

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. Variables included in the systematic review

Domain	Variables
Study characteristics	Authors, affiliations, SIH diagnostic criteria, study design (prospective/retrospective, observational/interventional), number of patients.
Demographics	Age (mean, SD, range), sex (male/female).
Risk factors	Patients with connective tissue disorders, spinal pathologies, other risk factors.
Clinical presentation	Symptoms duration (mean, SD, range), headache (n. patients and characteristics), nausea/vomiting, neck pain/stiffness, hearing impairment, tinnitus, other ear signs/symptoms, dizziness, vertigo, photophobia, diplopia, other visual signs/symptoms, reduced level of consciousness, cognitive disturbances, back pain, movement disturbances, other signs/symptoms.
Brain MRI	N. of investigations performed, diffuse pachymeningeal enhancement, subdural collections, brain sagging, pituitary gland enlargement, venous engorgement, slit ventricles, tonsillar descent, normal brain MRI appearances, other findings.
Spinal imaging	For each type of spinal investigation: n. of investigations performed, n. of extradural CSF detection, type of leak detection (specific leak site, broad area, unspecified). Type of investigations: spine MRI, CT myelogram, radionuclide cisternography, MR myelography (with and without intrathecal gadolinium), other spinal investigations.
CSF leak location	N. of leaks identified, leaks location (cervical, cervico-thoracic, thoracic, thoraco-lumbar, lumbar, lumbo-sacral, sacral, multiple leaks).
CSF pressure	N. of lumbar punctures (or CSF pressure measurements), pressure findings: low (<60 mmH ₂ O), normal (60-200 mmH ₂ O), high (>200 mmH ₂ O).
Treatments and outcomes	Conservative treatment: n. of patients treated, duration of treatment, outcomes, type (bed rest, hydration, caffeine, analgesia, steroids); EBP: n. of patients treated, duration of treatment, outcomes, n. of EBPs, type (targeted, nontargeted, large(>20ml), small); Other treatments.
CSF: Cerebrospinal Fluid; EBP: Epidural Blood Patch; SD: Standard Deviation.	

eTable 2. Inclusion criteria for meta-analyses

Metanalyses	Inclusion criteria for metanalyses
Age	Mean age and SD specified.
Sex	N. of males/females specified.
Symptoms duration	Mean duration and SD specified.
Sign/Symptoms	For each sign/symptom: n. of patients with the sign/symptom specified.
Brain MRI	N. of investigations, type of positive findings and proportion of positive findings specified.
Spinal imaging	N. of investigations, type of investigations and proportion of positive findings (extradural CSF) specified.
CSF pressure	N. of investigations and findings (n. low pressure, normal pressure and high pressure) specified. Studies in which all patients had low CSF opening pressure were excluded.
Outcomes of conservative treatment	N. of patients who received treatment and n. good outcomes specified. Studies in which all (or none) of the patients had good outcomes were excluded.
Outcomes of first EBP	N. of patients who received treatment and n. good outcomes after 1 st EBP specified. Studies in which all (or none) of the patients had good outcomes were excluded.
Outcomes of nontargeted/targeted EBP	N. of patients who received treatment, type of EBP (nontargeted or targeted) and n. good outcomes after 1 st EBP specified. Studies in which all (or none) of the patients had good outcomes were excluded.
Outcomes of small/large EBP	N. of patients who received treatment, type of EBP (small or large) and n. good outcomes after 1 st EBP specified. Studies in which all (or none) of the patients had good outcomes were excluded.
All	Studies with 0% or 100% proportion of findings were excluded. For each meta-analysis, if more than one study from the same author met the inclusion criteria, only the study reporting the largest number of patients was included.
CSF: Cerebrospinal Fluid; EBP: Epidural Blood Patch; SD: Standard Deviation.	

eTable 3. List of selected studies and inclusion for meta-analyses

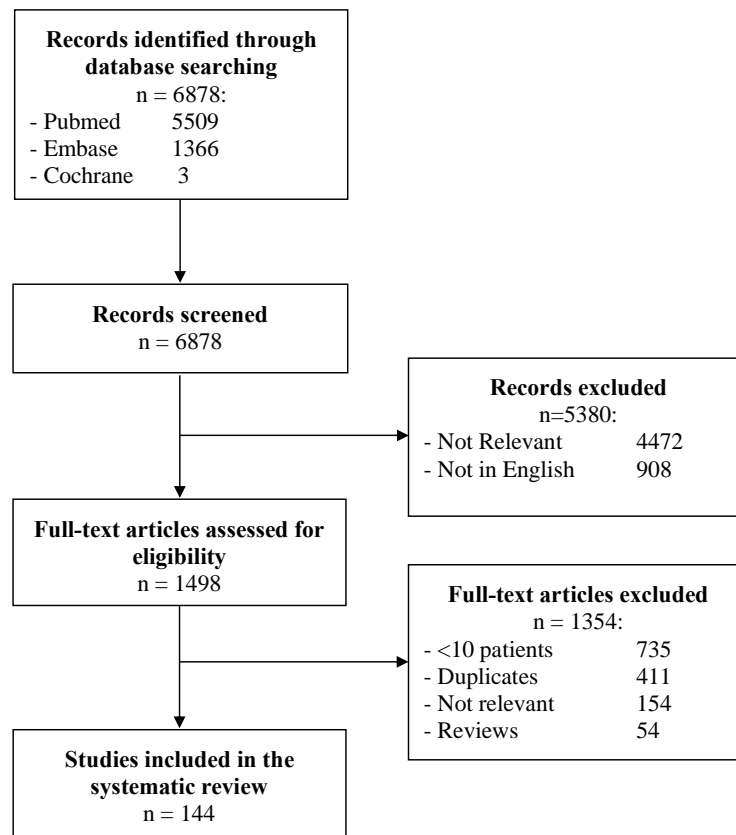
Reference	Author (year)	Quality grading ^a	Patients (n)	Meta-analyses
(1)	Cebeci et al (2020)	Fair	20	Age, sex, other symptoms, MRMG, leak location
(2)	Davies et al (2020)	Good	86	Sex, other symptoms, conservative treatment
(3)	Wang et al (2020)	Good	20	
(4)	Dobrocky et al (2019)	Good	56	Age, sex, brain MRI
(5)	Li et al (2019)	Fair	40	Age, sex, clinical presentation, brain MRI, LPOP
(6)	Levi et al (2019)	Good	101	Age, sex, headache, other symptoms, nontargeted EBP, small EBP
(7)	Kim et al (2019)	Good	43	Age, sex, symptoms duration, headache, other symptoms, brain MRI
(8)	Schievink et al (2019)	Good	113	Age, symptoms duration, headache
(9)	Schievink et al (2019)	Good	49	DSM
(10)	Pagani-Estévez et al (2019)	Fair	202	First EBP
(11)	Fichtner et al (2019)	Fair	27	LPOP, leak location
(12)	Martin et al (2019)	Fair	94	Other symptoms, first EBP
(13)	Kinsman et al (2019)	Fair	144	Sex
(14)	Farb et al (2019)	Fair	31	Sex, brain MRI, spine MRI, DSM, leak location
(15)	Griffin et al (2019)	Good	92	
(16)	Ohtonary et al (2018)	Fair	19	Age, sex, headache, other symptoms, LPOP, leak location, conservative,
(17)	Murakami et al (2018)	Good	38	Age, sex
(18)	Lee et al (2018)	Fair	62	Age, sex, leak location, first EBP, targeted EBP
(19)	Schievink et al (2018)	Good	29	Conservative treatment
(20)	Xia et al (2018)	Good	156	Conservative treatment
(21)	Ahn et al (2018)	Good	116	Sex, brain MRI, spine MRI, CTM, leak location, first EBP, nontargeted EBP, targeted EBP
(22)	Yagi et al (2018)	Fair	37	Sex, symptoms duration, other symptoms, brain MRI, leak location, conservative, first EBP, large EBP
(23)	Tsai et al (2018)	Fair	27	Symptoms duration, brain MRI
(24)	Takai et al (2018)	Fair	11	Symptoms duration, LPOP
(25)	Dobrocky et al (2018)	Fair	14	
(26)	Clark et al (2018)	Fair	101	
(27)	Ferrante et al (2018)	Fair	35	
(28)	Beck et al (2018)	Fair	47	
(29)	Schievink et al (2018)	Fair	15	
(30)	Yao et al (2017)	Fair	206	Age, sex, symptoms duration, headache, brain MRI, LPOP
(31)	Wu et al (2017)	Good	150	Age, sex, symptoms duration, headache, other symptoms, brain MRI, MRM, leak location, first EBP, targeted EBP
(32)	Beck et al (2017)	Good	31	Other symptoms
(33)	He et al (2017)	Good	165	Other symptoms, CTM, MRM, leak location, conservative, first EBP, targeted EBP, small EBP
(34)	Choi et al (2017)	Good	95	Sex, headache, other symptoms, brain MRI, leak location, first EBP, nontargeted EBP, targeted EBP, small EBP
(35)	Kim et al (2017)	Fair	128	Sex, headache, headache location, other symptoms, brain MRI, first EBP
(36)	Kranz et al (2017)	Good	22	
(37)	Chen et al (2017)	Good	19	
(38)	Chen et al (2017)	Good	23	
(39)	Chen et al (2016)	Fair	45	Age, sex, headache, other symptoms, conservative, first EBP
(40)	So et al (2016)	Fair	34	Age, sex, symptoms duration, headache, leak location, first EBP, small EBP
(41)	Amemiya et al (2016)	Good	15	Age, symptoms duration, other symptoms
(42)	Kranz et al (2016)	Good	99	CTM
(43)	Schievink et al (2016)	Good	53	DSM
(44)	Ferrante et al (2016)	Fair	106	First EBP, large EBP

Reference	Author (year)	Quality grading ^a	Patients (n)	Meta-analyses
(45)	Amrhein et al (2016)	Fair	35	First EBP, targeted EBP, small EBP
(46)	Fichtner et al (2016)	Good	39	Headache
(47)	Monteith et al (2016)	Fair	12	Headache, brain MRI, RIC
(48)	Schievink et al (2016)	Good	568	Sex
(49)	Hori et al (2016)	Good	22	Sex, brain MRI
(50)	Karm et al (2016)	Fair	104	Sex, brain MRI, first EBP, targeted EBP
(51)	Ansel et al (2016)	Fair	16	Sex, brain MRI, spine MRI, leak location, first EBP, nontargeted EBP, small EBP
(52)	Takahashi et al (2016)	Fair	169	Sex, headache, brain MRI, RIC, LPOP, leak location, conservative, first EBP
(53)	Capizzano et al (2016)	Fair	41	Sex, headache, other symptoms, brain MRI
(54)	Tanaka et al (2016)	Good	40	Sex, headache, other symptoms, brain MRI
(55)	Kim et al (2016)	Fair	140	Sex, headache, other symptoms, brain MRI, spine MRI, conservative, first EBP, small EBP
(56)	Choi et al (2016)	Fair	18	Sex, leak location, first EBP, targeted EBP
(57)	Kranz et al (2016)	Good	89	Symptoms duration
(58)	Ferrante et al (2016)	Good	28	Symptoms duration, headache location
(59)	Beck et al (2016)	Good	15	
(60)	Verdoorn et al (2016)	Fair	129	
(61)	Wan et al (2016)	Fair	15	
(62)	Kranz et al (2015)	Good	106	Age, sex, brain MRI, LPOP
(63)	Idrissi et al (2015)	Fair	24	Age, sex, headache, headache location, other symptoms, brain MRI, spine MRI, RIC, leak location, conservative, first EBP,
(64)	Thielen et al (2015)	Fair	14	Leak location
(65)	Joo et al (2015)	Fair	76	Leak location, small EBP
(66)	Feltracco et al (2015)	Fair	18	Sex, brain MRI, first EBP, nontargeted EBP
(67)	Schievink et al (2015)	Fair	13	
(68)	Schievink et al (2015)	Good	42	
(69)	Xia et al (2015)	Fair	93	
(70)	Yoshida et al (2014)	Fair	12	Age, sex, headache, other symptoms, brain MRI, leak location, first EBP, targeted EBP, small EBP
(71)	Chazen et al (2014)	Good	24	Sex, CTM, MRMG, LPOP
(72)	Pimienta et al (2014)	Fair	50	
(73)	Schievink et al (2014)	Fair	338	
(74)	Tung et al (2014)	Good	17	
(75)	Hashizume et al (2013)	Fair	29	Age, sex, other symptoms, brain MRI, RIC, LPOP, conservative, first EBP, targeted EBP
(76)	Schievink et al (2013)	Fair	24	Headache location
(77)	Hosoya et al (2013)	Fair	100	Spine MRI, MRM
(78)	Ferrante et al (2013)	Fair	10	
(79)	Franzini et al (2013)	Fair	80	
(80)	Kranz et al (2013)	Good	19	
(81)	Reinstein et al (2013)	Good	50	
(82)	Albes et al (2012)	Fair	26	Age, sex, CTM, leak location, first EBP, targeted EBP, large EBP
(83)	Hasiloglu et al (2012)	Good	25	Age, sex, headache, LPOP, leak location
(84)	Hashizume et al (2012)	Fair	12	Leak location
(85)	Akbar et al (2012)	Fair	41	MRMG
(86)	Luetmer et al (2012)	Fair	151	Spine MRI
(87)	Balkan et al (2012)	Fair	11	Symptoms duration, other symptoms, brain MRI, first EBP, targeted EBP
(88)	Schievink et al (2012)	Good	33	
(89)	Schievink et al (2012)	Fair	20	
(90)	Takeuchi et al (2012)	Fair	15	
(91)	Yoon et al (2011)	Fair	30	LPOP
(92)	Cho et al (2011)	Good	56	Sex, headache, brain MRI, leak location, first EBP, nontargeted EBP, targeted EBP, small EBP
(93)	Bonetto et al (2011)	Fair	17	Sex, symptoms duration, headache, other symptoms, brain MRI, conservative, first EBP, nontargeted EBP
(94)	Watanabe et al (2011)	Fair	13	Symptoms duration, headache, small EBP
(95)	Franzini et al (2011)	Fair	74	

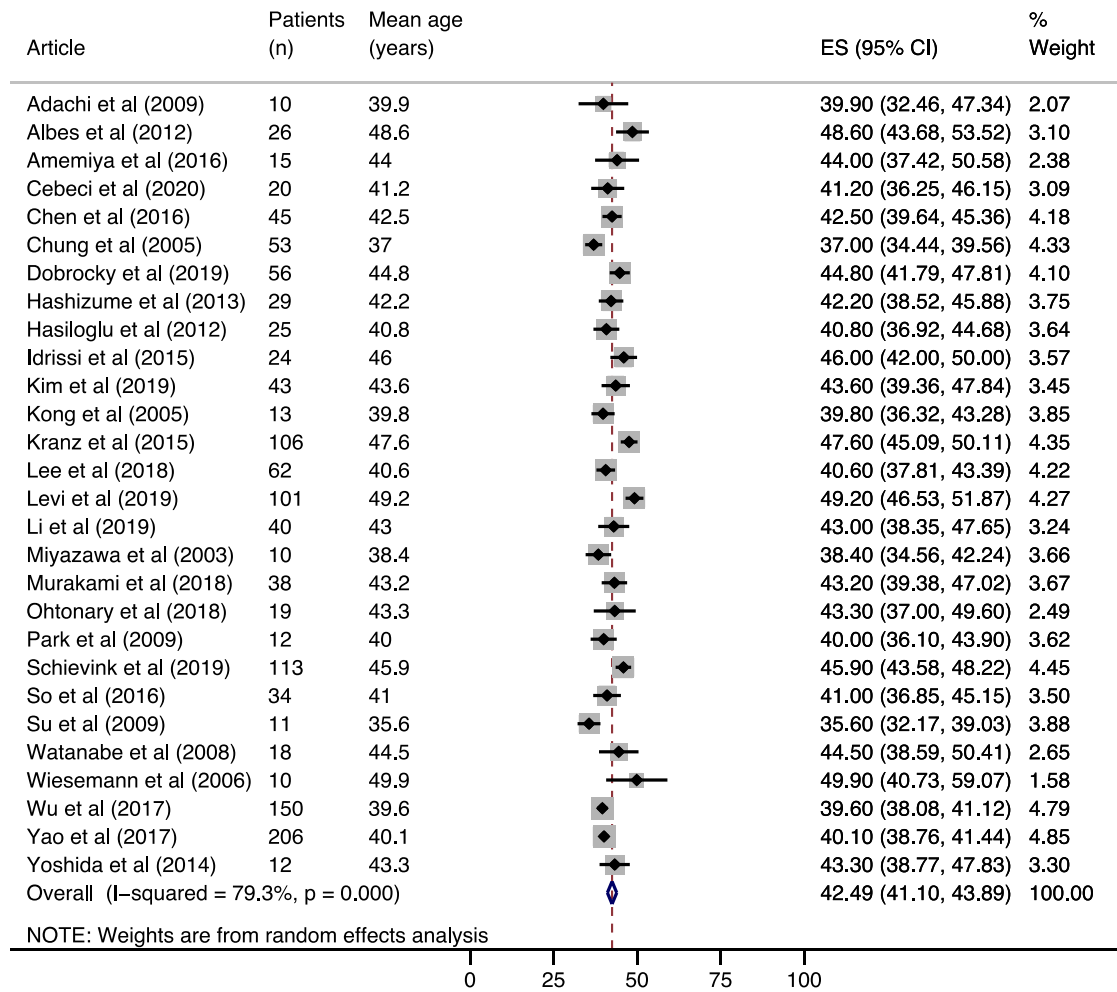
Reference	Author (year)	Quality grading ^a	Patients (n)	Meta-analyses
(96)	Liu et al (2011)	Good	55	
(97)	Franzini et al (2010)	Fair	28	Leak location
(98)	Medina et al (2010)	Fair	13	Sex, headache, spine MRI, first EBP
(99)	Ferrante et al (2010)	Fair	42	Spine MRI, MRM, RIC
(100)	Horikoshi et al (2010)	Fair	16	Targeted EBP
(101)	Adachi et al (2009)	Fair	10	Age, sex, headache, other symptoms
(102)	Park et al (2009)	Fair	12	Age, sex, headache, other symptoms, brain MRI, RIC, LPOP, conservative
(103)	Su et al (2009)	Fair	11	Age, sex, headache, other symptoms, brain MRI, spine MRI, leak location, first EBP, nontargeted EBP
(104)	Mea et al (2009)	Good	90	Brain MRI
(105)	Wang et al (2009)	Fair	19	CTM
(106)	Shankar et al (2009)	Good	17	Sex, brain MRI
(107)	Mea et al (2009)	Fair	90	
(108)	Watanabe et al (2008)	Fair	18	Age, headache, spine MRI, LPOP
(109)	Schievink et al (2008)	Fair	94	Brain MRI, LPOP
(110)	Yoo et al (2008)	Fair	15	MRM, RIC, first EBP
(111)	Albayram et al (2008)	Good	19	MRMG
(112)	Hyun et al (2008)	Good	30	Sex, headache, other symptoms, brain MRI, RIC, LPOP, leak location, conservative, first EBP, small EBP
(113)	Tomoda et al (2008)	Fair	27	Sex, other symptoms, conservative treatment, MRM, LPOP, first EBP
(114)	Fuh et al (2008)	Fair	53	
(115)	Mea et al (2008)	Fair	70	
(116)	Mea et al (2007)	Good	59	Sex
(117)	Chung et al (2007)	Fair	10	
(118)	Farb et al (2007)	Good	12	
(119)	Lai et al (2007)	Fair	40	
(120)	Schievink et al (2007)	Fair	11	
(121)	Schievink et al (2007)	Fair	80	
(122)	Tsai et al (2007)	Fair	17	
(123)	Wiesemann et al (2006)	Fair	10	Age, sex, symptoms duration, headache, other symptoms, brain MRI, LPOP, conservative
(124)	Chung et al (2006)	Fair	67	RIC
(125)	Hannerz et al (2006)	Fair	12	Sex, headache, other symptoms, brain MRI, conservative, first EBP, nontargeted EBP, large EBP
(126)	Cohen-Gadol et al (2006)	Fair	13	Sex, headache, other symptoms, brain MRI, leak location
(127)	Chung et al (2005)	Fair	53	Age, spine MRI, conservative treatment
(128)	Kong et al (2005)	Fair	13	Age, symptoms duration, spine MRI, CTM, RIC, LPOP, conservative
(129)	Schievink et al (2005)	Fair	33	Leak location
(130)	Schievink et al (2005)	Fair	20	
(131)	Ferrante et al (2004)	Fair	18	LPOP
(132)	Berrior et al (2004)	Fair	33	Sex, symptoms duration, headache, other symptoms, brain MRI, first EBP, nontargeted EBP
(133)	Ferrante et al (2004)	Fair	12	
(134)	Schievink et al (2004)	Good	18	
(135)	Schievink et al (2004)	Good	25	
(136)	Miyazawa et al (2003)	Fair	10	Age, headache, other symptoms, brain MRI, RIC, LPOP, leak location
(137)	Chen et al (2003)	Fair	13	
(138)	Schievink et al (2003)	Good	18	
(139)	Lin et al (2002)	Fair	15	LPOP
(140)	Schrijver et al (2002)	Good	20	
(141)	Chung et al (2000)	Fair	30	Headache location
(142)	Chen et al (1999)	Good	13	
(143)	Schievink et al (1998)	Good	10	
(144)	Schievink et al (1996)	Fair	11	Spine MRI, RIC

