Leprosy in a Canadian-Born Man with Seasonal Travel to Florida

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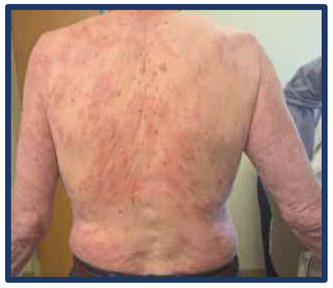
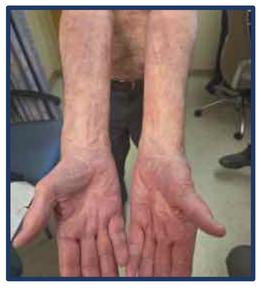
Case Description

75-year-old Canadian man presents with 18 months of Rash

- Numerous reddish-brown papules/plaques and occasional annular lesions over the torso, bilateral arms and upper legs
- Sparing of face, palms and soles
- Lesions were not pruritic, painful or anesthetic
- Neurologic Exam was normal; no sensory deficits, motor weakness or thickened nerves
- No contacts with similar symptoms
- CBC, liver enzymes, and CRP within normal limits





Biopsy Nov 2025:

Non-Necrotizing Granulomatous Inflammation. Fite Stain Positive with Negative Ziehl-Neelsen Stain.

→ *M. leprae* PCR Positive

Delayed Diagnosis From Lack of Traditional Risk Factors

- Born in Canada; Lives in Ontario
- No Travel Outside North America
- No Contacts with Known Cases
- No Contact with Migrant Workers
- From 2008-2018, spent winters at a horse farm in Florida; yard work in armadillo habitats

Increasing Leprosy in Florida

- Since 2000 there has been a gradual increase in leprosy incidence in Southeastern USA, particularly central Florida
- Between 2002-2014, Florida reported 10 cases a year, but since 2015 risen to 27 cases a year
- Approx. 1/3 of cases in Florida had no travel to endemic areas or known contact with infected individuals, suggesting locally acquired infection
- Some reports suggest leprosy should be considered endemic in Florida

Figure 2: Nine-Banded Armadillo
University of Georgia.

- The etiology for the rise in cases is not known but increased evidence for zoonotic infection
- Nine-banded armadillo is only known animal reservoir for leprosy. Expansion of infected armadillo population and land use changes may be responsible for increase in human cases.
- High percentage of human cases in southeastern USA involved a unique strain of *M. Leprae* that occurs amongst the local wild armadillos and not previously reported elsewhere
- Many cases had no direct contact with armadillos but had a history of environmental exposure such as landscaping or yard work in areas inhabited by armadillos and some research has suggested *M. leprae* may live temporarily in soil

Nine-Banded Armadillo
↓
Contaminated Soil in Habitat
↓
Exposure While Gardening in Endemic Areas

- Our case represents the reported case of *M. leprae* infection in Canadian-born individuals with no significant travel outside North America and no known positive contacts
- In all three cases, individuals had history of travel to SE USA
- In both prior cases, genotyping was consistent with the *M. leprae* zoonotic strain found in nine-banded armadillos
- Many Canadians seasonally travel to Florida, and more cases may occur

Conclusion

- Increasing cases that have no traditional risk factors or epidemiologic links suggests leprosy may be now endemic in Florida
- The strain of *M. leprae* involved suggests zoonotic transmission from 9-banded armadillos
- Risk factors may include environmental exposure to armadillo habitats even without direct animal contact
- Seasonal Travelers to Florida may acquire infection
- Clinicians must be aware since many Canadians winter in Florida

Bottom Line

Florida is increasingly recognized as endemic for leprosy. Leprosy should be on the differential for travelers to Florida with a compatible syndrome even in the absence of other traditional risk factors.

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A Systematic Review of Targeted Therapies for Helminthic Eosinophilic Meningitis (HEM): Implications for Refugee, Migrant, and Returning Traveller Populations

Preliminary Findings: Study in Progress – Final Results Pending

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BACKGROUND

HEM is a parasitic infection of the CNS, mainly caused by *Angiostrongylus cantonensis*, *Gnathostoma spinigerum*, and *Baylisascaris procyonis*. Refugees, migrants, and travellers from endemic areas are at increased risk due to contaminated food and water and may experience delays in diagnosis and treatment, leading to severe complications. There is currently no standardized treatment for HEM, resulting in varying outcomes. This systematic review assesses the effectiveness of targeted therapies for HEM.

OBJECTIVE

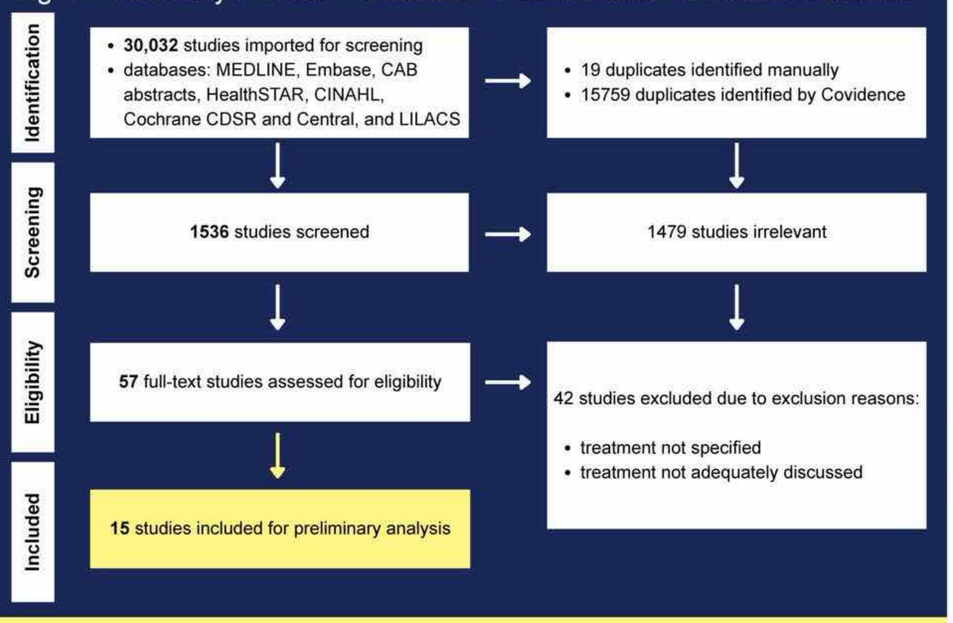
To systematically review and synthesize available literature on the use of targeted therapies for HEM and their relevance to migrant and traveller populations. Findings aim to support clinical decision-making across diverse global settings.

METHODOLOGY

Following PRISMA guidelines, we conducted a systematic search of relevant databases for studies on HEM treatment outcomes. We aim to assess the risk of bias and evidence quality and then perform narrative and subgroup data analyses to evaluate treatment effectiveness.

RESULTS

Fig 1. Preliminary PRISMA Flowchart for Identification of Relevant Studies:



CONCLUSION

Effective management of HEM depends on early detection and targeted treatment. Evidence from the included studies suggests that **a multimodal approach, combining supportive care, corticosteroids, and anthelmintics, particularly albendazole**, yields the most favourable clinical outcomes.

ANALYSIS

Study	Region of Helminth Acquisition	Region of Travel Origin	Region of Immigration / Presentation
1	China		
2	USA		
3	USA		
4	Cuba	Switzerland	
5	SE Asia		
	Caribbean	Mayotte Island	
	USA		
6	USA	SE Asia	
		Japan	
		Mexico	
		Ecuador	
	Latin America	USA	
7	Syria		Turkey
8	Brazil		
9	Vietnam		
10	USA		
11	Iraq		UK
12	Korea	USA	
13	Brazil		
14	USA		
15	Korea		

Fig 2. Geographic Distribution of Helminth Acquisition, Travel Origin, and Immigration/Presentation Sites in Included Studies (n = 15):

Table 1. Summary of six representative studies on HEM:

Study/ Design	Region	Causative Helminth	Transmission Mode	Intervention	Outcome
Bärtschi 2004 1 case report	Switzerland; travel to: Cuba	*A. cantonensis*	possible ingestion of helminth larvae during vacation in Cuba	Analgesics + LP	symptom resolu within 3 wks
Cattaneo 2021 2 case report	Mayotte Island	*A. cantonensis*	interaction or playing with snails	Albendazole + Analgesics + LP + Methyl-prednisolone + Prednisone	symptom resolu within a mo; normal neuro exam at 1 mo follow-up
Diaz 2009 3 review	travel to: SE Asia, Caribbean, USA	*A. cantonensis*	third-stage larvae in snail/slug intermediate hosts; ingestion of raw amphibians, fish, and mollusks reported in many cases	Albendazole + Praziquantel + LP + Corticosteroids	symptom resolu within a mo; spontaneous resolu of most cases with only supportive and nonspecific treatment
	travel to: USA	*B. procyonis*	embryonated eggs in raccoon feces; interaction with raccoons and their latrines reported in many cases	Albendazole + Corticosteroids + LP + Mannitol	usually partial symptom resolu; high mortality and morbidity; complete neuro recovery not possible in most cases
	travel to: SE Asia, Japan, Mexico, Ecuador	*G. spinigerum*	third-stage muscle encysted larvae in intermediate hosts; ingestion of raw freshwater fish in one case; ingestion of raw or undercooked fish, shrimp, crayfish, frogs, crabs, and chicken reported in many cases	Albendazole + Ivermectin + Analgesics + LP + Prednisolone	longer symptom resolu period; clinicians consider lack of migratory symptom recurrence within a median 12 m incubation period and resolu of PB and CSF EO presumptive evidence of cure; relapses have been reported requiring 2nd or 3rd courses of albendazole treatments
	travel to: Latin America, USA	*T. spiralis*	ova (eggs) excreted by a human pork tapeworm carrier; ingestion of contaminated or inadequately cooked pork meat reported in many cases	Albendazole + Praziquantel + Analgesics + Anticonvulsants + LP	risk of seizures in Hem caused by *T. spiralis* poses greater danger of patient health or recovery; neurosurgery may be required if medical treatments fail especially when large cysts are present
Elvan-Tuz 2021 4 case series	Turkey, migrated from: Syria	*Echinococcus* species	case 1: migrated from rural region of Syria case 2: prior lung and liver echinococcosis (3 yrs ago) and 3 cerebellar echinococcosis operations; lived in rural area with bovine animals case 3: frequently visited rural areas, which was inhabited by dogs	case 1: Neurosurgery + Albendazole + Analgesics + LP case 2: Neurosurgery + Albendazole + Analgesics + LP case 3: Neurosurgery + Albendazole + Analgesics + Antibiotics + LP	case 1: partial symptom resolu at 1 mo follow-up; elimination of HEM causing helminth case 2: patient was discharged 15 d after admission; at the 11th month follow-up no recurrence noticed case 3: cerebral abscess resolu after 56 d; partial resolu of rest of the symptoms
Hughes 2020 5 case report	UK; migrated from: Iraq	*Fasciola* species	frequent consumption of watercress from local river in Iraq before immigration to UK	LP + Antibiotics + Antituberculosis therapy + Prednisolone + Pyridoxine + Triclabendazole	symptom resolu within a mo; inappropriate antibiotics and antituberculosis therapies administered
Re 2002 6 case report	Philadelphia, USA; travel to: Korea	*G. spinigerum*	ate raw fish during Korea trip	LP + Amphotericin B + Antituberculosis therapy + Itraconazole + Fluconazole	symptom resolu after several mo; inappropriate antifungal therapy administered; neuro deficits or residual symptom presence not mentioned

Abbreviations: retro, retrospective; SE, Southeast; y, years; -ve, negative; *A. cantonensis*, *Angiostrongylus cantonensis*; PB, peripheral blood; CSF, cerebrospinal fluid; EO, eosinophil; d, day(s); wks, weeks; mo, month; resolu, resolution; LP, lumbar puncture; *B. procyonis*, *Baylisascaris procyonis*; *G. spinigerum*, *Gnathostoma spinigerum*; *T. spiralis*, *Taenia spiralis*; neuro, neurologic.

Fig 3. Interventions reported across 15 HEM studies:

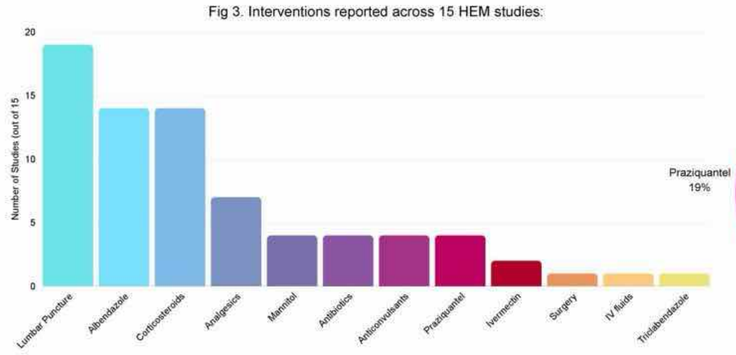


Fig 4. Proportion of Antihelmintic Use:

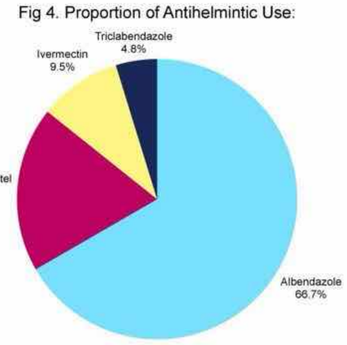
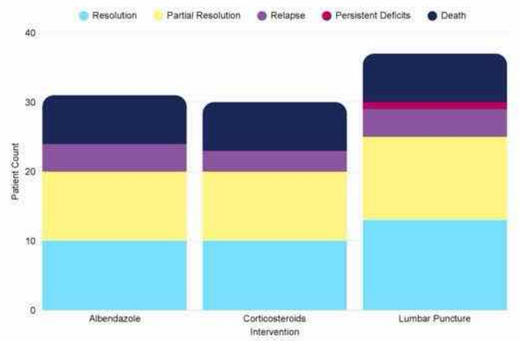


Fig 5. Outcomes by Major Intervention:



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LB-9235

A Systematic Review of Lifestyle Interventions for Neuropathy and Neuropathic Pain: Alcohol Avoidance

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Introduction

- Neuropathy and neuropathic pain (NP), affecting 7-10% of the global population and nearly all persons with leprosy, remain difficult to manage and are often complicated by underlying lifestyle factors
- Alcohol use, particularly in the context of chronic consumption or dependence, is a recognized contributor to peripheral nerve damage, yet its association with neuropathy/NP has not been systematically evaluated
- This systematic review synthesizes current evidence on alcohol exposure, including quantity, frequency, and dependency, and its relationship with neuropathy/NP incidence, prevalence, and severity

Methods

- Five databases (PubMed, Embase, Medline, Scopus, LILACS) were searched from inception to October 2025
- Included observational studies assessing alcohol consumption patterns or dependence in relation to neuropathy or NP outcomes
- Conducted in accordance with PRISMA guidelines while certainty & quality of evidence were evaluated via the GRADE framework

Results

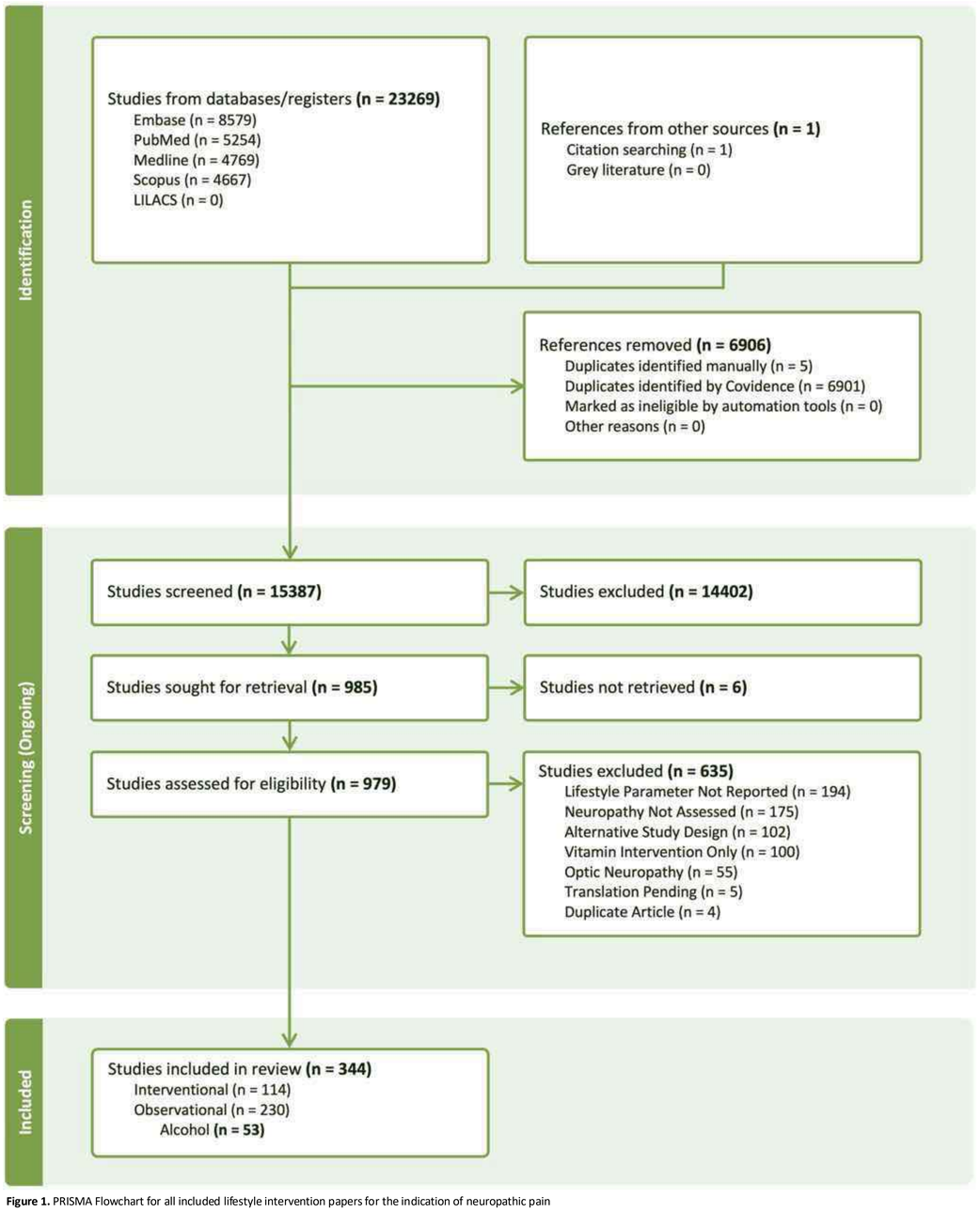

Figure 1. PRISMA Flowchart for all included lifestyle intervention papers for the indication of neuropathic pain

