Incidence rates of tumors in dogs in southern Italy – focus on the Campania region – 2018/2022

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Abstract

Neoplastic disease in dogs and humans has many similarities, including similar clinical manifestations, metastatic potential, and genomic instability. However, tumor latency is shorter in dogs, which may serve as a sentinel for the identification of carcinogenic environmental exposures. This study aims to describe the data collected in the Animal Tumor Registry (RTA) of the Campania Region in the period 2018-2022, with particular attention to the incidence rates of malignant tumors in dogs, divided by province. RTA tumor cases received by the *Istituto Zooprofilattico Sperimentale del Mezzogiorno* were analyzed; out of a total of 885 tumors, 70% were malignant, with a higher frequency in female dogs. The crude and standardized incidence rate of malignant tumors in dogs was calculated on a provincial basis. Caserta showed the highest incidence rate for both malignant tumors [incidence rate: 135.07 per 100,000; 95% confidence interval (CI): 135.01-135.13] and mammary tumors (incidence rate: 52.75 per 100,000; 95% CI: 52.69-52.80). The results highlight the importance of tumor monitoring in dogs as an indicator of potential environmental risk factors and underline the value of the RTA for the collection of data useful for the prevention and study of neoplastic diseases, as well as in humans.

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Introduction

Knowing the health status of synanthropic animals has enormous implications for human health. In fact, since these animals, especially dogs, share the same environment with humans, their health status can serve as a mirror of human health status. Neoplastic disease in dogs and humankind, in many circumstances, is characterized by the same clinical manifestation, metastatic potential, and genomic instability. The main difference is the latency, being shorter in dogs, making them a sentinel of an environmental alert. If we can understand what types of exposures are directly implicated in the mechanism of carcinogenesis in dogs, then we can apply prevention and screening measures in both species. The study of tumors in dogs can represent an important source of data on the temporal course and geographical distribution of neoplastic diseases; this information can, in turn, be useful and lay the foundation for in-depth studies of relevance not only for animals but also for human medicine (Glickman *et al*., 1983; Glickman *et al*., 1989; Hayes *et al*., 1995; Glickman *et al*., 2004). Recently, there has been an increase in the incidence of various chronic degenerative diseases in domestic animals, probably attributable to the lengthening of their life expectancy. Among these pathologies, tumors in dogs seem to be increasingly frequent (Komazawa *et al*., 2016). It has been discovered that neoplastic diseases cause up to 50% of deaths in both dogs and cats (Ciaputa *et al*., 2013). The increasing trend of tumors is believed to be attributable to various factors: nowadays, many dogs lead a life similar to that of humans, they eat too much and perhaps not always the healthiest products, they move little, they live in "high-risk" areas where it is presumed to be greater environmental contamination due especially to industrial settlements and densely populated urban areas. Tumors are one of the leading causes of death worldwide, and numerous studies have shown that exposure to environmental pollutants can play a significant role in the onset of these diseases in both humans and dogs. Toxic substances present in the environment, such as air pollutants, heavy metals, pesticides, and industrial chemicals, have been linked to an increased risk of developing various types of tumors, including lung, skin, and lymphatic cancers. Scientific research suggests that humans and dogs, being exposed to the same pollutants through air, water, and food, share similar vulnerabilities, making dogs a useful model for studying the effects of environmental pollution on tumor development.

The main tumors associated with environmental pollution include:

