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Snakebite in domestic animals: First global scoping review

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ABSTRACT

Snakebite is a Neglected Tropical Disease estimated to cause more than 100,000 human deaths and disable more than 400,000 victims each year. It primarily affects poor agricultural workers, farmers, and cattle herders living in rural areas of developing countries. It is thus an occupational disease. However, the impact of snakebite on these rural communities could be even higher if a One Health approach is taken to consider the direct impact on domestic animals and indirect impact on the livelihood of affected communities. To explore this hypothesis we developed the first scoping review to identify and characterize the global literature on snakebite in domestic animals.

Three bibliographic databases (*PubMed, Web of Science and Agricola*) were searched using terms related to snake, snakebite and domestic animals for publications up to December 31st, 2016. Two independent reviewers screened publications applying inclusion/exclusion criteria to select relevant material. Relevant information was then extracted from the selected literature.

The global literature on snakebite in domestic animals (n = 143 observational studies, reviews and letters) mainly represented North America, Europe and Australia (69%) with less information from Central and South America, Asia and Africa (31%). Observational studies (n = 119) mostly concerned pets (78%) and to a lesser extent livestock (22%). Thirty-four snake species were reported as responsible for bites in domestic animals. WHO's Medically Important Venomous Snakes were more frequently involved. The social-ecological determinants of snakebite were poorly documented but the reviewed literature suggested a strong seasonality and a diversity of habitat. Snakebite in animals caused neurotoxic, cytotoxic and hemotoxic envenomation syndromes similar to humans and death. Half of publications on envenomed livestock reported a fatality rate above 47%. There was no literature on the indirect impact of snakebite on livelihood caused by animal morbidity and mortality.

The results of this scoping review suggest a high and under-reported burden in terms of mortality in animals and a potential economic impact of snakebite in terms of losses in livelihood of affected communities. However, major knowledge gaps with respect to impact of snakebite on livestock and livelihood were identified. Filling these gaps is necessary for a full understanding of the impact of snakebite and to raise scientific, political and public awareness on this neglected issue.

1. Introduction

Snakebite envenoming (snakebite hereafter) kills and disables more than 100,000 and 400,000 people respectively worldwide each year (Gutiérrez et al., 2017). It affects poor and rural communities in South to Southeast Asia and sub-Saharan Africa, where encounters with venomous snakes are more frequent and access to adequate healthcare (*e.g.* antivenom) is limited (Warrell, 2010). In India, the most heavily affected country in the world, 1.4 million to 2.8 million snakebites occur every year resulting in at least 46,000 fatalities (Mohapatra et al.,

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2011). In West African countries, snakebite cause 3500 to 5350 deaths annually (Habib et al., 2015). In those high-income countries where venomous snakes are abundant, thousands of people are envenomed each year during recreational activities (*e.g.* 1,000–3,000 in Australia; 7,000–8,000 in the US) but deaths are very rare thanks to better access to appropriate health-care (White, 1998; CDC, 2018).

Snakebite has been severely neglected, falling out of major global health initiatives measuring human and animal disease such as the Global Burden of Disease (GBD, 2016), the first global assessment of foodborne disease (Havelaar et al., 2015), a mapping of poverty and zoonoses (Grace et al., 2012), studies on the burden of emerging infectious disease (World Bank, 2012), and estimates of animal and zoonotic diseases (OIE, 2012). Following the World Health Assembly of May 2017 snakebite was finally included in the World Health Organization (WHO) list of Neglected Tropical Diseases and in May 2019 the WHO launched the official snakebite envenoming road map with the ambition to reduce the number of deaths and disabilities by 50% before 2030 (WHO, 2019). This brings renewed political and scientific momentum and the need to address the socio-ecological complexity of this disease more comprehensively in rural and poor communities of the world.

Snakebite disproportionally affects agricultural workers, farmers, and cattle herders and is often described as an occupational disease (Alirol et al., 2010; Gutiérrez et al., 2017). In this context, snakebite in livestock is also a major concern (Abraha, 2007; Ndanu et al., 2012; Fison, 2016). In snakebite endemic countries such as Nepal, 80% of the population lives in rural areas (UN, 2018) and up to 88% of households keep livestock, including cattle, buffaloes, goats, sheep, pigs, or poultry (FAO, 2011). Since these rural communities are strongly dependent on these animals for food, work or as a direct source of revenue (Smith et al., 2013), livestock mortality or impaired productivity can heavily affect their livelihoods, especially because herd size is generally small. Thus, the impact of snakebite can go beyond direct impact on human health and associated healthcare costs urging for an integrated One Health approach (Zinsstag et al., 2015) to the study and response to snakebite in poor rural areas of the world.

To our knowledge, no review has addressed the impact of snakebite in the diversity of domestic animals in different ecological contexts of the world. To fill this gap, globally, we developed the first *Scoping Review* to summarize the extent, range and nature of the research in this domain highlighting the importance of the veterinary dimension of snakebite for a systemic understanding of the impact of snakebite in rural socio-ecological systems and improved both human and animal health in rural settings.

2. Material and methods

The scoping review methodology is well-suited to a highly interdisciplinary and multi-level review covering literature from veterinary and human medicine, public health, herpetology, ecology, and anthropology (Arksey and O'Malley, 2005; Levac et al., 2010). This review aimed to capture all published literature addressing the following aspects of snakebite in domestic animals: geographical distribution, diversity of animal victims and biting snakes, ecological context of snakebite, clinical implications and economic impact.

2.1. Review protocol

The scoping review followed the methodology proposed by Arksey and O'Malley (2005) and Levac et al. (2010). The protocol included source of information, search strategy, keywords, inclusion and exclusion criteria, and screening process.

2.2. Search strategy

Publications were obtained from *PubMed*, *Web of Science*, and *AGRICOLA*. *PubMed* provides publications in the health domain (*i.e.* human and animal medicine, epidemiology) and other life sciences (*e.g.* biology) whereas *Web of Science* has a broader multidisciplinary spectrum including papers related to livelihood and economic impact. *AGRICOLA* provided us with publications specifically related to domestic animals and their health. The combination of these sources ensured the needed multi-disciplinary coverage of the topic.

