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Contents

Headache Beyond Pain: Unraveling Migraine Prevalence, Mental Health Comorbidities, and Disability Among University Students in the Middle East and North Africa

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Abstract
Background: Migraine is a common primary headache disorder, affecting approximately 19% of university students worldwide. University students, in particular, encounter psychological and academic pressures that may precipitate migraines, resulting in functional impairment and impaired concentration, learning, and academic achievement, leading to impairment, decreased productivity, and absenteeism. Migraine is frequently correlated with stress, anxiety, depression, and sleeping disturbances. Despite its impact, migraine remains underdiagnosed and undertreated. Migraine management involves a multifaceted approach; however, in the era of precision medicine, it is evolving by integrating genomic, clinical, and imaging data to personalize treatment, improve response prediction, and reduce the time required to identify effective and tolerable treatments.
Objective: The present study aimed to assess migraine prevalence among university students in the Middle East and North Africa region (MENA) and determine its triggers, disability, and mental health comorbidities to inform personalized prevention and management strategies for this vulnerable population.
Methods: This multinational cross-sectional study was conducted in 11 low- and middle-income countries in the MENA region, using an anonymous, self-administered online questionnaire. The questionnaire assessed migraine characteristics, triggers, associated disability, and mental health comorbidities.
Results: A total of 5,954 were screened for migraine, with 26.1% screening positive. Of them, 72.5% had severe depression and 23.2% had severe disability. Sleeping disturbances and stress were the most common triggers. Females, older age, and non-medical field students were the primary predictors of migraine. Higher fluid intake, frequent exercise, adequate sleep, and adequate hydration were protective factors against migraines. A negative correlation between migraine disability score and academic performance was observed.
Conclusion: This study revealed a high prevalence of migraine, anxiety, depression, and disability among university students in the MENA region. These results emphasize the need for lifestyle changes, screening programs to support early detection, and targeted initiatives to raise awareness of migraine-related comorbidities.

Keywords: Migraine prevalence; university students; mental health comorbidities; migraine-related disability; MENA region.

The Efficacy of Different Types of Colonoscopies in Detecting Various Lesions in Lynch Syndrome Patients: Systematic Review and Network Meta-Analysis.

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Abstract
Background: Lynch syndrome patients are at a particularly high risk for developing colorectal cancer; thus, optimal surveillance strategies are required. Although colonoscopic imaging methods differ in diagnostic performance, direct comparisons in this population are not very common.
Aim: To evaluate the diagnostic performance of white-light endoscopy (WLE), chromoendoscopy, virtual chromoendoscopy (NBI, LCI, I-SCAN), and AI-assisted colonoscopy in identifying neoplastic and non-neoplastic lesions in individuals diagnosed with Lynch syndrome.
Methods: The PRISMA guidelines were followed in conducting a systematic review and network meta-analysis. Up until March 2025, PubMed and Scopus were searched. Relevant studies included observational or interventional designs that compared various colonoscopy techniques in adults with Lynch syndrome. The primary outcomes were lesion detection rate and number of lesions per colonoscopy. Secondary outcomes included total procedure time, withdrawal time, and adverse events.
Results: Nine studies were included. LCI demonstrated a significantly higher neoplastic lesion detection rate compared to WLE (RR = 1.42, 95% CI: 1.02–1.97) and also detected more lesions per procedure (MD = 0.23, 95% CI: 0.01–0.45). Chromoendoscopy was better at marking the non-neoplastic lesions (RR = 1.23, 95% CI: 1.05–1.44) but had the longest procedure and withdrawal times. AI-assisted and virtual approaches were better than WLE but not as effective as LCI or chromoendoscopy.
Conclusions: LCI is more efficient than WLE for detecting neoplastic lesions in Lynch syndrome. Chromoendoscopy remains valuable for non-neoplastic detection, but procedural time is a major drawback. AI-assisted technologies are promising but require additional investigation.

Keywords: Lynch syndrome; colonoscopy techniques; lesion detection rate; chromoendoscopy and LCI; network meta-analysis.