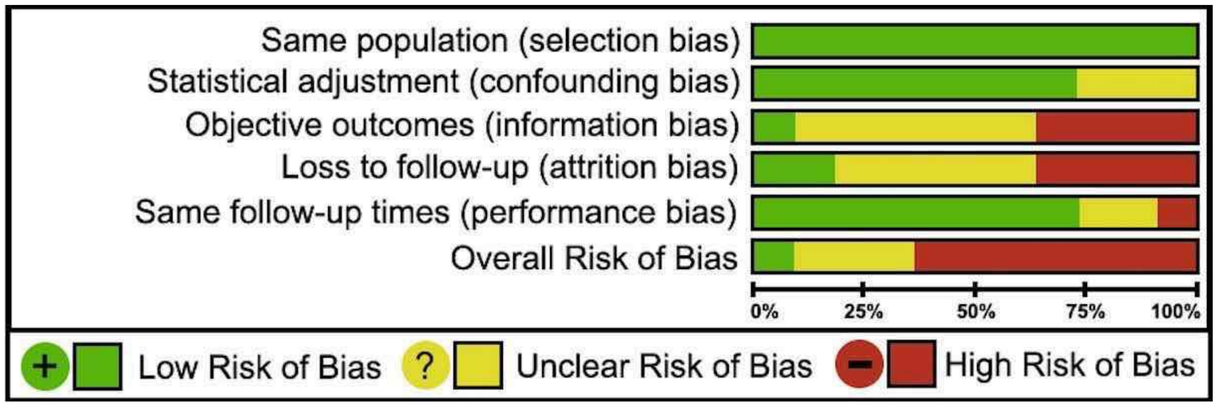

Figure 2. Summary of GRADE Risk of Bias Assessment for Included Cohort Studies

Results

Author (Year)	Study Design	Setting	N	Sex N (F-M)	Age (mean±SD, (range))	Population / ESiology	Lifestyle	Outcomes
Adler (1997)	Cohort Study	US	With Ne: 58; Without Ne: 230	With Ne: 1:57; Without Ne: 11:219	With Ne: 64.0; Without Ne: 61.5	DM + Incident Ne	Alcohol: CAGE score, history of treatment, current use	High (4) CAGE alcohol score was significantly associated with incident Ne (41.7% vs 58.3%, p=0.049; β=1.94, SE=0.7281, 6.96 [1.67-28.99], p=0.008).
Braffett (2020)	Cohort Study	US	With DPN: 455; Without DPN: 931	With DPN: 182:273; Without DPN: 475:456	* With DPN: 29 (24, 34); Without DPN 26 (21, 32)	T1DM + DPN	Occasional or regular alcohol use	Alcohol consumption was not significantly associated with DPN (1.14 [0.93-1.41], p>0.05).
Christensen (2020)	Cohort Study	Denmark	Overall: 5249; With DPoN: 938; With DPoN+Pain: 386	Overall: 2205:3144	* 65 (57, 72)	T2DM + DPoN + Pain	Alcohol: ≤14(F)/21(M) units, >14(F)/21(M) units	Alcohol consumption above recommended limit was significantly associated with increased prevalence of NP (aPR: 1.31 [1.01-1.69].
Khan (2023)	Cohort Study	US	TUD: 8009; TAUD: 1672; PSUD: 642; TUD Co: 8009; TAUD Co: 1672; PSUD Co: 642	TUD: 4660:3349; TAUD: 582:1090; PSUD: 233:409; TUD Co: 4665:3344; TAUD Co: 584:1088; PSUD Co: 234:408	TUD: 61.6±12.1; TAUD: 61.52±10.3; PSUD: 57.84±8.1; TUD Co: 61.6±12.1; TAUD Co: 61.42±10; PSUD Co: 57.88±8.1	T2DM + Hypertension + Ne	TUD: Yes, No; TAUD: Yes, No; PSUD: Yes, No	PSUD was associated with a significantly higher risk of DN (1.76 [1.33-2.32], p<0.05) compared to TUD, while TAUD vs TUD wasnt (1.04 [0.87-1.24], p>0.05).
Kindl (2021)	Cohort Study	Germany	With MSK: 255; With CRPS: 223	With MSK: 160:95; With CRPS: 173:50	With MSK: 54.6 (20-80); With CRPS: 50.9 (18-77)	CRPS or MSK, due to trauma	Alcohol Consumption: Yes, No, Daily, Weekly, Monthly	Alcohol consumption was significant within both the MSK (58%, p<0.001), and CRPS (43%, p<0.001) groups, and remained significantly associated with higher pain intensity (p<0.05) for MSK but not CRPS.
Lehtinen (1993)	Cohort Study	Finland	With ND: 12; Without ND: 101	With ND: 9:3; Without ND: 46:55	With ND: 57.2±4.7; Without ND: 55.4±10.4	DM + ND	Alcohol use (>30g/wk)	Alcohol use was not significantly different between ND groups (17% vs 30%, p>0.05).
Sreeram (2023)	Cohort Study	US	Overall 1034; With CIPN: 704; Without CIPN: 330	Overall: 797:237; With CIPN: 570:134; Without CIPN: 227:103	Overall: 57.1±10.9 (27-79); With CIPN: 55.8±10.8 (27-79); Without CIPN: 59.9±10.4 (27-79)	Cancer survivors + CIPN	Alcohol Use (Past 4 wks): Yes, No	Alcohol use was not significantly different between CIPN groups, or associated with CIPN prevalence (51.2% vs. 46.4%, 1.10 [0.81-1.49], p>0.05).
Doneddu (2020)	Case Control Study	Italy	Ca: 195; Co: 195	Ca: 109:86; Co: 109:86	NR	CIDP due to any etiology and their partners	Alcohol Consumption: Yes, No	Alcohol consumption was not significantly associated with CIDP (0.79 [0.50-1.24], p>0.05).
Fouchard (2023)	Case Control Study	France	Overall: 323; Ca: 162; Co: 161	Overall: 192:131; Ca: 88:74; Co: 104:57	Ca: 56±16; Co: 69±13	Cutaneous paresthesia + SFN via IENFD due to any etiology	Alcoholism: Yes, No	Alcohol consumption was not significantly different between SFN groups (3.7% vs 1.2%, p>0.05).
Franklin (1994)	Case Control Study	US	Ca: 77; Co: 200	Ca: 29:48; Co: 118:82	Ca: 61.7; Co: 58.6	NIDDM + DSN	Alcohol use: never, g/wk (<20, >20)	Alcohol (g/wk: <20, >20) was not significantly associated with DSN (0.71 [0.29-1.72] p=0.69, 1.03 [0.40-2.62]).
Gebabo (2021)	Case Control Study	Ethiopia	Overall: 528; Ca: 264; Co: 264	Ca: 101:163; Co: 105:159	Ca: <40: 43; 40-65: 178; 65+: 43; Co: <40: 64; 40-65: 178; 65+: 17	T1DM or T2DM + PN	Alcohol Consumption (Ever): Yes, No	Alcohol consumption was significantly higher among those with PN vs without (5.3% vs 1.5%, p=0.024).
Mondelli (2020)	Case Control Study	Italy	Ca: 220; Co: 460	Ca: 84:136; Co: 242:218	Ca: 51.7±11.8; Co: 47.8±12.4	Ca: UNE; Co: Upper limb complaints	Alcohol: u/wk or d	Alcohol consumption was not significantly different between UNE groups (p=0.463).
Pessione (1995)	Case Control Study	France	Ca: 32; Co: 58	Ca: 6:26; Co: 22:36	Ca: 49±10.1; Co: 46.8±9.6	Alcoholism + PN	Alcohol: parental history of alcoholism, alcohol dependence, weekly alcohol consumption (drinks)	Parental history of alcoholism, severe alcohol dependence, weekly alcohol consumption were all significantly higher in those with PN vs without (62.5% vs 15.5%, p<0.001); 81.2% vs 48.3%, p=0.002; 176.8±121.3 vs 106.9±85.6, p<0.006). Parental history of alcoholism, and weekly alcohol consumption remained significantly associated with PN on multivariate anlyses (6.8 [2.2-21.6] p<0.001; 2.4 [1.04-5.6] p=0.03).
Alessi (2020)	Cross Sectional Study	US	Overall: 934; Never Drinker: 103; Former Drinker: 89; Nonbinge Drinker: 567; Binge Drinker: 174	Overall: 569:365; Never Drinker: 61:42; Former Drinker: 51:38; Nonbinge Drinker: 373:194; Binge Drinker: 84:90	Overall: 38.3±15.8; Never Drinker: 31.8±16.8; Former Drinker: 44.1±16.1; Nonbinge Drinker: 39.8±15.8; Binge Drinker: 34±13	T1DM + PN	Alcohol Consumption: Never, Former, Current (Nonbinge), Current (Binge)	Ne is significantly lower in never vs former alcohol consumption (11% vs. 35%, p=0.006).
Asai (2022)	Cross Sectional Study	Japan	Overall: 817; With CP: 35; Without CP: 782	Overall: 431:386; With CP: 24:11; Without CP: 407:375	With CP: 63.91 [60.11-67.72]; Without CP: 63.75 [63.02-67.72]	Chronic neck/shoulder/upper limb pain due to any etiology	Current drinker: Yes, No	Alcohol consumption was not significantly different between CP groups (42.86% vs 47.19%, p>0.05).
Beulens (2008)	Cross Sectional Study	Europe	1857	893:964	(15-60)	T1DM + Ne	Alcohol consumption (g/wk)	Moderate alcohol consumption (30-70 g/wk) and drinking frequency (5-7 d/wk) were associated with significantly lower risks of Ne (0.61 [0.41-0.91], p<0.01; 0.49 [0.34-0.71], p<0.001), with alcohol consumption demonstrating a U-shaped relationship.
Correa (2023)	Cross Sectional Study	Brazil	Overall: 444; LLBP: 313; PNBP: 33; WP: 98	Overall: 289:155; LLBP: 188:125; PNBP: 26:7; WP: 75:23	Overall: 39.72±14.68; LLBP: 37.02±13.39; PNBP: 8.45±14.30; WP: 48.78±15.59	Chronic BP due to any etiology	Alcohol Abuse: Yes, No	Alcohol consumption reported between pain groups: LLBP: 12.1%, PNBP: 9.1%, WP: 12.2% (statistics NR).
Gyfadottir (2020)	Cross Sectional Study	Denmark	5514	2355:3159	64.1±10.9	T2DM + DPoN	Alcohol: >7(F)/14(M) units	Alcohol consumption above recommended limit was not significantly associated with DPoN (0.94 [0.74-1.18], p>0.05), or painful DPoN (1.09 [0.81-1.46], p>0.05), in multivariable logistic regression.
Hicks (2022)	Cross Sectional Study	US	Overall: 6902; With PN: 1181; Without PN: 5721	Overall: 3589:3313; With PN: 443:738; Without PN: 3101:2629	%(!) 40–49: 36 (0.9); 50–59: 27.8 (0.8); 60–69: 18.2 (0.6); 70–79: 12.8 (0.4); ≥80: 5.2 (0.3)	DM + PN	Alcohol: Never, Former, Current	Alcohol consumption reported between PN groups: Never: 16.4%, Former: 27.2%, Current: 56.5% vs 11.8%, 20.9%, 67.3% (statistics NR).
Jeyam (2020)	Cross Sectional Study	Scotland	Overall: 5558; With DPN 715; Without DPN 4842	Overall: 2449:3109; With DPN: 320:395; Without DPN 2129:2713	* Overall: 44.7 (33, 55.2); With DPN: 50.6 (41, 59.3); Without DPN: 43.7 (32, 54.4)	T1DM + DPN	Alcohol (u/wk): 2-6, 6-14, 14-21, 21-32, >32	Alcohol consumption below 32 u/wk was associated with lower odds of symptomatic DPN (0.47 [0.29-0.75], p<0.05), while consumption above 32 u/wk was not (0.88 [0.56-1.36], p>0.05). Authors suggest individuals with DPN may reduce alcohol intake due to medication use (reverse causation - protopathic bias).
Nielsen (2022)	Cross Sectional Study	Denmark	2839	High CIPN Score: 274:146; Low CIPN Score: 1193:870	^* High CIPN Score: 69; Low CIPN Score: 67; (18-99)	Cancer diagnosis at any stage of treatment + CIPN	Alcohol: yes/no + u/wk	Alcohol consumption was significantly different between CIPN groups (60.2% vs 73.5%, p<0.001), and high consumption (>14 u/wk) was significantly associated with high CIPN20 scores vs low consumption (<14 u/wk) in males (22% vs 11%, p<0.002).
Sahito (2022)	Cross Sectional Study	Pakistan	Overall: 1057; With PN: 607; Without PN: 450	Overall: 414:643; With PN: 230:377; Without PN: 184:266	30-40: 119; 41-50: 316; 51-60: 324; 61-70: 165; >70yrs: 133	T2DM + PN	History of alcohol intake: Yes, No	Alcohol intake reported between PN groups: 4.7% vs 1.4% (statistics NR).
Van der Velde (2020)	Cross Sectional Study	The Netherlands	Overall: 2401; High Sural SNAPA: 793; Med Sural SNAPA: 796; Low Sural SNAPA: 812	Overall: 1174:1227; High Sural SNAPA: 464:329; Med Sural SNAPA: 377:419; Low Sural SNAPA: 334:478	Overall: 59.3±8.2; High Sural SNAPA: 56.4±8.2; Med Sural SNAPA: 59.4±7.9; Low Sural SNAPA: 62±7.5	T2DM + PN	Alcohol: >7(F)/14(M) units	Alcohol consumption (% high) reported between PN groups (via sural SNAPA): High: 26.7%, Medium: 25.8%, Low: 27.6% (statistics NR).
Yokoyama (2020)	Cross Sectional Study	Japan	Overall: 9914; Without DPoN: 6180; With DPoN: 2745 (with DPoNS: 1689; with UDoPN: 989)	Overall: 3715:6139; Without DPoN: 2273:3904; With DPoN: 1041:1705 (with DPoNS: 664:1025, with UDPoN: 397:530)	^* Overall: 66 (69-73); Without DPoN: 65 (57-71); With DPoN: 70 (63-77) (with DPoNS: 69 (63-76), with UDPoN: 67 (59-75))	T2DM + DPoN	Alcohol: Current, Former, Never	Former alcohol consumption was associated with higher odds of DPN (2.02 [1.25–3.27], p=0.004), while current alcohol consumption was not. Authors suggest individuals with DPN may reduce alcohol intake due to emerging impairment (reverse causation - protopathic bias).

Table 1. Characteristics of Pooled Studies

Abbreviations: **aPR:** adjusted prevalence ratio; **Ca:** cases; **CIDP:** chronic inflammatory demyelinating polyradiculoneuropathy; **CIPN:** chemotherapy induced peripheral neuropathy; **CIPN20:** European Organisation for Research and Treatment of Cancer CIPN 20-item scale; **Co:** controls; **CP:** chronic pain; **CRPS:** complex regional pain syndrome; **d:** day; **DM:** diabetes mellitus; **DPN:** diabetic peripheral neuropathy; **DPoN:** diabetic polyneuropathy; **DPoNS:** diabetic polyneuropathy-related sensory symptoms/signs; **DSN:** distal symmetric neuropathy; **F:** female; **g:** grams; **IENFD:** intraepidermal nerve fiber density; **LLBP:** localised lower back pain; **M:** males; **MSK:** musculoskeletal pain; **Ne:** neuropathy; **ND:** neurophysiologically deteriorated; **NIDDM:** non-insulin dependent diabetes mellitus; **NP:** neuropathic pain; **NR:** not reported; **PN:** peripheral neuropathy; **PNBP:** peripheral neuropathic back pain; **PSUD:** polysubstance use disorder group (tobacco, alcohol, + 1 other); **SE:** standard error; **SFN:** small fibre neuropathy; **SNAPA:** sensory nerve action potential amplitude; **T1DM:** type 1 diabetes mellitus; **T2DM:** type 2 diabetes mellitus; **TAUD:** tobacco and alcohol use disorder group; **TUD:** tobacco use disorder group; **u:** units; **UDPoN:** unknown status diabetic polyneuropathy; **UNE:** ulnar neuropathy at the elbow; **wk:** week; **WP:** widespread pain; **y(s):** year(s); **β:** beta coefficient; **^:** Median (interquartile range); **^^:** Median (range); **‡:** Standard error; *All data reported as mean±SD, mean (range), or mean [95% CI]; outcome data reported as cases vs controls, or as "with Ne" vs "without Ne", with OR [95% CI], p-value (adj p-value when available) unless otherwise specified. Disease duration always reported in years, unless otherwisespecified.*

