HHS Public Access

Author manuscript

Prev Vet Med. Author manuscript; available in PMC 2024 August 08.

Published in final edited form as:

Prev Vet Med. 2014 February 01; 113(2): 249–256. doi:10.1016/j.prevetmed.2013.11.006.

Temporal patterns of human and canine *Giardia* infection in the United States: 2003–2009⋆

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Abstract

Giardia protozoa have been suspected to be of zoonotic transmission, including transmission from companion animals such as pet dogs to humans. Patterns of infection have been previously described for dogs and humans, but such investigations have used different time periods and locations for these two species. Our objective was to describe and compare the overall trend and seasonality of *Giardia* species infection among dogs and humans in the United States from 2003 through 2009 in an ecological study using public health surveillance data and medical records of pet dogs visiting a large nationwide private veterinary hospital. Canine data were obtained from all dogs visiting Banfield hospitals in the United States with fecal test results for *Giardia* species, from January 2003 through December 2009. Incidence data of human cases from the same time period were obtained from the CDC. Descriptive time plots, a seasonal trend decomposition (STL) procedure, and seasonal autoregressive moving-average (SARIMA) models were used to assess the temporal characteristics of *Giardia* infection in the two species. Canine incidence showed a gradual decline from 2003 to 2009 with no significant/distinct regular seasonal component. By contrast, human incidence showed a stable annual rate with a significant regular seasonal cycle, peaking in August and September. Different temporal patterns in human and canine *Giardia* cases observed in this study suggest that the epidemiological disease processes underlying both series might be different, and *Giardia* transmission between humans and their companion dogs seems uncommon.

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⋆The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Conflict of interest statement

The authors declare no conflict of interest.

Keywords

Ecological study; *Giardia* spp; Infectious disease; Protozoa; Temporal; Surveillance; Zoonosis

1. Introduction

Giardia protozoal parasites infect many species of domestic and wild animals as well as humans. Zoonotic transmission of some *Giardia* species/genotypes has been demonstrated experimentally, but its occurrence and clinical significance under natural conditions is unclear (Plutzer et al., 2010). Assemblages A and B which were considered to be human-specific have been isolated from a wide range of domestic, wild, and marine animals (Thompson et al., 2000), and these zoonotic assemblages have been shown to occur more commonly in dogs from the western United States compared to dog-specific assemblages (C and D) (Covacin et al., 2011). However, the relative importance of zoonotic transmission of *Giardia* spp. remains to be determined (Hunter and Thompson, 2005).

Human giardiasis in the United States is a nationally notifiable disease, with most states voluntarily reporting (Yoder et al., 2010). Approximately 20,000 human giardiasis cases were reported annually to the Centers for Disease Control and Prevention (CDC) from 2002 to 2009 (Yoder and Beach, 2007; Yoder et al., 2010), but CDC estimates the actual number of cases to be closer to 1.2 million cases per year due to under-reporting and under-diagnosis (Scallan et al., 2011). Documented cases of human giardiasis have been associated with a history of travel, outdoor recreational activities, and drinking contaminated water, but many cases may be subclinical (Eisenstein et al., 2008).

Cases of human giardiasis in the United States generally increase in late summer and early fall (Katz et al., 2006; Nakada et al., 2012; Yoder et al., 2010). The peak incidence of human giardiasis occurs during the spring in Europe and summer in Canada and the UK (Lal et al., 2012). The seasonality of canine giardiasis has been the subject of conflicting findings. For example, no seasonal pattern of canine giardiasis in the US was found in one study (Nolan and Smith, 1995), whereas a more recent study reported a highest prevalence in the month of November (Mohamed et al., 2013). The peak incidence of canine giardiasis has been reported to occur in the winter in Italy (Bianciardi et al., 2004), the summer in Spain (Díaz et al., 1996), and in the fall in Argentina (Fontanarrosa et al., 2006).

Time-series analysis is a method for describing the occurrence of common events over time while accounting for the serial correlation (autocorrelation) between observations. Few studies have used a time-series approach to describe the temporal pattern of *Giardia* (Naumova et al., 2000; Nolan and Smith, 1995). However, no studies have compared the temporal patterns of *Giardia* infections across species. Similarities in temporal patterns could potentially indicate common source etiologies or cross-species transmission.

