

S1. Data base used and search strategy used in each one.

Data base	Search strategy
PubMed	<p>#1 (((((((("Chagas disease") OR ("Trypanosoma cruzi")) OR ("cruzi, Trypanosoma")) OR ("American Trypanosomiasis")) OR ("Trypanosomiasis, American")) OR ("Trypanosomiasis, South American")) OR ("South American Trypanosomiasis")) OR ("Trypanosoma cruzi Infection")) OR ("Infection, Trypanosoma cruzi")) OR ("Infections, Trypanosoma cruzi")) OR ("Trypanosoma cruzi Infections")) OR ("Chagas' Disease")</p> <p>#2 Search: (Esophagus) OR (Colon)</p> <p>#3 Search: (((((((("Myenteric plexus") OR ("Nervous system")) OR ("Plexus, Myenteric")) OR ("Auerbach's Plexus")) OR ("Auerbach Plexus")) OR ("Auerbachs Plexus")) OR ("Plexus, Auerbach's")) OR ("Nervous Systems")) OR ("System, Nervous")</p> <p>Combination: #1 AND #2 AND #3</p>
Web of Science	<p>#1 TS= ("Chagas disease" OR "Trypanosoma cruzi" OR "cruzi, Trypanosoma" OR "American Trypanosomiasis" OR "Trypanosomiasis, American" OR "Trypanosomiasis, South American" OR "South American Trypanosomiasis" OR "Trypanosoma cruzi Infection" OR "Infection, Trypanosoma cruzi" OR "Infections, Trypanosoma cruzi" OR "Trypanosoma cruzi Infections" OR "Chagas' Disease")</p> <p>#2 TS= (Esophagus OR colon)</p> <p>#3 TS= ("Myenteric plexus" OR "Plexus, Myenteric" OR "Auerbach's Plexus" OR "Auerbach Plexus" OR "Auerbachs Plexus" OR "Plexus, Auerbach's" OR "Nervous system" OR "Nervous Systems" OR "System, Nervous")</p> <p>Combination: #1 AND #2 AND #3</p>
EMBASE	<p>#1 ('chagas disease' OR 'trypanosoma cruzi' OR 'cruzi, trypanosoma' OR 'american trypanosomiasis' OR 'trypanosomiasis, american')</p>

Lilacs	<p>OR 'trypanosomiasis, south american' OR 'south american trypanosomiasis' OR 'trypanosoma cruzi infection' OR 'infection, trypanosoma cruzi' OR 'infections, trypanosoma cruzi')</p> <p>#2 esophagus OR colon</p> <p>#3 'myenteric plexus' OR 'plexus, myenteric' OR 'auerbach plexus' OR 'auerbachs plexus' OR 'nervous system' OR 'nervous systems' OR 'system, nervous'</p> <p>Combination: #1 AND #2 AND #3</p> <p>("Chagas disease") OR ("Doença de Chagas") OR ("Enfermedad de Chagas") OR ("Trypanosoma cruzi") AND (Esophagus) OR (Esôfago) OR (Esófago) OR (Colon) OR (colón) AND ("Myenteric plexus") OR ("Plexo mioentérico") OR ("plexo mientérico") OR ("Nervous system") OR ("sistema nervoso") OR ("sistema nervioso")</p>
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S2. Screened articles and final status for inclusion in the systematic review.

Title	Final situation	Ref.
Aspirin prevents atrophy of esophageal nitrenergic myenteric neurons in a mouse model of chronic Chagas disease	Included	Massocatto et al., 2015
Could Cyclophosphamide exert a protective role avoiding esophagic neuron loss in Calomys callosus infected with Trypanosoma cruzi?	Included	Caetano et al., 2007
Does cyclophosphamide play a protective role against neuronal loss in chronic T. cruzi infection?	Included	Caetano et al., 2008
Effect of acetylsalicylic acid on total myenteric neurons in mice experimentally infected with Trypanosoma cruzi	Included	Souza et al., 2019
Substance P enhances neuronal area and epithelial cell proliferation after colon denervation in rats	Excluded (Does not use an experimental model for Chagas disease)	Buttow et al., 2003
Treatment with low doses of aspirin during chronic phase of experimental Chagas' disease increases oesophageal nitrenergic neuronal subpopulation in mice	Included	Massocatto et al., 2017

Beneficial immunomodulatory and neuro digestive effect in Trypanosoma cruzi infection after Lycopodium clavatum 13c treatment	Included	Aleixo et al., 2017
Myenteric neuroprotective role of aspirin in acute and chronic experimental infections with Trypanosoma cruzi	Included	Oda et al., 2017
Influence of Trypanosoma cruzi Chronic Infection in the Depletion of Esophageal Neurons in Calomys callosus	Included	Caetano et al., 2006

S3. SYRCLE tool risk of bias criteria adapted and met.

Criteria used for risk of bias analysis

1. Was the allocation sequence adequately generated and applied??
2. Were the groups similar at baseline or were they adjusted for confounders in the analysis?
3. Was the allocation to the different groups adequately concealed during?
4. Were the animals randomly housed during the experiment?
5. Were the caregivers and/or investigators blinded from knowledge which intervention each animal received during the experiment?
6. Were animals selected at random for outcome assessment?
7. Was the outcome assessor blinded?
8. Were incomplete outcome data adequately addressed?
9. Are reports of the study free of selective outcome reporting?
10. Was the study apparently free of other problems that could result in high risk of bias??

Fonte: SYRCLE's RoB tool (HOOIJMANS et al., 2014)