^aBased on NIH Quality Assessment Tool for Case Series Studies
CTM: CT myelography, EBP: Epidural Blood Patch, LPOP: Lumbar Puncture Opening Pressure, MRM: MR Myelography, MRMG: MR myelography with intrathecal Gadolinium, RIC: Radionuclide Cisternography

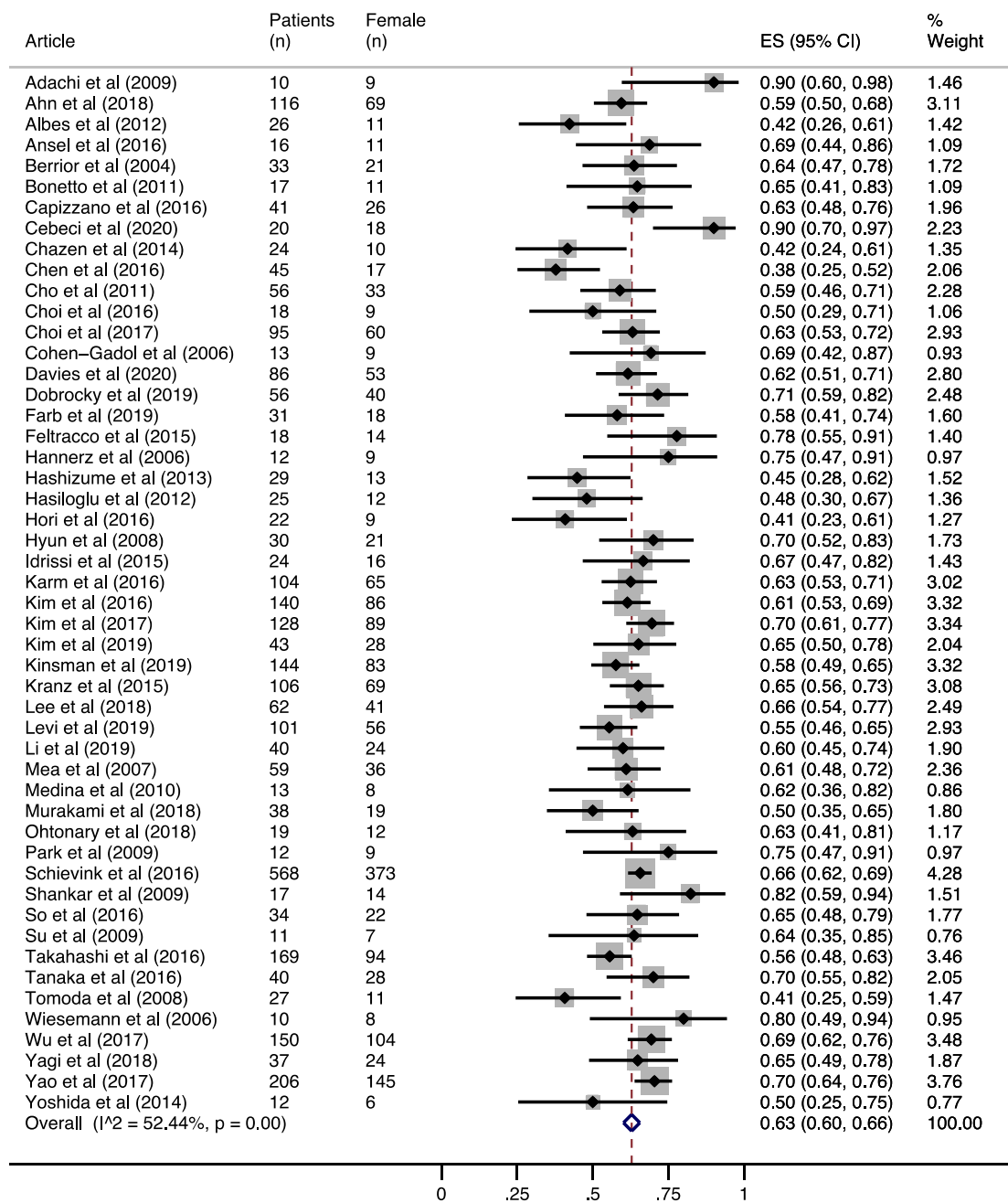
eFigure 1. Flowchart of the selection process for articles



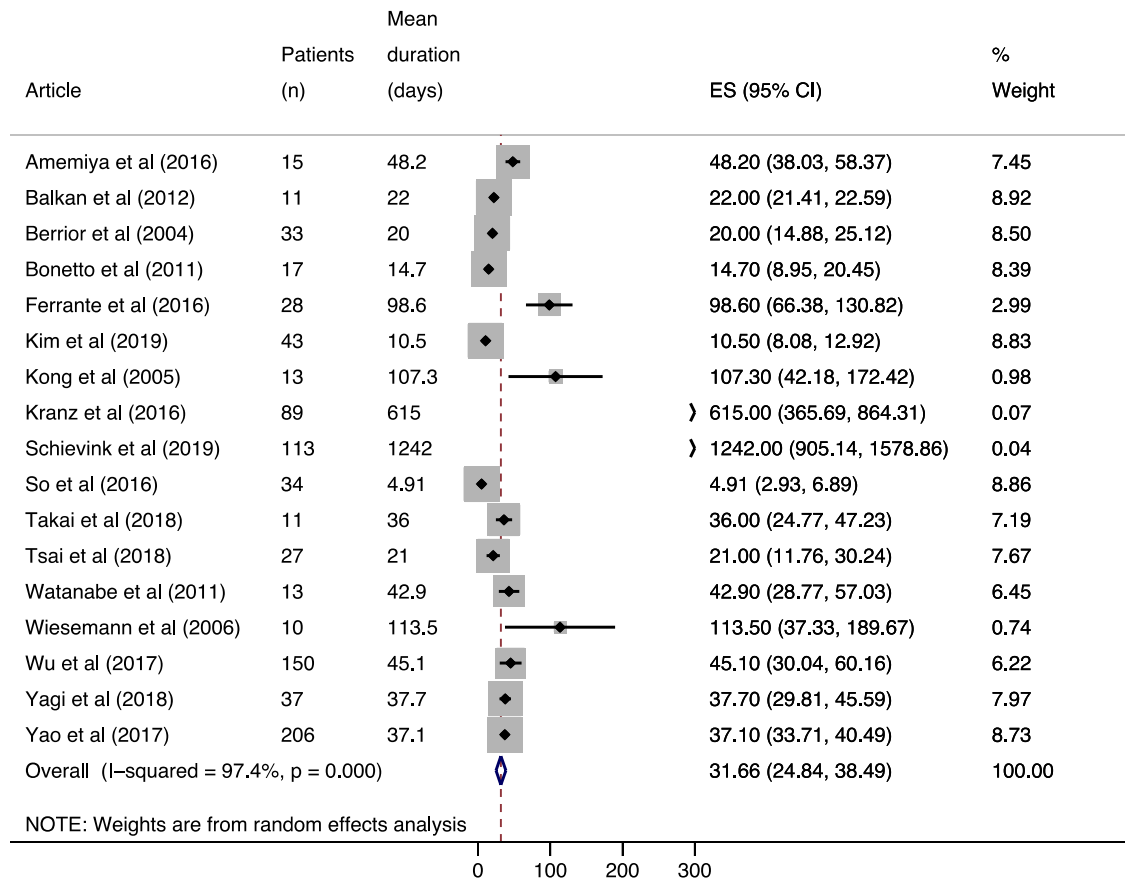
eFigure 2. Age meta-analysis (mean years)



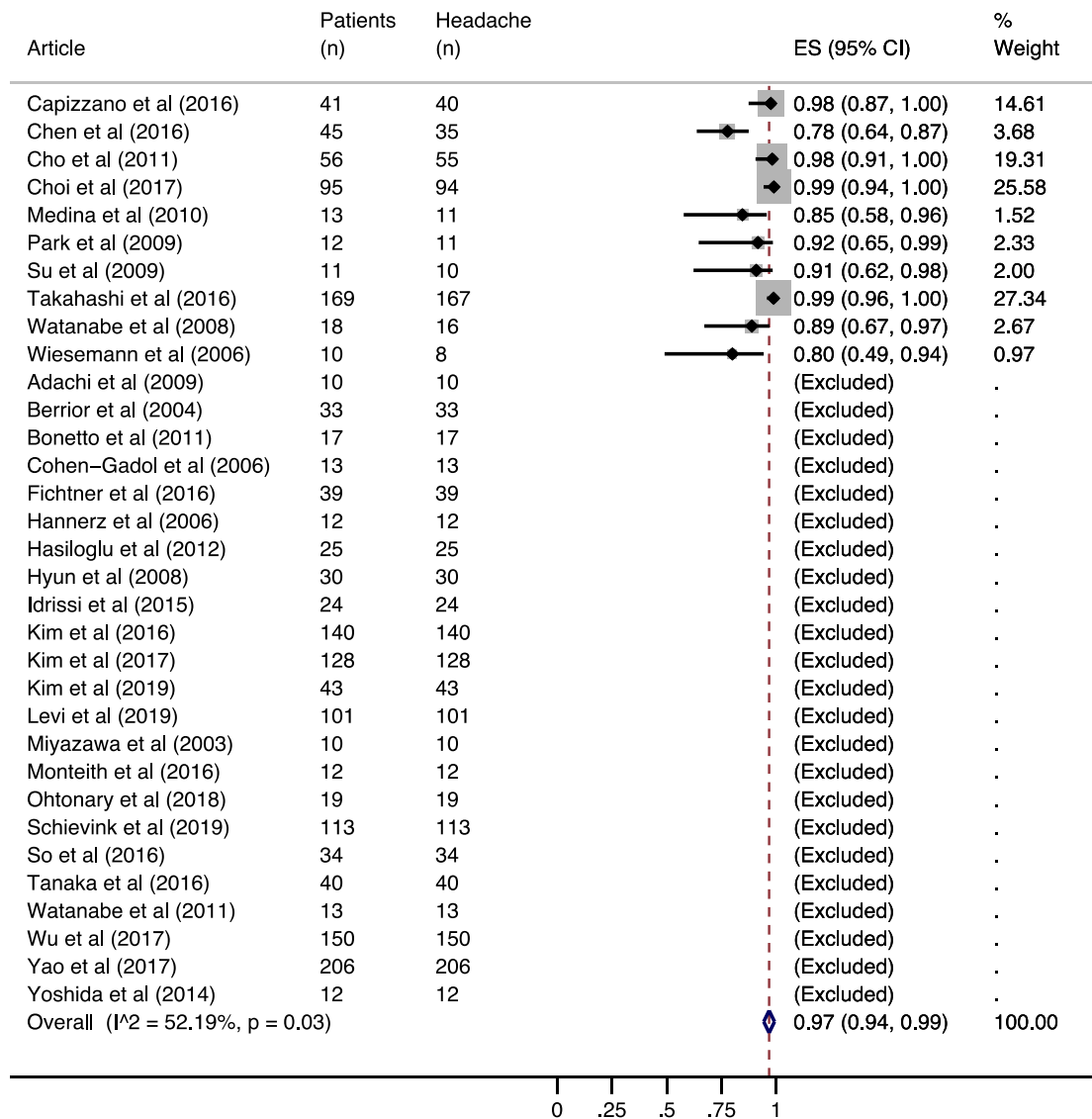
eFigure 3. Sex meta-analysis (proportion of female patients)



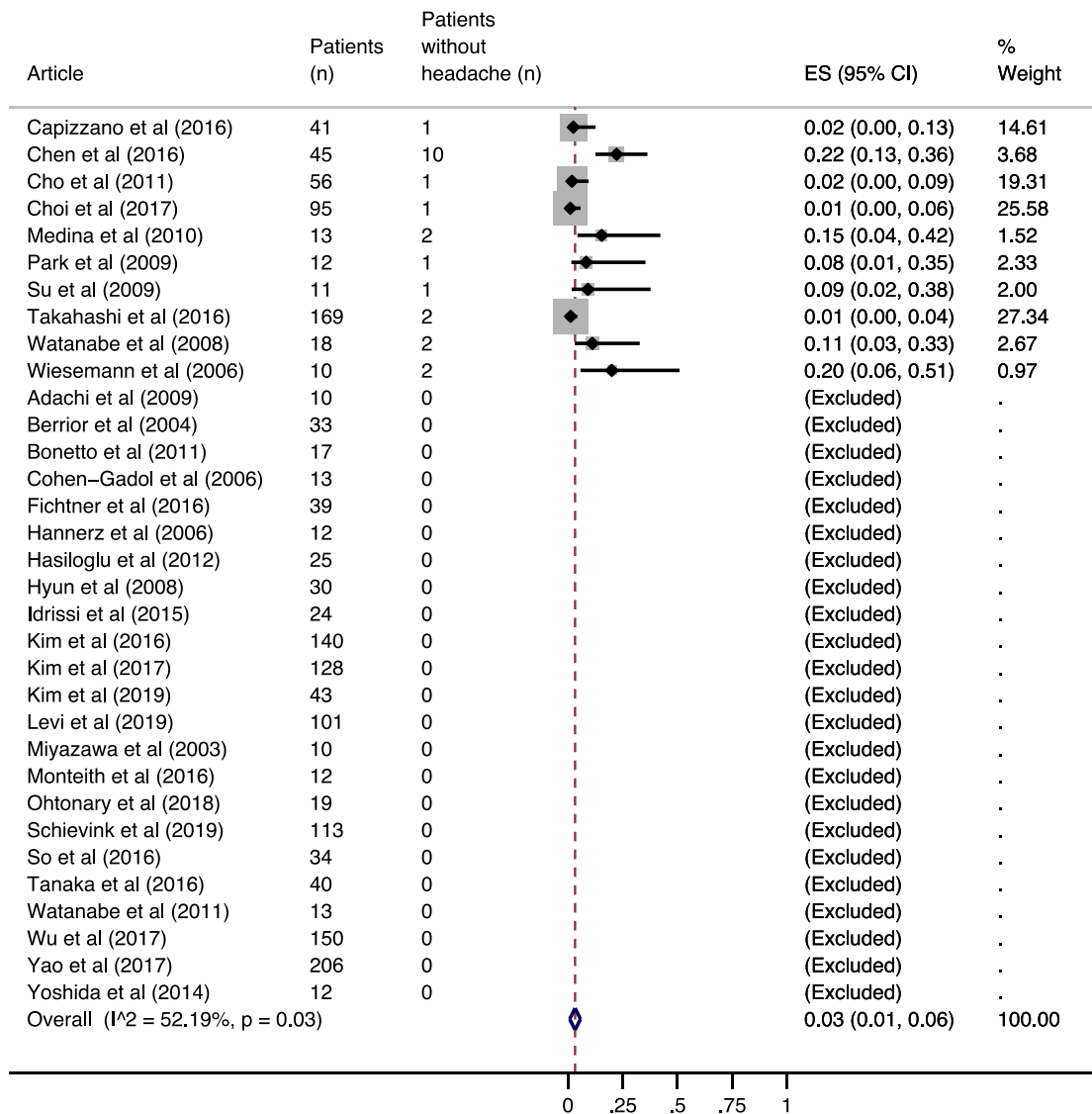
eFigure 4. Symptoms duration meta-analysis (mean days)