The literature was searched using a combination of keywords related to *snakes* (n = 142), *domestic animal affected* (n = 68) and *snakebite* (n = 8) (Table S1a supplementary data). The keywords related to *snakes* were selected in two steps: first, general terms (*e.g.* snakes, ophidian, serpentes, rattlesnake) were selected. Second, keywords specific to the list of 219 Medically Important Venomous Snakes (MIVS) from WHO (WHO, 2010) (genus or common and scientific name) were used. The keywords related to *domestic animal affected* were selected from the Veterinary Science Subset from *PubMed* (NLM, 2017). The *snakebite*-related terms were extracted from the literature. Database search was done on May 11^{th}, 2017, using the syntax combination described in Table S1b. The database searches were extended by hand-searching literature reviews, and by using Google scholar to be as comprehensive as possible. Dr. J.P. Chippaux and experts from the *African Society of Venimology* and in veterinary toxicology were consulted for additional references.

2.3. Criteria for inclusion and exclusion of publications

The review considered peer-reviewed articles, including original qualitative and quantitative studies, reviews, viewpoints and conference proceedings, as well as book chapters, and dissertations, published before December 31st, 2016. The literature search included all geographical areas of the world and languages. Publications not containing any of the keywords in the title and/or abstracts or not relevant to the topic of the review were excluded. Publications focusing on antivenom production using horses, sheep or other animals and articles on experimental envenomation of animals were also excluded.

2.4. Screening process and literature refinement

Titles and abstracts were screened by two independent reviewers (IB, MF) and full publications were read for final selection. Information by the two reviewers was compared and discussed in an iterative process to ensure consistency and completeness of the review. No quality assessment of the publications selected was made to allow the maximum breadth in the research. Results were merged using citation software EndNote X7 and duplicates were removed.

2.5. Charting the data

Selected publications were reviewed and the following information was extracted and described statistically: publication identifiers (authors, first author affiliation, journal, type of publication, year of publication, language), study identifiers (design, country of study, affected animals and their number), ecological context of snakebite (habitat, season), biting snake identifiers (family, genus, species), impact of snakebite on the animal (bite site, local and systemic clinical signs, treatment, outcome and sequelae), and indirect impact on animal owners (economic, emotional).

3. Results

3.1. Scoping review descriptive statistics

A final selection of 143 publications was obtained out of 2055 publications retrieved from the initial literature search (Fig. 1).

The majority of these publications were original articles (82%) in English (90%) published after 2007 (55%) (Table 1). Based on first

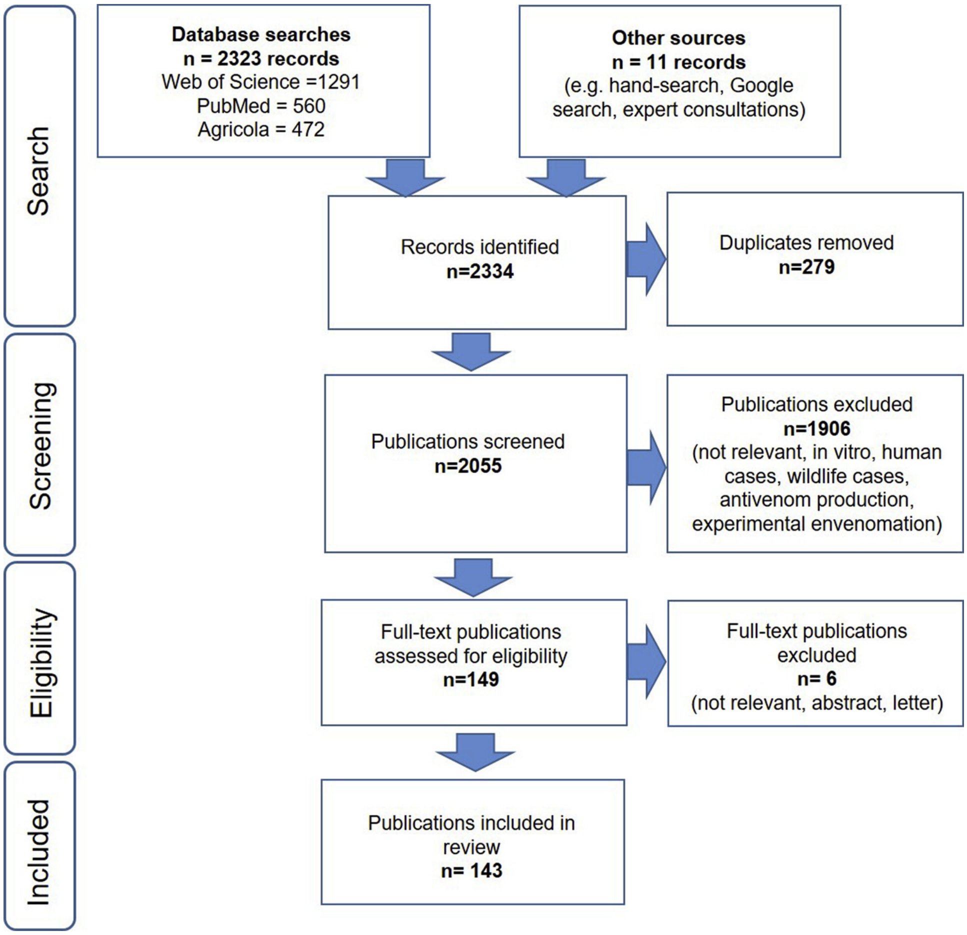

Fig. 1. Selection of publications through the scoping review process.

author affiliation, 69% of publications were produced by experts based in North America, Europe and Australia, and 31% in Central and South America, Asia and Africa. These publications were part of 53 scientific journals and a thesis, mostly confined to the veterinary clinical field (Table S2). 119 publications (83%) were observational studies reporting natural snakebite.