The Efficacy of Alpha-Lipoic Acid in Migraine: A Systematic Review and Meta-Analysis

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Background: Despite assumptions about the role of oxidative stress in the pathogenesis of migraine, the effectiveness of antioxidant-based preventive treatments remains uncertain. Alpha-lipoic acid (ALA), with its anti-inflammatory properties, is a promising compound for migraine prevention. Therefore, this study aims to evaluate the current evidence on ALA's effectiveness in migraine prevention.
Methods: We conducted searches of PubMed, Web of Science, Scopus, and OVID up to April 2025 to identify randomized controlled trials (RCTs) investigating the efficacy of ALA for patients with migraine. We used the Cochrane risk-of-bias tool to assess the quality of the studies.
Results: 5 RCTs, including 255 patients, proved eligible. Results suggested a significant improvement in MMF in two subgroups as ALA as monotherapy and as combination with values (MD= -1.43, 95% CI: [-2.48, -0.390; p=0.007), (MD= -2.32, 95% CI: [-3.18, -1.46; p=0.001) respectively. For MMD, three studies were included, and the meta-analysis showed a significant decrease in ALA compared to control (MD = -5.2, 95% CI: [-9.43, - 0.98]; p = 0.02). For a 50% reduction in migraine frequency, three studies were included, and a meta-analysis showed a significantly higher risk with ALA compared to control (RR=2.00; 95% CI [1.34, 3.00], p=0.0008). No serious adverse events were reported in the studies.
Conclusion: Our results suggest that ALA is a safe intervention with potential benefits for reducing migraine frequency. Further studies are critical to support the evidence and improve our understanding of its effectiveness.

Keywords: Alpha-lipoic acid; migraine prevention; oxidative stress; randomized controlled trials; meta-analysis

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Impact of Gender and Race on Gastrointestinal Diseases in Patients with Parkinson's Disease: A Nationwide Analysis

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Abstract
Background: Gastrointestinal (GI) diseases are common non-motor features of Parkinson's disease (PD), significantly impacting quality of life. Racial and gender disparities influence these diseases, but their impact remains underexplored. This study examines the association of race and gender with GI syndromes in hospitalized PD patients.
Methods: A retrospective study using the National Inpatient Sample was conducted, including 124,345 hospitalized PD patients. Multivariable logistic regression was used to assess associations between GI conditions and race/ethnicity (White, Black, Hispanic) and sex, adjusting for confounders.
Results: Overall prevalence of GI diseases was 49.07%. Compared with White males, Black males had higher odds of dysphagia (aOR 1.27, 95%CI 1.04–1.56), and both Black (aOR 2.19, 95%CI 1.48–3.36) and Hispanic patients (aOR 1.7, 95%CI 1.05–2.77) had significantly higher odds of gastrostomy tube placement. White females had significantly higher odds of gastroesophageal reflux (GERD) (aOR 1.35, 95%CI 1.25–1.46), constipation (aOR 1.34, 95%CI 1.23–1.59), gastroparesis (GP) (aOR 3.44, 95%CI 2.23–5.31), and IBS (aOR 3.1, 95%CI 2.2–4.2), but lower odds of dysphagia (aOR 0.82, 95%CI 0.74–0.91), compared with White males.
Conclusion: Significant racial and gender disparities were observed in GI diseases among hospitalized PD patients. White females showed higher odds of GERD, constipation, GP, and IBS, while Black and Hispanic patients were more likely to require gastrostomy tube placement. These patterns highlight the need for tailored, equitable care strategies and for further research to understand better and address disparities in PD-related GI outcomes.

Keywords: Parkinson's disease; Gastrointestinal diseases; Gender; Races.

Phosphorylated Tau Isoforms (pTAU-181, pTAU-217, pTAU-231) as Reliable Biomarkers for Alzheimer's Disease: A Grade-Based Meta-Analysis of Diagnostic Accuracy in CSF and Plasma