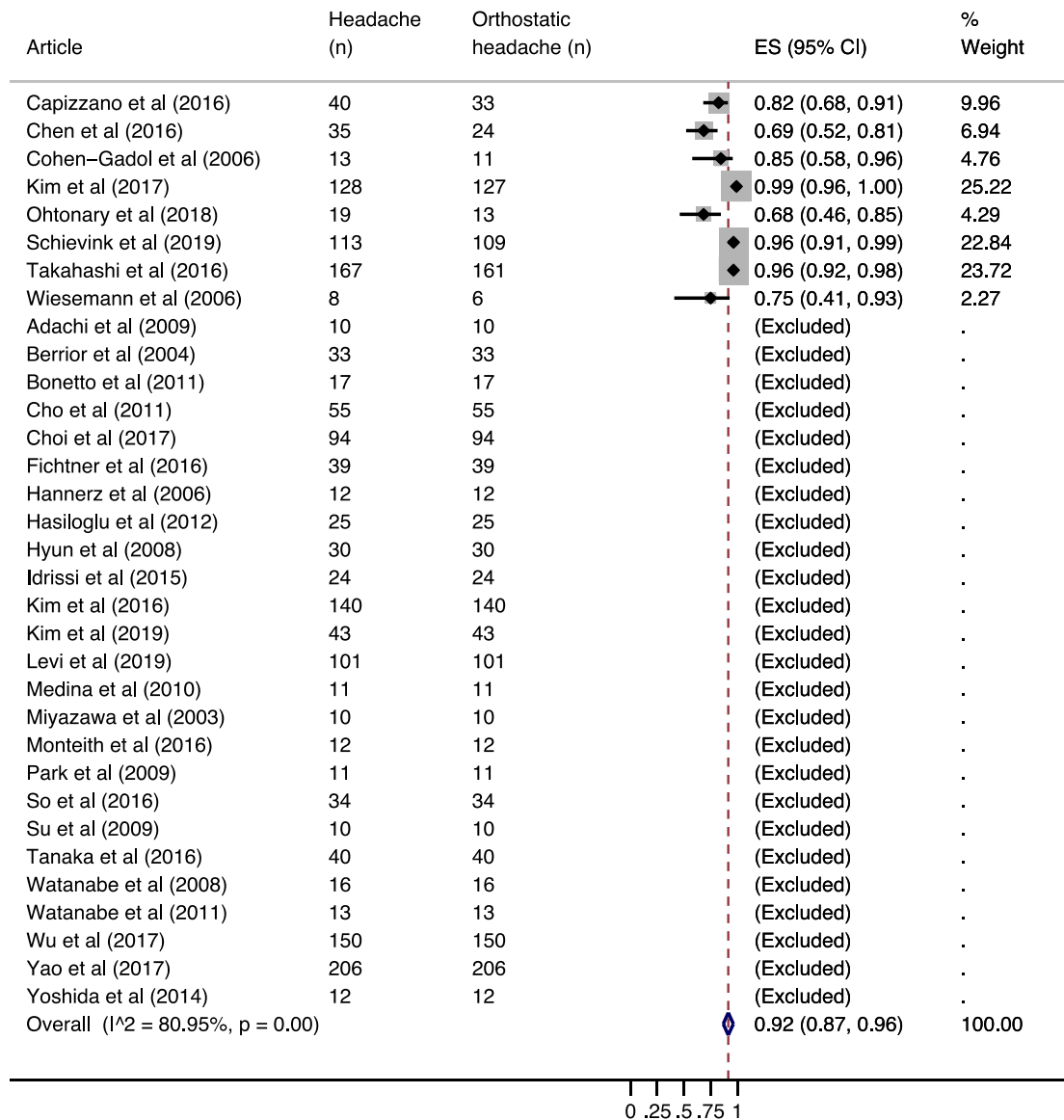
eFigure 5a. Meta-analysis of proportions of patients with headache



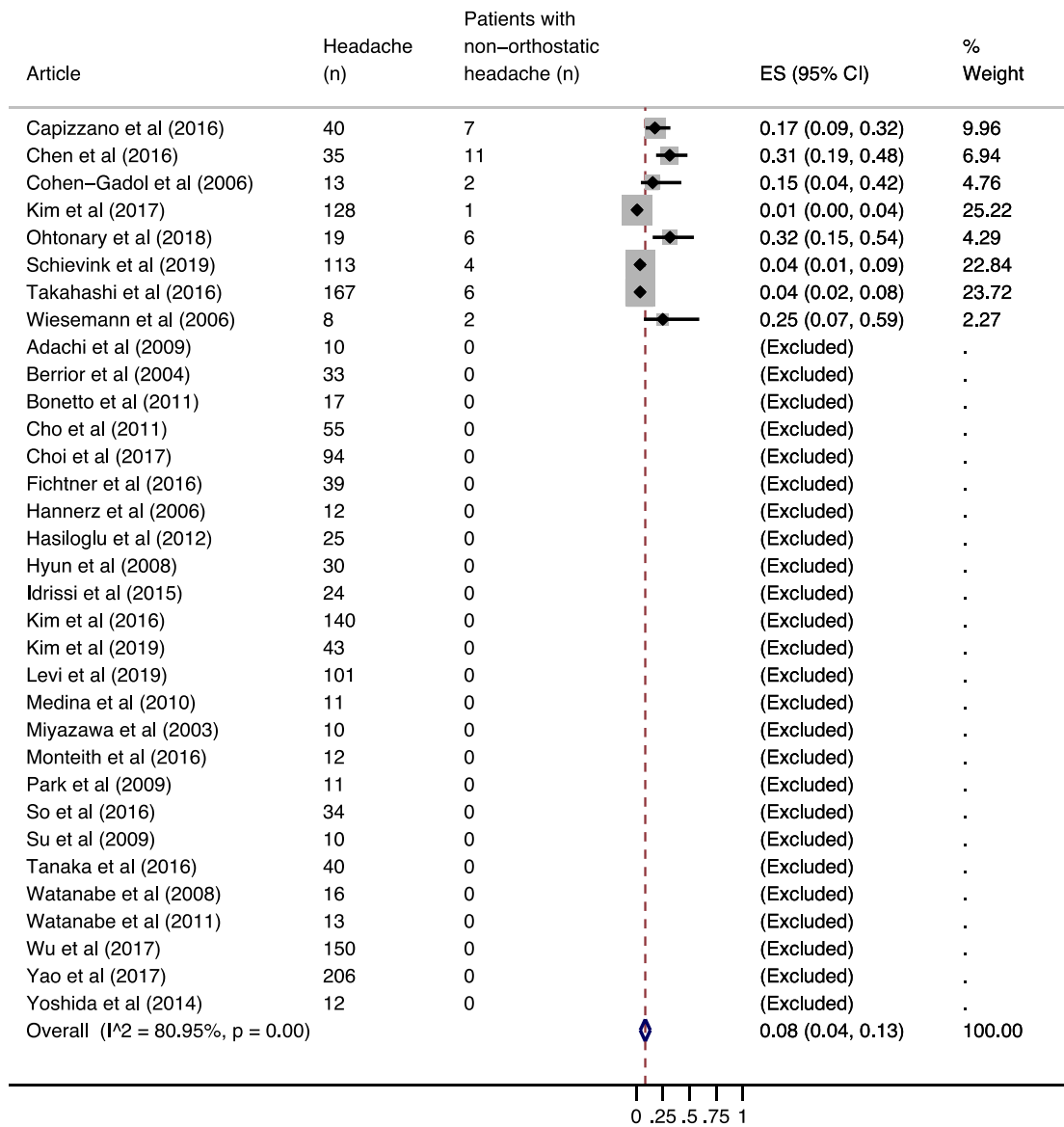
eFigure 5b. Meta-analysis of proportions of patients without headache



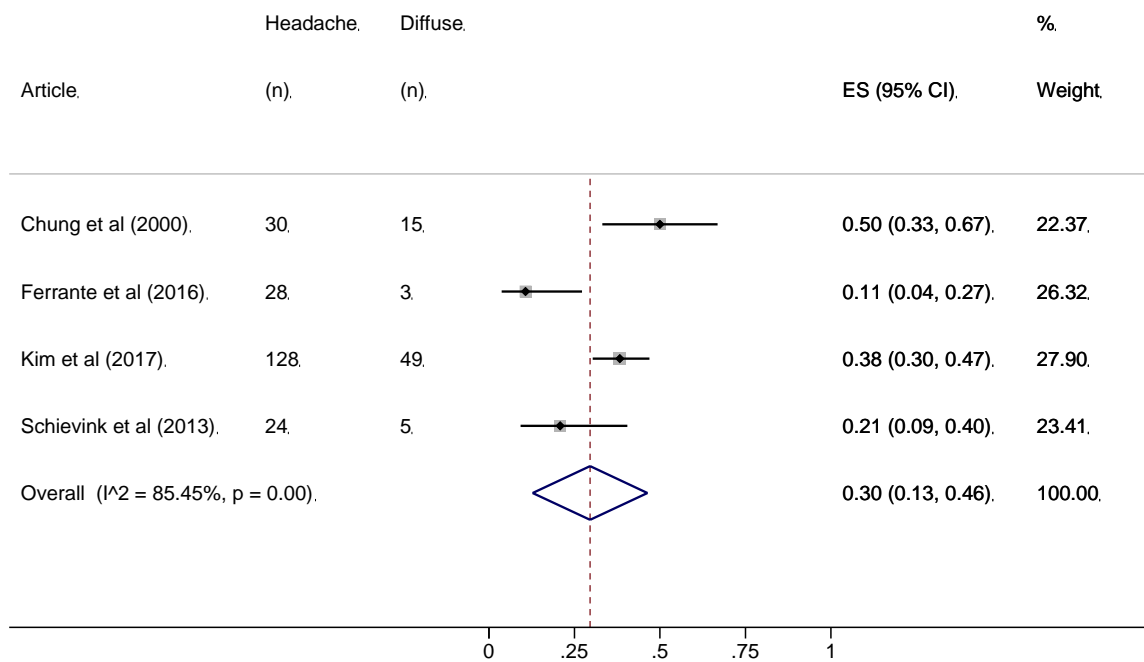
eFigure 6a. Meta-analysis of proportions of patients with orthostatic headache



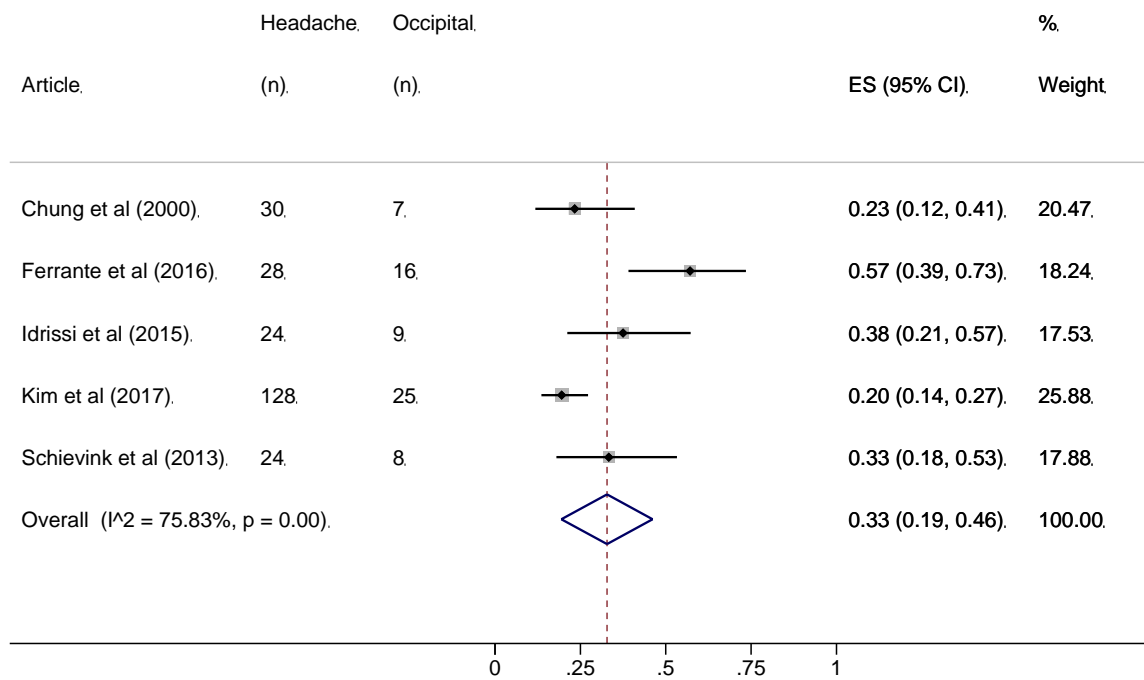
eFigure 6b. Meta-analysis of proportions of patients with non-orthostatic headache



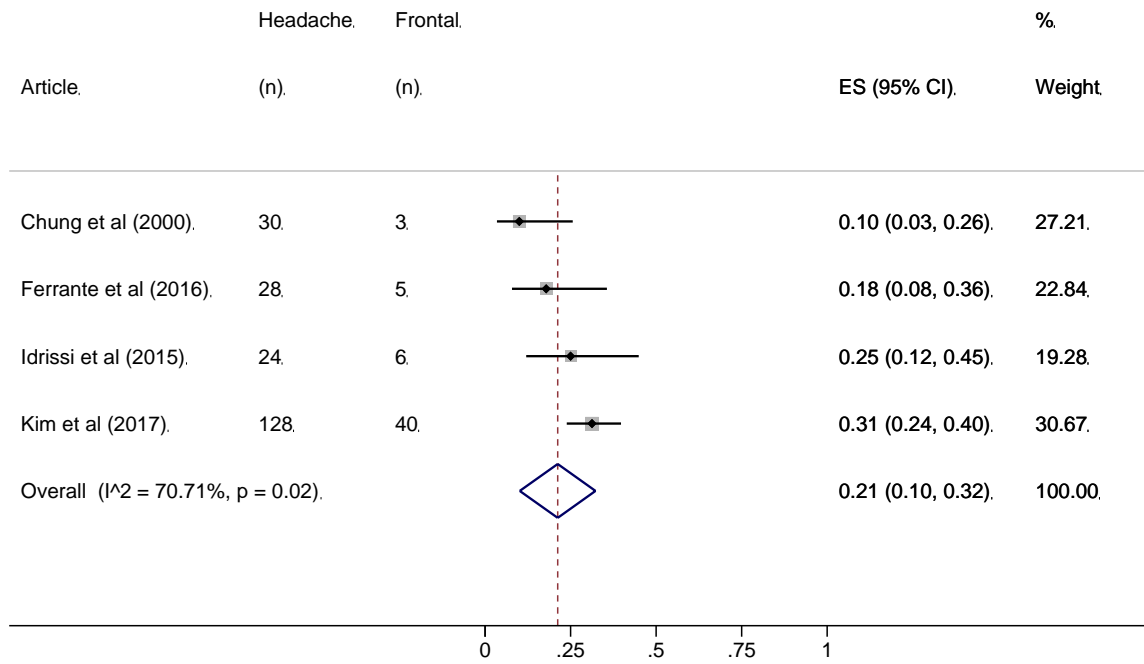
eFigure 7a. Meta-analysis of proportions of headache location (diffuse)



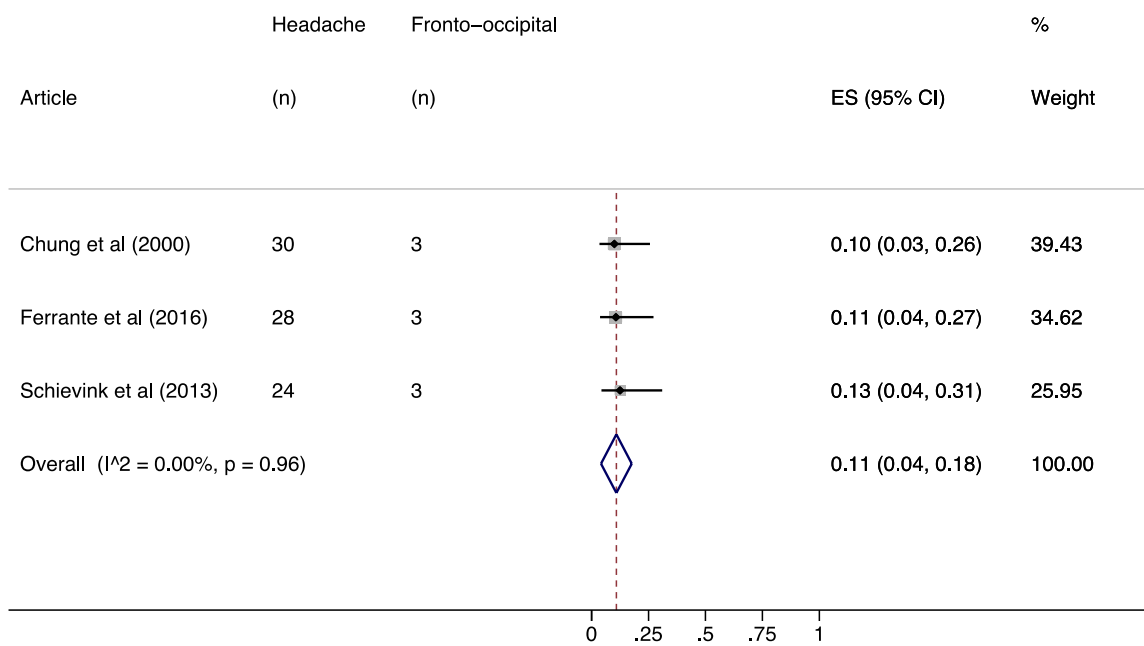
eFigure 7b. Meta-analysis of proportions of headache location (occipital)



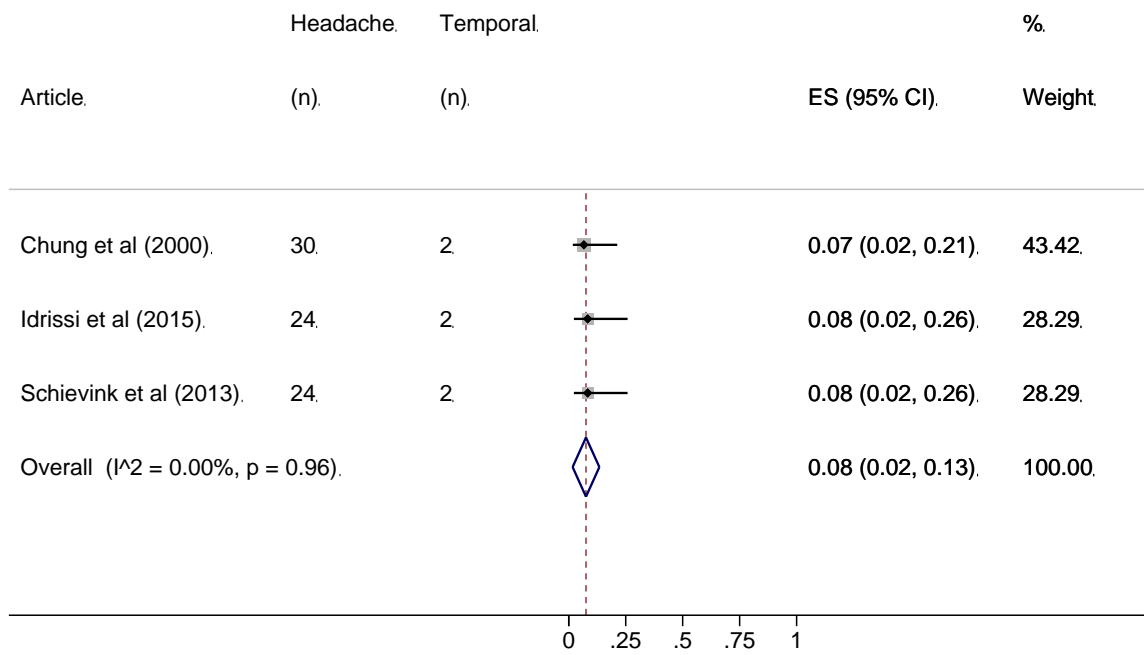
eFigure 7c. Meta-analysis of proportions of headache location (frontal)



