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Zoonotic Transmission of Waterborne Disease: A Mathematical Model

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1 **Zoonotic transmission of waterborne disease: a**
2 **mathematical model**

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6
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8 **Abstract** Waterborne parasites that infect both humans and animals are
9 common causes of diarrheal illness, but the relative importance of transmis-
10 sion between humans and animals and vice versa remains poorly understood.
11 Transmission of infection from animals to humans via environmental reser-
12 voirs, such as water sources, has attracted attention as a potential source of
13 endemic and epidemic infections, but existing mathematical models of water-
14 borne disease transmission have limitations for studying this phenomenon, as
15 they only consider contamination of environmental reservoirs by humans. This
16 paper develops a mathematical model that represents the transmission of wa-
17 terborne parasites within and between both animal and human populations.
18 It also improves upon existing models by including animal contamination of
19 water sources explicitly. Linear stability analysis and simulation results, using
20 realistic parameter values to describe *Giardia* transmission in rural Australia,
21 show that endemic infection of an animal host with zoonotic protozoa can

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22 result in endemic infection in human hosts, even in the absence of person-
23 to-person transmission. These results imply that zoonotic transmission via
24 environmental reservoirs is important.

25 **Keywords** Mathematical model · Protozoa · Zoonoses · Waterborne disease

26 **Mathematics Subject Classification (2000)** 92D30 · 92D40 · 92B05

27 1 Introduction

28 Waterborne protozoa that infect both humans and animals, including *Cryp-*
29 *tosporidium* and *Giardia* species, are significant public-health problems, with
30 about 58 million cases of childhood diarrhea worldwide due to protozoan in-
31 fection annually (Savioli et al, 2006). The exact role of zoonotic (animal to
32 human) transmission in the epidemiology of these infections is still poorly un-
33 derstood, with *Giardia* and *Cryptosporidium* both classed as neglected tropical
34 diseases because of the lack of research attention they have received relative to
35 their epidemiological importance (Kline et al, 2013). Correlational studies have
36 attempted to elucidate the importance of direct zoonotic transmission (Fayer
37 et al, 2010, 2007, 2006; Swaffer et al, 2014) but have not definitively proven
38 the relative importance of environmentally mediated zoonotic transmission,
39 where parasites enter a water source from an animal host's faeces and are
40 then ingested by humans, compared to direct person-to-person or animal-to-
41 human transmission. For the two most common waterborne pathogenic proto-
42 zoa, *Cryptosporidium* and *Giardia*, transmission from person-to-person (either
43 directly or via the environment) is thought to be more important than zoonotic
44 transmission (Chalmers et al, 2011; Nasser et al, 2012), but this may not be
45 true for some species of *Cryptosporidium*, particular *Cryptosporidium parvum*
46 (Hunter and Thompson, 2005). Whilst a number of mathematical models ex-
47 ist of the transmission of water-borne infections via environmental reservoirs
48 (Chick et al, 2002; Eisenberg et al, 2002, 2004; Li et al, 2009; Tuite et al, 2011),
49 these models have humans as the source of pathogens in the environmental
50 reservoir and are therefore inappropriate for studying the importance of en-
51 vironmentally mediated zoonotic transmission. In this paper, a more complex
52 model, which instead incorporates animals as the source of pathogens in the
53 environmental reservoir, is devised. The model is analysed mathematically,
54 showing that the importance of environmentally mediated zoonotic transmis-
55 sion may be underestimated; in fact, endemic infection with waterborne pro-
56 tozoa in humans may be completely explained by this transmission route.
57 The model is then applied to the study of waterborne protozoan disease in
58 rural Australia. Australia appears to be particularly vulnerable to outbreaks
59 of waterborne disease; of 199 documented waterborne disease outbreaks be-
60 tween 2004 and 2010, 46.5% occurred in Australia (Baldursson and Karanis,
61 2011). From 2003 to 2009 acute *Cryptosporidium* infections in the Australian
62 state of New South Wales increased almost tenfold (from 2.7 to 19.8 cases per
63 100,000 people) (Waldron et al, 2011) and *Giardia* cases increased by approx-
64 imately 30% Australia-wide over a similar period (Kirk et al, 2014). *Giardia*

