Supplemental Online Content

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This supplemental material has been provided by the authors to give readers additional information about their work.

eTable 1. Summary of studies examining the association between migraine and anxiety and depressive symptoms/disorders (n=74)

Study	Design	Location	Setting	Sample size	Ages	Sex	Outcome	Exposure	Unadjusted results	Adjusted results	Quality
Açlkel B et al, 2021[22]	Case-control	Turkey	Cases recruited from a neurology clinic and controls recruited from community	N=94 (37 with migraine, 22 with TTH, 35 controls)	8-18 years	N= 56 females (59.6%); 38 males (40.4%)	1. Primary headache diagnosis according to ICHD-II criteria 2. General quality of life: Pediatric Quality of Life Inventory (Peds QL)	1. Anxiety symptoms measured using the Screen for Child Anxiety Related Emotional Disorders (SCARED) 2. Depression symptoms measured using the Child Depression Inventory (CDI)	1. Mean SCARED score was not significant different in migraine vs. control group (31.2±17.8 vs. 24.8±14.6; ANCOVA F(2)=1.586, p=0.211) 2. Mean CDI score was higher in migraine vs. control group* (15.6 ±5.8 vs. 9.6±5.7; ANCOVA F(2)=5.563, p=0.005)	N/A	6/7 domains adequate
Albanês Oliveira Bernardo A et al, 2020[23]	Cross-sectional	Recife, Brazil	Recruitment from pediatric clinics	N=300 (253 with migraine, 47 with TTH)	6-17 years	Not reported for entire group; N= 132 females with migraine(52.1%); 121	Primary headache diagnosis according to ICHD-III criteria	1. Clinical anxiety ascertained using a clinical cut-off of 41 on the State-Trait Anxiety	1. N=61 (24.1%) of the migraine group had anxiety 2. N=4 (1.6%) of the	N/A	5/10 domains adequate

						males with migraine (47.8%)		(STAI) Inventory to define anxiety 2. Clinical depression ascertained using a clinical cut-off of 17 on the Children's Depression Inventory (CDI) to define depression	migraine group had depression		
Andrasik F et al, 1988[34]	Case-control	Florida, USA	Recruitment from pediatric clinics and the community	N = 64 (32 cases, 32 controls)	8-17 years	Not provided	Migraine as per Prensky and Sommer criteria	1. Depressive symptoms, measured using Children's Depression Inventory (CDI) for 8-13yo, or Beck Depression Inventory (BDI) for ≥14yo; Child Behavior Checklist-Internalizing Score (CBC-I) for all ages; Children's	1. Mean CDI scores for 8-12yo: 8.7 for migraine vs. 4.0 for control group*; Mean BDI scores for ≥14yo: 9.1 for migraine vs. 3.1 for control group*; Mean CBC-I scores: 60.9 for migraine vs. 55.1 for control group*; Mean	1. Migraine group scored higher on depression measures * (ANOVAs with age and sex): CDI, F (1, 34)=8.33, p<0.007; BDI F (1,21)=6.76, p<0.017; CDRS, F (1,52)=7.16, p<0.01;	4/7 domains adequate

								Depression Rating Scale (CDRS) for all ages 2. Anxiety symptoms, measured using State-Trait Anxiety Inventory for Children (STAIC) for 7-12yo, or State-Trait Anxiety Inventory Form X (STAIX) for ≥13yo	Children's Depression Rating Scale for all ages: 20.7 for migraine group vs. 17.6 in control group* 2. Mean STAIC for 7-12yo: not reported; Mean STAIX for >13yo: 39.1 for migraine vs. 30.2 for control group*	CBC-I F (1,54)=4.96, p<0.03 2. ≥13yo migraine group scored higher on STAIX*: F (1, 25)=7.16, p<0.04	
Anttila P et al, 2004[45]	Cross-sectional	Turku, Finland	Population-based	N=183 (32.2% migraine, 35.6% TTH, 32.2% no headache)	11-13 years (sixth grade students)	N=90 females (49.1%); 93 males (50.8%)	Primary headache diagnosis according to ICHD	1. Depressive symptoms, measured using Children's Depression Inventory (CDI) 2. Internalizing symptoms measured using Child Behavior Checklist (CBCL) given to parents	1. No difference in CDI depression scores between migraine (5.2 ± 4.7) vs. no headache (4.4 ± 4.3) (p=0.59 in ANOVA) 2. CBCL internalizing subscale significantly higher in	1. No difference in CDI depression scores between migraine (5.2 ± 4.7) vs. no headache (4.4 ± 4.3) (p=0.55 in ANCOVA) after controlling for	9/10 domains adequate

									migraine (7.0 ± 5.4) vs. no headache*(4.4 ± 3.8) (p<0.01 in ANOVA)	gender, age, and socioeconomic status 2. CBCL internalizing subscale significantly higher in migraine (7.0 ± 5.4) vs. no headache (4.4 ± 3.8) (p=0.03 in ANCOVA) after controlling for gender, age, and socioeconomic status	
Araujo G et al, 2020[56]	Case-control	Missouri, USA	Cases recruited from clinics (not specified what type) and unclear where controls were	N=40 (57.5% chronic migraine; 42.5% controls)	12-17 years	N=31 females (77.5%); 9 males (22.5%)	Not provided	Depression symptoms measured using the Children's Depression Inventory (CDI), and clinical cut-offs used and	The migraine group had higher CDI scores* (50.2±9.7 vs. 43.4 ±7.7); there was no significant difference between migraine vs.	N/A	3/7 domains adequate

			recruited from					defined as a T score ≥60	control group on proportion with clinically elevated depression (p=0.06)		
Arruda M et al, 2012[67]	Cross-sectional	São Paulo, Brazil	Population-based	N=1,856 (23% migraine, 28.9% TTH and 18.6% controls)	5-12 years	N=897 females (48.3%); 959 males (51.7%)	Primary headache diagnosis according to ICHD-2	Clinically relevant anxious/depressed and internalizing symptoms measured using cut-offs from the Child Behavior Checklist (CBCL)	Children with migraine were more likely to have clinically relevant anxious/depressed scores* (15.0% vs. 3.5%, RR=4.3, 95% CI=2.4-7.8, p<0.01) as compared to no headache group, and more likely to have clinically relevant internalizing scores* (56.8% vs. 19.1%, RR=2.7, 95% CI=2.1-3.4, p<0.01)	Children with migraine were more likely to have clinically relevant anxiety/depression (p<0.05) and internalizing scores (p<0.05) compared to controls, after controlling for age, race, gender, headache frequency, and income	9/10 domains adequate
Bektas Ö et al, 2015[78]	Cross-sectional	Ankara, Turkey	Population-based	N=5,355 (10.3% migraine, 9.8% probable migraine, 16.5% TTH, 2.9% other headache,	9-18 years (mean 13.4 ± 2.68)	N=2,708 females (50.6%); 2,647 males (49.4%)	Primary headache diagnosis according to ICHD-2	1. Clinically relevant depression measured using cut-off of Child Depression Scale from	1. Mean depression score 13.6 ± 6.80 for migraine vs. 9.3 ± 6.17 for no headache*; Migraine group more	Anxiety was associated with migraine* (OR=1.45, 95% CI=1.16-1.82, p=0.001)	9/10 domains adequate

				60.6% no headache)				Association of Turkish Child Psychiatry (validated) 2. Clinically relevant anxiety using cut-off from Turkish version of Beck Anxiety Score *Diagnoses confirmed by child psychiatrist	likely to have clinically relevant depression* (29.6% vs. 13.8%, p<0.05) 2. Mean anxiety score 17.5 ± 12.19 for migraine vs. 10.2 ± 8.88 for no headache*; Migraine group more likely to have clinically relevant anxiety* (43.5% vs. 19.8%, p=0.001)	after controlling for maternal education, obesity, low grade point average and PedMIDAS score	
Blaauw B et al, 2014[89]	Cross-sectional	Nord-Trondelag County, Norway	Population-based	N=4,872 (Recurrent headache 29.0%, migraine 2.8%)	12-17 years	Not provided	Participants read description of migraine, TTH and non-classifiable headache in accordance with ICHD criteria and	Symptom Check List (SCL-5) used to measure depression and anxiety symptoms	Not reported separately for migraine (reported as recurrent headache vs. headache free)	Migraine group aged 12-14 years had higher odds of symptoms of anxiety and depression* (OR=1.69, 95%CI=1.15-2.49, p=0.007) after adjusting for sex and	8/10 domains adequate

							classified according to validated "recognition-based" headache diagnosis approach by nurse			family condition/single parenthood; Migraine group aged 15-17 years had higher odds of symptoms of anxiety and depression* (OR=2.12, 95%CI=1.65-2.72, p<0.001) after adjusting for sex and family condition/single parenthood	
Braccili T et al, 1999[94]	Cross-sectional	Rome, Italy	Not described	N=73 with migraine	8-14 years	N=34 females (46.6%); 39 males (53.4%)	Migraine diagnosis according to ICHD-I criteria	1. Depressive symptoms measured with Child Depression Scale (CDI) 2. Anxiety symptoms measured with Anxiety Scale Questionnaire for Evolutive Age	Participants divided into 3 groups: 1. Anxiety and depression = 21.9% 2. Depression = 53.4% 3. No anxiety or depression = 24.6% NB. used "Sample Classification" to define	N/A	3/10 domains adequate

									groups, unclear if validated cut-offs; no hypothesis testing done		
Cooper P et al, 1987[95]	Case-control	Halifax, Canada	Cases recruited from a neurology clinic and controls were best friend controls from community	N=78 (39 with migraine, 39 controls)	6-16 years	N=40 females (51.2%) ; 38 males (48.7%)	Migraine diagnosis according to Prensky criteria	1. Anxiety symptoms measured using State-Trait Anxiety Inventory for Children (STAIC), the Revised Children's Manifest Anxiety Scale (RCMAS), and parent-reported child anxiety via the Revised Personality Inventory for Children (PIC-R) 2. Depression symptoms, parent-reported child depression via the Revised Personality Inventory	1. Anxiety: No significant differences between migraine vs. controls and all patients had normal range anxiety scores (STAIC trait mean 35.8 $\pm$ 7.4 for migraine vs. 33.8 $\pm$ 7.4 for controls; RCMAS mean 51.6 $\pm$ 8.6 for migraine vs. 49.2 $\pm$12.1 for controls 2. Depression: PIC-R parent-reported depression scores higher in migraine vs. controls* (t=4.74,	N/A	5/7 domains adequate

								for Children (PIC-R)	p<0.001), but scores in normal range in migraine group		
Cunningham S et al, 1987[24]	Case-control	Ottawa, Canada	Cases recruited from a neurology clinic, pain controls were suffering from chronic musculoskeletal pain and recruited from outpatient clinics, and no pain hospital controls recruited from outpatients clinics	N=60, 20 with migraine, 20 with musculoskeletal pain, and 20 no-pain hospital controls	9-17 years	N=30 females (50%); 30 males (50%)	Migraine diagnosis by neurologist using unvalidated criteria	1. Anxiety symptoms measured using State-Trait Anxiety Inventory (STAI) administered to secondary school participants, the "How I Feel Questionnaire" was used for primary school participants, and the Child Behavior Checklist (CBCL) given to parents and teachers 2. Depressive symptoms measured using the Birleson	1. Anxiety: CBCL teacher-reported mean anxiety scores higher for migraine than for other groups* (61.9 for migraine, 57.4 for pain controls and 57.2 for no pain controls, F(2,48)=4.0, p<0.05); no differences seen on STAI or "How I Feel Scores" 2. Depressive symptoms: No significant differences found between groups on	N/A	3/7 domains adequate

								Self Rating Scale and the Child Behavior Checklist (CBCL) given to parents and teachers	any of the measures (no raw data given) 3. Internalizing symptoms (combined): CBCL parent-reported internalizing mean scores higher for migraine than for no pain controls* (63.7 for migraine, 60.4 for pain controls and 53.6 for no pain controls, F(2,57)=5.4, p<0.01)		
D'Andrea G et al, 1989[25]	Case-control	Vincenza, Italy	Cases recruited from a headache clinic, controls recruited from hospital personnel (offspring of hospital personnel)	N=40 (20 with migraine, 20 controls)	7-11 years	N=25 females (62.5%); 15 males (37.5%)	Migraine diagnosis according to Ad Hoc Committee on Classificatiof Headache	Anxiety symptoms measured using a 48-item anxiety questionnaire developed by Busnelli, Faina, and Dall'Aglio	Anxiety symptoms were higher in the migraine group (52.7 ± 26) vs. controls* (31.8 ± 19.4) (p<0.01)	N/A	5/7 domains adequate

