

## GENERALIZED LINEAR MODELS AND CAPTURE-RECAPTURE METHOD IN A CLOSED POPULATION: STRENGTHS AND WEAKNESSES

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### 1. INTRODUCTION

The Capture-Recapture Method is one of the most common method to estimate the size of an unknown population. This methodology was initially developed in ecology to estimate the size of wildlife populations. Animals were trapped, marked, and released on a number of occasions, and the individual trapping histories were then used to estimate the size of the whole population.

The first application to human populations data occurred in 1949 by Sekar and Deming. In this case, “being captured by the sample  $i$ ” is replaced by “being included in the list  $i$ ”. In epidemiology the Capture-Recapture method is attempt to estimate or adjust for the extent of incomplete ascertainment using information from overlapping lists of cases from distinct sources (see International Working Group for Disease Monitoring and Forecasting, 1995a,b).

This technique has been widely used to estimate the prevalence of drug users (see for example Frischer, 2001; Gemmell, 2004; Hope, 2005) and the number of people infected with the Human Immunodeficiency Virus (Abeni, 1994; Davies et al., 1999; Bartolucci and Forcina, 2006). Other areas of application include the estimation of deaths due to traffic accidents (Razzak and Luby, 1998), prostitution (Roberts and Brewer, 2006) and the prevalence of other diseases (see for example Tilling and Stern, 2001; Zwane and van der Heijden 2005).

In a closed Capture-Recapture Model, we assume that there are no births, deaths or migrations, so that the population size is constant over trapping times. The demographic closure assumption is usually valid for data collected in a relatively short time.

Traditionally, discrete-time capture-recapture models assume that the samples are independent, but in epidemiology lists dependence and heterogeneity (the behaviour component) are the norm and Log-Linear Models are particularly useful in modeling these phenomena (Schwarz and Seber, 1999).

The dependence may be due to dependence between lists within each subject (the capture in one sample has a direct causal effect on the subject capture in an

other sample) and/or to heterogeneity among subjects (the capture probability may be influenced by subject's characteristics). Recently Hwang and Huggins (2005) have demonstrated that the effect of ignoring heterogeneous capture probabilities may lead to biased estimates of the population size.

This can be overcome by modeling the heterogeneity and using covariates or auxiliary variables in the statistical analysis of capture-recapture data (Pollock *et al.*, 1984; Huggins, 1989; Ahlo, 1990; Pledger, 2000; Pollock, 2002).

In presence of continuous covariates the standard Log-Linear Model assumes that the covariates are stratified. As the stratification is subjective, it is possible that for the same data set researchers using different stratifications can arrive at different estimates of the population size. Furthermore, the direct dependence between lists is incorporated by introducing interaction terms between lists, while continuous covariates can be introduced using a dummy variable for each value of the covariate. In this case the dimension of the parameters space can be large. When this dimension is close to the number of observations, the maximum likelihood estimate may be inconsistent or biased (Baker 1994, Tilling e Stern 1999) and the Multinomial Conditional Logit Model (MCLM) is preferable because allows to treat continuous covariates in their original scale (Zwane and van der Heijden, 2005).

In this work we show some open problems in using the MCLM in a closed population, particularly in the presence of a large number of lists and one or more continuous covariates.

Finally, a comparison with a Multinomial Bayesian Model (Ghosh and Norris 2005), that allows to treat the heterogeneity in absence of observed covariates, will be showed.

## 2. MATERIALS

### 2.1. *Simulated datasets*

Three datasets, different in terms of dependence among three lists and observed heterogeneity, were generated with an expected population size of 4000 subjects:

- A. Independence among the three lists + continuous covariate effect
- B. Dependence among the first two lists + continuous covariate effect
- C. Dependence among the first two lists + dependence with continuous covariate.

A. The first generated dataset is characterized by independence between sources and a significant effect of the continuous covariate.

We started by randomly assigning to each subject of a population of 4000 individuals a value of covariate extracted from a Gaussian density function  $N(40,6)$ . Then, we proceeded to divide these values into quintiles. Finally, using these five classes as strata we extracted independently 3 samples of 400 subjects so that the proportion of subjects for each strata was equal to 10%, 15%, 20%, 25%, 30% respectively.

B. In the second dataset, besides the significant effect of the continuous covariate we introduce a dependency between the first two sources.

The following extraction technique was applied to a population of 4000 individuals, each of which was associated with a value of a random normal vector  $N(40,6)$  and then categorized in five strata as in the previous point. First, we extracted a sample of 400 subjects so that the percentage of subjects for each strata was equal to 10%, 15%, 20%, 25%, 30% respectively. Then, we set aside the 20% of these subjects (80 subjects) and added the remaining 80% to the 3600 subjects not captured in the first instance to get a new population of  $3600+400*0.8 = 3920$  subjects. From this new population we drew a sample of 320 subjects in order to have a percentage of subjects in the five strata equal to 10%, 15%, 20%, 25%, 30% respectively.

Finally, we added this 320 subjects to the  $400 * 0.2 = 80$  subjects set apart after the first extraction in order to obtain an overall number of individuals marginally captured on the second occasion of 400 subjects. This technique allowed us to introduce dependency between the first and the second source. In fact, not all subjects captured the first time have the same chance of being captured in the second occasion because 80 of them are forced to be captured on both occasions. Finally, we extracted from the whole population of 4000 individuals a sample of 400 subjects, proportionally in the five strata as we did in the first occasion.

C. In the third and last dataset, besides the dependency between the first two sources and a significant effect of the covariate, we introduced also an association between the first two sources and the covariate.

The simulation procedure follows essentially that adopted in B with the only difference that the 20% of the 400 subjects drawn in the first capture (the 80 subjects set aside) was extracted proportionally from the five strata in the following proportions: 10%, 15%, 20%, 25%, 30% respectively.