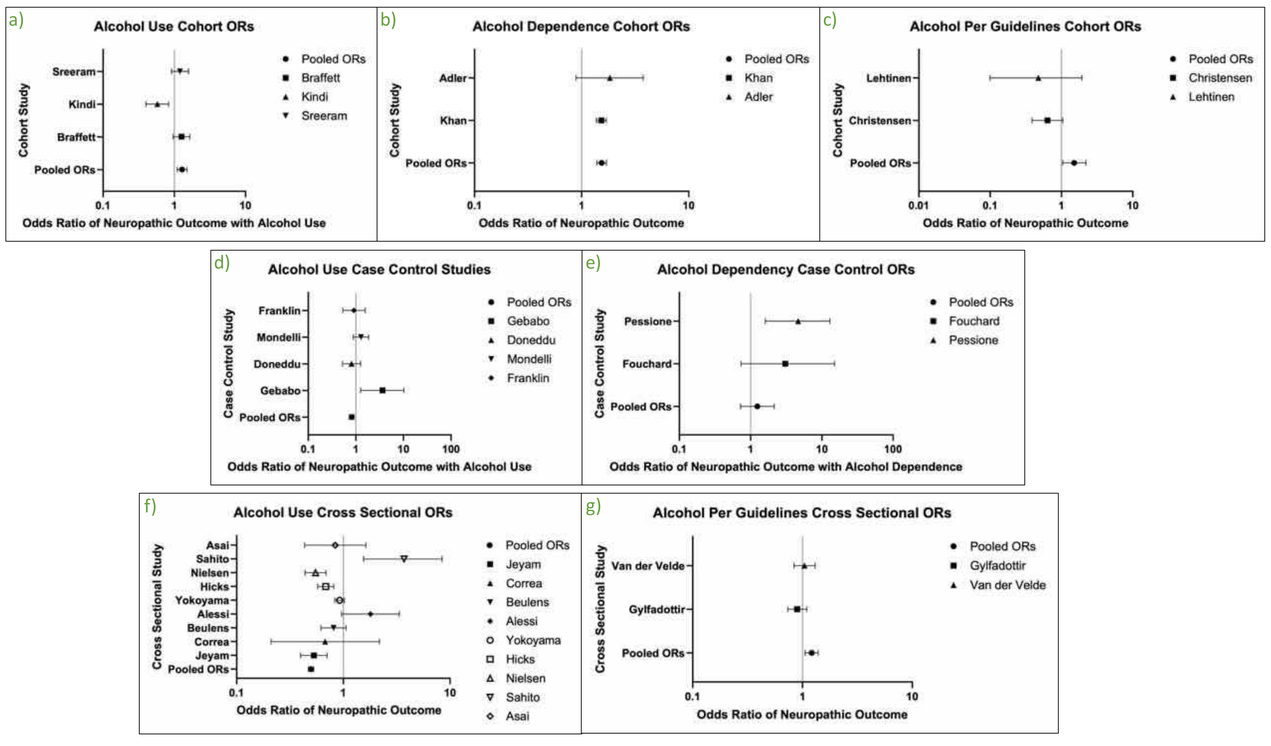

Figure 3. Forest plots of odds ratios of neuropathic outcome according to alcohol consumption variables in cohort (a-c), case-control (d, e), and cross sectional (f, g) studies

Discussion

- Following screening, fifty-three studies were identified for final inclusion and analysis (Figure 1)
- While associations varied by study design and exposure category, alcohol dependence and consumption were more consistently linked with increased neuropathy risk and severity, including electrophysiological deterioration (Table 1)
- Significant heterogeneity and risk of bias were present, largely due to the subjective classification of alcohol exposure and a lack of objective neuropathy measurement tools (Figure 2)
  - Despite this multiple pooled estimates, reached statistical significance (Figure 3)
- Alcohol abstinence was linked to clinical improvements in neuropathy/NP symptoms
- Evidence supports a potential role for alcohol use, especially dependence, in the development and progression of neuropathy/NP
  - Abstinence may offer therapeutic benefit, though further interventional studies are required to clarify causality and guide low-cost, adjunctive strategies

References

Targeted Pharmacological Interventions for the Prevention and Treatment of Viral Hemorrhagic Fever: A Systematic Review of Updated Intelligence from the 74th Annual Meeting of the American Society of Tropical Medicine and Hygiene

Michael Klowak[1,2], Gregory Hawley[1,2,3], Jamal Tarrabain[2,3], Sandy Wang[2,3], Amanda Hempel[2,3], Keshini Abeyewardene[2,3], Jahmar Hewitt[2], Candice Madakadze[2], Asal Adawi[2], Aquilla Reid-John[2], Zain Ahmad[2], Andrea K. Boggild[1,2,3]

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Introduction

- Viral hemorrhagic fevers (VHF) are high-consequence, life-threatening illnesses characterized by systemic disease, hemorrhage, and high mortality
- The American Society of Tropical Medicine and Hygiene (ASTMH) Annual Meeting functions as a major international forum for the presentation of emerging data on infectious diseases, including novel pharmacologic and biologic interventions for VHF
- While ASTMH presentations provide timely and high-impact insights, there is no consolidated synthesis of this rapidly evolving evidence base
- Given the acute, outbreak-prone nature of VHF and the need for rapid translation of emerging data into clinical and public health practice, a structured synthesis of these data is warranted.

Methods

- This systematic review follows PRISMA guidelines and is limited to presentations delivered at the ASTMH Annual Meeting in Toronto (November 9-13, 2025) to capture evolving evidence as it emerges
- Titles and abstracts were screened for inclusion and eligible symposia, oral presentations, and poster abstracts, attended in person, have undergone preliminary data extraction
- Studies of all designs evaluating vaccines, chemoprophylactic agents, or targeted biological therapies for the prevention or treatment of VHF in adults and children will be included
- Methodological quality will be assessed using the GRADE framework, with risk of bias evaluated using JBI tools
- Data will be extracted on incidence of VHF among exposed populations, safety, toxicity, and tolerability of preventive and therapeutic interventions, and morbidity and mortality outcomes among treated individuals
- Secondary outcomes will include hospitalization length-of-stay, economic outcomes, and measures of feasibility, acceptability, accessibility, and health equity

Results

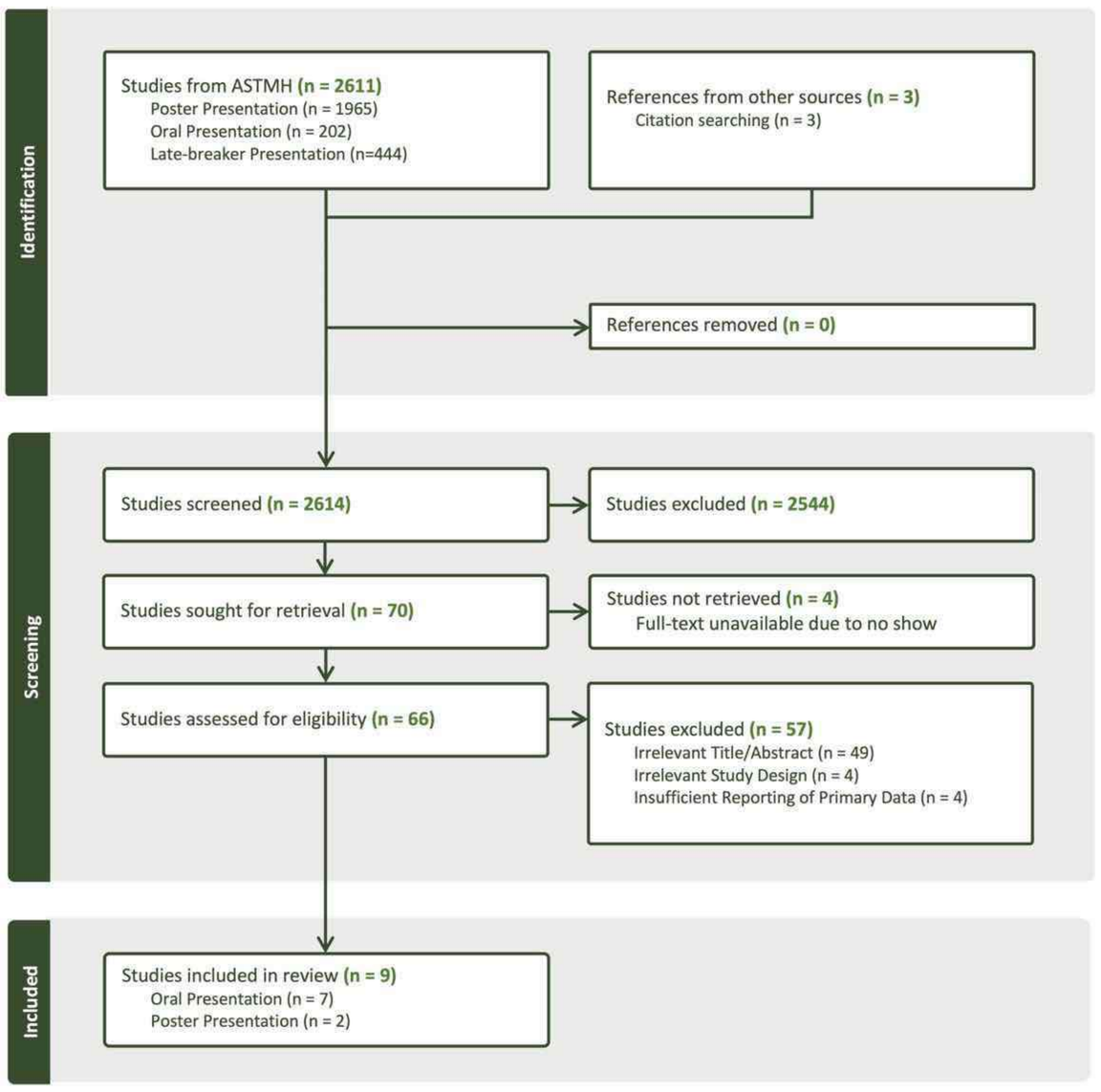

Figure 1. PRISMA flowchart

Results

Author (Year)	Type of Presentation	Study Design	Type of VHF	Population Characteristics	Intervention	Outcomes
Malkevich et al. (2025) [1]	Poster Presentation	Phase 1 Trial	Ebola – Sudan virus (SUDV)	14 cases and 34 controls	rVSVΔG-SeboV-GP vaccine: IM dose of 2x10E6 - 2x10E8 pfu	**Primary:** vaccine was safe and well tolerated with no serious vaccine-related adverse events; mild-to-moderate local pain and tenderness were reported. **Secondary:** rapid vaccine study implementation within 5 days of outbreak confirmation demonstrated feasibility of emergency outbreak response using pre-approved protocols, in-country vaccine availability, and existing collaborations.
Njenga et al. (2025) [1]	Oral Presentation	Post-outbreak Survivor Cohort Study	Ebola – Sudan virus (SUDV)	Outbreak of 142 cases with 55 fatalities and 87 survivors	N/A	**Primary:** 57.5% of SUDV survivors developed persistent multi-system clinical sequelae over 2 years, most commonly involving ophthalmologic, central nervous system, and reproductive manifestations.
Tremblay et al. (2025) [1]	Oral Presentation	Randomized Control Trial	Ebola virus (ZEBOV)	Adults and adolescents	Ebola Virus Vaccine (rVSV-ZEBOV-V) and placebo	**Primary:** vaccine recipients developed sustained GP-ELISA and PRNT responses through 1 year, with geometric mean titres 42-fold higher than placebo recipients; adverse events were primarily injection-site pain, headache, fatigue, and arthralgia.
Berrian et al. (2025) [1]	Poster Presentation	Cross Sectional Study	Ebola virus (unspecified)	1200 participants including 696 females and 504 males with a mean age of 40yrs (18-80)	Survey to identify community-based Ebola preparedness and vaccination readiness strategies	**Secondary:** outbreak preparedness, healthcare infrastructure, vaccine availability/effectiveness, and trust in healthcare systems were associated with increased likelihood of vaccination during outbreaks; affordable healthcare and community preparedness were identified as predictors of vaccine uptake.
Gilbert et al. (2025) [1]	Oral Presentation	Phase 1 Trial	Nipah virus	Sentinel cohort including 6 adults and main cohort including 45 adults	ChAdOx1 NipahB Vaccine and saline placebo (n=5)	**Primary:** no serious adverse events were reported; asymptomatic thrombopenia occurred in 2 volunteers, including 1 potentially spurious result that resolved on repeat testing. **Secondary:** clinical efficacy assessment was not considered feasible because of sporadic/low Nipah virus case numbers and absence of an established correlate of protection.
Heppner et al. (2025) [1]	Oral Presentation	Phase 1 Trial	Nipah virus	A. 61 healthy adults; B. 120 healthy adults	Nipah Virus Vaccine (PHV02); A: One IM dose of 1.0e5:1.0e6:1.0e7:placebo (1:1:1:1 pfu) with 5.0e8 booster at 1 yr; B: Two IM dose of 2.5e6:2.5e7:2.5e8:placebo (1:1:1:1 pfu) 28 days apart	**Primary:** all vaccine doses were well tolerated; neutralizing antibody seroconversion occurred after single-dose vaccination and increased following booster vaccination, reaching 96% in the two highest dose groups by day 57.
Playford et al. (2020) [2]	Oral Presentation	Phase 1 Trial	Hendra virus and Nipah virus (henipaviruses)	40 healthy adults including 16 females, and 24 males, aged 18-50 yrs old	Monoclonal antibody m102.4 (n=30), and placebo (n=10)	**Primary:** m102.4 was safe and well tolerated with no deaths, life-threatening events, serious adverse events, or study discontinuations; treatment-emergent adverse events were similar between placebo and treatment groups, with headache being the most common treatment-related adverse event.
Nsanzimana et al. (2025) [3]	Oral Presentation	Emergency Phase 2 Trial during active outbreak	Marburg virus	A. 66 laboratory-confirmed MVD cases (21 female (32%), 45 male (68%), with median age 31.5 yrs) with 6340 persons tested overall; B. 1710 frontline workers and high-risk contact vaccinated as preventive outbreak-response	A. remdesivir, MBP091; B. ChAd3-MARV vaccine	**Primary:** case fatality rate was 23% (15/66 patients); respiratory failure requiring mechanical ventilation developed in 9 patients, of whom 7 died; both patients requiring hemodialysis died. No serious vaccine-related adverse events were reported during emergency ChAd3-MARV vaccine rollout.
Hamer et al. (2023) [4]	Oral Presentation	Phase 1 Trial	Marburg virus	40 healthy adults including 25 females (63%), and 15 males (38%) with a mean age of 34.9 yrs (range 19–48)	chimpanzee adenovirus type 3-vectored Marburg virus vaccine (cAd3-Marburg): IM dose at 1×10^{10} pu (n=20) and 1×10^{11} pu (n=20)	**Primary:** vaccine was safe and well tolerated with no serious vaccine-related adverse events, including mild injection site pain/tenderness, malaise, headache, and myalgia. Glycoprotein-specific antibody responses developed in 95% of participants after a single vaccination and remained elevated at 48 weeks. **Secondary:** findings supported potential emergency deployment and outbreak-response use of the vaccine.

Table 1. Preliminary Characteristics of Included Studies
Abbreviations: **IM:** intramuscular; **MVD:** Marburg virus disease; **PFU:** plaque-forming units; **PRNT:** plaque reduction neutralization test; **yrs:** years.

Discussion

- Across Ebola, Nipah, and Marburg virus studies, preventive and therapeutic interventions were generally safe and well tolerated, with no serious vaccine-related adverse events reported in vaccine trials and strong immunogenicity demonstrated through sustained antibody responses and high seroconversion rates (Table 1)
- Findings also highlighted major operational and clinical challenges in VHF response, including persistent long-term sequelae among SUDV survivors, substantial mortality and organ-support requirements in MVD, and the importance of outbreak preparedness, healthcare infrastructure, regulatory readiness, and rapid deployment capacity for effective implementation of VHF countermeasures (Table 1)
- This systematic review will provide a rapid, structured synthesis of targeted pharmacological interventions presented as emerging evidence at an expert scientific venue, while addressing the current lack of a consolidated accessible summary of emerging VHF evidence
- By rapidly organizing and evaluating these data, this work facilitates timely interpretation and application in clinical and public health settings where rapid decision-making is critical

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A case of concurrent dengue and *Plasmodium vivax* malaria in a returned traveler to India

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INTRODUCTION

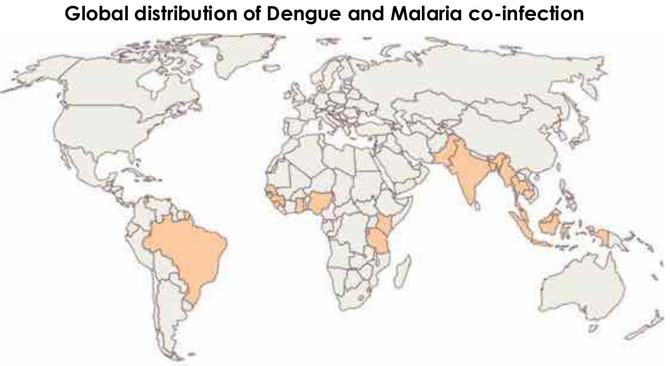
Dengue and malaria are common vector-borne tropical diseases

They are associated with high morbidity and mortality

Co-infection of malaria and dengue is underestimated due to parsimonious approach once the diagnosis of either is made

Herein, we describe a case of a 27-year-old man of Indian origin residing in Canada who took a 15-day trip to India to visit friends and relatives (VFR), and thereafter presented to hospital for evaluation of high fever, fatigue, myalgia, headache and generalized weakness.

Global distribution of Dengue and Malaria co-infection



Salam et al. BMC Public Health (2018) 18:710

CASE TIMELINE

Day 1:
Return to Canada following 15 days trip to New Delhi, India

Day 10:
fatigue, myalgia, headache

Day 12:
Symptoms worsened with fever with chills

Day 13:
Travelled to Cancun, Mexico

Day 15:
Presented to ED for high fever of 40.5 C

Workup: CBC
Mild anemia with hemoglobin of **127**g/L
WBC 4.9 x 10^9/L with moderate lymphopenia of **0.3** x 10^9/L
Profound thrombocytopenia of **66** x 10^9/L

Infectious workup:
Initial malaria RDT: positive pan-*Plasmodium* aldolase, negative *P. falciparum*-specific HRP-2 antigen
Thin blood smear demonstrated intraerythrocytic stages of *P. vivax* at a parasitemia level of 0.7%.

Blood cultures and serologic testing for hepatitis A, hepatitis B, and dengue virus

Rx: atovaquone-proguanil 1000/400 mg daily for 3 days

Day 20:
TDU clinic-*P. vivax* strain confirmed by PHOL

Rx: primaquine phosphate 30-mg PO daily for 14 days for radical cure

Day 27: Follow up
Dengue serology: reactive IgM and IgG by EIA **confirming the diagnosis of malaria and dengue co-infection**

Repeat parasitemia 0%
Repeat CBC demonstrated resolution of lymphopenia (2.1 x 10^9/L) and thrombocytopenia (platelets 232 x 10^9/L).
Remaining infectious work up negative

Day 69: Final follow up
clinically well
CBC normal range
repeat parasitemia level was 0%.

CLINICAL OUTCOME

Investigations

Initial work up for malaria while present in the ED by rapid diagnostic test (RDT) demonstrated positive pan-*Plasmodium* aldolase and negative *P. falciparum*-specific histidine rich protein-2 (HRP-2) antigen, most suggestive of a non-falciparum malaria. However, the few cases of HRP-2 mutant strains of *P. falciparum* reported from the Indian sub-continent necessitate interpreting a negative HRP-2 band cautiously. Thin blood smear demonstrated intraerythrocytic stages of *P. vivax* at a parasitemia level of 0.7%.

Dengue serologic testing performed during his first visit to the ED (drawn on day 8 of fever) was reported as **reactive** IgM and IgG by enzyme immunoassay (EIA), confirming the diagnosis of malaria and dengue co-infection.