Donnelly T et al, 2017[26]	Cross-sectional	Australia	Cases and controls recruited from a twin study (Australian Twin Registry) which is a community-based registry	N=2,525 (149 with migraine, 2,376 controls)	3-18 years	N=1,290 females (51%), 1,235 males (49%)	Migraine diagnosis according to ICHD-II beta criteria	Anxious-depressed syndrome measured using the Achenbach System of Empirically Based Assessment (ASEBA) Child Behavior Checklist (CBCL) for 3-5yo, and the CBCL for 6-18 yo, where 98th %ile score was used as clinical cut-off to define clinical anxiety/depression	The odds of clinical anxious/depressed syndrome were higher among those with migraine vs. controls* (OR=6.52, 95% CI=3.15-13.5, p<0.001)	N/A	7/10 domains adequate
El-Heneedy Y et al, 2019[27]	Case-control	Tanta, Egypt	Cases recruited from headache clinic; not reported where controls were recruited from	N=60 (40 with migraine, 20 controls)	11.13 $\pm$ 2.85 (range not given)	Not described for whole sample; for migraine group: 23 females (57.5%); 17 males (42.5%)	Migraine diagnosis according to ICHD-III beta criteria	Internalizing symptoms measured using the Child Behavior Checklist (CBCL)	Higher anxious/depressed CBCL scores in migraine vs. control group* (67.18 $\pm$4.67 vs. 58.7 $\pm$4.38, t=16.985, p=0.001), and higher withdrawn/depressed CBCL scores in	N/A	5/7 domains adequate

									migraine vs. control group* (65.7 ±9.73 vs. 58.6 ±5.63, t=9.072, p=0.004)		
Ertem D et al, 2019[28]	Case-control	Istanbul, Turkey	Cases recruited from a headache clinic, and hospital controls recruited (patients without neurological disorder diagnosed with any other health condition)	N=238 (115 with migraine, 80 with TTH, 43 controls)	6-16 years	N=130 females (54.6%); 108 males (45.4%)	Primary headache diagnosis according to ICHD-III beta criteria	1. Anxiety symptoms measured using the Social Anxiety Scale for Adolescents (SAS-A) 2. Depression symptoms measured using the Children's Depression Inventory (CDI)	1. Anxiety: SAS-A scores did not differ between groups (40.2 ± 12.3 for episodic migraine, 41.6 ± 11.8 for chronic migraine, 38.8 ± 10.5 for TTH, and 40.4 ± 12.0 for controls, p=0.712) 2. Depression: CDI scores did not differ between groups (12.8 ± 7.7 for episodic migraine, 14.7 ± 8.7 for chronic migraine,	N/A	2/7 domains adequate

									12.8 ± 6.7 for TTH, and 12.5 ± 5.8 for controls)		
Fuh JL et al, 2009[29]	Cross-sectional	Taitung County, Taiwan	Recruited from community (school-based recruitment)	N=3,963 (928 with migraine or probable migraine, 1,092 with TTH, 445 with other headache, 1498 no headache)	13-15 years	N=1,923 females (48.5%); 2,040 males (51.5%)	Primary headache diagnosis according to ICHD-II criteria	Depression: Ascertained using the Adolescent Depression Inventory (ADI)	Migraine group (13.4 ±6.90 had higher ADI scores than controls (6.7 ±5.8) and than TTH (8.7 ±6.0, p<0.001)*	N/A	9/10 domains adequate
Galli F et al, 2007[30]	Case-control	Rome, Italy	Cases recruited from headache clinic, recurrent abdominal pain controls recruited from gastroenterology department, and healthy controls recruited from schools	N=210 (42 with migraine, 28 with TTH, 70 with recurrent abdominal pain, and 70 controls)	4-18 years	N=111 females (52.9%), 99 males (47.1%)	Primary headache diagnosis according to ICHD-II criteria	Child Behavior Checklist (CBCL)	Mean internalizing score was higher for migraine group (12.52 ± 6.89) vs. for controls (8.27 ± 5.39), p<0.05*; mean anxiety/depression score was not different for migraine group (5.02 ± 3.47) vs. for control group (4.58 ± 3.33)	N/A	6/7 domains adequate
Gibson J 2004[31]	Case-control (dissertation)	Columbus, USA	Cases recruited from headache	N=120 (68 with migraine, 40 controls)	6-12 years	N= 51 females (47%); 57	Primary headache diagnosis according	1. Anxiety: measured using the Revised	1. Anxiety: RCMAS anxiety scores	N/A	4/7 domains

			clinic, controls recruited from pediatric clinic or community			males (53%)	to ICHD criteria	Children's Manifest Anxiety Scale (RCMAS), and the Child Symptom Inventory-4 (CSI-4) 2. Depression: measured using the Children's Depression Inventory, and the Child Symptom Inventory-4 (CSI-4) NB. Those with screening cut-offs or with past psychiatric diagnosis had a follow-up semi-structured interview with parents using DSM-IV diagnostic criteria (Barkley & Murphy, 1998 method)	were higher for migraine* (48.23 ± 13.59 vs. 38.78 ± 10.52, t(102) =-3.75, p<0.001); semi-structured interviews revealed migraine group more likely to have generalized anxiety disorder* (OR=6.7, 95% CI not given, chi square = 4.10, p<0.05) 2. Depression: CSI-4 scores in normal range for migraine, TTH and controls; Higher CSI-4 depression scores for		adequate

									migraine vs. controls* (53.26 ± 6.95 for migraine vs. 50.85 ± 2.82 for controls, t(106)=-2.09, p<0.05) and higher dysthymia scores for migraine vs. controls* (57.32 ± 9.75 for migraine vs. 53.10 ± 5.14 for controls, (t(106)=-2.54, p<0.05); CDI scores in normal range for migraine, mean CDI scores higher for migraine* (43.4 ± 7.74 vs. 40.39 ± 5.7, t(91)=-2.02,		

									p<0.05); no data reported on depressive disorders from semi-structured interviews		
Gladstein J et al, 1996[32]	Cross-sectional	Baltimore, United States	Cases of chronic daily headache recruited from headache clinic	N=37 (5 with chronic/transformed migraine, 13 with new daily persistent headache, 15 with other/comorbid pattern)	7-17 years	N=29 females (78%); 8 males (22%)	Primary headache diagnosis as per Silberstein et al criteria	Child Behavior Checklist (CBCL)	Internalizing scale scores on CBCL were no different across the chronic daily headache groups (migraine = 58.2 ± 7.3; new daily persistent headache = 56.9 ± 8.6; other/comorbid = 54.7 ± 10.2)	N/A	4/10 domains adequate
Gozubatik-Celik R et al, 2021[33]	Case-control	Istanbul, Turkey	Recruitment from neurology clinic	N=92 (N=29 with migraine, N=32 with TTH, N=31 controls)	8-18 years	N=55 females (59.8%); 37 males (40.2%)	Primary headache diagnosis according to ICHD III criteria	1. Anxiety symptoms measured using the Screen for Child Anxiety-Related Disorders (SCARED) 2. Depression symptoms	1. The mean SCARED score was higher in the migraine vs. control group* (32.0±3.1 vs. 8.0±1.3, p=0.001) 2. The mean CDI score	N/A	6/7 domains adequate

								measured using the Children's Depression Inventory (CDI)	was higher in the migraine vs. control group* (22.0±2.7 vs. 10.0±4.0, p=0.002)		
Guidetti V et al, 1987[35]	Case-control	Rome, Italy	Cases recruited from headache clinic, controls recruited from community (schools)	N=86 (43 with migraine, 43 controls)	8-14 years	Not reported	Migraine diagnosis according to Ad Hoc Committee criteria	Personality Inventory for Children (PIC) administered to mothers	Migraine group had significantly higher scores on the depression subscale* (p<0.01) and the anxiety subscale* (p<0.01)	N/A	3/7 domains adequate
Guidetti V et al, 1998[36]	Cohort	Rome, Italy	Cases randomly selected from a clinical cohort in a headache clinic	N=100 (64 with migraine, 36 with TTH)	4-18 years	N=60 females (60%); 40 males (40%)	Primary headache diagnosis according to ICHD criteria	Psychologists performed structured clinical interviews using DSM-II-R criteria; anxiety was also measured using the Anxiety symptoms measured using State-Trait Anxiety Inventory for Children (STAIC), and parent-reported	1. Anxiety disorders: For baseline (1998), 15.6% of migraine vs. 2.8% of TTH group; anxiety disorders were significantly associated with migraine* (chi square=3.88, df=1, p<0.05); at follow-up	N/A	5/8 domains adequate

								anxiety and depression were measured using the Revised Personality Inventory for Children (PIC-R)	(1996), 81.8% of migraine vs. 10% of TTH had anxiety disorders 2. Depression: Did not report group results for baseline (1988); At 8-year follow-up (1996) 54.5% with migraine vs. 9.7% with TTH had depression 3. Anxiety and depression: At 8-year follow-up 45.5% of migraine vs. 3.2% of TTH had both anxiety and depression		
Guidetti V et al, 2013[37]	Case-control (abstract)	Rome, Italy	Unclear where cases and controls were recruited from	N=200 (60 with migraine without aura, 10 with migraine with aura, 15 with TTH, 10 with	8-14 years	N=101 females (50.5%), 99 males (49.5%)	Unclear how primary headache diagnoses were ascertained	Anxiety and depression measured with the Self Administrated Psychiatric Scales for Children and Adolescents	No differences in anxiety or depression subscales between groups, except for depressed mood scale, for which	N/A	2/7 domains adequate

				chronic daily headache and 5 with benign paroxysmal vertigo, plus 100 controls)				(SAFA) Anxiety (A) and Depression (D) scales, respectively	higher scores were observed in the migraine with aura group* (p=0.024)		
Guler G et al, 2017[38]	Cross-sectional	Turkey	Unclear	N=140 (98 with migraine, 42 with TTH)	12-18 years	N=91 females (65.0%); 59 males (42.1%)	Primary headache diagnosis according to ICHD-3 beta criteria	Psychiatric disorders ascertained using DSM-IV criteria, depression and anxiety ascertained using "Depression Scale" and the "State-Trait Anxiety Scale for Children", respectively	No difference between migraine and TTH in depression and anxiety prevalence, but rates high: 1. Depression : 27.6% of migraine group vs. 21.4% of TTH group had depression (p=0.57) 2. Anxiety: 30.6% of migraine group vs. 38.1% of TTH group had anxiety disorders (p=0.50)	N/A	3/10 domains adequate
Gunalan S et al, 2012[39]	Case-control (abstract)	Australia	Case-control twin study (community sample)	N=455 (did not report number of cases vs. controls)	3-18 years	Not reported	Not reported	ASEBA Behavioral Checklists	Migraine twins had higher anxious depression scores than control twins*	N/A	4/7 domains adequate

									NB. Scores reported to be significantly higher in migraine twins but no raw data given		
Hammond N et al, 2019[40]	Cohort	Canada	Population-based	N=2,313 (3.1% with migraine)	14-15 years	N=1,182 females (51.1%); 1,131 males (48.9%)	Migraine ascertained by person most knowledgeable reported health professional diagnosed migraine in their adolescent	Depression and separation anxiety symptoms measured using Ontario Child Health Study scale	Mean depressive/anxiety symptoms score higher for those with migraine (3.53 $\pm$ 2.78 in migraine group vs. 2.65 $\pm$ 1.99 in other headache group, p=0.016)	N/A	6/8 domains adequate
Heinrich M et al, 2007[41]	Cross-sectional	Southern Lower Saxony, Germany	Population-based	N=5,474 (411 with migraine, 5,063 without migraine)	7-14 years	N=2,704 females (49.4%); 2,770 males (50.6%)	Primary headache diagnosis according to ICHD criteria	Child Behavior Checklist (CBCL) internalizing scores	Headache group had higher mean internalizing symptoms that non-headache group* (1.47 for headache vs. 0.95, F=138.03, df=1,5395, p<0.001); migraine group had higher mean internalizing symptoms than	N/A	6/10 domains adequate

									TTH and unclassifiable headache* (1.87 for migraine, 1.57 for unclassifiable headache, 1.16 for TTH, F=28.45, df=2,2867, p<0.001)		
Hommer R et al, 2021[42]	Cross-sectional	USA	Population-based	N=10,123 (N=162 (1.6%) with migraine with aura, N=1,114 (11.0%) with migraine without aura, N=1,448 (14.3%) with non-migraine headache)	13-18 years	N=5,170 females (51.1%); 4,953 males (48.9%)	Primary headache diagnosis according to ICHD III criteria	Psychiatric diagnoses made according to a modified World Health Organization Composite Diagnostic Interview (CIDI)	1. Major depressive disorder present in 27.0%±4.9 % of migraine with aura, 17.2±1.4 of migraine without aura, and 8.8%±0.6 % of controls 2. Anxiety disorders present in 47.6%±6.1 % of migraine with aura, 29.9%±1.5 % of migraine without aura, and	N/A	8/10 domains adequate

									17.0%±0.6 % of controls *Modeling associations are reported but no comparison between migraine vs. controls, only all headache vs. controls or migraine with vs. without aura		
Huss et al, 2008[43]	Case-control	Kentucky, United States	Cases recruited from neurology clinic or community; controls recruited from hospital or community	N=53 (21 with migraine, 32 controls)	7-12 years	N= 26 females (49.1%); 27 males (50.9%)	Migraine according to ICHD criteria	Anxiety measured using the Multidimensional Anxiety Scale for Children (MASC)	Mean MASC scores were higher in the migraine group as compared to the control group* (55.9 vs. 50.22, $F(1,51)=6.30$, $p<0.05$, $d=0.71$)	N/A	4/7 domains adequate