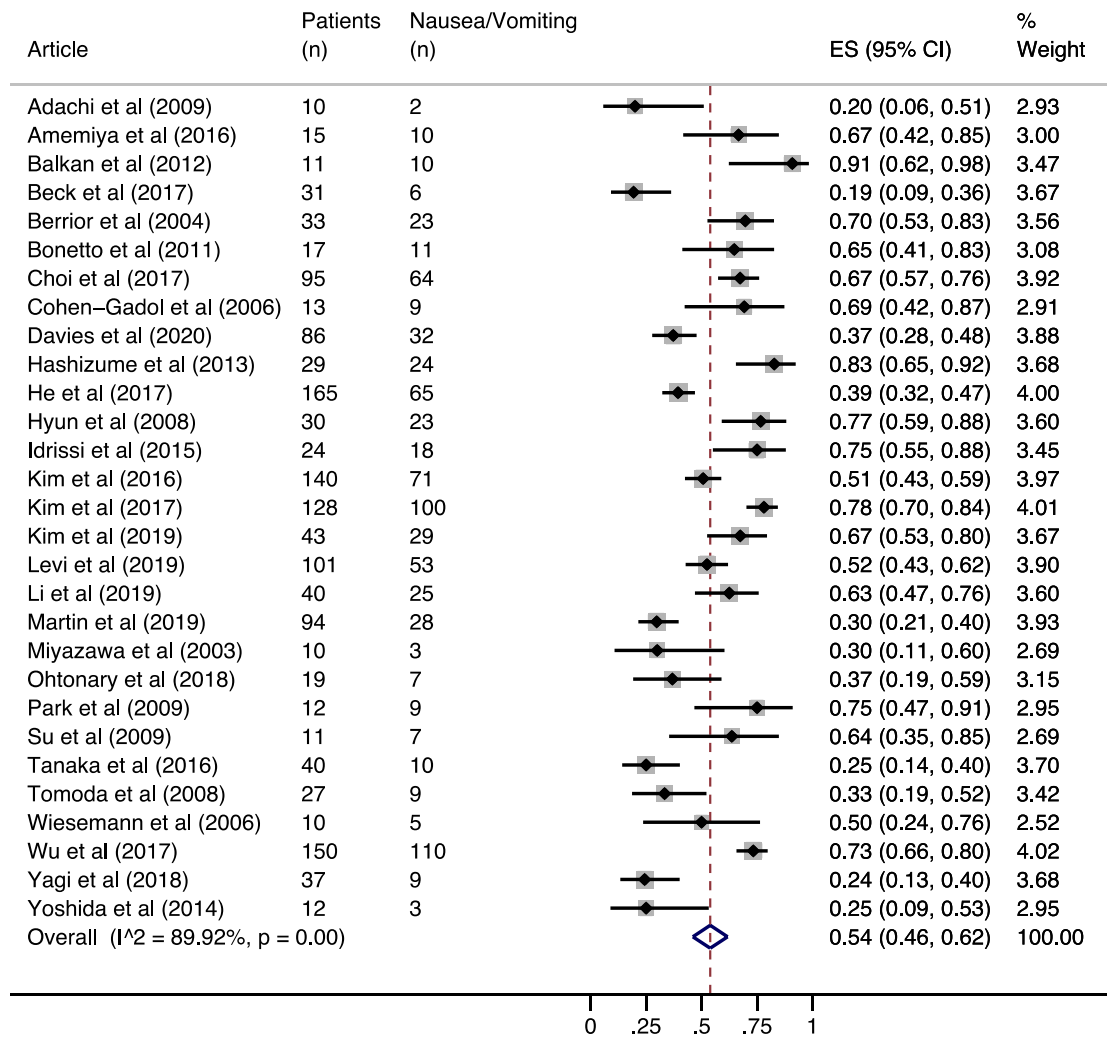
eFigure 7d. Meta-analysis of proportions of headache location (fronto-occipital)



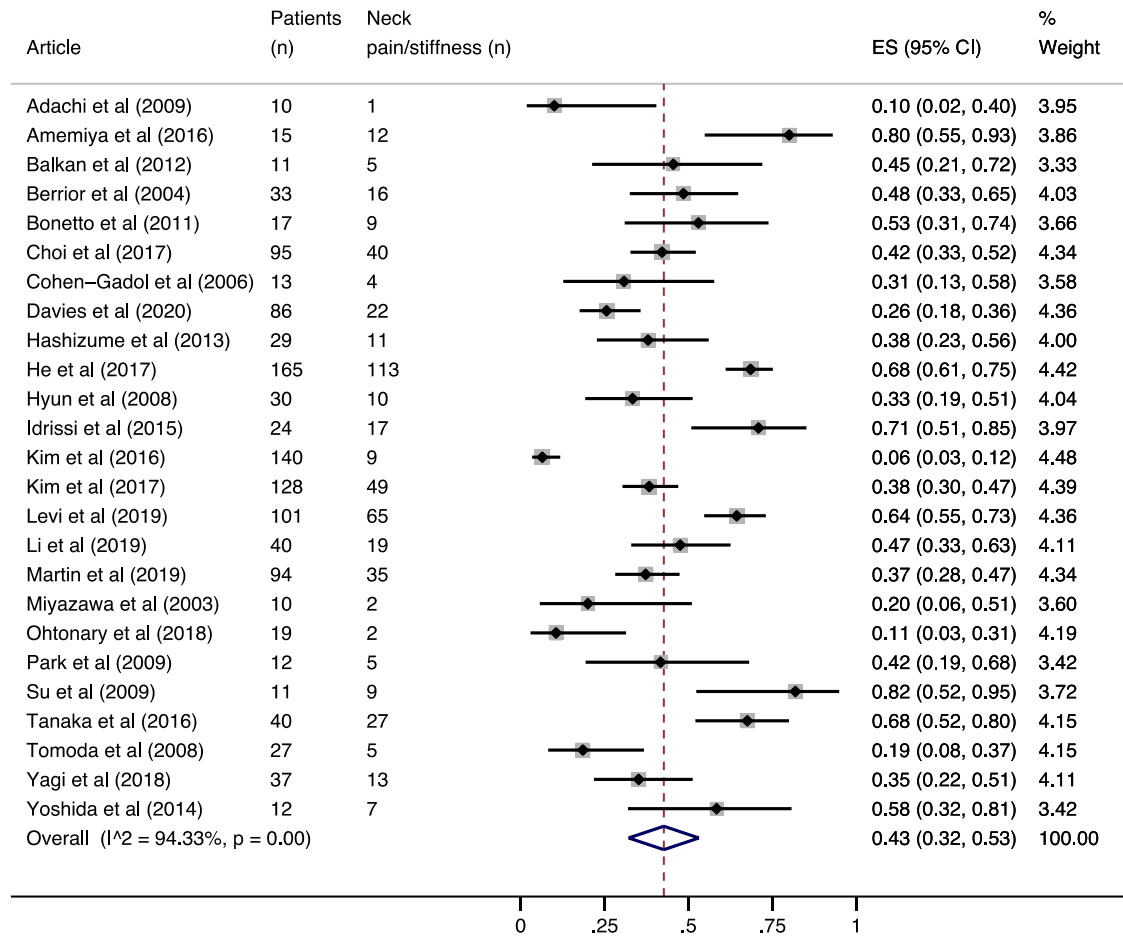
eFigure 7e. Meta-analysis of proportions of headache location (temporal)



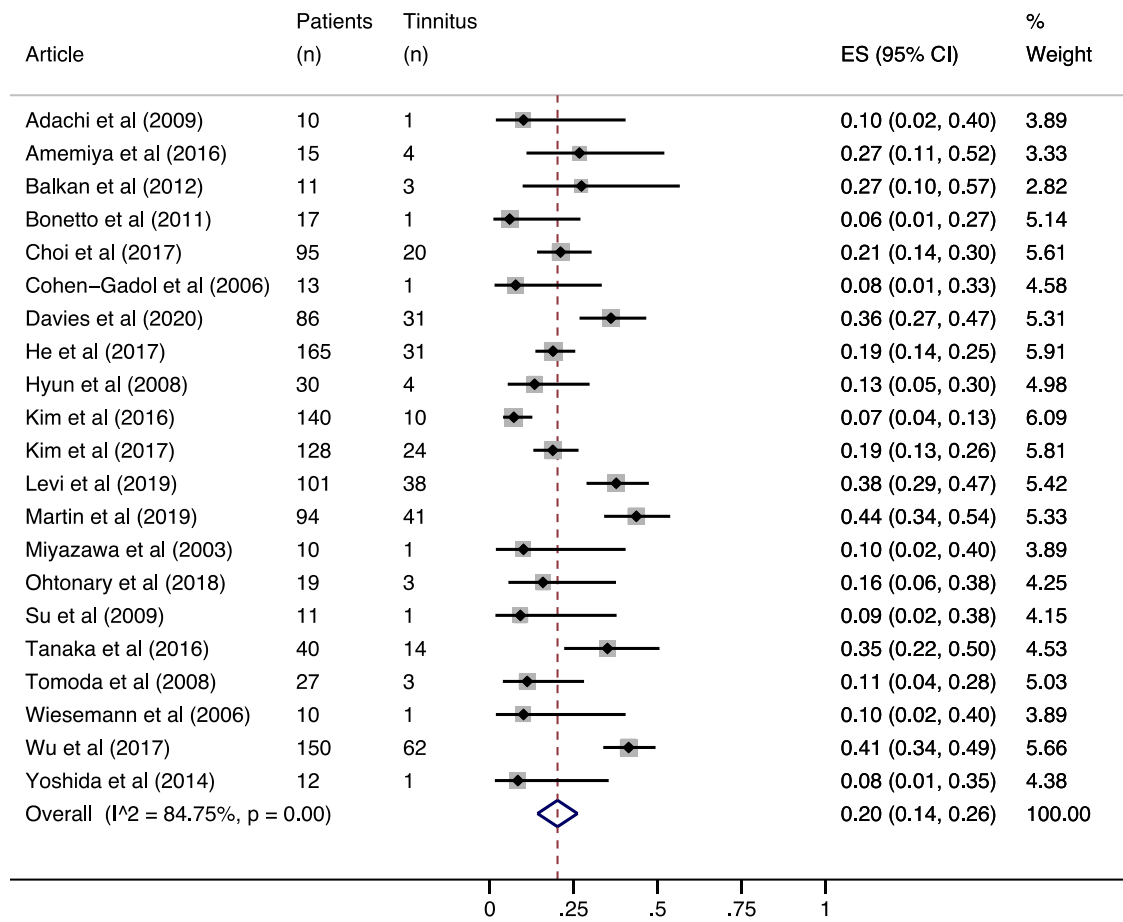
eFigure 8a. Meta-analysis of proportions of patients with nausea/vomiting



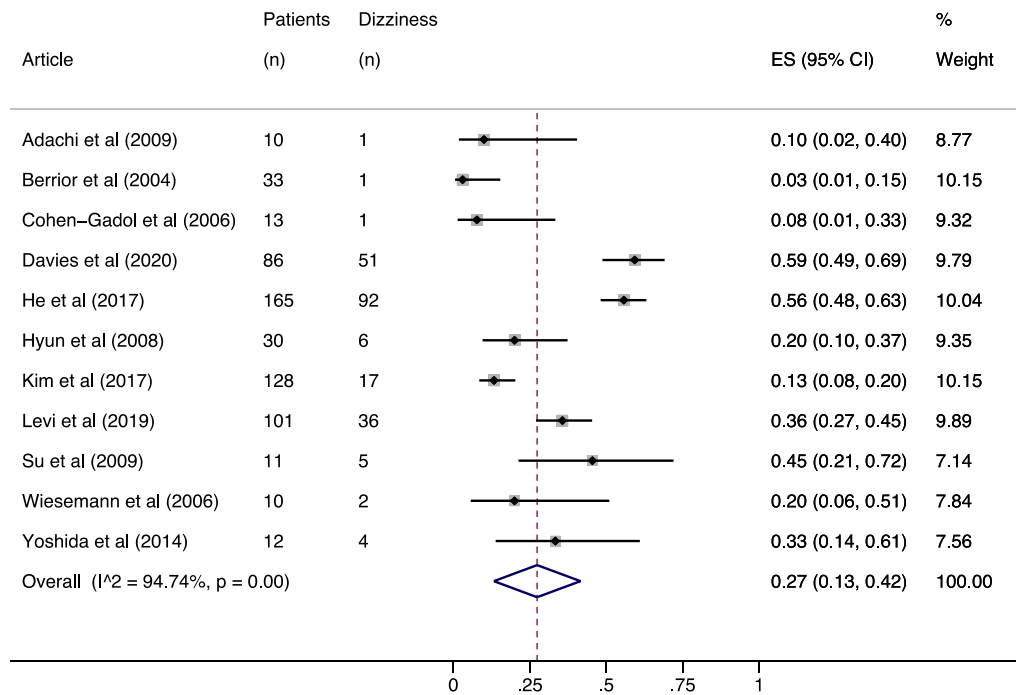
eFigure 8b. Meta-analysis of proportions of patients with neck pain/stiffness



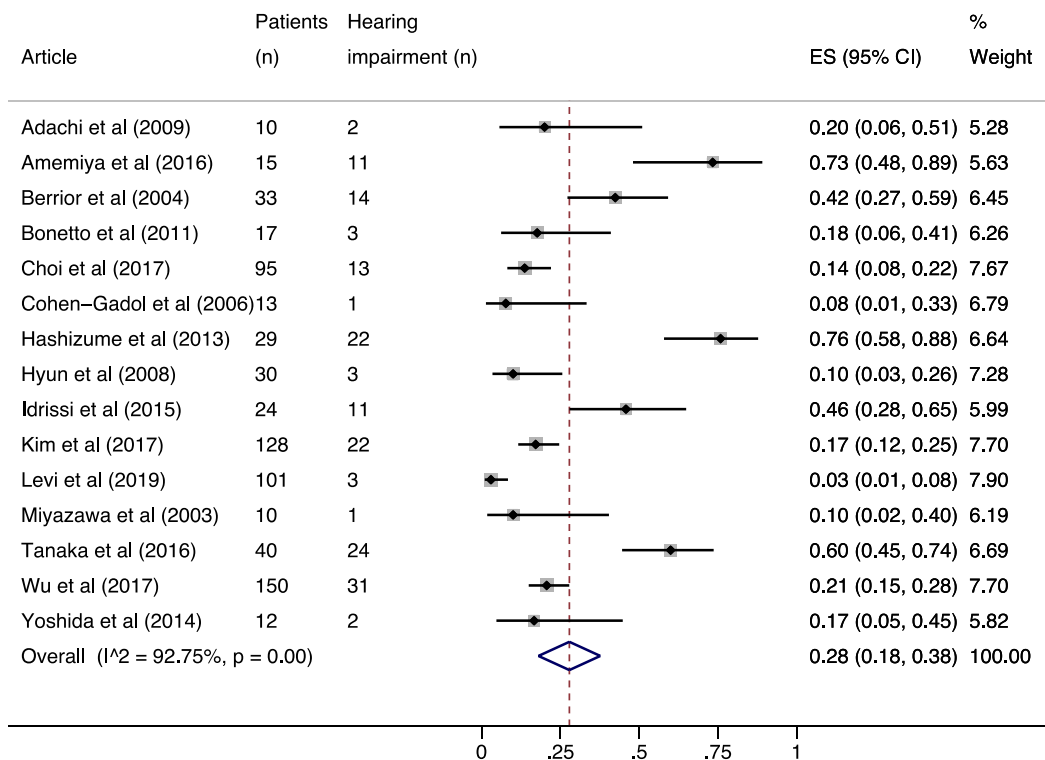
eFigure 8c. Meta-analysis of proportions of patients with tinnitus



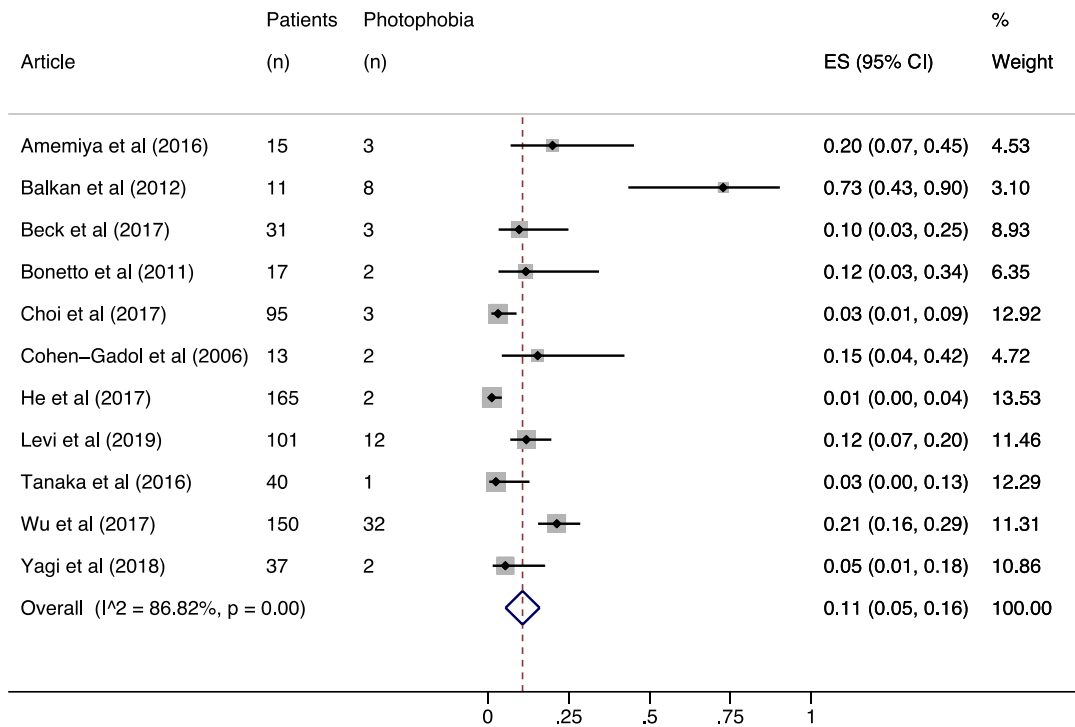
eFigure 8d. Meta-analysis of proportions of patients with dizziness