For each of the three simulated datasets, the number of subjects captured from only one source (s1, s2, s3), two sources (s12, s13, s23) and three sources (s123) are reported in table 1.

TABLE 1  
*Capture profiles of the simulated datasets*

| Type of datasets | s0 | s1  | s2  | S3  | s12 | s13 | s23 | s123 |
|------------------|----|-----|-----|-----|-----|-----|-----|------|
| A                | ?  | 314 | 307 | 312 | 40  | 35  | 42  | 11   |
| B                | ?  | 233 | 321 | 312 | 120 | 29  | 41  | 18   |
| C                | ?  | 242 | 314 | 309 | 112 | 37  | 45  | 9    |

### 2.1. Real datasets: Drug users in Liguria Region(2002)

The Capture-Recapture method was widely used to assess the estimated prevalence of drug abuse in Europe: Glasgow (Frisher 1991); Dundee (Hay 1996); Amsterdam (Buster 1997); Barcelona (Brugal 1999); Cheshire (Hickman 1999); North East Scotland (Hay 2000); Brighton, Liverpool and London (Hickman 2004); Manchester (Gemmel 2004). Moreover, studies of this type was done in Australia

(Hall, 2000), Bangkok (Bohning, 2004) and Russia (Platt 2004). Following the directives of the Italian National Observatory, which in turn operates in conjunction with the European one, an integration of data from four distinct capture sources was activated in the Liguria Region. It is essential in the implementation of prevalence studies to identify and define the connection between information sources, connecting health information flows with those of social nature.

According to above considerations in this study we will take into account database from:

- s1) Public services for drug addiction (SerT);
- s2) Operational units for Drug Addiction at the Prefectures (NOT), dealing with subjects identified by the police and in possession of illegal substances, Article 75 (possession for personal use) and 121 (compulsory treatment) of the D.P.R. 309/90;
- s3) Accredited private social services, therapeutic communities (CT);
- s4) The hospital discharge records (SDO).

In the SerT list there are people with a chronic problem of drug use. Subjects in SDO list, identified by hospital discharge records, have received an ICD 9 diagnosis that refers to dependence, abuse, or poisoning by specific drug. Moreover these diagnoses have also subcategories indicating if this dependence, abuse or poisoning is continuous/episodic/in remission. The therapeutic community list (CT list) generally contains people who received a clinical evaluation and were identified as patients that may prevent chronicity if treated properly. Finally the NOT list (preventive social services list) includes subjects arrested for possession and who use illegal drugs.

Each person has an anonymous identification code and the following auxiliary variables: kind of drug, gender and age. As can be seen in Table 2 the observed data for the cocaine are much less numerous than those for the opiates. Furthermore, in some crosses there are not observed subjects and, as we will see later, this could bring to a questionable convergence in the Maximum Likelihood Estimation.

TABLE 2  
*Capture profiles of the drug users in Liguria Region (2002)*

| Drug    | s0 | s1   | s2  | s3  | s4  | s12 | s13 | s14 | s23 | s24 | s34 | s123 | s124 | s134 | s234 | s1234 |
|---------|----|------|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|------|------|------|-------|
| Cocaine | ?  | 292  | 108 | 37  | 68  | 13  | 7   | 2   | 0   | 3   | 0   | 0    | 1    | 0    | 0    | 0     |
| Opiate  | ?  | 3590 | 165 | 180 | 226 | 149 | 201 | 220 | 2   | 3   | 16  | 12   | 14   | 39   | 3    | 5     |

### 3. METHODS

#### 3.1. Capture-Recapture Method in a closed population

The simplest capture-recapture model consists of two catches and can be set out in a 2x2 table. The goal is to estimate the number of subjects not caught in both the occasions ( $n_{00}$ ). This number can be estimated using the information on subjects captured in both samples and on subjects captured only in one sample, thus providing the total population size  $N$ .

The capture-recapture model requires that three assumptions are satisfied:

A. There is no change in the population during the period under investigation; that is, there are no births, deaths or migrants (closed population). This implies that each individual in the population has a non-zero probability of being observed in all the samples.

B. For each sample, each individual has the same chance of being included in the sample (homogeneity of inclusion probabilities). If the assumption A does not hold also the assumption B will not hold, as the cases which stay in the population are clearly likely to have higher “catchability” than those who migrate or die.

C. The two samples are independent. This assumption actually follows from assumption B since the latter implies that marked and unmarked individuals have the same probability of being caught in the second sample, so that the capture in the first sample does not affect the capture in the second sample.

If the three assumptions hold, then the estimated number of subjects not caught in both the occasions ( $n_{00}$ ) is given by the well known Petersen-Estimator (or Dual-System Estimator):

$$\hat{n}_{00} = \frac{n_{10}n_{01}}{n_{11}} \quad (1)$$

and the resulting estimate of the total population size will be  $\hat{N} = \hat{n}_{00} + n_{10} + n_{01} + n_{11}$

Usually, the first assumption may be controlled by the researcher as it is sufficient to carry the two captures at a relatively short time. In contrast, the second and third assumption may not always be controlled because they are related to intrinsic characteristics of individuals belonging to the population.

In this case the estimate obtained by (1) will be distorted. For example, consider the situation where two groups of the same species have different sizes and hence the larger has a higher probability of being captured than the smaller.

Ignoring the size of the animal we violate the assumption B and hence the C, as we induce dependence between the two catches. When there are only two sources of capture, the information regarding covariates is available and the covariates may somehow affect the capture probability, a commonly used approach is to stratify the population by the covariates, to estimate the missing number in each strata by using the estimator (1) and then to pool these estimates to obtain the total population size.

Moreover, when two or more sources of capture are available, instead of stratifying according to the observed covariates, it is possible to handle the direct dependence between sources and to model the observed heterogeneity induced by covariates by using the Generalized Linear Model (GLM).