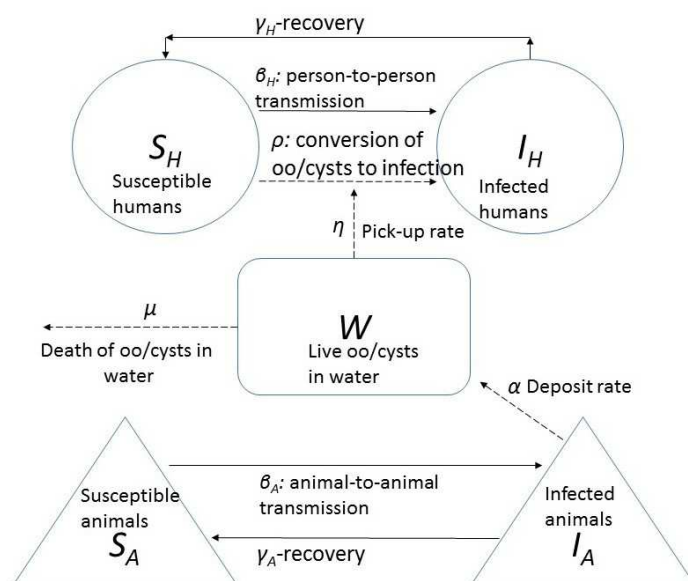


Fig. 1 Graphical representation of the process of environmentally-mediated transmission of protozoan infections from animals to humans, as described by the system of equations (6). The term oo/cyst is used to denote the free living life stage of a protozoa.

65 infection is, however, more severe than *Cryptosporidium* infection, resulting in
 66 the loss of three times as many disability adjusted life years annually (Gib-
 67 ney et al, 2014). For this reason, this paper uses the model to study *Giardia*
 68 transmission, though it can easily be adapted to the study of *Cryptosporid-*
 69 *ium* (Thompson and Smith, 2011). Using realistic parameter values, we find
 70 that environmentally mediated transmission via an endemically infected host
 71 could drive infection in the human population. These results suggest zoonotic
 72 transmission of *Giardia* could be more important than commonly thought and
 73 support the conclusions drawn from mathematical analysis of our model. The
 74 importance of environmentally mediated zoonotic transmission of waterborne
 75 protozoa should be further studied.

76

77 2 Mathematical model

The susceptible–infected–susceptible (*SIS*) framework, where infected hosts become susceptible once again after recovering from infection (Anderson and May, 1991), formed the basis of our model of rural *Giardia* infection, as the best fit to the currently poorly understood epidemiology of many protozoan parasites. Factors supporting use of the *SIS* framework are that it is apparent that the symptomatic state (assumed to be infectious) can reoccur within the same individual and that any immunity conferred is at best partial (Casman

et al, 2000; Esch and Petersen, 2013; Newman et al, 2001). The existence of partial or temporary immunity might support using a *SIRS* model that includes a recovered state, but unfortunately it is unclear how the recovered state relates to asymptomatic carriage of protozoan infections, which may be both protective and potentially infectious (Quilliam et al, 2013; Tysnes et al, 2014). These factors, and the undeniably endemic nature of protozoan infection in some communities (certainly for children) (Asher et al, 2014; Desai et al, 2012), support the parsimonious choice of the simplest possible model for endemic infections: the *SIS* model (Clancy and Mendy, 2011). From this basic framework, a deterministic compartmental model, represented schematically in Figure 1, was developed to include three types of state entities: 1) humans, divided into susceptible (S_H) and infectious (not necessarily symptomatic) (I_H) states; 2) animals, divided into susceptible (S_A) and infectious (not necessarily symptomatic) (I_A) states, and live pathogen in water (W). The term oo/cyst is used to describe the free-living life stage of a protozoan pathogen in water; the free-living stage of the two most common pathogens, *Cryptosporidium* and *Giardia*, is an oocyst or cyst, respectively. The dynamics of infection in the animal population as a function of time are modelled using the *SIS* equations

$$\begin{aligned}\dot{S}_A &= (-\beta_A S_A + \gamma_A) I_A \\ \dot{I}_A &= (\beta_A S_A - \gamma_A) I_A,\end{aligned}\tag{1}$$

where β_A is the transmission rate per animal per unit time and γ_A the recovery rate per unit time. For the remainder of this paper, the unit of time is assumed to be one day, the shortest increment of time that would be useful in most practical applications of this model. Assuming that the host animal population is of constant size $N_A = S_A + I_A$, (1) can be reduced to the single logistic equation

$$\dot{I}_A = (\beta_A N_A - \gamma_A) I_A - \beta_A I_A^2.\tag{2}$$

The change in the number of live oo/cysts per litre of water ($W =$ oo/cysts per litre), as a function of time, is given by the ordinary differential equation

$$\dot{W} = \alpha I_A - \eta W (S_H + I_H) - \mu W.\tag{3}$$

78 In (3), μ is the rate per unit time at which oo/cysts are eliminated from water
 79 by naturally dying; α is the oo/cysts per animal per litre per unit time rate
 80 at which infected animals contaminate water; and η is the rate per person per
 81 unit time at which humans ingest cysts by consuming water.