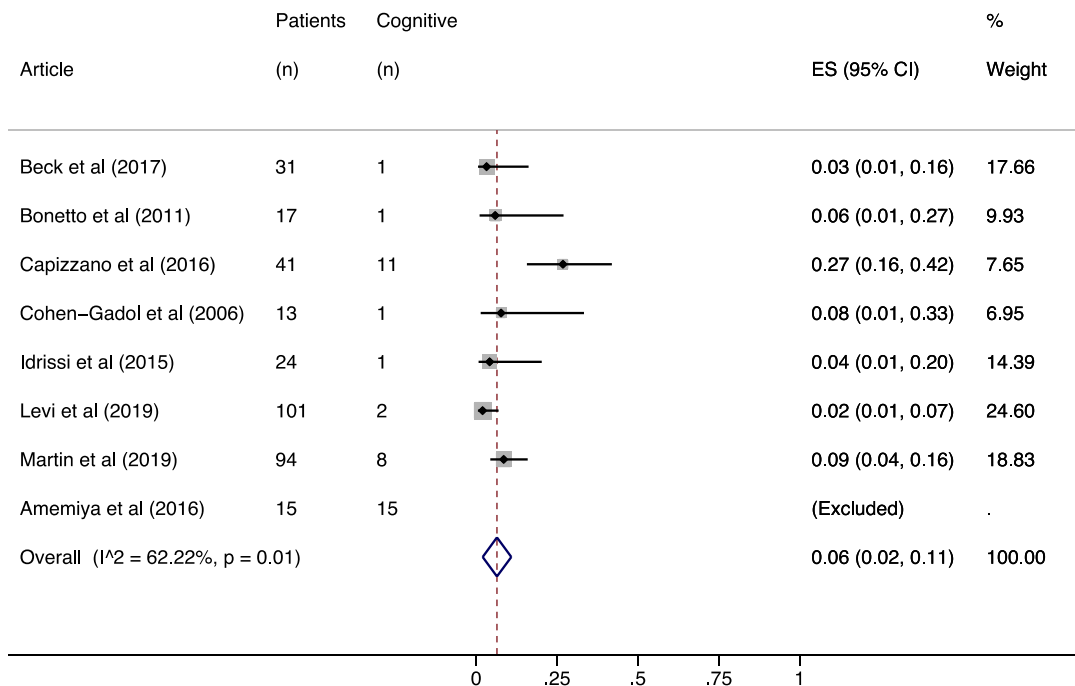
eFigure 8e. Meta-analysis of proportions of patients with hearing disturbances



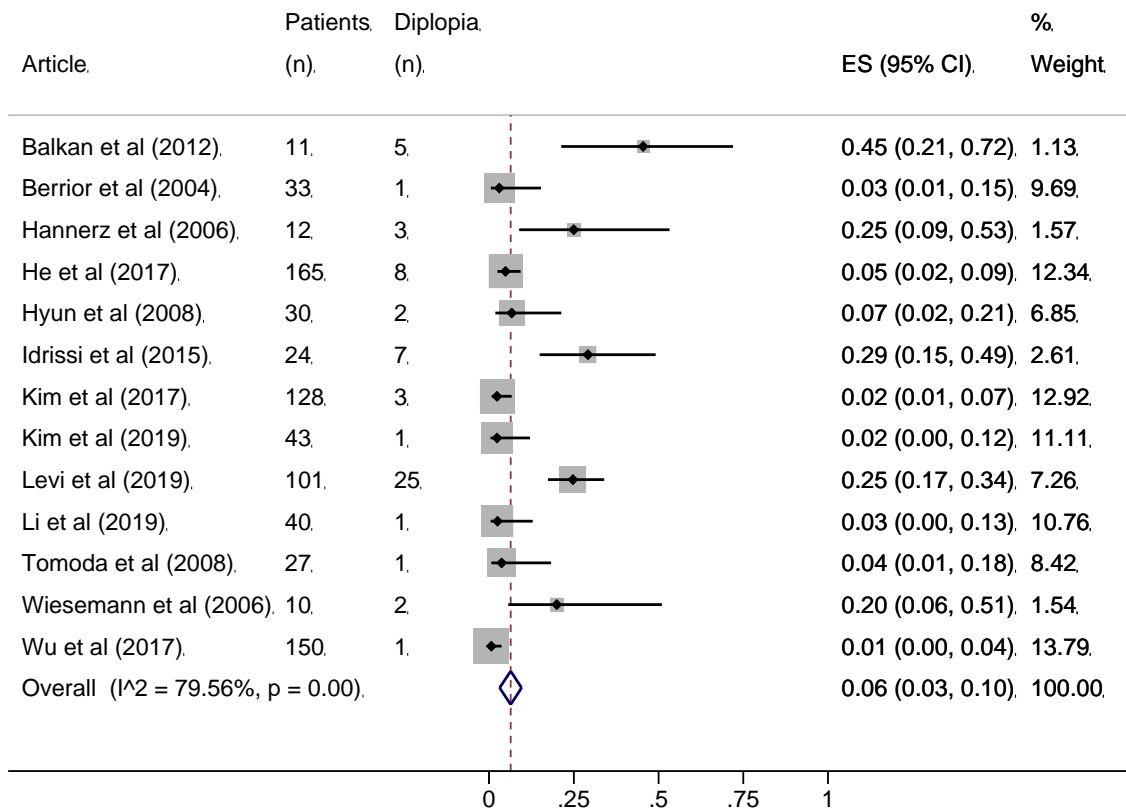
eFigure 8f. Meta-analysis of proportions of patients with photophobia



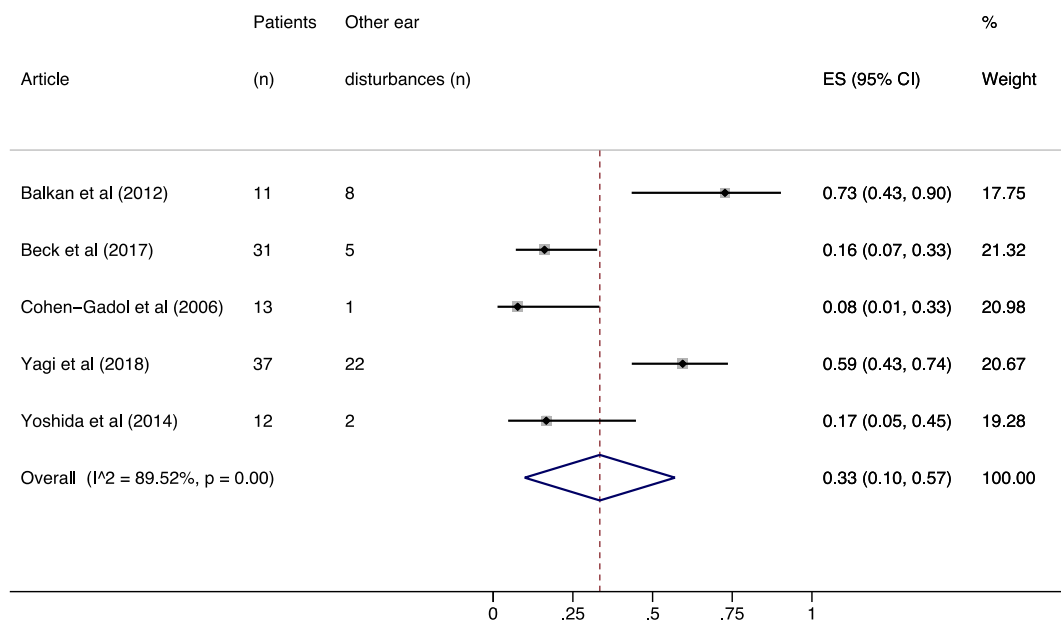
eFigure 8g. Meta-analysis of proportions of patients with cognitive symptoms



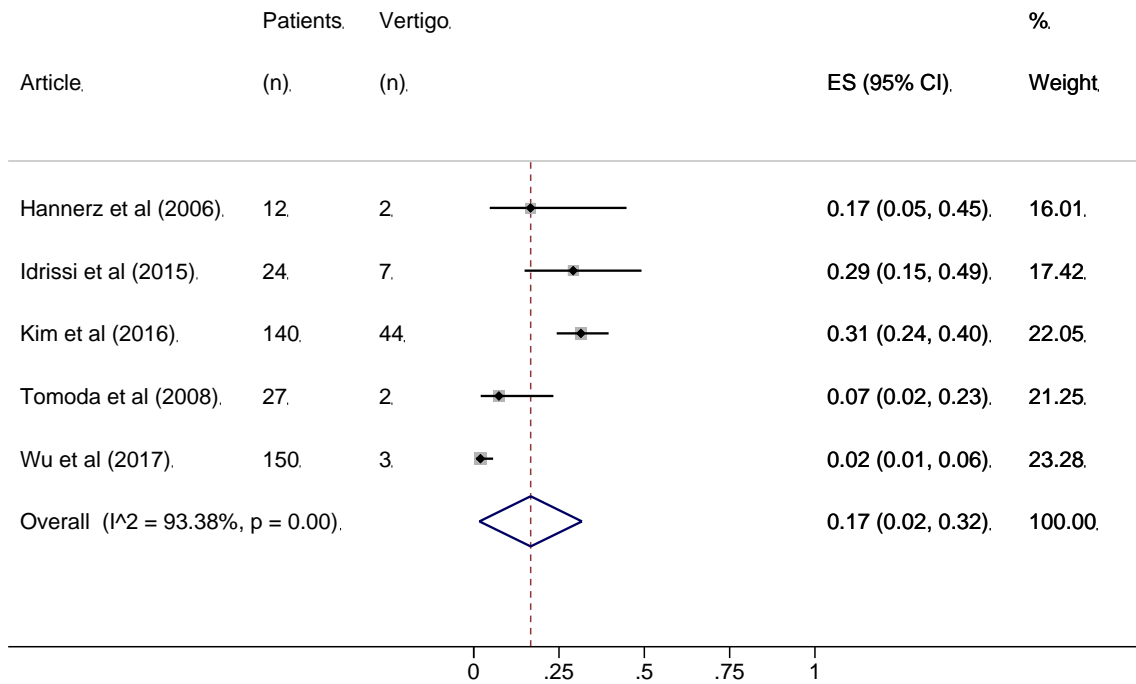
eFigure 8h. Meta-analysis of proportions of patients with diplopia



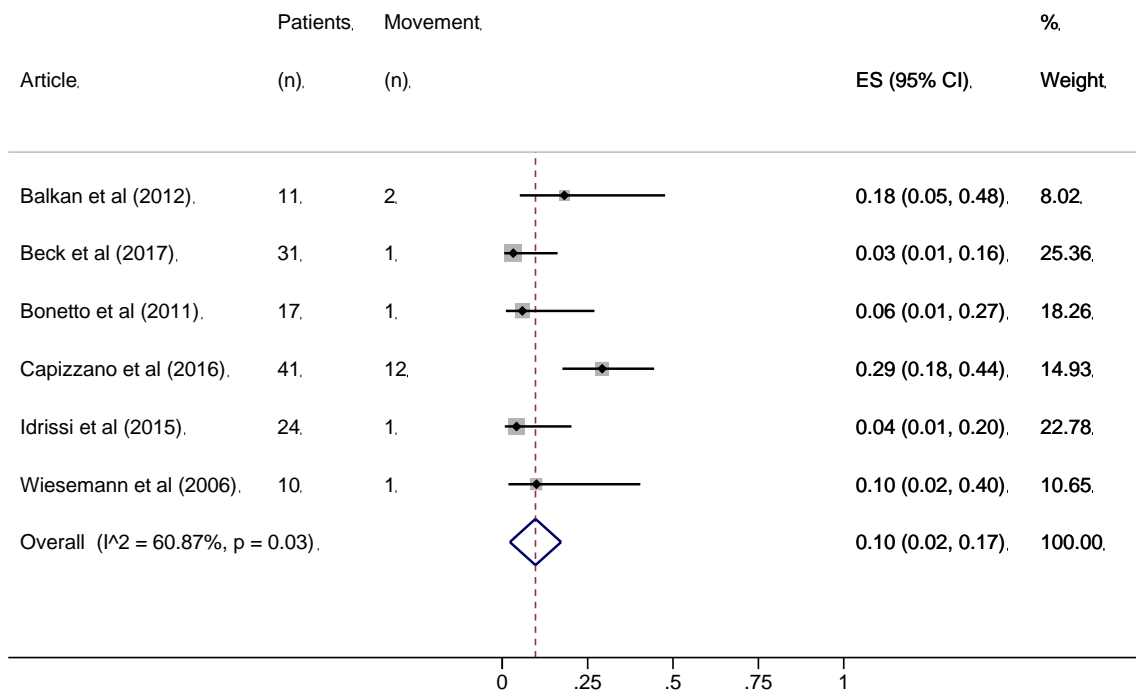
eFigure 8i. Meta-analysis of proportions of patients with other ear-related symptoms



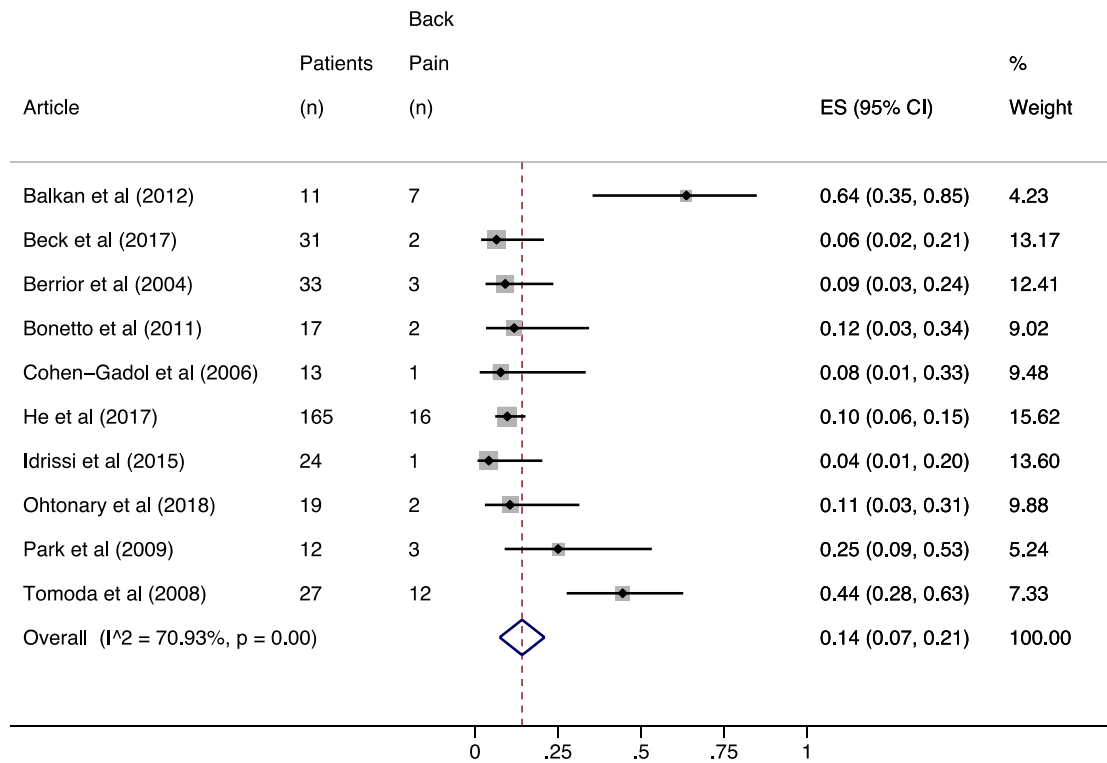
eFigure 8l. Meta-analysis of proportions of patients with vertigo



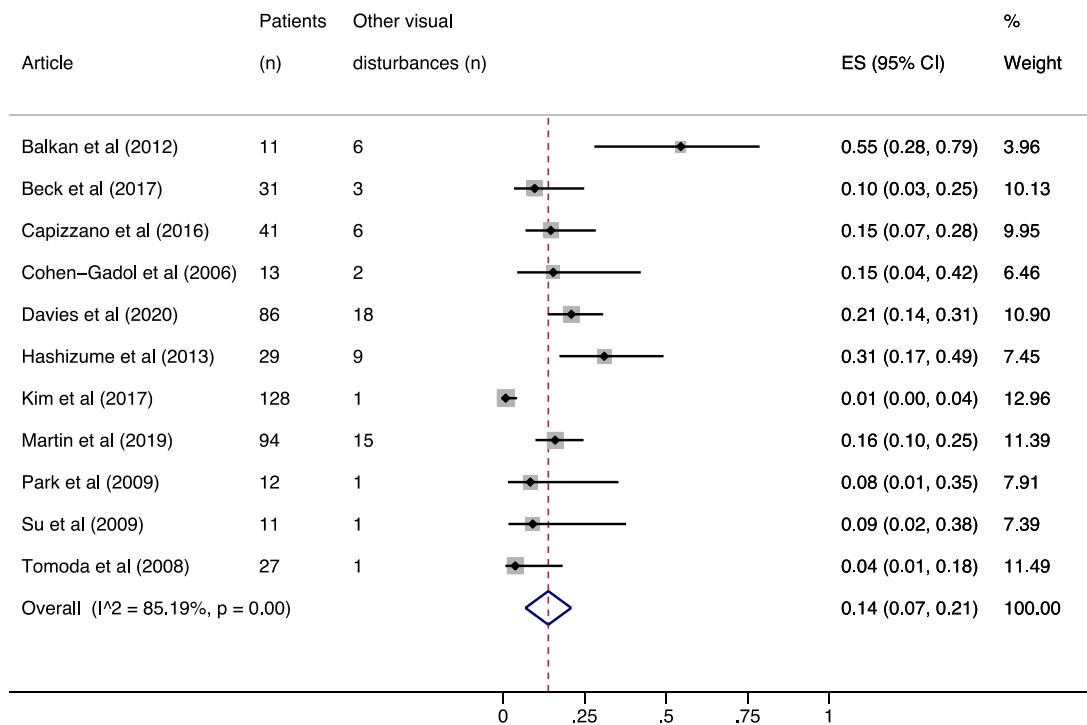
eFigure 8m. Meta-analysis of proportions of patients with movement disorders



