

A review of methods used to adjust for cluster effects in explanatory epidemiological studies of animal populations

J.J. McDermott^{*,a,b}, Y.H. Schukken^{a,c}

^a*Department of Population Medicine, Ontario Veterinary College, University of Guelph, Guelph, Ont. N1G 2W1, Canada*

^b*Department of Public Health, Pharmacology and Toxicology, Faculty of Veterinary Medicine, University of Nairobi, Nairobi, Kenya*

^c*Department of Herd Health and Reproduction, University of Utrecht, Utrecht, Netherlands*

(Accepted 21 July 1993)

Abstract

This paper reviews explanatory studies in the veterinary epidemiology literature, in which clusters (herds) were sampled and individual responses were measured. The studies were taken from the first ten volumes of *Preventive Veterinary Medicine*. The objectives of the review were: (1) to describe the statistical methods used to adjust for cluster effects; (2) to provide estimates of intracluster correlations for various health and production outcomes; and (3) for studies ignoring cluster effects, to estimate the proportion of significant inferences that would be rejected if cluster effects were included.

Of the 67 papers reviewed, 36 (54%) used some form of adjustment for clustering. Using a fixed effect for herd was employed most frequently (27 papers). Four of the 67 papers used a matched design, two used a weighted analysis, and three papers included a random herd effect.

An estimate of the intracluster correlation (ρ) was calculated when sufficient data were present. This estimate ranged from 0.0017 (lamb mortality data), to 0.46 (prevalence of brucellosis positive serotiter). Most intracluster correlations ranged from 0.01 to 0.15. In the papers where ρ was estimated from the data, the variance inflation factor ranged from 1.1 to 13. In 36 of the 67 (54%) papers reviewed, all inferences were accepted. In 30 of these 36, the authors correctly accounted for clustering, and in the other six the inference would not have changed after adjustment for clustering. In the remaining 31 (46%) papers, changes in inference were predicted. The proportion of incorrect inferences could be estimated in 20 of these 31 papers.

Introduction

Livestock populations are commonly clustered into herds, flocks or other groups. The importance of considering herd factors as well as the individual animal factors that influence the health and production indices of livestock has long been appreciated. Herd health programmes (developed from the

*Corresponding author at: Department of Population Medicine, Ontario Veterinary College, University of Guelph, Guelph, Ont. N1G 2W1, Canada.

1950s) have been a practical response to addressing production and health at both the individual animal and herd levels. The relative importance of herd vs. individual animal effects can be of great practical importance in targeting animal health and production interventions more effectively (Dohoo et al., 1984b).

In recent years, veterinary epidemiologists have undertaken many explanatory studies to investigate factors influencing health and production in livestock populations. Given the structure of livestock populations, herds are usually the sampling units. The unit of interest may be the individual animal, the herd, or both (McDermott and Shoukri, 1991).

The statistical models used to analyze such studies often assume that the outcomes are independent. The most obvious violation of the independence assumption occurs when herds are sampled and individual animal responses are assessed. Less obviously, independence of individual animal responses is also assumed when herd proportions or counts (number of animals in a defined risk category) are the outcomes of interest (Haseman and Kupper, 1979). If the responses of herd mates are correlated, statistical tests based on an assumption of independence will be incorrect and the estimated variance will be too low. The degree by which the variance will need to be inflated will be related to the degree of intraherd correlation and the herd size.

A wide variety of methods can be used to adjust for herd effects. Traditionally, ANOVA methods which estimate herd effects as either fixed or random have been used (Shoukri et al., 1991). For non-normally distributed (binomial or Poisson) outcomes, herd effects (either random or fixed) have been estimated using mixture distributions (likelihood) (Curtis et al., 1988b) or overdispersion parameters (quasi-likelihood) (McDermott et al., 1988).

In this paper, explanatory studies in which herds were sampled and individual responses were measured are reviewed. The studies were taken from the first ten volumes of *Preventive Veterinary Medicine*. The objectives of the review are: (1) to describe the statistical methods used to adjust for cluster effects; (2) to provide estimates of intracluster correlations for various health and production outcomes; and (3) for studies ignoring cluster effects, to estimate the proportion of significant inferences that would be rejected if cluster effects were included.

Materials and methods

Criteria for inclusion of papers

All papers in Volumes 1–10 of *Preventive Veterinary Medicine* with the exceptions of two special conference proceeding issues (Volume 2, Numbers 1–4 and Volume 8, Numbers 2–3) were eligible for inclusion. Initially, papers chosen as eligible were explanatory (as opposed to purely descriptive) studies

in which more than one cluster of animals was investigated. From these papers, the subset in which either individual animal responses (continuous and categorical) or herd proportions or counts were the outcomes of interest were chosen for detailed review. Papers in which herds were classified as high/low or in which herd scores were assigned were not included, since the herd was the unit of analysis and individual animal independence was not a necessary assumption.

Classification of papers

Each of the chosen papers was reviewed by both authors independently. Each paper was described when possible under the following headings: major outcome(s); animal unit of interest; method of cluster adjustment; number of clusters; average cluster size; presumed or estimated intraherd correlation; variance inflation from independence; and the proportion of inferences presented in the paper that would be rejected if the variance inflation estimate was utilized. After the initial review phase the authors compared their findings until a consensus was reached.

Estimation of intraherd correlation and variance inflation

For each paper in which sufficient data were presented (i.e. herd proportions or counts given or individual animal responses classified by herd), the intraherd correlation or variance inflation factor was estimated. For papers in which sufficient data were not presented, a range of presumed intraherd correlations based on literature estimates or our best guesses were provided. In general, three ranges of intraherd correlations were used: low (<0.05), medium (0.05–0.10) and high (0.10–0.20). When possible, intraherd correlations were estimated using a one-way ANOVA method (Snedecor and Cochran, 1980; Fleiss, 1981). The intraclass correlation coefficient ($\hat{\rho}$) was estimated as:

$$\hat{\rho} = (\text{MSW} - \text{MSB}) / (\text{MSW} + (n - 1) * \text{MSB})$$

where: MSW is the within cluster mean square; MSB is the between cluster mean square; and n is the mean cluster size (Donald and Donner, 1988).

