



Estimating the intra-cluster correlation coefficient for evaluating an educational intervention program to improve rabies awareness and dog bite prevention among children in Sikkim, India: A pilot study

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ABSTRACT

Background: Educational initiatives targeting at-risk populations have long been recognized as a mainstay of ongoing rabies control efforts. Cluster-based studies are often utilized to assess levels of knowledge, attitudes and practices of a population in response to education campaigns. The design of cluster-based studies requires estimates of intra-cluster correlation coefficients obtained from previous studies. This study estimates the school-level intra-cluster correlation coefficient (ICC) for rabies knowledge change following an educational intervention program.

Methods: A cross-sectional survey was conducted with 226 students from 7 schools in Sikkim, India, using cluster sampling. In order to assess knowledge uptake, rabies education sessions with pre- and post-session questionnaires were administered. Paired differences of proportions were estimated for questions answered correctly. A mixed effects logistic regression model was developed to estimate school-level and student-level ICCs and to test for associations between gender, age, school location and educational level. **Results:** The school- and student-level ICCs for rabies knowledge and awareness were 0.04 (95% CI: 0.01, 0.19) and 0.05 (95% CI: 0.2, 0.09), respectively. These ICCs suggest design effect multipliers of 5.45 schools and 1.05 students per school, will be required when estimating sample sizes and designing future cluster randomized trials. There was a good baseline level of rabies knowledge (mean pre-session score 71%), however, key knowledge gaps were identified in understanding appropriate behavior around scared dogs, potential sources of rabies and how to correctly order post rabies exposure precaution steps. After adjusting for the effect of gender, age, school location and education level, school and individual post-session test scores improved by 19%, with similar performance amongst boys and girls attending schools in urban and rural regions. The proportion of participants that were able to correctly order post-exposure precautionary steps following educational intervention increased by 87%.

Conclusion: The ICC estimates presented in this study will aid in designing cluster-based studies evaluating educational interventions as part of disease control programs. This study demonstrates the likely benefits of educational intervention incorporating bite prevention and rabies education.

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1. Introduction

Given the cost, logistical constraints and poor availability of sampling frames, the use of cluster randomization (where interventions are randomized to individuals in clusters such as schools

or communities) is increasingly utilized in public health research in developing countries (Donner and Klar, 2004; Janjua et al., 2006). Because intervention outcomes such as knowledge or awareness levels of participants within a cluster or community tend to be similar (Eldridge and Kerry, 2012) outcome measures lack independence and this lack of independence must be taken into account when calculating the required number of individuals to take part in a study. Correlation between members of a cluster, or variation between clusters is quantified using intra-cluster correlation (ICC)

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estimates. ICCs are used in the design phase of cluster intervention trials to increase sample size estimates to account for lack of independence in study outcomes arising from individuals within the same cluster (e.g. schools) (Parker et al., 2005).

1.1. Rabies in the South-East Asia region

Rabies is a fatal zoonotic disease, posing a major public health risk in countries where it is endemic (Knobel et al., 2005). While rabies is 100% preventable through prompt administration of post-exposure prophylaxis to bite victims and can be controlled through mass vaccination of domestic dogs (Hampson et al., 2015), it remains a neglected disease in many developing countries. The risk and burden of rabies falls disproportionately on the most vulnerable sectors of society (Hampson et al., 2008), with 40% of human rabies deaths occurring in children younger than 15 years, particularly from rural, low-resource communities (World Health Organization, 2013). The highest human incidence is reported in India, where an estimated 18,000 to 20,000 (Fahrion et al., 2016) of approximately 59,000 human rabies cases worldwide (Gongal and Wright, 2011) occur annually. Dogs are the most important reservoir of rabies, with dog bites being the primary cause of 96% of human rabies cases in the South-East Asia Region (SEAR) (World Health Organization, 2011). Approximately 17 million dog bite cases are reported to occur annually in India (Menezes, 2008). It is estimated that only around 20% of the 19 million humans bitten by dogs in the SEAR receive one or more doses of rabies vaccine (Gongal and Wright, 2011).

