



NEOPLASTIC DISEASE

The Swiss Canine Cancer Registry: A Retrospective Study on the Occurrence of Tumours in Dogs in Switzerland from 1955 to 2008

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Summary

Diagnostic records are a key feature of any cancer epidemiology, prevention or control strategy for man and animals. Therefore, the information stored in human and animal cancer registries is essential for undertaking comparative epidemiological, pathogenic and therapeutic research. This study presents the Swiss Canine Cancer Registry, containing case data compiled between 1955 and 2008. The data consist of pathology diagnostic records issued by three veterinary diagnostic laboratories in Switzerland. The tumours were classified according to the guidelines of the International Classification of Oncology for Humans on the basis of tumour type, malignancy and body location. The dogs were classified according to breed, age, sex, neuter status and place of residence. The diagnostic data were correlated with data on the Swiss general dog population and the incidence of cancer in dogs was thus investigated. A total of 67,943 tumours were diagnosed in 121,963 dogs and 47.07% of these were malignant. The most common tumour location was the skin (37.05%), followed by mammary glands (23.55%) and soft tissue (13.66%). The most common tumour diagnoses were epithelial (38.45%), mesenchymal (35.10%) and lymphoid tumours (13.23%). The results are compared with data in other canine registries and similarities in tumour distribution and incidence are noted. It is hoped that this study will mark the beginning of continuous registration of dog tumours in Switzerland, which, in turn, will serve as a reference for research in the fields of animal and human oncology.

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Keywords: cancer registry; dog; epidemiology

Introduction

Cancer is a leading cause of death in man and dogs (Pinho *et al.*, 2012); however, current medical research is hampered by the complex biology of the disease. Murine cancer models are highly standardized and have contributed tremendously to knowledge of cancer mechanisms and treatment regimes, but such models are often limited in representing spe-

cific aspects of spontaneously arising human cancer such as long time latency, recurrence and metastasis (Porello *et al.*, 2006; Thamm and Dow, 2009; Martić-Kehl *et al.*, 2012; Ranieri *et al.*, 2013). Such information is best derived from cancer registries, which provide data on the epidemiology of cancer over space and time. In many countries, human cancer registration has been practiced since the 1940s (Bronden *et al.*, 2007).

Companion animal cancer registries were introduced in the 1960s, following increasing mortality

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due to spontaneously arising tumours. The study of companion animal tumours offers benefits not only for animal epidemiology, but also for comparative epidemiological, pathogenic and therapeutic research. Companion animals have a life span that allows them to develop tumours resembling equivalent human cancers in their morphology and biological behaviour. Companion animals also benefit from oncological therapies that are used in human medicine. Companion animals share the same environment as their owners and can therefore act as sentinels for recognition of environmental factors implicated in oncogenesis (Bukowski and Wartenberg, 1997; Backer *et al.*, 2001; Gamlem *et al.*, 2008; Marconato *et al.*, 2009; Bettini *et al.*, 2010). Companion animals, and dogs in particular, share significantly more of their genome with man than do rodents (Pinho *et al.*, 2012). Therefore, investigations of spontaneously arising cancer in dogs can provide a partial alternative to animal testing (Bukowski and Wartenberg, 1997; Thamm and Dow, 2009).

In the 1960s and 1970s three population-based animal registries were reported in the USA: the California Animal Neoplasm Registry (1963–1966; Dorn, 1967), the Kansas University Neoplasm Registry (1961–1971; Strafuss, 1976) and the Tulsa Registry of Canine and Feline Neoplasms (1972–1977; MacVean *et al.*, 1978). Since the late 1980s several animal cancer registries have been established and are still being updated: the Purdue Comparative Oncology Program (since 1979; Purdue Comparative Oncology Program, 2006), the Cancer Registry and Surveillance System for Companion Animals, Cornell (since 1980; Page, 2004), the Animal Tumour Registry of Genoa (since 1985; Merlo *et al.*, 2008), the Norwegian Cancer Project (since 1990; Gamlem *et al.*, 2008), the VetCancer Registry (since 1994; Brønden *et al.*, 2007), the Registry on Canine Tumours in Sweden/Agria (since 1995; Egenvall *et al.*, 2011), the Danish Veterinary Cancer Registry (since 2005; Brønden *et al.*, 2010), the Animal Tumour Registry of the Vicenza and Venice provinces (since 2009; Vascellari *et al.*, 2009) and the Guelph Companion Animal Cancer Epidemiologic Registry (since 2010; Nødtvedt *et al.*, 2011).

The Swiss Canine Cancer Registry (1955–2008) was assembled as part of the project ‘One Medicine – One Oncology: Incidence and Geographic Distribution of Companion Animal Cancer in Switzerland, 1955–2008’. Additionally, the project benefits from information about the general canine population at risk, since microchipping and registration of dogs in Switzerland has been compulsory since 2006. The general dog population was surveyed with an accu-

racy reaching 95% in 2008 (personal information, Gesellschaft Schweizer Tierärztinnen und Tierärzte, the Swiss Society of Veterinarians). These latest data, together with data originating from previous research on the Swiss general dog population, allows data in the registry to be analysed against the background of the total population of dogs in Switzerland (Pospischil *et al.*, 2013).

The aim of this paper is to present the Swiss Canine Cancer Registry, which was compiled between 1955 and 2008. Data consists of pathology diagnostic records issued by three veterinary diagnostic laboratories in Switzerland. The tumours were classified according to the guidelines of the International Classification of Oncology for Humans (ICD-O-3) on the basis of tumour type, malignancy and body location (WHO, 2013). The dogs were classified according to breed, age, sex, neuter status and place of residence. The analysis provides a retrospective overview of the incidence of malignant and benign neoplasms in the Swiss canine population. The findings are related to the general dog population and the tumours are characterized by type, biological behaviour, body location, age of animal and diagnostic method.

Materials and Methods

Data Source

The dog tumour registry comprises 121,963 diagnostic records provided by three veterinary diagnostic laboratories in Switzerland: the Vetsuisse Faculty, Institut für Veterinärpathologie, Zürich (IVPZ), the Institut für Tierpathologie, Bern (ITP) and the Zyto-Histo Diagnostics private veterinary diagnostic laboratory (based in Rorbas Freienstein).