3.2. Geographic distribution of snakebite in domestic animals

Globally, and based on the geographic location of the snakebite cases, publications on snakebite in domestic animals were available from 23 countries (Fig. 2 and S1). The US (31/119 publications) and Australia (23/119 publications) together produced almost half of the observational studies. Brazil, Germany, India, Israel, South Africa, Sweden and the UK produced between 4 and 9 publications each while the remaining 14 countries published only one or two articles each.

3.3. Diversity of animal victims and biting snakes

3.3.1. Animal victims

Snakebite was reported in 14 groups of domestic animals, including both companion and livestock animals (Table 2). Snakebite in dogs and cats was more frequent (94/119 publications, 18 countries) and livestock followed with 28/119 publications from 14 countries. Snakebite in food-producing animals was reported in low-income countries including Nepal, Nigeria and Zimbabwe (cattle, goat, poultry, and pig) and in middle-income countries including Brazil and Costa Rica (cattle, sheep, and goat).

3.3.2. Snakes responsible for envenomation in domestic animals

A total of 34 biting snake species were reported by 78/119 publications (Table 3). In the remaining 41/119 publications, the snake species was “suspected” or the identification was at the genus level, common name (*e.g.* rattlesnake) or simply not mentioned. Snake identification was more frequent when snakebite affected dogs or cats (66/94) than livestock (14/28). Out of the 34 snake species, 30 (88%) were MIVS according to WHO. For Australia, Tiger snake (*Notechis scutatus*) and Common brownsnake (*Pseudonaja textilis*) were the most frequently cited MIVS (15/23 publications), and Eastern diamondback rattlesnake (*Crotalus adamanteus*) and Western rattlesnake (*Crotalus viridis)* were for North America (10/21 publications).

3.4. Ecological context of the snakebite

3.4.1. Seasonality of snakebite in domestic animals

Seasonality of snakebite was described in 35/143 publications. The incidence of snakebite in animals was seasonal in Australia, Brazil, France, Germany, Israel, South Africa, the UK and US with most cases occurring in the warmer months of the year for both dogs, cats and livestock. In Australia, Israel or the UK some cases of snakebite in dogs and cats did also occur in the cooler months. In South Africa, seasonality depended on the snakes with the highest incidence of puff-adder bites in autumn and cobra in summer (Lobetti and Joubert, 2004).

3.4.2. Environmental context of animal victims at the time of envenoming

The environmental context of the snakebite was documented in 29/94 publications with dogs/cats and 17/28 publications with livestock. Snakebite in dogs/cats occurred mostly in rural and peri-urban areas in

Table 1
General characteristics of included publications (number of publications = 143).

Category		Count (%)
Type of publication	Original article	118 (82 %)
	Review	20 (14 %)
	Letter	4 (3 %)
	Thesis	1 (1 %)
Language	English	130 (90 %)
	German	5 (3 %)
	Portuguese	3 (2 %)
	French	2 (1 %)
	Spanish	2 (1 %)
	Dutch	1 (1 %)
Year of publication	1956	1 (1%)
	1957–1966	1 (1 %)
	1967–1976	6 (4 %)
	1977–1986	6 (4 %)
	1987–1996	18 (12 %)
	1997–2006	33 (23 %)
	2007–2016	78 (55 %)
Geographical Region[a]	North America	42 (30 %)
	Europe	32 (22 %)
	Australia	25 (18 %)
	Central and South America	15 (10 %)
	Asia	15 (10 %)
	Africa	14 (10 %)
Type of study	Observational study[b]	119 (83 %)
	Case report or case-series	63 (44 %)
	Retrospective study	31 (22 %)
	Prospective study	13 (9 %)
	Clinical investigation[c]	7 (5 %)
	Survey	3 (2 %)
	Randomized controlled trial	1 (1 %)
	Treatment recommendation	1 (1 %)
	Review/Letter	24 (17%)

[a] Based on first author affiliation.
[b] Defined as reports and studies on natural envenomation.
[c] Defined as specific investigation or analysis conducted on envenomed animals (*e.g.* study of myocardial cell damage, renal impairment) when there is no follow-up of the animals (not prospective) nor control groups (not RCT).

Australia, Germany and Israel. A retrospective study on 327 dogs in Israel over a 13-year period did not report significant difference in cases distribution between urban and rural areas. Some specific environments described are the owner's garden or close to owner's house (6 publications), wooded areas (4 publications), and on or close to a farm (2 publications). Snakebite was reported in pasture for cattle, horses and sheep in Australia, Brazil, the UK, and US (5 publications), in agro-ecosystems such as farms for camels and sheep in Brazil and Saudi Arabia (4 publications), and on an oil palm plantation for cows in Costa Rica (1 publication). Horses, pigs and poultry were also bitten indoors, in stalls or pens (3 publications).

3.5. Clinical implications of snakebite in domestic animals

3.5.1. Diagnosis and clinical signs

81/119 observational studies described the part of the body where snakebite had occurred. The head/face/neck were most frequently bitten in dogs (1337/1765) while in cats it was the limb (27/52). Horse, llama, and alpaca were mainly bitten on the head/face/muzzle (145/166). Besides the head, sheep, goat, pig and cow were also bitten in their limbs. In poultry, several studies pointed to the breast, wings and head.

Diagnostic criteria varied between publications. Depending on studies, diagnosis of snakebite was based on clinical signs consistent with snake envenomation by the local snake species and one or more other criteria including evidence of a contact with a snake, presence of snakebite puncture wounds, potential for exposure (hot weather, wooded area), laboratory findings, and exclusion of other differential diagnoses. Some authors emphasize the difficulty of snakebite diagnosis in animals when the history of snakebite is absent and fang marks not found, especially in areas where the disease is uncommon (*e.g.*, adder bites to dogs in some parts of the UK (Sim, 2000)) or poorly recognised (*e.g.* snakebite to livestock in Nepal (Chapman et al., 1998)).