82

The change in the number of infected people as a function of time is modelled using the *SIS* equations

$$\begin{aligned}\dot{S}_H &= -\rho\eta W S_H - \beta_H S_H I_H + \gamma_H I_H \\ \dot{I}_H &= \rho\eta W S_H + \beta_H S_H I_H - \gamma_H I_H,\end{aligned}\tag{4}$$

where β_H is the per person per unit time and γ_H the per unit time rate at which susceptible persons acquire infection from other individuals and recover from infection. The parameter ρ is the rate at which individuals who have ingested oo/cysts become infectious, with units of persons per oo/cysts per litre. Let the human population be of constant size $N_H = S_H + I_H$, such that (4) can be rewritten as the single extended logistic equation

$$\dot{I}_H = \rho\eta W(N_H - I_H) + (\beta_H N_H - \gamma_H)I_H - \beta_H I_H^2. \quad (5)$$

The three equations (2), (3) and (5) together comprise the system of equations

$$\begin{aligned} \dot{I}_A &= (\beta_A N_A - \gamma_A)I_A - \beta_A I_A^2 \\ \dot{W} &= \alpha I_A - \eta W N_H - \mu W \\ \dot{I}_H &= \rho\eta W(N_H - I_H) + (\beta_H N_H - \gamma_H)I_H - \beta_H I_H^2, \end{aligned} \quad (6)$$

83 which describes the environmentally mediated transmission of protozoan in-
84 fection from animals to humans, as shown schematically in Fig. 1.

85

The system (6) has three equilibrium points: the disease-free equilibrium $(0, 0, 0)$, endemic disease in the human population as a result of human-to-human transmission $(0, 0, N_H - \gamma_H/\beta_H)$, and a third equilibrium with endemic disease in both the human and animal populations, mediated by waterborne transmission. The solution at this third equilibrium point is given by the vector

$$\begin{pmatrix} \hat{I}_A \\ \hat{W} \\ \hat{I}_H \end{pmatrix} = \begin{pmatrix} N_A - \frac{\gamma_A}{\beta_A} \\ \frac{\alpha N_A - \frac{\alpha \gamma_A}{\beta_A}}{\eta N_H + \mu} \\ \frac{-B \pm \sqrt{B^2 - 4AC}}{2A} \end{pmatrix}, \quad (7)$$

where

$$\begin{pmatrix} A \\ B \\ C \end{pmatrix} = \begin{pmatrix} \beta_A \beta_H (\eta N_H + \mu) \\ \rho \eta \alpha \gamma_A \left(\frac{\beta_A N_A}{\gamma_A} - 1 \right) + \beta_A \gamma_H (\eta N_H + \mu) \left(1 - \frac{\beta_H N_H}{\gamma_H} \right) \\ \rho \eta \alpha \gamma_A N_H \left(1 - \frac{\beta_A N_A}{\gamma_A} \right) \end{pmatrix}. \quad (8)$$

The three eigenvalues (λ_i) of the Jacobian matrix of (6) evaluated at the

equilibrium point (7) are

$$\begin{pmatrix} \lambda_1 \\ \lambda_2 \\ \lambda_3 \end{pmatrix} = \begin{pmatrix} \gamma_A \left(1 - \frac{\beta_A N_A}{\gamma_A}\right) \\ -\eta N_H - \mu \\ \frac{-\rho\eta\alpha\gamma_A \left(\frac{\beta_A N_A}{\gamma_A} - 1\right)}{\beta_A(\eta N_H + \mu)} + \gamma_H \left(\frac{\beta_H N_H}{\gamma_H} - 1\right) - 2\beta_H \hat{I}_H \end{pmatrix}. \quad (9)$$

Under the assumption that realistic values for all parameters are all greater than or equal to zero, $\lambda_1 < 0$ when $R_{0A} = \beta_A N_A / \gamma_A > 1$, and $\lambda_2 < 0$ always. Define the basic reproduction number R_{0i} as the number of new infections arising in a population of species i ; commonly, when this number exceeds one, an epidemic can commence in host i (Anderson and May, 1991; Keeling and Rohani, 2007). Were the normal dynamics of the *SIS* model to apply, the existence of a stable equilibrium with disease in the animal and human populations would require that $R_{0i} > 1$ for both humans and animals. Whilst it is clear that $R_{0A} > 1$ is required for stability, solving the inequality $\lambda_3 < 0$ shows that the behaviour of the model is different to the standard *SIS* model, as endemic disease in the animal population drives infection in the human population even while $R_{0H} < 1$. Given $\beta_A N_A / \gamma_A > 1$ (since $\lambda_1 < 0$) and assuming that only positive values of \hat{I}_H are meaningful, the first and third terms in λ_3 are negative. When $R_{0H} = \beta_H N_H / \gamma_H < 1$, the second term in λ_3 is also negative, and hence $\lambda_3 < 0$ overall. Therefore a stable equilibrium with disease in both the animal and human population exists only if $R_{0A} > 1$ and $R_{0H} < 1$.