The IVPZ provided three sets of diagnostic records ($n = 97,759$; 1955–2008) from canine post-mortem, biopsy and cytology samples. The datasets originated from three time periods during the history of this institution. The IVPZ-GL (1955–1964) provided 3,797 records from canine post-mortem samples. These records were originally handwritten documents that were later digitized in an Excel file. The IVPZ-SLK (1964–1988) provided 33,100 records from canine post-mortem and biopsy samples. These records were originally transcribed onto punch cards using diagnostic key words (Keydex, Fa. Royal McBee; Stünzi and Lott-Stolz, 1967) and were digitized by Scydoc, an external company based in Zug, Switzerland. The results were crosschecked using the original typed reports. The IVPZ-APPX (1987–2008) provided 60,862 records from canine post-mortem, biopsy and cytology samples. The records were stored in the electronic patient record

system of the IVPZ. In 1987, when the digitized collection of data started, a punch card system was still used. There was no overlapping of data since dogs were only recorded in one system.

The ITP provided a set of diagnostic records ($n = 20,674$; 1983–2008) from canine post-mortem and biopsy samples and Zyto-Histo Diagnostics provided a set of diagnostic records ($n = 3,530$; 2007–2008) from canine biopsy samples. All samples from the IVPZ, ITP and Zyto-Histo Diagnostics were examined by histopathology.

Data Preparation

The datasets were compiled in a FileMaker database, which was exported into a Stata database (StataCorp LP, College Station, Texas, USA). Individual diagnostic records were standardized according to age, sex, neuter status and breed. The diagnoses were then coded according to the tumour topographical and morphological keys of the ICD-O-3 (Tables 1 and 2) and checked for plausibility using the original patient records. All tumour diagnoses were confirmed by histopathology. Epidermal cysts were excluded. Diagnoses were grouped for future comparison with human cancer and for this reason some of the groups may be unusual for veterinary pathologists. The groups are described in Table 3. The term ‘epithelial tumour’ is used in two different ways: firstly as an overall group including all types of epithelial tumours and secondly as a narrow group: ‘epithelial* tumour’ (Table 3).

Tumour groups included both malignant and benign tumours (i.e. adenoma and adenocarcinoma

Table 1
Coding and grading of tumour diagnoses according to ICD-O-3

Diagnosis	ICD-O code
Odontogenic neoplasia	ICD-O 9270–9330
Trophoblastic tumours	ICD-O 9104
Epithelial tumour	ICD-O 8010–8587, ICD-O 9050–9058
Germ cell tumour	ICD-O 9060–9085
Lymphangioma, lymphangiosarcoma	ICD-O 9590–9960
Lymphoid tumour	ICD-O 9590–9960
Melanoma	ICD-O 8720–8730
Mesenchymal tumour	ICD-O 8680–8711, ICD-O 8800–9040, ICD-O 9120–9150, ICD-O 9580
Skeletal tumour	ICD-O 9180–9262
Neural tumour	ICD-O 9380–9570
Gonadal tumours	ICD-O 8610–8670
Unspecified tumours	ICD-O 8000

Table 2
Coding of tumour locations according to ICD-O-3

Location	ICD-O C code
Blood, haemopoietic system	ICD-O C 42
Neoplasia of bones, joints, cartilage	ICD-O C 40–41
Brain, meninges, other parts of CNS	ICD-O C 70–72
Mammary gland	ICD-O C 50
Endocrine gland	ICD-O C 73–75
Gastrointestinal tract	ICD-O C 16–26.8
Lymph nodes	ICD-O C 77
Male sexual organs	ICD-O C 60–63.2
Oral cavity, pharynx	ICD-O C 2.9–11
Other female sex organs	ICD-O C 51–58
Peripheral nerves, autonomic nervous system	ICD-O C 47
Respiratory system, intrathoracic organs	ICD-O C 30–39
Retroperitoneum, peritoneum	ICD-O C 48
Skin	ICD-O C 44
Soft tissues	ICD-O C 49
Urinary organs	ICD-O C 67–68

were categorized as one group ‘adenoma, adenocarcinoma’). Each diagnostic record gave information about the tumour malignancy grade in an additional field. To investigate malignancy, each tumour group was divided into ‘benign’ (malignancy grade 0–2) and ‘malignant’ (malignancy grade 3–6) according to the ICD-O-3 classification. Because benign tumours can develop into malignant tumours of the same type, tumours such as adenoma and adenocarcinoma were not treated as separate groups. The same procedure was applied to related tumour groups; for example, lymphangioma and lymphangiosarcoma, osteoma and osteosarcoma, naevi and melanoma, myxoma and myxosarcoma. As different pathologists had worked on the samples, there were two different approaches to specifying the location of fibrosarcomas in subcutaneous tissue. Some pathologists used ‘skin’ as the location because skin biopsy was used to collect the sample, while others used ‘soft tissue’ to describe the origin of the tumours. We combined these two locations and recoded ‘skin’ as ‘soft tissue’ for fibrosarcomas.

Breed allocation was based on information in the diagnostic records. Mixed breed dogs were assigned according to the first-named breed or were classed non-specifically as crossbreed dogs. The 17 most common breeds, each comprising >900 individuals, were investigated further. The remaining breeds and records in which breed was recorded as ‘unknown’ were listed as ‘other breeds’. The breed category ‘shepherd’ included German shepherd dogs, Beauceron Berger de Beauce, white shepherd dogs, Berger de Picardie, Berger de Savoie, Berger des Pyrénées, Groenendael, Laekenois, Malinois and Tervueren. Diagnostic records for dogs residing outside Switzerland were excluded from the analysis.

