

# Bats in the Bedroom, Bats in the Belfry: Reanalysis of the Rationale for Rabies Postexposure Prophylaxis

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**Background.** We assessed the scientific basis and practical implications of recommendations made since the late 1990s to offer rabies postexposure prophylaxis (RPEP) for occult bat encounters, including recommendations to offer RPEP to persons with bedroom exposure to a bat while sleeping without evidence of direct physical contact.

**Methods.** The number needed to treat after bedroom exposure to a bat was calculated as the percentage of population exposed multiplied by the inverse of crude rabies incidence. Bedroom exposure was estimated in a population survey of 14,453 households. Incidence was based on reported human cases in Canada and the United States, 1990–2007.

**Results.** In the population surveyed, bedroom bat exposure while sleeping and without known physical contact occurred at an annual rate of 0.099%. We estimate that <5% of eligible persons with bedroom exposure receive RPEP as recommended. The incidence of human rabies due to bedroom bat exposure without recognized contact was 1 case per 2.7 billion person-years. The number needed to treat to prevent a single case of human rabies in that context ranges from 314,000 to 2.7 million persons. A total of 293–2500 health care professionals working full-time for a full year would be required to prevent a single human case of bat rabies due to bedroom exposure without recognized contact. Amounts of Can \$228 million to Can \$2.0 billion are additionally required for associated material costs.

**Conclusions.** Human rabies acquired through bedroom exposure to a bat while sleeping and without recognized contact is rare. Conversely, such exposures are not uncommon in the population, and the resources required for associated RPEP are orders of magnitude higher than those required for most interventions that are considered to be reasonable. Current RPEP recommendations related to occult bat contact should be reconsidered.

During the mid-1990s, the Centers for Disease Control and Prevention in the United States began highlighting human cases of bat rabies in the absence of recognized bat contact [1–3]. Accompanying editorials initially emphasized that “because some bat bites may be less severe—and therefore more difficult to recognize—than bites inflicted by larger animals, rabies postexposure prophylaxis should be considered for any phys-

ical contact with bats when bite or mucous membrane contact cannot be excluded” [1, p. 272]. Follow-up reports were expanded to include emphasis on physical proximity to a bat, with editorials further suggesting that postexposure prophylaxis (RPEP) be “considered in all situations in which there is reasonable probability that contact with a bat may have occurred” [2, p. 400; 3].

These reports culminated in a summary by the Advisory Committee on Immunization Practice (ACIP) in 1999 that revealed that, of 21 individuals with bat rabies since 1980, only 1–2 had a recognized bite, 10–12 had physical contact with no bite, and 7–10 had no bat contact; thus, the ACIP concluded that RPEP “can be considered for persons who were in the same room as the bat and who might be unaware that a bite or direct contact had occurred” [4, p. 9]. Cited examples of such occult bat contact, recently reiterated in updated ACIP guidelines in 2008, included a deeply sleeping person awakens to find a bat in the room or an adult witnesses

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a bat in the room with a previously unattended child, mentally disabled, or intoxicated person [4, 5]. Similarly, in Canada beginning in 1998 and as recently as 2006, the National Advisory Committee on Immunization recommended that when persons are sleeping unattended in a room where a bat is present and they cannot reasonably exclude the possibility of a bite, rabies postexposure prophylaxis should be initiated [6, 7]. In providing guidance, the ACIP includes the following qualifier: “These situations should not be considered exposures if rabies is ruled out by diagnostic testing of the bat, or circumstances suggest it is unlikely that an exposure took place” [5, p. 13]. Frontline public health staff and clinicians, however, remain in the difficult position of having to adjudicate individual exposures that expert committees have simultaneously emphasized may well be undetectable.

We present a reanalysis of the risks and recommendations for RPEP after occult bat contact, taking into account not only numerator data (case reports) but also the proportion of the population exposed, the proportion of eligible persons reached, and the incidence of preventable disease, summarized by the number needed to treat (NNT) per case prevented and interpreted in the context of the benefit-to-risk ratio. We describe the practical implications in terms of human and material resources required to prevent a single human case of rabies associated with bedroom exposure.

