, 20, 30, 40 and 50) were used, based on previous field studies (Dubey et al., 1995; Mateus-Pinilla et al., 1999). After initial seeding, the number of cats on the farm was a dynamic variable that changed over the course of a simulation.

2.3.3. Duration of oocyst survival (*s*)

Three values for duration of oocyst survival (52, 39 and 26 weeks) were used. Oocysts can survive in the environment for up to 18 months (Frenkel et al., 1975). Preliminary simulations with oocyst survival of 52 weeks produced values of *T. gondii* prevalence in finishing pigs that were 30% higher than the maximum estimated from previous field studies (16.7%) (Dubey et al., 1995). Oocyst survival was decreased under the assumption that environmental conditions influence the infectivity and survival of oocysts (Yilmaz and Hopkins, 1972; Dubey and Beattie, 1988; Dubey, 1998). Thus, lower estimates of oocyst survival (39 and 26 weeks) were also used in the simulations. This variable was constant throughout a simulation run.

2.3.4. Proportion of cats captured (*κ*)

Three values (0, 50 and 75%) were used for the proportion of cats captured. The 0% capture represented a strategy of no vaccination; this was the control condition for comparison to the vaccination conditions. Mark-recapture data from the field trial (Mateus-Pinilla et al., 1999) were used to estimate population size, which was used to estimate proportion of cats captured (number of individual cats captured/estimated population size) (Mares et al., 1981). The median “proportion of cats captured” for all the farms that participated in the field vaccine trial was 50%. This value was used as one simulation condition. The value of 75% also was used to explore the impact of increasing the proportion of cats captured. The proportion of cats captured was used to calculate the vaccine efficacy in Eq. (6). This variable was constant throughout a simulation run.

2.3.5. Vaccination schedules

This variable was relevant only for conditions where the proportion of cats captured was >0%. Two vaccination schedules were used. One schedule (*field*) involved trapping and vaccination at weeks 18, 26 and 35 each year, which were the median weeks of vaccination for each of the three seasons of the field trial (Mateus-Pinilla et al., 1999). The second “weaning-vaccination” schedule involved trapping and vaccination at weeks 27 and 40 of each year, designed to coincide with the movement into the susceptible compartment of weaned cats from each of the two simulated birth waves. This variable was constant throughout a simulation run.

There were 225 simulation runs: one deterministic run under each biologically possible combination of experimental factors. Any proportion of cats captured other than 0% was
irrelevant under the no-vaccination scenario. There were 45 simulations without vaccination and 180 with vaccination.

2.4. Statistical methods for simulation results

The primary outcome variable examined was the prevalence of *T. gondii* in finishing pigs, calculated as the average prevalence during the final year (year 10) of each simulation run. Also, we determined whether elimination of *T. gondii* from finishing pigs had been accomplished at the end of a simulation run. The predictors analyzed for their association with *T. gondii* prevalence in finishing pigs were the experimental factors listed above.

The association of each experimental factor with the dichotomous outcome elimination (yes or no) of *T. gondii* infection from finishing pigs was evaluated using contingency-table analysis. The association of each experimental factor with the continuous outcome *T. gondii* prevalence in finishing pigs was analyzed using multiple linear regression. The categorical independent variable “vaccination” was coded using two orthogonal contrasts (Cohen and Cohen, 1983). The first contrast compared vaccination (regardless of capture schedule) with no vaccination and the second compared the two vaccination schedules (*field* vs. *weaning-vaccination schedule*).

Two sets of multiple linear regression analyses were conducted. The first set included as independent variables the experimental factors manipulated in the computer simulation model. The second evaluated the effects of the experimental factors in conjunction with the risk of exposure to *T. gondii* (*Et*). The effects of vaccination (versus not vaccinating) were not apparent in the first multiple regression model due to the high correlation of this variable with the proportion of cats captured (*r* = 0.91), where 0% represented no vaccination. Thus, a multiple regression model was run, omitting the variable “proportion of cats captured”. Furthermore, to correct for model deficiencies (serial correlation of residuals and heterogeneity of residual variance), an arcsin transformation of the dependent variable (i.e., prevalence values in finishing pigs) was conducted and, to remove remaining deviant residuals, simulations with initial number of farm cats equal to 10 were deleted because these all resulted in swine *T. gondii* prevalence outcomes of 0%.

