Transition models to assess risk factors for new and persistent trypanosome infections in cattle -analysis of longitudinal data from the Ghibe valley, Ethiopia

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Abstract
Transition models were used to distinguish between factors associated with both incident and persistent trypanosome infections. Data were analysed from a long-term study of 2559 cattle in 8 herds in which both trypanosome infections (a total of 101,240 cattle sampling-months) and tsetse (*Glossina spp*.) challenge were monitored monthly from March 1986 to March 1998. Over this period, both tsetse control and drug treatment programs were implemented.. In general, the duration of infection increased during the study, despite the regular treatment with diminazene. The odds of new infections, however, decreased by two-thirds to one-half due to tsetse control and mass treatments with diminazene. Both the number of previous infections and the age of an animal were associated with variations in new infection risk and duration of infection.

Introduction
This paper aims to assess risk factors for both incidence and persistence of trypanosome infections for cattle in the Ghibe valley between 1986 and 1998 using transition models. The relative importance of these factors on the incidence and persistence of trypanosome infections and their implications for control and treatment of trypanosomosis are highlighted. Finally, the merits of transition models for the assessment of longitudinal data on parasite infections are discussed.

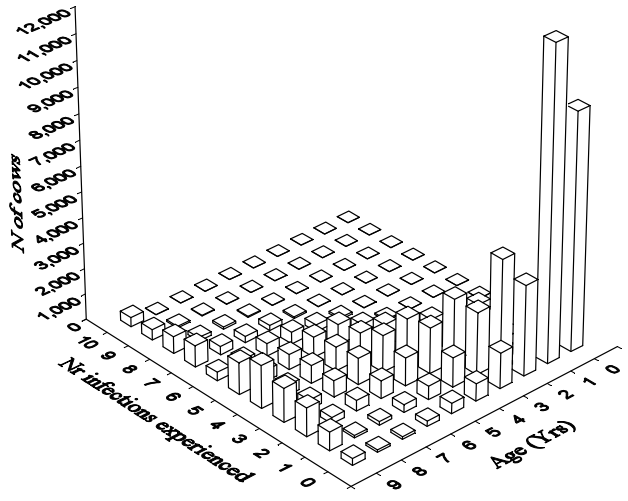
Materials and Methods
The study area was the Ghibe valley in southwest Ethiopia (Leak et al. 1996). Data on tsetse and cattle populations were collected monthly from March 1986 to March 1998. A number of tsetse and trypanosomosis control measures were undertaken during this period. Tsetse populations were monitored for 5 consecutive days per month using 16-baited biconical traps as described by Leak et al. (1996). The tsetse apparent density was the mean number of flies per trap per day in a month. Blood samples from cattle located in 8 herds in the valley were tested monthly for trypanosomes, using the phase-contrast, buffy-coat technique, and for the determination of packed cell volume (PCV) (Rowlands et al., 2001). Parasitaemic animals with a PCV below 26% were treated by intramuscular injection with diminazene aceturate (Berenil®; Hoechst, Germany) at a dose of 3.5-mg/kg bw. Cattle with a PCV below 26% and which showed clinical signs of trypanosomosis, although not detected as parasitaemic, were also treated with the same dose. Leak et al. (1996) and Rowlands et al. (1993) have described the study methods in more detail. The general structure of the transition multivariable model that was used for analyzing the data was: $\text{logit}(\text{inf}_t) = \text{intercept} +$

risk factors + inf_{t-1} + inf_{t-1}* risk factors + error, where inf_t is the infection status at the current sampling and inf_{t-1} is the infection status at the previous sampling. The intercept is the baseline risk of a new infection and the intercept + inf_{t-1} is the baseline risk of remaining infected (non-cure). The error was complex, allowing for the inclusion of compound or serial correlation in the error.

Results

The parameter estimates and odds ratios for terms significant ($p<0.05$) in the model are presented in Table 1 for new (incident) infections (infections flowing two months of no detectable infection). An increase in rolling geometric mean tsetse density by one fly per trap per day increased the odds of a new infection by 1.49. There was also a significant seasonal pattern in incidence.. Risk of new infections was influenced by both control operations. During the control periods in which targets were placed, June 1990 - May 1991and June 1991 to May 1992, and when pour-on was used, January 1994 - March 1998, the odds of new infections decreased by two-thirds to one-half due to targets (OR = 0.38 and 0.57) and one-half due to pour-on (0.49), respectively ($p<0.0001$). Mass treatments with diminazene (in mid-1990 and early 1994) also were associated with an almost 50% decrease in the risk of new infections (Table 1). Both the number of previous infections and the age of an animal were associated with variations in new infection risk (see Figure 1 for detailed patterns). The predicted prevalence closely matched the observed prevalence. At a prediction cut-off of 0.5, 88% of infected and 85% of non-infected cattle-observations were correctly classified. A very small but statistically significant serial correlation remained in the residuals using this first-order Markov process (0.14 in the first lag, .05 in the second lag and .04 in the third lag). This was not felt to be important enough to justify the added complexity of a second-order process.