## METHODS

**NNT per case prevented.** NNT is defined as the inverse of the absolute risk reduction [8]. The absolute risk reduction is derived as the incidence without intervention minus the incidence with intervention. We allowed 100% RPEP efficacy so that incidence in the intervention group was not influential and could be excluded. The NNT was then derived as

$$\begin{aligned} \text{NNT} &= \frac{1}{\left( \frac{\text{No. of human cases due to given exposure without intervention}}{\text{Percentage of exposed persons per year} \times \text{cumulative population in person-years}} \right)} \\ &= \text{Percentage of exposed persons per year} \\ &\quad \times \frac{1}{\text{Crude incidence without intervention}} \end{aligned}$$

As this equation indicates, the NNT will increase as the proportion of the population with a given exposure increases or as the number of human cases associated with that exposure decreases. In our analysis, the NNT included the investigation of the eligible exposure and the administration of RPEP (immunoglobulin plus 5 spaced doses of vaccine).

**Proportion of the population exposed annually.** To estimate the proportion of the population with bat exposure an-

nually, we conducted a random-digit-dial telephone survey from 15 January through 30 March 2007 in Québec, Canada (population, 7.6 million). Approximately half the population of Québec lives in the metropolitan area of Montreal. Because this may have influenced the likelihood of bat exposure, the sample was stratified and weighted for the population of each region to ensure a valid overall estimate for the province. After providing verbal consent, participants were asked whether they had been in the presence of a bat from 1 January through 31 December 2006. When the answer was affirmative, the rest of the interview was recorded. Additional questions sought details related to bat exposure and intervention. Participants were asked to describe the age and sex of other household members and whether any household members had also been in the presence of a bat during the same period. If so, these persons were interviewed individually. Parents responded for and with the help of exposed children aged <14 years. This study was approved by the ethics committee of the Centre Hospitalier Universitaire de Québec.

Exposure was classified as direct contact if there was recognized physical contact with a bat. Household exposure in the absence of recognized physical contact was divided into 3 categories. According to the National Advisory Committee on Immunization and ACIP RPEP recommendations, bedroom exposure refers to the presence of a bat in the room where an individual was sleeping when exposed. Bedroom access exposure refers to a bat found elsewhere in the house with a door open to allow bat access to the individual while sleeping. All other noncontact exposures were classified as “other.” A public health nurse with experience in the investigation of bat exposures reviewed the taped recordings for classification accuracy. Analysis was adjusted for clustering by household and stratification by region with 95% confidence intervals, as shown in the Appendix.

**Proportion of RPEP-eligible persons reached.** The proportion of RPEP-eligible persons reached was estimated by dividing the annual number of notifications of bat exposures by the expected number of persons exposed annually. The mean annual number of notified bat exposures was taken from a previous publication documenting all such notifications in Québec during a 2-year period [9]. The expected number of persons exposed annually was calculated by multiplying the population of Québec by the estimated proportion of the population that was exposed annually.

**Incidence of preventable disease.** The crude incidence rate (cases per person-year) was calculated by dividing the number of cases with a given exposure by the sum of the populations from each year during 1990–2007 [10]. Population data were obtained from the US Census Bureau [11, 12] and Statistics Canada [13].

**Practical implications.** In a previous publication, we es-

estimated the professional time required for exposure investigation and RPEP administration on the basis of 189 exposure investigations and 49 persons who were administered RPEP, as summarized in table 1 [9]. In this study, we derived the human and material resources required per case prevented by multiplying the previously estimated costs for professional time, biological products, and virologic testing by the NNT. A full-time equivalent (FTE) of professional time was assumed to be 1650 h per year.