Management

The patient was started on atovaquone-proguanil 1000/400 mg daily for 3 days with fatty meals

Once the reference laboratory confirmed that his malaria was caused by *P. vivax* strain, he was additionally started on primaquine phosphate 30-mg PO daily for 14 days for radical cure, after confirming a normal G6PD level of 8.3 U/g Hb.

Symptomatic management for dengue ensued

Outcome

The patient improved clinically rapidly and during the follow up at our clinic 6 weeks from symptom onset he continued to remain clinically well.

His CBC at the time of 6-week follow-up was within normal range

Routine repeat day 28 parasitemia level was 0%.

LEARNING POINTS

This case highlights that dengue and malaria intercurrent infection might be more common than previously estimated, particularly as vector ranges expand with global warming and climatologic events permissive to mosquito generation.[1]

The severity of the intercurrent infection can be mitigated by early diagnosis and treatment of the malaria component while supportive measures are instituted for dengue.[2,3]

This case underscores the importance of patients presenting with either infection acquired from areas endemic for both coupled with the trifecta of low parasitemia level, moderate to severe thrombocytopenia and leukopenia, support the diagnosis of intercurrent infection. [4]

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Rifampin-Ofloxacin-Minocycline (ROM) for the Treatment of Paucibacillary Leprosy: A Systematic Review

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Introduction

- Standard WHO multi-drug treatment (MDT) for leprosy consists of medications that are potentially harmful and cause a range of adverse systemic effects
- Paucibacillary leprosy, characterized by limited skin lesions and a low bacillary load, may be most amenable to a fluoroquinolone-based treatment protocol
- Monthly- or single dosing of ROM has emerged as a potential treatment option for leprosy, however, a synthesis of the evidence supporting ROM does not exist

Methods

- Abstracts reporting the efficacy & safety of monthly ROM treatment in paucibacillary leprosy in human patients were targeted using combinations of search terms related to "leprosy" (including "Hansen's disease" and "*M. leprae*") and "rifampin," "ofloxacin," "minocycline," and "ROM," along with their common synonyms and trade names (from inception to June 2025)
- Inclusion Criteria: Systematic reviews, randomized controlled trials, clinical trials, cohort studies, observational studies, case-control studies, case series (N>5), English and non-English publications
- Exclusion Criteria: Case reports, case series (N<4)

Results

Study	Country	Study Design	Sample Size, No.	Mean Age, y	Male, %	Follow-Up, (SD), mo	Diagnosis of Leprosy	# Lesions	Treatment	Comparator
[1]Alam et al., 2007	Bangladesh	Retrospective	270	-	-	96	Not reported	Single	ROM, single dose	No Comparator
[2]Babu et al., 1997	India	Randomized Control Trial	1483	23	42.28	12	Clinical	Single	ROM, single dose	WHO-MDT
[3]Desikan & Gupte, 2001	India	Randomized Control Trial	236	-	46.19	12-18	Clinical + Histological	2-3	ROM, single dose	WHO-MDT
[4]Deshmukj et al., 2003	India	Randomized Control Trial	32	-	75	6	Clinical + Histological	1-3	ROM, single dose	WHO-MDT
[5]Diniz et al., 2010	Brazil	Cohort	54	31	31.48	12	Clinical + Histological	Single	ROM, single dose	No Comparator
[6]Ebenezer et al., 1999	India	Case series	13	26 (11.4)	62	12	Clinical	1-3	ROM, single dose	No Comparator
[7]Emmanuel & Gupte, 2005	India	Randomized Control Trial	51	-	58.82	24	Clinical + Histological	2-3	ROM, single dose	WHO-MDT
[8]Ganapati et al., 1999	India	Case series	634	-	-	-	Clinical	2-5	ROM, single dose	No Comparator
[9]Girdhar et al., 2011	India	Randomized Control Trial	300	30.9 (16.2)	41	36.76 (14.8)	Clinical	Single	ROM, single dose	ROM + clarithromycin
[10]Gomes et al., 2008	Brazil	Cohort	259	32.4 (16)	38.2	36	Clinical + Histological	Single	ROM, single dose	No Comparator
[11]Kumar et al., 2015	India	Randomized Control Trial	268	-	37.7	60	Clinical	1-5	ROM, monthly	WHO-MDT
[12]Kumar et al., 2014	India	Cohort	289	41.6	61.8	12	Clinical	1-5	ROM, monthly	WHO-MDT
[13]Majumder et al., 2000	India	Clinical Trial	90	-	-	12	Clinical + Histological	Single	ROM, single dose	ROM, single dose + Convit vaccine*
[14]Mane et al., 1997	Senegal	Case series	220	-	60	12	Clinical + Histological	2-5	ROM, monthly	No Comparator
[15]Manickam et al., 2012	India	Randomized Control Trial	1526	27	47.5	36	Clinical	2-5	ROM, single dose	WHO-MDT
[16]Martelli et al., 2000	Brazil	No outcomes reported	259	32.4 (16.0)	38.22	-	Clinical + Histological	Single	ROM, single dose	No Comparator
[17]Pai et al., 1999	India	Case series	634	-	-	-	Clinical	1-5	ROM, single dose	No Comparator
[18]Ravenkar et al., 2002	India	Cohort	335	-	-	6-70	Clinical	2-5	ROM, single dose	No Comparator
[19]Shetty et al, 2011	India	Retrospective cohort	62	-	-	-	Clinical + Histological	1-5	ROM, single dose	i) WHO-MDT, ii) dapsone, iii) RO
[20]Shinde et al., 2000	India	Case series	26	-	-	-	Clinical	Single	ROM, single dose	No Comparator
[21]Shukla et al., 2000	India	Clinical Trial	61	-	55.7	12	Clinical + Histological	Single	ROM, single dose	No Comparator
[22]Sousa et al., 2007	Brazil	Case series	135	30.5 (15.4)	44.4	31.4	Clinical	Single	ROM, single dose	No Comparator
[23]Stefani et al., 2003	Brazil	Case series	39	33.4 (15.3)	51.28	32.4 (16.0)	Histological	Single	ROM, single dose	No Comparator
[24]Vivekkumar et al., 2010	India	Randomized Control Trial	72	-	61	6	Clinical	1-5	ROM, single dose	RLM, single dose

Table 1. Preliminary Baseline Characteristics of Included Studies
Abbreviations: Rifampin + Ofloxacin (RO); Standard World Health Organization Multi-drug therapy (WHO-MDT); Rifampin + Levofloxacin + Minocycline (RLM)
*Low-dose Convit vaccine contained $1.6x10^7$ heat-killed *M. leprae* in 0.1ml saline and $1.5x10^7$BCG in 0.1ml saline

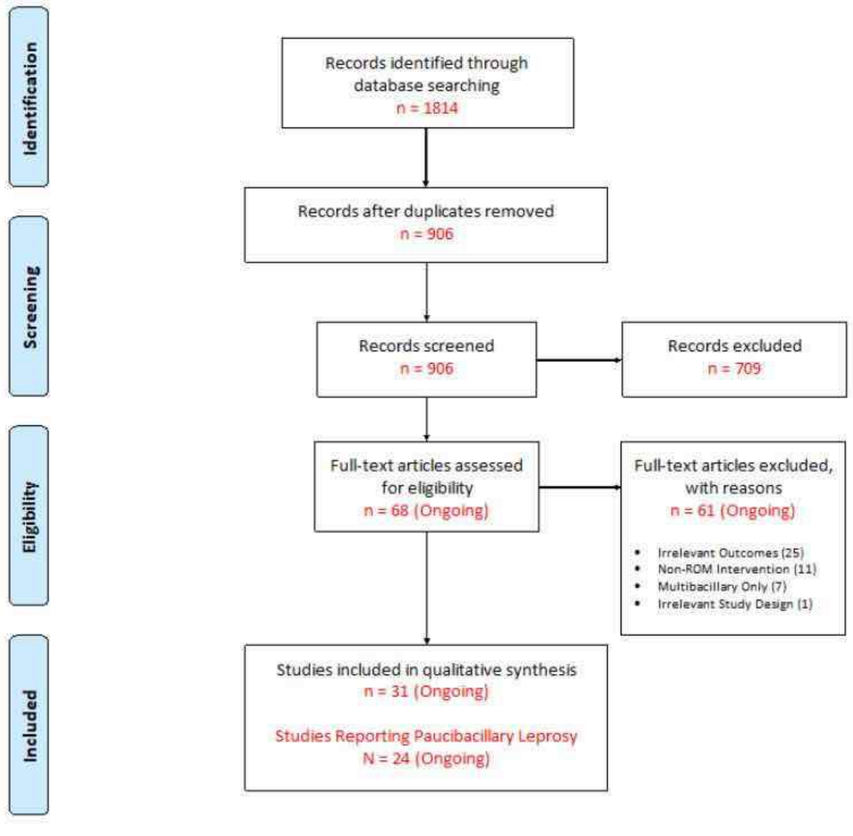

Figure 1. PRISMA Flowchart

Outcome	Study	ROM		Comparator		Difference (%)
		% of patients	Proportion	% of patients	Proportion	
Lesion Clearance	[6]Alam et al., 2007	75.93	205/270	-	-	-
	[2]Babu et al., 1997	44.25	327/739	50.27	374/744	-6.02
	[3]Desikan & Gupte, 2001	96.22	102/106	96.15	100/104	0.07
	[5]Diniz et al., 2010	85.20	45/54	-	-	-
	[6]Ebenezer et al., 1999	84.62	11/13	-	-	-
	[7]Emmanuel & Gupte, 2005	-	-	-	-	-
	6mo	3.85	1/26	16.00	4/25	-
	12mo	38.46	10/26	44.00	11/25	-
	18mo	42.31	11/26	60.00	15/25	-
	24mo	46.15	12/26	64.00	16/25	-
	Mean of first 4 f/u	32.69	-	46.00	-	-13.31
	[10]Gomes et al., 2008	80.69	209/259	-	-	-
	[9]Girdhar et al., 2011	-	-	-	-	-
	6mo	72.85	110/151	78.52	117/149	-
	12mo	89.40	135/151	89.26	133/149	-
	18mo	94.59	140/148	91.72	133/145	-
	Mean of first 3 f/u	86.61	-	86.50	-	0.11
	[11]Kumar et al., 2015	97.22	105/108	93.27	97/104	3.95
	[13]Majumder et al., 2000	46.67	14/30	33.30	20/60	13.37
	[14]Mane et al., 1997	25.00	14/56	-	-	-
	[15]Manickam et al., 2012	72.11	486/674	72.12	494/685	-0.01
	[18]Ravenkar et al., 2002	98.74	626/634	-	-	-
	[23]Stefani et al., 2003	44.00	11/25	-	-	-
	[24]Vivekkumar et al., 2010	36.11	13/36	75.00	27/36	-38.89
	Mean	**52.73**	-	**57.42**	-	**-4.69**
	Median	**75.93**	-	**73.56**	-	**2.37**
	Range	**25.00-98.74**		**33.33-96.15**		**Negative in favour for ROM**
Treatment Failure	[3]Desikan & Gupte, 2001	3.77	4/106	3.85	4/104	-0.08
	[11]Kumar et al., 2015	0.93	1/108	3.87	4/104	-2.94
	[13]Majumder et al., 2000	23.33	7/30	18.33	11/60	5.00
	[14]Mane et al., 1997	0.98	1/102	-	-	-
	[15]Manickam et al., 2012	0.30	2/674	0.58	4/685	-0.28
	[18]Ravenkar et al., 2002	3.79	24/634	-	-	-
	[22]Sousa et al., 2007	1.48	2/135	-	-	-
	[23]Stefani et al., 2003	2.70	1/37	-	-	-
	Mean	**4.66**	-	**6.66**	-	**-2.00**
	Median	**2.09**	-	**3.86**	-	**-1.77**
	Range	**0.30-23.33**		**0.58-18.33**		**Positive in favour for ROM**
Relapse	[1]Alam et al., 2007	3.70	10/270	-	-	-
	[2]Babu et al., 1997	0.81	6/739	0.81	6/744	0.00
	[5]Diniz et al., 2010	9.3	5/54	-	-	-
	[18]Ravenkar et al., 2002	1.49	5/335	-	-	-
	[9]Girdhar et al., 2011	2.22	3/135	1.43	2/140	0.79
	[11]Kumar et al., 2015	2.78	3/108	6.73	7/104	-3.95
	[15]Manickam et al., 2012 *		29/100py	-	9/100py	20/100py
	Mean	**3.38**	-	**2.99**	-	**0.39**
	Median	**2.50**	-	**1.43**	-	**1.07**
	Range	**0.81-9.3**	-	**0.81-6.73**	-	**Negative in favour for ROM**
Side Effects	[2]Babu et al., 1997	0.68	5/739	0.94	7/744	-0.26
	[3]Desikan & Gupte, 2001	0.00	0/118	1.69	2/118	-1.69
	[13]Majumder et al., 2000	0.00	0/30	0.00	0/60	0
	[14]Mane et al., 1997	0.00	0/220	-	-	-
	[16]Martelli et al., 2000	5.79	15/259	-	-	-
	[24]Vivekkumar et al., 2010	0.00	0/36	0.00	0/36	0
	Mean	**1.08**	-	**0.66**	-	**0.42**
	Median	**3.24**	-	**1.32**	-	**1.93**
	Range	**0.68-5.79**	-	**0.94-1.69**	-	**Negative in favour for ROM**
Reversal Reactions (Type 1&2)	[2]Babu et al., 1997	0.95	7/739	0.40	3/744	0.55
	[5]Diniz et al., 2010	1.85	1/54	-	-	-
	[7]Emmanuel & Gupte, 2005	7.69	2/26	0.00	0/25	7.69
	[10]Gomes et al., 2008	16.20	42/259	-	-	-
	[14]Mane et al., 1997	3.33	1/30	-	-	-
	[21]Shukla et al., 2000	6.50	4/61	-	-	-
	[22]Sousa et al., 2007	14.81	20/135	-	-	-
	[23]Stefani et al., 2003	33.33	13/39	-	-	-
	Mean	**8.35**	-	**0.2**	-	**8.15**
	Median	**7.69**	-	**0.2**	-	**7.49**
	Range	**0.95-33.33**	-	**0.00-0.40**	-	**Negative in favour for ROM**

Table 2. Preliminary Summary of Primary Outcomes; *Not included in mean/median/range

Discussion

- Interim findings suggest that patient lesion clearance and treatment failure is greater in the comparator group (+4.69% and +2% respectively)
  - Relapse, side effects, and reversal reactions are greater in the ROM group (+0.39%, +0.42%, and +8.15% respectively). This suggests that ROM is slightly less efficacious than its comparator, however a more robust analysis is necessary.

- Qualitatively, several determinants of health were identified throughout this analysis including:
  - **Social environments** – 50% of non-adherent patients denied having leprosy due to potential loss of jobs and/or marriage prospects[25]
  - **Patient education** – 86% of respondents did not understand the concept of their disease[12]
  - **Gender** – Women completed treatment at a rate of 65.6% and men at 79.2% ($p<0.05$)[26]
    - Further investigation to better understand gender- and sex-based influences on treatment and prognosis warranted

- Synthesizing the current evidence discussing the efficacy of monthly ROM, will strengthen the current body of knowledge surrounding the treatment of paucibacillary leprosy, and may allow for the development of standardized fluoroquinolone-based treatment protocols.

References

LB-9384

Leptospirosis Following Freshwater Adventure Travel

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Introduction

Leptospirosis is an emerging zoonotic infection in travelers[1]

Transmission via direct or indirect contact with infected animal urine[2,3]

Freshwater recreation, such as kayaking and rafting, are implicated in transmission[2,3,4]

Clinical Cases

Three cases of leptospirosis acquired during whitewater rafting in Ecuador

2024

Two patients referred via ED for acute febrile illness after a 3-week rafting trip

- Case 1: 20s M, no pmhx, on finasteride (hair loss)
- Case 2: 50s M, no pmhx, no medications

2025

One patient referred via ED following a convalescent episode of acute febrile jaundice on a 6-week rafting trip

- Case 3: 20s F, no pmhx, no medications

Case 1 Timeline

Day 0 — Returns from Ecuador

Day 6 — Fever, myalgia, n/v

Day 8 — ED visit
- **WBC 10.2**, **ANC 9.4**
- Bili 16 umol/L, **ALT 44 U/L**
- **COVID-19 NP +ve**
- Malaria screen –ve
- Blood cx, Dengue IgM, viral hep serologies sent

Day 9 — Tropical Disease Unit
- New non-bloody diarrhea & headache
- Persistent fever (38.3°C)
- Ddx: acute gastroenteritis versus leptospirosis
- *Leptospira* serology sent
- Tx: ciprofloxacin 500 mg BID x 3 days

Day 10 — News Alert: Outbreak of leptospirosis in Ecuador from heavy rains
- Ongoing fever and diarrhea (>30 BM/day)
- **New proteinuria (0.3 g/L)**
- **New anemia (128 g/L)**
- **Elevated bili (23 umol/L)**
- Dx: leptospirosis (clinical)
- Tx: doxycycline 100 mg BID x 7 days

Day 11
- Clinical improvement within 24 hours
- **Stool cx *Campylobacter coli* and *Campylobacter jejuni***

Day 17
- Complete clinical and biochemical resolution
- *Leptospira* IgM returns negative
- Blood cultures, Dengue IgM, viral hepatitis serologies negative

Case 2 Timeline

Day 0 — Returns from Ecuador

Day 5 — Fever, arthralgia, myalgia, n/v, abdo pain

Day 8 — ED visit
- **Plt 103**; **lymphopenia**
- **Bili 41 umol/L**, ALT 38 U/L
- **Cr 129 umol/L** (no baseline)
- Malaria screen –ve
- *Leptospira* serology sent
- Blood cx, Dengue IgM, CHIKV IgM sent

Day 9 — Tropical Disease Unit; News Alert: Outbreak of leptospirosis in Ecuador from heavy rains
- Afebrile, conjunctival injection, abdminal tenderness
- **UA: proteinuria (1 g/L)**
- Dx: leptospirosis (clinical)
- Leptospira serology sent
- Tx: doxycycline 100 mg BID x 7 days
- Returns to ED with vomiting of doxycycline

→ Admitted to GIM
- **Plt 78, Hb 123**
- **Bili 70, Cr 123**
- Tx: ceftriaxone 2g IV daily

Day 12
- Improving, tolerating PO
- D/c home with 5 days of doxycycline (7 days total)

Day 26
- Complete clinical and biochemical resolution
- *Leptospira* IgM returns negative

Two Months
- Convalescent *Leptospira* serology ordered → ***Leptospira* IgM positive, MAT negative**

Case 3 Timeline

Travel to rural Ecuador: 6-week rafting trip

~1 wk
- Acute, non-bloody diarrhea. No systemic symptoms.
- Rx Secnidazole, Albendazole, 10 days of Ciprofloxacin

2-3 days later
- Symptoms worsening despite treatment
- New fever & jaundice

→ Admitted to hospital
- Dx: acute liver failure
- Reports IVF but no antimicrobial therapy
- D/c after a few days

~3 wk
- Complete symptom resolution → resumes rafting

~4 wk
- New acute febrile illness
- Reports dx of Dengue

→ Admitted to hospital for 5 days for monitoring

Returns to Canada (~6 weeks)

6 wk — Tropical Disease Unit
- No infectious symptoms
- **ALT 62, AST 41, bili 62**
- *Leptospira* serology sent
- Negative Dengue IgM/IgG
- Reactive Hep A IgG (h/o pre-travel HAV vaccine)

7 wk
- ***Leptospira* IgM positive, MAT negative**
- ALT, AST normalized
- **Bili 32 umol/L**

Discussion

- Leptospirosis can present as anicteric or icteric infection; Wiel's Disease is the feared complication
- Treatment is with doxycycline; IV therapy is indicated for severe disease or inability to tolerate oral intake

Learning Points

- Suspect leptospirosis in febrile travelers with freshwater exposure
- Diagnosis is often clinical due to limitations in microbiologic testing
- Start empiric treatment with high clinical suspicion before testing returns
- Prophylaxis with doxycycline 200 mg PO once weekly is effective[4] → consider in all travelers with recreational water travel

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LB-9393

Recurrent Pyogenic Cholangitis Unveiling Latent Clonorchiasis in a Filipino Migrant to Canada: Implications for Diagnosis and Management

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Background

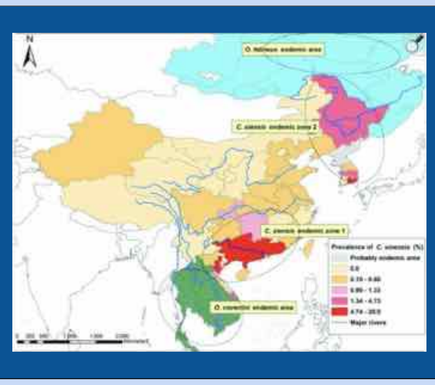
- *Clonorchis sinensis* is a liver fluke endemic to East Asia, transmitted via ingestion of raw or undercooked freshwater fish.
- Chronic infection can cause biliary inflammation, stone formation, and recurrent pyogenic cholangitis (RPC).
- With increased global migration, cases are emerging in non-endemic regions where diagnostic familiarity is low.