An additional multiple regression analysis was conducted to identify factors more proximate than initial number of cats on the farm. In particular, environmental oocyst load (*E_t*), as determined from Eq. (2), was considered a more direct predictor of the probability of infection and, thus, this variable replaced total number of cats at *t_0* and initial cat *T. gondii* prevalence as predictors in the regression model. The heterogeneity of residual variance of this model was corrected with an arcsin transformation of the dependent variable. The transformed model corrected model deficiencies.

Although statistical methods were used to obtain measures of association between variables, in this deterministic model there was no variance in outcome for a specified set of seeded model parameter values. Thus, no sampling distribution exists and *P*-values were not calculated. Instead, the percentage of variance in outcome accounted for by an independent variable (based on its squared semipartial correlation coefficient (sr^2_)) was used as a criterion for determining its importance.
3. Results

In all cases, by 2 years of simulation, the population dynamics for cats and pigs stabilized with fluctuations around an equilibrium point. After the first year of the simulation runs, *T. gondii* prevalence in cats and finishing pigs followed a somewhat regular time series. The proportion of infected cats decreased immediately following the mass release of weaned cats into the susceptible pool and increased gradually until the next release. The weekly prevalences for finishing pigs reflected the changes in the risk of exposure to *T. gondii*, with a lag of several weeks allowing time for susceptible cats to become infected and shed oocysts. The oscillations in pig prevalences were less pronounced because the pig population size was stable. To illustrate these cases, Fig. 2 represents the changes in the risk of exposure to *T. gondii*, as defined by Eq. (5) for the simulation conditions with the weaning-vaccination schedule, 50% of cats captured and 26 weeks of oocyst survival. Likewise, Figs. 3 and 4 represent the changes in *T. gondii* prevalence in swine and cats, respectively, as the initial number of cats changed from 10 to 50, under the same treatment and environmental conditions.

In 71 (32%) of the 225 simulation runs, the *T. gondii* prevalence in the finishing pig sector dropped to 0%. The factors that were most important in increasing the probability of elimination of *T. gondii* in finishing pigs were decreased oocyst survival and a decrease in the initial number of cats on the farm (Table 1). To a lesser extent, vaccination improved the probability of *T. gondii* elimination over no vaccination and the weaning-vaccination schedule improved the probability of elimination over the field vaccination schedule. There was no association of initial *T. gondii* prevalence in cats with the probability of *T. gondii* elimination in swine.

![Fig. 2. Change in the risk of exposure to *T. gondii* (Ei) (i.e., number of cats that contributed to the environmental contamination with oocysts at any time t). Simulation conditions included: initial number of cats (10, 20, 30, 40 and 50), 26 weeks of oocyst survival, 50% of cats captured, 60% feline prevalence at time 0 and interval of time between calculations (.dt) = 1 week.](image-url)
Examination of *T. gondii* simulation-prevalence values indicated a mean decrease in *T. gondii* prevalence in finishing pigs of $-1.5\%$ (median $=-1.6\%$, range: $0$ to $-3.6\%$) associated with the field-vaccination schedule compared to no vaccination. The mean change from no vaccination to the weaning-vaccination schedule” was $-5.5\%$ (median $=-5.9\%$, range: $0$ to $-12.3\%$).

Fig. 3. Change in *T. gondii* prevalence (%) in finishing pigs, resulting from changes in the risk of exposure to *T. gondii*. Simulation conditions included: initial number of cats (10, 20, 30, 40 and 50), 26 weeks of oocyst survival, 50% of cats captured, 60% feline prevalence at time 0 and interval of time between calculations $dt = 1$ week.

Fig. 4. Change in *T. gondii* prevalence (%) in cats, resulting from changes in the risk of exposure to *T. gondii*. Simulation conditions included: initial number of cats (10, 20, 30, 40 and 50), 26 weeks of oocyst survival, 50% of cats captured, 60% feline prevalence at time 0 and interval of time between calculations $dt = 1$ week.
An examination of *T. gondii* prevalences for cats also indicated a decrease in *T. gondii* prevalence in cats associated with the field and weaning-vaccination conditions compared to no vaccination. The mean difference in *T. gondii* prevalence in cats associated with field-vaccination conditions (compared to no vaccination) was $-11.5\%$ (median = $-9.7\%$, range = $-2.5\%$ to $-26.4\%$) and the mean difference in *T. gondii* prevalence in cats associated with the weaning-vaccination condition was $-30.9\%$ (median = $-31.1\%$, range: $-4.35$ to $-49.4\%$). The prevalence of *T. gondii* in cats never dropped to 0%; the lowest value among all simulations was 0.021%. After arcsin transformation of the dependent variable, multiple linear regression analysis (Table 2, Model A) indicated that the factors resulting in decreased *T. gondii* prevalence in finishing pigs were the weaning-vaccination schedule (compared to the field schedule) and vaccination (vs. no vaccination). The factors resulting in increased *T. gondii* prevalence in finishing pigs were an increase in the initial number of cats on the farm and an increase in the duration of oocyst survival. The initial feline prevalence of *T. gondii* on the farm explained almost none of the variance in outcome.