## RESULTS

**Proportion of the population exposed annually.** Of the 27,795 telephone numbers generated for the population survey, 22,833 (82%) were valid household numbers; 14,453 (63%) of these households participated. The participating households included 36,445 persons, among whom there were 5 significant direct contacts that involved 4 persons; an 11-year-old child contributed 2 exposures (1 outdoor and 1 indoor) (figure 1). None of these 4 persons believed that they were bitten but could not rule out the possibility. The adjusted proportion of persons with direct bat contact without evidence of a bite was 0.0098% (table 1). Of the 152 persons with indoor proximity to a bat but without direct contact, 34 described bedroom exposure, 41 described bedroom access, and 77 had other exposure. For any household proximity to a bat without direct physical contact, the proportion was 0.43%, distributed as 0.099% for bedroom exposure, 0.12% for bedroom access exposure, and 0.21% for other exposure.

**Proportion of RPEP-eligible persons reached.** Two (5%) of the 41 individuals with bedroom access exposure sought medical advice, and both received RPEP. In contrast, neither the 34 individuals with bedroom exposure nor the 4 with direct physical contact without evidence of a bat bite sought medical advice.

The expected annual number of persons in Québec who had direct physical contact without evidence of a bat bite was ~751

( $0.0098\% \times 7.6$  million persons). The mean annual number of notifications for this type of exposure was 53 [8]. We thus estimate that RPEP reached 53 (7.1%) of the 751 eligible persons (table 2). Similarly, for bedroom exposure without recognized physical contact, 245 (3.2%) of 7548 eligible persons were reached.

**Incidence of preventable disease.** From 1990 through 2007, 36 individuals were reported to have indigenously acquired bat rabies in Canada and the United States; 19 had a history of direct bat contact [10]. Of the 17 individuals without recognized physical contact, 2 had bedroom exposure, 4 had other household exposure, and 11 had no known bat exposure [10]. Of the 11 individuals with rabies found from 1990 through 2007 who had a history of a bat in the bedroom, 9 reported being bitten or awakened by direct contact with the bat.

The cumulative number of person-years during 1990–2007 in Canada and the United States was 5.4 billion. The preventable incidence thus varies from 1 case per 2.7 billion person-years, for the 2 cases strictly defined as bedroom exposure, to 1 case per 318 million person-years, if bedroom, other household, and other unknown exposures are included as RPEP eligible under the revised recommendation for sleeping exposure (table 3).

**NNT per case prevented.** The NNT to prevent 1 human case of rabies associated with direct contact with a bat without evidence of a bite is ~59,000 persons ( $0.0098\% \times 601$  million persons) (table 3). The NNT to prevent 1 case of rabies associated with bedroom exposure is ~2.7 million ( $0.099\% \times 2706$  million persons). As such, the risk of rabies associated with physical contact would be 45-fold greater than that associated with bedroom exposure. In sensitivity analysis, if we assume that all 17 patients with rabies who did not have known history of direct bat contact acquired their disease through bedroom exposure, the NNT would be ~314,000 ( $0.099\% \times 318$  million persons) (table 3).