- lung cancer: exposure to air pollutants such as cigarette smoke, fine particles [particulate matter (PM) 2.5], and nitrogen oxides has been clearly linked to an increased risk of lung cancer. Epidemiological studies have shown that air pollution increases the risk of developing lung cancer, particularly in smokers, but also in non-smokers (Hammond *et al*., 1980; Cohen and Pope, 1995);
- skin cancer: exposure to ultraviolet radiation and other chemical agents in the environment, such as benzene and industrial chemicals, has been linked to an increased risk of melanoma and other skin cancers (Armstrong and Kricker, 2001; Yusuf *et al*., 2022);
- bladder cancer: exposure to chemical pollutants, particularly compounds containing benzene and other industrial chemicals, has been linked to an increased risk of bladder cancer, one of the most common tumors related to pollution (Letašiová *et al*., 2012; Bladder Cancer Epidemiology, 2013)
- breast cancer: some environmental pollutants, such as pesticides and industrial chemicals, have been associated with an increased risk of breast cancer. Specifically, dioxins and other persistent chemicals in the environment have been studied for their potential influence on breast health (Ma *et al*., 2024);
- leukemias and lymphomas: exposure to pesticides, organic solvents, and ionizing radiation has been linked to an increased risk of leukemias and lymphomas. Environmental pollution, particularly in areas with high industrial activity, has shown a negative impact on hematological health (Hernán *et al*., 2004);
- gastrointestinal tumors: pollutants such as cadmium, lead, and other heavy metals have been associated with an increased risk of gastrointestinal tumors, including those of the colon, rectum, and stomach (Kiani *et al*., 2021; Yan *et al*., 2025).

Both dogs and humans, at present, are increasingly exposed to additives, the effects of which are still not entirely clear. Furthermore, the increased sensitivity of tumor diagnosis must also be considered, attributable both to the improvement of diagnostic procedures and to the growing willingness of owners to diagnose and sometimes treat tumors in their pets. Synanthropic animals reflect the natural onset and evolution of typical human tumors, presenting the same genomic affinities but shorter onset and progression times; therefore, it is possible to complete research studies related to the metastatic process and to obtain survival data much more quickly than similar clinical studies conducted on humans (Gray *et al*., 2020). The collection of cases allows not only to make a comparison with the data present in the human tumor registry but also to conduct specific studies relating to a single type of tumor, such as, for example, osteosarcoma, whose annual incidence rates in dogs are significantly higher than those in humans; their relative abundance highlights their potential model for oncological research. Therefore, monitoring animal tumors can provide useful information on the evolution of the epidemiological picture also for humans, offering important support to regional prevention and public health plans (Morrison *et al*., 2025).

Over the years, the Campania Region has developed a particular scientific sensitivity regarding the in-depth analysis of the connections between environmental exposure and health, conducting several studies aimed at evaluating the effect of the correlation between environment/polluting factors and human health in a One Health perspective. In particular, the SPES study, conducted following the so-called "land of fires" emergency and the critical issues detected, has allowed us to acquire information on the spatial distribution of the sources of contamination and on the concentration of contaminants in different matrices, within the Integrated Monitoring Plan "Campania Transparent" (Pierri *et al*., 2020).

To track data and acquire useful information for the analysis of neoplastic pathologies, the Animal Tumor Registry (RTA) was established: a national information system that records new cases of tumors that occur in the canine population resident in a specific territory and classifies them based on their location and morphology. In Italy, the first population-based canine tumor registry was established in Genoa in 1985 (Merlo *et al*., 2008), followed by several other registries, such as the one in Campania (Vascellari *et al*., 2009; Baioni *et al.*, 2017).

Currently, there is a national tumor registry managed by the National Reference Center for Veterinary and Comparative Oncology (CEROVEC), which is fed by the various Italian regions; the latter, including Campania, has improved the data collection system over time to ensure increasingly standardized and usable information that is periodically sent to CEROVEC. Unfortunately, however, there are still criticisms related to the correct establishment of animal tumor registries, as data collection depends on many factors, including the incomplete or incorrect implementation of the RTA and/or the lack of data due to the failure to continue the process (Manuali *et al*., 2019).

The aim of this study was to analyze the data collected by the ATR of the Campania Region, received at the *Istituto Zooprofilattico Sperimentale del Mezzogiorno* (IZSM), over a 5-year period (2018-2022), to identify the incidence rates of tumors in dogs in the different provinces of the Campania region and identify any areas with a higher incidence of malignant tumors.