Just U et al, 2003[44]	Case-control	Mannheim and Heidelberg, Germany	Cases recruited from community or neurology clinic; controls recruited from community	N=211 (70 migraine without aura, 33 migraine with aura, 25 TTH, 83 controls)	6-18 years	N=99 females (46.9%); 112 males (53.1%)	Primary headache diagnosis according to ICHD criteria	1. Anxiety: measured using the Anxiety Questionnaire for Pupils (AFS) and the Child Behavior Checklist (CBCL) 2. Depression: measured using the Depression Inventory for Children and Adolescents (DIK) and the Child Behavior Checklist (CBCL)	1. Anxiety: no significant differences between groups on the AFS subscales; CBCL anxiety/depression scores higher in migraine with aura* (p=0.002) and migraine without aura *(p<0.001) than controls; CBCL internalizing scores higher in migraine with aura* (p<0.001) and migraine without aura* (p<0.001) than controls 2. Depression: DIK scores	N/A	5/7 domains adequate

									significantly different between groups* (F=3.41, df=3, p=0.019) but not reported separately for migraine; CBCL scores as per above		
Kaczynski K et al, 2013[46]	Cross-sectional	Boston, USA	Cases recruited from headache clinic	N=262 (109 with migraine, 153 with TTH)	11-17 years	N=179 females (68.5%); 83 males (31.7%)	Primary headache diagnosis according to ICHD-II criteria	1. Anxiety: measured using the Revised Children's Manifest Anxiety Scale (RCMAS) 2. Depression: measured using the	1. Anxiety: Migraine group mean RCMAS score (11.23 ±8.12) did not differ from TTH group mean score	See Table 2 in manuscript	6/10 domains adequate

								Children's Depression Inventory (CDI)	(12.39 ±8.58) 2. Migraine group had lower mean CDI score (8.52 ±7.26) as compared to TTH group (10.32 ±7.93) (t(289)= -2.57, p<0.05, d=0.30)		
Kafle M et al, 2022[47]	Cross-sectional	USA	Cases of migraine who were hospitalized in different centers for migraine manage-ment identified in an administra-tive health database (Pediatric Health Information System – PHIS)	N=21,436	6-18 years	N=15,419 females (72%), 6,017 males 28%)	Migraine diagnosis according to International Classifica-tion of Diseases, 9th and 10th editions	Psychiatric diagnoses ascertained using the International Classification of Diseases, 9th and 10th editions	1. Anxiety disorder: 11.2 % (2,415) of the migraine cases had an anxiety disorder 2. Depressive disorder: 6.7% (1,433) of the migraine cases had a depressive disorder	N/A	8/10 domains adequate
Kandemir et al, 2018[48]	Case-control	Ankara, Turkey	Case recruited from	N=100 (50 with	8-18 years	N=73 females (73.0%);	Migraine diagnosis according	1. Anxiety: Measured using the	1. Anxiety: Migraine group had	N/A	6/7 domains

			neurology clinic; controls were hospital controls recruited from pediatric clinics	migraine, 50 controls)		27 males (27.0%)	to ICHD-III beta criteria	Screen for Child Anxiety Related Emotional Disorders (SCARED) and the Kiddie Schedule for Affective Disorders and Schizophrenia for School-Age Children – Present and Lifetime Version (Kiddie SADS) 2. Depression: Measured using the Children's Depression Inventory (CDI), and the Kiddie SADS	higher prevalence of Kiddie SADS anxiety disorders vs. controls* (44% % vs. 18%, χ^2=6.857, p=0.009); no difference between the groups in the mean SCARED scores (28.84 ±13.49 for migraine vs. 28.08 ±14.67 for controls, t=0.270, p=0.78) 2. Depression: Migraine group had higher prevalence of Kiddie SADS depressive disorders vs. controls* (18% vs.		adequate

									4%, p=0.025); no difference between the groups in the mean CDI scores (13.02 ±9.12 for migraine vs. 11.68 ±7.14 for controls, t=0.817, p=0.41)		
Kashikar-Zuck S et al, 2013[49]	Cross-sectional	USA	Cases recruited from headache clinic; juvenile fibromyalgia group recruited from rheumatology clinics	N=304 (153 with chronic migraine; 151 with juvenile fibromyalgia)	10-18 years	N=261 females 85.9%); 43 males (14.1%)	Chronic migraine diagnosis according to ICHD-II criteria	1. Anxiety: measured using the Adolescent Symptom Inventory-4 – Generalized Anxiety Subscale (ASI-4) 2. Depression: measured using Children's Depression Inventory (CDI)	N/A	1. Anxiety: Mean ASI-4 scores lower in the chronic migraine group vs. juvenile fibromyalgia group, controlling for age and sex (1.03 ±0.15 vs. 2.46 ±0.15, F=45.18	6/10 domains adequate

										, p<0.001) 2. Depression: Mean CDI scores lower in the chronic migraine group vs. juvenile fibromyalgia group, controlling for age and sex (7.98 ±0.54 vs. 12.92 ±0.55, F=40.36 , p<0.001)	
Kroner J et al, 2013[50]	Cohort (abstract)	Cincinnati, USA	Recruited from headache clinic	N=115 with migraine	11-18 years	Not reported	Migraine diagnosis according to ICHD-II criteria	Internalizing symptoms measured using the Behavior Assessment Scale for Children (BASC-II)	Baseline: BASC-II internalizing symptoms score elevated at baseline* (M=60.86, at-risk range, p<0.0001)	N/A	4/8 domains adequate

Kröner-Herwig B et al, 2012[51]	Cross-sectional	Southern Lower Saxony, Germany	Population-based	N=3,399 (N=314 with migraine, N=1,010 with TTH; N=808 with unclassified headache and 1,267 with no headache)	9-15 years	N=1,725 females (50.7%); 1,674 males (49.2%)	Primary headache diagnosis according to ICHD-II criteria	Internalizing symptoms were measured with the Youth Self-Report (YSR)	Mean YSR internalizing score was significantly higher comparing the headache groups and the controls (migraine group 1.93 ±0.60, no headache group 1.50 ±0.45, F=89.30, p<0.01 across)	The odds of migraine were significantly higher with higher YSR internalizing scores, after controlling for age and sex (OR=4.05, 95% CI=3.13-5.23, p<0.01)	8/10 domains adequate
Lateef T et al, 2019[52]	Cross-sectional	USA	Population-based	N=10,123 (104 with migraine with aura, 578 with migraine without aura, 586 with other headache, 8,855 with no headache)	13-18 years	N=5,170 females (51.1%); 4,953 males (48.9%)	Primary headache diagnosis according to ICHD-III criteria	Modified World Health Organization Composite International Diagnostic Interview (CIDI version 3.0) administered by lay interviewers	Migraine was more prevalent in youth who had a diagnosis of a mood or anxiety disorder in the past 12 months: Wald chi square for mood disorder=9.1, df=3, p<0.001*; Wald chi square for anxiety disorder=16.1, df=3, p<0.001* (see Table 1 in publication for	N/A	6/10 domains adequate

									raw data details)		
Laurell K et al, 2005[53]	Cross-sectional	Uppsala, Sweden	Population-based	N=130 (42 with migraine, 37 with TTH, 49 controls)	7-17 years	N=70 females (53.8%); 60 males (46.2%)	Primary headache diagnosis according to ICHD criteria	The Child Behavior Checklist (CBCL) was used to measure internalizing symptoms	Migraine group had higher mean CBCL internalizing scores than TTH and controls* (4.2 ±4.0 vs. 2.2 ±2.2 vs. 3.3 ±2.9, F(4,115)=2.39, p=0.05); CBCL anxious-depressed subscale scores did not differ between groups (raw data not given)	N/A	6/10 domains adequate
Lucarelli E et al, 2009[54]	Cross-sectional	Bari, Italy	Cases recruited from neurology clinic	N=52 (29 with migraine, 23 with TTH)	5-16 years	N=31 females (60%); 21 males (40%)	Primary headache diagnosis according to ICHD-II criteria	1. Anxiety: measured using the Screen for Child Anxiety Related Disorders (SCARED), the Youth Self Report, the Child Behavior Checklist (CBCL),	1. Anxiety: 14% of migraine group had anxiety disorders, 24% of migraine group had "anxious-depressive" temperament; 43.5% of TTH group had anxiety	N/A	3/10 domains adequate

								and the Kiddie Schedule for Affective Disorders and Schizophrenia Present and Lifetime Version (Kiddie SADS) 2. Depressive symptoms: measured using the Children's Depression Inventory (CDI), the Youth Self Report, the Child Behavior Checklist (CBCL), and the Kiddie SADS	disorders, and 26% of TTH had "anxious-depressive" temperament 2. Depression: No patients in migraine group had depressive disorders, 24% of migraine group had "anxious-depressive" temperament, 8.7% of TTH group had depressive disorders, and 26% of TTH had "anxious-depressive" temperament NB. No hypothesis testing done		

									for group comparisons		
Machnes-Maayan D et al, 2014[55]	Case-control	Petah Tikva, Israel	Cases recruited from a headache clinic or gastroenterology clinic, hospital controls recruited from general outpatient clinics (recent discharges from hospital for brief acute illness)	N=116 (N=32 migraine, 32 with TTH, 19 with recurrent abdominal pain, and 33 controls)	5-17 years	N=72 females, 44 males	Primary headache diagnosis according to ICHD-II criteria	Development and Well-Being Assessment (DAWBA) semi-structed interview to diagnose psychiatric disorders, administered by trained non-clinical interviewers, based on DSM-IV	1. Depressive disorders on DAWBA: 4 (12.5%) in the migraine group vs. 0 (0%) in the control group vs. 8 (25%) in the TTH group 2. Anxiety disorders on DAWBA: 18 (56.3%) in the migraine group vs. 3 (9.1%) in the control group vs. 22 (68.8%) in the TTH group NB. Overall there were group differences but too small to analyze for migraine vs. controls specifically (analyzed for	N/A	4/7 domains adequate

									all pain groups vs. controls) NB2. Specific DAWBA diagnosis rates in manuscript Table 2		
Maleki N, 2016[57]	Cross-sectional (abstract)	Boston, USA	Cases recruited from hospital clinic (not specified what type of clinic)	N=1,425 with migraine	10-15 years	N=1,425 females (100%); 0 males (0%)	Not reported	Not reported in detail; chart reviews were carried out to identify prevalence of other diseases in this sample of females with migraine	Anxiety occurred in 13% of this sample; depression prevalence is not reported but is stated to be uncommon in this sample	N/A	0/10 domains adequate
Mar S et al, 2009[58]	Case-control (abstract)	St Louis, MO, USA	Unclear	N=17 (10 with chronic migraine, 7 controls)	12-17 years	Not reported	Chronic migraine diagnosis according to ICHD-II criteria	Depression ascertained using Children's Depression Inventory (CDI)	CDI scores were higher in the chronic migraine group compared to the controls* (54 vs. 47; no hypothesis testing reported)	N/A	3/7 domains adequate
Mar S et al, 2010[59]	Case-control (abstract)	Not reported	Not reported	N=40 (23 with chronic migraine, 17 controls)	12-17 years	Not reported	Not reported	Not reported, labeled as "neuropsychological testing"	Migraine group had higher depression scores on neuropsychological testing* ($p<0.05$)	N/A	2/7 domains adequate
Marates J et al, 1982[60]	Case-control	London, England	Cases recruited from headache	N=50 (36 with migraine, 14 controls)	5-15 years	Not reported	Migraine ascertained with Research	Standardized psychiatric interview as developed by	1. Depression: 4 (11%) with migraine vs.	N/A	4/7 domains

			clinic, controls recruited from dental clinic				Group on Migraine and Headache of the World Federation of Neurology definition	Rutter and Graham	0 (0%) controls had depression 2. Anxiety: 6 (13.3%) with migraine vs. 1 (3.7%) controls had anxiety NB. No hypothesis testing done		adequate
Mazzone L et al, 2006[61]	Case-control	Catania, Italy	Cases recruited from headache clinic; controls recruited from pediatric clinic data (well child visits)	N=150 (67 with migraine, 47 with TTH, 36 controls)	6-16 years	N=69 females (54%); 81 males (46%)	Primary headache diagnosis according to ICHD criteria	1. Depression: The Child Behavior Checklist was used to measure internalizing symptoms; the Children's Depression Inventory (CDI) was used to measure depressive symptoms 2. The Child Behavior Checklist was used to measure	1. Internalizing: CBCL internalizing scores higher in migraine and TTH group compared to controls* (61.59 ±9.87 vs. 66.03 ±10.79 vs. 51.02 ±7.21, F=25.67, p<0.0001); high proportion of migraine group with pathological CBCL internalizin	N/A	5/7 domains adequate

								internalizing symptoms; the Multidimensional Anxiety Scale for Children (MASC) was used to measure anxiety symptoms	g scores than controls* (33% vs. 0%, p<0.01) 2. Depression: CDI scores higher in migraine and TTH as compared to controls* (9.57 ±6.47 vs. 11.0 ±6.72 vs. 7.2 ±1.14, F=4.52, p<0.05); no difference in proportion with pathological CDI scores between migraine vs. TTH vs. control group (10% vs. 13% vs. 0%, NS)		

