

A Systematic Review of Scorpion Envenomation Therapeutics and Antivenom Accessibility

Avinash N. Mukkala,^{1,*} Christian Lecce,^{2,*} Aisha Khatib,^{3,4} Michael Klowak,⁵ Priyanka Challa,⁶ Tianna Chong-Kit,⁷ Eric Shao,⁸ Jason Kwan,⁹ Emma Hagopian,¹⁰ Mofe Adeosun,¹¹ Dylan Kain,⁴ Jamie Sookhoo,¹² Apira Ariya, Andrea K. Boggild^{1,3,4,13,}

¹Institute of Medical Science, University of Toronto, Toronto, ON, Canada; ²Faculty of Engineering & Architectural Science, Ryerson University, Toronto, ON, Canada; ³Tropical Disease Unit, UHN-Toronto General Hospital, Toronto, ON, Canada; ⁴Department of Medicine, University of Toronto, Toronto, ON, Canada; ⁵Faculty of Science, McMaster University, Hamilton, ON, Canada; ⁶Faculty of Arts and Science, University of Toronto, Toronto, ON, Canada; ⁷Department of Biochemistry, University of Waterloo, Waterloo, ON, Canada; ⁸Department of Microbiology and Immunology, University of Western Ontario, London, ON, Canada; ⁹Faculty of Health Science, McMaster University, Hamilton, ON, Canada; ¹⁰Faculty of Arts and Science, University of Toronto, Toronto, ON, Canada; ¹¹Dalla Lana School of Public Health, University of Toronto, Toronto, ON, Canada; ¹²University of the West Indies, St. Augustine, Trinidad and Tobago; ¹³Public Health Ontario Laboratories, Toronto, ON, Canada. *Both authors contributed equally to this work.



Figure 2. Preliminary qualitative data

Introduction:

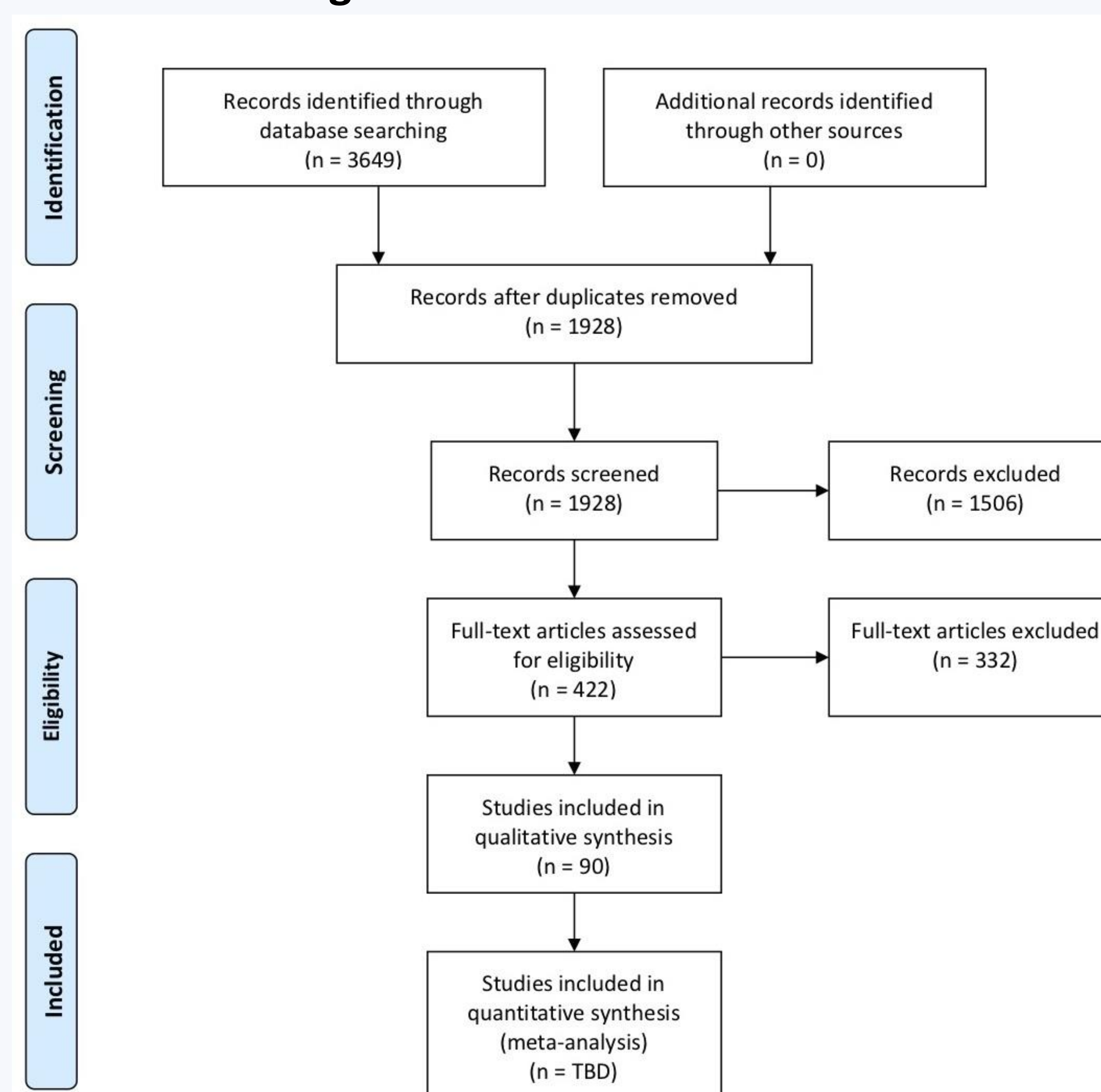
- Scorpions (*Scorpiones*) are eight-legged arthropods of the class *Arachnida*
- Increased human migration and transcontinental produce shipment may cause the incidence of scorpion envenomations to increase in non-endemic areas¹
- We aim to synthesize existing evidence around prevention and treatment of scorpion envenomation's into a clinical resource, including provision of information on access to, and indications for, antivenom usage