For papers in which the intraherd correlation was estimated, the variance was multiplied by a factor (c), estimated as:

$$c = 1 + (n - 1) * \hat{\rho}$$

(Brier (1980) for multinomial data; Donald and Donner (1988) for binomial data; Snedecor and Cochran (1980) for continuous data). This method assumes that all cluster sizes were equal. For papers in which the intraherd

Table 1
Methods of herd adjustment and impact of clustering on analyses from studies in which clusters were sampled and individual animal characteristics recorded

Reference	Outcome variable	Unit of interest	Method of cluster adjustment	Number of clusters	Mean cluster size	Estimated ^a or presumed ^b correlation	Variance inflation from independence	Proportion ^c of significant inferences rejected
<i>Volume 1</i>								
Hird and Robinson (1982)	Calf mortality	Dairy calf	None	45	48 ^d	0.01 ^b	1.5	2/6
Nabuurs et al. (1982) Exp. 1	Post-wean mortality	Piglet	None	22	100	0.12 ^a	12.6	0/3
Hird and Robinson (1983)	Milk production	Dairy cow	Individual cow matching	17	47	0.10-0.20 ^b	5.6-10.2	NA
Lutnaes and Simensen (1983)	Abomasal bloat	Lamb	None	28	170 ^d	0.06 ^a	11.1	9/10 ^f
<i>Volume 2</i>								
Dohoo et al. (1984a)	Diseases	Dairy cow	Fixed effect	32	63	0.01-0.10 ^b	1.6-7.2	NA ^f
Dohoo and Martin (1984a)	Diseases	Dairy cow	Case-control	32	63	0.01-0.10 ^b	1.6-7.2	NA
Dohoo and Martin (1984b)	Milk production	Dairy cow	Herd matching	32	63	0.10-0.20 ^b	7.2-13.4	NA ^f
Dohoo and Martin (1984c)	Culling	Dairy cow	Fixed effect	32	63	0.05-0.10 ^b	4.1-7.2	NA
Huffman et al. (1984)	Pyometra	Dairy cow	Fixed effect	4	197 ^d	0.02 ^a	4.9	NA
<i>Volume 3</i>								
Dohoo et al. (1984b)	Milk production and diseases	Dairy cow	None	32	63	0.01-0.20 ^b	1.6-13.4	Some ^e

Grohn et al. (1984)	Ketosis	Dairy cow	Herd-season fixed effect	??	??	0.01 ^a	??	NA	
Pappaioanou et al. (1984a)	Echinococcus prevalence	Dog	Weighted least squares	528	11	0.08–0.12 ^a	2.0	NA	
Pappaioanou et al. (1984b)	Hydatid prevalence	Sheep	Weighted least squares	278	45	0.03–0.07 ^b	2.3–4.1	NA	
Goodger and Kushman (1985)	Herd health and milk production	Dairy cow	None	9	555	0.05–0.20 ^b	27–110	Some ^e	
Bigras-Poulin et al. (1985)	Milk production and diseases	Dairy cow	None	102	36	0.01–0.20 ^b	1.3–8.2	Some	
Algers and Hennichs (1985)	Fertility/culling	Dairy cow	Matched on cooperative	106	20	0.01–0.05 ^b	1.2–2.0	0/2 ^f	
Zessin et al. (1985)	CBPP prevalence	Cattle	None	400	18	0.06 ^g	2.0	0/3	
Andersson and Emanuelson (1985)	Ketoneamia/fertility	Dairy cow	Fixed effect	126	24	0.05–0.10 ^b	2.1–3.3	NA	
<i>Volume 4</i>									
Bartlett et al. (1986a)	Days open and milk production	Dairy cow	Adjusted for herd mean (fixed effect)	21	60 ^d	0.05–0.20 ^b	7.7–27.8	NA ^f	
Markusfeld (1986)	Displaced abomasum	Dairy cow	Mantel-Haenszel	7	250 ^d	0.005–0.01 ^a	2.2–3.5	NA	
Rowlands and Lucey (1986)	Milk production	Dairy cow	Fixed effect	4	183 ^d	0.10–0.20 ^b	19.2–37.4	NA	
Rowlands et al. (1986)	Clinical diseases	Dairy cow	Fixed effect	4	223 ^d	0.01–0.10 ^b	3.2–23.2	NA ^f	
Bartlett et al. (1986b)	Days open and milk production	Dairy cow	Adjusted for herd mean (fixed effect)	22	60 ^d	0.05–0.20 ^b	9.5–35.0	NA ^f	
Bendixen et al. (1986a)	Clinical diseases	Dairy cow	None	943	20 ^d	0.05–0.10 ^b	2.0–2.9	4/48 ^f	
Bendixen et al. (1986b)	Dystocia	Dairy cow	None	943	20 ^d	0.05–0.20 ^b	2.0–4.8	2/20	

Table 1 (continued)

Reference	Outcome variable	Unit of interest	Method of cluster adjustment	Number of clusters	Mean cluster size	Estimated ^a or presumed ^b correlation	Variance inflation from independence	Proportion ^c of significant inferences rejected
<i>Volume 4 (continued)</i>								
Bendixen et al. (1987a)	Retained placenta	Dairy cow	None	943	20 ^d	0.05-0.10 ^b	2.0-2.9	5/49
Hueston et al. (1987)	High SCC prevalence	Dairy herd	Weighted by herd size	1325	58	0.05-0.15 ^b	3.8-9.6	Some ^e
Dohoo et al. (1987)	Conception rates	Sheep	Fixed effect	4	170	0.06 ^a	11.1	NA
Salman and Meyer (1987)	Weight gain	Lamb	Fixed effect	2	174	0.05-0.20 ^b	9.6-35.6	NA
	Herd <i>Brucella</i> prevalence	Dairy herd	None	110	150	0.05-0.10 ^b	8.4-15.9	3/4
<i>Volume 5</i>								
Dobbelaar et al. (1987)	γ -globulin levels	Dairy calf	None	6	30	0.05-0.15 ^b	2.5-5.4	Some ^e
Bendixen et al. (1987b)	Parturient paresis	Dairy cow	None	943	20 ^d	0.05-0.10 ^b	2.0-2.9	3/26
Bendixen et al. (1987c)	Ketosis	Dairy cow	None	943	20 ^d	0.10-0.20 ^b	2.9-4.8	5/28
McDermott et al. (1987a)	CBPP and brucellosis reactors	Cow	None	32	18	0.06 ^a	2.0	0/0
	Brucellosis reactors	Cow	None	37	20	0.46 ^a	8.7	2/2
McDermott et al. (1987b)	Brucellosis reactors	Cow	None	35	10	0.08 ^a	1.7	2/3
Schukken et al. (1988)	Retained placenta	Dairy cow	Fixed effect	34	65	0.05-0.10 ^b	4.2-7.4	NA
Bendixen et al. (1988a)	Mastitis	Dairy cow	None	943	20 ^d	0.05-0.10 ^b	2.0-2.9	3/38