Snake envenomation of domestic animals causes a combination of local and systemic clinical signs with considerable variations depending on the species of the biting snake and the bitten animal. Clinical signs of envenomation by Elapidae, Viperidae/Crotalinae (pit vipers), and Viperidae/Viperinae snakes in dogs/cats were described in 26, 27, and

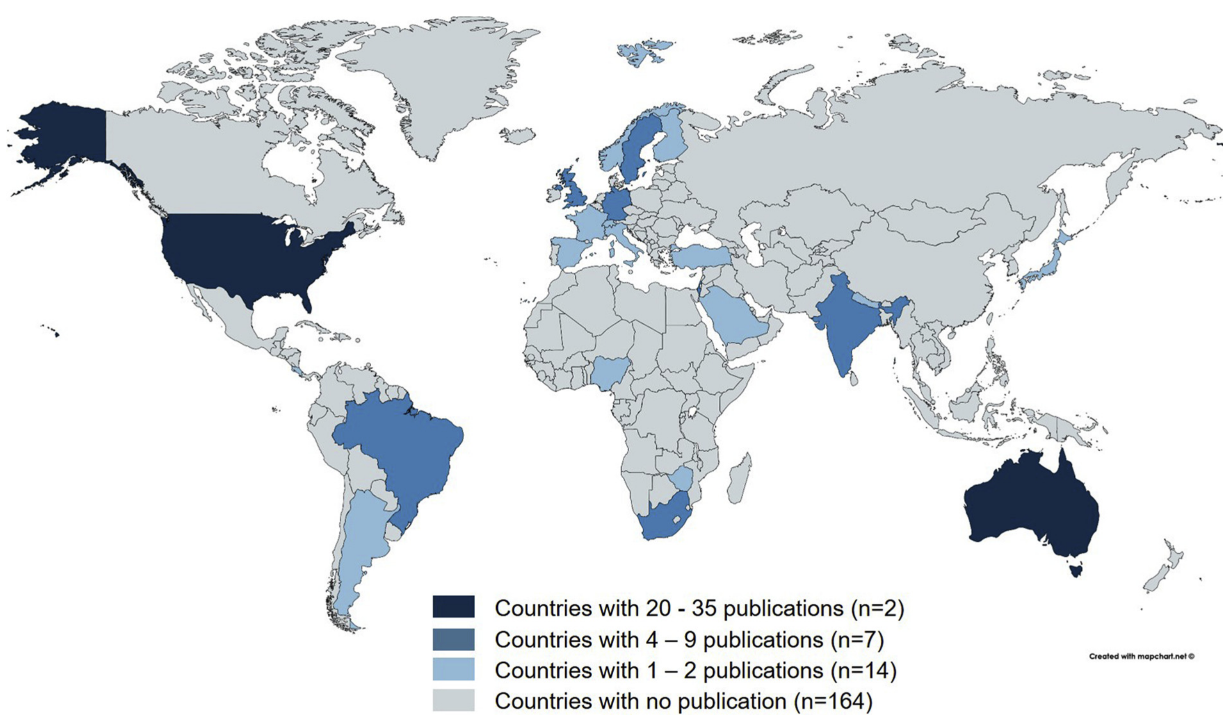

Fig. 2. Countries with published literature on local snakebite in domestic animals (Original figure created with mapchart.net (https://mapchart.net/).

Table 2
Animal victims of snakebite.

Animal victims	Number of publications[a]	Country of snakebite occurrence (number of publications)
Companion animals (94/119 publications)		
Dog, Cat	94	USA (24), Australia (21), Israel (8), South Africa (7), UK (7), Germany (4), Sweden (4), Brazil (3), India (3), Argentina (2), Finland (2), France (2), Turkey (2), Italy (1), Japan (1), Norway (1), Spain (1), Switzerland (1)
Livestock animals[b] (28/119 publications)		
Horse	12	USA (4), Australia (3), Brazil (2), France (1), Israel (1), Sweden (1)
Cattle (Cow, Buffalo)	6	Costa Rica (2), UK (1), France (1), Nepal (1), Australia (1)
Sheep	4	Brazil (3), Germany (1)
Goat	3	Brazil (1), Nepal (1), USA (1)
Poultry (Chicken, Duck, Turkey)	2	Nigeria (2)
New world camelid (Alpaca, Llama)	2	USA (2)
Camel	2	India (1), Saudi Arabia (1)
Pig	1	Zimbabwe (1)

[a] Some publications reported snakebite cases both in companion and livestock animals.
[b] Livestock refers to "any domestic or domesticated animal including bovine (including buffalo and bison), ovine, porcine, caprine, equine, poultry and bees raised for food or in the production of food (FAO, 2001)".

Table 3
Snake species involved in bites in domestic animals.

Geographical Region of Snakebite Occurrence	Biting Snake Species	Number of Publications	WHO MIVS[a]
Africa	***Bitis arietans***	3	Yes
	Dispholidus typus	2	Yes
	Naja annulifera	2	Yes
	Causus rhombeatus	1	No
	Haemachatus haemachatus	1	Yes
	Naja mossambica	1	Yes
	Thelotornis capensis	1	Yes
Asia	***Daboia palaestinae***[b]	8	Yes
	Naja naja	1	Yes
Australia	***Notechis scutatus***	10	Yes
	Pseudonaja textilis	5	Yes
	Oxyuranus scutellatus	2	Yes
	Pseudechis porphyriacus	2	No
	Acanthophis antarcticus	1	Yes
	Echiopsis curta	1	No
	Pseudonaja affinis	1	Yes
	Pseudonaja modesta	1	No
Central and South America	***Crotalus durissus***	2	Yes
	Bothrops asper	1	Yes
	Bothrops diporus	1	Yes
	Bothrops jararaca	1	Yes
	Bothrops neuwiedi	1	Yes
	Bothrops pauloensis	1	Yes
Europe	***Vipera berus***	19	Yes
	Vipera aspis	3	Yes
North America	***Crotalus adamanteus***	6	Yes
	Crotalus viridis	4	Yes
	Agkistrodon contortrix	2	Yes
	Agkistrodon piscivorus	2	Yes
	Crotalus oreganus	2	Yes
	Micrurus fulvius	2	Yes
	Crotalus atrox	1	Yes
	Crotalus horridus	1	Yes
	Sistrurus miliarius	1	Yes

[a] MIVS, Medically Important Venomous Snake.
[b] Current taxonomy for *Vipera palaestinae* / *Vipera xanthina palaestinae*.