**Practical implications.** For the investigation of direct phys-

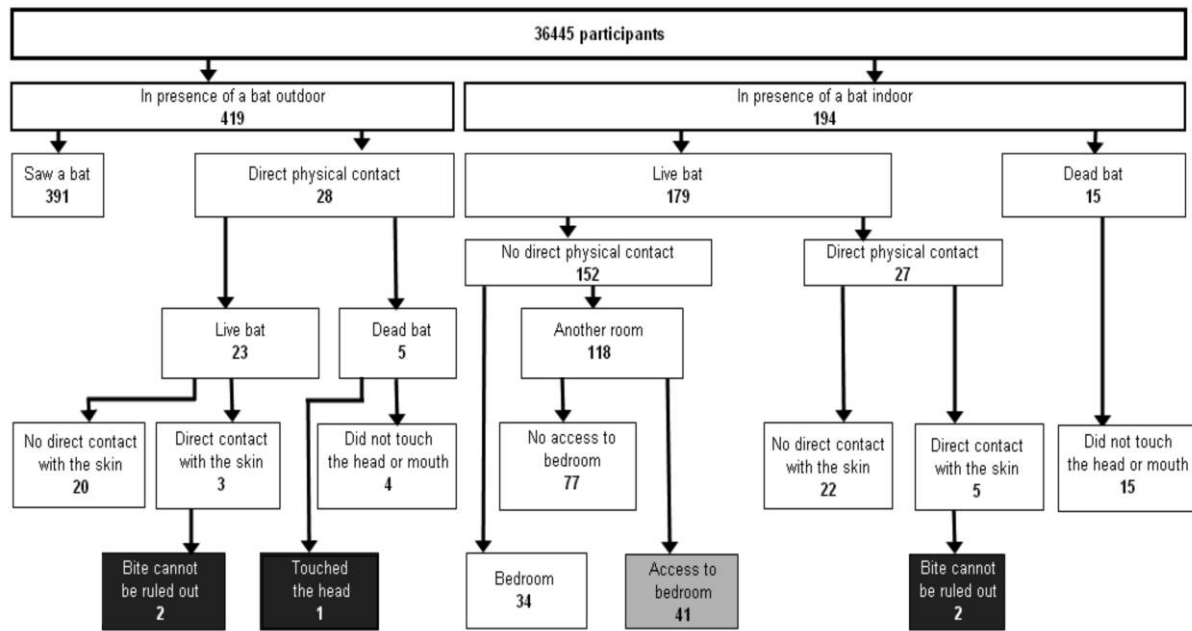
**Table 1. Estimated human and material resources required to investigate bat exposure and administer rabies postexposure prophylaxis (RPEP).**

Variable	Direct contact without evidence of a bite	Bedroom exposure without direct contact
Percentage of bats tested	25	32
Percentage of bats testing positive for rabies	12	2
Percentage of exposed individuals who would receive RPEP in absence of bat testing	100	100
Nurse or physician time to investigate bat exposure, h <sup>a</sup>	1	0.33 <sup>b</sup>
Nurse time to administer RPEP, h <sup>a</sup>	1.5	1.5
Veterinarian time for bat analysis, h <sup>a</sup>	1	0.5 <sup>b</sup>
Cost of vaccine and immunoglobulins for a complete course of RPEP, Can \$	1000	1000
Cost of virologic analysis, Can \$	250	250

**NOTE.** Data are from Huot et al. [9].

<sup>a</sup> A total of 91% of the time was for nurses, and 9% was for physicians.

<sup>b</sup> Accounts for a mean of 2 exposed persons per bedroom exposure investigated.



**Figure 1.** Exposure chart for persons exposed to bats in Québec, Canada, from 1 January through 31 December 2006

ical contact without evidence of a bite, 5304 physician hours (3 FTEs), 53,627 nursing hours (33 FTEs), and 14,733 veterinarian hours (9 FTEs) are required. Administration of RPEP would require an additional 68,949 nursing hours (42 FTEs). The cost of biological products and virologic analyses would add an additional Can \$48 million (table 3).

For bedroom exposure, the number of hours needed to investigate ~2.7 million exposed persons would correspond with 49 physicians, 491 nurses, and 259 veterinarians working full-time for a full year; 1665 additional nurse FTEs would be required to administer RPEP, and nearly Can \$2.0 billion would be required for biological products and virologic analyses to prevent a single case. In sensitivity analysis, by varying assumptions about RPEP eligibility for other types of household exposure, estimated costs are intermediary but never below 293 professional FTEs and Can \$228 million in added biological product and virologic analysis costs per case prevented (table 3).

## DISCUSSION

Rabies is a tragic and frightening disease. With the notable exception of 1 human survivor [14], the disease is without cure in humans thus far. Because of the already sinister image of bats, it is not difficult to understand how bat rabies in humans may have become dreaded out of proportion to its threat. To overcome the possible influence of emotive distortion, risk analysis to inform public policy requires the consideration of data beyond case reports (i.e., beyond numerator data alone). Quantifying risk and its potential impact requires additional population considerations, including the proportion of persons

exposed, the proportion of persons reached by the intervention, and the incidence of preventable disease. These concepts are conventionally summarized in the standard epidemiologic measure of the NNT per case prevented.