This class of models is certainly one of the most common in Epidemiology to solve problems in the capture-recapture field because it allows to treat in an easy way simultaneously both the dependence among sources and the heterogeneity.

### 3.1.1. Classical Log Linear Model and Capture-Recapture Method

In this section we briefly introduce how capture-recapture data with multiple samples and observed heterogeneity can be handled in the standard framework of the Poisson Log-Linear Model (Fienberg, 1972; Cormack, 1989; Chao 2001). We describe the case with three capture sources (Table 3) because the generalization to more than three captures is immediate.

TABLE 3  
Representation of 3 sources Capture-Recapture data by a contingency-table

| Capture 3 | Capture 2 | Capture 1     |   |
|-----------|-----------|---------------|---|
|           |           | 0             | 1 |
| 0         | 0         | $n_{000}$ (?) | 0 |
|           | 1         | $n_{010}$     |   |
| 1         | 0         | $n_{001}$     | 1 |
|           | 1         | $n_{011}$     |   |

The analysis of capture-recapture data by the Log-Linear-Model starts from the definition of a contingency table in which subjects are grouped according to one of the following capture profiles  $C = (000, 100, 010, 001, 110, 101, 011, 111)$ , where the subjects not captured in any of the three occasion ( $n_{000}$ ) are missing. For example, the profile 101 tells us that the subject was captured by the first and third source but not by the second. The Log-Linear approach allows us to model the logarithm of the expected value of the observed number of subjects in each capture profile through the following linear equation:

$$\log[E(n_{ijk})] = u + u_1 I_{(i=1)} + u_2 I_{(j=1)} + u_3 I_{(k=1)} + u_{12} I_{(i=j=1)} + u_{13} I_{(i=k=1)} + u_{23} I_{(j=k=1)}$$

where  $I_A$  is the Indicator Function of the event  $A$ .

The unknown number of subjects ( $n_{000}$ ) is given by:  $E(n_{000}) = \exp(u)$ .

To take into account the effect of a dichotomous covariate we need to include in the model a term for the covariate and interaction terms between covariate and capture profiles. The resulting model is

$$\begin{aligned} \log[E(n_{ijk|c})] = & u I_{(i=j=k=0|c=0)} + u_1 I_{(i=1|c=0)} + u_2 I_{(j=1|c=0)} + u_3 I_{(k=1|c=0)} + u_{12} I_{(i=j=1|c=0)} + \\ & + u_{13} I_{(i=k=1|c=0)} + u_{23} I_{(j=k=1|c=0)} + u_c I_{(i=j=k=0|c=1)} + u_{1c} I_{(i=1|c=1)} + u_{2c} I_{(j=1|c=1)} + \\ & + u_{3c} I_{(k=1|c=1)} + u_{12c} I_{(i=j=1|c=1)} + u_{13c} I_{(i=k=1|c=1)} + u_{23c} I_{(j=k=1|c=1)} \end{aligned}$$

In the two levels of the covariate the subjects never captured by any source will be given by  $E(n_{000|0}) = \exp(u)$  and  $E(n_{000|1}) = \exp(u + u_c)$ , where  $u$  and  $u_c$  are the intercepts related to the first and second level of the covariate and  $n_{000|0}$ ,  $n_{000|1}$  are the subjects never captured by any source in the two levels of the covariate.

The extension to more dichotomous covariates is straightforward. In situations where continuous covariates are available, Poisson Log-Linear Model may show some disadvantages associated with the need of handling such covariates in a categorized manner, as reported in the introduction.

### 3.1.2. Multinomial Conditional Logit Model and Capture-Recapture Method

Multinomial Conditional Logit Model, unlike the Poisson Log-Linear Model, can treat continuous covariates in their original measurement scale, overcoming problems regarding the Maximum Likelihood Estimation.

The MCLM or Bock's Multinomial Logit Model, which are two different parameterizations of the same model, extends the logistic approach, proposed by Huggins (1989) and Ahlo (1990) for two independent sources, to multiple dependent sources(see Zwane and van der Heijden (2005) for a more detailed discussion).

This model allows, stratifying for each subject, to model different capture probabilities for each of them according to the information regarding the overlapping sources and the individual covariates.

These probabilities  $\pi'_i = (\pi_{1|i}, \dots, \pi_{k|i}, \dots, \pi_{K|i})$  of belonging to one of K capture profiles (defined so that  $n_{k|i} = 1$  if the i-th individual belongs to the profile k and 0 otherwise) are estimated by:

$$\pi_{k|i} = \frac{\exp(\sum_{b=1}^H \sum_{j=1}^J x_{ib} \lambda_{bj} y_{jk})}{\sum_{r=1}^K \exp(\sum_{b=1}^H \sum_{j=1}^J x_{ib} \lambda_{bj} y_{jr})} \tag{2}$$

where  $x_{ib}$  are elements of the covariates matrix  $\mathbf{X}_{n \times H}$ ,  $\lambda_{bj}$  are elements of the regression parameters matrix  $\mathbf{\Lambda}_{H \times J}$  and  $y_{jk}$  are elements of the design matrix  $\mathbf{Y}_{J \times K}$ . Once estimated these quantities, it's possible to calculate the probability of

not being captured by any source:  $\hat{\pi}_{0|i} = \frac{\hat{m}_{0|i}}{1 + \hat{m}_{0|i}}$  where, for three sources,

$$\hat{m}_{0|i} = \frac{\hat{\pi}_{1|i} \cdot \hat{\pi}_{2|i} \cdot \hat{\pi}_{3|i} \cdot \hat{\pi}_{7|i}}{\hat{\pi}_{4|i} \cdot \hat{\pi}_{5|i} \cdot \hat{\pi}_{6|i}}.$$

Finally, we can get the estimated population size:

$$\hat{N} = \sum_{i=1}^n n_i + \hat{n}_{000} = \sum_{i=1}^n \hat{N}_i = \sum_{i=1}^n \left( \frac{1}{1 - \hat{\pi}_{0|i}} \right) \tag{3}$$

where  $\hat{N}_i$  represents the individual contribution to the total unknown popula-

tion. The Log-likelihood of the MCLM is given by  $l_{mult} = \sum_{i=1}^n \sum_{k=1}^K n_{k|i} \log(\pi_{k|i})$  and can be fitted with available software by exploiting the similarity of the likelihood function with that of the Stratified Proportional Hazards Model (Chen and Kuo, 2001; Zwane and van der Heijden, 2005).