Materials and Methods

The data were extracted from: SIGLA (Laboratory Management System) of the IZSM and the national canine registry database [unified database (BDU)], which is a system for the mandatory registration of dogs in Italy. It is managed by the Veterinary Services of the AASSLL (Local Health Authorities) and contains information on registered dogs equipped with microchips, including the details of the owners and vaccinations.

Descriptive statistical analysis was performed using R version 4.3.2. (R Foundation for Statistical Computing) as the fundamental tool to conduct data analysis. Before proceeding with statistical analyses, the dataset was subjected to a cleaning phase to ensure data integrity and consistency. Subsequently, descriptive statistical analyses were performed to explore the distribution and main characteristics of the dataset. RStudio features, including graph generation, facilitated the exploratory analysis.

A descriptive analysis of the data on tumor cases in the canine species was performed, taking into account the age at first diagnosis (difference between sampling date - date of birth), sex, breed, benign/malignant tumor behavior code, and tumor localization.

The distinction between malignant and benign tumors was made based on the "Histological Classification of Tumors of

Domestic Animals" of the World Health Organization, assigning to each neoplasm the corresponding International Classification of Diseases for Oncology code, a common coding system developed from the consolidated model used in the medical field, appropriately adapted to animal species. The original dataset had some gaps in the information relating to the sex and date of birth of the dogs. In some cases, sex was easily deduced based on the type of tumor found. Regarding the date of birth, most of it was retrieved from the BDU. However, in cases where both the date of birth and the microchip information were missing, these data were eliminated from the dataset, as they were fewer than the total number of records in the dataset with all the information.

The age at diagnosis was obtained by subtracting the date of birth from the sampling date and was divided into four age classes based on the basic statistical indices of the age distribution variable (>0 to ≤3 years; >3 to ≤7 years; >7 to ≤11 years; >11 years). The dogs in the dataset were also divided into "purebred dogs" and "non-purebred dogs". The geographical representation of cases by province was performed using Q-GIS version 3.24 software.

Direct standardization was performed to compare the incidence rates of malignant tumors among the different provinces of Campania; subsequently, based on the results obtained from the descriptive analyses, a focus was carried out on malignant tumors of the mammary gland. The incidence rates were calculated per 100,000 dogs.

The standard population was identified as follows: i) identification of living dogs in the period 2018-2022; ii) the age of each dog was calculated from the difference between the date of death and the date of birth (where the date of death was empty, December 31, 2022, was inserted); iii) elimination of dogs whose sex had not been recorded; iv) creation of a new variable with the age classes, according to the statistical indices of the distribution; v) calculation of the population for the period considered divided by sex and age classes.

Data standardization is important to reduce the distortion attributable to possible confounders: without standardization, the observed differences in incidence could also be due to differences in the demographic characteristics (age, sex) of the populations under study. Indeed, neoplastic pathologies, being chronic degenerative pathologies, occur more frequently in elderly subjects. In particular, to compare the incidence rates of the mammary gland on a provincial basis, a standardization was carried out by sex in addition to age.

The non-parametric Kruskal-Wallis test was applied to evaluate the possible statistically significant difference between the standardized rates of the different provinces of the Campania region.

Results

In the 5 years considered, 885 cases of primary tumors in dogs were analyzed, of which over 70% were malignant (Table 1). 70% of malignant tumors were detected in females; in both sexes, the greatest number of malignant tumors occurred in dogs aged 8 to 11 years (Figure 1) 83% of tumors were detected in non-purebred dogs, and the majority (73%) were malignant (Figure 2).

The mean age at first diagnosis was similar in both sexes, with small differences in breed and tumor behavior: non-breed dogs were slightly older than breed dogs at first diagnosis (Table 2).

To evaluate which sites of malignant tumors were most frequent, we constructed two frequency tables, one for females and one for males: in both sexes, the most common tumors were those of epithelial origin, followed by breast cancer (26%) in females and tumors of the blood, hematopoietic system and sexual organs (16%) in males (Figure 3).

Table 1. Distribution of 885 cases of primary tumors in dogs analyzed in the period considered

Tumor behaviour	No. cases	%
Benign	242	27
Malignant	643	73
Total	885	100

Table 2. Average age at first diagnosis of cancer in dogs, broken down by sex, breed and tumor behavior.

