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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

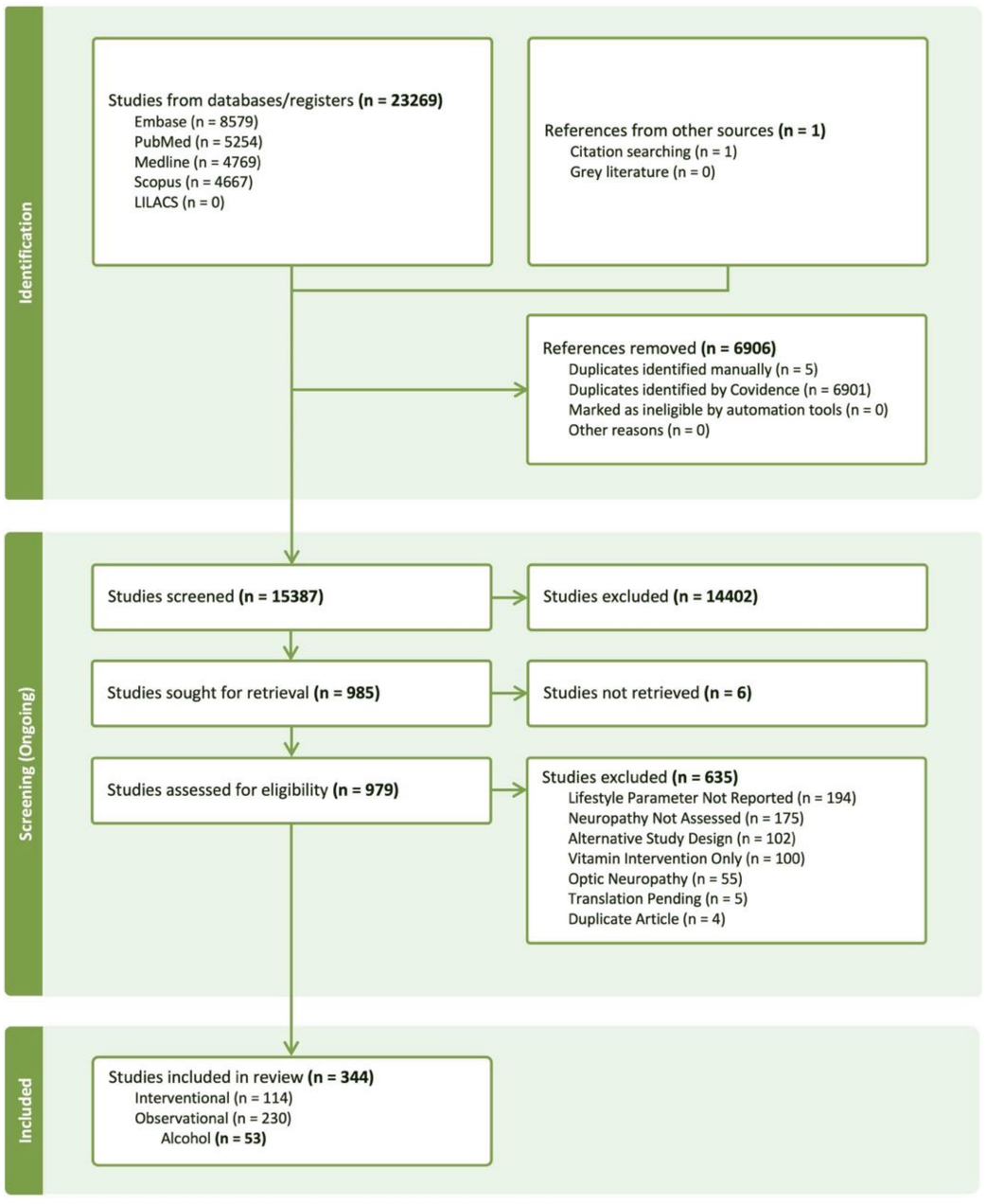

Figure 1. PRISMA Flowchart for all included lifestyle intervention papers for the indication of neuropathic pain