### 3.1.3. Bayesian approach to Capture-recapture method

In this chapter the main characteristics of the General Mixture Model ( $M_{bb}$ ) proposed by Ghosh and Norris (2005) will be briefly described. This type of model can be seen as a Bayesian version of the MCLM previously described.

The dependency between sources (b) and the heterogeneity among subjects (h) are treated by the appropriate definition of certain parameters related to the distribution of the vector of individual capture-recapture probabilities  $(p_{1m}, p_{2m})$ , where  $p_{1m}$  and  $p_{2m}$  denote the capture chance of the m-th subject if he has not been or has been previously captured.

It is assumed that the distribution of the two-dimensional discrete distribution of this random vector  $G(p_1, p_2) = \Pr(p_{1m} \leq p_1, p_{2m} \leq p_2)$  will have a maximum of  $r=4$  support points and density distribution  $\Pr(p_{1m} = p_1, p_{2m} = p_2) = \sum_{i=1}^r \pi_i I(p = \theta_i)$ , where  $I(A)$  is the Indicator-Function of the event A and  $\theta_i = (\theta_{1i}, \theta_{2i})$ ,  $i = 1, \dots, r$ , are its support points with unknown probability  $\pi_1, \dots, \pi_r$ ,  $\sum_{i=1}^r \pi_i = 1$  and  $0 \leq \theta_{11} < \dots < \theta_{1r} \leq 1$ .

For each fixed value of  $r$  the following Multinomial Likelihood Function can be defined:

$$L(N, G) \propto \binom{N}{S} \prod_{j=1}^k \prod_{l=1}^{k-j+1} P_{jl}^{f_{jl}} \left( 1 - \sum_{j=1}^k \sum_{l=1}^{k-j+1} P_{jl} \right)^{N-S}$$

where  $S$  is the total number of subjects caught in the  $k$  catches and  $P_{jl}$  is the probability that a subject will be first captured by source  $j$  for a total of  $l$  sources.

Finally the model is completed, according to the Bayesian perspective, with the definition of the non-informative joint prior distribution of parameters.

Ghosh and Norris (2005) proposed the GGC as model selection index. This index follows the decision-theoretic framework of Gelfand and Ghosh (1998), is based on the posterior predictive distribution and can be used to compare different models. The model with the smallest GGC value is selected.



### 3.2. Model selection

One of the most critical point in the capture-recapture analysis using GLMs is the selection of the best model. In fact, it is not always easy to evaluate all possible models because of their fast growth with increasing sources and/or covariates. For example, if we consider only the capture sources, the number of all possible models is:

$$N = \sum_{k=0}^{n-1} \frac{n!}{k!(n-k)!} + 1, \quad \text{where} \quad n = \sum_{b=2}^{f-1} \frac{f!}{b!(f-b)!} + 1$$

$N$  = number of all possible models

$f$  = number of sources

$n$  = number of parameters

$b$  = order of the interaction between sources

$k$  = combination of parameters

Of course, with two sources there is only one model to be evaluated, with three sources there are 8 models and with four sources we have 1024 possible models.

With four capture sources the number of models is very large and their evaluation is impractical. So a solution may be to consider only hierarchical models. In this case the total number of model reduces to 79, according to the following formula:

$$N_G = \sum_{l=2}^{f-1} \frac{m!}{l!(m-l)!} + 1 \quad \text{where} \quad m = \frac{f!}{b!(f-b)}$$

$N_G$  = all possible hierarchical models

$f$  = number of sources

$b$  = order of the interaction between sources

$m$  = number of parameters into hierarchy

$l$  = number of combinations of parameters into hierarchy

At this point, if we want to insert some covariates in the analysis we come back to a situation where to evaluate all possible models is again not feasible in practice.

These considerations led us to consider alternative strategies to search the best model according to the number of involved sources and covariates:

a) to evaluate all possible models with only sources effect and, after adding and selecting covariates effects, to choose the best one according to AIC, BIC or BW-0.05 (only significant coefficients are present in the model). This can be considered the best strategy, but increasing the number of sources and/or covariates there are too many models to be evaluated and then it's necessary to find alternative strategies.

b) to evaluate all possible hierarchical models with only source effects and, after adding and selecting covariates effects, to choose the best one according to

AIC, BIC or BW-0.05. Furthermore, in order to restrict the analysis to a minor number of models, it can be convenient to evaluate covariates effects only on those models  $i$  having a distance  $\Delta_i \leq 10$  (in terms of AIC or BIC) from the model with minimum index.

c) to select directly the best model from all possible hierarchical models with only sources effects according to AIC, BIC or BW-0.05 and then, after adding and selecting covariate effects, to choose the best one.

### 3.3 Multi-Model approach

To overcome difficulties regarding the selection of the best model a methodology known as multi-model estimation has been proposed in literature (Burnham and Anderson 2004) in order to mitigate the error we make assuming the existence of a single optimal model. It's based on a weighted average of those models having a maximum distance of 10, in terms of AIC or BIC values, from the model with minimum index.