32 publications respectively. Signs reported were diverse but consistent and converged to the same envenoming syndromes as those reported in human, *i.e.*, progressive weakness and flaccid paralysis caused by Elapidae bites, progressive swelling and hypotensive shock caused by Crotalinae bites or local swelling and inflammation with or without systemic signs caused by Vipera bites. Neurological signs were also reported for Crotalinae bites occurring in Argentina and Brazil (*Bothrops diporus, Crotalus durissus terrificus*) (Esteso et al., 1990; Koscinczuk et al., 2000; Conceicao et al., 2007). In two retrospective studies involving large series of dogs in the UK and Israel, respectively 33% and 85% of dogs bitten by Vipera developed local effects alone (Aroch and Harrus, 1999; Sutton et al., 2011). Three publications from South Africa reported rare cases of dog envenomation by snakes from the Colubridae family (*Dispholidus typus, Thelotornis capensis*) with a clinical picture of severe bleeding (VaughanScott and Lobetti, 1995; Otto and Blaylock, 2003; Hoole and Goddard, 2007). Many reviews also addressed the physiopathology of dog/cat envenomation by snakes in the US (Senter and Carson, 1999; Peterson, 2006a, b; Najman and Seshadri, 2007; Gilliam and Brunker, 2011), South Africa (Leisewitz et al., 2004), Australia (Heller et al., 2007), and Brazil (Ferreira Júnior and Barravieira, 2004).

On the other hand, the clinical picture of livestock animal envenomation by Elapidae, Viperidae/Crotalinae, or Viperidae/Viperinae snakes was less documented (in 3, 14, and 8 publications respectively), and not reported for all livestock species (Table 4). No study described clinical signs of elapid envenomation in cattle and sheep. However, their envenomation by crotalids was addressed by five publications from Latin America (Mendez and Rietcorrea, 1995; Berrocal et al., 1998; Tokarnia et al., 2008; Leal et al., 2013; Rodríguez et al., 2016) and three reviews from Colombia (Estrada-Gómez et al., 2014) and Brazil (Tokarnia and Peixoto, 2006; Tokarnia et al., 2014). Swelling and hemorrhage at the bite site, bristling, lethargy and bleeding from the nose, ears or skin are among the clinical signs reported. In sheep, death can occur within 24–48 h of the bite, especially in young animals (Mendez and Rietcorrea, 1995; Leal et al., 2013). In cattle, late detection of the envenomation (after 8–12 h) led to more severe symptoms with animals lying on the ground, coughing froth or found dead (Rodríguez et al., 2016). Clinical description of envenoming in food-producing animals in developing countries is limited to two case reports on poultry envenomation in Nigeria (Onoviran et al., 1976; Lawal et al., 1992) and one report on pig envenomation in Zimbabwe (Stewart, 1974).

3.5.2. Mortality

Death associated with snakebite occurred in all animal species. We analysed dog/cat mortality secondary to snake envenomation in studies reporting large number of snakebite cases. In the US, dog mortality rates to snakebite ranged from 1% to 7.8% (Hackett et al., 2002; McCown et al., 2009; Peterson et al., 2011; Katzenbach and Foy, 2015; Witsil et al., 2015) but went as high as 19.4% and 30% in studies

Table 4
Clinical signs in envenomed livestock in relation to the snake family/subfamily. Available clinical descriptions were grouped according to the biting snake family/subfamily.

Snake Family/Subfamily	Number of publications	Country of snakebite occurrence	Clinical signs
Elapidae	3	Australia, Nigeria	(horse) Staggering and trembling, muscle fasciculation, recumbency, lameness, inability to stand, reluctance to move, absence of muscle tone, depression, pupillary dilation, drooping of the eyelid, sweating, pulse barely detectable, depression of gastrointestinal activity, tachycardia, tachypnea. (chicken, duck and turkey) Edema, cyanotic hemorrhagic area around bite sites, depression, prostration and nervous signs.
Viperidae/Crotalinae	14	Brazil, Costa Rica, USA	(cattle, sheep, goat, horse, and new world camelid) Severe facial/muzzle/limb swelling with marked lameness depending on the bite site, spontaneous bleeding from eyes, ears, nose, gingiva, skin, lethargy, recumbency, tachypnea, respiratory distress, fever, tachycardia, cardiac arrhythmia, blood in stool and urine, diarrhea, necrosis and sloughing of the skin (limb in a goat).
Viperidae/Viperinae	8	Europe, Israel, India, Zimbabwe	(camel, cow, horse, pig, sheep) At the bite site, marked swelling (foot, facial with case of upper airway obstruction), severe pain, blood oozing from fang marks and nose. Other signs included bacterial infection, ptyalism, lameness, depression, tachycardia, dysphagia, tissue necrosis, black spots on the skin (pig), staggering and lameness. (chicken) Recumbency, droopy wings, eyes closed, head rested on the floor.

reporting bites by the deadly Eastern diamondback rattlesnake (*Crotalus adamanteus*) (Schaer, 1984; Willey and Schaer, 2005). Mortality of envenomed dogs was 3.8% in the UK (Bates and Warrell, 2013), 4% in Israel (Segev et al., 2004), 10.3% in South Africa (Lobetti and Joubert, 2004), and between 19.2% to 34.5% in Australia (Barr, 1984; Mirtschin et al., 1998). Similarly, cat fatality rates differed between countries and was 5.7% in the US (Pashmakova et al., 2013) and between 15.7% to 18.8% in Australia (Barr, 1984; Mirtschin et al., 1998).