For completeness, we will discuss the stability of the first two equilibrium points. The three eigenvalues of the Jacobian matrix evaluated at the disease-free equilibrium and the second equilibrium point, corresponding to endemic disease in the human population as a result of human-to-human transmission, can be shown to be

$$\begin{pmatrix} \gamma_A \left(\frac{\beta_A N_A}{\gamma_A} - 1\right) \\ -\eta N_H - \mu \\ \gamma_H \left(\frac{\beta_H N_H}{\gamma_H} - 1\right) \end{pmatrix} \text{ and } \begin{pmatrix} \gamma_A \left(\frac{\beta_A N_A}{\gamma_A} - 1\right) \\ -\eta N_H - \mu \\ \gamma_H \left(1 - \frac{\beta_H N_H}{\gamma_H}\right) \end{pmatrix}, \quad (10)$$

respectively. As stated before, we should assume only positive parameter values as meaningful. By examining the eigenvalues (10), the disease-free point is stable (all three eigenvalues are less than zero) if both R_{0A} and R_{0H} are less than one. On the other hand, the second equilibrium point is stable when $R_{0A} < 1$ and $R_{0H} > 1$.

109 Summarising the results presented here, if $R_{0i} > 1$ for either humans or
110 animals, the disease-free state is unstable. Where $R_{0H} > 1$ and $R_{0A} < 1$, the
111 system tends towards the second equilibrium point with disease in the human
112 population only; if $R_{0A} > 1$ but $R_{0H} < 1$, the system tends towards the third
113 equilibrium point, where endemic disease in the animal population is sufficient
114 to cause endemic disease in the human population also.

116 3 Application of the model to the case of *Giardia* transmission 117 from possums to humans

118 Numerical methods were employed to demonstrate the implications of Section
119 2 for understanding the phenomenon of high *Giardia* prevalence in rural Aus-
120 tralia. In Australia, as in other parts of the world, pockets of symptomatic
121 *Giardia* infection (giardiasis) occur in rural locations (Fletcher et al, 2014; Lal
122 et al, 2013). A number of explanations have been proposed for the clustering
123 of *Giardia* infection in rural areas. Larger populations of agricultural livestock
124 and wild animals in rural areas suggest that increased zoonotic transmission
125 of *Giardia* infection in rural areas may be important (Borchard et al, 2010),
126 but the epidemiological evidence for any direct transmission from either agri-
127 cultural or wild animals to humans remains weak (Cacció et al, 2005; Hunter
128 and Thompson, 2005). A more likely explanation for the crowding of *Giardia*
129 infection in rural areas is the higher use of alternative water sources such as
130 rain or bore water (Fletcher et al, 2014). One author estimates that as high
131 as 82% of rural households in rural New South Wales, Australia, rely on rain-
132 water tanks for household drinking water (Lye, 2002). Rainwater tanks and
133 other alternative water sources are associated with many outbreaks of water-
134 borne disease in Australia (Dale et al, 2010) and often become contaminated
135 with *Giardia* cysts shed in animal faeces (Ahmed et al, 2012). Under this hy-
136 pothesis, zoonotic transmission is environmentally mediated rather than due
137 to direct contact between humans and animals. Bird and possum¹ faeces are
138 possible sources of *Giardia* contamination of rainwater tanks (Ahmed et al,
139 2012). Mice and rats are other mammals known to carry *Giardia* (McKenna,
140 2009) and also have the potential to faecally contaminate rainwater (Abbasi
141 and Abbasi, 2011). Of these hosts, possum faeces most commonly contain *Gi-*
142 *ardia* cysts ($\sim 30\%$) (Ahmed et al, 2012), so possums were chosen to be the
143 example animal host in these examples. Two examples are used in this sec-
144 tion to demonstrate that both the second and third equilibrium solutions of
145 the model (6) can be fitted to the high target prevalence of *Giardia* in rural
146 Australian people. The target prevalences of interest were the proportions of
147 infectious humans and possums. A person or animal was considered infectious
148 if their faeces contained *Giardia* cysts; they did not have to be symptomatic
149 in terms of presenting with diarrhea. There are reasonable estimates of the

¹ Possums are native Australian marsupials, here assumed to be of *Trichosurus vulpecula* species.

150 proportion of human and possum faeces containing cysts: 7.6% (Feng and
 151 Xiao, 2011; Lasek-Nesselquist et al, 2009; Read et al, 2002) and 30% (Ahmed
 152 et al, 2012), respectively. Given constant population sizes $N_H = 1000$ and
 153 $N_A = 500$, at equilibrium the numbers of infectious humans and possums are
 154 76 and 150. Using these values as the target prevalence values, the second and
 155 third equilibrium points of (6) are $(0, 0, 76)$ and $(150, 150/(\alpha(-\eta N_H - \mu)), 76)$.
 156 It is apparent that fitting (6) to the second equilibrium point depends only
 157 on optimising the parameters of the third equation for disease in the human
 158 population, which is equivalent to (5). Considering the third equilibrium point
 159 $(150, 150/(\alpha(-\eta 1000 - \mu)), 76)$, observe **that**, because the target prevalence
 160 of infection in the possum population and the size of the human population
 161 are known, fitting the model can be reduced to the problem of optimising
 162 the parameters α , η and μ . Substituting these equilibrium values into (6), ob-
 163 serve that each of these parameters to be optimised, plus the final unknown
 164 parameter ρ , appears in the third equation — for disease in the human popula-
 165 tion. Thus the problem of fitting the model to the third equilibrium point can
 166 also be addressed by analysing the third equation in (6) only, equivalent to (5).
 167