Recent studies carried out assessing existing control strategies for canine-mediated rabies focus on implementation of mass dog vaccination campaigns, alongside improvement of human post-exposure prophylaxis (PEP) availability. Although timely administration of human rabies PEP vaccination and immunoglobulin prevents exposed individuals from developing clinical disease, unlike canine vaccination, it has no effect on transmission of the virus from the animal reservoir and therefore does not prevent future human exposure. Cost analyses of rabies control programs show that the procurement and wastage rates of PEP vaccine and immunoglobulin were found to greatly influence total program costs (Abbas et al., 2014), contributing to the excessive global expenditure on rabies control (estimated at US \$583.5 million annually (Knobel et al., 2005)). Additional drivers of program costs include the incidence of dog bites (Abbas et al., 2014) which account for 90% of human post-exposure rabies treatments (Yoak et al., 2014). For these reasons, actions to prevent human infection by vaccination of dogs and reduction in the incidence of dog bites by health education have the potential to reduce global expenditure on rabies by reducing the amount of PEP required as well as reducing the overall human-rabies prevalence.

Recent knowledge, attitude and practice (KAP) studies have identified a lack of awareness, a disregard of post-exposure precautionary measures and/or an inadequate availability of primary health care services as leading factors for the high incidence and maintenance of rabies endemicity in the SEAR (Agarvval and Reddaiah, 2003; Garg et al., 2013; Matibag et al., 2007; World Health Organization, 2011). A multi-country, multicenter study showed that only 15% of patients reported learning about rabies at school (Dodet et al., 2008). There is a critical need to encourage community involvement to address the existing gaps in community-based and formal health education, particularly in children given the high proportion of childhood rabies deaths (Dodet et al., 2008). Studies indicate that students express a high commitment to school-based, participatory health education. It has been shown that once children have acquired basic knowledge of how disease is transmitted and prevented, they are able to take

initiatives to prevent disease incidence through their role as change agents (Mwanga et al., 2008).

In this study, a community-based rabies health education and dog-bite prevention program was implemented, with a target demographic of local school children in Sikkim, India. The feasibility of evaluating the effectiveness of the intervention using pre- and post-session questionnaires was analyzed, in addition to baseline levels of awareness and gaps in knowledge. Using the pilot data, the ICC was calculated. An appropriate ICC estimate will inform design of cluster randomized trials that enroll an appropriate number of students and schools, allowing differences in the effect of alternative educational interventions to be estimated with increased confidence.

2. Material and methods

2.1. Study design

This was a two-wave panel study. The study involved the following sessions: a pre-questionnaire administered to students to assess baseline levels of knowledge of rabies, a 45-min education session on rabies and repeat administration of the questionnaire to assess knowledge uptake. The outcome of interest was the difference in the proportion of questions that were correctly answered before and after the training (pre- and post- training questionnaires).

2.2. Study location and study population

The study was carried out in Sikkim, a landlocked state of northeast India. The state is comprised of four districts, an area of 7096 km² and human population of 610,557, of which approximately 25% live in urban regions and 75% live in rural villages (The Government of India, 2011). A sampling frame comprised of name and address details of all schools in Sikkim was obtained from the state Department of Education. In March 2014, the principal of each school was sent a letter describing the aims and objectives and an invitation to take part in the study. The study population comprised students that attended schools where the principal agreed to participate in the study. From the group of consenting schools, seven were randomly selected using computer-generated random numbers. Four of the seven schools were located in the urban districts of Sikkim and the remaining three schools in rural districts. Six out of the seven schools were government funded.

