



# Geographical characteristics influencing the risk of poisoning in pet dogs: Results of a large population-based epidemiological study in Italy

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## ABSTRACT

Pets can act as sentinels for human health and thus surveillance of pet dogs has the potential to improve awareness of emerging risks for animal and public health. The aim of this study was to investigate factors associated with the risk of canine poisoning. In a large population-based epidemiological investigation in Italy performed from January 2015 to January 2016 and April 2016 to April 2017, descriptive statistics were acquired and analysed to determine variables associated with poisoning events in pet dogs. Results were validated in a test population and forecast analysis of risk was performed. The cumulative incidence of poisoning events was low (10.2/1000 dogs/year). Anticoagulant rodenticides, organophosphate pesticides, metaldehyde and strychnine were the most frequent causes of intoxications. Territory characteristics significantly modulated both the frequency and the nature of the involved substances. The seashore area was associated with poisoning by rodenticides (odds ratio, OR, 1.81, 95% confidence interval, CI, 1.54–2.13) and metaldehyde (OR 1.61, 95% CI 1.16–2.28). The hill country area was associated with poisoning by organophosphate pesticides (OR 1.73, 95% CI 1.38–2.15), metaldehyde (OR 2.26, 95% CI 1.53–3.25) and strychnine (OR 1.86, 95% CI, 1.34–2.57). The mountain area was associated with strychnine poisoning (OR 3.79, 95% CI 2.84–5.06). The prospective cumulative incidence of poisoning over 10 years was 9.74% (95% CI 9.57–9.91). These results may be useful for predicting the risk of poisoning and for estimating the risk index related to specific toxic compounds in specific territories. This study suggests that poisoning events in dogs may represent a problem of public health with the potential to affect wildlife and human beings.

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## Introduction

Pet dogs share several risk factors with their owners, since they live in the same habitats and potentially are exposed to the same environmental risk factors. For this reason, pet dogs may serve as sentinels for disease in human beings (Eleni et al., 2014). An epidemiological study using the data base of the United States National Animal Poison Control Centre (NAPCC) recognised dogs as the most common sentinel animal for outdoor exposure to environmental toxins, such as insecticides and herbicides (Hungerford et al., 1995). Pet dogs respond to most poisoning events

analogously to human beings and are not necessarily affected by the same lifestyle risk factors (Backer et al., 2001). Veterinary clinics may represent a valuable source of information for epidemiological studies on potential risks to public health. Surveillance in small animal practices may be an effective tool for improving public health awareness of emerging toxicological risks (Dorea et al., 2011).

Poisoning events in pet dogs are influenced by biological variables, such as age, body weight, metabolism, sex, breed and stress, as well as environmental variables, such as indoor vs. outdoor exposure, territory characteristics and habitat (Peterson and Talcott, 2001; Wingfield, 2001; Ettinger and Feldman, 2010). In the European Union (EU), there are relatively few links among national and/or regional poison control centres for notification of accidental poisoning events (Berny et al., 2010). Furthermore, only

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a few European States are supported by such centres; these include the Centre National d'Informations Toxicologiques Veterinaires (CNITV, France), the Laboratory of Toxicology of Ghent University (LTGU, Belgium) and the Centro Antiveneni di Milano (CAV, Italy). Although the available data are fragmented and limited, and the flow of information among countries and regions is far from optimal, current toxico-epidemiological evidence indicates that poisoning in pet dogs is a frequent and serious veterinary problem in Europe (Berny et al., 2010).

In Italy, several decrees endorsed by the National Ministry of Health have made notification of intentional poisoning episodes in animals and the illegal use of poisoned baits mandatory to competent authorities. The role of institutions and professionals involved in the management of animal poisoning events have been defined, and pathological and toxicological investigations must be performed by specific public veterinary health institutions (Istituti Zooprofilattici Sperimentali).<sup>1,2,3</sup>

The relatively small number of poison control centres may be related to an underestimation of the prevalence and risk of poisoning in veterinary species. A broader knowledge of the causes and types of poisoning in pet dogs may help diagnosis, treatment and prevention of poisoning events. The aim of this study was to investigate the factors influencing the risk of poisoning in pet dogs in Italy through a large, population-based, epidemiological investigation.

## Materials and methods

### Study design

A cross-sectional study (study A) was conducted using information obtained from January 2015 to January 2016 from the data bases of 72 veterinary clinics located in central Italy. The canine population included in this phase of the study represented a training population that was used to analyse the factors associated with poisoning events in dogs.

Study A was followed by another cross-sectional study (study B) from April 2016 to April 2017. Data on poisoning events were collected from a population of dogs treated at 12 veterinary clinics located in central Italy. This population (test population) included different dogs from different territories and different dates compared to those of study A. The test population was used as a validation set to verify if the variables identified from the training population might be applicable in different territories.