Once the best model is selected according to AIC or BIC, the following difference  $\Delta_i = AIC_i - AIC_{\min}$  is calculated for each  $i$ -th model, and all models with  $\Delta_i > 10$  are excluded from the analysis.

Finally, a new estimate is calculated as weighted average of the estimates obtained by all models  $i$  with  $\Delta_i \leq 10$  according to the following weights:

$$w_i = \frac{\exp(-\Delta_i / 2)}{\sum_{r=1}^R \exp(-\Delta_r / 2)} \quad (4)$$

where  $R$  is the total number of considered models.

Because it is impractical to evaluate all possible models, with increasing sources and/or covariates it's necessary to try different strategies for obtaining Multi-Model estimates:

a) to evaluate all possible models without covariates effects and to select those with  $\Delta_i \leq 10$  in terms of AIC or BIC values. To add and select covariates effects and, finally, to select the best model among the final models with covariates effects. Once checked again the distances  $\Delta_i$ , a weighted average is calculated according to  $\sum_{i=1}^n w_i \hat{N}_i$ .

b) to evaluate all possible hierarchical models with covariates effects and to select those with  $\Delta_i \leq 10$  to be used in Multi-Model estimates. In order to restrict the analysis to a smaller number of models, it can be convenient to evaluate covariates effects only on those models with a distance  $\Delta_i \leq 10$  when the covariates are without the model.

c) to select directly the best model from all possible hierarchical models with-

out covariates effects according to AIC or BIC values. Then, after adding and selecting the effects of the covariates, to use all models with a  $\Delta_i \leq 10$  into the weighted average.

#### 4. RESULTS

##### 4.1. Analysis of simulated datasets

We analyzed the three simulated datasets characterized by different types of association among capture sources and between sources and a continuous covariate. The results obtained by the MCLM and the Bayesian approach are shown and compared.

##### 4.1.1 MCLM estimates

In this section the results obtained by the MCLM are showed. We verified that the three model selection strategies, just described in Section 3.2, lead to select the same optimal models.

The analytical estimates of the total population (N), the Bootstrap-estimates and the confidence intervals, both parametric and nonparametric (Zwane and van der Heijden, 2003), are reported in Table 4.

TABLE 4  
Estimated population size (N), Bootstrap Mean, Median and 95% C.I.

| Type of dataset | Selected model                | Selection index   | Analytical N | Bootstrap Mean | C.I. (95%) Parametric | Bootstrap Median | C.I. (95%) Non-parametric |
|-----------------|-------------------------------|-------------------|--------------|----------------|-----------------------|------------------|---------------------------|
| A               | s1 s2 s3 s1x s2x s3x          | AIC, BIC, BW-0.05 | 3843         | 3901           | 3150 - 4652           | 3877             | 3250 - 4760               |
| B               | s1 s2 s3 s12 s1x s2x s3x      | AIC, BIC, BW-0.05 | 4001         | 4062           | 3253 - 4871           | 4027             | 3368 - 5009               |
| C               | s1 s2 s3 s12 s1x s2x s3x s12x | AIC, BW-0.05      | 3957         | 4037           | 3082 - 4992           | 3987             | 3252 - 5150               |
|                 | s1 s2 s3 s12                  | BIC               | 3336         | 3356           | 2816 - 3896           | 3342             | 2845 - 3972               |

x: covariate

It has already been discussed at length that the symmetric (or asymptotic) confidence intervals are inappropriate for capture recapture studies. The International Working Group for Disease Monitoring and Forecasting (1995a) noted that for all models proposed in Capture-Recapture literature the distribution of the population size estimate is skewed. In literature several authors have used a nonparametric bootstrap in the presence of continuous covariates (see Huggins, 1989; Tilling and Sterne, 1999) but, as noted by Norris and Pollock (1996), this bootstrap method could result in a variance estimate which is likely to be smaller than the true variance.

For each of the three simulated datasets we selected the optimal model according to AIC, BIC or BW-0.05. Then, from each dataset we extracted with replacement 1,000 samples of sample size equal to that observed.

For each of these samples the total population size ( $N$ ) was estimated using the model selected on the starting dataset. This procedure conducts to a final distribution of the parameter  $N$  which can be used to produce point statistics and confidence intervals both parametric and nonparametric. For each of the three simulated datasets the models selected according to the AIC showed exactly the intended simulated effects. The models selected according to the AIC and BW-0.05 estimated a total population size very close to that of the real population of 4000 subjects. In the third dataset the model selected according to the BIC yielded a heavy underestimate of the population size.

#### 4.1.2 Multi-Model estimates

Here we compare the estimates derived from the models selected by AIC and BIC with those obtained by the Multi-Model technique. When three capture sources and one covariate are present, all the three strategies previously described in 3.3 can be applied. However, our results (Table 5) did not show to be a great advantage in applying the Multi-Model technique. For BIC selected models the Multi-Model technique essentially confirmed results obtained using the best model only. For the C dataset both estimation methods underestimated the real population size. Regarding the models selected by the AIC, the estimates obtained by the Multi-Model technique seem to be slightly worse than those obtained by the single best model.

TABLE 5  
*Estimated population size by the optimal model  
and the Multi-Model technique according to AIC and BIC selection index*

| Type of dataset | Best Model estimates |      | Multi-Model estimates<br>(Strategy a and b) |      | Multi-Model estimates<br>(Strategy c) |      |
|-----------------|----------------------|------|---|------|---------------------------------------|------|
|                 | AIC                  | BIC  | AIC   | BIC  | AIC                                   | BIC  |
| A               | 3843                 | 3843 | 4033  | 3843 | 3843                                  | 3830 |
| B               | 4001                 | 4001 | 4180  | 4001 | 4166                                  | 4008 |
| C               | 3957                 | 3336 | 3107  | 3328 | 3957                                  | 3338 |

#### 4.1.3 Bayesian estimates

The simulated datasets were also processed using the Bayesian methodology. Recent developments in the software for the statistical analysis (WinBUGS, Spiegelhalter et al. 2001) permitted to apply these models and to overcome the problem of performing complex integrations, which has severely limited the application of this approach in the past. The software implements Gibbs sampling with Metropolis-Hasting steps to obtain samples from the posterior distribution. Practically, through a proper definition of the prior distribution and a Multinomial-Likelihood function we arrive to a posterior distribution of the total population size ( $N$ ) by using Markov Chain Monte Carlo (MCMC) method. Point estimates and confidence intervals can be derived from the posterior distribution.