Table 1 (continued)

Reference	Outcome variable	Unit of interest	Method of cluster adjustment	Number of clusters	Mean cluster size	Estimated ^a or presumed ^b correlation	Variance inflation from independence	Proportion ^c of significant inferences rejected
<i>Volume 8</i>								
Bigras-Poulin et al. (1990a)	Milk production	Dairy cow	Fixed effect	34	47	0.10-0.20 ^b	5.6-10.2	NA
Bigras-Poulin et al. (1990b)	Clinical diseases	Dairy cow	Fixed effect	34	22	0.01-0.10 ^b	1.2-3.1	NA
Grohn et al. (1990a)	Reproductive disorders	Dairy cow	Community-fixed effect	76	552	0.05-0.10 ^b		Some ^c
Grohn et al. (1990b)	Mastitis	Dairy cow	Community-fixed effect	76	804	0.05-0.10 ^b		Some ^c
Slettbakk et al. (1990)	Individual SCC	Dairy heifer	Random effect	1987	2	0.10 ^a	1.1	NA
<i>Volume 9</i>								
Debnath et al. (1990)	Mortality	Calf	None	4350	3	0.01 ^b	1.02	0/3
Oltenucu et al. (1990)	Milk production and diseases	Dairy cow	Mean herd production effect	4334	16	0.01-0.20 ^b	1.2-4.0	Some ^c
Mousing et al. (1990)	Chronic pleuritis	Slaughter pig	Subset checked with herd fixed effect	632	8	0.05-0.10 ^b	1.3-1.7	3/7
Hueston et al. (1990)	High SCC prevalence	Dairy herd	Weighted by herd size	78	55	0.05-0.15 ^b	3.7-9.1	Some ^c
Reeves et al. (1991)	Colic survival	Horse	None	10	67	0.06 ^a	5.0	6/7
Markusfeld (1991)	Disease recurrence	Dairy cow	Mantel-Haenszel	7	800	0.01-0.20 ^b	9.0-161	NA ^f
Bell et al. (1991)	Newcastle disease	Chicken	None	5	482	0.056	27.4	0/1
		Turkey	None	5	75	0.028	3.1	0/1

Volume 10										
Akhtar et al. (1991a)	Milk production	Dairy cow	3	178	0.10-0.20 ^b	18.7-36.4	NA			
Akhtar et al. (1991b)	<i>C. fetus</i> reactors	Dairy cow	4	210	0.05-0.10 ^b	10.4-21.9	Some ^c			
Reinhardt et al. (1991)	BVD/MD reactors	Cow	40	24	0.01 ^b -0.36 ^d	1.2-9.3	3/6			
Bigras-Poulin et al. (1991)	Clinical diseases	Dairy cow	34	65	0.01-0.10	1.6-7.4	8/11			
Schukken et al. (1991)	Clinical mastitis	Dairy herd	125	40	0.17 ^a	7.7	NA			
Emanuelson and Bendixen (1991)	Cystic ovaries	Dairy cow	11,000	35	0.05-0.10	2.7-4.4	2/16			
Chaarani et al. (1991)	Lamb mortality	Lamb	16	120	0.0017 ^a	1.1	0/5			

^aEstimated from data or references provided in the paper.

^bPresumed based on other studies or the authors' best guess.

^cUsing mean variance inflation from independence, $P < 0.05$.

^dCalculated average herd size, in studies with multiple observations per animal.

^eImpact on inference could not be estimated from the paper, some effect likely for binomial outcomes.

^fSome additional cluster effects due to multiple observations per animal, multiple herd observation years or other causes may remain.

^aEstimate from McDermott et al. (1987a).

^bEstimated from data used in Martin et al., (1989).

^cEstimated from data used in Houe and Meyling (1991).

correlation was presumed, the same formula was used to calculate a range for the variance inflation.

For papers in which herd proportions or counts were the outcome and individual herd proportions or counts were not provided, the variance inflation was estimated as the ratio of the observed variance to the expected variance. For proportions, the expected variance was calculated from the binomial distribution as $\hat{p}\hat{q}/n$ (Mood et al., 1974). For counts, the expected variance was equated to the mean response, assuming a Poisson variate (Mood et al., 1974).

Results

The ten issues of *Preventive Veterinary Medicine* yielded 67 papers that met the eligibility criteria. The results of our review on each paper are listed in Table 1. Dairy cows or calves were studied most frequently. Outcome variables were either mortality, disease, or production. Most frequently, the individual animal was the unit of interest.

Of the 67 papers in the sample, 36 (54%) used some form of adjustment for clustering. Including a fixed effect for herd (or other cluster) was employed most frequently (27). This was performed by including dummy variables in linear models, using Mantel–Haenszel statistics, or by adjusting for mean herd production. Four of the 67 papers used a matched (by herd) de-