168 Bifurcation analysis was used to find the optimal value of $R_{0H} > 1$ by
 169 solving (5) given the constraint $\hat{I}_H = 76$ and setting the values of all param-
 170 eters other than β_H and γ_H to zero. In the deterministic *SIS* model (5), the
 171 removal rate, $\gamma_H/\beta_H N_H$, is equal to $1/R_{0H}$, or equivalently, to the proportion
 172 susceptible at endemic equilibrium in homogeneously mixed populations (An-
 173 derson and May, 1991; Hethcote, 2000). Therefore a plot of increasing values
 174 of the bifurcation parameter R_{0H} can be used to determine the point at which
 175 the desired prevalence $(1 - 1/R_{0H})$ is attained.² Values of R_{0H} ranging from
 176 1.07687–1.0881 produced the target prevalence of 7.6 (± 0.5)% in the human
 177 population (see Fig. 2).
 178

To fit the model to the third equilibrium point, deterministic optimisation
 methods were used to solve the following non-linear programming problem.

$$\begin{aligned} \text{Minimize: } & 0\alpha + 0\eta + 0\mu + 0\rho & (11) \\ \text{Subject to: } & \rho\eta \left(\frac{\hat{I}_A}{\alpha(\eta N_H + \mu)} \right) [N_H - \hat{I}_H] + N_H\beta_H\hat{I}_H - \gamma_H\hat{I}_H - \beta_H\hat{I}_H^2 = 0, \\ & \hat{I}_A = 150, \hat{I}_H = 76, \\ & \alpha, \eta, \rho > 0, \mu \geq 0. \end{aligned}$$

179 By setting the objective function equal to zero, as defined in (11), we cast this
 180 problem as a feasibility problem rather than a strict optimisation problem.

² This approach was used because of the lack of reliable estimates of γ_H and β_H in the literature. Estimates of the duration of *G. lamblia* infection in humans only describe the duration of symptoms (Gibney et al, 2014; Rendtorff, 1954; Robertson et al, 2010), not infectiousness as defined in this paper, and vary substantially from 2–60 days (Gibney et al, 2014; Nash et al, 1987; Nygård et al, 2006).

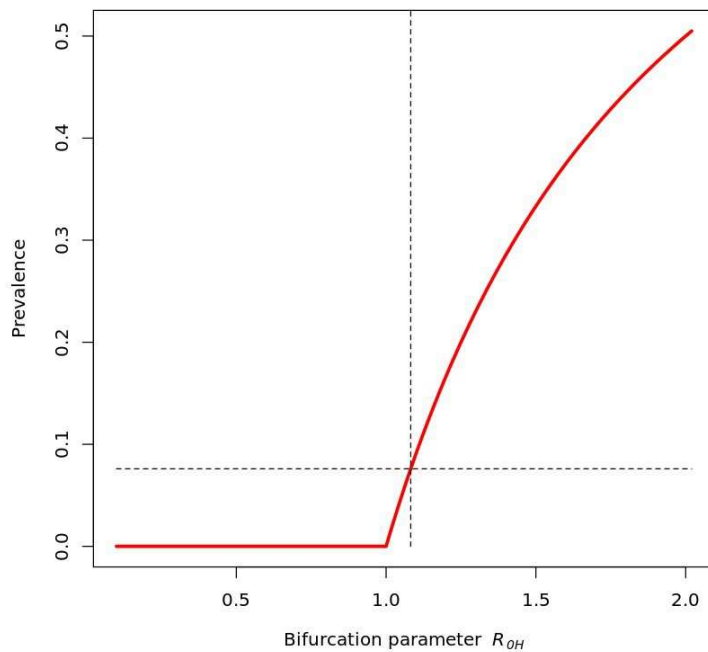


Fig. 2 Bifurcation plot showing that the target *Giardia* prevalence of 7.6% (Feng and Xiao, 2011; Lasek-Nesselquist et al, 2009; Read et al, 2002) is attained in the human population with an R_{0H} value of 1.082.

Table 1 Parameter values and constraints used in optimising the parameters of (5) given $\hat{I}_H = 76$, $\hat{I}_A = 150$ and $\hat{W} = 150/(\alpha(-\eta 1000 - \mu))$.