Case Description

- A 39-year-old Filipino woman living in Canada presented with 2-year history of intermittent right upper quadrant pain and persistently elevated cholestatic liver enzymes.

Investigations

- **Laboratory results:** ALT 151 U/L, AST 112 U/L, ALP 532 U/L, GGT 749 U/L, normal eosinophils, IgE 408 Viral hepatitis and serologic testing for other helminths negative..
- **Stool O&P testing:** negative on three occasions.
- **Imaging:**
  - Ultrasound → intrahepatic ductal dilation.
  - MRI → multiple intrahepatic stones, right-lobe atrophy, and periductal enhancement consistent with recurrent pyogenic cholangitis.



Global distribution of three major species of liver flukes (2)

Clinical Course

(1) •Referred to the Toronto Centre for Liver Disease at the University Health Network due to a persistent elevation of liver enzymes in a cholestatic pattern.

(2) •Referred to Hepatology: Abdominal Ultrasound and MRI showed results consistent with recurrent pyogenic cholangitis
•Referred to the Tropical Disease Unit

(3) •Tropical Medicine unit: intermittent right upper quadrant pain over 2–3 years, worsened by fatty meals, and unintentional weight loss of 6 kilograms over 6 months.
•No jaundice, fever, pruritus, nausea, vomiting, diarrhea, constipation and dyspepsia.

(4) •Empiric treatment with praziquantel (25 mg/kg TID × 2 days) initiated given imaging findings, exposure history of frequent raw fish consumption in the Philippines, and persistent symptoms

(5) •2 months later: Liver enzymes showed partial improvement.
•Repeat MRI showed persistent intrahepatic stones, moderate biliary dilatation, hepatic atrophy, and microabscesses. No malignancy.

Management

- Given the suggestive imaging, exposure history, and negative stool results, *empiric praziquantel* (25 mg/kg TID × 2 days) was initiated.
- Two months later: marked symptomatic improvement, normalization trend in liver enzymes, and decreased inflammatory changes on repeat MRI.
- Treatment was well-tolerated with transient dizziness only.
- Continued hepatology follow-up arranged for surveillance of chronic biliary changes.

Discussion

- *Clonorchiasis* is often missed in non-endemic settings due to non-specific findings and limited diagnostic access.
- Stool microscopy sensitivity can fall below 30% in chronic or low-burden infections.
- Imaging features (intrahepatic duct dilation, pigmented stones, lobar atrophy) are often the most reliable diagnostic clues.
- Empiric treatment is justified in high-suspicion cases to prevent long-term complications including cholangiocarcinoma.

Learning Points

- Recurrent pyogenic cholangitis may signal chronic *Clonorchis sinensis* infection **even with negative stool tests** .
- Clinical suspicion should be heightened in **migrants from endemic areas presenting with biliary disease**.
- Empiric praziquantel therapy is **safe**, **effective**, and may **prevent irreversible hepatobiliary damage**.
- Long-term surveillance is warranted due to **increased lifetime risk of cholangiocarcinoma**.

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Reactivation of Old World Tegumentary Leishmaniasis Following Iatrogenic Immunosuppression: Occurrence and Role for Secondary Prophylaxis

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Introduction

- Old world tegumentary leishmaniasis (OWTL) is a neglected tropical disease caused mainly by the species *L. donovani*, *L. aethiopica*, *L. tropica*, *L. major* & *L. infantum*
- Recent increases in global migration, travel, and climate change contribute to the growing burden of OWTL[1]
- Iatrogenic immunosuppression can increase the risk of reactivation and severe disease manifestations due to weakened immunological control[2]
- The role for secondary prophylaxis in preventing such outcomes is currently unknown

- **Objective:** We aim to synthesize available data surrounding leishmaniasis reactivation and immunosuppressive regimens as well as the potential role of secondary prophylaxis to guide healthcare providers on clinical management

Methods

- Five databases were searched from database inception to March 2024
- Conducted in accordance with PRISMA guidelines
- Certainty & quality of evidence evaluated via the GRADE framework[3]

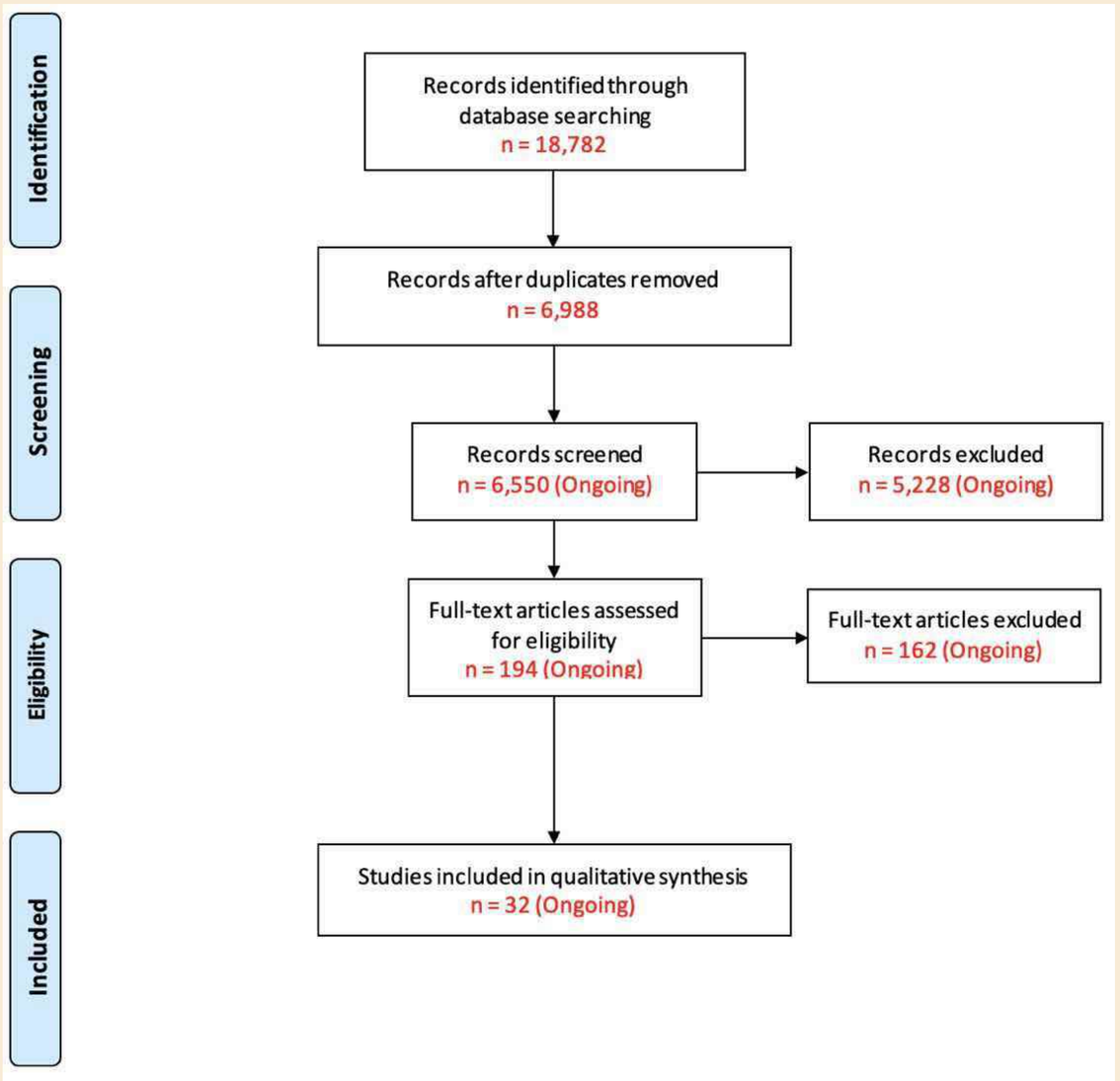

Figure 1. PRISMA Flowchart

Results

First Author, Year	Country	Species	Manifestations (primary → reactivations)	Iatrogenic Immunosuppresion	Primary Treatment	Treatment for Reactivations	Secondary Prophylaxis Regimen	Outcomes
Richter, 2011	Germany (history of travel to Spain)	*L. infantum*	ML → ML	Treatment for systemic lupus erythematosus	L-AmB	Miltefosine	Extended Miltefosine	Success. No recurrence.
Perez-Jacoiste Asin, 2017	Spain	Unspecified	VL → ML → VL	**Kidney Transplant Regimen:** Prednisone, tacro, MPA	L-AmB	**Reactivation 1:** L-AmB **Reactivation 2:** Miltefosine	L-AmB for 12 months	Success. No third recurrence.
Darcis, 2017	Belgium (history of travel to Spain)	*L. infantum*	VL → CL → CL → CL + ML	**1. EBV-negative classical Hodgkin lymphoma Treatment:** C-MOPP*+ radiation therapy for EBV-negative **2. Rheumatoid arthritis:** Entanercept (later switched to Rituximab), ciclosporin, methylprednisolone	L-AmB	L-AmB	Monthly AmB	Implementation after primary infection and reactivation 1 resulted in failure. Secondary prophylaxis was not used after reactivation 2 and 3.
Micallef, 2014	Malta	*L. donovani*	CL (no recurrence to date)	**Treatment for seronegative arthritis:** Adalimumab, anti-TNF, methotrexate	Sodium stibogluconate	n/a	Monthly sodium stibogluconate	No recurrence to date.
Nieto Gomez, 2019	Spain	not specified	CL (no recurrence to date)	**Treatment for psoriatic arthritis:** Infliximab and methotrexate	L-AmB	n/a	Monthly L-AmB	No recurrence to date but patient is still being followed up.

Table 1. Summary of preliminary data on cases of OWTL reactivation and outcomes of secondary prophylaxis.
Abbreviations: Cutaneous leishmaniasis (CL), Epstein–Barr virus (EBV), Liposomal amphotericin B (L-AmB), Mucocutaneous leishmaniasis (ML), Mycophenolic acid (MPA), Tacrolimus (tacro), Tumor necrosis factor inhibitor (anti-TNF), Visceral leishmaniasis (VL); *Chemotherapy regimen: Cyclophosphamide, Vincristine (Oncovin), Procarbazine, Prednisone

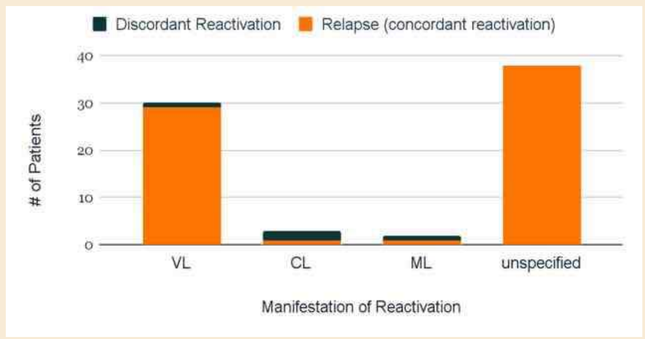

Figure 2. Clinical manifestations of reactivation in solid organ transplant (SOT) recipients upon use of immunosuppressive regimens.
Abbreviations: Cutaneous leishmaniasis (CL), Mucocutaneous leishmaniasis (ML), Visceral leishmaniasis (VL)

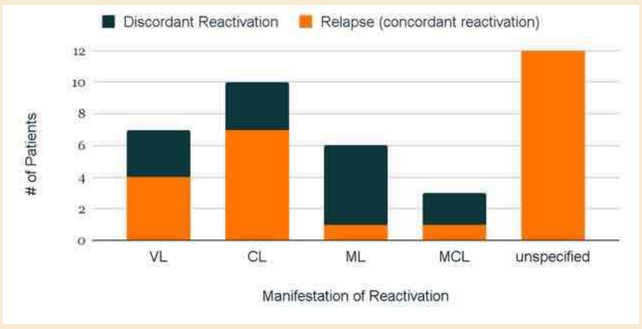

Figure 3. Clinical manifestations of reactivation upon use of immunosuppressive treatments for inflammatory diseases.
Abbreviations: Cutaneous leishmaniasis (CL), Mucocutaneous leishmaniasis (MCL/ML *per original reporting), Visceral leishmaniasis (VL)

Discussion

- VL and CL were shown to be the most common forms of reactivation in transplant recipients and inflammatory disease patients, respectively (Figure 2 & 3)
- Review papers support the use of secondary prophylaxis in preventing relapse of VL, but the same confidence does not exist for OWTL
- The role of secondary prophylaxis in the context of OWTL remains inconclusive due to the dearth of data around this topic
- This systematic review aims to further investigate the role of prophylaxis to guide clinical management in this patient population

References

Fruit-Bearing Plant Ethnopharmaceuticals for the Treatment of Old World Cutaneous Leishmaniasis: A Systematic Review

D. Fernando[1,2], R. Kariyawasam[3,4], M. Klowak[1,6], K. Shahzad[6], E. Aluko[1,7], E. Bado, S. Bhasker[6], J. Kwan[6], S. Igboanugo[6], A. K Boggild[1,6,7]

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Introduction

- **Old World Cutaneous Leishmaniasis (OWCL):** a neglected parasitic disease caused by members of the genus *Leishmania,* passed onto humans by the bite of sandflies[1]
- Better drugs are needed due to the toxicity, accessibility limits, and expense of first-line treatment options
- **Ethnopharmaceuticals:** plant-based compounds with potential anti-leishmanial effects found in and around local endemic communities[2]
- Potential to overcome the aforementioned therapeutic challenges using ethnopharmaceuticals is supported by anecdotal evidence of efficacy

Objective: Aim to synthesize existing evidence around available fruit-bearing ethnopharmaceuticals to promote drug discovery for the prevention and treatment of OWCL.

Results

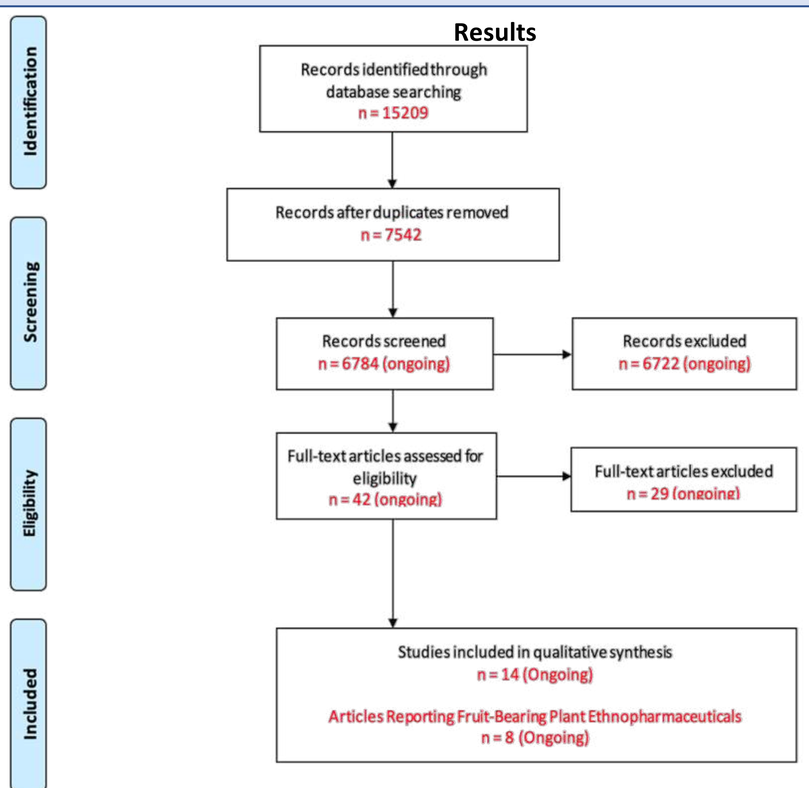

Figure 1. PRISMA Flow Diagram for studies captured in the search strategy.