The objective of this ecological study therefore was to describe the temporal pattern of giardiasis among dogs and humans in the United States using medical records of dogs visiting private veterinary hospitals and reports of human giardiasis by state health departments to the CDC for the period from January 2003 through December 2009. Our

hypothesis was that temporal correlations of human and canine infection could provide supportive evidence for either zoonotic transmission or a common source of infection affecting both species.

2. Materials and methods

2.1. Data

2.1.1. Canine—Fecal test information was obtained from Banfield, The Pet Hospital, Portland, Oregon. Banfield, The Pet Hospital, is a small animal general practice with more than 700 hospital locations in metropolitan areas in the United States. The practice estimates that their hospitals provide health care for approximately 5% of the US pet population. Fecal testing was performed as part of routine diagnostic or preventive veterinary care of symptomatic and asymptomatic pet dogs during visits to Banfield veterinary hospitals. Fecal flotation without centrifugation using 1.18 SG $ZnSO_4$ was performed to detect *Giardia* cysts in the stool and the results reported as positive or negative; no attempt was made to identify specific *Giardia* assemblages. All fecal tests were conducted by trained hospital staff following a standard protocol. The medical records from all Banfield hospitals nationwide are downloaded weekly and stored in a central electronic data warehouse using proprietary software (PetWare, Banfield, The Pet Hospital, Portland, OR). Each record includes a unique patient and hospital identifier. Demographic data for each dog including hospital visit date and the results of fecal flotation tests from January 1, 2003, through December 31, 2009, were downloaded from the central database. All dogs had a recorded fecal flotation test, and only results from the first fecal test for each dog were used in the analysis. Data related to clinical signs and specific treatments were not available.

The main dataset for canine data was organized into a subset containing all positive fecal test results indexed by the test date and a second full set containing all fecal tests (positive and negative) indexed by the test date. A monthly incidence ($MP_{d,i}$) per 100 dogs was estimated as the number of positive fecal tests for each month i (NPT_i) divided by the total number of tests for the same month (TNT_i): $MP_{d,i} = (NPT_i / TNT_i) \times 100$.

2.1.2. Human—The number of human *Giardia* cases reported to CDC's National Notifiable Disease Surveillance System from each state by month ($TNRC_i$) from January 2003 through December 2009 was obtained from CDC. Confirmed and probable cases of giardiasis are reported voluntarily by states. Positive diagnostic testing includes visual detection of cysts via staining or direct fluorescent antibody methods, or *Giardia* antigen detection by immunodiagnostic tests (Yoder et al., 2010). An estimate of the total population for each state included in the study for each of the seven years was obtained from the federal census web-site (US Census Bureau, 2009). The total population (TP_i) for each state was used as the denominator to estimate a monthly incidence of *Giardia* ($MP_{h,i}$) per 100,000 people: $MP_{h,i} = (TNRC_i / TP_i) \times 100{,}000$.

2.2. Analysis

Monthly incidence rates of canine and human *Giardia* infection were graphed. The seasonal-trend decomposition procedure based on loess (STL) method (Cleveland et al., 1990;

Barnett and Dobson, 2010) was then used to decompose the complete time series in order to visualize temporal patterns. This procedure is based on decomposing the time-series into trend, seasonal, and remainder components. The seasonal component is found by local linear regression (loess) smoothing the seasonal sub-series of the overall time series. The seasonal values are removed, and the deseasonalized remainder smoothed to find the trend. The remainder component is the residuals from the seasonal plus trend fit. Monthly data were plotted as a cycle-subseries, displaying monthly averages (horizontal bars) with accompanying deviations from the mean for each year (vertical bars). The horizontal and vertical bars allow a visual assessment for trends and/or a time-variant nature of the data.

2.2.1. Model fitting—A seasonal autoregressive integrated moving average (SARIMA) model was used to describe the times series of each species. SARIMA is an extension of the autoregressive integrated moving average (ARIMA) models and is used to model time series with a seasonal or cyclic component of length S (Box et al., 2008). Accordingly, SARIMA includes seasonal and non-seasonal components; candidate models were first selected on the basis of exploratory analysis that took into consideration the time plot structure, properties of the model residuals' autocorrelation (ACF) and partial autocorrelation (PACF) plots for each series. Diagnostics of the residuals and Akaike information criterion (AIC) values were then used to select the final model that best fit the data and appeared to satisfy statistical assumptions. Integration order, autoregressive (AR), and moving-average (MA) coefficients were selected based on minimizing AIC for the seasonal and non-seasonal components of the model. The Ljung-Box Q test of residuals (Ljung and Box, 1978) was used to assess goodness-of-fit of the final models. All statistical analyses were conducted using R (R Development Core Team, 2012; Hyndman and Khandakar, 2008) and an α value of less than 0.05 was selected as the significance level.