Table 3
Example of tumour grouping for four selected groups

<i>Diagnosis group</i>	<i>Single diagnosis</i>	<i>Number</i>	<i>Percentage [%]</i>	
Skeletal tumour ICD-O 9180–9262	Adamantinoma of long bones	103	8.7	
	Chondroblastoma	22	1.86	
	Chondroma, fibrochondrosarcoma	168	14.19	
	Osteochondroma	11	0.93	
	Osteofibroma	38	3.21	
	Osteoma, osteosarcoma	842	71.11	
Total of skeletal tumours		1,184	100	
Gonadal tumours ICD-O 8610–8670	Granulosa cell tumour, granulosa cell carcinoma	93	8.72	
	Leydig cell tumour	450	42.17	
	Luteoma	9	0.84	
	Sertoli cell adenoma, Sertoli cell carcinoma	423	39.64	
	Sertoli-Leydig cell tumour	92	8.62	
Total of gonadal tumours		1,067	100	
Gonadal germ cell tumour ICD-O 9060–9085	Embryonal carcinoma	3	0.45	
	Seminoma	632	95.47	
	Teratoma	8	1.21	
	Germ cell tumours	19	2.87	
Total of germ cell tumours		662	100	
Epithelial tumour ICD-O 8010–8587, ICD-O 9050–9058	Adenocarcinoma of anal glands	2,421	9.27	
	Adenocarcinoma with squamous metaplasia	190	0.73	
	Adenoma, adenocarcinoma	12,348	47.27	
	Adenomatous polyp, adenocarcinoma in adenomatous polyp	321	1.23	
	Adrenal cortical adenoma, adrenal cortical adenocarcinoma	168	0.64	
	Basal cell carcinoma, adenoma	499	1.91	
	Carcinoma, anaplastic type	296	1.13	
	Cholangioma, cholangiocarcinoma	48	0.18	
	Composite carcinoid	43	0.16	
	Epithelial* tumour ICD-O 8010–9053	1,677	6.42	
	Epithelioid mesothelioma	37	0.14	
	Epithelioma	958	3.67	
	Hepatoma, hepatocarcinoma	155	0.59	
	Insulinoma	52	0.2	
	Intracystic papillary adenoma, intracystic papillary adenocarcinoma	79	0.3	
	Intraductal papilloma, intraductal papi	12	0.05	
	Mesothelioma, biphasic, malignant	42	0.16	
	Multifocal superficial basal cell carcinoma	231	0.88	
	Papillary adenoma, adenocarcinoma	112	0.43	
	Papillary carcinoma	871	3.33	
	Pilomatrixoma	503	1.93	
	Pulmonary adenomatosis, bronchiolo-alveolar adenocarcinoma	45	0.17	
	Sebaceous adenoma, sebaceous adenocarcinoma	1,456	5.57	
	Secretory carcinoma of the mammary gland	329	1.26	
	Spindle cell carcinoma	72	0.28	
	Squamous cell carcinoma	1,324	5.07	
	Squamous papillomatosis	10	0.04	
	Sweat gland adenoma, sweat gland adenocarcinoma	427	1.63	
	Thymoma	96	0.37	
	Transitional cell papilloma, transitional cell carcinoma	168	0.64	
	Trichoepithelioma	1,132	4.33	
	Total of epithelial tumours		26,122	100

Results

Dataset

A total of 121,963 dogs were examined through histopathology, of which 63,214 (51.83%) were diagnosed with tumours. Of those, 59,124 (93.53%) had a single tumour and 4,090 (6.47%) had multiple tumours. A to-

tal of 35,232 (52.93%) of the tumours were benign and 31,336 (47.07%) were malignant. The proportion of tumour bearing patients versus patients without a tumour differed according to the method of examination: by biopsy histopathology 64.81% of the patients were diagnosed with a tumour, by cytological examination 41.96% and by post-mortem examination 31.04%.

Table 4
The 17 most common breeds out of a total of 183 breeds among 121,963 dogs

Breed	Number	Percentage [%]
Shepherd	12,354	10.13%
Crossbreed	12,193	10.00%
Retriever	11,429	9.37%
Swiss Mountain dog	7,774	6.37%
Poodle	7,214	5.91%
Dachshund	6,499	5.33%
Boxer	6,368	5.22%
Schnauzer	2,796	2.29%
Collie	2,206	1.81%
Yorkshire terrier	2,157	1.77%
Cocker spaniel	2,127	1.74%
Setter	2,105	1.73%
Great Dane	1,598	1.31%
Doberman pinscher	1,596	1.31%
Rottweiler	1,470	1.21%
West Highland white terrier	1,316	1.08%
Bulldog	1,016	0.83%
Parson Jack Russell terrier	981	0.80%
Other breeds (including dogs of unknown breed)	38,764	31.78%
Total of all breeds	121,963	100%

Breed Distribution

The dataset included 182 different dog breeds ($n = 101,281$). A large number of these were cross-breeds ($n = 12,193$) and some were of unclassified breed ($n = 8,489$). The most frequent breed was the Shepherd dog (10.13%), closely followed by cross-breeds (10.00%) and retrievers (9.37%) (Table 4).

Incidence Rates

Fig. 1 shows the influence of the examination methods on the annual tumour incidence rate. Post-mortem examination had a relatively stable annual incidence rate: 13 cases of neoplasia per 100,000 dogs in 1955 and 20 cases in 2008. A peak of 65 cases per 100,000 dogs was observed in the 1980s. Conversely, the overall annual tumour incidence rate rose from 13 cases of neoplasia per 100,000 dogs in 1955 to 695 cases in 2008. This trend is comparable with the rise in the incidence rate of biopsy and cytology cases, which increased from 141 cases of neoplasia per 100,000 dogs in 1968 to 675 cases in 2008.

Distribution of the Most Common Diagnoses

The most common tumours were epithelial (38.45%), mesenchymal (35.1%), lymphoid (13.23%), melanoma (3.90%), skeletal (1.74%) and gonadal tumours (1.57%). Fig. 2 presents a more detailed distribution of the diagnoses, with adenoma and adenocarcinoma (32.62%) at the top (see Fig. 3).

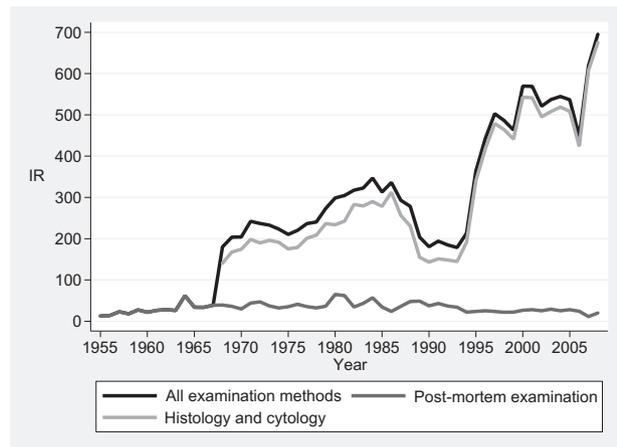


Fig. 1. The influence of examination methods on the annual tumour incidence rate (IR; i.e. number of tumours diagnosed per 100,000 dogs in the Swiss dog population).