									3. Anxiety: MASC scores higher in migraine and TTH group as compared to controls* (41.77 ±13.9 vs. 46.4 ±18.49 vs. 36 ±6.06, F=5.45, p<0.001)		
McGinley J et al, 2019[62]	Cohort	USA	Population-based	N=5,608	Grade 7-12 students followed through 4 survey waves over 14 years	Not reported	Migraine as per parent report at Wave 1 (baseline in adolescents)	Centers for Epidemiologic Studies Depression (CES-D) measure at each wave	The main effect growth curve (multilevel) model demonstrated that depression scores were higher in the migraine vs. control group (p<0.0001)*	N/A	4/8 domains adequate
Nardello R et al, 2014[63]	Case-control (abstract)	Palermo, Italy	Cases recruited from hospital and controls recruited from	N=18 (6 with migraine, 12 controls)	6-9 years	N=15 (83.3%) females, 3 (16.7%) males	Migraine diagnosis according to ICHD criteria	Kiddie – Schedule for Affective Disorders and Schizophrenia for School Aged Children	None of the children with migraine nor the controls met criteria for any psychiatric diagnoses	N/A	5/7 domains adequate

			community					(Kiddie SADS)			
Nesterovskiy Y et al, 2015[65]	Cross-sectional (abstract)	Moscow, Russia	Not reported	N=187 with migraine	7-16 years	Not reported	Migraine diagnosis according to ICHD-II criteria	Anxiety disorders diagnosed according to ICD-10 diagnostic criteria, and severity of anxiety symptoms ascertained with the Spence Children's Anxiety Scale	46% (N=86) of migraine patients had "manifestations" of anxiety disorders, with 49% (N=56) having mild, 32% (N=37) having moderate, and 19% (N=16) having severe manifestations; 12% had generalized anxiety disorder, 33% had social anxiety disorder, and 55% had specific phobias	N/A	2/10 domains adequate
Nita S et al, 2020[65]	Case-control	Bucharest, Romania	Unclear where cases and controls were recruited from	N=34 (18 with migraine, 16 controls with other headache disorders)	5-17 years	Not reported	Migraine diagnosis according to ICHD-III criteria	Anxiety symptoms were measured using the Achenbach System of Empirically Based Assessment (ASEBA) and clinical cut-off for anxiety	1. The mean ASEBA anxiety scale score was no different between groups (p=0.083; no raw scores given) 2. There was no	N/A	4/7 domains adequate

								set at percentile ≥93	difference in clinical levels of anxiety comparing the migraine vs. other headache group (80% vs. 75%, p=0.739) 3. The odds of anxiety did not differ between migraine vs. other headache group (OR=0.75 ± 0.866, 95% CI=0.137-4.095, p=0.740)		
Onofri A et al, 2019[66]	Cross-sectional (abstract)	L'Aquila, Italy	Migraine cases recruited from neurology hospital clinic	N=106 (N=76 with migraine without aura, N=30 with migraine with aura)	4-17 years	N=62 females (58.5%), 44 males (41.5%)	Migraine diagnosis according to ICHD-III criteria	Child Behavior Checklist (CBCL)	No difference in the prevalence of internalizing disorders for migraine without aura vs. migraine with aura (56% of migraine without aura	N/A	2/10 domains adequate

									vs. 66% of migraine with aura group; total 41.5% of sample had internalizing disorders; raw CBCL scores not available)		
Oztop D et al, 2016[68]	Case-control	Turkey (details not specific)	Migraine cases recruited from neurology clinic; unclear how cases were recruited	N=70 (N=35 with migraine, N=35 controls)	9-16 years	N=52 (74.3%) females, 18 (25.7%)males	Migraine diagnosis according to ICHD criteria	1. Depression: Ascertained using Kiddie – Schedule for Affective Disorders and Schizophrenia for School Aged Children (Kiddie-SADS) and Kovacs Children Depression Inventory (Kovacs-CDI) 2. Anxiety: Ascertained using Kiddie-SADS, State-	1. Depression: major depression in 2 (5.7%) of migraine cases, adjustment disorder in 3 (8.6%) of migraine cases; mean Kovacs-CDI scores were higher in the migraine group* (11 vs. 7, Z=2.426, p=0.015) 2. Anxiety: generalized anxiety in 1 (2.9%) of migraine cases,	N/A	4/7 domains adequate

								Trait Anxiety Inventory for Children (STAIC) for those <12yo, and Spielberg State-Trait Anxiety Inventory for >12yo	separation anxiety in 4 (11.4%) of migraine cases; no significant differences were found between migraine and control groups on STAIC (Table 1 in manuscript)		
Pakalnis A et al, 2005[69]	Case-control	Columbus, USA	Cases recruited from headache clinic, controls recruited from pediatric clinics during routine physicals	N=80 (47 with episodic migraine, 33 controls)	6-17 years	N=21 females with migraine (44.6% of migraine sample), 26 males with migraine (55.3% of migraine sample)	Migraine diagnosis according to ICHD criteria	Child Symptom Inventory (CSI-4) or Adolescent Symptom Inventory (ASI-4); those with high scores had semi-structured interview with psychologist using Barkley & Murphy 1988 interview	1. Depression association: 1 (2.1%) of migraine group vs. 0 (%) of controls had depression; no difference between CSI-4 and ASI-4 depression scores (55.24 $\pm$ 8.32 for migraine vs. 55.36 $\pm$ 5.3 for controls)	N/A	4/7 domains adequate

									2. Anxiety association: 7 (14.9%) of migraine group vs. 1 (3.0%) of controls had anxiety; CSI-4 and ASI-4 generalized anxiety disorder scores were higher in migraine than controls* (59.24 ± 9.44 in migraine vs. 54.36 ± 6.64 in controls) t(62)=-4.87, p<0.05), though all migraine scores were within normal range		
Pakalnis A et al, 2009[70]	Case-control	Columbus, USA	Cases recruited from headache clinic; controls recruited	N=48 (N=15 with episodic migraine, N=15 with chronic migraine,	13-17 years	N=25 females (52.0%); N=23 (48.0%)	Migraine diagnosis according to ICHD-II criteria	1. Depression: measured using the Child Depression	1. Depression: depression T scores were higher among the	N/A	4/7 domains adequate

			from pediatric clinics	N=18 controls)				Inventory (CDI), and the Adolescent Symptom Inventory-4 (ASI-4) 2. Anxiety: measured using the Adolescent Symptom Inventory-4 (ASI-4)	migraine group as compared to the controls on the CDI* (mean=50.9 in migraine vs. 41.9 in control group, p<0.01), and on the ASI-4* (mean=62.4 in migraine vs. 52.6 in control group, p<0.05); dysthymia T scores on the CDI were also higher in the migraine group* (64.8 in migraine vs. 57.2 in control group, p<0.05); chronic migraine group had higher		

									dysthymia T scores than episodic migraine group* (69.4 for chronic vs. 60.5 for episodic migraine group, p<0.05) 2. Anxiety: generalized anxiety T scores on the ASI-4 were higher in the migraine group* (62.4 vs. 51.8, p<0.01)		
Pavone P et al, 2012[71]	Case-control	Catania, Italy	Cases recruited from pediatric clinics, controls recruited from hospital	N=560 (N=280 with headache – N=56 with migraine and N=224 with TTH; N=280 controls)	4-14 years	N=210 (37.5%) females, N=350 (62.5%) males	Migraine diagnosis according to ICHD-II criteria	1. Depression: ascertained using Clinical Diagnostic Interview, Child Behavior Checklist (CBCL) 2. Anxiety: Ascertain	1. Depression: anxiety-depression was more frequent in migraine group than in TTH group* (44.6 vs. 27.7%) p=0.014) 2. Anxiety: anxiety-	N/A	6/7 domains adequate

								ed using Clinical Diagnostic Interview, CBCL, and Children's Yale-Brown Obsessive-Compulsive Scale (CY-BOCS)	depression was more frequent in migraine group than in TTH group* (44.6 vs. 27.7%) p=0.014); OCD was more frequent in migraine group than in TTH group* (8.9 vs. 1.3%, p=0.002) *NB. Results not compared for migraine vs. controls		
Rabner J et al, 2018[72]	Cross-sectional	Boston, USA	Recruited from headache clinic	N=527 (52.7% with migraine, 29.8% with TTH, 17.5% with new daily persistent headache)	7-17 years	N=344 (65.3%) females; 183 (34.7%) males	Primary headache diagnosis according to ICHD-II criteria	1. Depression: Ascertained using the Children's Depression Inventory (CDI) 3. Anxiety: Ascertained using	1. Depression: Mean CDI T score 48.03 ± 9.75 for migraine group, 51.7 ± 12.86 for TTH group and 52.63 ± 12.50 for NDPH group	N/A	6/10 domains adequate

								the Revised Children's Manifest Anxiety Scale-2nd Edition (RCMAS)	(p<0.001 for group comparisons); depression was lower in migraine as compared to TTH and NDPH groups* 3. Anxiety: Mean RCMAS T score 44.91 ± 9.52 for migraine group, 47.89 ± 11.63 for TTH group and 47.98 ± 11.11 for NDPH group (p=0.05 for group comparisons); anxiety was lower in migraine as compared to TTH and NDPH groups*		

Reale L et al, 2011[73]	Case-control	Catania, Italy	Cases recruited from neurology clinic, controls recruited from database of healthy children visiting pediatric clinics	N=60 (N=20 with migraine, N=21 with benign paroxysmal vertigo, N=19 controls)	4-15 years	N=34 females (56.7%); 26 males (43.3%)	Primary headache diagnosis according to ICHD-II criteria	1. Depression: measured using the Child Behavior Checklist (CBCL), and the Children's Depression Inventory (CDI) 2. Anxiety: measured using the Child Behavior Checklist (CBCL), and the Multidimensional Anxiety Scale for Children (MASC)	1. Depression: migraine group had higher mean CBCL internalizing score than control group* (66.47 ±6.33 vs. 58.27 ±7.94 ($p<0.01$); migraine group had higher mean CDI score than control group* (13.74 ±7.85 vs. 7.0 ±4.96, $p<0.001$); a larger proportion of the migraine group had pathological CBCL internalizing scores as compared to controls* (60% vs.	N/A	5/7 domains adequate

									21%, p<0.05) 2. Anxiety: migraine group had higher mean MASC score than control group* (60.05 ±7.28 vs. 46.57 ±6.74, p<0.001); a larger proportion of the migraine group had pathological MASC scores than control group* (65% vs. 0%, p<0.001)		
Rousseau-Salvador C et al, 2013[74]	Cross-sectional	Paris, France	Cases recruited from a headache clinic	N=368 (N=88 with migraine, N=32 with TTH, N=248 with mixed migraine and TTH)	8-17 years	N=201 females (54.6%); 167 males (45.4%)	Primary headache diagnosis according to ICHD-II criteria	1. Depression: measured using the Multiscore Depression Inventory for	1. Depression: the mean MDI-C score for the migraine group was 49.4 ±8.5 vs. 50 ±10 for normative	N/A	7/10 domains adequate

								Children (MDI-C) 2. Anxiety: measured using the Revised Children's Manifest Anxiety Scale (RCMAS)	data (no hypothesis test on this comparison); the migraine group did not differ from the general population in clinically relevant depression levels (3.4% vs. 5%) 2. Anxiety: the mean RCMAS score for the migraine group was 49.4 $\pm$9.6 vs. 50 $\pm$10 for normative data (no hypothesis test on this comparison); the migraine group did not differ from the general population		

									in clinically relevant anxiety levels (9.4% vs. 5%)		
Rousseau-Salvador C et al, 2014[75]	Cross-sectional (same population as Rousseau-Salvador et al, 2013, analyzed differently)	Paris, France	Cases recruited from a headache clinic	N=368 (N=297 with episodic headache, N=15 with chronic migraine, and N=56 with chronic TTH)	8-17 years	N=201 females (54.6%); 167 males (45.4%)	Primary headache diagnosis according to ICHD-II criteria	1. Depression: measured using the Multiscore Depression Inventory for Children (MDI-C) 2. Anxiety: measured using the Revised Children's Manifest Anxiety Scale (RCMAS)	1. Depression: the chronic migraine group had higher mean MDI-C scores than the chronic TTH group* (59.5 ±7.0 vs. 51.4 ±8.4, t(69)=3.39, p<0.001) 2. Anxiety: the chronic migraine group had higher mean RCMAS scores than the chronic TTH group* (57.7 ±11.9 vs. 50.8 ±10.1,	N/A	5/10 domains adequate

									t(69)=2.25, p<0.05)		
Salerno M et al, 2017[76]	Case-control	Palermo, Italy	Not described	N=350 (N=119 with migraine without aura; N=231 controls)	Unclear (mean age listed as ±7.59 ±1.78 – no range given)	N=167 females (47.7%); 183 males (52.3%)	Migraine without aura diagnosis according to ICHD-III criteria	Separation anxiety measured using the separation anxiety subscale of the Screen for Child Anxiety Related Emotional Disorders (SCARED)	Social anxiety subscale scores of the SCARED were higher in the migraine group vs. the control group* (6.83 ±0.97 for migraine vs. 4.72 ±0.32 for control group, p<0.001)	N/A	5/7 domains adequate
Salvadori F et al, 2007[77]	Case-control	Pisa, Italy	Cases recruited from neurology clinic; controls recruited from community (local schools)	N=60 (N=30 with migraine; N=30 controls)	7-16 years	N=48 females (80.0%); 12 males (20.0%)	Migraine diagnosis according to ICHD-III criteria	Mother completed the Child Behavior Checklist (CBCL) for three time periods: the present, when the child was aged 0-3 years, and when the child was aged 4-6 years	The migraine group had significantly higher CBCL internalizing scores than the control group for all time periods* (0-3 years: 45.8 ±10.1 vs. 41.3 ±6.2, p<0.05; 4-6 years: 56.1 ±8.6 vs. 41.8 ±7.2, p<0.001; present: 55.8 ±11.0 vs. 44.1 ±9.0, p<0.001); the migraine group also had significantly CBCL anxious/depressed subscale	N/A	7/7 domains adequate

									scores for all periods* (0-3 years: 53.9 ±6.4 vs. 50.5 ±2.4, p<0.01; 4-6 years: 56.5 ±6.3 vs. 50.5 ±1.7, p<0.001; present: 56.2 ±7.1 vs. 51.2 ±2.8, p<0.01)		
Smith M et al, 2003[79]	Case-control	Seattle, USA	Cases recruited from headache clinic; controls recruited from community (school)	N=308 (N=179 with migraine; N=97 with chronic fatigue, and N=32 controls)	11-18 years	N=193 females (62.7%); 115 males (37.3%)	Not reported	1. Anxiety: measured using the Trait form of the Spielberger State-Trait Anxiety Inventory (STAI) Form X2 2. Depression: Measured using the Children's Depression Inventory (CDI)	1. Anxiety: Mean STAI scores were higher in the migraine group vs. control group* (44.9 ±7.2 vs. 39.1 ±9.3, overall ANOVA F=7.766, p<0.001) 2. Depression: Mean CDI scores did not differ between the migraine vs. control group (7.7 ±7.1 vs.	N/A	5/7 domains adequate