3. Results

A total of 135,802 cases of human giardiasis were reported to the CDC during the period from 2003 through 2009 from all states except Indiana, Kentucky, North Carolina, Mississippi, and Texas where notification was not required during this period. The total annual number of reported human cases remained relatively stable (ranging from 18,478 in 2009 to 20,751 in 2004) whereas the total number of cases reported from month to month fluctuated with noticeable increases during late summer and early fall. Reported human cases were generally lowest in February (1216) and highest in August (2383) during the study period.

Using the first fecal test available in the medical record for each dog, the total number of canine fecal tests included in the study was 2,468,359. These tests were obtained from 777 Banfield veterinary hospitals in 43 states, approximating the same geographical area as the human data. The number of canine fecal samples tested annually for *Giardia* increased from 288,803 in 2003 to 483,016 in 2009, concurrent with increasing number of hospitals. Meanwhile, the percentage of dogs testing positive for *Giardia* infection annually declined during the study period ranging from 0.61% (1760/288,803) in 2003 to 0.27% (1326/483,016) in 2009. There was slight monthly variation in percentage of tests positive from a low of 0.39% (725/185,371) in November to a high of 0.52% (1108/214,466) in

January. Time plots of monthly incidence of human giardiasis (per 100,000) and monthly incidence (per 100) of canine positive fecal tests are shown in Fig. 1A and B, respectively.

Examination of human case data with the STL procedure showed no clear overall trend over time as the incidence was relatively constant in the calculated trend throughout the seven-year study period, from a high of 0.75 (cases per 100,000) in 2005 to 0.70 in 2009 (Fig. 2). A regular seasonal pattern was noticeable with a large magnitude of variation (approximately 0.4 cases/100,000) peaking in July through October (Fig. 3). In contrast, the canine series trend indicated a general decline over study period from a high of 0.70 (per 100 dogs) in 2003 to 0.30 (per 100 dogs) by the end of 2009 (Fig. 4). The seasonal pattern for this data series however was irregular with a small magnitude of variation (±0.03 cases/100) (Fig. 5).

Fitting a SARIMA model for the human series indicated a non-seasonal moving-average and an annual integrated seasonal moving-average term; both terms were statistically significant (Table 1). In comparison, the canine model included an integrated non-seasonal moving average and a 4-month seasonal moving-average term, yet only the non-seasonal term was statistically significant. Both models were deemed to adequately fit the data given the uncorrelated residuals and that the Ljung-Box Q test of the residuals was not significant.

4. Discussion

To the best of our knowledge, this is the first study to use time-series techniques to analyze temporal patterns of *Giardia* infection among dogs and people over multiple years in the United States. Because there is no common database of information regarding fecal test results of dogs and their owners, two separate data sources were used in this ecological study. Ecological studies use aggregates of individuals for analysis, but observed associations may differ from an association existing at the individual level – a phenomenon known as the ecological fallacy (Last, 2001). Our hypothesis was that temporal similarities in infection might support a possible zoonotic risk and promote further investigation. However, the datasets used different denominators, not only in species, but also in diagnostic test indications.

Human data compared with canine data seemed to follow two different temporal patterns suggesting that the generating processes underlying both series might be different, and that *Giardia* transmission from dogs to humans and from humans to dogs might be uncommon. The human data series exhibited a strong and regular annual cycle with peaks observed in July through October months, but the canine series did not demonstrate any clearly defined seasonality. Further research will be needed to determine if humans and dogs are simply infected by different assemblages, or if the same assemblage/organism comes from different sources. The seasonal pattern of human giardiasis observed here is in agreement with prior CDC reports and other studies that reported peaks of human giardiasis in the late summer and early fall (Furness et al., 2000; Naumova et al., 2000). Although the main risk factors for giardiasis in humans include contaminated water or food, the increased incidence during late summer months may be attributable to increased human outdoor activities resulting in increased exposures. Interestingly, the human incidence remained relatively constant

throughout the seven-year period based on national data. Other trends may have occurred at the state level, but this was not investigated in this study. The ‘stable’ incidence in people may indicate the need for increased efforts to educate the public about potential infection sources and appropriate preventive measures.