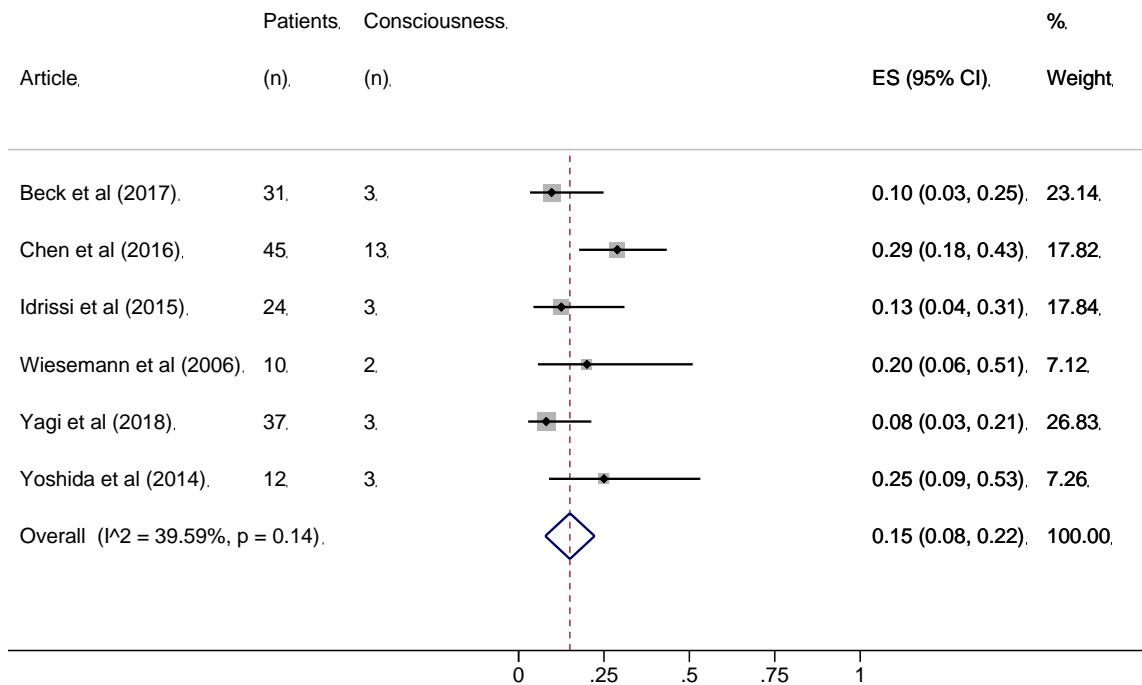
eFigure 8n. Meta-analysis of proportions of patients with back pain



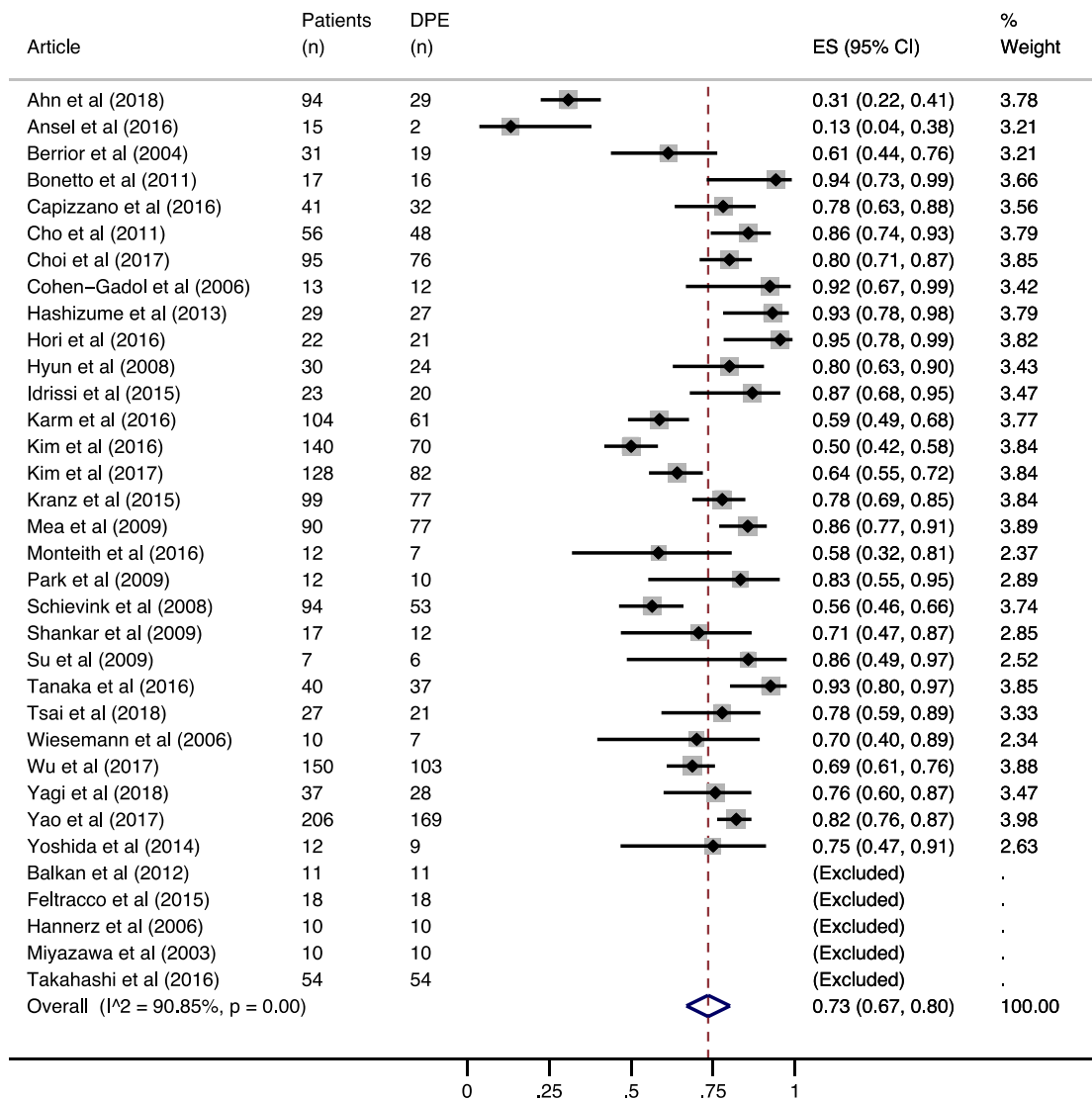
eFigure 8o. Meta-analysis of proportions of patients with other visual symptoms



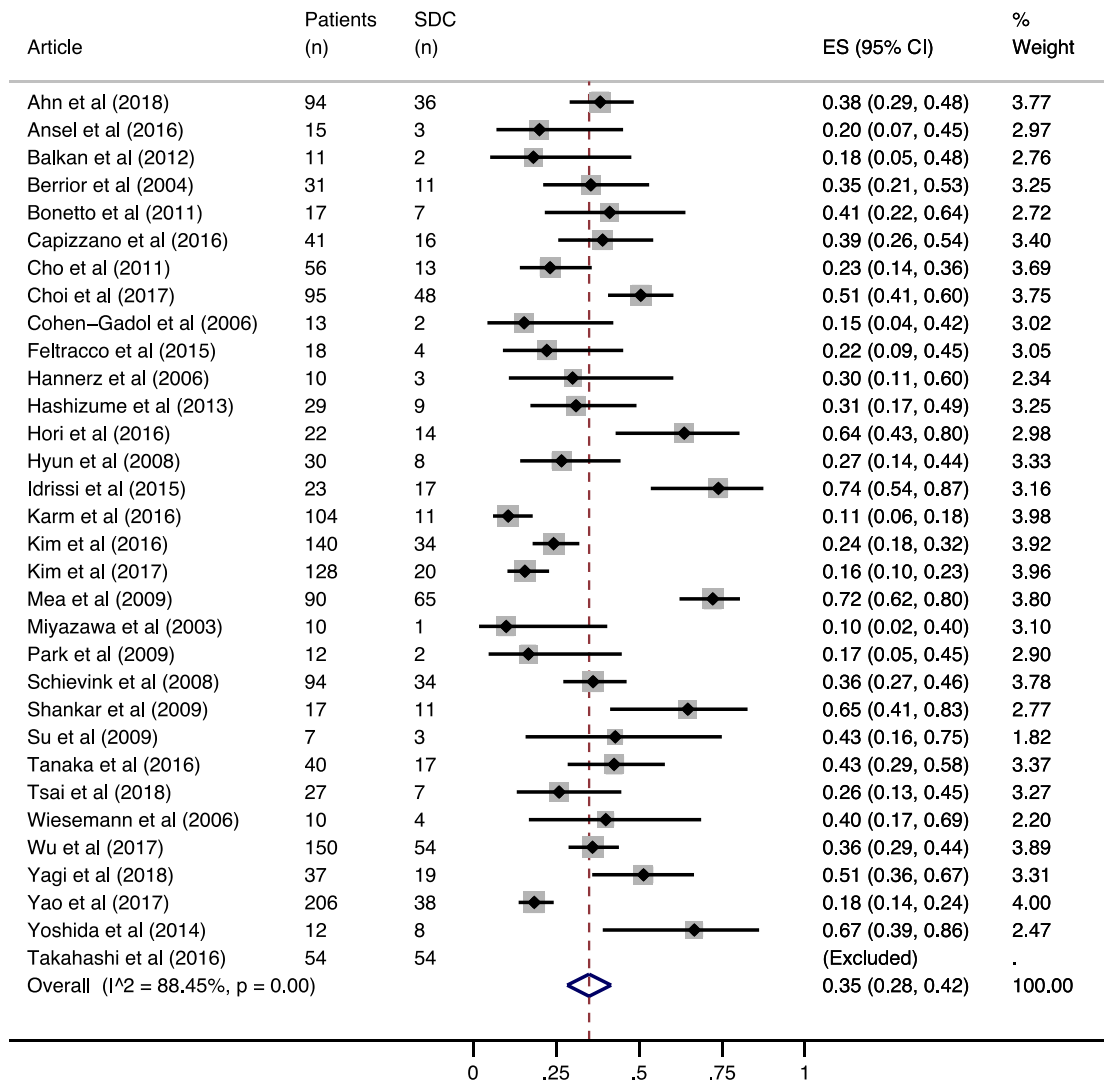
eFigure 8p. Meta-analysis of proportions of patients with reduced consciousness



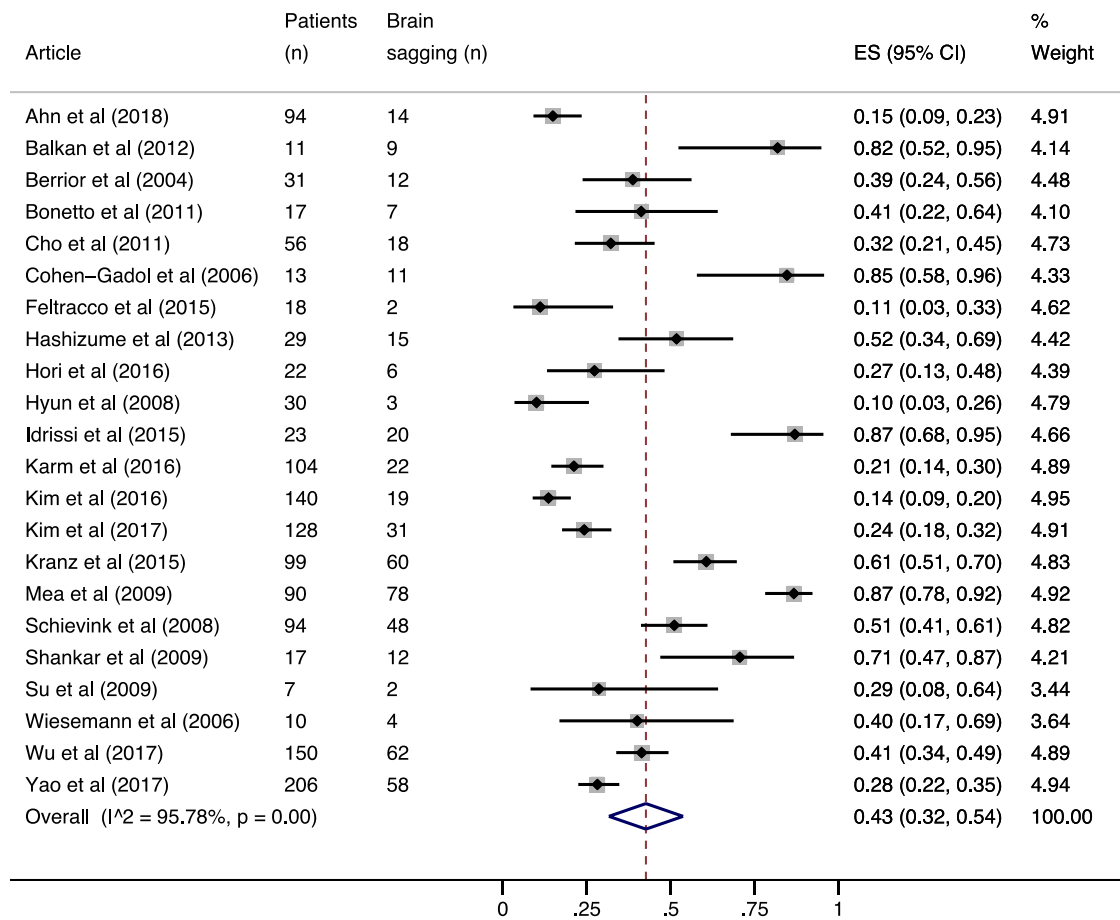
eFigure 9a. Meta-analysis of proportions of diffuse pachymeningeal enhancement (DPE) in brain MRI



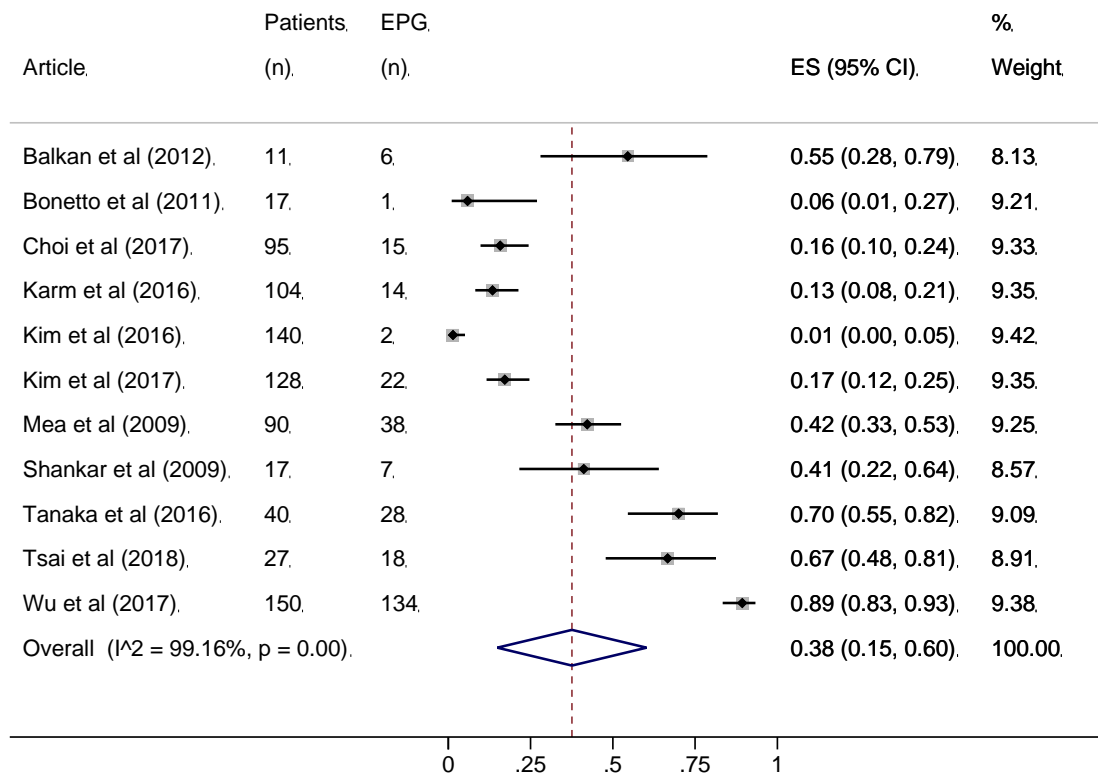
eFigure 9b. Meta-analysis of proportions of subdural collections (SDC) in brain MRI



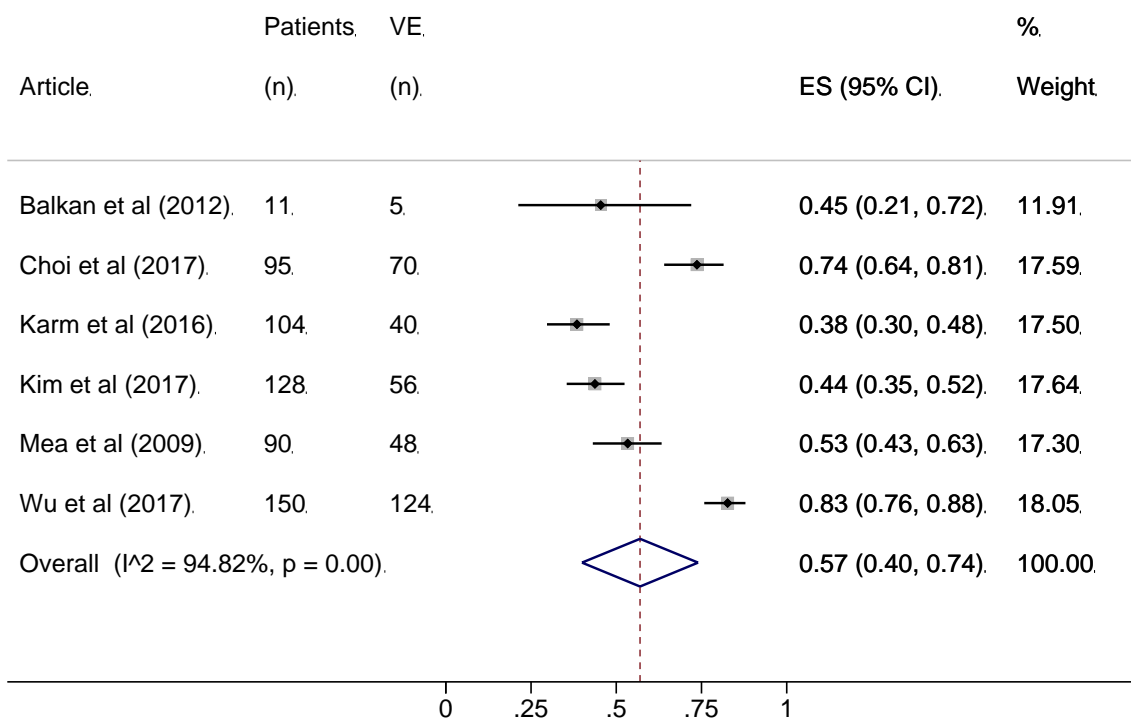
eFigure 9c. Meta-analysis of proportions of brain sagging brain MRI