Gender/breed	Avarage age at diagnosis/benign	Average age at diagnosis/malignant
Female/non breed dog	10.9	10.9
Male/non breed dog	10.7	10.5
Female/breed dog	9.7	8.7
Male/breed dog	8.9	9.3

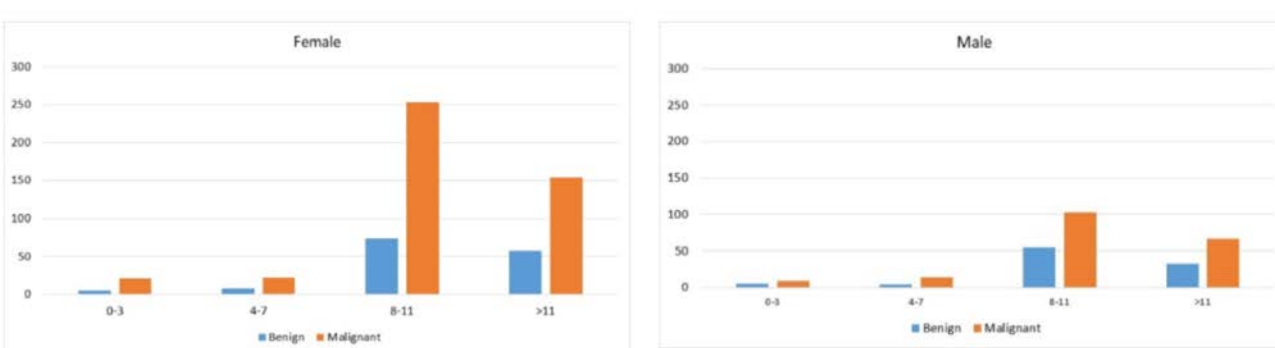

Figure 1. Histogram of the distribution of malignant tumors in dogs based on sex and age group.

The province with the highest crude incidence rate for malignant tumors was Caserta; direct standardization, by age, confirmed the crude data:

- Standardized rate Avellino: 37.23 per 100,000 [95% confidence interval (CI): 37.18-37.27]
- Standardized rate Benevento: 58.28 per 100,000 (95% CI: 58.21-58.34)
- Standardized rate Caserta: 135.07 per 100,000 (95% CI: 135.01-135.13)
- Standardized rate Napoli: 64.26 per 100,000 (95% CI: 64.23-64.29)
- Standardized rate Salerno: 82.93 per 100,000 (95% CI: 82.89-82.97)

The very narrow CIs suggest that the estimates are very precise, and the lack of overlap in the CIs indicates that the difference is statistically significant.

After calculating the standardized incidence rates for all the provinces of the Campania region, the possible presence of a statistically significant difference between the various rates was assessed.

The Shapiro-Wilk test was first applied to verify the normality of the distribution: the data are not normally distributed ($p<0.05$). Therefore, the non-parametric Kruskal-Wallis test was applied, and it was found that there is no statistically significant difference between the standardized rates of the provinces ($p>0.05$).

Below, we propose maps depicting the incidence rates of malignant tumors on a provincial basis, pre- and post-standardization (Figure 4).

The focus on breast cancer revealed the following:

- Standardized rate Avellino: 14.56 per 100,000 (95% CI: 14.52-14.59)
- Standardized rate Benevento: 15.93 per 100,000 (95% CI: 15.88-15.98)
- Standardized rate Caserta: 52.75 per 100,000 (95% CI: 52.69-52.80)

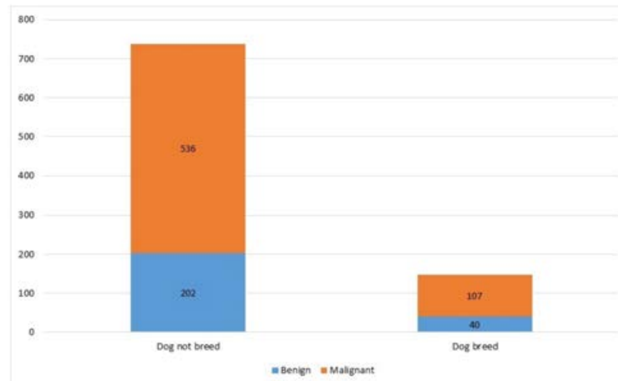

Figure 2. Histogram of the distribution of tumors in dogs based on breed.