Figure 1. Number of cattle sampling months by age and number of previous detected infections.



Discussion

Different patterns of infection incidence and persistence were associated with cattle age and previous infection history. The incidence of new infections, when adjusted by the model for the number of previous infections, decreased with age. However, the

number of infections varied greatly for individual cattle with a few cattle hardly ever acquiring detectable new infections. Declining incidence with increasing age might normally be associated with the acquisition of a limited degree of immunity over time; however, the age and previous infection history patterns of duration of infection do not support this. Both increasing age and increasing numbers of previous infections were associated with longer duration infections in some cows which made detection of new infections more difficult. These patterns deserve more detailed further investigation, particularly by different trypanosome species for they may indicate differences in genetic ability to control trypanosome infections in the local cattle population that could be exploited. Rowlands et al. (2001) observed longer duration infections with *T. congolense* as compared to *T. vivax*. There is also evidence from other studies that *T. vivax* prevalence and incidence declines more with increasing age than *T. congolense*. Interestingly, in this study, the average duration of infection of multiple-species infections (combinations of *T. brucei*, *T. congolense* and *T. vivax*), as detected microscopically, was shorter than for single-species infections. The real benefit of using a transition model to investigate infection dynamics of trypanosomes in cattle is its ability to assess, simultaneously, factors influencing both incidence and persistence of trypanosome infections. This was particularly useful because increased duration of infection could be examined when adjusting for factors such as tsetse control and chemotherapy programs that influenced infection incidence.. Transition models, thus, appear to offer solid promise as a tool in better understanding infection dynamics of parasite infections in natural settings as they distinguish between factors associated with new infections and those influencing persistence.

Table 1. Risk factors for new trypanosome infections in cattle sampled monthly in the Ghibe valley, Ethiopia, March 1986 – March 1998.

Variable	Estimate or Range of Estimates	Odds Ratio (OR) or Range of ORs	Confidence limits for Odds Ratio (OR) Lower 95%	Higher 95%	P-value
Intercept	-2.78	-	-	-	<.0001
Rolling geometric mean tsetse fly density	0.40	1.49	1.38	1.61	<.0001
Control period (baseline class: no control from June 1992 – Dec 1993)					
1986	0.93	2.53	2.18	2.93	<.0001
1987	-0.08	0.92	0.82	1.04	0.21
1988	0.05	1.05	0.95	1.16	0.36
Mar 1989 – May 1990	-0.30	0.74	0.66	0.83	<.0001
June 1990 – May 1991	-0.97	0.38	0.34	0.42	<.0001
June 1991 – May 1992	-0.56	0.57	0.51	0.63	<.0001
Jan 1994 – March 1998	-0.71	0.49	0.46	0.53	<.0001

Season (baseline class: long wet season)					
Dry season	0.14	1.15	1.09	1.20	<.0001
Short wet season	-0.20	0.82	0.78	0.86	<.0001
Blanket treatment 1	-0.54	0.58	0.41	0.83	0.003
Blanket treatment 2	-0.53	0.59	0.38	0.92	0.02
Number of previous infections (baseline class: never)					
from 1-10	(1.80, 4.61)	(6.05, 101)	-	-	<.0001
Age (10 classes, baseline class: age 25-36 months)					
from 0 to >108 months	(-1.31, 2.01)	(0.27, 2.01)	-	-	<.0001
Sex (male versus female)	0.30	1.35	1.19	1.53	<.0001
Sex*Age interaction (baseline class: males 25 – 36 months)					
males, 0 to > 108 mths	(-0.30, 0.23)	(0.74, 1.25)	-	-	<.0001

Acknowledgements

The contribution of technical staff in these institutes is gratefully acknowledged as is the long-term co-operation of farmers involved in this study. The analysis of data was funded by a grant by the United States Agency for International Development (USAID) to ILRI and Cornell University.

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