For the second multiple regression analysis (which substituted risk of exposure to *T. gondii* ($E_t$) for initial number of cats and initial *T. gondii* prevalence in cats), the same factors decreased *T. gondii* prevalence in finishing pigs while the factors resulting in increased prevalence were an increase in the risk of exposure to *T. gondii* and an increase in

<table>
<thead>
<tr>
<th>Experimental factor</th>
<th>Level</th>
<th>Number of simulations</th>
<th>Percent with <em>T. gondii</em> elimination in finishing pigs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaccination</td>
<td>Vaccination</td>
<td>180</td>
<td>33</td>
</tr>
<tr>
<td></td>
<td>No vaccination</td>
<td>45</td>
<td>27</td>
</tr>
<tr>
<td>Vaccination schedule</td>
<td>Weaning</td>
<td>90</td>
<td>39</td>
</tr>
<tr>
<td></td>
<td>Field</td>
<td>90</td>
<td>27</td>
</tr>
<tr>
<td>Proportion of cats captured (%)</td>
<td>0</td>
<td>45</td>
<td>27</td>
</tr>
<tr>
<td></td>
<td>50</td>
<td>90</td>
<td>32</td>
</tr>
<tr>
<td></td>
<td>75</td>
<td>90</td>
<td>33</td>
</tr>
<tr>
<td>Oocyst survival (weeks)</td>
<td>26</td>
<td>75</td>
<td>47</td>
</tr>
<tr>
<td></td>
<td>39</td>
<td>75</td>
<td>28</td>
</tr>
<tr>
<td></td>
<td>52</td>
<td>75</td>
<td>20</td>
</tr>
<tr>
<td>Initial <em>T. gondii</em> prevalence in cats (%)</td>
<td>30</td>
<td>75</td>
<td>31</td>
</tr>
<tr>
<td></td>
<td>60</td>
<td>75</td>
<td>32</td>
</tr>
<tr>
<td></td>
<td>90</td>
<td>75</td>
<td>32</td>
</tr>
<tr>
<td>Initial number of cats</td>
<td>10</td>
<td>45</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>20</td>
<td>45</td>
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<tr>
<td></td>
<td>50</td>
<td>45</td>
<td>0</td>
</tr>
</tbody>
</table>
the duration of oocyst survival (which explained most of the variance) (Table 2, Model B). The multiple $R^2$ for this model ($58\%$) was less than for the previous model ($R^2 = 94\%$).

Fig. 5 shows the mean difference in $T. gondii$ prevalence in finishing pigs for the last year of the simulation for the two vaccination treatments (weaning and field schedules) compared to no vaccination, under different environmental conditions of number of cats and oocyst-survival time. There is an apparent interaction of vaccination schedule with

![Figure 5](image.png)

**Fig. 5.** Mean difference in prevalence of $T. gondii$ in finishing (%) pigs, for the last year of the simulation, under simulation conditions of: field and weaning-vaccination schedules, oocyst-survival time (Oo. Surv.) and number of cats.

Table 2

Results for the final regression models evaluating: the effect of the simulation experimental factors on $T. gondii$ arcsin-prevalence in finishing pigs (Model A; multiple $R^2 = 0.94$) and the effect of the experimental factors and the risk of exposure to $T. gondii$, on the $T. gondii$ prevalence (after arcsin transformation) in finishing pigs (Model B; multiple $R^2 = 0.58$)

<table>
<thead>
<tr>
<th>Model</th>
<th>Model variables</th>
<th>Proportion of variance ($sr^2$)</th>
<th>Regression coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model A</td>
<td>Initial number of cats</td>
<td>0.47</td>
<td>0.011</td>
</tr>
<tr>
<td></td>
<td>Oocyst survival</td>
<td>0.35</td>
<td>0.0096</td>
</tr>
<tr>
<td></td>
<td>Vaccination (vs. no vaccination)</td>
<td>0.045</td>
<td>−0.061</td>
</tr>
<tr>
<td></td>
<td>Weaning-vaccination schedule (vs. field schedule)</td>
<td>0.072</td>
<td>−0.052</td>
</tr>
<tr>
<td></td>
<td>Initial $T. gondii$ prevalence in cats</td>
<td>&lt; 0.001</td>
<td>−0.0057</td>
</tr>
<tr>
<td>Model B</td>
<td>Risk of exposure to $T. gondii$ ($E_t$)</td>
<td>0.16</td>
<td>0.005</td>
</tr>
<tr>
<td></td>
<td>Oocyst survival</td>
<td>0.35</td>
<td>0.0096</td>
</tr>
<tr>
<td></td>
<td>Vaccination (vs. no vaccination)</td>
<td>0.045</td>
<td>−0.061</td>
</tr>
<tr>
<td></td>
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<td>0.072</td>
<td>−0.052</td>
</tr>
</tbody>
</table>