The canine data showed a marked downward trend over the study period despite an increased number of dogs being tested at Banfield veterinary hospitals for intestinal parasitism. This trend is unlikely to reflect changes in patient demographics, or in diagnostic methods as all samples were examined by trained staff following a standardized protocol in all Banfield hospitals. Previous research by our group documented a higher risk of *Giardia* infection in pure breed vs. mixed breed dogs and in younger vs. older dogs (Mohamed et al., 2013). The decreasing prevalence of *Giardia* infection in dogs in this study may suggest that fewer puppies are coming from large puppy mills, where the prevalence of intestinal parasites is often greater than in private homes or less crowded group settings (Barr and Bowman, 1994). Alternatively, these sources may be employing more methods in treatment or prevention. The lack of seasonality in the canine series is not totally unexpected, however, and is in agreement with the only available study that analyzed *Giardia* infection among dogs using time-series techniques – albeit at a single hospital location (Nolan and Smith, 1995). Although an earlier study reported some seasonal patterns (Kirkpatrick, 1988), less rigorous analytic methods in a smaller population were used.

Time-series techniques such as the ones used in this study are useful to analyze and interpret temporal patterns of infection observed using routinely collected surveillance or hospital data. These methods are commonly used in fields such as econometrics, but their application to veterinary medical data has been limited (Benschop et al., 2008; Sanchez-Vazquez et al., 2012). A recent paper (Christiansen et al., 2012) that reviewed methods used to assess seasonality in epidemiological studies of human infectious disease did not include STL and ARIMA/SARIMA.

The STL decomposition procedure provides an effective tool to visualize and explore time-series events by dividing them into trend, seasonal, and remainders components that best fit the data (Cleveland et al., 1990). Other methods used to analyze epidemiological data collected over time include generalized linear models (GLM) focusing on evaluating change-point of time parameters rather than decomposing and describing its elements (Christiansen et al., 2012). The SARIMA approach is another equally effective time-series analysis method (Jiang et al., 2010) and was used here to provide some contrast and to verify results obtained from descriptive analyses, i.e. STL. The SARIMA model confirmed that human series follow an annual cycle with a highly significant seasonal component whereas seasonality of the canine series was rather weak.

It is also possible to fit a lagged regression type model, or a SARIMA(X) model, where the human incidence series is regressed against the lags of canine incidence series. As a first step, the number of lags of the canine incidence series to be included has to be estimated. To do this, so-called prewhitening (Shumway and Stoffer, 2011) has to be applied to both sides of the regression equation. This operation transforms the input (canine giardiasis) series into the white noise, and then the cross-correlation between the transformed output (human

giardiasis) series and the aforementioned white noise is assessed. In our specific case, the resulting cross-correlation did not have a single significant lag which indicated that there is very little, if any, dependence between the temporal/seasonal patterns of human and canine giardiasis series.

It is important to point out that both time series have some shortfalls that could limit the scope of interpreting the observed results. The human data were based on passive surveillance of *Giardia* infection which is believed to be highly underreported (Nakada et al., 2012). However, testing for *Giardia* in humans is usually prompted by clinical signs and the attending physician's consideration of protozoal infection. By comparison, the canine data was based on a routinely performed fecal flotation testing which, with sensitivity estimated at 49%, is less sensitive compared to other diagnostic techniques such as centrifugal flotation and ELISA (Rishniw et al., 2010; Zajac et al., 2002; Dryden et al., 2006). Additionally, the fecal *Giardia* test results from dogs did not distinguish whether the dog being tested was asymptomatic and the test was part of a routine wellness exam, or whether it was showing clinical signs associated with an intestinal illness. This may have resulted in a differential bias in which seasonal patterns in dogs were obscured by broader testing protocols. In contrast, a higher proportion of the human fecal tests were probably performed on individuals who were clinically symptomatic at the time. Due to its retrospective nature, this ecological study was limited in its capability to assess zoonotic risk or source of infection in either species. Ideally, these would be evaluated by performing fecal tests on dogs and humans in the same household at the same time. However, an ecological approach may initially be necessary when medical data of interest, e.g. human and canine, are collected independently. Despite problems in interpretation, ecological studies may generate initial leads for pursuit in more definitive studies.