Some problems were encountered by using this methodology such as: a long waiting times to obtain posterior distribution, the need to define a priori an upper

bound of the total population size, the lack of functionality of the proposed selection-index (GGC) and a non-convergence of the MCMC method in some circumstances.

Table 6 and Figure 1, 2 and 3 summarize nonparametric estimates of the total population size (Median, 2.5 and 97.5 percentiles of the posterior distribution) obtained for the three simulated data sets according to the upper bound a priori imposed on the distribution of the total population size.

TABLE 6  
*Bayesian estimated population size and Non Parametric C.I. according to the a priori upper bound (Bayesian Capture-Recapture model)*

| Type of dataset | Upper Bound | Median | Non Parametric C.I. (95%) | MCMC Convergence | GGC Selection Model index |
|-----------------|-------------|--------|---------------------------|------------------|---------------------------|
| A               | 15000       | 4325   | 2634-12340                | si               | 0.056                     |
|                 | 10000       | 4134   | 2503-9211                 | si               | 0.054                     |
|                 | 8000        | 4072   | 2472-8445                 | si               | 0.055                     |
|                 | 6000        | 3975   | 2508-6832                 | si               | 0.054                     |
|                 | 5000        | 3796   | 2471-5843                 | no               | 0.055                     |
|                 | 4000        | 3575   | 2474-4951                 | si               | 0.054                     |
|                 | 3000        | 3323   | 2363-4020                 | no               | 0.054                     |
|                 | 2000        | 2806   | 2271-3049                 | no               | <b>0.052</b>              |
| B               | 15000       | 4503   | 2751-11500                | si               | 0.074                     |
|                 | 10000       | 4435   | 2596-10070                | no               | 0.074                     |
|                 | 8000        | 4289   | 2590-8312                 | no               | 0.075                     |
|                 | 6000        | 4242   | 2606-6834                 | no               | 0.074                     |
|                 | 5000        | 4001   | 2628-5900                 | si               | 0.075                     |
|                 | 4000        | 3730   | 2595-4973                 | si               | 0.074                     |
|                 | 3000        | 3345   | 2418-4033                 | si               | 0.074                     |
|                 | 2000        | 2836   | 2301-3065                 | si               | <b>0.073</b>              |
| C               | 15000       | 4281   | 2487-11330                | si               | 0.0787                    |
|                 | 10000       | 4232   | 2544-9943                 | no               | 0.0782                    |
|                 | 8000        | 4094   | 2560-8225                 | si               | 0.0788                    |
|                 | 6000        | 3953   | 2577-6653                 | no               | <b>0.0787</b>             |
|                 | 5000        | 3969   | 2557-5864                 | si               | 0.0792                    |
|                 | 4000        | 3584   | 2433-4934                 | si               | 0.0788                    |
|                 | 3000        | 3308   | 2440-4023                 | si               | 0.0787                    |
|                 | 2000        | 2803   | 2278-3056                 | si               | 0.0791                    |

The analysis was performed using three support points for the posterior distribution of the parameter of interest and three Markov chains. The proposed model selection index (GGC) doesn't seem to work well in selecting an appropriate upper bound in two of the three analyzed datasets, leading to a heavy underestimate of the population size. The selected upper bound was 2000 for the A and B datasets and 6000 for the C dataset. Non parametric estimates of the population size and corresponding 95% C.I., according to the upper bound of the posterior distribution, are reported in Figures 1, 2 and 3. As can be seen there is an asymptotic trend of the median, which tends to stabilize around the expected estimate of 4000 with increasing upper bound. Finally, we observed that the confidence interval increases with the upper bound, even if the point estimates are very similar. In conclusion we can say that the most critical point in a Bayesian perspective is the choice of the upper bound for the posterior distribution. Furthermore, for the three data sets the Bayesian model does not improve the estimates of the population size obtained by the MCLM with covariates.

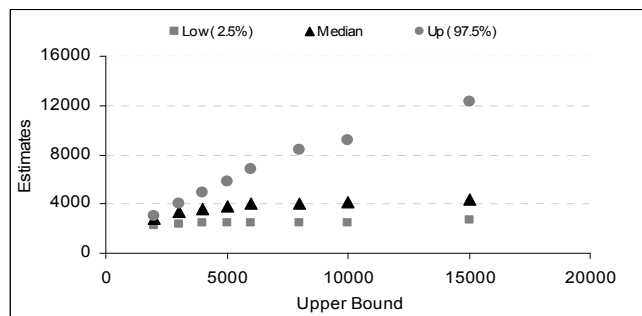


Figure 1 – Dataset A) Independence among sources and significant effect of continuous covariate: non parametric point estimates of the population size and 95% C.I. according to the upper bound (Bayesian Capture-Recapture model).

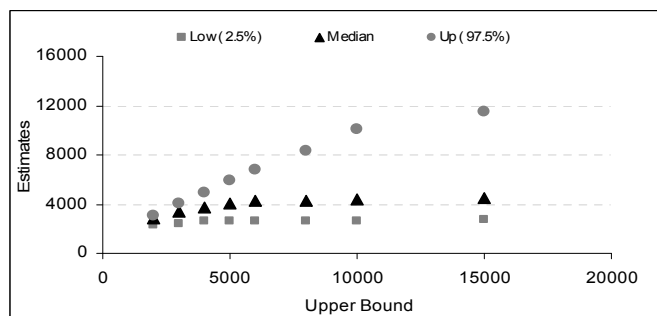


Figure 2 – Dataset B) Independence among sources and a significant effect of continuous covariate: non parametric point estimates of the population size and 95% C.I. according to the upper bound (Bayesian Capture-Recapture model).