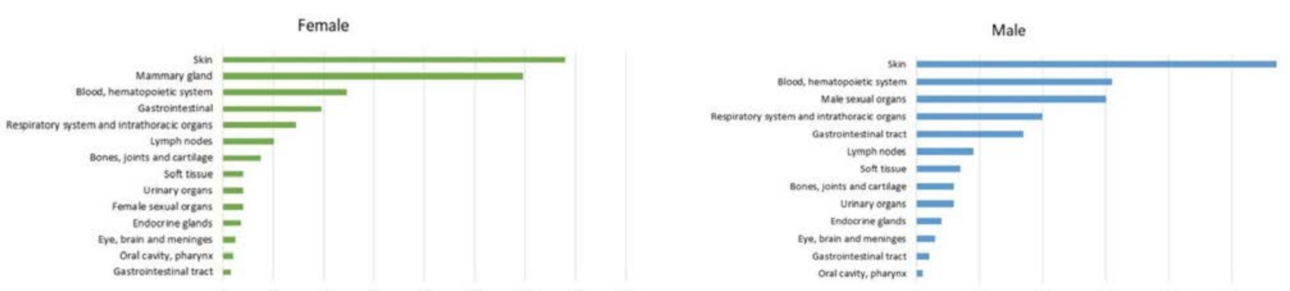

Figure 3. Histogram of the frequencies of the main types of malignant tumors divided by sex.

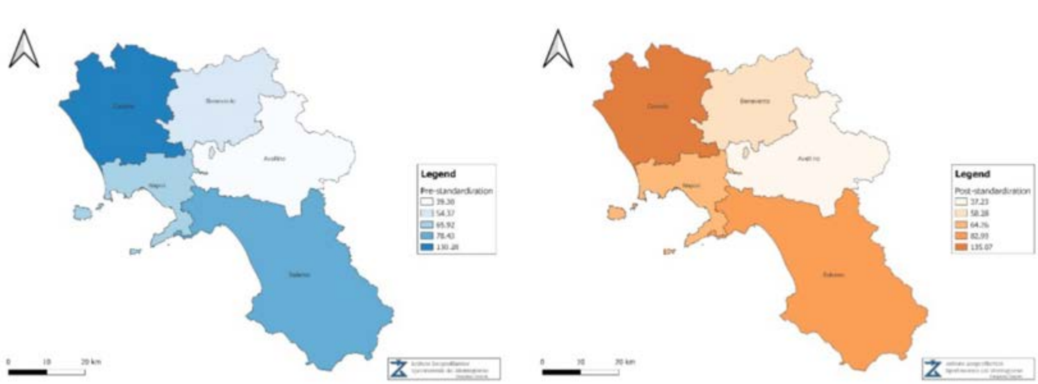

Figure 4. Distribution of the incidence of malignant tumors in the provinces of Campania, before (left) and after(right) standardization by age.

- Standardized rate Naples: 25.19 per 100,000 (95% CI: 25.17-25.21)
- Standardized rate Salerno: 30.31 per 100,000 (95% CI: 30.27-30.34)

Also, regarding breast cancer, the province with the highest incidence rate is the province of Caserta (Figure 5).

The Kruskal-Wallis test was applied to the standardized rates of breast cancer for each province to evaluate any statistically significant difference between the various provincial rates. Also in this case, with $p>0.05$, the absence of a statistically significant difference was confirmed. Below, we propose maps depicting the incidence rates of breast cancer on a provincial basis, pre- and post-standardization (Figure 6).