Parameter	Initial value	Final value	Constraint
Rate of conversion of ingested cysts to infection ρ (persons per cysts per litre)	0.02 (Rose et al, 1991)	0.02	$\rho > 0$
Deposit rate α (cysts per litre per animal per day)	0.01	0.49	$\alpha > 0$
Pick-up rate η (per person per day)	0.01	3.4×10^{-4}	$\eta > 0$
Decay rate in the environment μ (per day)	0.36 (Bingham et al, 1979; DeRegnier et al, 1989)	0.03	$\mu \geq 0$

181 This approach is appropriate because there is no established notion of an opti-
 182 mal parameter set for this problem, but there are **well-established** biological
 183 constraints limiting solutions to a feasible region. Additionally, problem (11)
 184 has non-linear constraints, which **makes** it difficult to solve exactly. By us-
 185 ing our **approach**, all solutions to the objective function will equal zero and
 186 be equally optimal, making the problem easy to solve, but biological realism
 187 is preserved by the fact that not all of these solutions are feasible given the
 188 constraints. In general, recasting such optimisation problems in this way is
 189 an efficient option as feasible solutions can be readily identified by sophisti-
 190 cated optimisation tools, such as those in **Matlab**. To solve (11) given the
 191 constraints, we utilised an algorithm that checks first-order necessary condi-
 192 tions for an optimiser, namely, the built-in **fmincon** function that exists within
 193 the **Matlab** Optimization Toolbox. The formulation of the problem assumed
 194 constant values of all other parameters and variables. Values of β_H and γ_H
 195 were chosen that gave a value of the bifurcation parameter R_{0H} close to zero
 196 (0.01) to convincingly demonstrate that high *Giardia* prevalence in the human
 197 population could be driven solely by environmentally mediated transmission
 198 from the possum population. There are no estimates of the transmissibility of
 199 *Giardia* or the duration of infectiousness in possums, so bifurcation analysis
 200 was used to determine the optimal value of R_{0A} (as described above for the
 201 human population) and appropriate values of β_A and γ_A were inferred from
 202 this. Values of R_{0A} between 1.418 and 1.439 produced the target prevalence
 203 of 30.0 (± 0.5)%. Initial values for all other parameters are given in Table 1.
 204 Initial values of α and η were set close to zero in the absence of data. The
 205 solution to (11) is given in Table 1. The solution shows that, with realistic
 206 values of the parameters α , η , μ and ρ , the target *Giardia* prevalence in the
 207 human population can be produced with almost zero person-to-person trans-
 208 mission. This numerical analysis shows the realism of our analytical findings
 209 and has important implications for the study of *Giardia* and other zoonotic,
 210 waterborne pathogens.

211
 212 Deterministic sensitivity analysis was conducted by iteratively solving (11)
 213 for $\hat{I}_H \in [71, 81]$ (the tolerance region set around the target prevalence above).
 214 The parameters η , ρ and μ increased linearly in response to increasing values
 215 in \hat{I}_H . In contrast, the parameter α decreased linearly. This is depicted in
 216 **Figure 3** below. The parameter variations are shown in Table 2.

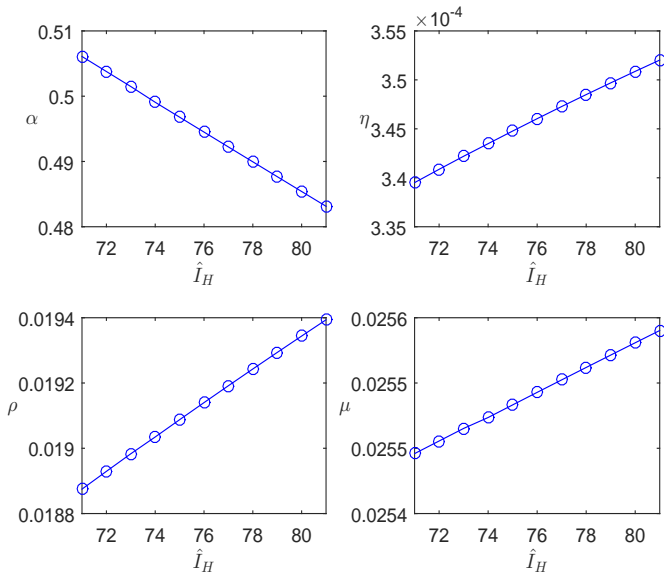


Fig. 3 The variation in parameter values with respect to the change in \hat{I}_H .

Table 2 Change in parameter values for changes in the equilibrium number of infectious humans $\hat{I}_H \in [71, 81]$.