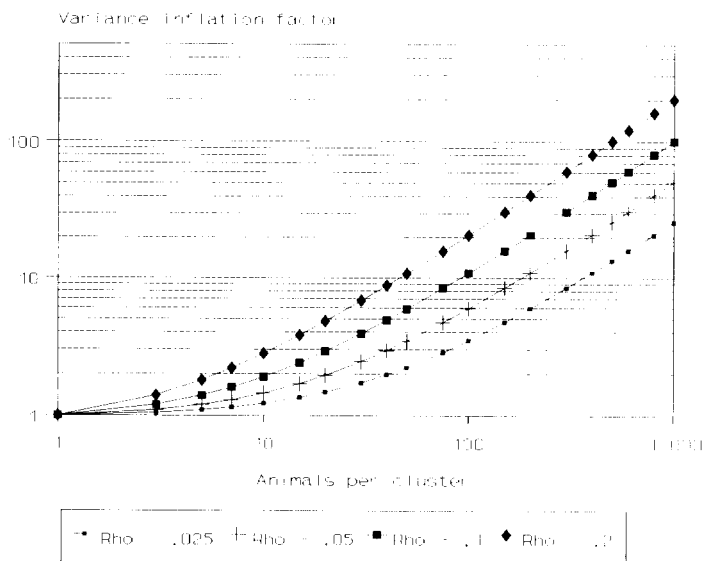
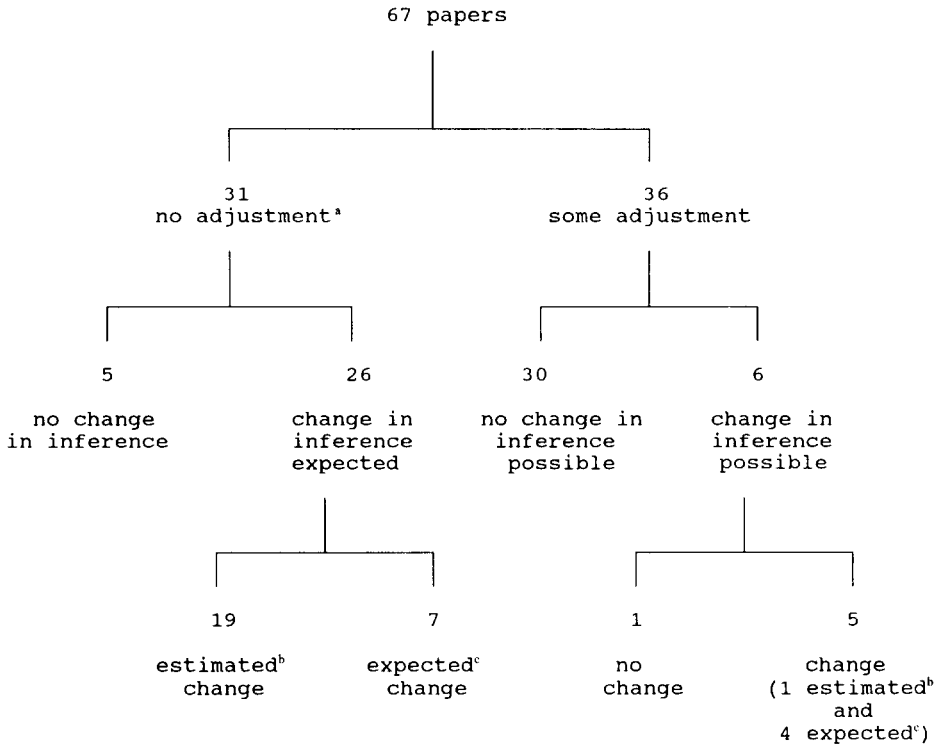


Fig. 1. The effect of intracluster correlation (ρ) and cluster size on the variance inflation factor ($c = 1 + (n - 1)(\rho)$).



^a includes 4 papers that weighted by size.

^b see Table 1 for estimates of the proportion of inferences rejected.

^c changes in inference expected but the effect of clustering could not be estimated from the data presented.

Fig. 2. Classification of 67 reviewed papers by adjustment for clustering and correctness of inference.

sign, two used a weighted analysis, and three papers included a random herd effect.

When the data were available, an estimate of the intracluster correlation was calculated. This estimate ranged from 0.0017 (lamb mortality data), to 0.46 (prevalence of brucellosis positive serotiter). Most intracluster correlations ranged from 0.01 to 0.15. The effect of this correlation on the variance inflation depended strongly on cluster size. The relation between intracluster correlation (ρ), cluster size and variance inflation is shown in Fig. 1. In the papers where $\hat{\rho}$ was estimated from the data, the variance inflation factor ranged from 1.1 to 13.

The expected change in inference was the most important issue examined

(Fig. 2). In 36 of the 67 (54%) papers, all inferences would be accepted. In 30 of these 36, no change was expected as the authors had correctly adjusted for clustering, and in six no change of inference was noted after our post-hoc adjustment for clustering. In the remaining 31 (46%) papers, some change in inference was predicted. In 20 of these 31, the proportion of incorrect inferences could be estimated from the data provided.

Discussion

We suspected that a common source of mistaken inference in veterinary observational studies was that statistical analyses were conducted under the assumption that individual animals sampled in herds were independent. As *Preventive Veterinary Medicine* is a journal devoted to publishing (observational) studies in veterinary epidemiology, we reviewed the first ten volumes of this journal for observational studies conducted in more than one herd.

Our suspicion was confirmed by this review. Thirty-one of the 67 papers (46%) in which non-independence of herdmates could not be assumed, ignored the possibility. In 26 of these, we predict that changes in inference would result, based on the variance adjustment method we used. In addition, of the remaining 36 (54%) papers that made some adjustment for within-herd correlation, we conclude that five papers contained incorrect inferences. Thus, in our judgement, almost half of the papers reviewed contained incorrect inferences because of too small variance estimates.

The degree with which non-independence of herdmates affects variance estimates and leads to incorrect inference increases with the mean herd size and the level of within-herd correlation (Fig. 1). For subjective outcomes (e.g. farmer diagnosis of morbidity), the level of within-herd correlation may be affected by both biological factors and variations in diagnostic criteria between farms. Thus, much higher within-herd correlations were expected and usually found for subjective vs. objective outcome measures.

The similarity of individual animals within herds can be accounted for correctly by various study design and analytic methods. These are reviewed in a companion paper (McDermott et al., 1994). The method chosen should depend on the study objectives. Bendixen (1989) suggested that study design by either herd matching or exclusion was preferable to analytic control. Only one of the reviewed studies used herd matching (Dohoo and Martin, 1984a); in this study, only individual cow factors were of interest. However, if the study objectives include the investigation of both individual animal and herd factors for disease, matching on herd will preclude herd-level analyses. Exclusion has the same limitation; it also limits the extent to which study results can be generalized.

For studies in which the objective is to identify herd factors for disease, individual animal data are often aggregated into an overall herd score. In these

studies, herd disease status is classified as high/low or present/absent and the herd is the unit of interest and analysis. Herds and not individual animals are the units assumed independent. As there was no possibility of mistaken inference due to the correlation of individual animals within herds, these studies were not formally reviewed. However, this method was commonly used in the volumes of *Preventive Veterinary Medicine* reviewed (Elder et al., 1986; Waltner-Toews et al., 1986a,b; Faye and Lescourret, 1989; Cowen et al., 1989; D'Allaire et al., 1989; Barnouin, 1991). While the aggregation of individual data into herd scores prevents mistaken inference, much information may be lost, particularly when herd status is dichotomized. For example, if a present or absent classification is used, herds with a 1% prevalence are classified with herds having 100% prevalence. Obviously, herd prevalences would be more informative. Invariably, the aggregation of individual animal data into an overall herd score leads to a loss of statistical power.