2.3. Selection of study subjects and sample size

Sample size calculations were carried out to determine the appropriate number of students to be surveyed within each school using Stata version 14.1 (StataCorp, 2015). At least 80 students per school were required to provide 80% power of detecting an absolute difference of 25% in proportions (improvement in performance) in questions answered correctly between repeated (paired) samplings using McNemar's test assuming a 5% chance of making a type I error and low correlation (25%) between individual student's answers to pre- and post-training questionnaires (Thrusfield, 2013). School students were chosen as study participants, given the high proportion of childhood rabies deaths. The study was carried out with students in classes 6–10 (ages ranged from 10 to 17 years), to ensure a moderate to good level of English competency. To make the tasks more accessible and minimize language barriers for the students, cartoon-style images and videos were utilized during the sessions. An average of 37 students were administered pre- and post-training questionnaires in each of the 7 clusters (Table 1). Although not studied here as considered unreliable to measure, targeting similar interventions and research at school children younger than 10 years

Table 1
Characteristics of the study population (n = 261) from the Sikkim Anti Rabies and Animal Health (SARAH) education program, 2014, by school.

School	Location	Respondents	Male respondents (%)	Education level (class)	Questionnaire sections administered
1	Urban	39	19 (49)	6	I & II
2	Urban	22	14 (64)	7 & 8	I & II
3	Urban	37	0 (0) ^a	9	I & II
4	Urban	25	10 (40)	10	I & II
5	Rural	25	14 (56)	7	I & II
6	Rural	78	78 (100) ^a	10	I & II
7	Rural	35	20 (57)	6 & 7	III only

^a School 3 is a girls only school whereas School 6 is a boys only school.

of age would be possible with materials available from the Global Alliance for Rabies Control (GARC: <https://rabiesalliance.org>).

2.4. Educational sessions

The educational sessions, which lasted for approximately an hour, were pre-arranged with the schools prior to conducting sessions in April 2014 and delivered to a total of 8700 students. The content presented during the educational sessions was formulated on the basis of the three areas of knowledge: the ability to interpret dog behavior, the level of awareness of rabies, and knowledge of appropriate prevention measures (prompt washing of bite wounds and scratches (Dodet et al., 2008; World Health Organization, 2013), PEP). Written educational materials, questionnaires and program structure were designed and carried out by the researchers (AA, ASC, TVZ).

2.5. Questionnaire design and administration

The questionnaire was designed to assess and compare initial awareness levels of students and to evaluate the degree of knowledge uptake. Closed questions focusing on the three areas of knowledge addressed in the educational sessions were included within the questionnaire; Section I, interpretation of dog; Section II, awareness of rabies and Section III appropriate prevention measures. The questionnaire was provided in English, with all questions answered individually. One point was given for each correct answer with a maximum overall score of 24 possible. The same questionnaire was used for the pre- and post-training assessment to enable paired comparisons and to assess the effect of the training. Due to time constraints, section III of the post-training questionnaire was only administered at one school.

2.6. Ethical approval

All research was conducted with the approval of the University of Melbourne Human Research Ethics Committee, application number 1341381.

2.7. Statistical analyses

Test scores at the commencement and conclusion of a student's engagement in the intervention were compared to evaluate the effectiveness of the training (Australian Council for Educational Research, 2013). The data were checked, with incomplete and inconsistent responses excluded from further analyses. Initially, data were analyzed using contingency tables. McNemar's paired test for differences between proportions was used to compare the proportion of questions that were answered correctly in the pre- and the post-training questionnaires.

Our primary objective was to obtain a point estimate of the school-level intra-cluster correlation coefficient as well as an indication of the uncertainty around this estimate. To achieve this, a mixed effects logistic regression model was developed to test

for associations between increasing levels of awareness pre- and post-training, adjusting for confounders such as gender, age, school location (urban versus rural) and the education level of respondents. The outcome variable was the proportion of correct answers (out of 12) constructed by summing the binary responses (questions answered correctly) to Sections I and II of the questionnaire, including six questions each from the sections on 'Interpretation of dog behavior' and 'Knowledge of rabies and its transmission' (Table 2). As the questions requiring students to correctly order post-exposure precaution steps (Section III) were only administered in one school, these were not included in the score. We tested all one-way interaction terms incorporating a variable representing the session (pre- versus post-) and increases in score for variables representing each of the following: gender, age, urban versus rural school location and educational level. Interaction terms were removed sequentially, followed by statistically non-significant ($P > 0.05$) main effects.