									6.6 ±6.8, overall ANOVA F=3.206, p<0.05)		
Tereshchenko et al, 2017[80]	Case-control (abstract)	Krasnoyarsk, Russia	Cases recruited from tertiary medical center, unclear where controls were recruited	N=404 (N=89 with migraine, N=109 with TTH, N=26 with mixed headache, N=180 controls)	12-18 years	Not reported	Not reported	Development and Well-Being Assessment (DAWBA) semi-structed interview to diagnose psychiatric disorders	1. Depression: Predicted probability of depressive disorder was higher in migraine vs. controls (3.26 vs. 1.11, p=0.002) 2. Anxiety: Predicted probability of generalized anxiety disorder (1.07 vs. 0.10, p<0.001) and posttraumatic stress disorder (1.10 vs. 0.08, p=0.008) was higher in migraine vs.	N/A	3/7 domains adequate

									controls; no differences in specific phobia, social phobia, or obsessive compulsive disorder		
Trent H et al, 2020[81]	Cross-sectional (abstract)	USA (unclear if Indiana or Ohio)	Recruitment from headache clinic	N=374	6-18 years	Not reported	Not reported	Not reported	N=57 (15.2%) of the total participants with migraine were categorized as depressed (unclear how this was ascertained)	N/A	1/10 domains adequate
Uçar H et al, 2020[82]	Case-control	Turkey	Cases recruited from headache clinic, controls recruited from hospital (routine check-up visits)	N=112 (N=71 with migraine without aura, N=41 controls)	12-17 years	N=81 females (72.3%); N=31 males (27.7%)	Migraine without aura diagnosis according to ICHD-III beta criteria	Anxiety symptoms measured using the Screen for Child Anxiety Related Emotional Disorders (SCARED)	The migraine group had significantly higher mean SCARED scores compared to the control group* (23.11±12.68 vs. 13.34±8.64, t=4.832, p<0.001)	In the ANCOVA model, the migraine group had higher SCARED scores compared to controls after controlling for the effect of age, gender, family income, and parental education levels*	6/7 domains adequate

										(F=15.153, p<0.001)	
Uyar Cankay T et al, 2021[83]	Case-control	Rize, Turkey	Cases recruited from neurology clinic, controls recruited from community (classroom peers)	N=100 (N=50 with chronic migraine, N=50 controls)	12-18 years	N=78 females (78%); N=22 males (22%)	Chronic migraine (CM) diagnosis according to ICHD-III criteria	1. Psychiatric diagnoses ascertained using Kiddie – Schedule for Affective Disorders and Schizophrenia for School Aged Children (Kiddie-SADS) 2. Psychiatric symptoms measured using the DSM-V Level 1 Cross-Cutting Symptom Measure (CCSM-5)	1. Anxiety: N=6 (12%) with CM had generalized anxiety disorder; N=1 (2%) with CM had obsessive compulsive disorder; Mean anxiety symptoms on CCSM-5) higher in CM group than in control group* (59.49 vs. 41.51, Z=-3.125, p=0.002) 2. Depression: N=8 (16%) with chronic migraine had major depressive disorder; Mean depression symptoms on CCSM-	N/A	6/7 domains adequate

									V higher in CM group than in control group* (65.49 vs. 35.51, Z=-5.223, p<0.001)		
Valeriani M et al, 2009[84]	Case-control	Rome, Italy	Cases recruited from headache clinic, unclear how controls were recruited	N=38 (N=18 with migraine without aura, N=10 with TTH, N=10 controls)	Age range not reported (mean 10.5 ± 2 for migraine, 12.8 ± 2.8, 11.8 ± 2.5)	N=20 (52.6%) females, 18 (47.4%) males	Primary headache diagnosis according to ICHD-II criteria	Parents completed the Child Behavior Checklist (CBCL)	Scores on the internalizing subscale of the CBCL were highest in the TTH group (12.6 ± 6.1), intermediate in the migraine group (9.7 ± 7.4), and lowest in the control group (5.2 ± 3.3) ($F_{2,34}$=8.77, p=0.0005)	N/A	4/7 domains adequate
Vannatta K et al, 2008[85]	Case-control	Ohio, USA	Cases recruited from headache clinic; controls recruited from schools	N=93 (N=47 with migraine; N=46 controls)	8-14 years	N= 42 females (45.2%); 51 males (54.8%)	Migraine diagnosis according to ICHD-II criteria	1. Internalizing: Measured using the Child Behavior Checklist (CBCL) 2. Depression: Measured using the Children's Depression	1. Internalizing: Mothers reported higher CBCL internalizing scores in migraine vs. control group* (57.18 ±10.15 vs. 49.84 ±8.83,	N/A	5/7 domains adequate

								Inventory (CDI)	t(89)=3.83, p=0.00); mother also reported higher CBCL anxious-depressed scores in migraine vs. control group* (57.96 ±9.95 vs. 53.06 ±5.39, t(89)=2.76, p=0.01); mothers reported higher proportion of CBCL internalizing scores above the clinical cut-off in the migraine vs. control group* (38% vs. 11% χ^2 (1,91)=8.99, p<0.01), fathers' scores did not differ		

									between groups 2. Depression: Mean CDI scores did not differ between migraine vs. control group (7.28 ±5.73 vs. 5.65 ±6.21, t=1.38, p=0.17); no difference between migraine vs. controls on proportion with CDI score above clinical cut-off (6% vs. 7%, χ^2 (1,93)=0.001, p<0.05)		
Wagner J et al, 2014[86]	Case-control	South Carolina, USA	Cases and controls identified through a surveillance database	N=32,530 (N=10,495 with migraine, N=6,730 with	6-18 years	N=15,288 (47.0%)females, N=17,242 (53.0%) males	Migraine, epilepsy, and fracture diagnoses identified	Comorbid mental health diagnoses identified by searching ICD-9 codes	1. Depression: Higher odds of depression in the migraine	1. Depression: Higher odds of depression in	3/7 domains adequate

				epilepsy, N=15,305 with fractures)			by searching ICD-9 codes		group as compared to fracture group in both 6-12yo* (OR=1.85, 1.50-2.27) and 13-18yo* (OR=3.56, 95% CI=3.20-3.97) 2. Anxiety: Higher odds of anxiety in the migraine group as compared to the fracture group in both 6-12yo* (OR=2.67, 95% CI=2.15-3.32), and 13-18yo* (OR=3.95, 95% CI=3.50-4.46)	the migraine group as compared to fracture group in both 6-12yo (aOR=1.29, 1.04-1.60) and 13-18yo (aOR=1.82, 95% CI=1.61-2.06) 2. Anxiety: Higher odds of anxiety in the migraine group as compared to the fracture group in both 6-12yo (aOR=1.93, 95% CI=1.54-2.42), and 13-18yo	

										(OR=1.89, 95% CI=1.65-2.16)	
Waldie K et al, 2014[87]	Cross-sectional (from cohort study, data of interest cross-sectional)	Waitemata or Auckland, New Zealand	Community birth cohort of small for gestational age infants and random sample of average for gestational age infants	N=617 (N=65 with migraine, N=115 with TTH, N=337 no headache)	11 years	N (migraine subgroup)= 31 (47.4%) females; 34 (52.3%) males; larger group sex distribution not reported	Incidence of primary headaches at 11 years old, with diagnosis according to ICHD criteria	Depression ascertained at 11 years old using The Centre for Epidemiological Studies Depression Scale for Children (CES-DC) with cut-off scores	12.5% of migraine group had depression vs. 5.9% of controls (no hypothesis testing done to compare proportions); Symptoms of depression at age 11 were not significantly associated with migraine when compared to TTH (OR=2.26, p=0.06)	N/A	4/10 domains adequate
Wang SJ et al, 2007[88]	Cross-sectional	Taitung County, Taiwan	Recruited from community (school-based recruitment)	N=121 with chronic daily headache, selected from larger cohort study (81 with chronic migraine)	12-15 years	N=90 females; 31 males	Chronic daily headache diagnostic subgroups classified according to ICHD-II criteria	Depressive and anxiety disorders ascertained using the Mini-International Neuropsychiatric Interview for Children and Adolescents (MINI-Kid, version 1.01)	1. Depressive disorders: Chronic migraine diagnosis associated with MDD* (OR=4.6, 95% CI=1.3-16.4, p=0.01);	1. Depressive disorders: Chronic migraine with aura associated with any depressive disorder	7/10 domains adequate

								administered by a psychiatrist	2. Anxiety: Chronic migraine diagnosis associated with any anxiety disorder* (OR=3.8, 95% CI=1.5-9.5, p=0.004), panic disorder* (OR=6.6, 95% CI=1.5-30.0, p=0.006), social phobia* (16.0% vs. 0%, p=0.005) NB. Results for any depressive disorder, OCD and generalized anxiety disorder NS NB2. Raw data in Table 3	* (OR=4.1, 95% OR=1.0-16.4, p<0.05) after controlling for sex and gender, not significant for chronic migraine without aura; chronic migraine with and without aura not associated with dysthymia (NS) 2. Anxiety disorders: Chronic migraine without aura (OR=3.7, 95%=1.	

										4-9.7, p<0.01) and chronic migraine with aura (OR=4.6, 95% CI=1.2-17.6, p<0.01) associated with any anxiety disorder * after controlling for age and gender NB. Results for specific disorders in manuscript Table 3	
Wang SJ et al, 2009[90]	Cross-sectional	Taitung County, Taiwan	Recruited from community (school-based recruitment)	N=3,963 (928 with migraine, 3,331 other or no headache)	13-15 years	N=1,923 females (48.5%); 2,040 males (51.5%)	Migraine diagnosis according to ICHD-II criteria	Depression: Ascertained using the Adolescent Depression Inventory (ADI)	Migraine group had higher mean ADI scores than those without migraine* (12.0 ± 6.7 vs. 7.9 ± 6.0, p<0.001)	N/A	7/10 domains adequate
Wilcox S et al, 2018[91]	Cross-sectional	Boston, USA	Recruited from pediatric	N=359 with migraine	≤18 years (range	N=210 females (58.1%),	Migraine as diagnosed	1. Depression: Ascertain	1. Depression: 13.2% of migraine	N/A	4/10 domains

			headache clinic		not specified, mean 12.5± 3.1)	149 males (41.5%)	by a neurologist (criteria used not specified)	ed using the Child's Depression Inventory (CDI-2); if elevated score, clinical interview done and DSM-IV diagnosis made 2. Anxiety: Ascertained using the Revised Children's Manifest (RCMAS-2); if elevated score, clinical interview done and DSM-IV diagnosis made	patients had a depressive disorder 2. Anxiety: 32.8% of migraine patients had an anxiety disorder 3. Both anxiety and a depressive disorder: 9.8% had both an anxiety and a depressive disorder NB. No hypothesis testing done to look at association between migraine and internalizing disorders		adequate
Williams R et al, 2017[92]	Case-control	Rome, Italy	Cases recruited from pediatric headache clinic; controls recruited	N=100 (100 with migraine, 100 controls)	8-18 years	N=101 females (50.5%); 99 males (49.5%)	Migraine diagnosis according to ICHD-III criteria	Anxiety measured using the Self-Administered Psychiatric Scales for Children and	The migraine group had significantly higher scores on all SAFA subscales*: generalized anxiety	N/A	7/7 domains adequate

			from community (schools)					Adolescents (SAFA)	disorder (47.92 ±9.65 vs. 41.53 ±8.26, t(196)=5, p<0.0001); scholastic anxiety (49.48 ±10.32 vs. 42.89 ±5.53, t(196)=5.61, p<0.0001); separation and loss anxiety (45.31 +8.32 vs. 40.85 +9.76, t(196)=3.46, p<0.001); social anxiety disorder (51.07 +9.93 vs. 45.24 +8.04, t(196)=4.54, p<0.0001)		
Yilmaz et al, 2017[93]	Case-control (abstract)	Ankara, Turkey	Cases recruited from neurology clinic; did not report where controls were recruited from	N=90 (50 with migraine, 40 controls)	6-17 years	Not reported	Not reported	Depression measured using the Children's Depression Inventory (CDI)	No significant difference was found comparing migraine group to control group on CDI scores (raw scores not published)	N/A	2/7 domains adequate

