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The Capture-Recapture Method in the Analysis of a Measles Epidemic in the County of Cluj, Romania

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Abstract
Aim: Measles is an infectious disease that has been proposed to be eliminated, but epidemics continued to appear mainly due to unvaccinated persons who refused to be vaccinated. The aim of our study was to estimate, using the capture-recapture method, the real number of cases that existed in a measles epidemic which evolved in the Cluj County's population. *Material and Method:* A survey to compare the cases of measles that were declared to the Cluj County Public Health Authority during the 1993 epidemic, with those registered in the medical records from Family Doctors' Offices, was conducted between February and March 1994. Descriptive statistics for the characterisation of non-normal distributed samples were performed using XLSTAT software. *Results:* In the survey, two samples were constituted, the first sample comprised of declared cases (1,404 cases), and the second sample comprised of the field-identified cases (2,383). The monthly cases' in the samples were not different (Mann-Whitney upper-tailed test), with a cold period seasonality. For the field-identified sample, 1,667 cases were undeclared and 716 were declared and identified ("recaptured") in the field investigation. The estimated number of cases at the Cluj County level was 4,673 cases, of which the declared ones represented 30% of all cases. *Conclusion:* The capture-recapture method is an easy methodology to apply, that can indicate the magnitude of an epidemic by the estimated number of cases in a specific time period and can also provide some details regarding a disease's epidemiological characteristics.

Keywords: Capture-Recapture; Measles; Epidemic

Introduction

Measles is a highly contagious viral disease, which is prevented by vaccinations and can be eradicated through a well-run vaccination programme and sustained epidemiological surveillance. In practice, after the introduction of population vaccination programmes, the burden of disease dropped rapidly and measles outbreaks and infections have even been eliminated from some regions, such as the USA, who declared in 2000 the disappearance of indigenous cases of measles [1, 2]. However, after the recent surge in anti-vaccination opinions, triggered by the false assumption that there exists a strong correlation between autism and the measles-mumps-rubella (MMR) vaccine, many people have refused the measles vaccination [3, 4]. Despite the proven absence of a causal link between the administration of the MMR vaccine and the occurrence of autism in children, many people still

continue to refuse the MMR vaccination [4-7]. Therefore, this has resulted in the increased number of measles outbreaks in several countries, recorded deaths related to these outbreaks [2, 8]. These issues have also been observed in Romania, and several epidemics appeared after 1979, when the national measles vaccination program was implemented [9].

Due to the passive status of the national epidemiological surveillance system, that only included records completed by medical practitioners, discrepancies in the number of diagnosed cases reported were expected [10]. The occurrence of cases of measles infection requires immediate intervention to protect the people who have come into contact with the infected person through vaccination, the administration of immune globulins (total), and medical surveillance [2, 3].

In this context, we can have suggestive information regarding the mode of measles population manifestation. In addition, having supplementary information could aid in the development and implementation of more appropriate intervention measures, particularly regarding innovative and long-term recommendations at population level.

In this paper we propose to perform an estimation of the actual number of measles cases that have occurred during a measles epidemic in the Romanian county of Cluj, using the capture-recapture method.

Material and Method

Study Design

During the analysis of the 1993 measles epidemic that occurred in Romania, some unreported cases that occurred during this period were observed, leading to the development of a survey, in the first trimester of 1994, for the identification of unreported cases in the county of Cluj. With the aid of the Cluj County Public Health Authority, a list of all the reported cases of measles was compiled, which included the name, date of birth and residential address of all reported cases. For the identification of cases, two teams each comprised of a field epidemiologist and a nurse, compared and matched the cases from the list of reported cases with the measles cases registered in the entire year of 1993, using medical records obtained from Family Doctors. The unreported cases were registered in a complementary list with actively identified cases.

Case identification and data collection were conducted between February and March 1994 (twenty-four working days), and the medical offices in urban and rural areas of the Cluj County, who agreed to participate in the survey, were each checked once.

Statistical Analysis

Descriptive statistics were used to characterise the data obtained from the two independent samples observed during data collection. The monthly distribution of the number of measles cases was tested with the normality tests and Fisher coefficient to determine the skewed deviations. For the comparison of the distribution of monthly cases in the two samples, the Mann-Whitney upper-tailed test was done. In the interpretation, the null hypothesis stated that the monthly distribution of the two investigated samples were equal, with 0.05 as the alpha level for the statistical significance. The graphic visualizations for the one tailed Mann-Whitney test values under the null hypothesis, with the critical and observed value, was done with a distribution chart and a scattergram was chosen for the comparison distribution of the monthly number of cases. All statistical analysis and presentations have been conducted using the XLSTAT software in Excel for Windows [11].