All publications on envenomed livestock reported deaths. Animal victims were either found dead by their owner (pig, poultry), died without receiving medical care (poultry, sheep), were dead at presentation (new world camelid), died hours or days after receiving veterinary medical care (sheep, goat, horse) or were culled due to deterioration of condition or owing to financial constraints (horse, cow, new world camelid). Snakebite was the third cause of camel mortality in a dairy camel farm in Saudi Arabia (Agab, 2006). For each publication, where available, we reported the fatality rate in livestock animals (Table 5). Although sample size is often small, case fatality rates are high with half of the publications reporting fatality rate above 47%.

3.5.3. Sequelae

Outcome and long-term follow-up of the victims was documented in 44/94 publications with dog/cat victims and 13/28 publications with livestock victims. Most often animals surviving the bite fully recovered. Rare cases of necrosis occurred in dog, sheep, and horse (Schaer, 1984; Mendez and Rietcorrea, 1995; Mamak and Aytekin, 2009; Schaer et al., 2015), some leading to subsequent surgical debridement or a decision to amputate. Facial nerve paralysis was described in horse, goat, and dog (Fielding et al., 2011; Smith et al., 2015; Martins et al., 2016). Vision loss, cataract, and retinal degeneration followed periocular or ocular snakebite in dog/cat (Kibar et al., 2014; Martins et al., 2016). Cardiac complications, such as severe cardiac dysrhythmia, were diagnosed in horses up to two years after rattlesnake envenomation. Two cases of congestive heart failure led to euthanasia, and one case of persistent tachycardia led to severe exercise intolerance (Dickinson et al., 1996; Fielding et al., 2011; Gilliam et al., 2012). One case of a secondary bacterial infection occurred in an envenomed cow (Arbuckle, 1991).

3.6. Veterinary treatment and traditional medicine

Snakebite treatment included a combination of supportive measures such as intravenous fluid therapy, corticosteroids, broad-spectrum antibiotics, analgesics, atropine, furosemide, antihistamines, oxygen and mechanical ventilation. Horses and new world camelids bitten near muzzle with subsequent head swelling and obstruction of nasal passages required airway support nasal intubation or tracheostomy (Dickinson et al., 1996; Dykgraaf et al., 2006; Anlén, 2008; Fielding et al., 2011; Sonis et al., 2013).

Antivenom was administered in dog/cat (72/94 publications) and in goat, chicken, horse, cow, and new world camelid (13/28 publications). In most studies, the small number of animals treated with antivenom or the lack of prior measurement of envenomation severity did not allow drawing conclusions as to the effect of antivenom administration on survival. However, in Australia, dogs and cats envenomed by Elapidae snakes had a higher survival rate if treated with antivenom (Barr, 1984; Mirtschin et al., 1998). In the US, dogs envenomed by Eastern diamondback rattlesnakes (*Crotalus adamanteus)* and administered antivenom had a higher survival rate than those not receiving antivenom (Willey and Schaer, 2005), whereas most dogs envenomed by Prairie rattlesnakes (*Crotalus viridis*) did not require antivenom for resolution of clinical signs (Hackett et al., 2002; Katzenbach and Foy, 2015). In Israel and the UK, the administration of antivenom in dogs bitten by vipers did not significantly increase survival (Segev et al., 2004; Bates and Warrell, 2013). Delay between envenomation and presentation to a veterinarian has been reported as a problem for antivenom use in livestock (Berrocal et al., 1998; Dykgraaf et al., 2006). Antivenom administration more than 8 h after envenomation was associated with significantly higher mortality in cattle than when administered within 6 h of envenoming (Rodríguez et al., 2016).

Surveys of farmers and cattle herders in local communities of the Northwestern part of Nigeria and Botswana revealed the use of traditional medicine in the management of snakebite in livestock (Ismaila and Adamu, 2012; Setlalekgomo, 2015). Traditional remedies included medicinal plants, bloodletting, milk taken orally, and various parts of a snake mixed with medicinal herbs.

3.7. Snakebite in domestic animals: Implications for owners

Livestock losses due to snakebite were reported in resource-poor countries. For instance, snakebite caused a high fatality rate in poultry flocks in Nigeria (Lawal et al., 1992) and in pigs in Zimbabwe (Stewart, 1974). Chapman et al. (1998) stressed the loss of livestock due to snakebite and its implications for local farmers in the Terai Region of Nepal. In Botswana, snakebite is a serious problem to cattle, and 67% of the farmers surveyed used medication to treat snakebite in cattle (Setlalekgomo, 2015). In these countries, rural communities rely on livestock for their livelihood. However, no publications were identified that examined the economic consequences of snakebite in livestock for farmers in terms of costs of treatment, impaired productivity, animal loss etc. In addition, no studies analysed the psychological or emotional impact of losing an animal due to snakebite on owners. Emotional

Table 5
Outcomes of livestock animals bitten by snakes.