Individual student-level and school-level random effect terms were included in the model to account for lack of independence in the data. In the multilevel model the level 1 (individual test) variance was constrained to 1 (that is, no extra-binomial variation was permitted). Because this variance was expressed on the binomial rather than the logit scale, the estimates of the proportion of variation of each level of the hierarchy (test, individual and school) were computed assuming the level 1 variance on the logit scale was $\pi^2/3$, where $\pi = 3.1416$. This calculation is based on interpreting the responses to questions (correct or incorrect) as the result of an underlying latent process with a continuous, logistic distribution (Tom et al., 1999). The school-level and student-level (repeated measures) ICCs were calculated as proportions of the sum of the variances of the test-level, individual-level and school-level random effect terms (Dohoo et al., 2001).

All statistical analyses were implemented using the R statistical package version 3.1.1 (R Core Team, 2012), using the library 'lme4' to compute mixed effects models (Bates et al., 2014).

3. Results

Of the 226 students that completed pre- and post-training questionnaires, 123 (54%) attended schools in urban districts and 60% were boys. Students were from classes 6–10 (age range 10–17 years) (Table 1). The 35 students from the single rural school that completed Section III were from classes 6 and 7 only and 57% were boys.

3.1. Dog behavior and knowledge of rabies

A total of 81% of students were aware of rabies before the educational session. There was a good baseline level of rabies knowledge, however, key knowledge gaps were identified in understanding appropriate behavior around scared dogs and potential sources of rabies infection. Paired and complete responses for all questions in Sections I and II were available for 103 of the 226 students from the four urban and two rural schools. For these students, there was a

Table 2

Pre- and post-education session test results from the Sikkim Anti Rabies and Animal Health (SARAH) education program, 2014.

No.	Details	Pre- (% correct)	Post- (% correct)	Δ% (95% CI)	P-value ^a
Section I: Interpretation of dog behavior					
1	Identify a scared dog	174/218 (80)	177/218 (81)	1.4 (−6.5, 9.3)	0.80
2	Would the participant approach a scared dog	54/207 (26)	117/207 (56)	30 (21, 40)	<0.001
3	Identify an aggressive dog	202/218 (93)	208/218 (95)	2.7 (−2.1, 7.6)	0.24
4	Would the participant approach an aggressive dog	137/206 (66)	148/206 (72)	5.3 (−4.0, 15)	0.11
5	Ability to identify a 'happy' dog	140/218 (64)	187/218 (86)	22 (13, 30)	<0.001
6	Would the participant approach a 'happy' dog	174/204 (85)	179/204 (88)	2.4 (−4.7, 9.6)	0.53
Section II: Knowledge of rabies and its transmission					
7	Recognize rabies as a virus	117/218 (81)	217/218 (99)	18 (13, 24)	<0.001
8	Recognize that only mammals transmit rabies	153/211 (72)	186/211 (88)	16 (7.7, 24)	<0.001
9	Identify cows transmit rabies	37/144 (26)	105/144 (73)	47 (36, 58)	<0.001
10	Identify that dogs transmit rabies	183/202 (91)	197/202 (97)	6.9 (1.9, 12)	0.006
11	Identify that snakes do not transmit rabies	97/140 (69)	116/140 (83)	14 (3.0, 24)	<0.001
12	Identify dogs as the main reservoir of rabies	149/187 (80)	144/187 (77)	−2.7 (−12, 6.2)	0.54
Section III: Ability to correctly order post-exposure precaution steps					
13	Correctly order post-exposure precaution steps	16/35 (46)	30/35 (86)	40 (17, 63)	<0.001
14	Identify vaccine as best means of prevention	28/35 (80)	30/35 (86)	5.7 (−15, 26)	0.62

CI: Confidence Interval.