Discussion and Conclusions

The analysis showed a higher frequency of malignant tumors compared to benign ones, a finding that reflects the studies conducted by CEROVEC on the national territory (Crescio *et al.*, 2022). Furthermore, it was found that females develop tumors more frequently than males, which is in agreement with the results of several studies (Merlo *et al.*, 2008; Vascellari *et al.*, 2009; Brønden *et al.*, 2010; Baioni *et al.*, 2017; Crescio *et al.*, 2022). However, this result could be influenced by the higher incidence of sex-specific tumors. Of course, mammary gland tumors, as well as genital and skin tumors, which are more represented in the analyzed dataset, are more easily recognizable than visceral tumors, which require specific diagnostic tests that are sometimes very expensive and therefore difficult to implement, and which may therefore cause a lack of data (Global Burden of Disease Tumour Collaboration, 2019). In this regard, the analyzed dataset showed that most visceral tumors were diagnosed through autopsy, while most skin and mammary gland tumors were diagnosed in cases referred by private veterinarians.

The province of Caserta shows the highest standardized incidence rate for both malignant tumors and mammary gland tumors; the standardized incidence rate of breast cancer in the province of Caserta, equal to 52.75, indicates that, if the population of Caserta had the same age and sex structure as the standard population of the entire Campania region, there would be approximately 53 cases per 100,000 dogs (about double the number of the provinces of Salerno and Naples and triple that of the remaining ones). This data could be related to the territory: in other words, it could be hypothesized that the negative impact of some environmental contaminants on the onset of cancer. In this regard, it would be desirable to carry out further investigations and correlate the data on tumors with those related to environmental matrices, also taking into account what emerged from the environment-health studies; Pierri *et al.*, 2020). However, it cannot be ruled out that in some areas of the provinces of Salerno, Benevento, and Avellino, characterized by less urbanized territories than Naples and Caserta, there is a lower level of awareness and consciousness towards dogs as "pets" on the part of owners, and this could have generated a possible underdiagnosis of cancer cases due to the failure to send biopsy samples. In fact, the value obtained could be considered as perhaps underestimated, but no less reliable data, able to describe the temporal trend and the geographical distribution of the phenomenon; the results obtained suggest the opportunity to conduct in-depth and targeted studies in a One Health perspective and provide useful indications to orient and/or focus research in certain areas. The completeness of the informative case history relating to tumor cases represents a fundamental element to increase knowledge on the real distribution of tumors in the pet population and can be considered at the same time a tool for monitoring fluctuations in the onset of neoplastic pathology and its contextual geographical diffusion. In this regard, it is necessary to underline that this work represents a starting point; although it has allowed us to describe the oncological situation of the canine species in the Campania Region, confirming what was described by previous works, it has highlighted critical issues relating to the information

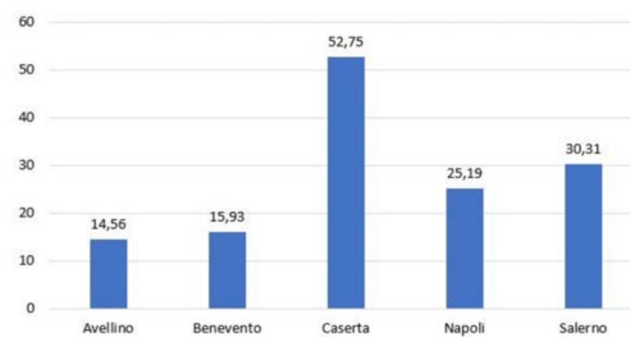

Figure 5. Histogram of the incidence of breast cancer standardized by age in the provinces of Campania.