Methods

- PubMed (NCBI), Medline (OVID), Embase (OVID), and Web of Science (BioSIS) were searched using combinations of the search terms and related concepts of **"cutaneous leishmaniasis"** and **"ethnopharmaceuticals"**
- Inclusion criteria: CL patient from the Old World (Africa, Asia, Europe), treated with an ethnopharmaceutical, patient outcome(s) reported after treatment
- GRADE approach used to assess the quality of studies reporting therapeutic interventions[4]
- Data were grouped and summarized by *Leishmania* spp. and plant species

Discussion & Conclusions

- 14 studies were included evaluating a number of topical applications of ethnopharmaceuticals including: *Cassia fistula*, garlic, and pepper. 8 out of the 14 pertained to fruit-bearing ethnopharmaceuticals.
- Most trials tested interventions in combination with standard therapies (e.g., Glucantime), not as stand-alone treatments.
- Some agents (e.g., *Cassia fistula*, *Juniperus excelsa*) have shown cure rates comparable to or superior to those of conventional drugs.
- Variability in study design, small sample sizes, and inconsistent reporting limit the certainty of evidence.
- Adverse events were generally mild and tolerable, supporting feasibility in clinical use.
- Highlights the potential of ethnopharmaceuticals to inform drug discovery pipelines, particularly in resource-limited settings.
- Future work requires rigorous, well-designed RCTs and testing of novel compounds identified in preclinical models.

Author, Year	Setting	Population	Design/Sample Size	Study Period	Species	Type of Fruit-Bearing Plant	Treatment/Intervention	Outcomes
Jaffary 2009	Iran	Inclusion: Confirmed CL on smears, lesions (<5 in quantity, <3cm). Exclusion: Lesions close to the eyelids, pregnant or breastfeeding mothers.	RCT; 140 Patients. Group A: 70. Group B: 70.	Not reported	Not reported	*Cassia Fistula*	Group A: 70% topical gel containing 2% DMSO from C. fistula 1x/day for 1-4 weeks + Glucantime (1- 2.5mL) 2x/week up to 4 weeks. Group B: placebo gel 1x/day for 1-4 weeks + Glucantime (1-2.5mL) 2x/week up to 4 weeks.	Complete recovery at week 4: Group A (28/70) Group B (25/70) (p=0.0945). Relative recovery at week 4: Group A (28/70) Group B (22/70). Complete recovery at week 12: Group A (47/70) Group B (29/70) (p<0.001. Relative recovery at week 12: Group A (20/70) Group B (21/70). Mean complete recovery time: Group A (7.9+/-0.5) Group B (8.2+/-0.4) (p=0.005). Adverse events: Group A (9), Group B (9) - Erythema and itchiness (p=0.25).
Jaffary 2014CF	Iran	Inclusion: Confirmed CL on smears, age 6-60 years old, lesions (<5 in quantity, <3cm, <12 weeks old, not near eye)	RCT; 165 Patients. Group A: 55. Group B: 55. Group C: 55.	16 weeks	Not reported	*Cassia fistula*	Group A: boiled extract- soaked gauze applied 1x/day up to 4 weeks. Group B: hydroalcoholic extract soaked gauze applied 1x/day up to 4 weeks. Group C: intralesional Glucantime (0.5-2mL) 2x/week up to 4 weeks.	Complete cure at 16 weeks: Group A - 22 (40%), Group B - 20 (36.4%), Group C - 36 (65.5%) (p=0.02). Adverse Events: Group A - 3 (5.5%), Group B - 2 (3.6%), Group C - 2 (3.6%) due to allergic reaction.
Jaffary 2014AM	Iran	Inclusion: Severe CL for >5 years, lesions (<5 in quantity, <5cm^2)	RCT; 60 Patients. Group A: 60 Group B: 60	January 2009-Feburary 2010	Not reported	*Achillea millefolium*	Group A: IV Glucantime 20mg/kg/day x4 weeks + topical gel of 5% yarrow 2x/day. Group B: IV Glucantime 20mg/kg/day x4 weeks + placebo gel of 5% chlorophyll 2x/day	Complete or partial cure at 12 weeks: Group A (21/30) Group B (18/30) (p=0.0351). Adverse Event at 6 weeks: Group A (10/30) Group B (12/30) (p>0.05). Mild to moderate itching at 12 weeks: Group A (8/30) Group B (2/30) (p=0.014). Increased wound discharge: Group A (1/30).
Mozafari 2019	Iran	Inclusion: Confirmed CL on smears, lesions (>14 days old). Exclusion: Pregnant women, known adverse reactions to treatment, treatment within the last month, lesions (>3 months old, near the eyelids, nose, mouth, and eyes).	RCT; 110 Patients. Group A: 55. Group B: 55.	December 2017-June 2018	Not reported	*Samacucus ebulus*	Group A: 5% *S.ebulus* gel + Glucantime 2x/day up to 12 weeks. Group B: placebo gel + Glucantime 2x/day up to 12 weeks.	Duration of recovery: Group A (mean 26.64(16.24) days) Group B (mean 30.05(18.54) days) (p=0.31). Complete recovery (total epithelialization): Group A (30) Group B (29) (p=0.87). Medium recovery (>50% decrease in lesion size): Group A (8) Group B (10). Mild recovery (<50% decrease in lesion size): Group A (9) Group B (9). Failure: Group A (5) Group B (7).
Parvizi 2017	Iran	Inclusion: Confirmed CL on smears, age 18-70 years old, no previous treatment in the last 4 months, lesions (<4 in quantity, <5cm^2, <4 months old)	RCT; 62 patients. Group A: 33. Group B: 29	Not reported	*Leishmania major* and *Leishmania infantum*	*Juniperus excelsa*	Group A: Topical cream of 5% hydroalcoholic leaf extract 3x/day + Cryotherapy. Group B: Placebo cream 3x/daily + Cryotherapy.	Complete cure: Group A (82%) Group B (34%). Partial cure: Group A (9%) Group B (14%). Treatment failure: Group A (9%) Group B (52%). Adverse events: Group A (85%) Group B (100%).
Sattar 2012	Pakistan	Inclusion: Patients with CL, age 6-70 years old	Cohort; 40 (30M 10F)	6 weeks	*Leishmania donovani*	*Morinda citrifolia*	1% dry methanol leaf extract gel 3x/day then weekly up to 6 weeks	Excellent response: 20/40 (50%). Good response: 12/40 (30%. No response: 8/40 (20%). Adverse events: none.
Rahman 2012	Iran	Patients with CL	Cohort; 100 Patients (35 at 2 week follow- up)	Not reported	Not reported	*Physalis minima*	25% methanolic extract with white soft parrafin-based petroleum gel	Cure: 23/35 (65.71%) of patients showed excellent response and recovery by topical application
Zerehs az 1999	Iran	Inclusion: Confirmed CL on smears for <4 months. Exclusion: Severe CL and pregnancy.	RCT; 171 patients. Group A: 86. Group B: 85.	Not reported	Not reported	Z-HE herbal extract (*Althaea rosa, Althaea officinalis, Leguminosae, Faliaceae, Malvaceae*, and *Lythrace*)	Group A: topical Z-HE x5 days + 0.5mL saline injection x20 days. Group B: topical placebo x5 days + 15- 20mL/kg/day Glucantime x20 days.	Complete cure: Group A (74.4%) Group B (24.1%). Partial cure: Group A (11.6%) Group B (14.1%). Failure: Group A (14%) Group B (58.8%). Adverse Events: Group B had urticaria and generalize pruritis.

Table 1. Summary of findings tables for studies included in this study.

QR for References

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Influence of Host Nutriome on Immunological Control of *Leishmania* Infection

Ranie Ahmed[1], Michael Klowak[1], Mariyam Mohammed[2], Rachel Lau[3], Afia Birago[2], Kalsoom Shahzad[2], Chelsia Watson[1], Andrea K. Boggild[1,2,4*]

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Introduction

- Immunologic control of parasitic infections arises from a combination of humoral and cellular mechanisms
- Micronutrient depletion or over-repletion may impair the functioning of the immune system
- Leishmaniasis is a tissue-dwelling parasitic infection in which disease severity is determined by the host's immune system along with parasitologic factors
- Research suggests that acquired factors such as nutritional inadequacies play a significant role in immunosuppression & pathogenicity

Methods

- Five electronic databases were searched from database inception to September, 2025
- Conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, and the Grading of Recommendations Assessment, Development, & Evaluation (GRADE) approach

Results

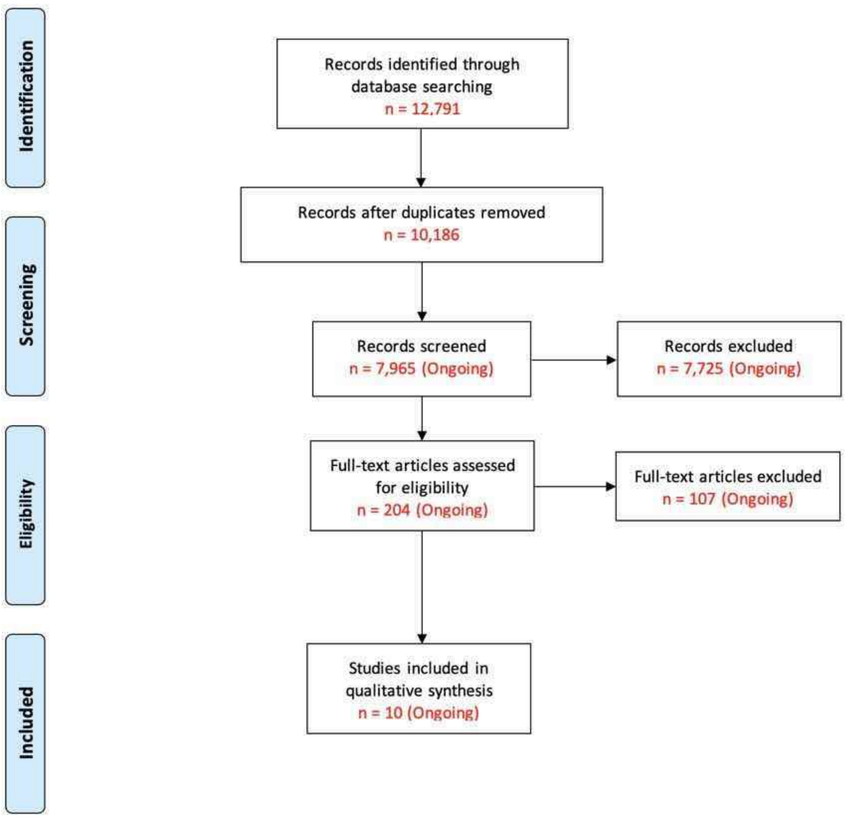

Figure 1. PRISMA Flowchart

Author, Year	Country	Design	Population	Sample Size	Assessment / Intervention	Mean Age ± SD	Sex (F:M)	Outcomes
[1]Goyonlo, 2020	Iran	Case-Control	Diagnosis of CL confirmed by Geimsa-stained direct smear versus age and sex matched controls	220 Cases (149) Control (71)	Nutritional status and Vitamin A intake via FFQ	21.32 ± 17.62	Cases (82:67) Contorls (45:26)	Daily intake of Vitamin A (p<0.001) was significantly lower among the CL group, as well as energy intake, fiber, Vitamin E, and potassium
[2]Guzman-Rivero, 2014	Bolivia	Case-Control	Patients aged 15-50 with confirmed CL on blood, or microbiological/biochemical analysis.	29 Cases (14) Controls (15)	Zinc gluconate (315mg) vs placebo (315mg cornstarch) for 60 days	Not Reported	Not Reported	A statistically significant biological or clinical effect due to zinc was not found
[3]Maciel, 2014	Brazil	Case-Control	Children with clinical and laboratory confirmed VL versus healthy controls	26 Cases (10) Controls (16)	Serum vitamin A (retinol) status and immune response (CD4+CD24Foxp3+ T cells)	Cases (7.99 ± 7.85) Controls (8.82 ± 6.26)	Cases (7:3) Contorls (5:11)	Vitamin A (retinol) status (p=0.013) and immune cells (p=0.011) were significantly lower in cases versus controls
[4]Maciel, 2008	Brazil	Case-Control	Biochemically confirmed cases of paediatric VL versus healthy controls	149 Cases: Active VL (20) History of VL (33) Antigen Response to VL (40) Controls (56)	Nutritional status via anthropometry, and serum Vitamin A (retinol) level	Cases: Active VL (4.7 ± 3.9) History of VL (10.1 ± 3.3) Antigen Response to VL (11.2 ± 2.4) Controls (8.1 ± 3.4)	Cases: Active VL (11:9) History of VL 19(:14) Antigen Response to VL (20:20) Controls (31:25)	Serum retinol was significantly lower in patients with active VL versus controls (p=0.037)
[5]Cerf, 1987	Brazil	Case-Control	Children aged 0-15 years old with at least 2 consecutive years of anthropometric and serologic data confirming presence of VL	1066	Nutritional status via weight-for-age index	Not Reported	Not Reported	Low weight-for-age was significantly higher In VL children versus controls (p < 0.0001)
[6]Kumar, 2014	India	Case-Control	Patients with confirmed, active, and untreated cases of VL versus healthy controls	40 Cases (20) Controls (20)	Nutrition status via weight-to-height ratios and immune response (including ROS activity, cytokine levels, leishmania antigen) via biochemistry	Not Reported	Not Reported	Patients found to be malnourished had a statistically significant weakened immune response to VL on several accounts as compared to healthy controls: antigen responsiveness, monocytes, & ROS activity (p<0.05), CD62-L (p<0.001)
[7]Kocyigit, 2002	Turkey	Case-Control	Patients with laboratory confirmed CL versus healthy controls	50 Cases (28) Controls (22)	Serum nutrient levels: copper, zinc, and iron, and immunoregulatory cytokines: IL-1B, IL-2R, IL-6, IL-8, TNF-a	Cases (27.3 ± 3.8) Controls (28.4 ± 4.1)	Not Reported	Plasma selenium, zinc, iron, and IL-2r levels were significantly lower and plasma copper, IL-1B, IL-8, IL-6, and TNF-a were significantly higher in cases versus controls (p<0.01)
[8]Al-Jurayyan, 1995	Saudi Arabia	Cohort Study	Infants and children undergoing active treatment for Leishmania donovani	94	Haematological findings including nutrition via biochemistry	1.8	39:55	Patients with active infection were found to be immunocompromised and iron deficient
[9]Carbone, 2018	Brazil	Clinical Trial	Patients with parasitologically confirmed presence of VL	67 Intervention: With Zinc (33) Without Zinc (29) Controls (15)	Zinc (2mg/kg/day) plus standard treatment (amphotericin B (0.5-1mg/kg/day) or glucantime (20mg/kg/day)) for 20 days versus standard alone	Intervention: With Zinc (46.20 ± 9.66) Without Zinc (43.76 ± 6.50) Controls (44.60 ± 10.20)	Intervention: With Zinc (12:11) Without Zinc (18:11) Controls (9:6)	Patients who received Zinc supplementation exhibited a more rapid reduction in spleen size compared to controls (p<0.05)
[10]Mengesha, 2014	Ethiopia	Cross-Sectional	Patients age >17 years and non pregnant women with a confirmed diagnosis of VL	403	Nutritional status via BMI	Only Range Provided: 68% 18-27 years old 25.8% 28-37 years old 6.2% >37 years old	6:397	The prevalance of malnutrition and VL infection was 95.5% while presence of intestinal parasitic infection was statistically associated with severe malnutrition in VL patients (p<0.001)

Table 2. Preliminary Data Extraction of Included Studies
Abbreviations: Cutaneous Leishmaniasis (CL), Visceral Leishmaniasis (VL), Food Frequency Questionnaire (FFQ), Reactive Oxygen Species (ROS), Body Mass Index (BMI), Interleukin (IL), Tumor Necrosis Factor (TNF)

Discussion

- Following full-text screening 10 articles remained for absolute inclusion
- Deficiencies reported thus far include malnourishment in general, vitamin A, zinc (n=3 each), iron (n=2), fiber, vitamin E, potassium, selenium, and copper (n=1 each), which variably intersected with clinical disease manifestations and progression
- Disruptions to immune cell count (n=3), and antibody levels (n=1) were also noted
- The data will be summarized to systematically map published literature that will illuminate a number of ways in which nutrient deficiencies or abnormal micronutrient status alter and impair immune function in persons with leishmaniasis
- This synthesized body of information will ultimately inform adjunctive therapeutic decisions in the context of leishmaniasis, which has the potential to improve patient prognosis

References

Dietary Lifestyle Interventions for Neuropathic Pain: Evaluation of the HEALM Quality Assessment Tool

Michael Klowak[1], Celine Lecce[2], Ranie Ahmed[2], Raesham Mahmood[2], Aquilla Reid-John[2], Ikeade Adeyinka[2], Shaleesa Clarke[2], Shveta Bhasker[2], Mariyam Mohammed[2], Katherine Tan[2], Jahmar Hewitt[2], Andrea K. Boggild[1,2,3,4*]

[1]Institute of Medical Science, University of Toronto, Toronto, ON, Canada; [2]Tropical Disease Unit, Toronto General Hospital, Toronto, ON, Canada; [3]Office of Access and Outreach, Temerty Faculty of Medicine, University of Toronto, Toronto, ON, Canada; [4]Department of Medicine, University of Toronto, Toronto, ON, Canada

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Introduction

- The "Grading of Recommendations, Assessment, Development and Evaluations" (GRADE) framework has emerged as a common and transparent approach to evaluating certainty (or "quality") of evidence for interventional and comparator studies
- However, design elements that are intrinsic to non-RCT lifestyle studies may contribute to poor grading of otherwise high quality and robust trials
- In order to mitigate this bias, the "Hierarchies of Evidence Applied to Lifestyle Medicine" (HEALM) framework has been developed
- This framework makes specific considerations for the pitfalls of traditional quality of evidence tools, however, lacks validation against a gold standard assessment tool
- As a result, this study seeks to validate the use of HEALM as a strength of evidence tool compared to GRADE for our **"Dietary Lifestyle Interventions for Neuropathic Pain"** systematic review, the objectives of which were to evaluate the effects of dietary lifestyle interventions on neuropathic pain outcomes

Methods

- A comprehensive search strategy was conducted using 5 databases from inception to October 2025, that resulted in 23,285 articles for screening
- Articles were screened independently by two reviewers and discrepancies were resolved by a tertiary arbitrator during title/abstract, and full-text screening
- A total of 6 articles were isolated for absolute inclusion / bias assessment
- GRADE and HEALM will be simultaneously implemented to assess their quality of evidence, followed by a comprehensive comparative analysis