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Abstract
Introduction: Alzheimer's disease (AD) remains the leading cause of dementia worldwide, yet accurate early diagnosis is often challenging. Recent advances highlight phosphorylated tau (pTau) isoforms—pTau-181, pTau-217, and pTau-231—in cerebrospinal fluid (CSF) and plasma as promising biomarkers capable of distinguishing AD from non-AD dementias and healthy controls (HC). We aimed to comprehensively assess their diagnostic accuracy through a systematic review and meta-analysis.
Methods: Following PRISMA guidelines and PROSPERO registration (CRD42025632278), we systematically searched PubMed, Scopus, Web of Science, and Ovid up to September 2025. Eligible studies evaluated pTau-181, pTau-217, or pTau-231 in CSF or plasma using accepted AD reference standards. Data were independently extracted and quality-assessed with QUADAS-2. Pooled sensitivity, specificity, diagnostic odds ratio (DOR), and area under the summary

receiver operating characteristic curve (AUC) were estimated using random-effects models. Clinical applicability was further explored using Fagan's nomogram to illustrate post-test probabilities, while potential publication bias was evaluated using Deeks' funnel plot asymmetry test. Moreover, certainty of evidence was evaluated using GRADE.
Results: A total of 48 studies encompassing diverse international cohorts were included. Compared with AD versus HC, CSF pTau-217 showed the strongest diagnostic performance, with a pooled sensitivity of 0.95 and specificity of 0.91, outperforming all other isoforms. CSF pTau-181 and pTau-231 also showed excellent accuracy (AUC = 0.90). Plasma assays demonstrated significant promise: plasma pTau-181 achieved a sensitivity of 0.88, a specificity of 0.81, and an AUC of 0.91, while plasma pTau-231 achieved a sensitivity of 0.84, a specificity of 0.87, and an AUC of 0.86, with particularly low heterogeneity across studies. Comparative analyses confirmed significantly elevated pTau isoform levels in AD versus both non-AD and HC groups. Certainty of evidence was rated moderate-to-high, supporting robust reliability of findings.
Conclusions: This meta-analysis establishes pTau isoforms—particularly CSF pTau-217—as highly accurate biomarkers for AD diagnosis. Importantly, plasma pTau-181 and pTau-231 emerge as minimally invasive, scalable alternatives with strong diagnostic validity, positioning them for clinical implementation and population-level screening. These findings support the integration of pTau assays into precision medicine frameworks, advancing early and accurate detection of AD.

Keywords: Alzheimer's disease; phosphorylated tau isoforms; CSF and plasma biomarkers; diagnostic accuracy; systematic review and meta-analysis.

Efficacy and Tolerability of First-Line Treatment Regimens for Extensive-Stage Small Cell Lung Cancer – A GRADE-assessed Network Meta-analysis of Randomized Controlled Trials

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Abstract
Background: The treatment landscape for extensive-stage small-cell lung cancer (ES-SCLC) has advanced with the introduction of immunotherapy, targeted therapy, and novel chemotherapy combinations. A comprehensive evaluation of safety and efficacy across these treatments remains essential. This study aimed to compare the outcomes of all first-line treatment regimens for ES-SCLC.
Methods: A systematic literature search of PubMed, Scopus, and Web of Science was conducted to December 2024 to identify randomized controlled trials of first-line treatments for ES-SCLC (CRD42024543408). Etoposide plus platinum (EP), the standard regimen, was the reference. Primary outcomes were overall survival (OS) and progression-free survival (PFS); secondary outcomes included objective response rate (ORR) and adverse events (AEs). Hazard ratios (HR) were used for survival, risk ratios (RR) for efficacy. A frequentist network meta-analysis was performed using Netmeta (v2.9- 0). Risk of bias was assessed with Cochrane RoB v2, and certainty of evidence with GRADE.
Results: This analysis included 34 studies with 10,658 participants and 22 treatment regimens. For OS, immunotherapy-based regimens such as Serplulimab + EP (HR = 0.63, 95% CI: 0.44–0.90, p = 0.01), Atezolizumab + EP (HR = 0.70, 95% CI: 0.49–1.00, p = 0.05), and Durvalumab + EP (HR = 0.71, 95% CI: 0.53–0.96, p = 0.02) showed significant improvements compared to EP. For PFS, Serplulimab + EP provided the greatest benefit (HR = 0.48, 95% CI: 0.31–0.75, p = 0.0012). Irinotecan + platinum was the only regimen to significantly improve the complete response rate (RR = 1.91, 95% CI: 1.06–3.46, p = 0.03). Safety outcomes varied: Atezolizumab + EP and Tiragolumab + Atezolizumab + EP demonstrated lower risks of treatment discontinuation. At the same time, regimens such as Ipilimumab + EP and Tislelizumab + EP were associated with increased risks of serious AEs. Heterogeneity was generally low, with moderate variability observed for PFS and AEs leading to discontinuation.
Conclusion: Immunotherapy-based combinations, particularly Serplulimab + EP, demonstrated superior survival outcomes while maintaining an acceptable safety profile in most cases. However, some regimens were associated with

increased AE risks. Future research should prioritize long-term outcomes and balance efficacy and tolerability to optimize therapeutic strategies.