Parameter	Range
Rate of conversion of ingested cysts to infection ρ (persons per cysts per litre)	[0.018, 0.019]
Deposit rate α (cysts per litre per animal per day)	[0.483, 0.506]
Pick-up rate η (per person per day)	$[3.4 \times 10^{-4}, 3.5 \times 10^{-4}]$
decay rate in the environment μ (per day)	[0.026, 0.027]

217 4 Discussion

218 A number of studies worldwide have suggested land-use as a risk factor for
 219 infection with *Giardia* (Borchard et al, 2010; Lal et al, 2013). The importance
 220 of this pathogen seems to be growing in Australia, with the incidence of symp-
 221 tomatic infections increasing by 30% Australia-wide in the period from 2000 to
 222 2010 (from 2,600 to 3,700 cases) (Kirk et al, 2014). According to some authors,
 223 this trend is likely to continue, with increasing use of rainwater and increasing
 224 temperatures due to climate change cited as risk factors for waterborne dis-
 225 ease (Fletcher et al, 2012). Whilst these factors have been studied in relation
 226 to other pathogens such as *Cryptosporidium* (McBride et al, 2014), this is the
 227 first paper that explicitly explores one of these factors—rainwater—in relation

228 to *Giardia* using a mathematical model.

229
230 This paper describes a new model that differs in two important ways from
231 previous models of the transmission of waterborne disease via drinking water.
232 Whilst a number of previous models of water-borne infections have environ-
233 mental reservoirs of the pathogen as the main source of transmission (Chick
234 et al, 2002; Eisenberg et al, 2002, 2004; Li et al, 2009; Tuite et al, 2011), these
235 normally have humans as the source of pathogens in the environmental reser-
236 voir. The model presented in this paper has animals as the source of pathogen
237 in the environment; in many scenarios, such as the example given of the con-
238 tamination of rainwater by possums, this is a more plausible source of pathogen
239 in the environment than human faeces. The model further differs from previous
240 similar models by including a compartmental model of the infection process in
241 the animal host. Linear stability analysis of the model is used to demonstrate
242 that disease in an animal host can drive endemic infection of the human popu-
243 lation, even if the basic reproduction number describing the number of people
244 infected by another person (R_{0H}) is less than one. This result supports the
245 hypothesis that environmentally mediated zoonotic transmission is important
246 in *C. parvum* epidemiology (Hunter and Thompson, 2005). This hypothesis is
247 also supported by the effectiveness of measures such as reducing cattle density
248 in reducing the occurrence of *C. parvum* infection (Xiao and Feng, 2008). On
249 the other hand, the result challenges existing assumptions about the epidemi-
250 ology of another important protozoa, *Giardia*. Some experts consider zoonotic
251 transmission to be less important for *Giardia* than for *C. parvum* (Hunter and
252 Thompson, 2005), suggesting that humans are more likely to infect animals
253 with the parasite rather than vice versa (Thompson and Smith, 2011). Our
254 results, which do not support this latter hypothesis, are obviously related to
255 our choice of model structure; nonetheless, if our model structure is in fact
256 an appropriate representation of the process of environmental transmission of
257 *Giardia*, our findings have the potential to cause us to rethink our attitudes
258 to this parasite.

259
260 It is notable that all the feasible parameter values identified during op-
261 timisation of the *Giardia* modelling scenario were plausible, given existing
262 empirical estimates. Similarly, the final value of the ρ parameter was identi-
263 cal to the best estimate for this parameter in the microbial risk assessment
264 literature – 0.0198 (95% CI 0.01,0.036) (Rose et al, 1991). Additionally, the
265 variation in ρ remained within these bounds during sensitivity analysis (see
266 Table 2). There is very little empirical information about the parameters α
267 and β , but the final values of both seem plausible. A value of $\alpha = 0.5$ implies
268 that the average infected animal deposits half a cyst into a litre of rain water
269 per unit time but that humans only ingest these cysts at a much lower rate
270 (3.4×10^{-4}); this seems feasible. Therefore the numerical simulations contained
271 in this paper show that the prevalence of just one waterborne pathogen (*Gia-*
272 *rdia*) in humans can be explained virtually entirely by zoonotic transmission
273 via environmental reservoirs, using realistic parameter values. The extent to

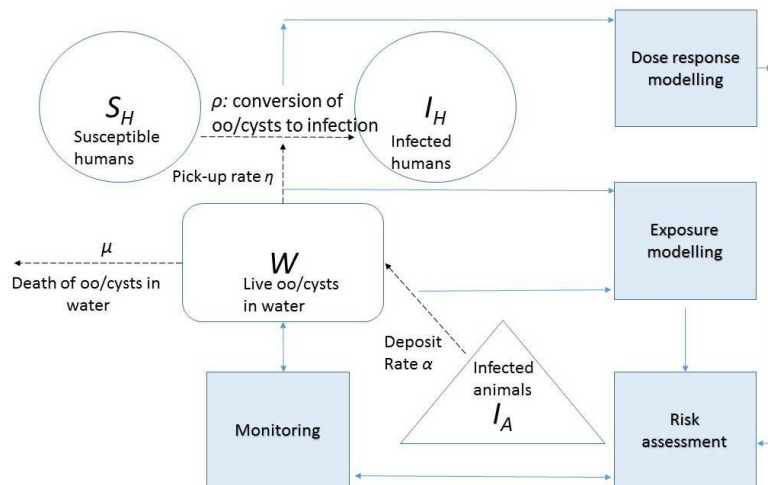


Fig. 4 Schematic showing how relevant processes within the transmission model (from Figure 1) are linked to monitoring and risk assessment activities (blue boxes).