^a P-values calculated using McNemar's paired difference of proportions test.

marked improvement in interpretation of dog behavior and knowledge of rabies, with a mean pre-session score of 8.6 out of 12 (71%; 95% CI 68% to 75%), and a mean post-session score of 10.2 out of 12 (85%; 95% CI 83% to 88%). Pre- and post-training questionnaire results are presented in Table 2.

The results of mixed effects logistic regression modeling of the pre- and post-session score data, adjusting for school location, school class and gender, are presented in Table 3. After adjusting for the effect of education level (school class), gender and region, and accounting for pairing and clustering of scores by school, the back-transformed log odds model outputs correspond to an absolute rise of 14% (95% CI 11% to 16%) in the proportion of correct test scores following the educational session. This amounts to a relative increase of 19% (95% CI 15% to 22%) compared with the mean pre-session score of 71%. Accounting for clustering of scores by school (Fig. 1), a direct relationship was observed between test scores and educational level. Test scores were comparable amongst students from rural and urban areas and between boys and girls for the sections of the questionnaires covering interpretation of dog behavior and knowledge of rabies. No interaction terms were statistically significant; similar improvements were observed by class, gender and region between pre- and post-questionnaires.

3.2. Knowledge of appropriate post-exposure prevention measures

Overall, there was a 40% absolute rise in the proportion of students able to correctly order the post-exposure precautionary steps following training (Table 2). This amounts to a relative increase of 87% (95% CI 37% to 138%) compared with the proportion of correct responses pre-training (46%). Insufficient data were available (due to time constraints) to stratify the analysis of Section III of the questionnaire by gender or class.

3.3. ICC estimates

After adjusting for the fixed effects included in the model, the school-level ICC was 4% (95% CI: 1–19%), the student-level ICC was 5% (95% CI: 2, 9%), whilst 91% of the variance in test scores between students in schools could be explained by other factors (including effectiveness of the sessions, educational level and gender of the students, and urban or rural location of the school, as well as those not investigated in this study), see Table 3.

4. Discussion and conclusions

As far as the authors are aware, this is the first study to evaluate a bite prevention and rabies education program, targeting school-age children in a rabies-endemic zone. Although previous evaluations have investigated the effectiveness of bite prevention educational interventions elsewhere, including (Dixon et al., 2013; Schwebel et al., 2011), none appear to have been conducted explicitly linked to rabies education targeting the most at-risk population, children in Asia and/or Africa. As a pilot study it is also the first to present ICC estimates that will inform the design of future planned cluster randomized trials (CRTs), helping to assess the feasibility of health educational interventions.

Given the nature of this type of CRT, with repeated observations made on the same individuals within the same clusters, correlation may exist at two levels (the individual and the cluster). This correlation results in a greater degree of homogeneity of study subjects compared with a study comprised of individuals selected at random from the general population, lowering the overall statistical power of the trial (Parker et al., 2005). In a recent review of educational interventions in children and adolescents for the prevention of dog bite injuries, all included studies undertaking CRTs failed to report an ICC on which their sample size calculations were based (Duperrex et al., 2009). By implication this means that the lack of independence in study outcomes was not accounted for and it is possible that insufficient numbers of study subjects and of clusters (schools) could reduce the study power (the ability to detect a true difference in outcome measures, given a true difference exists) (Campbell et al., 2004). The ICC estimate calculated in this study will allow future researchers to estimate the number of clusters (schools) and the number of students within each cluster to be included in a trial. To have adequate power and accommodate for clustering effect, standard sample sizes need to be inflated by a factor (known as the design effect, D) where $D = 1 + \rho \times (n-1)$, assuming n is the average cluster size (at this level) and ρ is the estimated ICC (for this level) (Kish, 1965).

In this pilot study, similar estimates for ICC were observed at the school-level and student-level (4–5%, with less certainty at the school level, due to the relatively smaller sample of schools relative to students). Calculation of appropriate sample sizes using the ICC value is crucial in efforts to detect a true effect, being effective educational intervention. The implication of an inappropriately small sample size calculation for future CRTs is a lack of evidence for stakeholders (particularly government authorities)

Table 3
Mixed effects logistic regression model of the proportion of correct responses to questions on interpretation of dog behavior and knowledge of rabies, from the Sikkim Anti Rabies and Animal Health (SARAH) education program, 2014.