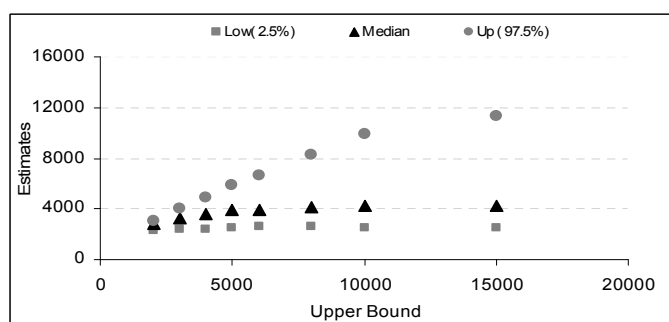


Figure 3 – Dataset C) Independence among sources and a significant effect of continuous covariate: non parametric point estimates of the population size and 95% C.I. according to the upper bound (Bayesian Capture-Recapture model).

The population size estimated by the MCLM without covariate and the Bayesian model using as upper bound 4000, that is the nonparametric upper limit of the 95% C.I. obtained using the MCLM without covariate, is reported in Table 7. The Bayesian estimates appear to be better than those obtained by the MCLM without covariate. Therefore, in absence of covariates a possible procedure to improve the estimate of the population size might be to determine the upper bound of the posterior distribution by the MCLM without covariates and then to use a Bayesian model.

TABLE 7  
*Population size estimated by the Bayesian model, with a priori upper bound equal to the upper limit of the nonparametric 95% C.I. obtained by the MCLM without covariate, compared with the population size estimated by the MCLM without covariate*

| Type of dataset | Bayes Median | Bayes Non Parametric C.I. (95%) | MCLM median | MCLM Non Parametric C.I. (95%) |
|-----------------|--------------|---------------------------------|-------------|--------------------------------|
| A               | 3575         | 2474-4951                       | 3313        | 2920-3817                      |
| B               | 3730         | 2595-4973                       | 3483        | 2947-4172                      |
| C               | 3584         | 2433-4934                       | 3342        | 2845-3972                      |

#### 4.2. Analysis of Real datasets

In this last section we compared methodologies presented above using the two real datasets. In order to obtain the estimated prevalence of opiate and cocaine users in the Liguria Region (2002) four sources of notification, one discrete (sex) and one continuous covariate (age) were used.

##### 4.2.1 Analysis without covariates

In this section the population size estimates, obtained using models without covariates, are described. The models were selected using Akaike Information Criteria (AIC), Bayesian Information Criteria (BIC) and BW-0.05. Since the total number  $n$  of models to be evaluated is too large when four capture sources are present, only hierarchical models ( $n=79$ ) were considered. The models selected by the three indices lead to different estimates. In general, the models selected by the BIC lead to lower estimates than those obtained by the models selected according to the AIC or BW-0.05 (Table 8).

For opiate users, some models selected by the AIC and BW- 0.05 were implausible even if convergent. For this reason we also considered models selected according to the second minimum AIC (AIC2).

For cocaine users, implausible estimates due to non-convergent models were found. Therefore, among convergent models we selected as best model the one with the lowest value of AIC or BIC.

Finally, Multi-Model technique seems to provide estimates very close to those obtained with the selected best models. This similarity is most marked when we consider the models selected by the BIC. Furthermore, among the models with  $\Delta_i \leq 10$ , non convergent models and/or models leading to implausible estimates were detected and excluded from the analysis.

TABLE 8  
*Analysis without covariates (Analytical and Multi-Model estimates)*

| Type of drug | Selected Models  | Selection Index  | Analytical Estimated Population Size | Analytical C.I.(95%) | Multi-Model Estimated Population Size |
|--------------|--|------------------|--------------------------------------|----------------------|---------------------------------------|
| Opiate       | s1 s2 s3 s4 s12 s13 s14<br>s23 s24 s34 s123 s124<br>s134 | AIC1,<br>BW-0.05 | 214581                               | 28368 - 1873618      | 134577 (45186°)                       |
|              | s1 s2 s3 s4 s12 s13 s14<br>s23 s24 s34 s234              | AIC2             | 13458                                | 10174 - 18758        | 17806°                                |
|              | s1 s2 s3 s4 s34  | BIC              | 8168                                 | 7806 - 8573          | 8187                                  |
| Cocaine      | s1 s2 s3 s4 s12 s13 s34                                  | AIC,<br>BW-0.05  | 16759                                | 4512-66679           | 17031°                                |
|              | s1 s2 s3 s4  | BIC              | 3447                                 | 2461-4936            | 6728                                  |

AIC1 = best AIC

AIC2 = second AIC

° = Non convergent models and/or models leading to implausible estimates were excluded from the analysis

#### 4.2.2 Analysis with covariates

In order to treat the observed heterogeneity, two covariates (sex and age) were also considered in the analysis.

In this case, characterized by too many capture sources and/or covariates, the model selection problem is not easy to solve. Strategy a) and b) aren't feasible due to an excessive number of models to be evaluated, therefore strategy c), as described in 3.2, was applied in order to find the best models according to the selection indexes. Also the Multi-Model estimates were obtained following the strategy c) as reported in 3.3. Furthermore, when covariates effects are present in the model it is not possible to derive analytical confidence intervals, therefore means, medians and nonparametric confidence intervals obtained by the bootstrap method were also assessed for the best model. The results are reported in Table 9. As can be seen, the covariates effect does not seem to be generally very strong, in fact point estimates and confidence intervals obtained from the selected models without covariates (Table 8) are very similar to those obtained from the selected models with covariates (Table 9). Also the multi model estimates were very similar to those of the best model. Furthermore, when the covariates are considered, models selected by the BIC continued to produce lower estimates than those obtained from the models selected by the AIC and/or the BW-0.05.