The Capture-Recapture Method

To estimate the number of measles cases existing in the Cluj County population, the cases that were declared to the Cluj County Public Health Authority were considered passive (first) identification and patients were marked on the reference list with all declared cases in the County. These cases have been coded with "M" as number of marked cases. In each Medical Office, the marked cases were searched and paired as recaptured, structuring the sample with "recaptured" cases

and coded by "R". The cases found outside of the list were considered unreported and counted in the sample of the field visit (or actively identified or the second visit identification). All cases identified at the visit in the Medical Office were coded by "T" (recaptured and unreported cases). Considering "X" as the unknown number of measles cases actually existing in the County population, this value will be calculated by the following formula (1) [12, 13]:

$$M/X = R/T$$
$$X= MT/R \quad (1)$$

Similarly, considering the number of cases in the second evaluation as being proportional to the number of cases in the whole population, this can be expressed as (2):

$$(M/X)*100=(R/T)*100 \text{ or } (M/X)*100=P_R(\%) \text{ of which } X=M/ P_R(\%) \quad (2)$$

In this equation $P_R(\%)$ represents the proportion of "recaptured" cases in the second sample. Both methods obtain the same result. The result obtained for the estimated number of cases shall be rounded to the nearest whole number, being an estimate referring to persons.

The Required Conditions for Capture-Recapture Method Application

The risk of over- or under-estimation is reduced by applying the method when the required conditions are met [13]. In this sense, the survey adhered to the following conditions:

- a stable Cluj County population counting 733,264 inhabitants in 1993, and a low birth rate and very low emigration [14];
- the same case definition and diagnostic methods provided by the National Measles Surveillance System have been applied by all physicians from the County;
- cases matching validation was made by double checking the data obtained from Medical Offices, which was carried out by the members of the field team;
- the capture homogeneity was given by performing the survey during an epidemic evolution and at the county level (meaning a large population);
- as data sources, for the measles surveillance system the cases were reported by family doctors and in their Medical Office the probability of identification of reported and unreported cases was the same;
- the active case identification, through the field visit, was not influenced (not dependent) by the passive case reporting in the ordinary surveillance system.

Results

Throughout the year 1993, a total of 1,404 measles cases were declared to the Cluj County Public Health Authority, by the family doctors. The declaration was made by filling in a standardized form on paper and submitting it to Public Health Authority, once a month.

During the survey, 63 Family Doctors' Offices, 39 from urban and 24 from rural areas of the county, had been checked for measles cases identification in their medical records. In total 2,383 cases were identified, exceeding the number of passively declared cases in the measles surveillance system by 979 cases (or 69.7%), (Table 1). The monthly distribution in both samples highlights a higher number of cases in the colder months of the year, certifying the continuation of seasonal outbreaks of measles. Systematically, more cases were identified in the survey than through the surveillance system, except in October when 2 less cases than those reported were actively identified (a negative difference).

In the test for normality (Lillieforts test), a ***p*** values of 0.026 for the surveys and 0.019 for the reported cases' sample, support the assumption that the variables do not follow a normal distribution. The Fisher coefficients, 1.779 for the survey and 1.59 for the reported cases sample, show a positive (right) skewedness due to the measles seasonality.

Table 1. The number of monthly cases identified in the survey that were declared through the surveillance system, and the differences in cases' identification between the two sources of data

Month	Cases from the survey	Cases reported in the surveillance system	Difference
January	70	42	28
February	315	202	113
March	905	490	415
April	584	353	231
May	259	149	110
June	152	98	54
July	55	35	20
August	17	11	6
September	11	9	2
October	7	9	-2
November	3	2	1
December	5	4	1
Year (total)	2,383	1,404	979

In Mann-Whitney upper-tailed test, no differences were found (p=0.302) between the samples' medians, and the scatter plot representation showed a similarity in the dispersion of the monthly number of cases (Figure 1). These indicate that there were no significant differences regarding the monthly measles cases' identification in the two samples. However, the difference in the number of cases of measles was significant (p<0.0001).