The NNT is directly related to the proportion of the population exposed. Our survey has revealed that the frequency of exposure to bats indoors is substantial when viewed on a population level. Overall, ~1 (0.43%) of 230 individuals provided a history of a bat in the household and ~1 (0.099%) of 1000 individuals admitted to RPEP-eligible bedroom exposure. Even with application of the lower limit of the 95% confidence interval (0.071%) for bedroom exposure, our estimate of the NNT is high (1.9 million persons). If our survey underestimated the proportion of the population with bedroom exposure, then the estimate for the NNT would be even higher and truly staggering. The NNT is also inversely related to disease incidence: the NNT decreases as the incidence increases. The true incidence of rabies associated with bedroom exposure may be >1 case per 2.7 billion person-years, but it is certainly lower than the estimate of 1 case per 318 million person-years, assuming all unknown exposures were also bedroom related. The incidence since 1990 is unlikely to have been decreased by RPEP administration for occult bat contact. We estimate that <5% of the eligible population is currently accessing RPEP for bedroom exposure, and thus, intervention is unlikely to have reduced the associated rabies incidence. With such a small proportion of eligible persons reached, full implementation would require 20- to 30-fold greater resources than are currently applied, and such an encompassing effort might be viewed as

**Table 2. Percentage of the population with bat exposure and the percentage of exposures reported.**

Variable	Direct contact without bite	Household exposure with no direct contact		
		Bedroom	Bedroom and bedroom access	Bedroom, bedroom access, and other
No. of persons exposed to bats	4	34	75	152
Crude percentage of persons exposed in the population	0.011	0.093	0.206	0.417
Adjusted percentage of persons exposed in the population (95% CI)	0.0098 (0.003–0.017)	0.099 (0.071–0.126)	0.214 (0.133–0.232)	0.427 (0.360–0.494)
Expected no. of exposed persons in Québec (population, 7.6 million persons)	751	7548	16,417	32,640
Mean annual no. of persons with notified exposure in Québec <sup>a</sup>	53	245 <sup>b</sup>	683	Not available
Percentage of reported persons currently reached by the RPEP intervention (mean no. reported/no. expected)	7 (53/751)	3 (245/7548)	4 (683/16,417)	Not available

**NOTE.** CI, confidence interval; RPEP, rabies postexposure prophylaxis.

<sup>a</sup> Data are from Huot et al. [9].

<sup>b</sup> After redistribution of persons with unknown data about the room where the bat was found.

inconceivably draining. Failure to intensely pursue a greater proportion of eligible persons then becomes paradoxical public policy: a recommendation that is known to be sustainable only if ignored by most eligible persons is of doubtful usefulness and questionable ethics.

This study has limitations. The 63% participation rate for the population survey is fairly good, but a lower rate of exposure to bats among nonparticipants (and, thus, a lower NNT overall) is possible. This is unlikely because bats were not mentioned before individuals agreed to participate. Respondents may have been unaware of exposures incurred by other household members. If more household members were exposed, however, this would only have resulted in a higher NNT. The frequency of bat exposure in Québec may be different from that of the rest of Canada or the United States, but results from elsewhere suggest that our estimates of the NNT are conservative. A similar study conducted in Oregon in 1998 found that 1.4% of 10,844 households surveyed had a bat in the home during the previous year, and in nearly one-quarter of households, the bat had been in the same room while a person slept [15]. Estimates of the NNT from that study are within the same order of magnitude as our estimates (800,000 persons). Similarly, in 1998, a Connecticut survey found that 1.0% of 1610 households had bats in the home during the previous year (R. Nelson, personal communication). Survey of additional areas may give added reassurance. Regions already surveyed, however, are unlikely to represent exceptional areas of greater bat exposure, because Québec, Oregon, and Connecticut each had a single indigenous human case of bat rabies from 1950 through 2007

[10]. Instead, because the density and diversity of bat populations may be anticipated to increase as the distance from Québec south toward the equator increases, any revision in estimates of bat exposure would likely be upward and, therefore, toward a higher NNT.