A further observation is that, when the bootstrap method was used, the selected model applied to some sampled datasets did not converge and/or produced implausible estimates.

Finally, the MCLM approach provided prevalence estimates of opiate and cocaine users consistent with those observed in other studies that addressed the problem of the drug addiction within the European Union. Our prevalence estimates for the Liguria Region, obtained considering four capture sources, two covariates and using as denominator the population of 15-64 years old (1,002,497 individuals) living in the Liguria Region in the 2002, were about 1.3‰ (95% C.I.: 1.0-1.9‰) for opiate users and 1.6‰ (95% C.I.: 0.7-3.6‰) for cocaine users, as obtained using the models selected by the AIC index (Table 10).



TABLE 9  
*Analysis with covariates (Analytical, Multi-Model and Bootstrap estimates)*

| Type of drug | Selection Index Without covariates | Selection Index with covariates | Analytical Estimated Size | Multi-Model Estimate | Bootstrap-Mean Estimated Size | Bootstrap-Median Estimated Size | Non Parametric Bootstrap CI (95%) |
|--------------|------------------------------------|---------------------------------|---------------------------|----------------------|-------------------------------|---------------------------------|-----------------------------------|
| Opiate       | AIC2, BW-0.05                      | AIC                             | 12734                     | 12761                | 13179                         | 12814                           | 9854-18756                        |
|              |                                    | BW-0.05                         | 12886                     |                      | 13292                         | 12921                           | 9819-19008                        |
|              |                                    | BIC                             | 13361                     | 13372                | 13824                         | 13415                           | 10187-19847                       |
|              | BIC                                | AIC                             | 8085                      | 8084                 | 8091                          | 8091                            | 7735-8485                         |
|              |                                    | BW-0.05                         | 8086                      |                      | 8092                          | 8092                            | 7736-8486                         |
|              |                                    | BIC                             | 8162                      | 8161                 | 8166                          | 8165                            | 7802-8565                         |
| Cocaine      | AIC, BW-0.05                       | AIC, BW-0.05                    | 16759                     | 16855                | 18897*                        | 16192*                          | 6868-36577*                       |
|              |                                    | BIC                             | 16759                     | 16759                | 18897*                        | 16192*                          | 6868-36577*                       |
|              | BIC                                | AIC, BW-0.05                    | 3503                      | 3484                 | 3651                          | 3527                            | 2616-5276                         |
|              |                                    | BIC                             | 3447                      | 3489                 | 3584                          | 3465                            | 2582-5148                         |

\* Bootstrap summary statistics obtained deleting implausible values from the final distribution of the parameter of interest

TABLE 10  
*Estimated prevalence ( $\times 1000$ ) obtained in similar studies*

| Country/Town | <i>Opiate</i>  |           | <i>Cocaine</i>                                       |           |
|--------------|--|-----------|--|-----------|
|              | World Drug Report 2006 (population: 15-64 years old)     | Years     | World Drug Report 2006 (population: 15-64 years old) | Years     |
| Italy        | 0.8  | 2004      | 1.02   | 2003      |
| UK           | 1.09   | 2001      | 2.04   | 2003      |
| Spain        |  |           | 2.07   | 2003      |
| London       | Hope et al. Addiction 2005 (population: 15-54 years old) |           |  |           |
| Brighton     | 1.2-1.6  | 2000-2001 | 1.5-1.9  | 2000-2001 |
| Liverpool    | 2  |           |  |           |
|              | 1.05   |           |  |           |

## 5. FINAL REMARKS

Our results, obtained using simulated and real datasets, indicate that the Multinomial Conditional Logistic Model is able to handle continuous covariates in their original measurement scale without incurring in an excessive parameterization and to produce reliable estimates of the unknown population size.

However, we found several critical points, among which the model selection in presence of many capture sources and/or covariates appears to be the main problem.

In this situation many models should be evaluated, therefore we proposed to apply a selection strategy consisting on selecting first the effects related to the dependence among sources and then the effects related to the heterogeneity due to the covariates. The Multi-Model estimation technique does not seem to make great advantages. Furthermore, different selection-indexes do not always provide consistent estimates. Selected models are not always convergent and lead to implausible estimates when the starting datasets have small counts in some intersection cells, as in the cocaine users dataset. Finally, also the Bayesian approach presents problems not easily solvable, mainly in small datasets (see cocaine users in

Table 2). Likewise, it is unclear what criterion to use for determining the upper bound of the posterior distribution.

However, on simulated data, the choice of an upper bound equal to the upper limit of the nonparametric 95% C.I. obtained from the MCLM without covariates and selected by the AIC seems to achieve results consistent with those obtained by the MCLM with covariates.

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#### SUMMARY

##### *Generalized linear models and Capture-Recapture Method in a closed population: strengths and weaknesses*

Capture-recapture methods are used by epidemiologists in order to estimate the size of hidden populations using incomplete and overlapping lists of cases. These models can be both continuous and discrete time and the particular population we want to obtain a quantitative evaluation can be assumed to be closed or open.

Here we specifically consider discrete-time models for closed population. The problem was treated using Generalized Linear Models as they allow to treat simultaneously both forms of dependence between sources than observed heterogeneity due to covariates effects.

Specifically, we analyzed the strengths and weaknesses of Multinomial Conditional Logistic Model and presented a comparison with a correspondent Bayesian approach. The estimates obtained on simulated and real data appear to be enough reliable.