*Statistically significant

NB. ICHD = International Classification of Headache Disorders; ICD = International Classification of Disease; TTH = tension-type headache; DSM = Diagnostic and Statistical Manual of Mental Disorders

eTable 2. Summary of studies examining migraine outcomes (n=18)

Study	Design	Location	Setting	Sample size	Ages	Sex	Outcome	Exposure	Unadjusted results	Adjusted results	Quality
Cooper P et al, 1987[95]	Case-control	Halifax, Canada	Cases recruited from a neurology clinic and controls were best friend controls from community	N=78 (39 with migraine, 39 controls)	6-16 years	N=40 females (51.2%); 38 males (48.7%)	1.Migraine diagnosis according to Prensky criteria 2.Prognostic outcome: Migraine group kept a daily headache diary for 4 months and headache frequency (over 4	Anxiety symptoms measured using State-Trait Anxiety Inventory for Children (STAIC), the Revised Children's Manifest Anxiety Scale (RCMAS), and parent-reported child anxiety via the Revised	1.Anxiety measures correlated with outcomes using Pearson correlations: Higher RCMAS total scores* (r=0.31, for frequency and 0.27 for severity), and higher STAIC	When Pearson correlations adjusted for sex, significance was lost except for the STAIC state score for females*, which was correlated with headache frequency	5/7 domains adequate

							months) and severity, on 1-3 scale, (sum of severity scores of all headaches over 4 months) assessed at 4-month follow-up	Personality Inventory for Children (PIC-R)	state* (r=0.55 for frequency and 0.53 for severity) and higher STAIC trait* (0.32 for frequency and 0.30 for severity) scores significantly associated with more frequent and severe headaches at follow-up 2. All anxiety measures placed in stepwise multiple regression model used to model the association between the prognostic outcomes and anxiety scores: 30% of the variance in headache frequency predicted and 27% of	and severity at follow-up ($p<0.002$) – raw data not presented	

									the variance in headache severity predicted by STAIC state scores*		
El-Heneedy Y et al, 2019[27]	Case-control	Tanta, Egypt	Cases recruited from headache clinic; not reported where controls were recruited from	N=60 (40 with migraine, 20 controls)	11.13 ± 2.85 (range not given)	Not described for whole sample; for migraine group: 23 females (57.5%); 17 males (42.5%)	Migraine diagnosis according to ICHD-III beta criteria	Internalizing symptoms measured using the Child Behavior Checklist (CBCL)	There was a significant positive correlation between CBCL anxious-depressed scores and PedMIDAS scores (shown in Figure 1, data not given)	N/A	5/7 domains adequate
Ertem D et al, 2019[28]	Case-control	Istanbul, Turkey	Cases recruited from a headache clinic, and hospital controls recruited (patients without neurological disorder diagnosed with any other health	N=238 (115 with migraine, 80 with TTH, 43 controls)	6-16 years	N=130 females (54.6%); 108 males (45.4%)	1. Primary headache diagnosis according to ICHD-III beta criteria 2. Visual analog scale for headache severity (not clear how it was measured) 3. Headache frequency (not clear	1. Anxiety symptoms measured using the Social Anxiety Scale for Adolescents (SAS-A) 2. Depression symptoms measured using the Children's Depression Inventory (CDI)	1. Anxiety: In the chronic migraine group, SAS-A and headache severity were correlated* (r=0.482, p=0.015) 2. Depression: In the episodic migraine group, CDI scores were correlated	N/A	2/7 domains adequate

			condition)				how it was measured)		with headache severity* (r=0.294, p=0.005) NB. No other significant correlations for migraine group		
Fuh JL et al, 2009[29]	Cross-sectional	Taitung County, Taiwan	Recruited from community (school-based recruitment)	N=3,963 (928 with migraine or probable migraine, 1,092 with TTH, 445 with other headache, 1498 no headache)	13-15 years	N=1,923 females (48.5%); 2,040 males (51.5%)	1. Primary headache diagnosis according to ICHD-II criteria 2. Pediatric Migraine Disability Scale (PedMIDAS)	Depression: Ascertained using the Adolescent Depression Inventory (ADI)	N/A	In the subgroup with migraine or probable migraine (N=928), higher ADI scores were associated with higher odds of moderate-severe disability on the PedMIDAS, after controlling for headache frequency and severity* (OR=3.1, 95% CI=0.7-3.7, p=0.001)	9/10 domains adequate
Gibson J 2004[31]	Case-control	Columbus, USA	Cases recruited	N=120 (68 with	6-12 years	N= 51 females	1. Primary headache	4. Anxiety: measured	N/A	Parent-reported	3/7 domai

	(dissertation)		from headache clinic, controls recruited from pediatric clinic or community	migraine, 40 controls)		(47%); 57 males (53%)	diagnosis according to ICHD criteria 2. General quality of life: measured using the Pediatric Quality of Life Inventory (PedsQL) 3. Headache-specific quality of life: modified version of the PedsQL with headache-specific questions	using the Revised Children's Manifest Anxiety Scale (RCMAS), and the Child Symptom Inventory-4 (CSI-4) 5. Depression: measured using the Children's Depression Inventory, and the Child Symptom Inventory-4 (CSI-4) NB. Those with screening cut-offs or with past psychiatric diagnosis had a follow-up semi-structured		headache-specific quality of life was associated with internalizing diagnoses* ($F(1,68)=7.377$, $p<0.05$, $R^2=0.071$), after controlling for age, sex, race, headache frequency, headache severity and externalizing disorders; no relationship between child-reported headache-specific quality of life and internalizing disorders after controlling for age, sex, race, headache frequency,	ns adequate

								interview with parents using DSM-IV diagnostic criteria (Barkley & Murphy, 1998 method)		headache severity and externalizing disorders; internalizing disorders were correlated with headache frequency *(r=0.229, p<0.05) after controlling for age, sex, race, headache frequency, headache severity and externalizing disorders; no relationship between internalizing disorders and headache-related impairment after controlling for age, sex, race, headache frequency, headache severity and	

										externalizing disorders; no significant relationships between parent- or child-reported PedsQL scores after controlling for age, sex, race, headache frequency, headache severity and externalizing disorders	
Guidetti V et al, 1998[36]	Cohort study	Rome, Italy	Cases randomly selected from a clinical cohort in a headache clinic	N=100 (64 with migraine, 36 with TTH)	4-18 years	N=60 females (60%); 40 males (40%)	Primary headache diagnosis according to ICHD criteria	1. Baseline (1988): Psychologists performed structured clinical interviews using DSM-II-R criteria; anxiety was also measured using the State-Trait Anxiety Inventory for Children	Anxiety disorders at baseline (1988) were predictive of persistence of headache at 8-year follow-up* (1996) (chi square=21.72, df=8, $p<0.05$); single comorbid disorders were related to headache persistence only in migraine	N/A	5/8 domains adequate

								(STAIC), and parent-reported anxiety and depression were measured using the Revised Personality Inventory for Children (PIC-R) 2. 8 year follow-up (1996): Psychologists administered the Structured Clinical Interview for DSM (SCID)	group; no association for depressive disorders		
Kaczynski et al, 2013[46]	Cross-sectional	Boston, USA	Cases recruited from headache clinic	N=262 (109 with migraine, 153 with TTH)	11-17 years	N=179 females (68.5%);	1. Primary headache diagnosis according to ICHD-II criteria 2. School functioning measured by the Pediatric Quality of	1. Anxiety: measured using the Revised Children's Manifest Anxiety Scale (RCMAS) 2. Depression: measured using the	N/A	In linear regression model, depressive symptoms were significantly associated with school functioning in migraine group (β=0.28,	6/10 domains adequate

							Life School Functioning Scale	Children's Depression Inventory (CDI)		p<0.05), while controlling for age, headache frequency, duration and severity, anxiety, protective parenting and passive coping; anxiety symptoms were not significantly associated with school functioning, while controlling for age, headache frequency, duration and severity, anxiety, protective parenting and passive coping	
Kafle M et al, 2022[47]	Cross-sectional	USA	Cases of migraine who were hospitalized in different centers	N=21,436	6-18 years	N=15,419 females (72%), 6,017 males 28%)	Migraine diagnosis according to International Classification of Diseases,	Psychiatric diagnoses ascertained using the International Classification of Diseases,	Having any psychiatric comorbidity was associated with a higher likelihood us receiving	After controlling for demographic variables, the differences	8/10 domains adequate

			for migraine manage-ment identified in an administra-tive health database (Pediatric Health Information System – PHIS)				9th and 10th editions	9th and 10th editions	medication treatment (see Table 1 in manuscript), with a longer mean length of stay (2.6 vs. 2.0 days, p<0.001), and with higher admission costs (8,749 vs. 7,040, p<0.001)*	between those with vs. without psychiatric comorbidities were still significant	
Karlson CW et al, 2013[97]	Cross-sectional daily diary study	Multicenter (Kansas and Ohio, USA)	Cases recruited from neurology or headache clinics (3 centers involved)	N=69 with migraine	7-12 years	N= 50 female (72.5%); 19 male (27.5%)	Migraine diagnosis according to ICHD-II criteria	Parents completed the Child Behavior Checklist (CBCL) and daily headache diaries were completed which included a daily mood rating using the Facial Affective Scale (FAS)	Baseline: Parents reported normal behavioral functioning on CBCL (subscale scores not reported)	1. Daily data – same day: Worse mood reported on headache days* (M=0.5 ±0.2 vs. 0.8 ±0.2; t(909)=17.81, p<0.001); worse mood associated with same-day headache occurrence* (t(883)=-	6/10 domains adequate

										8.75, p<0.001, longer headache duration* (z= -9.07, p<0.001), and more severe headache * (z=-19.05, p<0.001 2. Daily data – next day: Mood associated with next day headache severity* (z=2.11, p=0.04), but not next-day headache occurrence, or next day headache duration; neither headache occurrence, duration nor severity were	

										associated with next day mood NB. All of these analyses controlled for age, gender, quality of life, and headache-related disability (PedMIDAS scores)	
Nesterovskiy et al, 2015[64]	Cross-sectional (abstract)	Moscow, Russia	Not reported	N=187 with migraine	7-16 years	Not reported	Migraine diagnosis according to ICHD-II criteria	Anxiety disorders diagnosed according to ICD-10 diagnostic criteria, and severity of anxiety symptoms ascertained with the Spence Children's Anxiety Scale	Those with migraine and comorbid anxiety disorders have higher attack frequency than those without comorbid anxiety disorders (4.8 ±2.3 vs. 2.1 ±1.8, p<0.01)	N/A	2/10 domains adequate
Orr SL et al, 2019[98]	Cohort	Cincinnati, USA	Migraine cases recruited from headache clinic	N=5,316 (N=13,160 visit pairs)	13.4 ±3.7 years (range not reported)	N=3,586 females (67.5%); 1,730 males (32.5%)	1. Migraine diagnosis according to ICHD criteria 2. Clinical worsening defined as an	1. Depression: Ascertained using a single unvalidated question 2. Anxiety: Ascertaine	1. Depression: 16.9% (N=885) of the sample reported feeling depressed; in	1. Depression was associated with a higher odds of clinical worsening, after	4/8 domains adequate

							increase in 4 or more headache days/month in a 1-3 month follow-up window	d using unvalidated questions (endorsing any of the following: feeling anxious, feelings of low self-esteem, worrying a lot, or shyness)	univariate logistic regression models, depression was associated with a higher odds of clinical worsening* (OR=1.28, 95% CI=1.13-1.47, p=0.0004) 2. Anxiety: 45.8% (N=2,400) reported some anxiety symptoms; in univariate logistic regression models, anxiety was associated with a higher odds of clinical worsening (OR=1.17, 95%	adjusting for age, sex, disability score, and a variety of other predictors* (OR=1.31, 95% CI=1.13-1.51, p=0.0003) 2. Anxiety was not associated with odds of clinical worsening, after adjusting for age, sex, disability score, and a variety of other predictors	