$^a$ Squared semipartial correlation coefficient.
these environmental factors in affecting *T. gondii* prevalence in finishing pigs. Overall, the advantage of the weaning-vaccination schedule in decreasing *T. gondii* prevalence in finishing pigs is greater with an increase in oocyst-survival time and an increase in the number of cats on the farm. In fact, for both variables, the impact on vaccination effectiveness is different for the two vaccination schedules. The effectiveness of the field-vaccination schedule *decreases* with an increase in the number of cats on the farm and with an increase in oocyst-survival time. In contrast, the effectiveness of the weaning-vaccination schedule *increases* with an increase in the number of cats on the farm and with an increase in oocyst-survival time.

4. Discussion

The farms that participated in a prior field trial (Mateus-Pinilla et al., 1999) were selected from a pool of farms with the highest prevalence of infection in swine. If original estimates of prevalence on some of these farms were high due to sampling variation, the change in prevalence observed in the field trial could have been a consequence of regression towards the mean.

The computer-simulation experiment presented above was an alternative analytical approach to evaluate further the effectiveness of the feline vaccine in decreasing the exposure of swine to *T. gondii*. In addition to providing a control group (no vaccination), this approach also controlled for variables that were not possible to control under field conditions. The results of the computer-simulation experiment indicated that although vaccination of farm cats usually did not eliminate *T. gondii* infection in swine farms, it resulted in a decreased prevalence of *T. gondii* in cats and finishing pigs when all other conditions were kept constant—thereby supporting the conclusions of the field trial.

The computer model was used further to investigate the impact of improving the vaccination schedule. The simulated field-vaccination schedule consisted of vaccination of farm cats three times a year, as conducted in previous field work. The weaning-vaccination schedule targeted the largest number of susceptible cats, by simulating vaccination of recently weaned cats twice per year, after the simulated birth clusters (when cats entered the susceptible compartment). The weaning-vaccination schedule achieved an improvement in reducing the oocyst shedding by cats and thus decreased the risk of exposure of finishing pigs to *T. gondii*, compared to the field vaccination schedule, even with the elimination of one trapping and vaccination period. However, the effectiveness of this strategy under field conditions would require targeting the points in time when most of the susceptible cats (i.e., most of the recently weaned kittens) are present. Under natural conditions, cats are born over a somewhat extended period and not at two distinct points in time. Thus, under field conditions, it would be more difficult to target vaccination to times that maximize the encounter with susceptible cats. Maximizing the vaccination of susceptible cats could be accomplished by continuous administration of the vaccine (in either cat feed or bait). However, this mode of administration would not be feasible with the current version of the T-263 vaccine, which must remain frozen until delivery to keep the bradyzoites alive (Choromanski et al., 1995).
Although vaccination resulted in reduced *T. gondii* prevalence, even after vaccinating for 10 years and regardless of the vaccination schedule, *T. gondii* was not eliminated from finishing pigs in 67% of the simulations where cats received the vaccine. In addition, *T. gondii* was never eliminated from the cat population. The inability to eliminate *T. gondii* from the cat population could be due to a maintained environmental reservoir of *T. gondii*. This reservoir serves as a source of infection for susceptible cats. The high reproductive rate of cats provides a nearly constant supply of susceptibles (maintaining the cycle of transmission).

The most important finding was that a decrease in the initial number of farm cats had a greater impact on eliminating *T. gondii* infection in finishing pigs than vaccination of cats. *T. gondii* infection in finishing pigs was always eliminated when the initial cat-population size was as low as 10 cats, regardless of whether or not cats were vaccinated (on the other hand, *T. gondii* was not eliminated from finishing pigs in any simulations where there were 40 or 50 farm cats). Reducing the number of cats reduces the number of susceptible cats and therefore, it reduces future potential shedders of *T. gondii* oocysts into the environment. Thus, cat-population control appears to be a more effective strategy than vaccination of cats in the reduction of *T. gondii* infection in swine.