The Most Prevalent Diagnoses over Time (1955–2008). The proportion of epithelial tumours declined from 45.65% in 1955 to 34.46% in 2008, while the proportions of mesenchymal and lymphoid tumours, melanoma and gonadal tumours rose. Mesenchymal tumours rose from 28.26% in 1955 to 34.36% in 2008, lymphoid tumours from 8.70% to 14.69%, melanoma from 0.00% to 5.18% and gonadal tumours from 0.00% to 2.47% (Fig. 2).

Malignancy of the Most Common Tumour Diagnoses. Of the total tumours, 47.07% were malignant. The following tumour groups had malignancy rates higher than the overall rate: skeletal tumours (96.61%), melanoma (87.21%), gonadal germ cell tumours (86.38%), epithelial tumours (56.52%) and lymphoid tumours (52.79%). The following tumour groups had malignancy rates lower than the overall

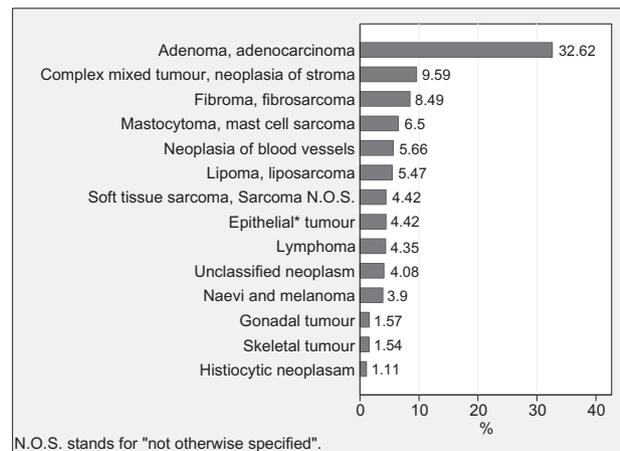


Fig. 2. Detailed most common tumour diagnoses (>1% of $n = 67,943$).

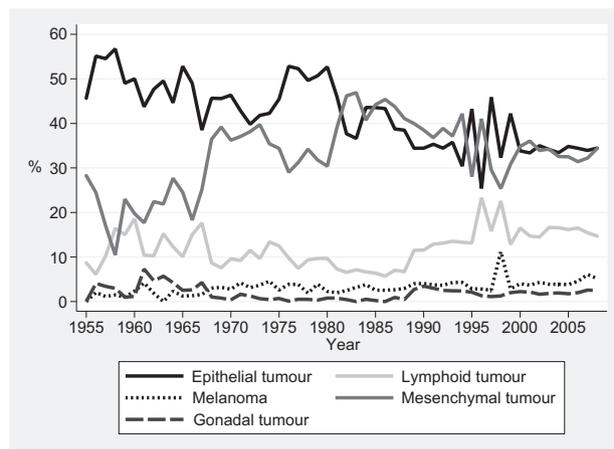


Fig. 3. The yearly most prevalent tumour diagnoses. The percentage of a tumour type among all tumour types diagnosed per year.

rate: neural tumours (43.38%), unclassified neoplasms (32.6%), mesenchymal tumours (29.65%), lymphangioma and lymphangiosarcoma (16.09%), gonadal tumours (8.15%) and odontogenic tumours (2.67%). Fig. 4 presents the malignancy rate of the most frequently occurring tumour groups.

A more accurate grouping shows that the following tumour groups had malignancy rates higher than the overall rate: mesothelial neoplasia (100%), complex epithelial neoplasia (99.47%), leukaemia (99.39%), transitional cell papilloma, transitional cell carcinoma (98.21%), other neoplasia of bones (96.45%), osteoma and osteosarcoma (95.49%), glial neoplasia (94.26%), epithelial* tumour (89.97%), soft tissue sarcoma (88.24%), naevi and melanoma (87.21%), gonadal germ cell tumour (86.38%), myxoma and

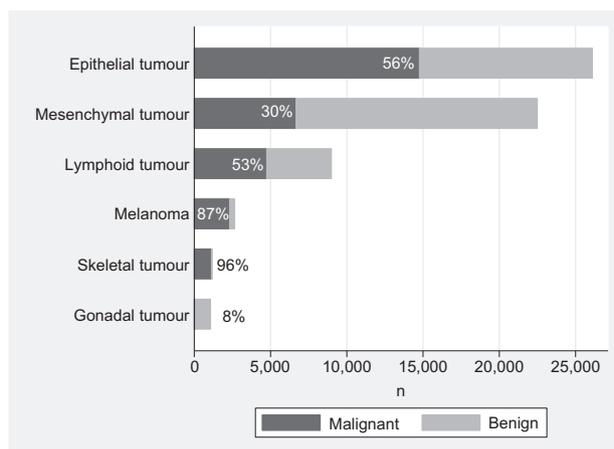


Fig. 4. Absolute (n) and relative (%) distribution of the malignancy in tumour diagnoses. In this figure, epithelial tumour includes ICD-O 8010–8587 and ICD-O 9050–9058.

myxosarcoma (83.24%), plasma cell neoplasia (82.44%), synovia-like neoplasia (53.49%), histiocytic neoplasia (52.13%), adenoma and adenocarcinoma (50.79%) and paraganglioma (48.5%).

Location of Tumours

Most of the tumours were located in the skin (32.29%), the mammary gland (20.53%) and the soft tissue (11.90%). Fig. 5 shows that the frequency of tumours in all other locations was below 10%. Due to the evaluation of all organs in post-mortem investigations, the distribution of locations of tumours is unbiased, as compared with biopsy and cytology samples (Fig. 6). The gastrointestinal tract (11.40%) and the respiratory system (10.63%) were the leading tumour locations. The largest variety of tumour types was found in the mouth and the pharynx, where seven different tumour types were identified (Fig. 7).

Age Distribution

The age distribution of the cases (Fig. 8) shows that most dogs, irrespective of tumour presence, were between 5 and 10 years of age (48.79%). Another large group consisted of dogs >10 years of age (21.42%). Only 16.80% of the dogs were between 1 and 5 years of age, and the group of dogs <1 year of age (6.84%) mainly consisted of animals without tumours (see Figs. 9 and 10).