Publication	Country	Biting Snake Species	Victim Species	Number of Animals Bitten	Number of Animals Treated (Antivenom (AV)/Supportive Drugs (SD)[a])	Spontaneous Death/ Euthanasia	
						Number	%
(Mirtschin et al., 1998)	Australia	*Pseudechis sp, Pseudonaja sp, Notechis sp*	Cow	36	13 AV/n[b] SD	18	50%
(Mirtschin et al., 1998)	Australia	*Pseudechis sp, Pseudonaja sp, Notechis sp*	Horse	27	12 AV/n SD	18	67%
(Fitzgerald, 1975)	Australia	*Notechis scutatus*	Horse	4	2 AV/4 SD	1	25%
(Cullimore et al., 2013)	Australia	*Notechis scutatus*	Horse	1	1 AV/1 SD	0	0%
(Mendez and Rietcorrea, 1995)	Brazil	*Bothrops neuwiedi*	Goat	1	0 AV/0 SD	1	100%
(Chiacchio et al., 2011)	Brazil	*Bothrops pauloensis*	Horse	3	3 AV/3 SD	0	0%
(Silva et al., 2011)	Brazil	*Bothrops spp (suspected)*	Horse	1	1 AV/1 SD	1	100%
(Tokarnia et al., 2008)	Brazil	*Bothrops jararaca*	Sheep	4	0 AV/ 0 SD	1	25%
(Leal et al., 2013)	Brazil	*Bothrops alternatus (suspected)*	Sheep	2	0 AV/ 0 SD	2	100%
(Mendez and Rietcorrea, 1995)	Brazil	*Bothrops neuwiedi*	Sheep	22	0 AV/ 0 SD	11	50%
(Rodríguez et al., 2016)	Costa Rica	*Bothrops asper*	Cow	31	30 AV/n SD	9	29%
(Berrocal et al., 1998)	Costa Rica	*Bothrops asper (suspected)*	Cow	1	1 AV/unknown	1	100%
(Roth et al., 2009)	Germany	*Vipera berus*	Sheep	1	0 AV/1 SD	1	100%
(Tagra and Yadav, 1998)	India	*Eristicophis macmahonii*	Camel	1	0 AV/ 1 SD	0	0%
(Hoffman et al., 1993)	Israel	*Vipera palaestinae*	Horse	2	Unknown	2	100%
(Onoviran et al., 1976)	Nigeria	*Echis carinatus (suspected)*	Poutry	1	0 AV/0 SD	1	100%
(Lawal et al., 1992)	Nigeria	*Walterinnesia morgani (suspected)*	Poultry	21	3 AV/3 SD[c]	20	95%
(Agab, 2006)	Saudi Arabia	Unknown	Camel	Unknown	Unknown	18	–
(Anlén, 2008)	Sweden	*Vipera berus*	Horse	7	2 AV/7 SD	3	43%
(Arbuckle, 1991)	UK	*Vipera berus (suspected)*	Cow	3	0 AV/3 SD	2	67%
(Smith et al., 2015)	USA	*Crotalus oreganus*	Goat	3	0 AV/3 SD	1	33%
(Gilliam et al., 2012)	USA	Rattlesnakes (sp unknown)	Horse	20	0 AV/15 SD	1	5%
(Dickinson et al., 1996)	USA	*Crotalus vididis viridis*	Horse	32	0 AV/29 SD	8	25%
(Fielding et al., 2011)	USA	Rattlesnakes (sp unknown)	Horse	58	9 AV/57 SD	5	9%
(Dykgraaf et al., 2006)	USA	*Crotalus atrox*	New world Camelid	12	3 AV/10 SD[c]	7	58%
(Sonis et al., 2013)	USA	*Crotalus viridis viridis*	New world Camelid	27	12 AV/24 SD[c]	9	33%
(Stewart, 1974)	Zimbabwe	*Bitis arietans (suspected)*	Pig	12	0 AV/0 SD	4	33%

Median = 47% Q1 = 25% (25th percentile).
Q3 = 98.8% (75th percentile).
[a] Most commonly used supportive drugs were antibiotics, corticosteroids, non-steroidal anti-inflammatory drugs, tetanus prophylaxis, and intravenous fluids.
[b] n = number of animals treated with supportive drugs unknown.
[c] Untreated animals were dead or had to be euthanized at arrival.

impact on animal owners could be significant especially when financial constraints forced them to refuse antivenom or to limit the number of doses administered or even to have their animal euthanized as has been reported in several studies (Hill and Campbell, 1978; Dykgraaf et al., 2006; Armentano and Schaer, 2011).

The literature reviewed did not address the aspects of a possible indirect impact on human health, namely the presence of animals and animal feed in or around the household as a potential risk factor for human cases.

4. Discussion

To our knowledge, this review is the first global and comprehensive description of the literature on snakebite in domestic animals. It provides insights on the epidemiology and clinical impact of snakebite in a diversity of domestic animal species across the world, stressing on the need for an integrated One Health approach to study and respond to snakebite in rural socio-ecological contexts. In addition, this review highlights major research gaps in veterinary medicine and public health.

We identified 143 scientific publications on snakebite in domestic animals published between 1956 and 2016. The US and Australia strongly dominated this literature while endemic countries were underrepresented. This likely reflects differences in research productivity between high-income countries and low-middle-income countries, which has already been described for the global snakebite burden in humans (Kasturiratne et al., 2008) and more recently for the geographical distribution of MIVS (Genevieve et al., 2018).

The literature is mainly confined to the veterinary clinical field focusing on diagnosis and treatment of snakebite, and health consequences for the animals. Snakebite in pets dominates the literature, particularly in high-income countries of the Americas and Europe. On the other hand, and despite their role in local economies and development, the study of snakebite in livestock has been poorly addressed, and its burden is highly underestimated or unknown at the local, national and global scales. Where data is better, the impact of snakebite on livestock is high. For example, in Costa Rica, Fer de Lance (*Bothrops asper)* is responsible for around 10,000 cases of envenomation in cattle per year only in the Central Pacific region of the country (Herrera et al., 2017). Clinical and epidemiological information on livestock envenoming for countries where snakebite is endemic is very limited. Only a few cases of poultry and pig envenomation have been reported in Nigeria and Zimbabwe (Stewart, 1974; Onoviran et al., 1976; Lawal et al., 1992). Despite this lack of information, some studies suggested that loss of livestock by snakebite could severely impact rural farmers (Chapman et al., 1998).

A diversity of venomous snake species is involved. Most of them belong to the WHO MIVS list and are thus also recognized as a threat to human health. In fact, animals could attract snakes to the households and increase potential risks for humans (Mise et al., 2016) or on the contrary, act as sentinels to prevent snakebite as suggested by Colling et al (2011), but this remains poorly studied. In general, the disease ecology of snakebite in both human and animals and the distribution and behavior of many of the most medically important species is still unknown, particularly in areas where snakebite burden is more important. A recent study has shown for example that the Forest cobra (*Naja melanoleuca*), a widespread snake species in tropical Africa, was actually five different cobra species (Wüster et al., 2018). This finding illustrates the complexity of snake taxonomy and ecology. The role of herpetologists is key to understanding, preventing and controlling snakebite, and new approaches based on digital and social innovation such as those described in Genevieve et al. (2018) are required to identify hotspots of snakebite risk to both human and domestic animals, and inform policy design on prevention and treatment of snakebite for humans and animals.