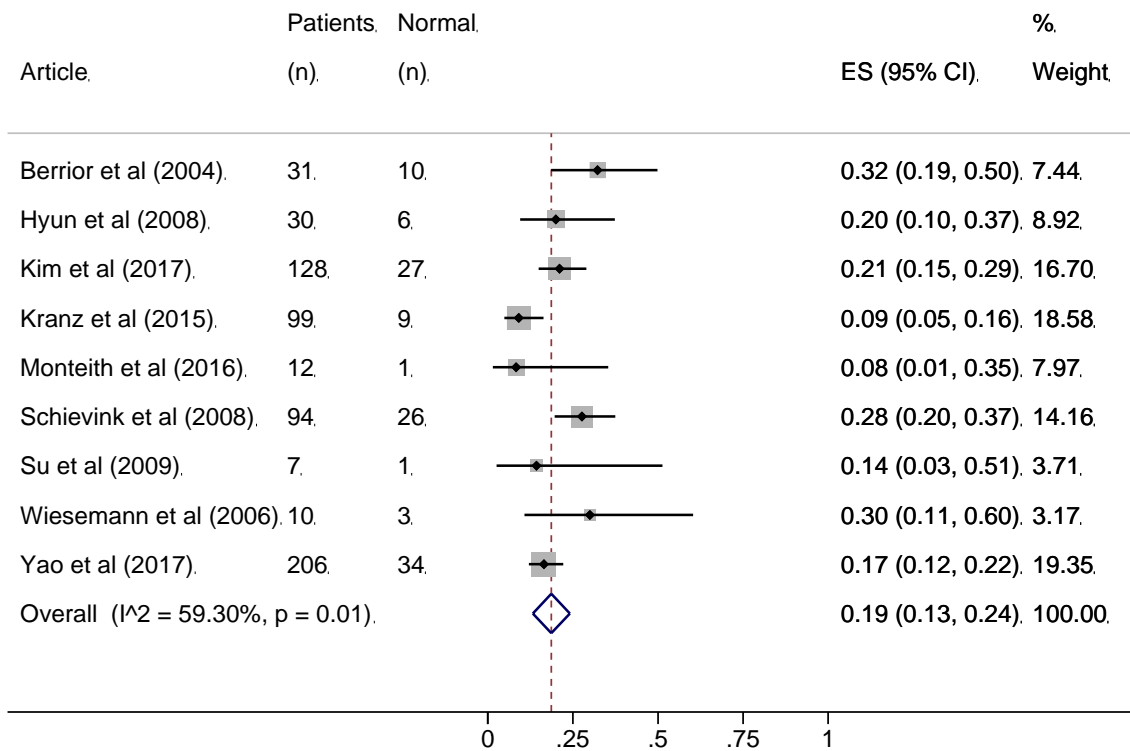
eFigure 9d. Meta-analysis of proportions of enlarged pituitary gland (EPG) in brain MRI



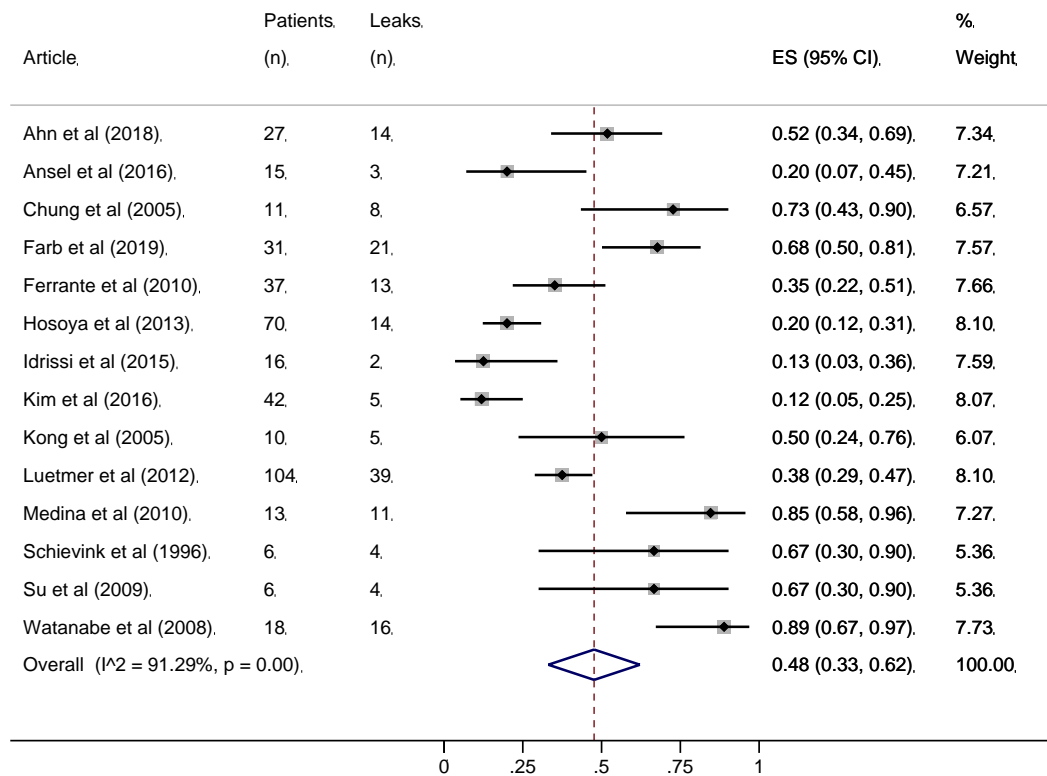
eFigure 9e. Meta-analysis of proportions of venous engorgement in brain MRI



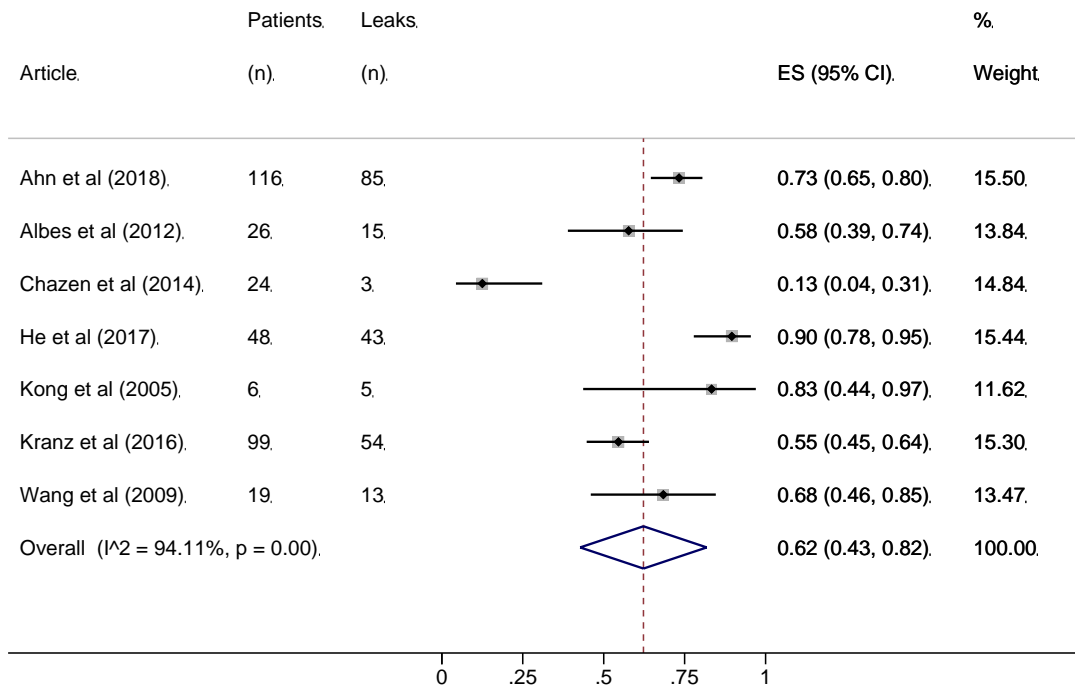
eFigure 9f. Meta-analysis of proportions of normal brain MRI



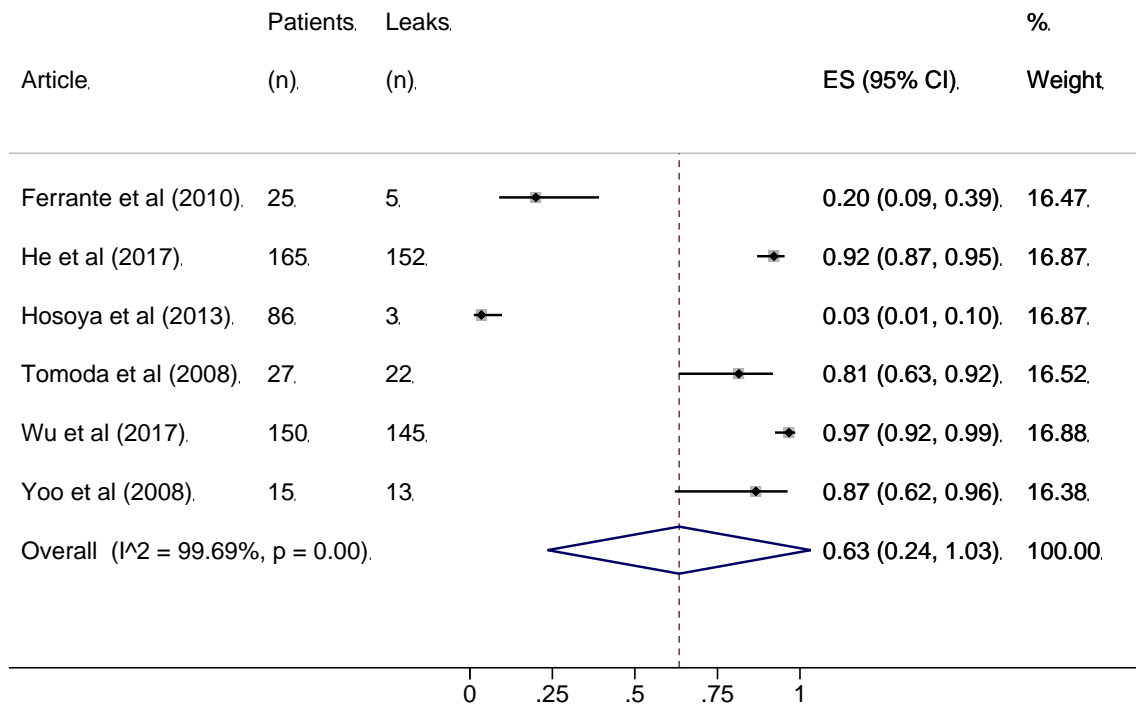
eFigure 10. Meta-analysis of proportions of positive findings in spinal MRI



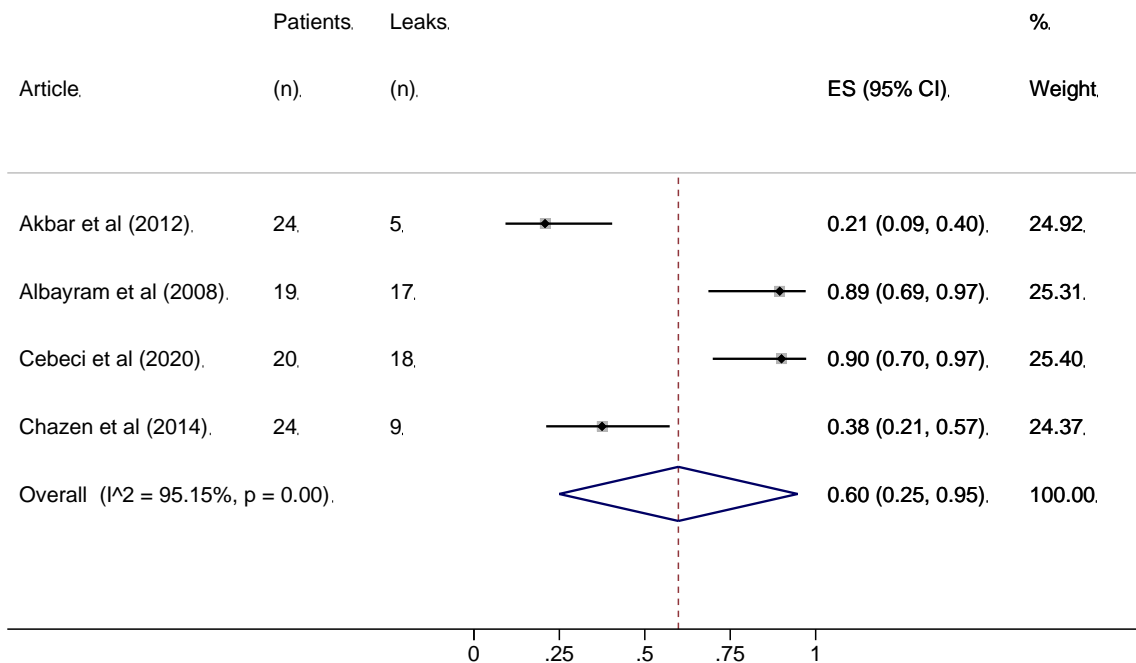
eFigure 11. Meta-analysis of proportions of positive findings in CT myelography (CTM)



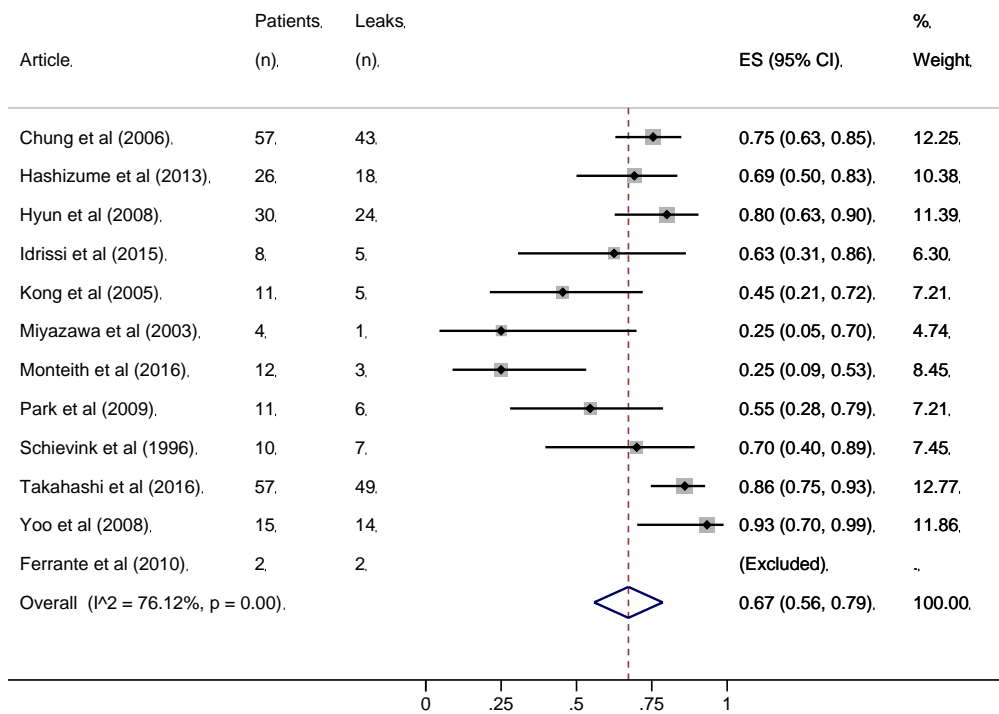
eFigure 12. Meta-analysis of proportions of positive findings in MR myelography



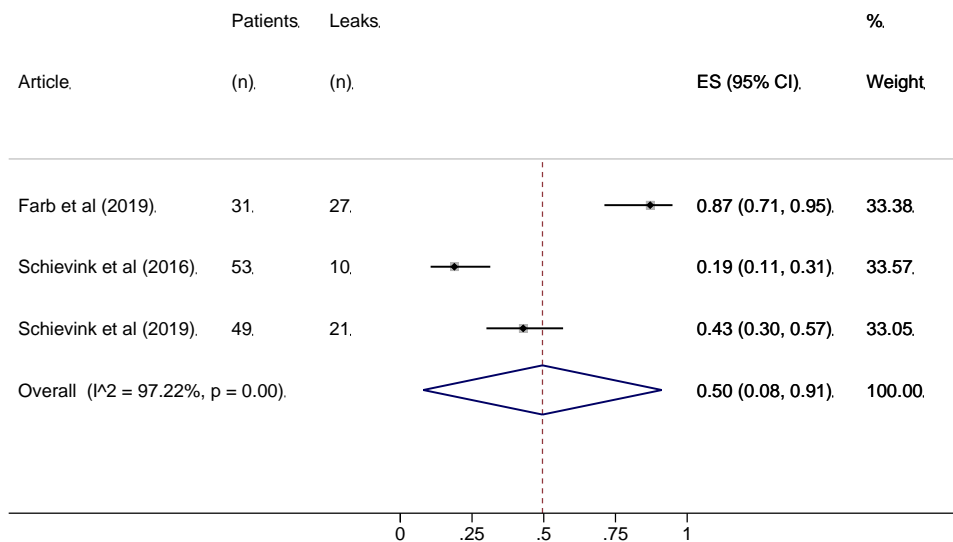
eFigure 13. Meta-analysis of proportions of positive findings in MR myelography with intrathecal gadolinium



eFigure 14. Meta-analysis of proportions of positive findings in radionuclide cisternography

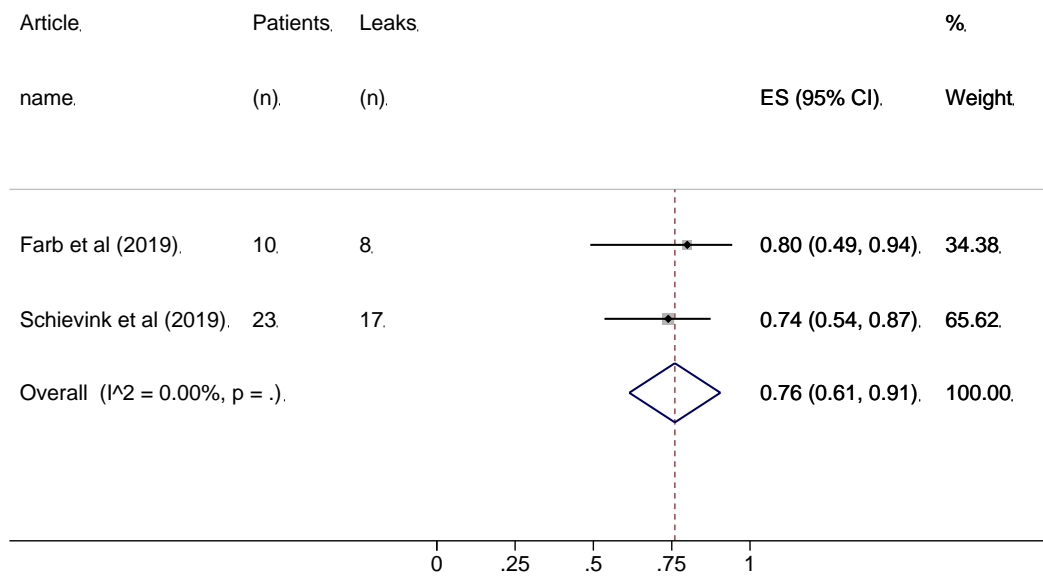


eFigure 15. Meta-analysis of proportions of positive findings in digital subtraction myelography