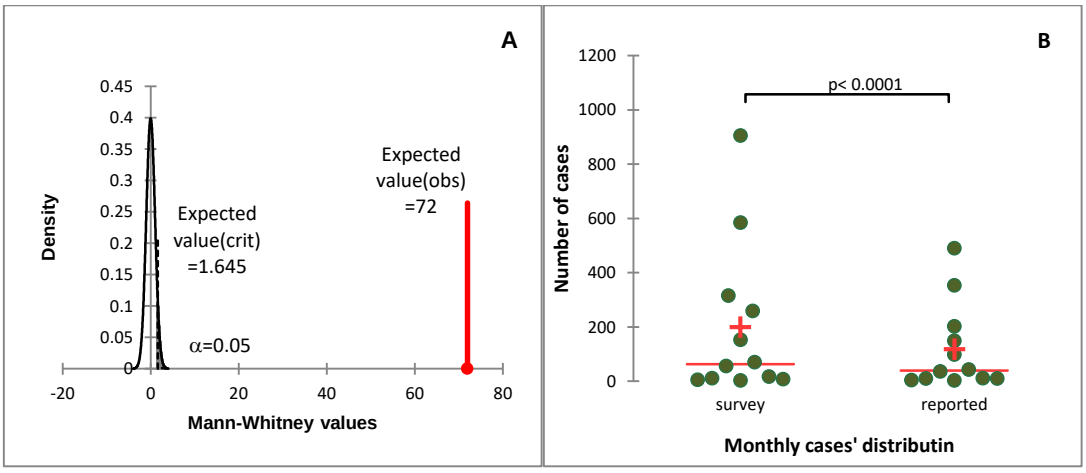

Figure 1. The results of comparisons between survey and reported cases' samples by the Mann-Whitney upper-tailed test: (A) the distribution of Mann-Whitney values under the null hypothesis with the observed (obs) and the critical (crit) values for statistical significance; (B) the scattergrams of the monthly number of cases identified in the two samples (green dots represent the number of cases each month, the red cross represents the mean, red line represents the median, and the *p* value of significance test).

In the survey sample, of the total number of cases 716 cases were matched ("recaptured") in both lists, representing the "recaptured" cases (Table 2). The 1,667 cases that were not reported were actively identified, exceeding those passively reported for the entirely year.

With these results, the number of estimated cases of measles in the county population was (3):

1,404*2,383/716 = 4,673 measles cases (3)

Table 2. The representation in a 2×2 contingency table of the number of cases identified in the two samples during the survey. (Legend: Y represents the unidentified cases; N represents all cases that existed in the population)

Cases provenance		Case found in the field visit		Total
		Yes	No	
Cases reported to the Cluj County Public Health Authority	**Yes**	716	688	1,404
	No	1667	Y	Y+1667
Total		2,383	Y+688	N

In proportion, regarding the 716 "recaptured" cases representing 30% of cases from the survey, the estimated number was (4):

$$1{,}404/0.3 = 4{,}673 \text{ measles cases} \quad (4)$$

Discussion

In Epidemiology, particularly for the diseases in the program of control or elimination, statistical methods are used to provide indirect evidence of the manifestation characteristics of a disease in a population. Based on such results and correlated with the data from the surveillance systems, more appropriate preventive measures can be applied [1].

Presently, this can be seen in cases of measles, which evolve with epidemics [8]. Their appearance needs to be explained by identifying the determinant factors that influence these epidemics. This was the main reason for writing our article, having the unpublished results of the survey made in 1994. Even though the study was conducted several years ago, it was the first capture-recapture method looking at measles cases (to our knowledge) and no similar studies have been carried out since then in Romania. At the same time, the study was performed rigorously with a meticulous verification of medical records. In this way we documented the presence of unreported cases in a surveillance system that was believed to be exhaustive for cases. Furthermore, the fact that we did not find the two cases that were reported for October, suggests deficiencies in registration procedure and preserving the patients' medical records.

The main characteristic in the analysis was the distribution of measles cases over time, because in epidemiological surveillance it is also the main aspect that defines epidemics [15]. Under this criterion, the absence of difference in monthly cases' identification shows that the measurement in the survey sample was not biased.

Regarding the measles epidemiology, the epidemic manifestation and the presence of seasonality demonstrate the partial influence of measles population manifestation by vaccination programmes [15]. In addition, the capture-recapture method revealed that the extent of the epidemic was much higher than documented by the local authorities. Due to the careful pairing of the cases, it is unlikely that there were errors of overestimation. Errors of underestimation are even less likely as the two samples were independent and the number of unreported cases, which were identified in the survey, was high.

Conclusions

The capture-recapture method gives us the possibility of estimating the number of existing measles cases in the population, in a short time-frame and cost-effective way, as this method does not require many resources. In addition, this method demonstrates the possibility of having unreported cases though the measles surveillance system, which in our study identified only a third out of all estimated existing cases. Referring to the epidemiology of measles, this study showed the influence of seasonality, a higher level of the real frequency of outbreaks, aspects that require re-

evaluation of the measles surveillance system, and the preventive recommendations for being more effective.

List of abbreviations

M: the marked measles cases
MMR: measles-mumps-rubella vaccine
p: p value of statistical test for significance
P_R(%): the proportion of "recaptured" cases
R: the "recaptured" measles cases
T: the "recaptured" and unreported measles cases
X: the unknown number of measles cases

Conflict of Interest

The authors declare that they have no conflict of interest.

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