Discussion

To our knowledge, the figures of 121,963 dogs and 67,943 tumour diagnoses collected over 53 years renders the Swiss Canine Cancer Registry the most comprehensive animal cancer registry at a national

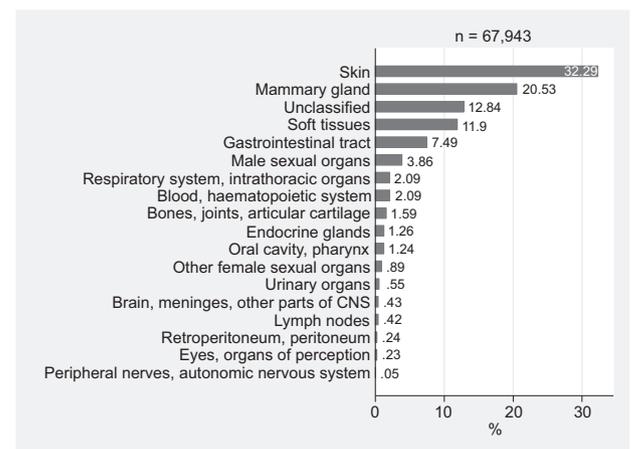


Fig. 5. Distribution of tumour locations diagnosed by all examination methods. n , number of all samples; %, proportion of tumour location.

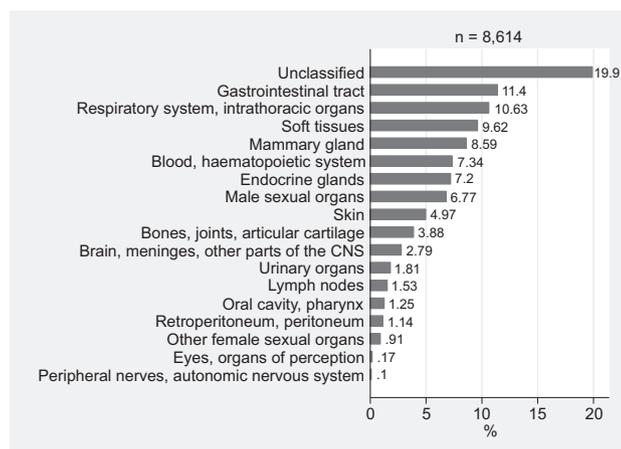


Fig. 6. Distribution of tumour locations diagnosed by post-mortem investigation. *n*, number of post-mortem samples; %, proportion of tumour location.

level. However, there are some shortcomings, which are typical of long-term retrospective studies. One such issue is that diagnoses were made by different pathologists at different time periods. The criteria for certain diagnoses may have changed over time and in some cases there may be a subjective factor in histopathological diagnostics. This problem was overcome by restricting data evaluation to those tumour entities that could be clearly identified and that have been known for a long time.

The yearly distribution of breeds in the Swiss Canine Cancer Registry reflects the change in breed fashion in the Swiss dog population (Pospischil *et al.*, 2013). In the 1950s and 1960s, poodles (13.80%), shepherds (12.66%), crossbreeds (10.61%), boxers (9.75%) and dachshunds (9.69%) were the most common breeds. From 1970 to 2008 the most common breeds were crossbreeds (10%), retrievers (9.97%), shepherds (9.87%) and Swiss Mountain dogs (6.53%).

During the study period, the Swiss dog population increased constantly and the relative tumour incidence rose dramatically, from 13 cases per 100,000 dogs at risk in 1955 to 695 in 2008. This trend could be explained by selection bias, due to the availability of new diagnostic methods, namely biopsy sampling (since 1968) and fine needle aspiration (since 1991). This trend may also have been influenced by a rising prevalence of tumours in dogs. In fact, similar to man, the life expectancy of dogs has risen continuously since 1955, due to advancements in veterinary medicine. An increased life expectancy, however, makes dogs more susceptible to tumours, since tumours tend to develop at an older age (Bonnett and Egenvall, 2010).

On the other hand, the tumour incidence rate in post-mortem samples did not increase over time. This might be explained partly by the decreasing relative number of post-mortem investigations, as dog owners increasingly tend to refuse a post-mortem examination. Moreover, since the introduction of biopsy sampling, tumours may have been diagnosed before death, so that a post-mortem investigation was no longer necessary.

Several additional factors may have contributed to the increasing canine tumour incidence rate in Switzerland. Firstly, the change in the role of dogs in society, from working dogs to family members, fully entitled to veterinary care, diagnostic examinations and therapeutic interventions. Secondly, the standard of living has generally risen over the years and dog owners can afford systematic diagnostic examinations. Thirdly, the density of licensed veterinary practices increased from two practices per 100,000 dogs to 346 practices per 100,000 dogs in Switzerland between 1955 and 2008 (personal information, *Gesellschaft Schweizer Tierärztinnen und Tierärzte*, the Swiss Society of Veterinarians). Fourthly, the evolution of environmental risk factors (e.g. UV radiation or air pollution) may have encouraged tumour development (Reif and Cohen, 1979; Porello *et al.*, 2006). Environmental factors responsible for dog tumours should be investigated in future research.

It is generally difficult to compare tumour incidences between animal cancer registries because of differences in the sampling methods (MacVean *et al.*, 1978; Brønden *et al.*, 2007, 2010; Vascellari *et al.*, 2009; Egenvall *et al.*, 2011). In order to estimate the population at risk, a telephone survey was undertaken in Northern Italy (Vascellari *et al.*, 2009). Data were collected from an animal health insurance company (Agria Ltd.) in Sweden (Egenvall *et al.*, 2011) or by counting the 'veterinarian-using' dogs in Tulsa, USA (MacVean *et al.*, 1978) and by legally regulated dog registration in Denmark in the Danish Dog Registry (Brønden *et al.*, 2010) and, since 2006, in Switzerland.