Because reducing the number of cats on a swine farm appears to be the most important factor in reducing exposure to *T. gondii*, strategies for reducing the cat population need to be explored. Programs to control cat populations have been based on capture and removal, or trapping, neutering and release (Mahlow and Slater, 1996). However, the number of cats present in a habitat might indicate the number of cats that a particular ecological niche can support. Thus, the removal of cats from a subsection of the niche (e.g., one swine farm) only creates an empty niche for additional cats (newborns or migrating cats) to occupy. The cats that fill this niche might not have been exposed previously to *T. gondii* and might be new contributors to oocysts shedding. Thus, trapping and removal of cats might only alleviate the problem temporarily and could exacerbate it if the new cat population is mostly susceptible to *T. gondii*. In contrast, neutering might be more effective in reducing cat-population size (Zaunbrecher and Smith, 1993; Mahlow and Slater, 1996) and reducing the introduction of new susceptible cats into the population. Neutering and vaccinating cats upon capture could be the most successful combined strategy for minimizing *T. gondii* transmission.

The computer-simulation model assumed a closed population of cats (i.e., no migration). Migration of cats can be considered a negligible source of environmental contamination with oocysts because cats usually become infected with *T. gondii* and shed oocysts within the first year of life (Weigel et al., 1995b), and migration occurs after puberty (8–10 months of age) (Pedersen and Wastlhuber, 1991). Model sensitivity analysis under the condition of no vaccination indicated that prevalences in finishing pigs were closest to prevalences from previous studies (Dubey et al., 1995; Weigel et al., 1995a) when the duration of oocyst survival was 26 weeks. Frenkel et al. (1975) estimated that oocysts could survive as long as 18 months in soil in Costa Rica. Although this is a maximum estimate, our simulation suggests the median survival time is considerably less in the US Midwest. However, it is nearly impossible to alter environmental conditions to decrease oocyst survival. Thus, strategies for reducing *T. gondii* infection in swine should focus on other means of reducing oocyst exposure.
The impact of number of cats, oocyst survival and vaccination on *T. gondii* prevalence on finishing pigs is actually more complex than is indicated by the analysis of the individual effects of these factors. The effectiveness of the weaning-vaccination schedule increased with an increase in the number of cats and an increase in oocyst survival. This can be interpreted as meaning that vaccination can be most effective as the oocyst load increases. In contrast, the effectiveness of vaccination under the field schedule decreased with an increase in the number of cats and an increase in oocyst survival perhaps because this vaccination schedule did not target the susceptible population prior to exposure to *T. gondii*. Thus, if vaccination is to be used, environmental conditions should be considered in evaluating its expected effectiveness and interventions should be timed to maximize their impact.

An unexpected finding of the computer simulation was the lack of association of the initial *T. gondii* prevalence in cats with prevalence in finishing pigs. However, it is the number of shedding cats that directly contribute to the current environmental load of oocysts rather than the overall prevalence of infection in cats, which contributes to the current risk of *T. gondii* infection for finishing pigs. This conclusion is consistent with that of Weigel et al. (1995b), who identified the number of juvenile cats infected with *T. gondii* on a farm as the primary risk factor for infection in finishing pigs.

The rodent sector of the population was excluded from the simulation, although previous studies identified rodents as a risk factors for the transmission of *T. gondii* to swine (Weigel et al., 1995b). Rodents were excluded due to insufficient population data to estimate accurately model parameters for the simulation. However, infection of rodents ultimately is traced back to the shedding of oocyst by cats (Dubey et al., 1986). Thus, inclusion of a rodent sector in this ecosystem model is unlikely to change results substantially.

Producer-initiated biosecurity measures (such as preventing cat access to swine barns, covering feed storage bins to prevent cats from defecating in the feed (Leman et al., 1992), rodent-control programs and removal of carcasses from swine pens) might decrease the risk of *T. gondii* infection for swine. However, the effects of these interventions compared to vaccination of cats or cat-population control are unknown.

Decreasing oocyst-survival time, decreasing oocyst shedding by cats through vaccination and reducing the number of cats all can reduce the risk of infection with *T. gondii*. However, the computer simulation conducted here has indicated that the intervention strategy needing the most attention is the reduction of cat-population size. This is the primary determinant of environmental contamination with *T. gondii*. Thus, field trials comparing the effectiveness of methods to reduce cat-population size and their impact on *T. gondii* infection in swine are warranted.

References