									CI=1.05-1.30, p=0.0066)		
Oztop D et al, 2016[68]	Case-control	Turkey (details not specific)	Migraine cases recruited from neurology clinic; cases were recruited from local schools	N=70 (N=35 with migraine, N=35 controls)	9-16 years	N=52 (74.3%) females, 18 (25.7%) males	1. Migraine diagnosis according to ICHD criteria 2. Pediatric Migriane Disability Assessment Scale (PedMIDAS)	1. Depression: Ascertained using Kiddie – Schedule for Affective Disorders and Schizophrenia for School Aged Children (Kiddie-SADS) and Kovacs Children Depression Inventory (Kovacs-CDI) 2. Anxiety: Ascertained using Kiddie-SADS, State-Trait Anxiety Inventory for Children (STAI)	Kovacs CDI scores were positively correlated with Pediatric Migraine Disability Assessment Scale (PedMIDAS) scores* (p=0.022); did not report on whether or not anxiety symptoms were associated with PedMIDAS scores	N/A	4/7 domains adequate

								for those <12yo, and Spielberg State-Trait Anxiety Inventory for >12yo			
Pakalnis A et al, 2005[69]	Case-control	Columbus, USA	Cases recruited from headache clinic, controls recruited from pediatric clinics during routine physicals	N=80 (47 with episodic migraine, 33 controls)	6-17 years	N=21 females with migraine (44.6% of migraine sample), 26 males with migraine (55.3% of migraine sample)	1. Migraine diagnosis according to ICHD criteria 2. Treatment response	Child Symptom Inventory (CSI-4) or Adolescent Symptom Inventory (ASI-4); those with high scores had semi-structured interview with psychologist using Barkley & Murphy 1988 interview	Prognosis at 3 months: Treatment response not different comparing those with comorbidity vs. those without (results not presented, unclear if depression and anxiety analyzed separately from other disorders)	N/A	4/7 domains adequate
Tarantino S et al, 2013[99]	Cross-sectional	Rome, Italy	Cases recruited from a headache clinic	N=62 with migraine without aura	8-16 years	N=33 females (53.2%); 29 males (46.8%)	Migraine without aura diagnosis according to ICHD-II criteria	Anxiety measured using the Self-Administered Psychiatric Scales for Children and Adolescents (SAFA)	Participants with low frequency of attacks (< 4 attacks/month) had higher SAFA separation anxiety scores than those with chronic	N/A	6/10 domains adequate

									migraine (≥15 attacks/month) group* (9.4 ±5.0 vs. 3.3 ±3.5, p=0.003)		
Tarantino S et al, 2019[100]	Cross-sectional (abstract)	Rome, Italy	Unclear where cases were recruited from	N=51 with migraine	Mean age=11.6± 2.1 years (no range given)	N=29 females (56.9%); 22 males (43.1%)	Not reported	Anxiety measured using the Self-Administered Psychiatric Scales for Children and Adolescents (SAFA)	There was no relationship between SAFA score and migraine frequency (no data given)	N/A	3/10 domains adequate
Tarantino S et al, 2020[101]	Cross-sectional	Rome, Italy	Case recruited from headache clinic	N=111 with migraine without aura	8-18 years	N=64 females (57.6%); 47 males (42.3%)	Migraine diagnosis according to ICHD-III criteria	Self-Administered Psychiatric Scales for Children and Adolescents (SAFA) used to measure both anxiety and depressive symptoms	1. Depression: Mean SAFA total depression score higher in high frequency migraine group (weekly-daily attacks) vs. low frequency migraine group (≤3 attacks/month) (31.7 ±19.5 vs. 24.3 ±15.2, p=0.042)*	N/A	5/10 domains adequate

									2. Anxiety: Mean SAFA generalized anxiety score higher in high frequency migraine group vs. low frequency migraine group (11.3 ±5.8 vs. 7.4 ±4.7, p=0.000)*		
Uyar Cankay T et al, 2021[83]	Case-control	Rize, Turkey	Cases recruited from neurology clinic, controls recruited from community (classroom peers)	N=100 (N=50 with chronic migraine, N=50 controls)	12-18 years	N=78 females (78%); N=22 males (22%)	1. Chronic migraine (CM) diagnosis according to ICHD-III criteria 2. Visual analog scale 3. Pediatric Migraine Disability Assessment Scale (PedMIDAS) score	1. Psychiatric diagnoses ascertained using Kiddie – Schedule for Affective Disorders and Schizophrenia for School Aged Children (Kiddie-SADS) 2. Psychiatric symptoms	There was no correlation between CCSM-V anxiety symptoms (r=-0.081, p=0.575) nor between CCSM-V depression symptoms (r=0.152, p=0.292) and VAS scores; there was no correlation between CCSM-V anxiety scores and	N/A	6/7 domains adequate

								measured using the DSM-V Level 1 Cross-Cutting Symptom Measure (CCSM-5) and clinical cut-offs used	PedMIDAS scores (r=0.018, p=0.903), nor between CCSM-V depression symptoms and PedMIDAS (r=0.112, p=0.438)		
Vannatta K et al, 2008[85]	Case-control	Ohio, USA	Cases recruited from headache clinic; controls recruited from schools	N=93 (N=47 with migraine; N=46 controls)	8-14 years	N= 42 females (45.2%); 51 males (54.8%)	1. Migraine diagnosis according to ICHD-II criteria 2. Headache frequency and severity at follow-up (average 3 month follow)	3. Internalizing: Measured using the Child Behavior Checklist (CBCL) 3. Depression: Measured using the Children's Depression Inventory (CDI)	1. Internalizing: Higher mother-reported internalizing CBCL scores were associated with higher headache frequency at follow-up* (r=0.45, p<0.05); higher father-reported CBCL internalizing scores were associated with higher headache severity at	N/A	5/7 domains adequate

									follow-up* (r=0.42, p<0.05) 2. Higher baseline CDI scores were correlated to higher headache frequency scores at clinical follow-up* (r=0.47, p<0.05)		

*Statistically significant

NB. ICHD = International Classification of Headache Disorders; ICD = International Classification of Disease; TTH = tension-type headache; DSM = Diagnostic and Statistical Manual of Mental Disorders

eTable 3. Summary of studies examining migraine incidence (n=2)

Study	Design	Location	Setting	Sample size	Ages	Sex	Outcome	Exposure	Unadjusted results	Adjusted results	Quality
Hammond N et al, 2019[40]	Cohort	Canada	Population-based	N=2,313 (3.1% with migraine)	14-15 years	N=1,182 females (51.1%); 1,131 males (48.9%)	Migraine ascertained by person most knowledgeable reported health professional diagnosed migraine in their adolescent	Depression and separation anxiety symptoms measured using Ontario Child Health Study scale at age 8-9 years	Symptoms of depression and anxiety at 8-9 years significantly mediated the association between early life stress from ages 0-5 years and incident migraine at 14-15 years (family dysfunction IE= 0.0209, 95% bias-corrected confidence interval-CI_{BC}=0.0014-0.0609; hostile parenting IE=0.0581, 95% CI_{BC}=0.0033-0.1238; punitive parenting IE=0.0271, 95% CI_{BC}=0.0036-0.0670;	Symptoms of depression and anxiety no longer significantly mediated the associated between family dysfunction from ages 0-5 years and incident migraine at 14-15 years after adjustment for sex, parental migraine status, and socioeconomic status	6/8 domains adequate

									parental depression IE=0.0443, 95% CIBC=0.0049-0.0883)		
Lu SR et al, 2013[102]	Cohort	Taitung County, Taiwan	Recruited from community (school-based recruitment)	N= 3,342 adolescents without chronic daily headache at baseline; total of 5,585 person-years of follow-up (94.3% had ≥1 annual follow-up); 63 cases of incident chronic daily headache, 37 (58.7%) of which had incident chronic migraine	13-14 years	N=1,641 females (49.1%); 1,701 males (50.9%)	Incidence of chronic daily headache at 1- or 2-year follow-up; diagnostic subgroups classified according to ICHD-II criteria	1. Depression: depressive disorders ascertained using the Adolescent Depression Inventory (ADI) with clinical cut-off and using the Mini-International Neuropsychiatric Interview for Children and Adolescents (MINI-Kid, version 1.01) administered by a psychiatrist 2. Anxiety: anxiety disorders ascertained using the Mini-International Neuropsychiatric Interview for Children and Adolescents (MINI-Kid, version 1.01)	Depression (ADI score above cut-off) was associated with increased risk of incident chronic migraine* (RR=4.32, 95% CI=2.11-8.86, p<0.001)	Depression (ADI score above cut-off) was associated with increased hazard of incident chronic migraine* (HR=2.47, 95% CI=1.08-5.62, p=0.032), with model that included the following covariates: migraine or probable migraine at baseline, baseline headache frequency ≥7 days/month, obesity and lower household socioeconomic status	7/8 domains adequate

								administered by a psychiatrist			

*Statistically significant

eTable 4. Risk of bias ratings for case-control studies

Meta-analyzed								
Study	***Selection***				***Comparability***	***Exposure***		***Total (out of 7 domains)***
	Case definition	Case representa-tiveness	Control selection	Control definition	Case-control comparability	Exposure ascertainment	Same ascertainment method case and controls	
Açlkel B et al, 2021[22]	★	-	★	★	★	★	★	6
Araujo G et al, 2020[56]	-	-	-	★	-	★	★	3
Cooper P et al, 1987[95]	★	★	-	★	★	-	★	5
D'Andrea G et al, 1989[25]	★	-	-	★	★	★	★	5
El-Heneedy Y et al, 2019[27]	★	-	-	★	★	★	★	5
Ertem D et al, 2019[28]	★	-	-	-	★	-	-	2
Galli F et al, 2007[30]	★	★	★	★	-	★	★	6
Gibson J 2004[31]	★	-	-	★	-	★	★	4

Gozubatik-Celik et al, 2021[33]	★	-	★	★	★	★	★	6
Kandemir et al, 2018[48]	★	★	-	★	★	★	★	6
Machnes-Maayan D et al, 2014[55]	★	-	-	★	★	-	★	4
Marates J et al, 1982[60]	★	★	-	★	-	-	★	4
Mazzone L et al, 2006[61]	★	-	★	★	-	★	★	5
Nardello R et al, 2014[63]	★	-	★	-	★	★	★	5
Nita S et al, 2020[65]	★	-	-	★	-	★	★	4
Oztop D et al, 2016[68]	★	-	-	★	★	-	★	4
Pakalnis A et al, 2005[69]	★	★	★	-	-	-	★	4
Pavone P et al, 2012[71]	★	★	-	★	★	★	★	6
Reale L et al, 2011[73]	★	-	★	★	-	★	★	5
Salerno M et al, 2017[76]	★	★	-	-	★	★	★	5
Salvadori F et al, 2007[77]	★	★	★	★	★	★	★	7
Smith M et al, 2003[79]	-	★	★	-	★	★	★	5
Uçar H et al, 2020[82]	★	★	-	★	★	★	★	6
Uyar Cankay T et al, 2021[83]	★	-	★	★	★	★	★	6
Valeriani M et al, 2009[84]	★	★	-	-	-	★	★	4

Vannatta K et al, 2008[85]	★	-	★	-	★	★	★	5
Wagner J et al, 2014[86]	-	★	-	-	-	★	★	3
Williams R et al, 2017[92]	★	★	★	★	★	★	★	7
Not fully meta-analyzed								
Study	***Selection***				***Comparability***	***Exposure***		***Total (out of 7 domains)***
	Case definition	Case representa-tiveness	Control selection	Control definition	Case-control comparability	Exposure ascertainment	Same ascertainment method case and controls	
Andrasik F et al, 1988[34]	★	-	-	★	★	★	-	4
Araujo G et al, 2020[56]	-	-	-	★	-	★	★	3
Cooper P et al, 1987[95]	★	★	-	★	★	-	★	5
Cunningham S et al, 1987[24]	-	-	-	★	★	★	-	3
Gibson J 2004[31]	★	-	-	★	-	★	★	4
Guidetti V et al, 1987[35]	★	-	★	-	-	-	★	3
Guidetti V et al, 2013[37]	-	-	-	★	-	-	★	2
Gunalan S et al, 2012[39]	-	-	★	★	-	★	★	4
Huss et al, 2008[43]	★	-	★	★	-	-	★	4
Just U et al, 2003[44]	★	★	★	-	★	-	★	5
Mar S et al, 2009[58]	★	-	-	-	-	★	★	3
Mar S et al, 2010[59]	-	-	-	-	★	-	★	2

Nita S et al, 2020[65]	★	-	-	★	-	★	★	4
Oztop D et al, 2016[68]	★	-	-	★	★	-	★	4
Pakalnis A et al, 2009[70]	★	-	-	★	-	★	★	4
Tereshchenko et al, 2017[80]	-	-	-	★	★	-	★	3
Yilmaz et al, 2017[93]	-	-	-	-	-	★	★	2

★ = domain satisfies quality requirement
- = domain does not satisfy quality requirement

eTable 5. Risk of bias ratings for cross-sectional studies

Meta-analyzed											
Study	***Study Methods***			***Selection***				***Exposure***	***Applicability***		***Total (out of 10 domains)***
	Design & sampling method	Report of estimates (CI, subgroup)	Adjust-ment for con-founders	Outcome definition	Case represent-tativeness	Sample size	Response rate	Exposure ascertain-ment	Study subject description	External validity	
Albanês Oliveira Bernardo A et al, 2020[23]	★	-	-	★	★	-	-	★	★	-	5
Anttila P et al, 2004[45]	★	★	★	★	★	★	★	★	★	-	9
Arruda M et al, 2012[67]	★	★	★	★	★	★	★	★	★	-	9
Bektas Ö et al, 2015[78]	★	★	★	★	★	★	★	★	★	-	9
Blaauw B et al, 2014[89] (12-14 years old)	★	★	★	★	★	★	★	★	-	-	8

Donnelly T et al, 2017[26]	★	★	★	★	-	★	-	★	★	-	7
Fuh JL et al, 2009[29]	★	★	★	★	★	★	★	★	★	-	9
Gladstein J et al, 1996[32]	★	★	-	-	★	-	-	★	-	-	4
Guler G et al, 2017[38]	★	-	-	★	-	-	-	★	-	-	3
Hommer J et al, 2021[42] (migraine with aura)	★	★	-	★	★	★	-	★	★	★	8
Kafle M et al, 2022[47]	★	-	★	★	★	★	★	★	★	-	8
Kaczynski K et al, 2013[46]	★	★	★	★	-	-	-	★	★	-	6
Kröner-Herwig B et al, 2012[51]	★	★	★	★	★	★	-	★	★	-	8
Laurell K et al, 2005	★	★	-	★	★	-	-	★	★	-	6
Lucarelli E et al, 2009[53]	-	-	-	★	-	-	-	★	★	-	3
Nesterov~~f~~skiy Y et al, 2015[64]	-	-	-	★	-	-	-	★	-	-	2
Rabner J et al, 2018[72]	★	-	-	★	★	-	★	★	★	-	6
Rousseau-Salvador C et al, 2013[74]	★	★	★	★	-	-	★	★	★	-	7
Rousseau-Salvador C et al, 2014[75]	★	★	-	★	-	-	-	★	★	-	5
Waldie K et al, 2014[87]	★	-	-	★	-	-	-	★	★	-	4