The additional information provided by using either herd proportions or counts has a cost, however. The assumption underlying the use of herd proportions or counts is that each contributing individual is independent (Hase-man and Kupper, 1979). Thus, while the herd is the unit of interest, the independence of individuals is required and mistaken inference can result if this independence assumption is violated. If individual animal responses are correlated within herds, statistical methods to adjust for within-herd correlation are necessary, just as if individual animals were the units of interest.

In the studies formally reviewed, most of those that controlled for within-herd correlation did so using statistical methods. Statistical methods for herd effects are relatively well developed for normally distributed outcomes but are an active area of research for counts and proportions (McCullagh and Nelder, 1989). In fact, of the 58 papers with counts or proportions as outcomes, only two (Martin et al., 1988; Schukken et al., 1991) adjusted for herd effects using models that relied on non-normal distributional assumptions. We could not judge whether such methods would have improved other papers.

Statistical control is not a panacea. An important problem in veterinary epidemiologic studies is that for fixed-effect models (the most common statistical method used) a large number of parameters have to be estimated, often over sparse data. For example, individual animal characteristics of interest (such as the previous occurrence of a particular disease) may not be present in all herds. This can lead to unstable parameter estimates and faulty inference. This is a particular problem when a large number of herds is studied. Bendixen et al. (1986a) explicitly recognized this problem. Their sensible approach was to reduce their significance level to 1%. As seen in Table 1, this led to relatively few mistaken inferences as judged by our variance inflation adjustment.

Other studies with large numbers of herds implicitly noted this problem as well, either by adjusting for larger aggregates such as regions (Grohn et al.,

1990a,b), by analyzing a subset of the data to estimate the effect of within-herd clustering (Mousing et al., 1990) or by using random-effect models (Slettbakk et al., 1990). Both the first and second approaches omit potentially useful information. The first method would be appropriate, however, if supporting information indicated that diseases or other outcomes clustered more by regions than by herds. The second method could be used to estimate the intracluster correlation by taking the ratio of the estimated coefficient variances with and without herd as a fixed effect. The third method, which unlike the second uses data from all herds, is to model herd effects with a single random effect parameter estimated across all herds (Schukken et al., 1991).

Given the potential importance of intracluster correlation, it is essential that authors consider and provide estimates of its possible impact. As a first step, the assumption of independence should be tested. For binomial data, the Pearson χ^2 can be compared with the residual degrees of freedom (McCullagh and Nelder, 1989) or the more formal method of Tarone (1979) can be used. For count data, the mean and variance can be compared (McCullagh and Nelder, 1989) or the method of Collings and Margolin (1985) used. If independence cannot be assumed, then the median (or mean) cluster size and the total number of clusters should be reported, $\hat{\rho}$, and the variance inflation should be estimated (or guessed), and significance tests for each outcome of interest should be adjusted post-hoc to account for clustering.

This method (while often adequate) may have important limitations under some circumstances. The two main assumptions required when inflating the variance by estimating a common correlation coefficient are that each herd is a homogenous unit and that within-herd correlations are equal for all herds. These assumptions are not always realistic and if violated can result in incorrect estimation of the relative contribution of herd vs. individual animal variability. For example, important heterogenous subgroups may be present in herds or marked differences in management or farmer behaviour may exist between herds. In a study of culling in beef breeding herds, McDermott et al. (1992) found that adjusting for $\hat{\rho}$ inadequately described the herd-to-herd variability in culling behaviour. Average culling policies were predictable, but cows were not culled consistently for these reasons on all farms. Thus, when statistical methods to adjust for clustering are used, potential violations of the assumptions underlying these models should be explored. We recommend that the equality of intracluster correlation estimates for the main subtypes of farms and for the main subgroups of animals within farms (e.g. heifers vs. cows) be compared using the methods of Donner (1986) or of Dunn and Clark (1974).

While we have focused on the importance of adjusting for herd effects in epidemiologic studies, production and disease outcomes may aggregate also in other naturally occurring units (e.g. farmer associations and ecological

zones). Under most circumstances, relatively simple adjustment methods (such as those used in this paper) are likely to be helpful in exploring initial hypotheses. As with techniques for estimating herd effects, further experience is needed to learn under what circumstances disease clustering at these levels might be important and when improved techniques are required to overcome too simplistic assumptions.

Acknowledgements

The comments of one reviewer (particularly the recommendation to include Fig. 2) have substantially improved the clarity of presentation.

References

- Akhtar, S., Riemann, H.P., Franti, C.E., Farver, T.B. and Thurmond, M.C., 1991a. The association between serological evidence of exposure to *Campylobacter fetus* and productivity in dairy cattle. *Prev. Vet. Med.*, 10: 1–14.
- Akhtar, S., Riemann, H.P., Franti, C.E., Farver, T.B. and Thurmond, M.C., 1991b. Multivariate logistic analysis of repeated cross-sectional surveys of *Campylobacter fetus* in dairy cattle. *Prev. Vet. Med.*, 10: 15–24.
- Algers, B. and Hennichs, K., 1985. The effect of exposure to 400 kV transmission lines on the fertility of cows. A retrospective cohort study. *Prev. Vet. Med.*, 3: 351–361.
- Andersson, L. and Emanuelson, U., 1985. An epidemiological study of hyperketonemia in Swedish dairy cows; determinants and the relation to fertility. *Prev. Vet. Med.*, 3: 449–462.
- Bartlett, P.C., Ngategize, P.K., Kanenee, J.B., Kirk, J.H., Anderson, S.M. and Mather, E.C., 1986a. Cystic follicular disease in Michigan Holstein-Friesian cattle: incidence, descriptive epidemiology and estimated economic impact. *Prev. Vet. Med.*, 4: 15–33.
- Bartlett, P.C., Kirk, J.H., Wilke, M.A., Kanenee, J.B. and Mather, E.C., 1986b. Metritis complex in Michigan Holstein-Friesian cattle: incidence, descriptive epidemiology and estimated economic impact. *Prev. Vet. Med.*, 4: 235–248.
- Barnouin, J., 1991. Components of the diet in the dry period as risk factors for milk fever in dairy herds in France. *Prev. Vet. Med.*, 10: 185–194.
- Bell, J.G., Belarbi, A. and Amara, A., 1991. A controlled vaccination trial for Newcastle disease under village conditions. *Prev. Vet. Med.*, 9: 295–300.
- Bendixen, P.H., 1989. The enigma of herd: a statistical problem or a question of study design? *Prev. Vet. Med.*, 7: 69–71.
- Bendixen, P.H., Vilson, B., Ekesbo, I. and Astrand, D.B., 1986a. Disease frequencies of tied zero-grazed dairy cows and of dairy cows on pasture during summer and tied during winter. *Prev. Vet. Med.*, 4: 291–306.
- Bendixen, P.H., Vilson, B., Ekesbo, I. and Astrand, D.B., 1986b. Disease frequencies of Swedish dairy cows. I. Dystocia. *Prev. Vet. Med.*, 4: 307–316.
- Bendixen, P.H., Vilson, B. and Ekesbo, I., 1987a. Disease frequencies in dairy cows in Sweden. II. Retained placenta. *Prev. Vet. Med.*, 4: 377–387.
- Bendixen, P.H., Vilson, B., Ekesbo, I. and Astrand, D.B., 1987b. Disease frequencies in dairy cows in Sweden. III. Parturient paresis. *Prev. Vet. Med.*, 5: 87–97.
- Bendixen, P.H., Vilson, B., Ekesbo, I. and Astrand, D.B., 1987c. Disease frequencies in dairy cows in Sweden. IV. Ketosis. *Prev. Vet. Med.*, 5: 99–109.