Fixed effects	Coefficient ^a	SE	95% CI	P-value ^b
Intercept	0.19	0.34	−0.47, 0.86	–
Session:				
Post-session	0.90	0.11	0.69, 1.11	<0.001
Pre-session	0	–	Reference	
Educational level (per unit increase in class)	0.23	0.11	0.02, 0.44	0.034
Gender:				
Female	0.21	0.18	−0.15, 0.57	0.25
Male	0	–	Reference	
Region:				
Rural	0.14	0.36	−0.56, 0.84	0.69
Urban	0	–	Reference	
Random effects	Variance	95% CI	ICC	95% CI
School	0.13	0.02, 0.69	0.04	0.01, 0.19
Student (within school)	0.17	0.06, 0.33	0.05	0.02, 0.09
Residual	3.29	–	0.91	–

$n = 103$; SE = Standard error of regression coefficient; ICC = intra-cluster correlation coefficient; 95% CI = 95% confidence interval.

^a Regression coefficient expressed as log odds.

^b P-values estimated using the likelihood ratio test statistic.

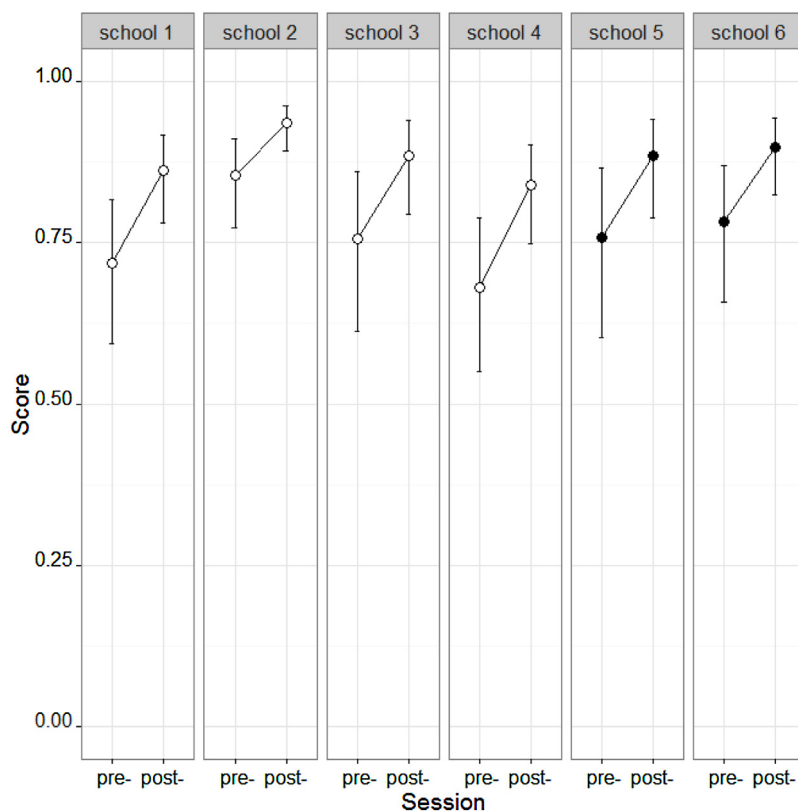


Fig. 1. Improvement in interpretation of dog behavior and knowledge of rabies from the Sikkim Anti Rabies and Animal Health (SARAH) education program, by school, 2014. Urban schools shown in white, rural schools in black, with error bars representing 95% confidence intervals accounting for paired measurements.