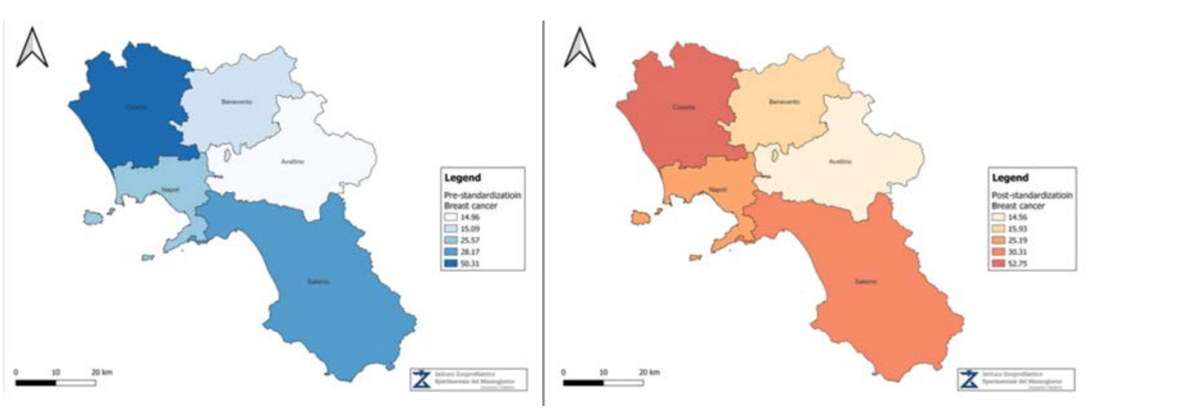

Figure 6. Distribution of breast cancer incidence in the provinces of Campania before (left) and after (right) standardization.

that represent reservations to the work itself. The results obtained must be read taking into account the explicit limitations that can potentially represent bias. The BDU source from which the denominator was obtained, *i.e.*, the population at risk in the period considered, is not completely and correctly implemented, even if over time this implementation has improved thanks to the greater degree of awareness and sensitization of the issue supported by the Campania Region. Similarly, regarding case studies, it should be noted that there may be missing cases of tumors in dogs diagnosed by freelancers: the latter, moreover, send samples for analysis to non-accredited laboratories that do not allow their inclusion in the RTA. In fact, only diagnoses provided by accredited laboratories are recorded in the tumor registry, currently only two in Campania (IZSM and University of Naples). A network is being created so that this data is not lost, given the importance of the information obtainable in light of One Health awareness and for comparative studies. The systematic and continuous implementation of the data will allow studies to be carried out on carcinogenesis factors, offering complementary ideas to traditional research approaches, and, at the same time, data analysis will help to identify the presence of geographical areas at greater risk, also creating targeted screening procedures based on territorial criticalities. Furthermore, it is not a single pollutant that causes disease, but rather a complex interaction between various environmental agents that contribute to the genesis of cancer. Scientific literature widely supports this view, indicating that the combination of multiple pollutants, rather than a single compound, is often responsible for the toxic and carcinogenic effects observed. Recent studies have shown that combined exposure to air pollutants (such as PM 2.5 fine particles and exhaust fumes) together with industrial chemicals (such as heavy metals or pesticides) can increase adverse health effects and contribute to an increased risk of cancer. The synergistic interaction between these substances can actually have an impact greater than the sum of the individual effects, creating an environment favorable to mutagenesis and carcinogenesis. Furthermore, individual susceptibility plays a crucial role, since various factors such as genetics, nutritional status, age, and pre-existing health conditions influence the body's response to exposure to pollutants. Therefore, it is essential to consider not only the nature of individual pollutants but also their combination and interaction with biological factors that determine individual responses. In conclusion, to address biases and improve the understanding of the mechanisms underlying cancer risk related to environmental pollution, it is essential to adopt an integrated approach that considers the multiple exposures and interactions between various agents. The combination of detailed environmental data, genetic information, and advanced statistical models will allow a better analysis of the complex interactions between pollutants and individual factors. Longitudinal studies on different cohorts and the adoption of standardized diagnostic guidelines will help reduce data variability and improve the quality of diagnoses. Furthermore, it is crucial to improve veterinary awareness and diagnostic infrastructure, ensuring accurate and timely collection of cases. Finally, a multidisciplinary approach, in line with the One Health perspective, will facilitate the investigation of the connections between human, animal, and environmental health, thus providing a solid basis for future research and targeted prevention policies.

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