- Bendixen, P.H., Vilson, B., Ekesbo, I. and Astrand, D.B., 1988a. Disease frequencies in dairy cows in Sweden. V. Mastitis. *Prev. Vet. Med.*, 5: 263-274.
- Bendixen, P.H., Vilson, B., Ekesbo, I. and Astrand, D.B., 1988b. Disease frequencies in dairy cows in Sweden. VI. Tramped teat. *Prev. Vet. Med.*, 6: 17-25.
- Bigras-Poulin, M., Meek, A.H., Martin, S.W. and McMillan, I., 1985. Attitudes, management practices and herd performance. A study of Ontario dairy farm managers. II. Associations. *Prev. Vet. Med.*, 3: 241-250.
- Bigras-Poulin, M., Meek, A.H. and Martin, S.W., 1990a. Interrelationships of health problems and age on milk production in selected Ontario Holstein cows. *Prev. Vet. Med.*, 8: 3-13.
- Bigras-Poulin, M., Meek, A.H. and Martin, S.W., 1990b. Interrelationships among health problems and milk production from consecutive lactations in selected Ontario Holstein cows. *Prev. Vet. Med.*, 8: 15-24.
- Bigras-Poulin, M., Meek, A.H., Martin, S.W. and McMillan, I., 1991. Health problems in selected Ontario Holstein cows: frequency of occurrences, time to first diagnosis and associations. *Prev. Vet. Med.*, 10: 79-89.
- Brier, S.S., 1980. Analysis of contingency tables under cluster sampling. *Biometrika*, 67: 591-596.
- Chaarani, B., Robinson, R.A. and Johnson, D.W., 1991. Lamb mortality in Meknes Province (Morocco). *Prev. Vet. Med.*, 10: 283-298.
- Collings, B.J. and Margolin, B.H., 1985. Testing goodness of fit for the Poisson assumption when observations are not identically distributed. *J. Am. Stat. Assoc.*, 80: 411-418.
- Correa, M.T., Curtis, C.R., Erb, H.N. and White, M.E., 1988. Effects of calfhoo morbidity on age at first calving in New York Holstein herds. *Prev. Vet. Med.*, 6: 253-262.
- Cowen, P., Schwabe, C.W., Rosenberg, H.R., BonDurant, R.H., Franti, C.E. and Goodger, W.J., 1989. Reproductive management practices among Tulare, California dairy herds. II. Analytical studies. *Prev. Vet. Med.*, 7: 101-111.
- Curtis, C.R., Scarlett, J.M., Erb, H.N. and White, M.E., 1988a. Path model of individual-calf risk for calfhoo morbidity and mortality in New York Holstein herds. *Prev. Vet. Med.*, 6: 43-62.
- Curtis, C.R., Mauritsen, R.H., Salman, M.D. and Erb, H.N., 1988b. The enigma of herd: a comparison of different models to account for group effects in multivariable analysis. *Acta Vet. Scand., Suppl.*, 84: 166-169.
- Curtis, C.R., White, M.E. and Erb, H.N., 1989. Effects of calfhoo morbidity on long-term survival in New York Holstein herds. *Prev. Vet. Med.*, 7: 173-186.
- D'Allaire, S., Morris, R.S., Martin, F.B., Robinson, R.A. and Leman, A.D., 1989. Management and environment factors associated with annual sow culling rate: a path analysis. *Prev. Vet. Med.*, 7: 255-265.
- Debnath, N.C., Sil, B.K., Selim, S.A., Prodhon, M.A.M. and Howlader, M.M.R., 1990. A retrospective study of calf mortality and morbidity on smallholder traditional farms in Bangladesh. *Prev. Vet. Med.*, 9: 1-7.
- Dobbelaar, P., Noordhuizen, J.P.T.M. and Van Keulen, K.A.S., 1987. An epidemiological study of gammaglobulin levels in newborn calves. *Prev. Vet. Med.*, 5: 51-62.
- Dohoo, I.R. and Martin, S.W., 1984a. Disease, production and culling in Holstein-Friesian cows. III. Disease and production as determinants of disease. *Prev. Vet. Med.*, 2: 671-690.
- Dohoo, I.R. and Martin, S.W., 1984b. Disease, production and culling in Holstein-Friesian cows. IV. Effects of disease on production. *Prev. Vet. Med.*, 2: 755-770.
- Dohoo, I.R. and Martin, S.W., 1984c. Disease, production and culling in Holstein-Friesian cows. V. Survivorship. *Prev. Vet. Med.*, 2: 771-784.
- Dohoo, I.R., Martin, S.W., McMillan, I. and Kennedy, B.W., 1984a. Disease, production and culling in Holstein-Friesian cows. II. Age, season and sire effects. *Prev. Vet. Med.*, 2: 655-670.