to support implementation of sustainable health education, for instance within the school curriculum. Conversely, sample size calculations that are too large may result in uneconomical studies, wasteful of resources. Our *pre hoc* estimate, assuming no clustering effects, was that a minimum of 80 children per school would need to be enrolled in future educational intervention studies to have 80% power of detecting an absolute difference of 25% in proportions (improvement in performance). Putting the findings of this pilot study into perspective (we observed a 14% absolute rise from a mean pre-session score of 71%, and ICCs of 0.047 and 0.037 at the student- and school-levels, respectively): To meet the requirements of a CRT, we now understand that the crude

sample size estimate is 107 students per school, and to account for repeated measurement of individuals we should multiply this sample size by a design effect of $1 + 0.05 \times (2-1) = 1.05$, resulting in an estimated requirement of 112 students per school. To then account, conservatively, for clustering at the school-level we should multiply this sample size by a further school-level design effect of $1 + 0.04 \times (112-1) = 5.45$. This implies that in order for future planned trials of similar educational interventions in similar regions of India (i.e. nearby states in Northern India) to accommodate for clustering, a minimum of 112 students per school from a minimum of 6 schools will be required. With caution, results may be used to inform the planning of similar studies in schools in nearby

highly endemic zones for terrestrial rabies in Bhutan, Nepal and Tibet.

A disadvantage of using an ICC calculated from a single pilot study is imprecision, given clusters involved in pilot studies are unlikely to be a random sample of the population of clusters from which the sample of a full trial will be drawn (Eldridge and Kerry, 2012). A conservative approach to addressing this issue would be to use the upper bound of the 95% confidence interval of the pilot study ICC for sample size calculations. Similarly, the relatively small number of clusters used in this study reduces the precision of the estimate (Donner and Klar, 2004). Given the pilot nature of the study, the process of selection of children chosen to participate in the study was limited by accessibility, time constraints and difficulties inherent in managing large classes of students. Therefore, results should be interpreted with caution in the face of potential selection and measurement biases.

It has been hypothesized that an inability to correctly interpret dog behavior, unsafe situations and inappropriate provocation contribute toward an increased risk of children being bitten by dogs (Lakestani et al., 2014; Wilson et al., 2003). In this study, overall test scores for interpretation of dog behavior and knowledge of rabies improved by 19%, suggesting that preventative education to improve the understanding of dog behavior may allow for a decline in the burden of dog bites amongst children, (and human rabies exposure) (Dixon et al., 2012). Prior to the educational sessions, only 46% (Table 2) of the children were able to correctly order the post-exposure precautionary steps taken following being bitten by a potentially rabid animal. This knowledge gap aligns with the dangerously low proportion of people exposed to rabies that seek PEP, principally due to a lack of knowledge or resources (Gongal and Wright, 2011). Despite being a small sample, the educational intervention appeared highly successful in improving knowledge of post-exposure precautionary steps amongst children in the rural school where this was tested (>85% of respondents correct in the post-training questionnaire versus 46% before training). Recently, school-based education campaigns implemented within an inter-sectoral rabies elimination program in the Bohol province of the Philippines, were found to directly increase the number of bite victims that not only reported bite incidents but also sought medical treatment after exposure, as a function of increased awareness (Lapiz et al., 2012), supporting the use of educational intervention in control efforts.

Changing the current public perceptions of rabies prevention and control is a fundamental aspect of ongoing rabies control efforts. Effective educational initiatives that target at-risk children are therefore vital to such efforts. ICC estimates calculated from this study will be useful in the design of cluster studies, evaluating rabies focused public-health education programs in developing countries. We suggest that estimates from larger scale studies be evaluated to improve calculation of sample sizes for future studies. Furthermore, follow-up assessment questionnaires 6–12 months after the training session should be administered to monitor and evaluate long-term knowledge uptake from training sessions. Future studies should be undertaken to establish whether there is evidence of educational programs reducing dog bite and human rabies case rates.

Conflict of interests

The authors have no conflicts of interest to declare.

Authors' contributions

AA led the design of the study. Written educational materials, questionnaires and program structure were designed and carried

out by AA, ASC, TVZ. AA, MAS and SMF performed the statistical analysis. AA wrote the first draft of the manuscript. All authors read and approved the final manuscript.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.actatropica.2016.12.032>.

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