274 which this is true for similar pathogens, such as *Cryptosporidium*, is an avenue
 275 for further research using the model formulated in this paper.

276

277 The model presented in this paper has a number of limitations that could
 278 be improved upon in future research. Use of the *SIS* framework is an oversim-
 279 plification, and future work should extend the model to incorporate at least
 280 temporary or partial immunity (Quilliam et al, 2013; Solaymani-Mohammadi
 281 and Singer, 2010; Tysnes et al, 2014). Another important avenue of future
 282 research is modelling the potential public health impact of different interven-
 283 tions targeting either the pick-up rate η or the deposit rate α , such as water
 284 filtration and treatment and the culling of animal hosts. Climatic variables
 285 such as rainfall and temperature have the potential to influence a number of
 286 parameters in the model, such as the deposit rate and survival of pathogens
 287 in the environment (Lal et al, 2013). Including the effect of climate on the
 288 pathogen load in the environment would also improve the model and make it
 289 more useful for exploring critical issues such as the impact of climate change
 290 on the spread of zoonotic waterborne disease (McBride et al, 2014).

291

292 The clear connection between our model and parameters used in risk as-
 293 sessment, such as pathogen concentration in water, pick-up rates and deposit
 294 rates, indicate the potential implications of the work contained in this paper
 295 for the field of quantitative microbial risk assessment (QMRA). QMRA is the
 296 most important tool for quantifying waterborne disease risks in general, and
 297 forms the basis of microbial risk management in major water-quality guide-
 298 lines, including the Australian Guidelines for Water Recycling (NRMCC et

299 al. 2006), the WHO Guidelines for the Safe Use of Wastewater, Excreta and
300 Greywater (WHO 2006) and the WHO's (2011) Guidelines for Drinking-water
301 Quality. Briefly, QMRA is a four-step process comprising (i) hazard identi-
302 fication, (ii) exposure assessment, (iii) dose-response modelling, and (iv) risk
303 characterisation. Practitioners and researchers utilising each of these processes
304 will be particularly interested in insights our model provides about likely values
305 of particular parameters, as shown in Figure 4. Hazard identification involves
306 determining the pathogen(s) of concern; exposure assessment comprises defin-
307 ing the exposure pathway so the dose of the pathogen(s) to which a person
308 is exposed can be determined; dose-response modelling defines the probability
309 of infection as a function of this dose; and the final step, risk characterisa-
310 tion, brings all this together to arrive at an estimate of the probability of
311 an adverse outcome, typically infection or illness. Many QMRA models have
312 been constructed for waterborne transmission of *Giardia* (Westrell et al, 2004;
313 Mota et al, 2009; Razzolini et al, 2011; McBride et al, 2013; Xiao et al, 2013),
314 but these models, like QMRA models generally, are limited by the fact that
315 they ignore the transmission of infection from person to person, animal to
316 animal and animal to person completely. QMRA and epidemiological models
317 like the one in this paper need not be mutually exclusive areas of research
318 though; rather, QMRA could readily be dovetailed into a modelling frame-
319 work such as the one presented here. As shown in this paper, an immediate
320 benefit of this type of modelling for QMRA is its ability to test common as-
321 sumptions. *Giardia*, unlike *Cryptosporidium*, is thought to be characterised by
322 high person-to-person transmission—but the results presented in this paper
323 show that the same prevalence of *Giardia* in the human population can be
324 arrived at through either high person-to-person or environmentally mediated
325 zoonotic transmission. Determining which of these scenarios is most important
326 is a topic for further research, but either scenario obviously has implications
327 for risk assessment using QMRA.

328

329 5 Conclusion

330 Waterborne protozoa, including *Giardia* and *Cryptosporidium*, are common
331 causes of diarrheal illness. These parasites infect both human and animal hosts,
332 but the relative importance of transmission between humans and animals and
333 vice versa remains poorly understood, as does the role of environmental reser-
334 voirs in this process. Existing mathematical models of water-borne disease
335 transmission between animals and humans via environmental reservoirs, such
336 as water sources, have limitations, as they only consider contamination of
337 environmental reservoirs by humans. This paper described a mathematical
338 model that represents the transmission of waterborne parasites within and be-
339 tween both animal and human populations. This model improves upon existing
340 models by including animal contamination of water sources explicitly. Linear
341 stability analysis and simulation results, using realistic parameter values to

342 describe *Giardia* transmission in rural Australia, show that endemic infection
343 of an animal host with zoonotic protozoa can result in endemic infection in
344 human hosts, even in the absence of person-to-person transmission. These re-
345 sults suggest that the importance of zoonotic transmission via environmental
346 reservoirs may be underestimated.

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