[1]GRADE	[2]HEALM
Common; transparent; iteratively refined over many years; gold standard	Newer framework (2019); specifically tailored towards lifestyle medicine
Reviewers make subjective judgements based on individual expertise	Reviewers make objective judgements based on a series of questions and criteria
Certainty/quality of evidence is rated up or down depending on specific considerations	Certainty/quality of evidence is given a grade: **A** (strong/decisive), **B** (moderate/suggestive), **C** (insufficient/inconclusive)
Considerations include: Study design: interventional (begins with **higher** rating) vs observational (begins with **lower** rating) Risk of bias, imprecision, inconsistency, indirectness, publication bias (can result in a **lower** rating) Large magnitude of effect, dose-response gradient, residual confounding decreases magnitude of effect (can result in a **higher** rating)	**Questions/criteria focus on:** Mechanisms of action, causality/attribution, generalizability in large populations, considerations of larger time periods (decades, lifetimes, generations) Answers to questions are assigned values: (**Yes** = 2, **Uncertain** = 1, **No** = 0), which contribute to the overall score: **A** (≥7), **B** (5-6), **C** (<5)
Critiqued for potential bias towards randomized controlled trials over observational studies	Considers common restrictions intrinsic to lifestyle trials including cost constraints, adherence challenges, difficulty blinding, limited generalizability (which all typically result in a lower rating)

Table 1. Comparison of quality of evidence, GRADE & HEALM frameworks

Results

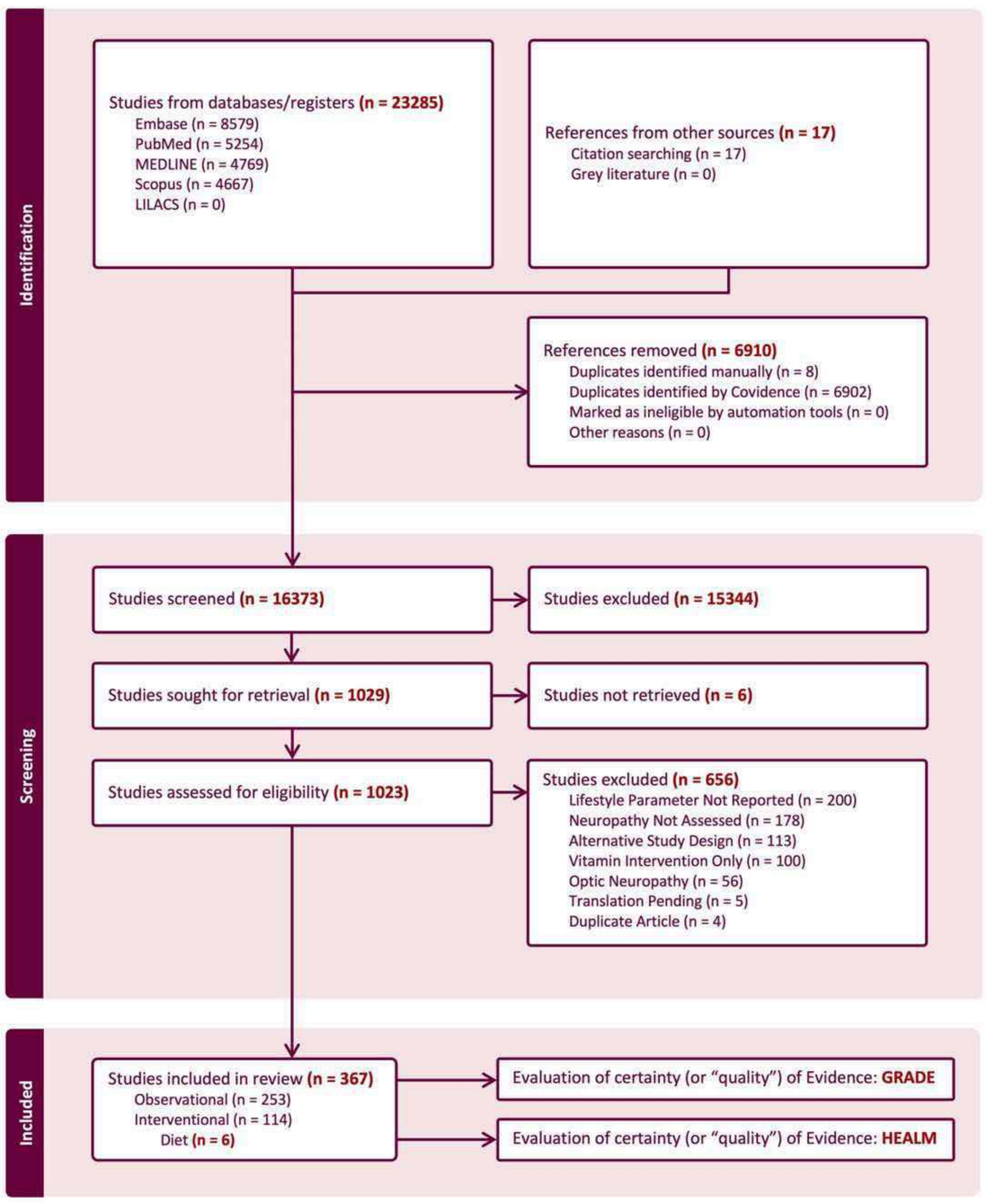

Figure 1. Modified PRISMA Flowchart

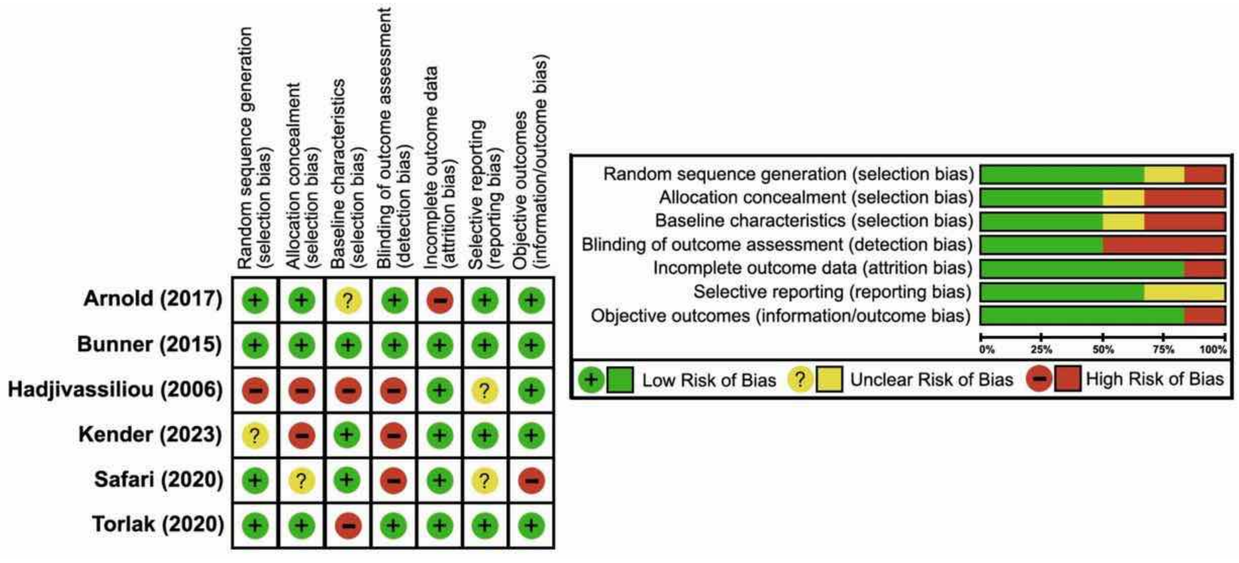

Figure 2. Risk of bias assessment for included articles by study and bias item

Discussion

- The reported quality of evidence for each article will be compared between tools to ascertain HEALM's utility and performance against the GRADE gold standard
- It is hypothesized that the quality/certainty of evidence from lifestyle trials will be considered more robust in HEALM vs GRADE due to the intrinsic pitfalls of such research and potential bias within each framework
- Overall, this validation project will allow for the succinct organization and dissemination of lifestyle-related outcomes by public health professionals, experts in the nutrition space such as nutritionists and dieticians, and clinicians worldwide

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An Update on the Role of Imaging in the Care of Patients with Genitourinary Schistosomiasis: A Systematic Review

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Introduction

- Schistosomiasis is a neglected tropical disease caused by worms of the genus *Schistosoma*.
- Genitourinary schistosomiasis is caused by *S. haematobium* which is endemic to Africa and the Middle East.
- For refugees and asylum seekers from countries where schistosomiasis is endemic, infection with the *Schistosoma* is common.
- Symptoms may begin shortly after arrival or years after migration or not at all.
- Chronic infection may lead to severe fibrosis of the urogenital tract and can cause serious lesions in organs like the bladder, kidney, and/or genital organs.
- Previously published guidance underscores the role of imaging as a risk stratification tool for intestinal schistosomiasis.

Methods

- Five databases were searched from inception to February 2025.
- Terms used in the search strategy were: “schistosomiasis” or “schisto*” AND “haematobium” or “haematob*” AND “CT” or “Computed And tomography” or “ultraso*” or “sonogr*” or “MRI” or “Magnetic AND resonance AND imaging” or “Echo”
- Screening and data extraction was performed by the reviewers.
- Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) was employed.
- Preliminary results were summarized narratively.

Objective

To synthesize available literature around the role of imaging in the evaluation of patients with genitourinary schistosomiasis for use in initial risk stratification and management.

Results and Discussion

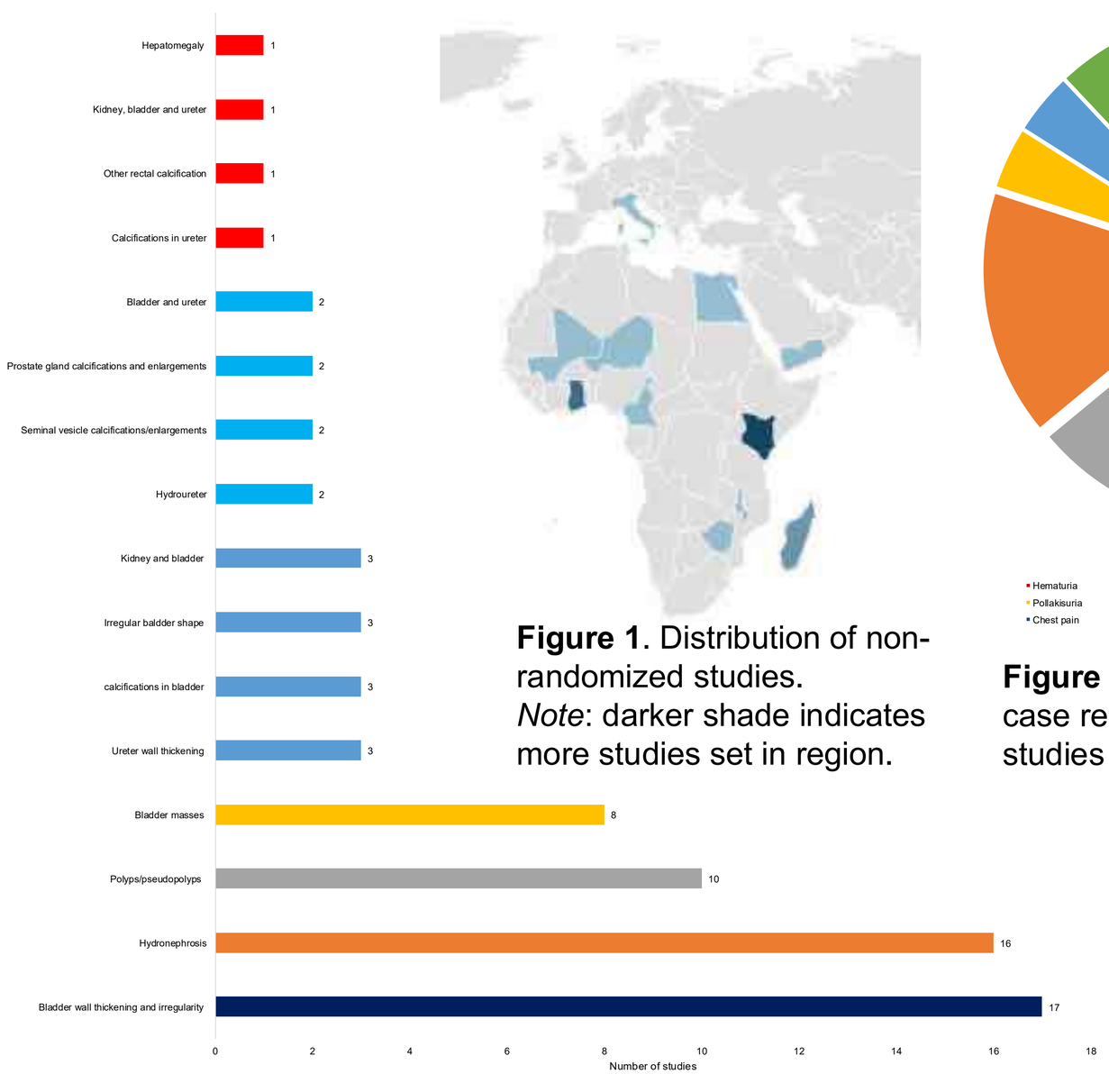

Figure 2 . Frequency of abnormalities detected across studies

Figure 1. Distribution of non-randomized studies.
Note: darker shade indicates more studies set in region.

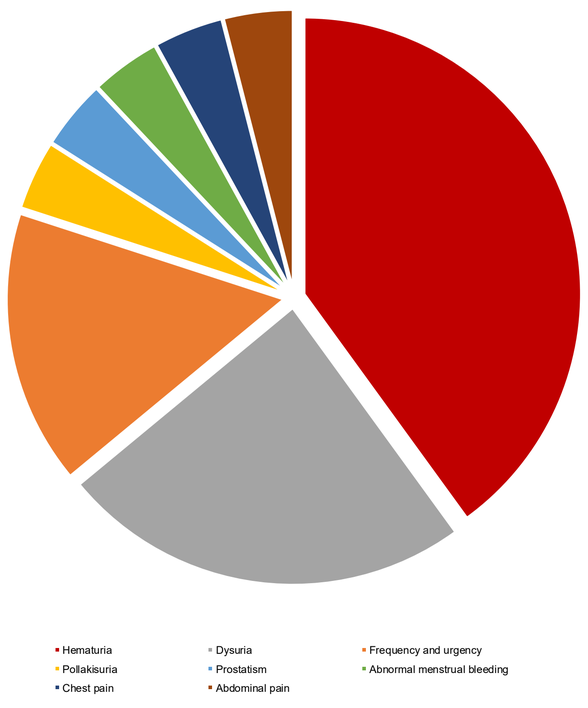

Figure 3. Presenting symptoms in case reports and case series across studies

- Both children and adults were represented with the majority of participants under 18 years of age. Most studies had more male participants.
- Most studies were conducted West Africa.
- Ultrasound and CT imaging were the most commonly used imaging modalities.
- Imaging showed bladder wall thickening or irregularities (most common), hydronephrosis, bladder masses, polyps or pseudo polyps in the bladder, calcifications along the urogenital tract, as well as abnormalities in ureter (dilations), and male genital organs.
- For case reports, most patients presented to health care with hematuria and dysuria.
- In countries endemic for the disease, imaging was able to diagnose and provide key information about disease progression, stage, and management.
- Findings can provide insights for developing clinical guidance to ensure timely detection and management of schistosomiasis for newcomers, thereby improving health outcomes.

References

Rifampin-Ofloxacin-Minocycline (ROM) for the Treatment of Multibacillary Leprosy: A Systematic Review

Michael Klowak[1], Jahmar Hewitt[2], Shveta Bhasker[2], Raesham Mahmood[1], Arghavan Omidi[2], Sahar Gholzom[2], Andrea K. Boggild[1,2,3,*]

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Introduction

- Patients who are affected by leprosy are at risk of several complications associated with the disease itself and its treatment
- Standard WHO multi-drug treatment (MDT) for leprosy consists of medications that are potentially harmful and cause a range of adverse systemic effects
- Alternative options for potential treatment have emerged such as Multibacillary leprosy, characterized by many skin lesions and a high bacillary load, may be most amenable to a fluoroquinolone-based treatment protocol
- Monthly dosing of ROM has emerged as a potential treatment option for leprosy, however, a synthesis of the evidence supporting ROM does not exist

Methods

- Abstracts reporting the efficacy & safety of monthly ROM treatment in multibacillary leprosy in human patients were targeted using combinations of search terms related to "leprosy" (including "Hansen's disease" and "*M. leprae*") and "rifampin," "ofloxacin," "minocycline," and "ROM," along with their common synonyms and trade names (from inception to June 2025)

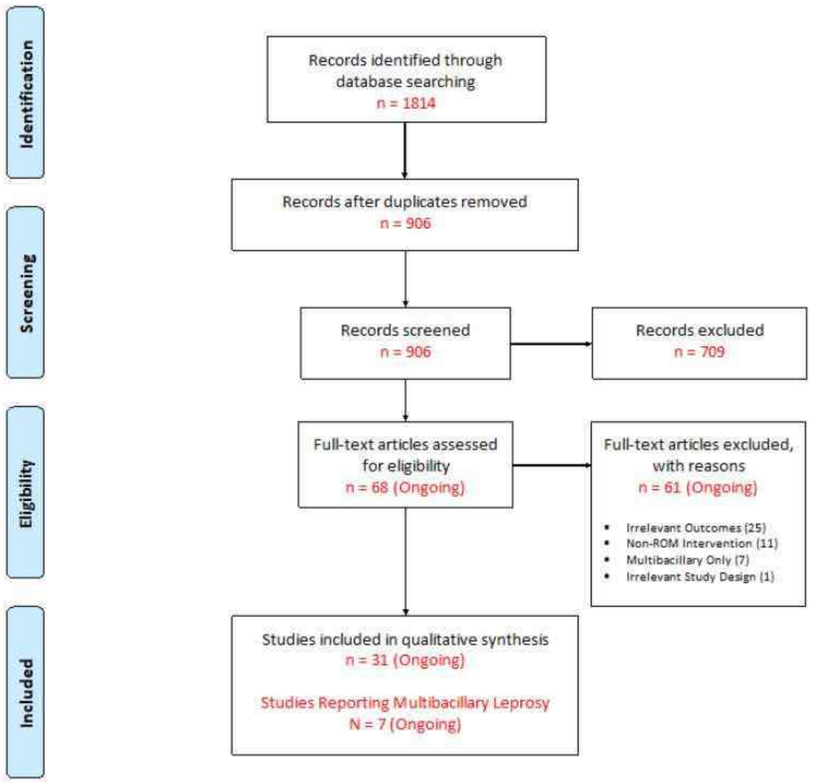

Figure 1. PRISMA Flowchart

Included	Excluded
Systematic reviews	Review articles
Randomized controlled trials	Case reports
Clinical trials	Case series (n<4)
Cohort studies	Editorials
Observational studies	Conference proceedings
Case-control studies	Animal studies
Case series (n>5)	Trial descriptions only