### Territory characteristics, geographical distribution and source of data

The territory characteristics of the areas included in this study were classified as 'seashore' (anthropurgic), 'flat land' (anthropurgic), 'hill country' (mixed anthropurgic/synanthropic) and 'mountain' (synanthropic) habitats (see Appendix: Supplementary material). The term 'anthropurgic' refers to an ecosystem created by human beings (e.g. cultivated pastures and urban areas), whereas 'synanthropic' refers to an ecosystem that is in contact with human beings (e.g. rural areas close to national parks) (Thrusfield, 1997). The veterinary clinics included in this study were randomly selected from the centre of Italy (see Appendix: Supplementary Fig. S1). The study was performed in agreement with local ethical rules with appropriate consent (see Appendix: Supplementary material). Data on poisoning events were recorded from veterinary clinics in studies A and B (see Appendix: Supplementary Fig. S2). Poisoning events were confirmed in the training and test populations by a clinical algorithm (see Appendix: Supplementary Fig. S3), history obtained at the time of presentation, inferred diagnosis through response to treatment and laboratory analysis (Peterson and Talcott, 2001; Wingfield, 2001; Ettinger and Feldman, 2010; Khan, 2012; Bates et al., 2015). Analytical methods included gas chromatography (GC), GC-low resolution (LR) mass spectrometry (MS), GC-MS/MS, and high-pressure liquid chromatography (HPLC)-MS/MS.<sup>4</sup>

### Statistical analysis

Descriptive statistics were acquired by calculating the territorial distribution of substances causing poisoning events in dogs and the cumulative incidence of poisoning events during a period of 1 year. The analysis of variables associated with poisoning events was carried out by calculating the odds ratios (ORs) and 95% confidence intervals (95% CIs) in both the training and the test population. The forecast risk of poisoning was estimated as described by Martin et al. (1987). Regression analysis was used to compare the variables associated with poisoning events between the training and the test population in order to validate the obtained results (Thrusfield, 1997). The rezoned risk matrix tool was applied for a semi-quantitative risk assessment, as described by Ni et al. (2010). The statistical analysis was carried out using GraphPad Prism and OpenEpi<sup>5</sup> (see Appendix: Supplementary material).  $P < 0.05$  was considered to be statistically significant.

## Results

### Descriptive statistics

The topographic distribution and altitudes of the veterinary clinics included in the study area are shown in Supplementary Fig. S4 (see Appendix). Details on population characteristics of study A and B are available as Supplementary material (see Appendix). The cumulative incidence of all poisoning events detected in the training area was 10.2/1000 dogs/year (1361 events). The most frequent cause of poisoning was anticoagulant rodenticides (3.4/1000 dogs/year; 453 events), followed by organophosphate pesticides (3.0/1000 dogs/year; 394 events), metaldehyde (1.5/1000 dogs/year; 202 events) and strychnine (1.3/1000 dogs/year; 178 events). Further substances were reported as uncommon causes of poisoning, with a cumulative incidence  $< 0.5/1000$  dogs/year. The cumulative incidence of compounds leading to poisoning in dogs, arranged by territory characteristics, is detailed in Table 1. Most poisoning events occurred in the seashore territory (37.8%), whereas the flat land area had the lowest frequency of poisoning events (Table 2).

### Analysis of variables associated with poisoning events

Sex, age and body weight variables were not significantly associated with poisoning events in the training population ( $P > 0.05$ ); conversely, the territory characteristics significantly modulated both the frequency of poisoning cases and the nature of the involved substances ( $P < 0.001$ ).

The strongest associations with poisoning events were identified in the seashore (OR 1.26; 95% CI 1.13–1.40;  $P < 0.001$ ) and hill country territories (OR 1.53; 95% CI 1.34–1.74;  $P < 0.001$ ). The subset analysis matching specific substances causing poisoning with territory characteristics showed that the mountain area, but not the flat land area, was associated with an increased risk of events of poisoning. In particular, the seashore area was significantly associated with poisoning by anticoagulant rodenticides (OR 1.81; 95% CI 1.54–2.13;  $P < 0.001$ ) and metaldehyde (OR 1.61; 95% CI 1.16–2.28;  $P < 0.01$ ), the hill country was associated with poisoning by organophosphate pesticides (OR 1.73; 95% CI, 1.38–2.15;  $P < 0.001$ ), metaldehyde (OR 2.26; 95% CI 1.53–3.25;  $P < 0.001$ ) and strychnine (OR 1.86; 95% CI 1.34–2.57;  $P < 0.001$ ), and the mountain territory was strongly associated exclusively with strychnine poisoning (OR 3.79; 95% CI 2.84–5.06;  $P < 0.001$ ) (Fig. 1).

### Poisoning risk forecast

Analysis of the prospective cumulative incidence indicated an overall risk of poisoning in the training population over 10 years of

<sup>1</sup> See: <http://www.gazzettaufficiale.it/eli/gu/2009/01/17/13/sg/pdf> (accessed 9 January 2018).

<sup>2</sup> See: <http://www.gazzettaufficiale.it/eli/gu/2012/03/09/58/sg/pdf> (accessed 9 January 2018).

<sup>3</sup> See: <http://www.gazzettaufficiale.it/eli/gu/2012/03/09/58/sg/pdf> (accessed 9 January 2018).

<sup>4</sup> See: <http://www.izs.it/IZS/Engine/RAServePG.php/P/938110010525/L/0> (accessed 9 January 2018).

<sup>5</sup> See: <http://www.openepi.com> (accessed 9 January 2018).

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