- Dohoo, I.R., Martin, S.W. and Meek, A.H., 1984b. Disease, production and culling in Holstein-Friesian cows. VI. Effects of management on disease rates. *Prev. Vet. Med.*, 3: 15–28.
- Dohoo, I.R., Heaney, D.P., Stevenson, R.G., Samagh, B.S. and Rhodes, C.S., 1987. The effect of Maedi-Visna virus infection on productivity in ewes. *Prev. Vet. Med.*, 4: 471–484.
- Donald, A. and Donner, A., 1988. The analysis of variance adjustment to chi-square tests when there is litter or herd correlation in surveys or field trials. *Acta Vet. Scand., Suppl.*, 84: 490–492.
- Donner, A., 1986. A review of inference procedures for the intra-class correlation coefficient in the one-way random effect model. *Int. Stat. Rev.*, 54: 67–82.
- Dunn, O.J. and Clark, V.A., 1974. *Analysis of Variance and Regression*. Wiley, New York, pp. 99–114.
- Elder, J.K., McKeon, G.M., Duncalfe, F., Ward, W.H. and Leutton, R., 1986. Epidemiological studies on the ecology of *Leptospira interrogans* serovars *pomona* and *hardjo* in Queensland. *Prev. Vet. Med.*, 3: 501–521.
- Emanuelson, U. and Bendixen, P.H., 1991. Occurrence of cystic ovaries in dairy cows in Sweden. *Prev. Vet. Med.*, 10: 261–271.
- Faye, B. and Lescourret, F., 1989. Environmental factors associated with lameness in dairy cattle. *Prev. Vet. Med.*, 7: 267–287.
- Fleiss, J.L., 1981. *Statistical Methods for Rates and Proportions*. 2nd edn. Wiley, New York, 277 pp.
- Goodger, W.J. and Kushman, J.E., 1985. Measuring the impact of different veterinary service programs on dairy herd health and milk production. *Prev. Vet. Med.*, 3: 211–225.
- Grohn, Y., Thompson, J.R. and Bruss, M.L., 1984. Epidemiology and genetic basis of ketosis in Finnish Ayrshire cattle. *Prev. Vet. Med.*, 3: 65–77.
- Grohn, Y.T., Erb, H.N., McCullough, C.E. and Saloniemi, H.S., 1990a. Epidemiology of reproductive disorders in dairy cattle: associations among host characteristics, disease and production. *Prev. Vet. Med.*, 8: 25–39.
- Grohn, Y.T., Erb, H.N., McCullough, C.E. and Saloniemi, H.S., 1990b. Epidemiology of mammary gland disorders in multiparous Finnish Ayrshire cows. *Prev. Vet. Med.*, 8: 241–252.
- Haseman, J.K. and Kupper, L.L., 1979. Analysis of dichotomous response data from certain toxicological experiments. *Biometrics*, 35: 281–293.
- Hird, D.W. and Robinson, R.A., 1982. Dairy farm wells in southeastern Minnesota: the relation of water source to calf mortality rate. *Prev. Vet. Med.*, 1: 53–64.
- Hird, D.W. and Robinson, R.A., 1983. Dairy farm wells in southeastern Minnesota: the relation of new water sources (new wells) to milk and milk production. *Prev. Vet. Med.*, 1: 97–104.
- Houe, H. and Meyling, A., 1991. Prevalence of bovine virus diarrhoea (BVD) in 19 Danish dairy herds and estimation of incidence of infection in early pregnancy. *Prev. Vet. Med.*, 11: 9–16.
- Hueston, W.D., Heider, L.E., Harvey, W.R. and Smith, K.L., 1987. The use of high somatic cell count prevalence in epidemiologic investigations of mastitis control practices. *Prev. Vet. Med.*, 4: 447–461.
- Hueston, W.D., Heider, L.E., Harvey, W.R. and Smith, K.L., 1990. Determinants of high somatic cell count prevalence in dairy herds practising teat dipping and dry cow therapy and with no evidence *Streptococcus agalactiae* on repeated bulk tank milk examination. *Prev. Vet. Med.*, 9: 131–142.
- Huffman, E.M., Mortimer, R., Olson, J.D., Ball, L. and Farin, P.W., 1984. Risk factors for prebreeding pyometra on four Colorado dairy farms. *Prev. Vet. Med.*, 2: 785–790.
- Lutnaes, B. and Simensen, E., 1983. An epidemiological study of abomasal bloat in young lambs. *Prev. Vet. Med.*, 1: 335–345.
- Markusfeld, O., 1986. The association of displaced abomasum with various periparturient factors in dairy cows. A retrospective study. *Prev. Vet. Med.*, 4: 173–183.