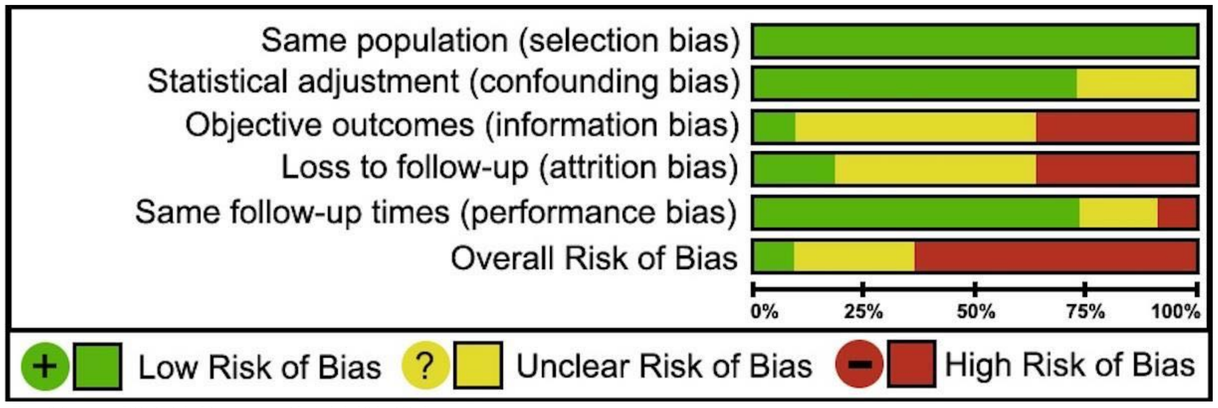

Figure 2. Summary of GRADE Risk of Bias Assessment for Included Cohort Studies

Results

Author (Year)	Study Design	Setting	N	Sex N (F-M)	Age (mean±SD, (range))	Population / Etiology	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: 3101:2620	%(!) 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 neuropathy 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.*

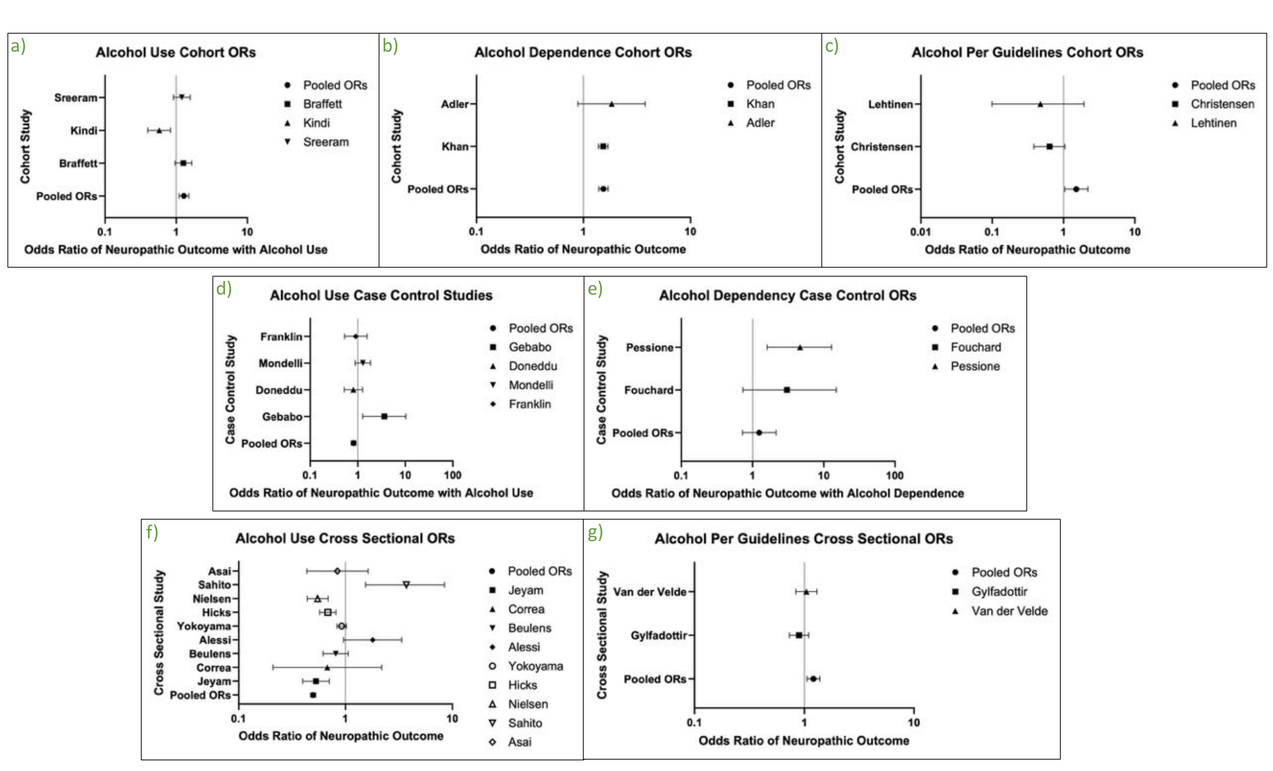

Figure 3. Forest plots of odds ratios of neuropathic outcome according to alcohol consumption variables in cohort (a-c), case-control (d, e), and cross sectional (f, g) studies

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