The associated resources required to prevent a single case of human rabies through RPEP for bedroom exposure appears to be overwhelming. This perspective is consistent with estimates previously reported by several others [15–17]. Even with application of the most conservative estimate of the NNT (314,000 persons), the human resources to prevent a single case caused by bedroom exposure would exceed what even the most conscientious physician could consider to be reasonable. It is tantamount that an institution dedicate 6 of its physicians and 257 of its nurses full-time for a full year to a single patient affected by a fatal disease. Even in the context of a deadly disease, most health care personnel from that institution would consider their other patients and the illnesses and deaths that could have been treated or prevented with such substantial resources. These practical translations expose the real and staggering opportunity costs associated with current RPEP recommendations, even without considering the added direct costs of biological products and virologic analysis (\$230 million) and the indirect costs (e.g., time, money, and worry) experienced by exposed individuals. It may be argued that the NNT is a theoretical concept: we would never actually consume those resources or subject such numbers of persons to RPEP. The NNT, however, is derived only for eligible persons who would actually receive the intervention; it is unaffected by the large proportion of persons who do not receive

**Table 3. Human and material resources per case prevented, by type of exposure.**

Variable	Direct contact without bite	Bedroom	Sensitivity analysis <sup>a</sup>		
			Rabies acquired through bedroom exposure	Rabies acquired through bedroom or bedroom access exposure	Rabies acquired through any household exposure
No. of cases during 1990–2007	9	2	17	17	17
Incidence, no. of cases/million person-years	1/601	1/2706	1/318	1/318	1/318
Percentage of persons exposed in the population	0.0098	0.099	0.099	0.214	0.427
No. of persons needed to treat <sup>b</sup>	59,000	2,668,000	314,000	681,000	1,359,000
Human resources, FTE					
Physician investigation	3	49	6	13	26
Nurse investigation	33	491	61	132	262
Nurse administering RPEP	42	1665	196	425	836
Veterinarian (bat analysis)	9	259	30	66	136
All professionals	86	2463	293	636	1260
Cost for biological products and virologic analyses, Can \$ million					
Vaccine and immunoglobulins	46	1831	215	468	920
Virologic analysis of bats	2	213	13	27	56
Total	48	2045	228	495	976

**NOTE.** FTE, full-time equivalent (1650 h of work); RPEP, rabies postexposure prophylaxis.

<sup>a</sup> Sensitivity analysis assumed that all persons ( $n = 17$ ) with no history of direct contact had been infected through the specific type of household exposure.

<sup>b</sup> Rounded to the thousand.

the intervention. Instead, the greater the proportion of eligible persons who do not receive RPEP, the longer it would take to achieve the goal of preventing a single case.

An NNT analysis can also provide insight into the benefit-to-risk ratio associated with an intervention, especially if rare but serious adverse events are associated with the intervention. Among the hundreds of thousands of required recipients, the frequency of adverse events that occur while preventing a single case must also be factored into the recommendation for RPEP and balanced against disease risk. The human diploid cell vaccine used in Canada and the United States is associated with allergic reactions (~1 case per 1000 vaccinated persons), 9% of which are type 1 anaphylactic reactions [5]. The Food and Drug Administration recently published a review of reports associated with the purified chick embryo cell rabies vaccine that were based on the Vaccine Adverse Events Reporting System in the United States from 1997 through 2005, a period during which ~1.1 million doses (equivalent to 220,000 RPEP administrations) were distributed [18]. No deaths occurred, but 24 of the 336 reported cases were classified as serious, including 1 case of acute demyelinating meningoencephalitis and 10 additional cases of various other neurologic events. Of the 20 patients with probable (14 patients) or possible (6 patients) anaphylaxis, 4 experienced anaphylaxis 15–30 min after leaving the immunization facility; 1 of these patients experienced the reaction while driving. No inferences about causality can be made from passive surveillance, because it does not include a control group, and no risk of severe adverse event attributable to the purified chick embryo cell vaccine can be validly cal-