- Markusfeld, O., 1989. The evaluation of a routine treatment with 1 α -Hydrovitamin D3 for the prevention of bovine parturient paresis. *Prev. Vet. Med.*, 7: 1–9.
- Markusfeld, O., 1991. Risk of recurrence of eight periparturient and reproductive traits of dairy cows. *Prev. Vet. Med.*, 9: 279–286.
- Martin, S.W., Darlington, G., Bateman, K. and Holt J., 1988. Undifferentiated bovine respiratory disease (shipping fever): is it communicable? *Prev. Vet. Med.*, 6: 27–35.
- Martin, S.W., Bateman, K.G., Shewen, P.E., Rosendal, S. and Bohac, J.E., 1989. The frequency, distribution and effects of antibodies to seven putative respiratory pathogens on respiratory disease and weight gain in feedlot calves. *Can. J. Vet. Res.*, 53: 355–362.
- McCullagh, P. and Nelder, J.A., 1989. *Generalized Linear Models*. Chapman & Hall, London, 124 pp.
- McDermott, J.J. and Shoukri, M.M., 1991. Simultaneous investigation of herd and individual-animal risk factors. In: S.W. Martin (Editor), *Proceedings of the 6th ISVEE Symposium, 12–16 August 1991, Ottawa, Canada*, pp. 81–83.
- McDermott, J.J., Deng, K.A., Jayatileka, T.N. and El Jack, M.A., 1987a. Cross-sectional cattle disease study in Kongor Rural Council, southern Sudan. I. Prevalence estimates and age, sex and breed associations for brucellosis and contagious bovine pleuropneumonia. *Prev. Vet. Med.*, 5: 111–123.
- McDermott, J.J., Deng, K.A., Jayatileka, T.N. and El Jack, M.A., 1987b. Cross-sectional cattle disease study in Kongor Rural Council, southern Sudan. II. Brucellosis in cows: associated factors, impact on production and disease control considerations. *Prev. Vet. Med.*, 5: 125–132.
- McDermott, J.J., Lesnick, T.G. and Martin, S.W., 1988. The analysis of individual risk for animals sampled in clusters. *Acta Vet. Scand., Suppl.*, 84: 459–461.
- McDermott, J.J., Allen, O.B. and Martin, S.W., 1992. Culling practices of Ontario cow-calf producers. *Can. J. Vet. Res.*, 56: 56–61.
- McDermott, J.J., Schukken, Y.H. and Shoukri, M.M., 1994. Study design and analytic methods for data collected from clusters of animals. *Prev. Vet. Med.*, 18: 175–191.
- Milian-Suazo, F., Erb, H.N. and Smith, R.D., 1989. Risk factors for reason-specific culling of dairy cows. *Prev. Vet. Med.*, 7: 19–29.
- Mood, A.M., Graybill, F.A. and Boes, D.C., 1974. *Introduction to the theory of statistics*. McGraw-Hill, New York, 89 pp.
- Mousing, J., Lybye, H., Meyling, A., Barford, K., Ronsholt, L. and Willeberg, P., 1990. Chronic pleuritis in pigs for slaughter: an epidemiological study of infectious and rearing system-related risk factors. *Prev. Vet. Med.*, 9: 107–119.
- Nabuurs, M.J.A., Bokhout, B.A. and Van der Heijden, Ph.J., 1982. Intraperitoneal injection of an adjuvant for the prevention of post-weaning diarrhoea and oedema disease in piglets: a field study. *Prev. Vet. Med.*, 1: 65–76.
- Oltenacu, P.A., Frick, A. and Lindhe, B., 1990. Epidemiological study of several clinical disease, reproductive performance and culling in primiparous Swedish cattle. *Prev. Vet. Med.*, 9: 59–74.
- Osteras, O. and Lund, A., 1988a. Epidemiological analyses of associations between bovine udder health and housing. *Prev. Vet. Med.*, 6: 79–90.
- Osteras, O. and Lund, A., 1988b. Epidemiological analyses of associations between bovine udder health and milking machine and milking management. *Prev. Vet. Med.*, 6: 91–108.
- Pappaioanou, M., Schwabe, C.W. and Polydorou, K., 1984a. Epidemiological analysis of the Cyprus anti-echinococcosis campaign. I. *Prev. Vet. Med.*, 3: 159–180.
- Pappaioanou, M., Schwabe, C.W. and Polydorou, K., 1984b. Epidemiological analysis of the Cyprus anti-echinococcosis campaign. II. *Prev. Vet. Med.*, 3: 181–195.
- Reeves, M., Curtis, C.R., Salman, M.D., Reif, J.S. and Stashak, T.S., 1991. A multivariable prognostic model for equine colic patients. *Prev. Vet. Med.*, 9: 241–257.

- Reinhardt, G., Riedeman, S., Ernst, S., Aguilar, M., Enriquez, R. and Gallardo, J., 1991. Seroprevalence of bovine viral diarrhoea/mucosal disease in southern Chile. *Prev. Vet. Med.*, 10: 73–78.
- Rowlands, G.J. and Lucey, S., 1986. Changes in milk yield in dairy cows associated with metabolic and reproductive disease and lameness. *Prev. Vet. Med.*, 4: 205–221.
- Rowlands, G.J., Lucey, S. and Russell, A.M., 1986. Susceptibility to disease in the dairy cow and its relationship with occurrences of other diseases in the current or preceding lactation. *Prev. Vet. Med.*, 4: 223–234.
- Salman, M.D. and Meyer, M.E., 1987. Epidemiology of bovine brucellosis in the coastal region of Baja California Norte, Mexico: results of path analyses in an area of high prevalence. *Prev. Vet. Med.*, 4: 485–502.
- Schukken, Y.H., Erb, H.N. and Smith, R.D., 1988. The relationship between mastitis and retained placenta in a commercial population of Holstein dairy cow. *Prev. Vet. Med.*, 5: 181–190.
- Schukken, Y.H., Casella, G. and Van den Broek, J., 1991. Overdispersion in clinical mastitis data from dairy herds: a negative binomial approach. *Prev. Vet. Med.*, 10: 239–245.
- Shoukri, M.M., Adams, J.E., McDermott, J.J. and Martin, S.W., 1991. On the adjustment for clustering effect in the one way ANOVA. In: S.W. Martin (Editor), *Proceedings of the 6th ISVEE Symposium, 12–16 August 1991, Ottawa, Canada*, pp. 84–86.
- Slettbakk, T., Jorstad, A., Farver, T.B. and Hird, D.W., 1990. Impact of milking characteristic and teat morphology on somatic cell counts in first-lactation Norwegian cattle. *Prev. Vet. Med.*, 8: 253–267.
- Snedecor, G.W. and Cochran, W.G., 1980. *Statistical Methods*, 7th edn. Iowa State University Press, Ames, IA, 243 pp.
- Tarone, R.E., 1979. Testing the goodness of fit of the binomial distribution. *Biometrika*, 66: 585–590.
- Traore, A. and Wilson, R.T., 1988. Livestock production in central Mali: environmental and pathological factors affecting morbidity and mortality of ruminants in the agropastoral system. *Prev. Vet. Med.*, 6: 63–75.
- Vagsholm, I., Carpenter, T.E. and Jasper, D.E., 1988. Impact of a mastitis control program in Valdres, Norway, during 1982–1985. *Prev. Vet. Med.*, 6: 223–234.
- Vaillancourt, J.P., Martineau, G.P., Lariviere, S., Higgins, R. and Mittal, K.R., 1988. Serological follow-up in breeding herds infected with *Actinobacillus pleuropneumonia* serotype 1 using the tube agglutination test with 2-mercaptoethanol. *Prev. Vet. Med.*, 6: 263–274.
- Waltner-Toews, D., Martin, S.W. and Meek, A.H., 1986a. Dairy calf management, morbidity and mortality in Ontario Holstein herds. III. Associations of management with morbidity. *Prev. Vet. Med.*, 4: 125–136.
- Waltner-Toews, D., Martin, S.W. and Meek, A.H., 1986b. Dairy calf management, morbidity and mortality in Ontario Holstein herds. IV. Associations of management with mortality. *Prev. Vet. Med.*, 4: 137–158.
- Zessin, K.H., Baumann, M., Schwabe, C.W. and Thorburn M., 1985. Analysis of baseline surveillance data on contagious bovine pleuropneumonia in the southern Sudan. *Prev. Vet. Med.*, 3: 371–389.