Methods:

- PubMed (NCBI), MEDLINE (OVID), EMBASE (OVID), Cochrane Database of Systematic Reviews (CIDR) and TOXLINE (TOXNET) were searched from inception to June 2018 using combinations of the search terms "scorpion", and "envenomation*"
- We **included**: observational studies, case reports, case series, and cohort studies, as well as clinical trials, and antivenom safety, tolerability, and efficacy.
- We **excluded**: Molecular epidemiology and purely mechanistic pathogenesis studies
- Abstracts underwent double reviewer screening and only titles about scorpions that had double inclusion responses were included for the full-text review.
- A different pair of authors screened the subsequent full-texts and only double inclusion responses were included in the systematic review.

Future: A tertiary arbitrator will mitigate any inclusion/exclusion discrepancies experienced during both abstract screening and full-text screening. The GRADE approach will be used to assess quality of studies reporting therapeutic interventions. Data will be grouped and summarized for ease of clinician use by prevention, therapeutic strategies, geographic location and species. The recommended mode of treatment and management will be provided on an evidence-based, per-species basis. Meta-analysis will be planned if sufficient efficacy measures exist.

Figure 1. PRISMA Flowchart



Results:

- 961 MEDLINE articles, 1053 PubMed, 1486 EMBASE, 0 CIDR and 149 TOXLINE records were retrieved for title and abstract screening; after a multi-step de-duplication pipeline, **1928** remained.
- Following the abstract screening protocol, **422** titles advanced to full-text review.
- Full-text screening resulted in the inclusion of **~90** titles to the systematic review.

Discussion:

Increased transcontinental movement of people and tropical produce has facilitated importation of scorpions to non-endemic regions where clinicians lack familiarity with envenomation syndromes and appropriate therapeutics. Synthesizing the current evidence around therapeutic strategies for scorpion envenomations can inform the development of appropriate treatment and prevention protocols.

Species	Antivenom Adverse Reactions	Pharmacological Treatments
Indian Red Scorpion (<i>Mesobuthus tamulus</i>)	<ul style="list-style-type: none"> Allergic reactions are possible Prazosin + Antivenom will reduce the risk of myocardial dysfunction as compared to Prazosin alone 	<ul style="list-style-type: none"> Hypertensive → nifepedipine and prazosin Tachycardic → prazosin, digoxin, aminophylline, and oxygen Pulmonary edema → digoxin, aminophylline, furosemide and prazosin Massive pulmonary edema → nitroprusside as well Children deteriorate quicker without antivenom+prazosin, prazosin alone is not enough
Yellow Scorpion (<i>Tityus serrulatus</i>)	<ul style="list-style-type: none"> Children with adrenergic manifestations after <i>T. serrulatus</i> scorpion sting had significantly lower anaphylactic reactions to antivenom than those without these manifestations This finding may also be true for adults victims 	<ul style="list-style-type: none"> Pain at the site of sting → dipyrone & metoclopramide Shock → intravenous infusion of dobutamine or dopamine Premedication with epinephrine, antihistamine plus or minus corticosteroid should be given parenterally to patients before antivenom injection to prevent early anaphylactic reactions Oral analgesics for pain
<i>Centruroides sculpturatus</i>	<ul style="list-style-type: none"> Minor vomiting Some diarrhea Rare residual amnesia No acute serum reactions → safe 	NA
Other medically relevant species	<i>Tityus stigmurus</i> , <i>Tityus obscurus</i> , <i>Hemiscorpius lepturus</i> , <i>Androctonus australis</i>	