Keywords: Extensive-stage small cell lung cancer; first-line treatment regimens; immunotherapy combinations; network meta-analysis; GRADE certainty of evidence.

Performance Anxiety, Autonomic Modulation, and Propranolol Use Among Healthcare Students in the MENA Region

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Abstract

Background: Anxiety is highly prevalent among healthcare students due to academic pressures, clinical responsibilities, and emotional burdens. Propranolol, a non-selective beta-blocker, is increasingly used for its anxiolytic effects, particularly during performance-related stress. However, patterns of use, motivations, and associated risks among healthcare students in the Middle East and North Africa (MENA) region remain underexplored.

Objectives: This study aims to assess the prevalence, patterns, motivations, and associated factors of propranolol use among healthcare students across the MENA region, in relation to their anxiety levels, as measured by the GAD-7 scale.

Methods: A cross-sectional online survey was conducted from June to October 2023 across 11 MENA countries. Data from 4,983 medical, pharmacy, and dentistry students were analyzed. The questionnaire included demographic data, propranolol use patterns, knowledge, and attitudes, alongside the GAD-7 anxiety assessment. Statistical analyses included chi-square tests, Mann-Whitney U tests, and logistic regression.

Results: Of 4,983 healthcare students surveyed across 11 MENA countries, 12.4% reported propranolol use, most commonly among medical students. The majority used propranolol for anxiety relief (64.5%), often without medical supervision (36.7% self-prescription). Reported doses were primarily 10–20 mg, and 38% indicated ongoing use at the time of the survey. Propranolol users demonstrated significantly higher GAD-7 scores (OR = 1.04 per point increase; $p < 0.001$), with self-prescribers showing greater anxiety severity than those with physician prescriptions ($p = 0.022$). Additional predictors of use included chronic disease (OR = 2.61, $p < 0.0001$), smoking (OR = 1.71, $p < 0.0001$), and advanced academic level (OR = 4.45 for sixth-year vs. first-year, $p < 0.001$). While 79.9% of users reported anxiety

improvement, 45.5% experienced adverse effects such as fatigue (22.6%), hypotension (14.8%), and sleep disturbances (13.5%).
Conclusions: Propranolol is widely used among healthcare students in the MENA region for anxiety management, often without medical oversight. The findings highlight the urgent need for improved mental health support, awareness campaigns on responsible medication use, and stronger regulatory control to mitigate potential misuse and health risks.

Keywords: Propranolol, Anxiety; GAD-7; Healthcare Students; MENA Region; Self-medication; Beta-blockers.

Exercise Effects on Breast Cancer Therapy-Related Cardiotoxicity: A Systematic Review and Meta-Analysis

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Abstract
Introduction: Cardiotoxicity is one of the most common side effects of cancer therapies. This systematic review aims to assess the effect of exercise on cardiotoxicity related to Breast cancer therapy in women.
Methods: We searched 4 databases (PubMed, Scopus, Web of Science, and Embase) to identify eligible studies. Randomized controlled trials (RCTs) published in English that reported the effects of exercise on cardiotoxicity in women with breast cancer were included. The PRISMA guidelines were followed. The risk of bias was assessed using the ROB-2 tool. The meta-analysis was performed using R 4.3.3.
Results: A total of 16 studies with 978 patients were included. Our findings revealed a mean change in LVEF of 2.193 (95% CI: -0.1 to 4.49; p = 0.058), which is slightly greater than the minimal clinically significant difference (MCID = 2.188). Peak oxygen consumption in the exercise group was 1.6 ml/kg/min greater than in the non-exercise group (95% CI: 0.69 to 2.47; p = 0.002), which is greater than the MCID of 0.975. For other outcomes, including cardiac biomarkers, global longitudinal strain (GLS), diastolic function (E/A ratio), hemodynamic measures (cardiac output, stroke volume, heart rate), and blood pressure, there was no significant difference between the two groups.
Conclusions: This study suggests that exercise may play a role in preventing or treating the cardiotoxicity caused by breast cancer therapy. However, as these findings represent a subclinical difference, further research is needed to confirm these results and determine their clinical significance.