5. Conclusion

Time-series analysis in an ecological study of *Giardia* infection among humans and dogs in the United States for the period from 2003 through 2009 showed that the temporal characteristics of the two data series were different. The human data series exhibited a strong annual seasonal cycle, peaking in August and September, and overall maintained a relatively constant incidence level during the study period. The canine series over the same seven-year period had weak and irregular seasonal fluctuation with an overall trend of declining incidence. These findings suggest that underlying transmission processes generating both series are likely to be different, raising additional questions regarding the significance and extent of the risk of zoonotic transmission of *Giardia* infection between dogs and people.

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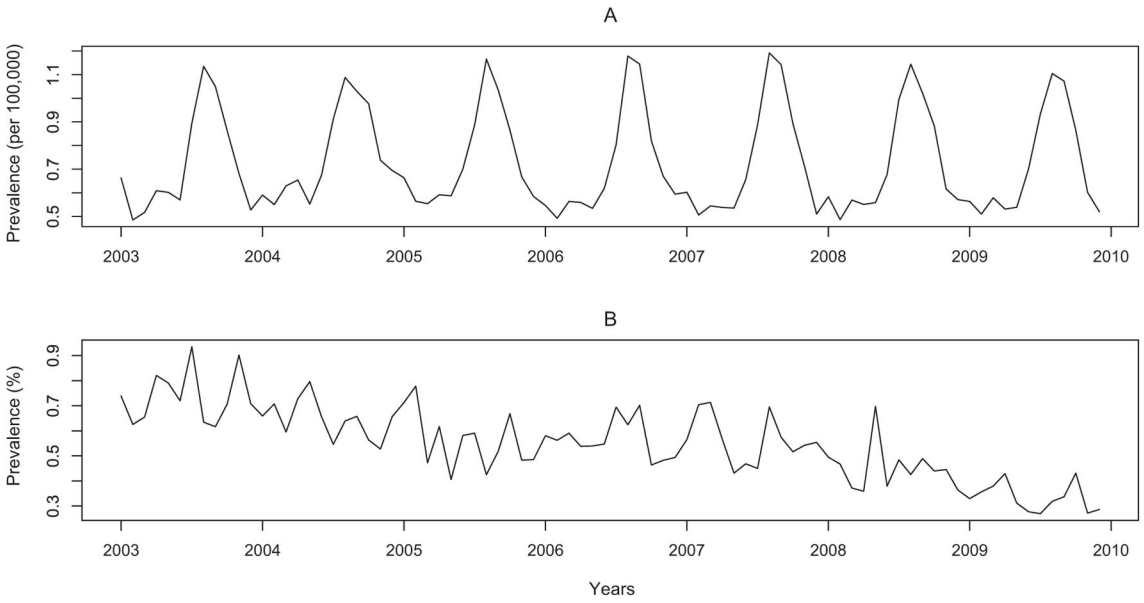

Fig. 1.

Time plots of human giardiasis (A) reported to CDC and percent of positive fecal canine tests (B) at Banfield Pet Hospital, by month, United States 2003–2009.