However, in Switzerland, the tumour incidence rate for 2008, which reached a value of 695 cases per 100,000 dogs, lies midway between the rates of other countries. For example, 282 cases per 100,000 dogs were observed in Northern Italy (Vascellari *et al.*, 2009), 500 cases per 100,000 dogs in Sweden (Egenvall *et al.*, 2005), 748 cases per 100,000 dogs in the UK (Dobson *et al.*, 2002) and 1,416 tumours per 100,000 dogs in Tulsa, USA (MacVean *et al.*, 1978). The observed malignancy distribution (47.07%) is similar to that of other cancer registries. It was reported as 38% by Brønden *et al.* (2010), 50% by

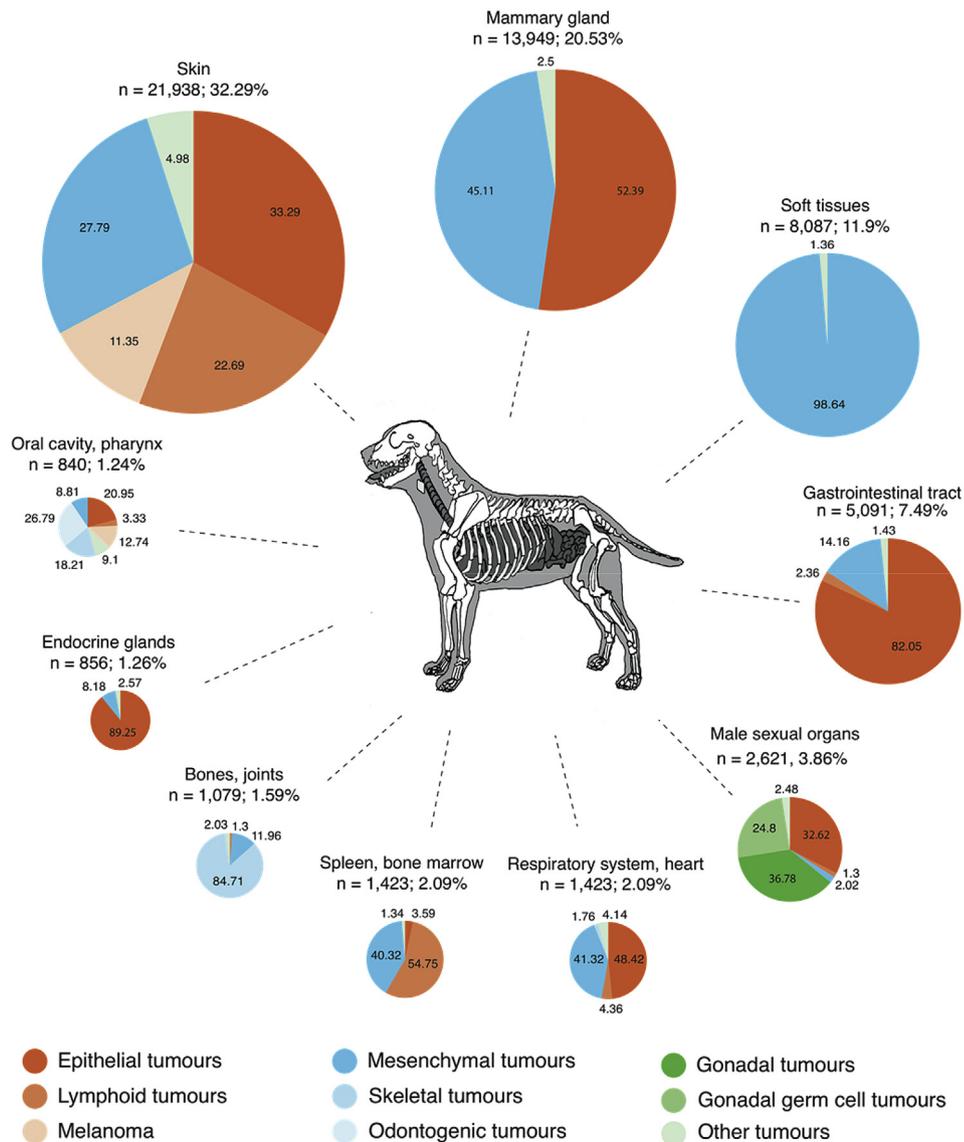


Fig. 7. Tumour location and diagnoses. *n*, number of tumours found in a location; %, proportion of the location compared with the total of locations. Figures in and around the slices show the relative proportion of tumour diagnoses/location. Tumour diagnoses <1% were added into 'other tumours'; locations <1% and unclassified locations were not listed. With the exception of 'male sexual organs', the listed locations are not sex specific.

Gamlem *et al.* (2008), 49% by Merlo *et al.* (2008) and 51% by Vascellari *et al.* (2009).

Skeletal tumours and melanomas showed the highest malignancy, with 96.61% and 87.21%, respectively. These figures are also similar to the results reported by Porello *et al.* (2006) and Ehrhart *et al.* (2013). Skin (32.29%), the mammary gland (20.53%) and soft tissues (11.90%) are the most frequent tumour locations, as confirmed by Dobberstein (1937), Mulligan (1949), Dorn (1967), MacVean *et al.* (1978), Bastianello (1983), Arnesen *et al.* (2001), Dobson *et al.* (2002), Gamlem *et al.* (2008), Vascellari *et al.* (2009) and Dobson (2013).

These results are influenced by the fact that both locations are easy to access and to observe, both for the dog owner and the veterinarian.

The ranking of the tumour locations diagnosed in post-mortem investigations shows the highest values for the gastrointestinal tract (14.23%) and the respiratory system (10.63), including thoracic organs (13.28%). In the ranking of all tumours sampled through post-mortem and biopsy, the gastrointestinal tract (7.49%) and the respiratory system, including thoracic organs (2.09%), hold places 4 and 6, respectively, similar to the observations of Dobson *et al.* (2002), Porello *et al.* (2006), Vascellari *et al.* (2009)

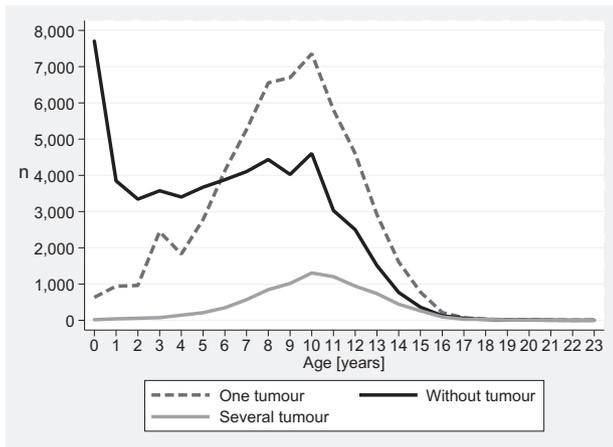


Fig. 8. Canine patients with none, one or several tumours per age. *n*, number of patients.