Wang SJ et al, 2007[88]	★	★	★	★	★	-	-	★	★	-	7
Wang SJ et al, 2009[90]	★	-	-	★	★	★	★	★	★	-	7
Not fully meta-analyzed											
Author	***Study Methods***			***Selection***				***Exposure***	***Applicability***		***Total (out of 10 domains)***
	Design & sampling method	Report of estimates (CI, subgroup)	Adjust-ment for con-founders	Outcome definition	Case represent-tativeness	Sample size	Response rate	Exposure ascertain-ment	Study subject description	External validity	
Bektas O et al, 2015[78]	★	★	★	★	★	★	★	★	★	-	9
Braccili T et al, 1999[94]	-	-	-	★	-	-	-	★	★	-	3
Heinrich M et al, 2007[41]	★	-	-	★	★	★	-	★	★	-	6
Kashikar-Zuck S et al, 2013[49]	★	★	★	★	-	-	-	★	★	-	6
Lateef T et al, 2019[52]	★	-	-	★	★	-	-	★	★	★	6
Maleki N, 2016[57]	-	-	-	-	-	-	-	-	-	-	0
Onofri A et al, 2019[66]	-	-	-	★	-	-	-	★	-	-	2
Trent H et al, 2020[81]	★	-	-	-	-	-	-	-	-	-	1
Wilcox S et al, 2018[91]	★	-	-	-	★	-	-	★	★	-	4

★ = domain satisfies quality requirement

- = domain does not satisfy quality requirement

eTable 6. Risk of bias ratings for cohort studies

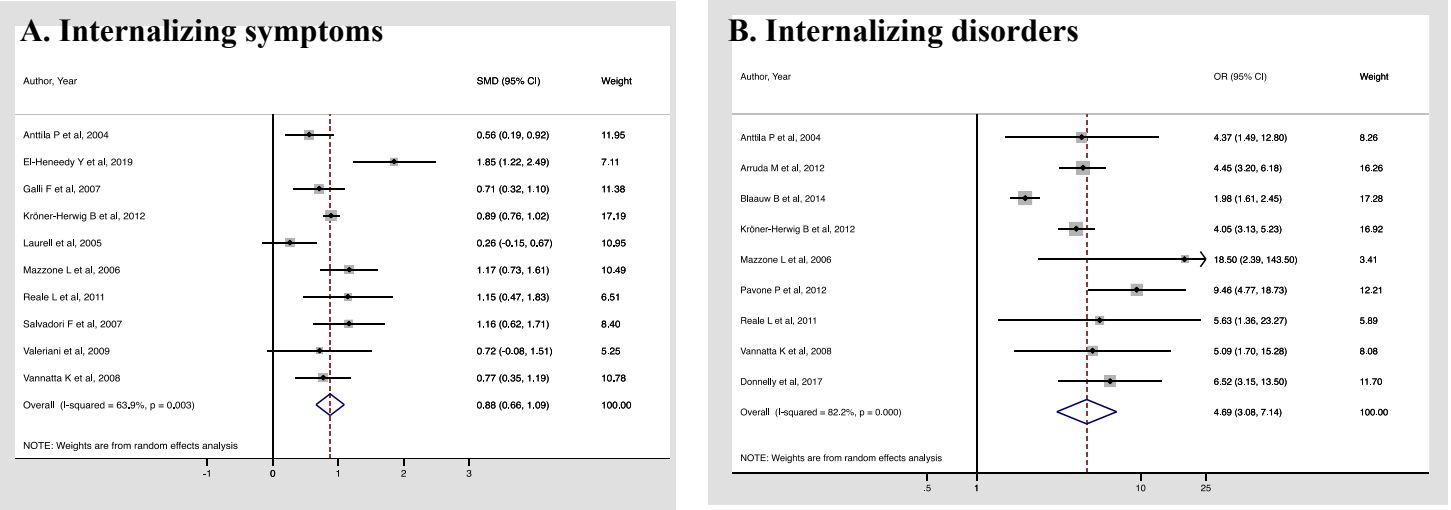
Meta-analyzed									
Author	***Selection***				***Comparability***	***Outcome***			***Total (out of 8 domains)***
	Cohort representa-tiveness	Selection of non-exposed cohort	Exposure ascertain-ment	Absence of outcome at start of study	Comparability of cohorts (design or analysis)	Outcome assessment	Duration of follow-up	Adequacy of follow-up	
Guidetti V et al, 1998[36]	-	★	★	★	-	★	★	-	5
Hammond N et al, 2019[40]	★	★	-	-	★	★	★	★	6
Not fully meta-analyzed									
Author	***Selection***				***Comparability***	***Outcome***			***Total (out of 8 domains)***
	Cohort representa-tiveness	Selection of non-exposed cohort	Exposure ascertain-ment	Absence of outcome at start of study	Comparability of cohorts (design or analysis)	Outcome assessment	Duration of follow-up	Adequacy of follow-up	

Kroner J et al, 2013[50]	★	★	-	-	-	★	★	-	4
McGinley J et al, 2019[62]	★	★	-	-	-	★	★	-	4

★ = domain satisfies quality requirement

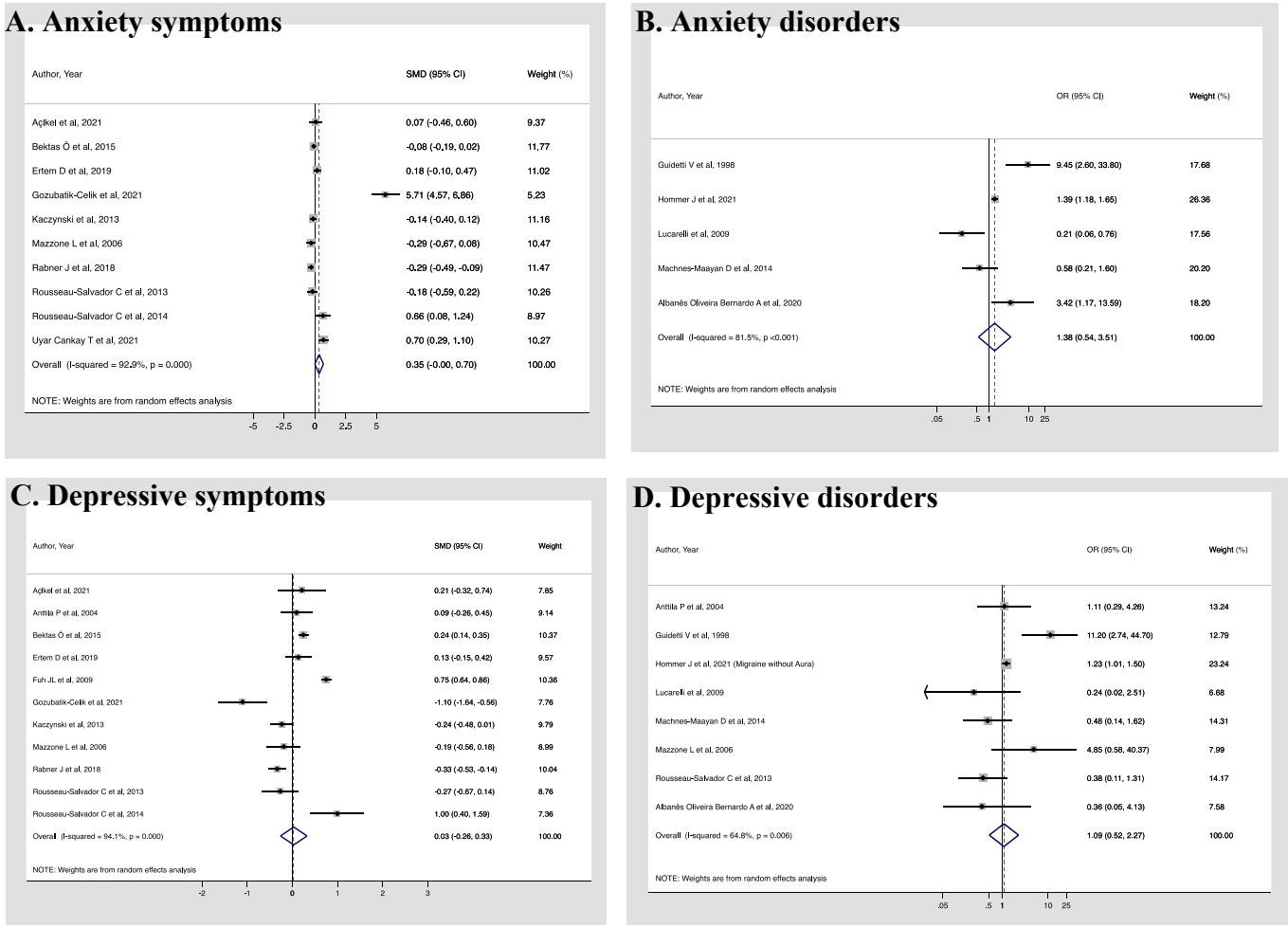
- = domain does not satisfy quality requirement

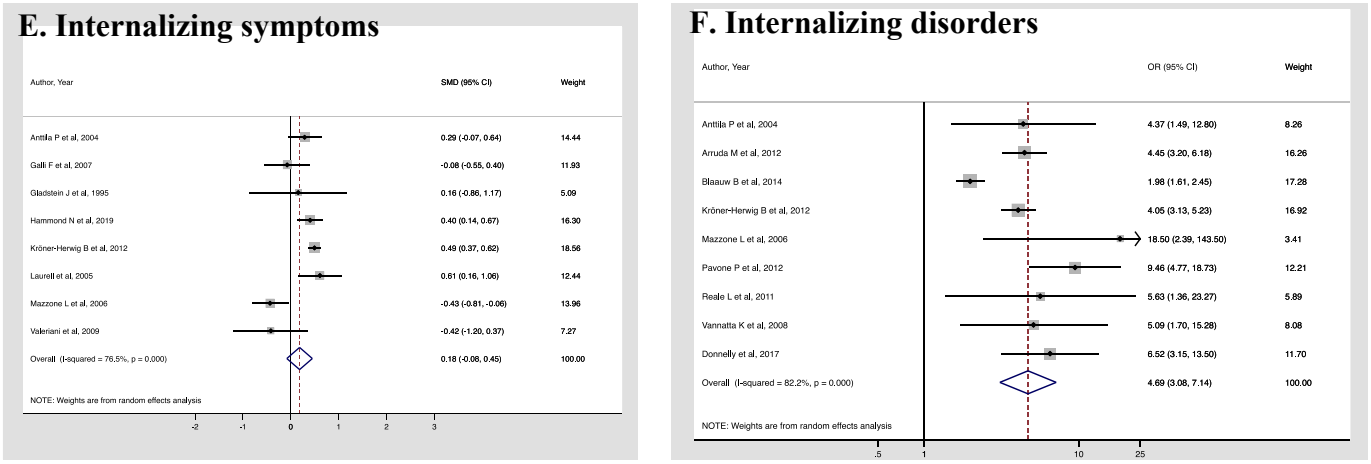
Figure e1. Results of meta-analyses comparing migraine to healthy controls for internalizing symptoms and disorders (presented in forest plots)



Forest plots illustrating pooled results of studies comparing migraine vs. healthy control samples on: A. internalizing symptoms[45,27,30,51,53,61,73,77,84,85] and B. internalizing disorders[45,67,89,51,61,71,73,85,26]

Figure e2. Results of meta-analyses comparing migraine to other headache controls (presented in forest plots)





Forest plots illustrating pooled results of studies comparing migraine vs. other headache control samples on: A. anxiety symptoms[22,78,28,33,46,61,72,74,75,83], B. anxiety disorders[36,42,54,55,23], C. depressive symptoms[22,45,78,28,29,33,46,61,72,74,75], D. depressive disorders[45,36,42,54,55,61,74,23], E. internalizing symptoms[45,30,32,40,51,53,61,84], and F. internalizing disorders[45,67,89,51,61,71,73,85,26]

eTable 7. Sensitivity analyses with removal of outlying studies

Studies					Sensitivity Analysis Data	
Exposure Type	*Control Group*	*Measure*	*N Studies in Original Analysis*	*N Studies in Sensitivity Analysis*	*Original Results*	*Sensitivity Analysis Results*
Anxiety symptoms	Healthy controls	SMD (95% CI)	16	15	1.13 (0.64-1.63)	0.82 (0.38-1.26)
Anxiety disorders	Healthy controls	OR (95% CI)	15	14	1.93 (1.49-2.50)	1.87 (1.47-2.37)
Depressive symptoms	Healthy controls	SMD (95% CI)	17	16	0.67 (0.46-0.87)	0.56 (0.38-0.74)
Depressive disorders	Healthy controls	OR (95% CI)	18	N/A	2.01 (1.46-2.78)	N/A (no outliers)
Internalizing symptoms	Healthy controls	SMD (95% CI)	10	9	0.88 (0.66-1.09)	0.80 (0.62-0.98)
Internalizing disorders	Healthy controls	OR (95% CI)	9	8	4.69 (3.08-7.14)	4.46 (2.93-6.79)