Table 1. Inclusion and exclusion criteria implemented during title and abstract screening

Primary Outcome Measures	Stratifiers
Lesion clearance	Social environments
Treatment failure	Education
Relapse	Socioeconomic status
Side effects	Sex / Gender
Reversal Reactions	Occupation

Table 2. Preliminary outcome measures, and stratifiers, to be assessed during full text screening

Results

Author, Year	Country	Study Design	Sample Size	Mean Age (SD), y	Male, %	Follow-Up, mo	Diagnosis of Leprosy	Treatment	Comparator
[1]Ji et al., 1998	Mali	Randomized Control Trial	20	34 (14)	80	0.25	Clinical + Histological	ROM, single dose	Ofloxacin + minocycline
[2]Kumar & Girdhar, 2014	India	Case Series	19	40.2 (4.0)	68.42	-	Clinical	ROM, monthly	No Comparator
[3]Kumar et al., 2014	India	Cohort	289	41.6	61.8	12	Clinical	ROM, monthly	WHO-MDT
[4]Mane et al., 1997	Senegal	Case series	220	-	60	12	Clinical + Histological	ROM, monthly	No Comparator
[5]Shetty et al., 2011	India	Retrospective cohort	62	-	-	-	Clinical + Histological	ROM, single dose	i) WHO-MDT, ii) dapsone, iii) RO
[6]Ura et al., 2007	Brazil	Randomized Control Trial	26	-	-	24	Clinical + Histological	ROM, monthly	WHO-MDT
[7]Villahermosa et al., 2004	Philippines	Randomized Control Trial	21	29.4	81.5	24	Clinical + Histological	ROM, monthly	WHO-MDT

Table 3. Preliminary Baseline Characteristics of Included Studies; Rifampin + Ofloxacin (RO), Standard World Health Organization Multi-drug therapy (WHO-MDT)

Outcome	Study	ROM		Comparator		Difference
		% of patients	Proportion	% of patients	Proportion	
Treatment Failure	*[7]Villahermosa et al., 2004*	0.00%	0	0%	0	0%
	Mean	**4%**	-	**6.29%**	-	-2.29%
	Median	**1%**	-	**0.58%**	-	0.42%
	Range	**3%**	-	**18.30%**	-	-15.30%
Relapse	*[7]Villahermosa et al., 2004*	0%	0/6	0%	0/10	0
	Mean	**1.53%**	-	**0.59%**	-	**0.94%**
	Median	**1.26%**	-	**0.35%**	-	**0.91%**
	Range	**3.60%**	-	**1.41%**	-	**2.19%**
Side Effects	*[1]Ji et al., 1998*	40%	4/10	20%	2/10	-2/10
	[7]Villahermosa et al., 2004	0%	0/21	100%	10/10	-100%
	Mean	**8%**	-	**60%**	-	**-52%**
	Median	**0%**	-	**10%**	-	**-10%**
	Range	**40%**	-	**100%**	-	**-60%**
Reversal Reactions (Type 1&2)	*[1]Ji et al., 1998*	0%	0/10	20%	2/10	-2/10
	Mean	**13%**	-	-	-	-
	Median	**9%**	-	-	-	-
	Range	**33.33%**	-	-	-	-

Table 4. Preliminary Summary of Primary Outcomes

Discussion

- Interim findings suggests that treatment failure and side effects are greater in the comparator group (+2.29% and +52% respectively)
  - Relapse is slightly greater in the ROM group (+0.94%). This suggests that ROM is slightly more efficacious than its comparator, however a more robust analysis is necessary)
- Several determinants of health were identified qualitatively throughout this analysis including:
  - **Social environments** – 50% of non-adherent patients denied having leprosy due to potential loss of jobs and/or marriage prospects[3]
  - **Patient education** – 86% of respondents did not understand the concept of their disease[8]
    - Indicating a clear opportunity for bedside quality improvement
  - **Gender** – Women completed treatment at a rate of 65.6% and men at 79.2% ($p<0.05$)[9]
    - Further investigation to better understand gender- and sex-based influences on treatment and prognosis warranted
- Synthesizing the current evidence discussing the efficacy of monthly ROM, will strengthen the current body of knowledge surrounding the treatment of paucibacillary leprosy, and may allow for the development of standardized fluoroquinolone-based treatment protocols.

References

Ethnopharmaceuticals for the Treatment of Cutaneous Leishmaniasis of the New World

Kalsoom Shahzad[1], Ruwandi Kariyawasam[2,3], Michael Klowak[1,4], Dileesha Fernando[1], Eunice Aluko[1], Ezra Bado[1], Shveta Bhasker[1,4], Jason Kwan[5], Sonia Igboanugo[6], Andrea Boggild[1,4,6,7,*]

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Introduction

- **New World Cutaneous Leishmaniasis (NWCL):** Neglected parasitic disease caused by members of the genus *Leishmania*, located primarily in Central and South America.[1]
- **Current challenge:** First-line therapies are costly, limited by toxicity and accessibility, and often ineffective.

- **Ethnopharmaceuticals:** Plant-based compounds with potential anti-leishmanial effects found in and around local endemic communities.[2]
- **Rationale:** These plant-based compounds, with potential anti-leishmanial effects, offer an opportunity to overcome the aforementioned therapeutic challenges. Many such interventions are also supported by anecdotal evidence.

Objective

This study aims to synthesize existing evidence around available ethnopharmaceuticals to promote drug discovery for the treatment of NWCL.

Methods

- PubMed (NCBI), Medline (OVID), Embase (OVID), Web of Science (BioSIS) and LILACS (VHL) were searched using combinations of the search terms and concepts, such as **"cutaneous leishmaniasis"** and **"ethnopharmaceuticals".**
- Inclusion and exclusion of search terms was employed to maximize relevant article extraction.

Inclusion criteria
- Observational studies
- Case reports
- Case series
- Cohort studies
- Clinical trials

Exclusion criteria
- Animal studies
- In vitro and in vivo studies
- Non ethnopharmaceuticals
- Non Leishmania spp. targets
- Mucosal, mucocutaneous or visceral leishmaniasis

- **GRADE** approach used to assess the quality of studies reporting therapeutic interventions.
- **LILACS** articles screened by native Spanish speaking individuals to ensure proper adherence to inclusion and exclusion criteria.
- Data will be grouped and summarized by *Leishmania* spp. and plant species.

Results

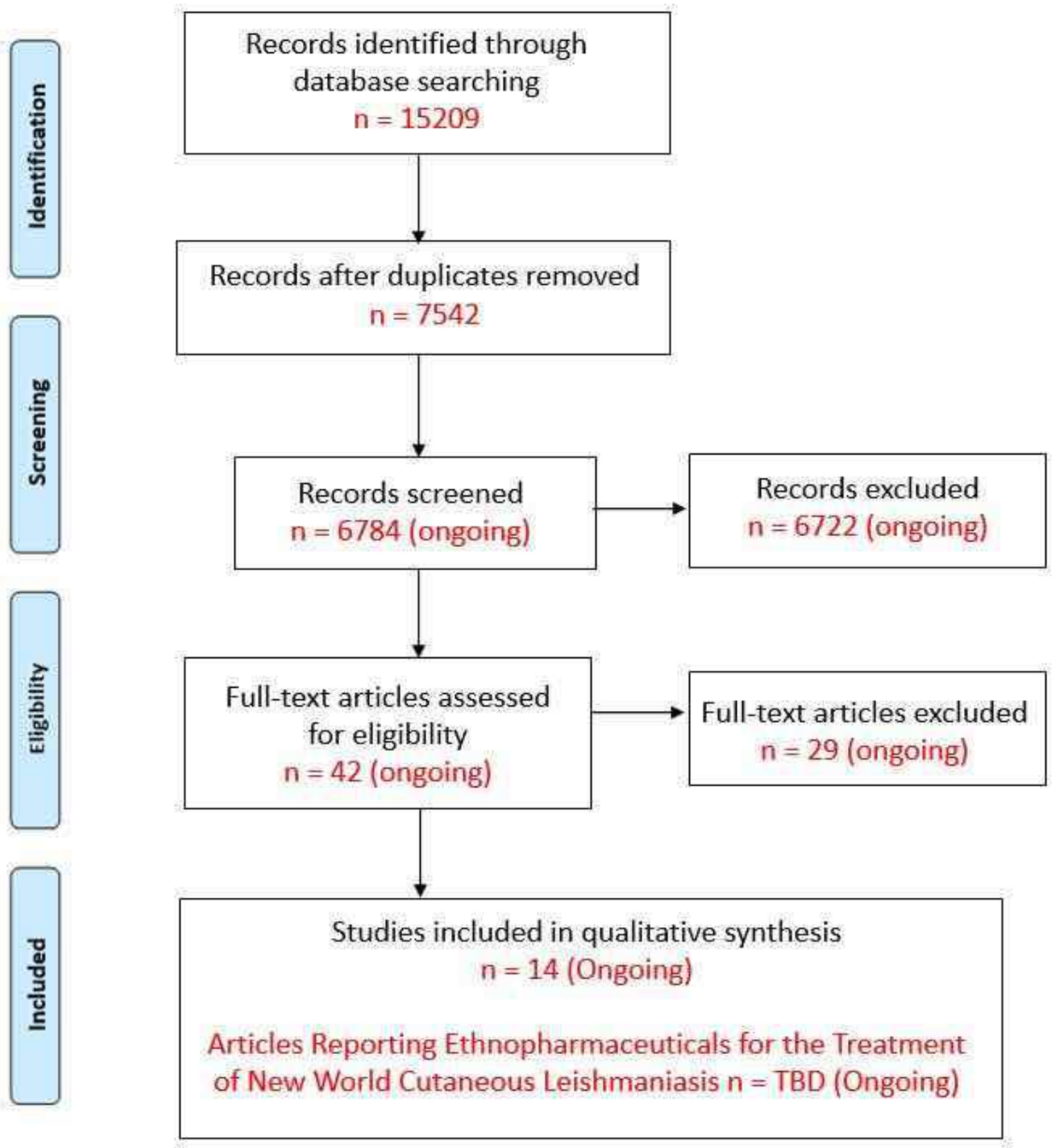

Figure 1: PRISMA flowchart.
The PRISMA flow diagram for the systematic review detailing the database searches, the number of abstracts screened and the full texts retrieved. Updated Feb. 2025.

Discussion & Conclusion

- Screening is ongoing (Figure 1). Focus of systematic review will be on the effects of ethnopharmaceuticals in the context of New World species.
- With climate change and increased human/vector migration, NWCL incidence may rise.

Advantages: Affordable, accessible, and culturally relevant alternatives to toxic and costly therapies. Strengthening drug discovery pipelines with ethnopharmaceutical evidence may guide development of novel therapeutics.
Conclusion: By synthesizing existing evidence, the study identifies promising candidates that may inform future drug discovery and development, particularly for severe cases caused by Leishmania species within the *Viannia* complex.

Future Directions

- Complete this systematic review by completing full text review of studies followed by qualitative analysis.
- Evaluate species-specific efficacy against New World Leishmania.
- Optimize topical formulations for safety, stability, and skin penetration.
- Explore combinatorial use with standard therapies to reduce toxicity and cost.
- Strengthen community-based research to integrate local knowledge into treatment strategies.

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An update on the role of imaging in the care of patients with intestinal schistosomiasis

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BACKGROUND:

- Intestinal schistosomiasis leads to significant morbidity and mortality worldwide, including severe hepatic disease with peri-portal liver fibrosis, portal hypertension and subsequent esophageal varices
- Previous guidelines recommended the use of abdominal imaging to detect early hepatic changes, thereby improving disease outcome [1]

METHODS:

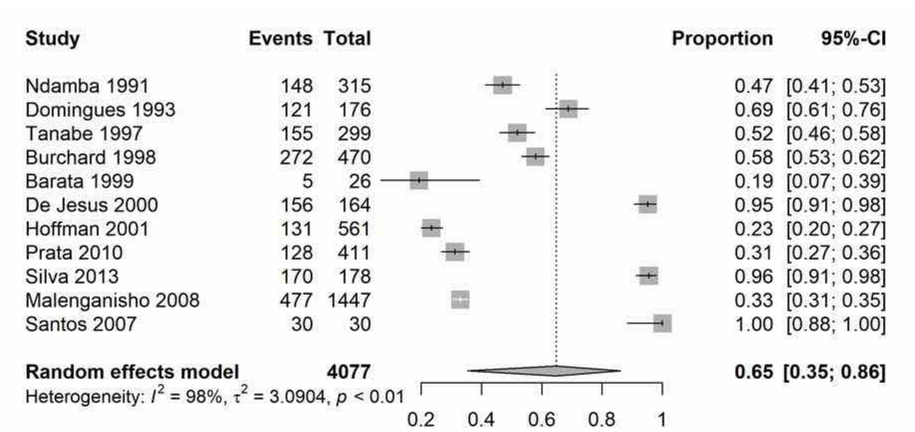
The search strategy was:

Schistosomiasis		Medical Imaging		Liver
Schistosomiasis		CT		Liver
Schistosoma mansoni		Computed tomography		Periportal fibrosis
Schistosoma japonicum		Ultrasound		Hepatic
		Ultrasonography		Echogenic
	AND	MRI	AND	Hepatosplenic
		Magnetic resonance imaging		Portal hypertension
		Echo imaging		
		Sonography		
		Sonogram		
Schistosomiasis OR (Schisto* AND (mansoni OR japonicum))		CT OR (computed AND tomography) OR Ultraso* OR Sonogr* OR MRI OR (Magnetic AND resonance AND Imaging) OR Echo OR Imaging		Liver OR periportal OR peri-portal OR fibrosis OR hepat* OR echogenic* OR (portal AND hypertension)

- Searched MEDLINE, Embase, Cochrane Library of Systematic Reviews, Epistemonikos, Global Health, NICE, TRIP and LILACS from database inception to August 1, 2025
- The study followed PRSIMA guidelines [13]
- Metanalysis was performed on R (Version 4.2.2)

RESULTS:

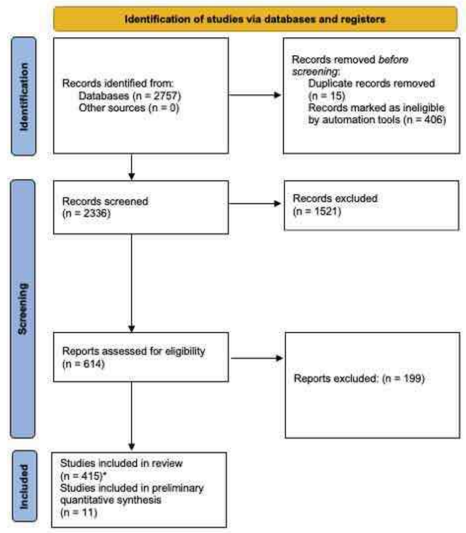
Prevalence of periportal fibrosis across 11 studies



- 11 studies included in this preliminary analysis
- 9 cross-sectional and 2 case-control
- All diagnosed with *Schistosoma mansoni*
- All studies used ultrasound imaging (none with CT or MRI)

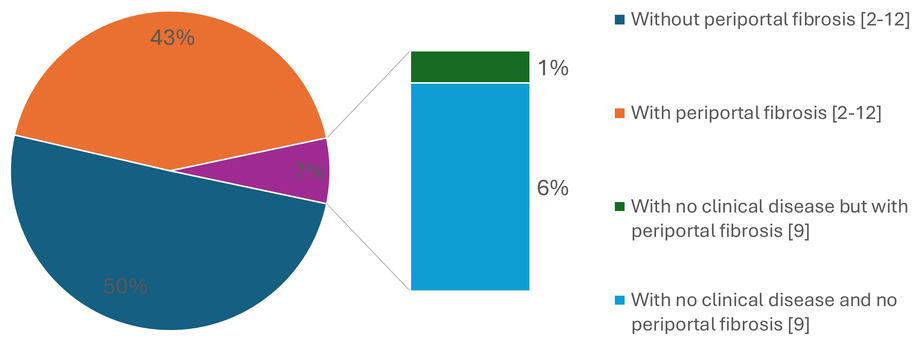
References:

RESULTS:

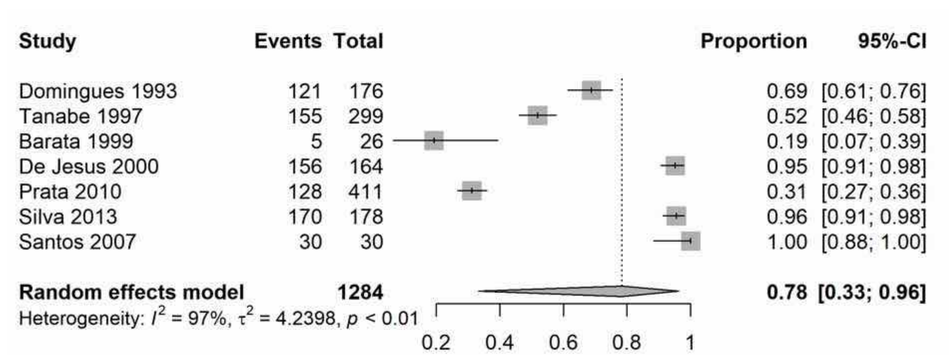


*Screening ongoing

Breakdown of schistosomiasis patients and liver disease



Sub-analysis of prevalence of periportal fibrosis in Brazil



- Of the 4,077 participants examined across 11 studies, the **pooled prevalence** of periportal fibrosis was **65%** and in Brazil, specifically it was **78%.**
- Abdominal ultrasound is an important **diagnostic tool** in the diagnosis of schistosomiasis related disease.

DISCUSSION:

- Abdominal imaging is able to detect liver fibrosis in the absence of clinical disease [9]
- Synthesizing the current literature on abdominal imaging in the evaluation of schistosomiasis can translate into clinical recommendations for improved risk stratification and management of schistosomiasis, and thereby overall improvement of disease outcomes