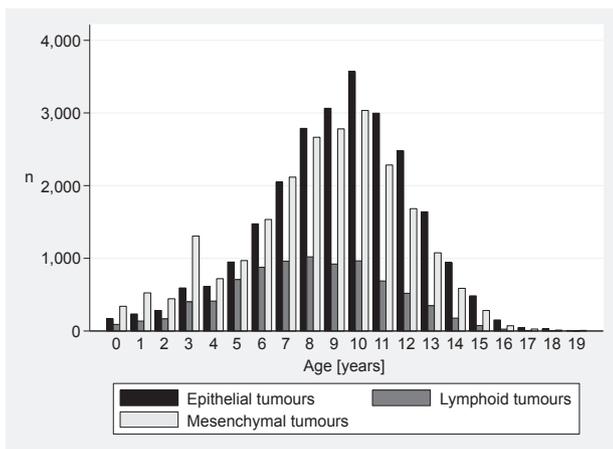


Fig. 9. Epithelial, mesenchymal and lymphoid tumours per age of patient. *n*, number of tumour types per age.

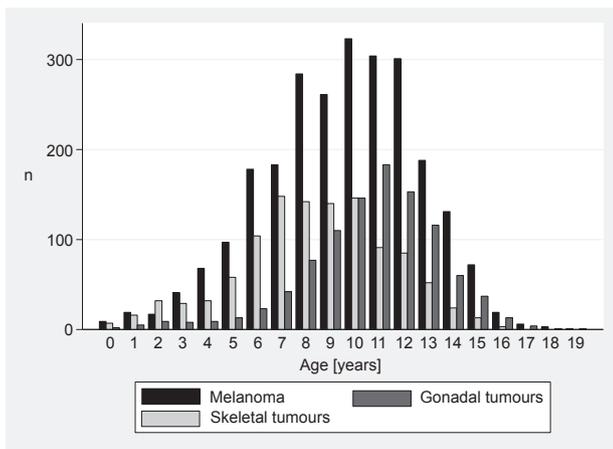


Fig. 10. Melanoma, gonadal neoplasia and skeletal tumours per age of patient. *n*, number of tumour types per age.

and Dobson (2013). The different frequencies in post-mortem samples and samples from biopsy suggest an over reporting of tumours at easily accessible locations, together with an underestimation of impenetrable locations.

The male sexual organs rank fifth (4.43%) in all examination methods and seventh (8.45%) in the post-mortem samples. Both results demonstrate that differences depend on the method of investigation and are similar to the findings of Dobberstein (1953), Mulligan (1949), Dorn (1967) and Bastianello (1983). Vascellari *et al.* (2009) observed that 13.4% of tumours were found in the male genital tract. In the Norwegian Canine Cancer Registry, tumours in the testes (2.4%) were less frequent than in the oral cavity (3.7%) (Gamlem *et al.*, 2008), which is an interesting difference in the distribution of these two tumour locations compared with those in the Swiss Canine Cancer Registry. Tumours of bones, joints and joint cartilage were similar in ranking for all examination methods and post-mortem investigations, with 1.82% and 4.84%, respectively. As previously mentioned, the investigation method had a strong impact on the distribution percentage. Gamlem *et al.* (2008) described tumours of bones, joints and joint cartilage as comparatively rare, with rates <1.00%. Oral tumours accounted for 1.24% of all tumours. Vascellari *et al.* (2009) found oral tumours more than twice as frequently in dogs in Northern Italy (2.6%) and Gamlem *et al.* (2008) found even more such tumours in dogs in Norway (3.7%). This discrepancy might be due to different sampling strategies. In the Swiss Canine Cancer Registry post-mortem data and biopsy samples were used, while in the Italian and Norwegian data, biopsy samples alone were used, where an overestimation of oral tumours might be expected. In accordance with the findings of Porello *et al.* (2006) and Thamm and Dow (2009), oral tumours represented the highest tumour type, including epithelial, lymphatic, mesenchymal, skeletal and odontogenic tumours and melanomas. Further research on these tumours may offer important insights for multimodality therapy in clinical investigations. For the development of new therapies it is advantageous that oral tumours develop rapidly and cannot be controlled by surgery alone (Porello *et al.*, 2006).

Adenoma and adenocarcinoma were the most frequent tumours in the Swiss Canine Cancer Registry, in concordance with the Tulsa Registry (MacVean *et al.*, 1978). In the Danish Veterinary Cancer Registry, the most frequently observed tumours were lipoma and adenoma (Brønden *et al.*, 2010). Another study reported histiocytoma, lipoma and adenoma as the most frequent tumours

(Dobson, 2013). The assigned tumour groups, however, are not always consistent, so comparison provides a rough overview only.

This study marks the beginning of a continuous registration of dog tumours in Switzerland, which will serve as reference for research in the fields of animal and human oncology. To be able to compare results of different registries in the future it is important that data collection is assimilated with other dog registries, as it is for human registries.

Acknowledgments

This study was financed through the financial support of the University of Zurich to A. Pospischil for acting as a fellow at the Collegium Helveticum during his fellowship period of 2009–2014. We thank Dr R. Dähler for his additional financial support and all colleagues of the Collegium Helveticum and the IVPZ, who contributed in various ways. We are grateful for the data from the veterinary pathology institutes, which made this and further studies possible. Finally, we thank H. Hofmann and H. Murray for revision of the English version.