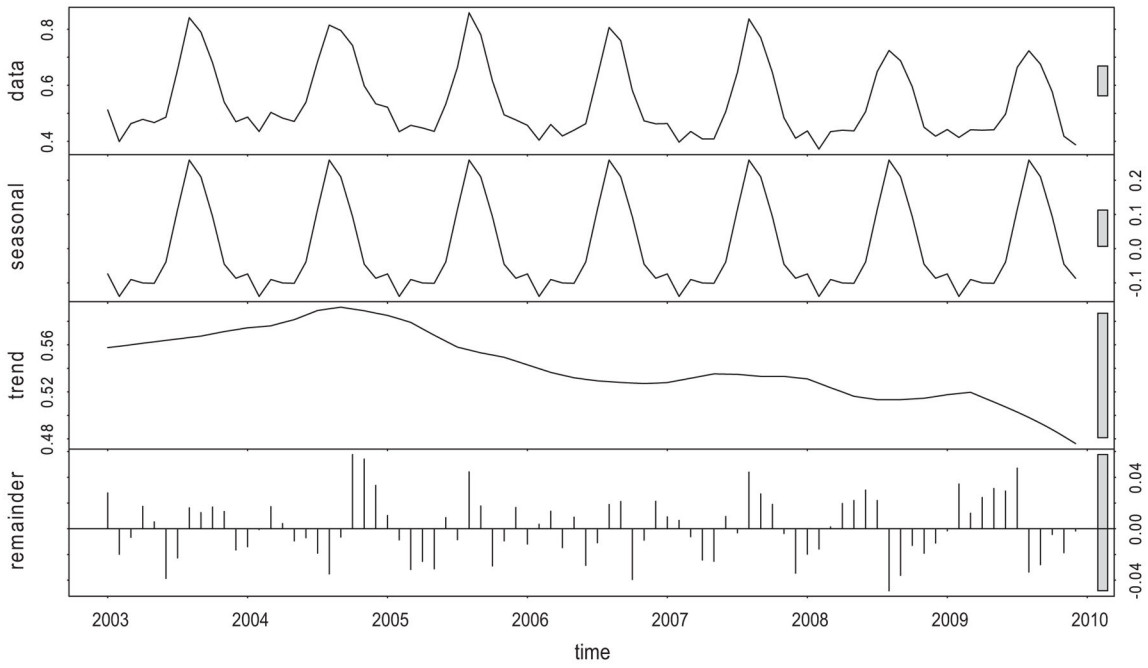

Fig. 2.

STL decomposition of human giardiasis by month, United States, 2003–2009, into seasonal, trend, and remainder components. The *y*-axis scale represents cases/100,000. As each component is drawn on its own scale, the gray bar on the right provides a relative magnitude of the variation in each component. Thus if panels were scaled so that the gray bars were all the same size, one would see how much of the variation in the original data is related to that component.

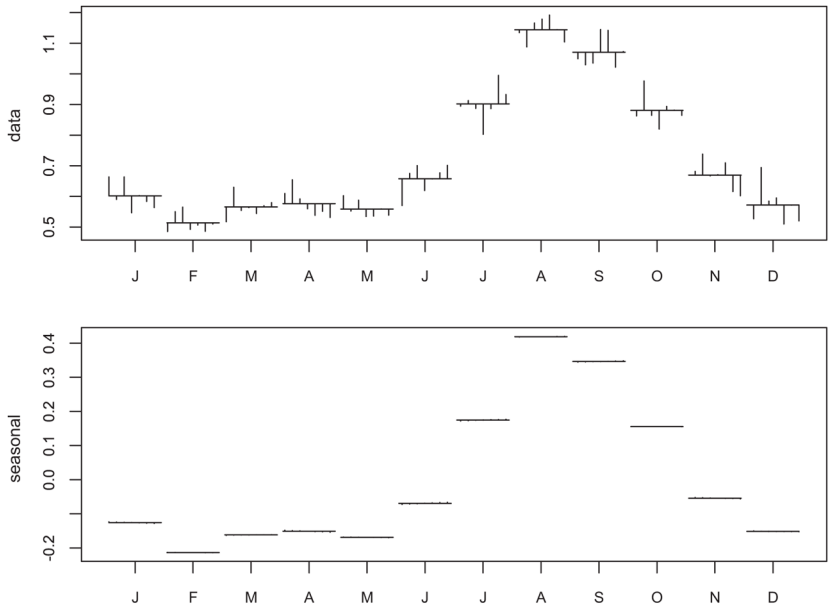

Fig. 3.

Plots of average monthly incidence of human giardiasis cases/100,000 (*y*-axis) from the surveillance raw data (top) and STL seasonal component (bottom), United States, 2003–2009.