Keywords: Breast cancer; exercise intervention; therapy-related cardiotoxicity; left ventricular ejection fraction; systematic review and meta-analysis.

Association Between Hepatitis B Virus Infection and Stroke Incidence: A Systematic Review and Meta-Analysis

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Abstract
Introduction: Stroke risk depends on many factors, including genetics, viral infections, and metabolism. Hepatitis B virus (HBV) infection is common and may affect stroke risk differently across populations. Understanding this variability is

essential for precision medicine approaches in stroke prevention. This study investigates the relationship between HBV infection and stroke incidence to explore whether HBV affects stroke risk differently in various study populations.
Methods: We conducted a systematic review and meta-analysis following the PRISMA guidelines, using four databases (PubMed, Scopus, Web of Science, and Cochrane) up to January 2025. Quality assessment was performed using the Newcastle-Ottawa Scale for cohort studies and the ROBINS-I tool for non-cohort studies. We used Comprehensive Meta-Analysis software, with odds ratios and event rates calculated for dichotomous outcomes.
Results: A total of 11 studies met the inclusion criteria with 2.67 million participants across diverse regions. The meta-analysis revealed a protective association between HBV and stroke (pooled OR: 0.89, 95% CI: 0.80- 0.99, $p < 0.05$). Most studies showed a protective association, except one study reported an increased risk. The event rate analysis demonstrated low stroke frequency in HBV-positive individuals (pooled rate: 3.3%, 95% CI: 0.018-0.060, $p<0.001$), with both fixed-effects (0.074, 95% CI: 0.072-0.075) and random effects (0.05, 95% CI: 0.02-0.08) models showing significant associations.
Conclusion: Findings suggest that HBV infection may influence stroke risk in a context-dependent manner, with evidence pointing towards a potential protective effect. The heterogeneity observed across populations highlights the importance of precision medicine. It underscores the need for future stratified studies to determine which patient subgroups may be protected or at higher risk, which could help guide the prevention and management of stroke.

Keywords: Hepatitis B virus; HBV; stroke; population variability; precision medicine; meta-analysis; systematic review

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Hybrid Strategy Combining Provisional Stenting and Drug-Coated Balloon in True Coronary Bifurcation: A Systematic Review and Meta-Analysis

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Abstract
Background: Management of side branches (SBs) in coronary bifurcation lesions during provisional stenting remains challenging. Drug-coated balloons (DCBs) are increasingly used; however, their benefit compared to uncoated balloons (UCBs) is not well established.
Methods: We conducted a systematic review and meta-analysis of randomized controlled trials (RCTs) and observational studies comparing DCBs and UCBs for SB treatment during provisional stenting. Searches were performed in PubMed, Embase, Scopus, and Web of Science until March 2025. Outcomes included postoperative SB diameter stenosis, late lumen loss (LLL), target lesion revascularization (TLR), target vessel revascularization (TVR), major adverse cardiovascular events (MACEs), myocardial infarction (MI), and cardiac death.
Results: Five studies (1,762 patients: 967 DCB, 795 UCB) were included. Pooled analyses showed DCBs significantly reduced postoperative SB diameter stenosis (MD: -1.42; 95% CI: -2.50 to -0.35; $P < 0.01$), LLL (MD: -0.21; 95% CI: -0.30 to -0.11; $P < 0.01$), MI (RR: 0.49; 95% CI: 0.33 to 0.73; $P < 0.01$), and MACEs (RR: 0.54; 95% CI: 0.39 to 0.75; $P < 0.01$) compared with UCBs. No significant differences were observed in TLR, TVR, or cardiac death. Subgroup analyses of RCTs and observational studies yielded consistent results. Certainty of evidence was high to moderate for RCT outcomes and low to very low for observational studies.
Conclusion: DCB use during provisional stenting for SB treatment provides superior angiographic and clinical outcomes compared with UCB. These findings support a hybrid approach of main-vessel stenting with DCB in non-complex bifurcation lesions.

Keywords: Coronary Bifurcation Lesions; Side Branch; Provisional Stenting; Drug-Coated Balloon; Uncoated Balloon