culated from the Vaccine Adverse Events Reporting System. On the other hand, adverse events are generally underreported through passive surveillance, which is intended only to detect signals of potential concern. The potential for concern is increased when vaccine is administered to hundreds of thousands of people. When the risk of rabies acquisition is high, the benefit of prophylaxis in preventing a uniformly fatal disease clearly outweighs any potential vaccine concern. However, in the context of exposure defined by the nearness of bats without physical contact, the benefit-to-risk ratio becomes less certain: among the hundreds of thousands of persons vaccinated to prevent a single case, reports of severe neurologic events with sequelae or a single adverse event causing death would entirely undo any potential benefit.

We conclude that bat rabies in humans is rare, especially without direct bat contact. Conversely, bedroom and other proximate bat exposures appear frequently in the population. Most bat-associated RPEP is administered for noncontact exposure (~80% of exposures) [5, 7, 9]. Despite this, only a small fraction (<5%) of eligible persons with such exposure seek RPEP. For noncontact bedroom exposure, the benefit-to-risk ratio of RPEP is unclear, the resources needed to prevent a single case of rabies are orders of magnitude higher than most interventions considered to be reasonable, and full implementation of the recommendation would be inconceivably resource intense. In the current context of global rabies vaccine shortage, administration of RPEP to persons other than those at highest risk is even less defensible. Recommendations since the mid-1990s to administer RPEP for bedroom or other occult bat

contact were introduced on the basis of numerator data alone; we urge that these recommendations be reconsidered in the context of this more complete risk analysis.

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## APPENDIX

The adjusted proportion of the population exposed to bats was estimated as follows. Estimator of the proportion in the province is

$$\hat{p} = \sum_{h=1}^{17} W_h \hat{p}_h = \sum_{h=1}^{17} \frac{N_h}{N} \hat{p}_h,$$

where  $W_h = \frac{N_h}{N}$  indicates the proportion of the population in the province living in region  $h$ ,  $N_h$  indicates the number of persons living in region  $h$ ,  $N$  indicates the number of persons living in the province,

$$\hat{p}_h = \frac{1}{m_h} \sum_{i=1}^{m_h} \frac{N_i}{N_h} p_i$$

is the estimate of the proportion exposed in region  $h$ ,  $m_h$  indicates the number of households in region  $h$ ,  $N_i$  indicates the number of persons in household  $i$ ,  $p_i$  indicates the proportion of persons exposed in household  $i$ ,  $\frac{N_h}{N}$  indicates the mean number of persons per household in region  $h$ , and  $M_h$  indicates the total number of households in region  $h$ .

Variance of the estimator is

$$var \hat{p} = var \sum_{h=1}^{17} W_h \hat{p}_h = \sum_{h=1}^{17} W_h^2 var \hat{p}_h = \sum_{h=1}^{17} \frac{N_h^2}{N^2} var \hat{p}_h,$$

where  $var \hat{p}_h = (1 - f_h) \frac{s_{ph}^2}{m_h}$  is the variance of the estimator  $\hat{p}_h$  and  $s_{ph}^2$  is the variance of the proportion of persons exposed in region  $h$  and is estimated as

$$s_{ph}^2 = \frac{1}{m_h - 1} \sum_{i=1}^{m_h} \frac{N_i}{N} p_i - \hat{p}_h^2.$$

$f_h = \frac{m_h}{M_h}$  is the proportion of households interviewed in region  $h$ .

The 95% confidence interval (CI) was estimated as  $95\%CI = [\hat{p} \pm 1,96\sqrt{var \hat{p}}]$ .

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