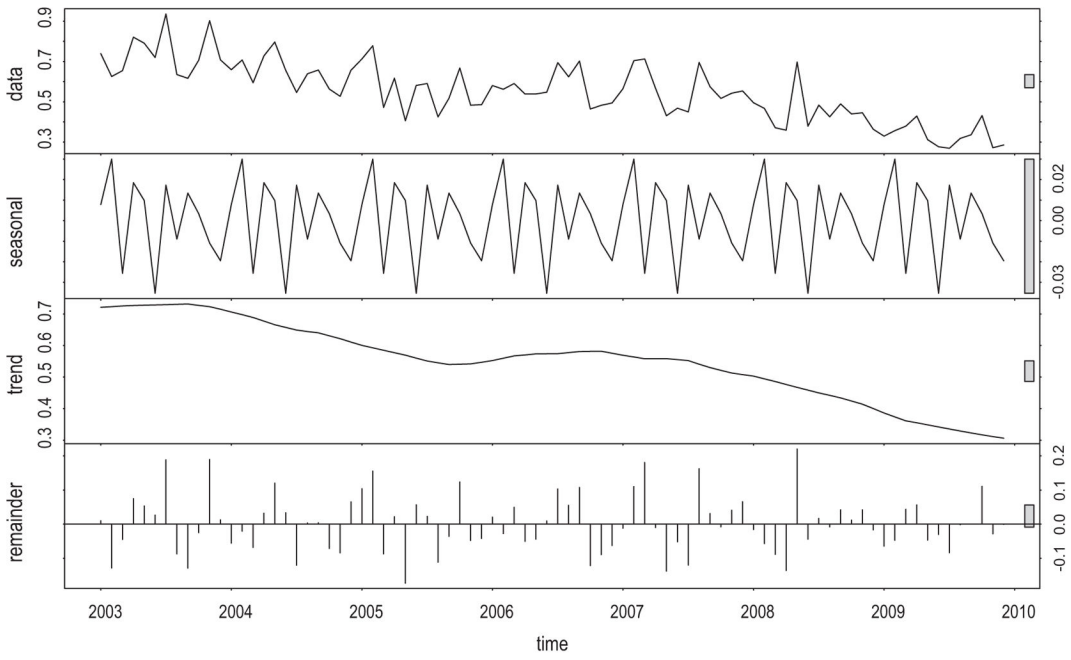

Fig. 4.

STL decomposition of canine giardiasis at Banfield hospitals, 2003–2009, into seasonal, trend, and remainder components. The *y*-axis scale represents positive fecal tests/100 dogs.

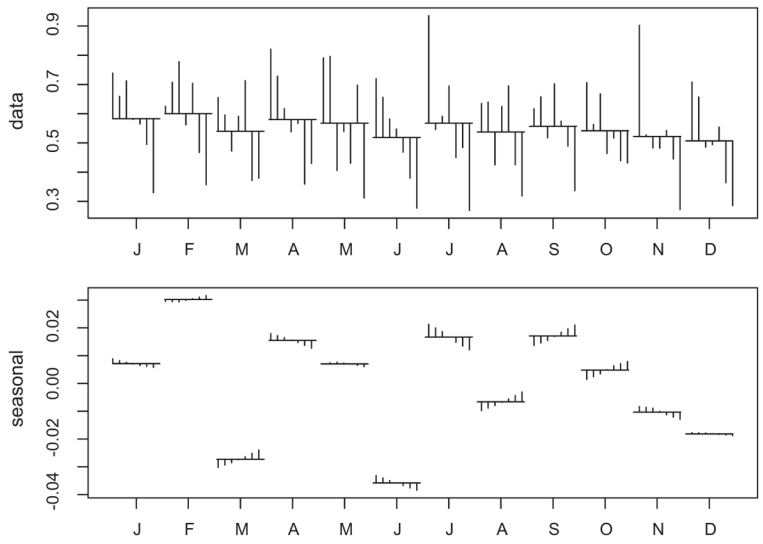

Fig. 5.

Plots of average monthly prevalence of positive fecal tests (*y*-axis) among dogs from the raw data (top) and STL seasonal component (bottom).

Table 1

Coefficients of the non-seasonal and seasonal terms, with corresponding standard errors (s.e.) of SARIMA models for human and canine data from 2003 to 2009. The numeric subscripts indicate model-determined time components of 12 months, i.e. annual, and 4 months for the human and canine series, respectively.

	Human series			Canine series		
Model	**SARIMA(0,0,1) × (0,1,1)$_{12}$**			**SARIMA(0,1,1) × (0,0,1)$_{4}$**		
Term	**Coefficient**	**s.e.**	***p*-value**	**Coefficient**	**s.e.**	***p*-value**
Non-seasonal	0.2015	0.124	0.026	−0.879	0.068	<0.001
Seasonal	−0.6231	0.158	<0.001	−0.0148	0.128	0.227