Conflict of Interest Statement

The authors declare no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

References

- Arnesen K, Gamlem H, Glatte E, Grøndalen J, Moe L *et al.* (2001) The Norwegian canine cancer register 1990–1998. Report from the project ‘Cancer in the dog’. *European Journal of Comparative Animal Practice*, **11**, 159–169.
- Backer LC, Grindem CB, Corbett WT, Cullins L, Hunter JL (2001) Pet dogs as sentinels for environmental contamination. *The Science of the Total Environment*, **274**, 161–169.
- Bastianello SS (1983) A survey on neoplasia in domestic species over a 40-year period from 1935 to 1974 in the Republic of South Africa. VI. Tumours occurring in dogs. *Onderstepoort Journal of Veterinary Research*, **50**, 199–220.
- Bettini G, Morini M, Marconato L, Marcato PS, Zini E (2010) Association between environmental dust exposure and lung cancer in dogs. *Veterinary Journal*, **186**, 364–369.
- Bonnett BN, Egenvall A (2010) Age patterns of disease and death in insured Swedish dogs, cats and horses. *Journal of Comparative Pathology*, **142**(Suppl. 1), 33–38.
- Brønden LB, Flagstad A, Kristensen AT (2007) Veterinary cancer registries in companion animal cancer: a review. *Veterinary and Comparative Oncology*, **5**, 133–144.
- Brønden LB, Nielsen SS, Toft N, Kristensen AT (2010) Data from the Danish Veterinary Cancer Registry on the occurrence and distribution of neoplasms in dogs in Denmark. *Veterinary Record*, **166**, 586–590.
- Bukowski JA, Wartenberg D (1997) An alternative approach for investigating the carcinogenicity of indoor air pollution: pets as sentinels of environmental cancer risk. *Environmental Health Perspectives*, **105**, 1312–1319.
- Dobberstein J (1937) Der Krebs der Haussäugetiere. *Berliner Tierärztliche Wochenschrift*, **7**, 101–102.
- Dobberstein J (1953) *Zur Statistik der Geschwülste der Tieren*. Akademie-Verlag, Berlin, pp. 1–50.
- Dobson JM (2013) Breed-predisposition to cancer in pedigree dogs. *ISRN Veterinary Science*, **94**, 1275–1298. Article ID 941275.
- Dobson JM, Samuel S, Milstein H, Rogers K, Wood JL (2002) Canine neoplasia in the UK: estimates of incidence rates from a population of insured dogs. *Journal of Small Animal Practice*, **43**, 240–246.
- Dorn CR (1967) The epidemiology of cancer in animals. *California Medicine*, **107**, 481–489.
- Egenvall A, Bonnett BN, Hedhammar A, Olson P (2005) Mortality in over 350,000 insured Swedish dogs from 1995–2000: II. Breed-specific age and survival patterns and relative risk for causes of death. *Acta Veterinaria Scandinavica*, **46**, 121–136.
- Egenvall A, Nødtvedt A, Roepstorff L, Bonnett B (2011) Integrating databases for research on health and performance in small animals and horses in the Nordic countries. *Acta Veterinaria Scandinavica*, **53**(Suppl. 1), 1–6.
- Ehrhart NP, Stewart RD, Fan TM (2013) Tumours of the skeletal system. In: *Withrow and MacEwen’s Small Animal Clinical Oncology*, 5th Edit., SJ Withrow, DM Vail, RL Page, Eds., Elsevier, St Louis, p. 463.
- Gamlem H, Nordstoga K, Glatte E (2008) Canine neoplasia – introductory paper. *Acta Pathologica, Microbiologica et Immunologica Scandinavica Supplementum*, **125**, 5–18.
- Gesellschaft Schweizer Tierärztinnen und Tierärzte GST. <http://www.gstsvs.ch>. [accessed 18th December 2014].
- MacVean DW, Monlux AW, Anderson PS, Silberg SL, Roszel JF (1978) Frequency of canine and feline tumours in a defined population. *Veterinary Pathology*, **15**, 700–715.
- Marconato L, Leo C, Girelli R, Salvi S, Abramo F *et al.* (2009) Association between waste management and cancer in companion animals. *Journal of Veterinary Internal Medicine*, **23**, 564–569.
- Martić-Kehl MI, Schibli R, Schubiger PA (2012) Can animal data predict human outcome? Problems and pitfalls of translational animal research. *European Journal of Nuclear Medicine and Molecular Imaging*, **39**, 1492–1496.
- Merlo DF, Rossi L, Pellegrino C, Ceppi M, Cardellino U *et al.* (2008) Cancer incidence in pet dogs: findings of the Animal Tumour Registry of Genoa, Italy. *Journal of Veterinary Internal Medicine*, **22**, 976–984.
- Mulligan RM (1949) *Neoplasms of the Dog*. Williams and Wilkins Company, Baltimore, pp. 1–135.

- Nødsvedt A, Berke O, Bonnett BN, Brønden L (2011) Current status of canine cancer registration — report from an international workshop. *Veterinary and Comparative Oncology*, **10**, 95–101.
- Pinho SS, Carvalho S, Cabral J, Reis CA, Gärtner F (2012) Canine tumors: a spontaneous animal model of human carcinogenesis. *Translational Research*, **159**, 165–172.
- Porello A, Cardelli P, Spugnini EP (2006) Oncology of companion animals as a model for humans. An overview of tumour histotypes. *Journal of Experimental and Clinical Cancer Research*, **25**, 97–105.
- Pospischil A, Hässig M, Vogel R, Salvini MM, Fabrikant S *et al.* (2013) Hundepopulation und Hunderassen in der Schweiz von 1955 bis 2008. *Schweizer Archiv für Tierheilkunde*, **155**, 219–228.
- Page RL (2004) *Summary of Cancer Surveillance and Registry Project from the Cornell University College of Veterinary Medicine*. <http://envirocancer.cornell.edu/research/animalreg/summarycompanion.pdf> [accessed 18. December 2014].
- Purdue Comparative Oncology Program. (2006). <http://www.vet.purdue.edu/pcop/videos/index.php> [accessed 18th December 2014].
- Ranieri G, Gadaleta CD, Patruno R, Zizzo N, Daidone MG *et al.* (2013) A model of study for human cancer: spontaneously occurring tumors in dogs. Biological features and translation for new anticancer therapies. *Critical Reviews in Oncology and Hematology*, **88**, 187–197.
- Reif JS, Cohen D (1979) *Canine Pulmonary Disease: A Spontaneous Model for Environmental Epidemiology. Animals as Monitors of Environmental Pollutants*. Office of Publications National Academy of Sciences, Washington DC, pp. 241–252.
- Strafuss AC (1976) Sebaceous gland adenomas in dogs. *Journal of the American Veterinary Medical Association*, **169**, 640–642.
- Stünzi H, Lott-Stolz G (1967) [Use of punch cards in veterinary pathology]. *Deutsche Tierärztliche Wochenschrift*, **74**, 182–184.
- Thamm D, Dow S (2009) How companion animals contribute to the fight against cancer in humans. *Veterinaria Italiana*, **45**, 111–120.
- Vascellari M, Baioni E, Ru G, Carminato A, Mutinelli F (2009) Animal tumour registry of two provinces in northern Italy: incidence of spontaneous tumours in dogs and cats. *BMC Veterinary Research*, **5**, 39.
- World Health Organization. (2013) *International Classification of Diseases for Oncology (ICD-O)*, 3rd Edit., WHO Press, Geneva, pp. 1–342.

[Received, January 16th, 2015]
[Accepted, February 23rd, 2015]