Studies on the impact of snakebite on domestic animals are mainly clinical, and their ecological determinants are not well documented. Some factors are similar to those affecting snakebite in humans, such as seasonality. Snakebite cases increased during the warmer months as shown for dogs in different parts of the world (Leisewitz et al., 2004; Segev et al., 2004; Sutton et al., 2011; Turkovic et al., 2015) and for humans in Europe or the Americas (Chippaux, 2012, 2017). With longer and hotter dry seasons, climate change may affect snakebite risk. Using ecological niche modelling and scenarios of future climatic changes, Yañez-Arenas et al. (2016) projected an expansion in snake distribution in North America and Latin America, and a subsequent increased risk of snakebite. Climate change is also expected to increase snakebite incidence in Sri Lanka (Ediriweera et al., 2018). Climate warming is likely to also affect the epidemiology of snakebite in domestic animals but this remains to be explored.

The habitat, for example pasture type (*e.g.*, Dickinson et al., 1996; Estrada-Gómez et al., 2014) or palm plantations (Rodríguez et al., 2016), and practices of animal husbandry, for example chicken raised in pens (Lawal et al., 1992), could also play a role in increasing the risk of snakebite.

Physiopathology varies considerably depending on the type of snake, the animal affected and the part of the body bitten, mainly head/face or limbs. Clinical signs of snakebite in dogs, cats, and to a lesser extent in horses are well described and tend to coincide with humans (Gutiérrez et al., 2017). In food-producing animals, this is poorly characterised and includes a diversity of signs, such as swelling, lameness, bleeding, and death, from small number of observations and studies. Further information on clinical presentation of natural livestock envenomation is needed to support snakebite diagnosis in livestock and the generation of epidemiological evidence.

The available literature indicates a high fatality rate in livestock following snakebite. This finding may be explained by the delay between envenomation and presentation to a veterinarian, which causes many bitten animals to die before having access to treatment. In fact, delayed access to healthcare has been repeatedly shown as one of the most important causes of death after snakebite in humans (Sharma et al., 2004; Alirol et al., 2010). A greater susceptibility of herbivores (horse, sheep, cattle, goat) to snake venom has also been reported for *Bothrops sp.* and brown snake venom (Kelloway, 1931; Ferreira Júnior and Barravieira, 2004; Tokarnia et al., 2014). If envenomed cattle are not rapidly treated with an adequate antivenom, animals could die in a matter of hours, potentially causing significant economic losses to owners. This has prompted the development of an innovative toxoid vaccine that extends the time window for antivenom administration and increases likelihood of survival (Herrera et al., 2017).

Despite the high fatality rate and the potential of sequelae (necrosis, cardiac complication, and vision loss) in bitten animals, animal losses and productivity impairment and the subsequent negative impact on livelihood has not yet been studied. This neglect further accentuates the already underestimated burden of snakebite in human populations. Therefore, studying the impact of snakebite on domestic animals, particularly in livestock animals, is indispensable for a real quantification of the burden of snakebite in rural areas of the world. This approach is supported by a study on the economic impact of cattle rabies in Ethiopia, which showed significant livelihood losses for affected households (Jibat et al., 2016).

Livestock envenomation is under-diagnosed and under-reported or not recorded at all by veterinary practices (Mirtschin et al., 1998; Chapman, 1998; Setlalekgomo, 2015). This is possibly because owners do not seek veterinary care for various reasons including cases going unnoticed, cost of or accessibility to medical treatment or death of the bitten animals before being found. A better understanding of snakebite burden in livestock in poor and rural communities of the world requires data collection at the community level, such as through cross-sectional surveys. A preliminary community-based survey developed in autumn 2016 in Akonolinga (Cameroon) showed that 50 out of 66 households (76%) have heard about or witnessed snakebite in domestic animals. Death was the most frequently reported outcome of snakebite and impacts on livelihood referred to food loss (57% of respondents), financial loss (18%) and emotional impact (24%) (Alcoba et al, *in prep*). The question on the impact of snakebite on animals and livelihoods will be further studied in an international and interdisciplinary project supported by the *Swiss National Science Foundation* (SNSF). This *Snake-byte* project led by the University of Geneva (incl. IB, SBM, RRdC) plans an unprecedented collection of data from 24,000 households through a regional and national integrated human-animal health survey in Nepal and Cameroon (SNSF, 2018).

One of the strengths of this scoping review is its global approach, with no limitations on geographical area, language and time frame, which enabled us to capture and compare published literature from a diversity of countries addressing a variety of domestic animal victims of snakebite. This differs from previous reviews, which focused only on one country/region or on a specific type of animal victim or biting snake. In addition, this review was highly exhaustive including three bibliographic databases (*PubMed*, *Web of Science*, and *AGRICOLA)* and an independent screening by two reviewers. We did not assess study quality in agreement with the methodological framework for scoping reviews (Arksey and O'Malley, 2005). As we focused only on naturally occurring envenomation by snakes, we did not include literature on experimental envenomation of livestock (unless they also reported cases of natural envenomation). This literature could have provided further information on the clinical course and pathology of snakebite in livestock. Grey literature (*e.g.*, social media, online forums) was also not included, potentially missing information on emotional impact on the owners of bitten animals. Other aspects might have also been neglected, such as the role of dogs to prevent snakebite in humans, as recently described in the press (BBC, 2018).

5. Conclusion

This scoping review identified several knowledge gaps on the epidemiology, burden, physiopathology, complications, and economic consequences of snakebite in domestic animals. Snakebite endemic countries and livestock species are strongly under-represented in the current published literature. The data gathered through this comprehensive overview of published evidence support the hypothesis that snakebite may have an important direct impact on livestock health causing loss of animals or impaired productive value and therefore could have consequences for livelihoods and impact on mental and physical health and wellbeing of farmers and their families and communities. We recommend a systemic approach to snakebite including a full societal cost analysis in humans and animals. Further assessments of the burden of snakebite on livestock will help raise scientific, political and public awareness on this neglected problem and reinforce the global political momentum on snakebite.

Declaration of Competing Interest

None.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.prevetmed.2019.104729.

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