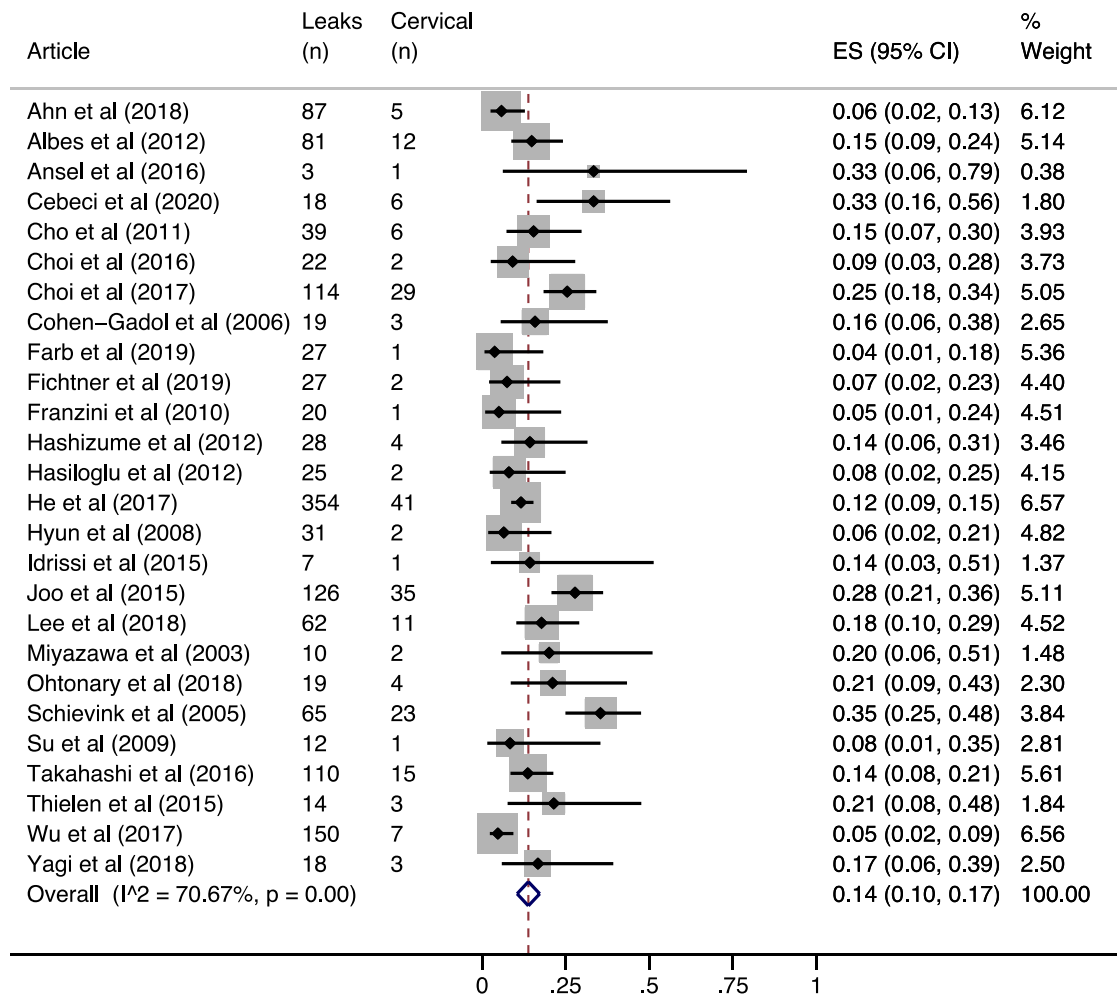


The two studies by Schievink *et al.* have clearly been reported to come from different groups of patients, therefore, they were both eligible for the meta-analysis.

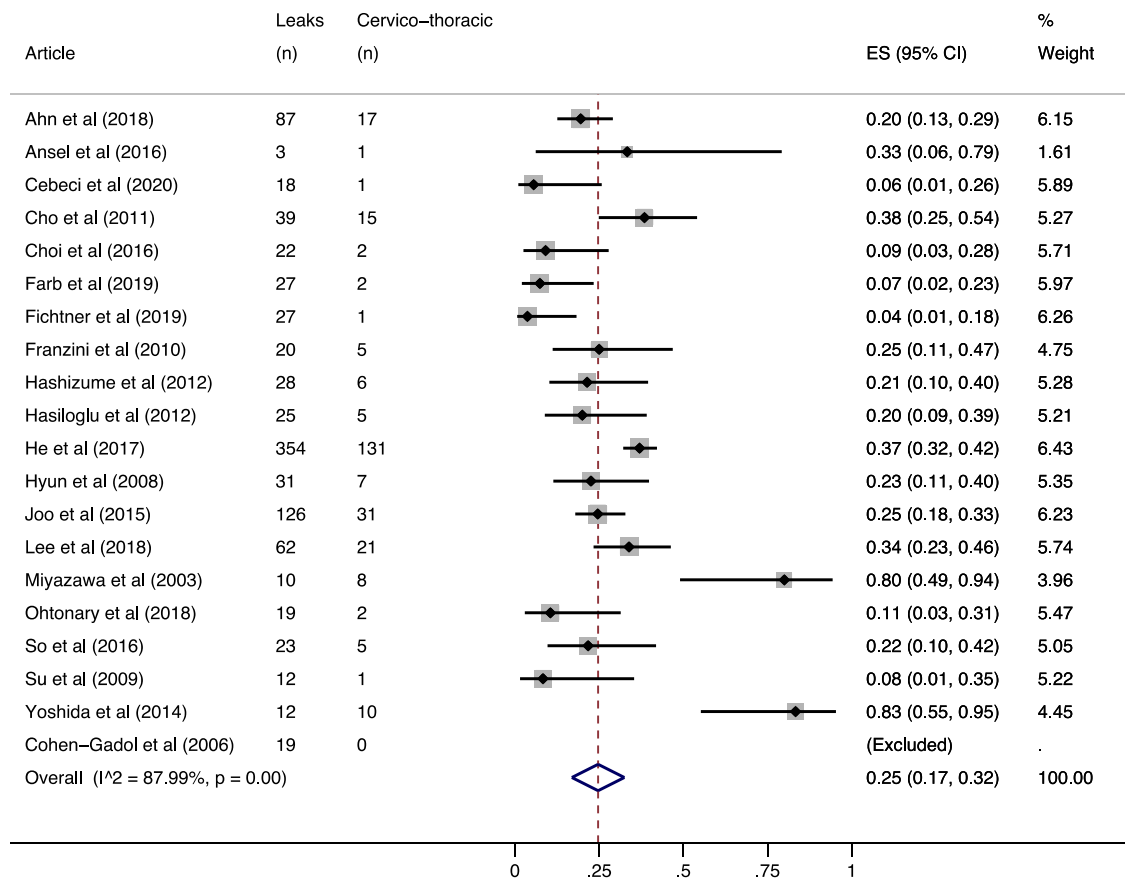
eFigure 16. Meta-analysis of proportions of positive findings in digital subtraction myelography performed in lateral decubitus position



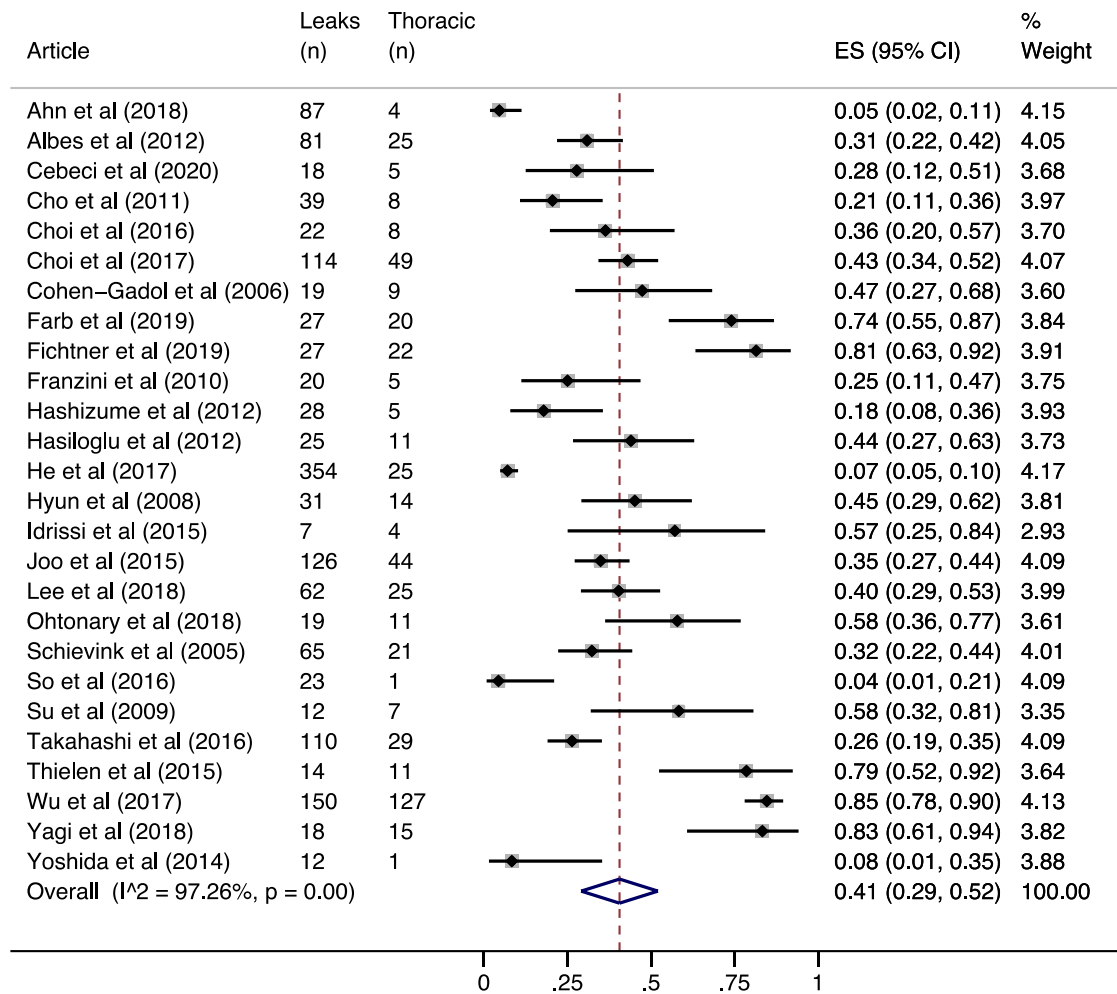
eFigure 17a. Meta-analysis of proportions of leak location (cervical)



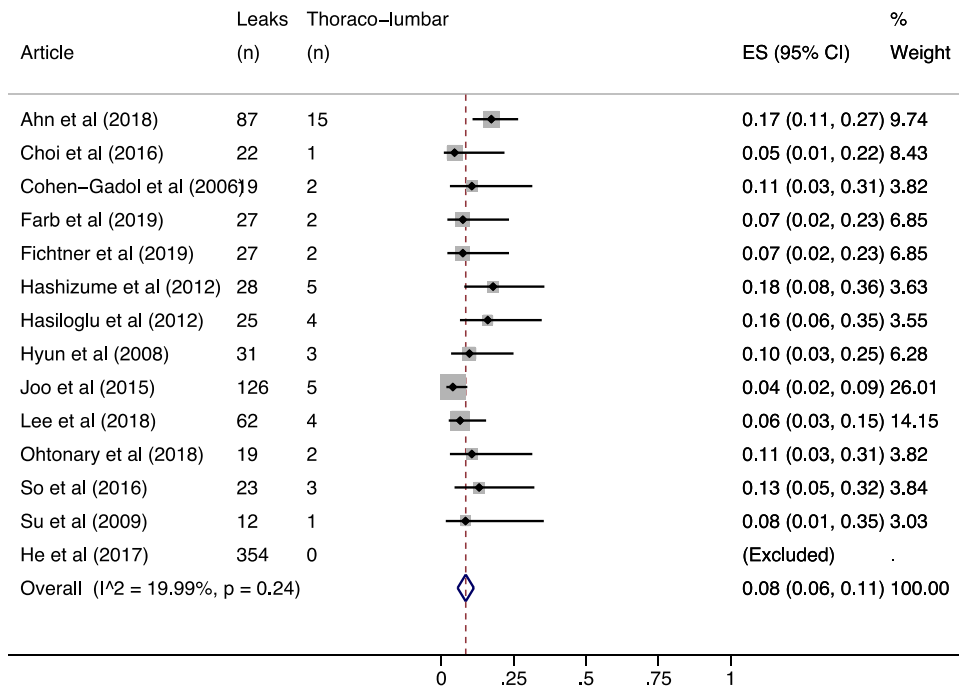
eFigure 17b. Meta-analysis of proportions of leak location (cervico-thoracic)



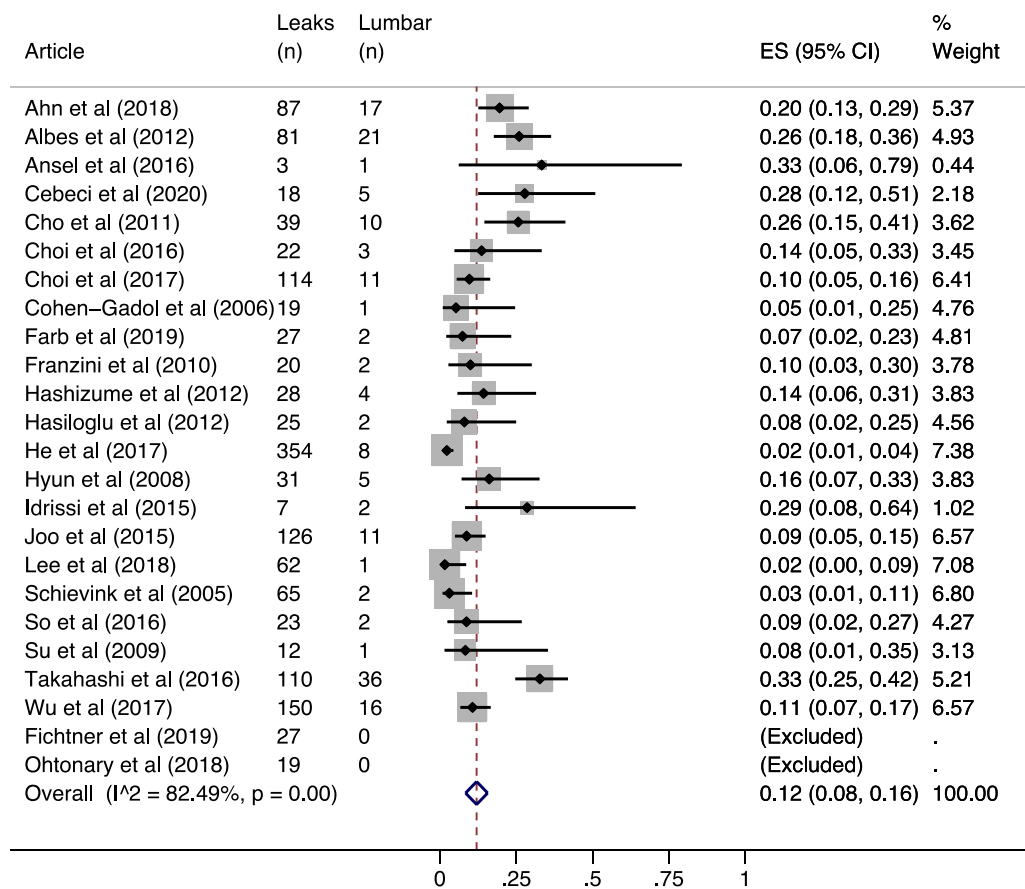
eFigure 17c. Meta-analysis of proportions of leak location (thoracic)



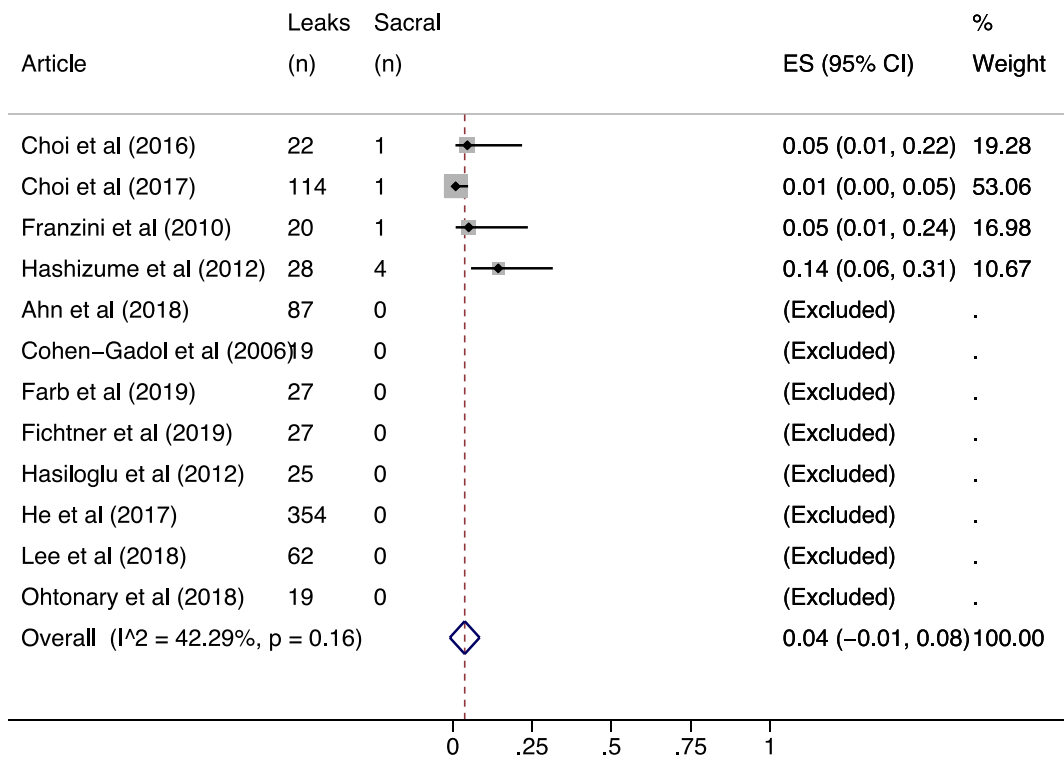
eFigure 17d. Meta-analysis of proportions of leak location (thoraco-lumbar)



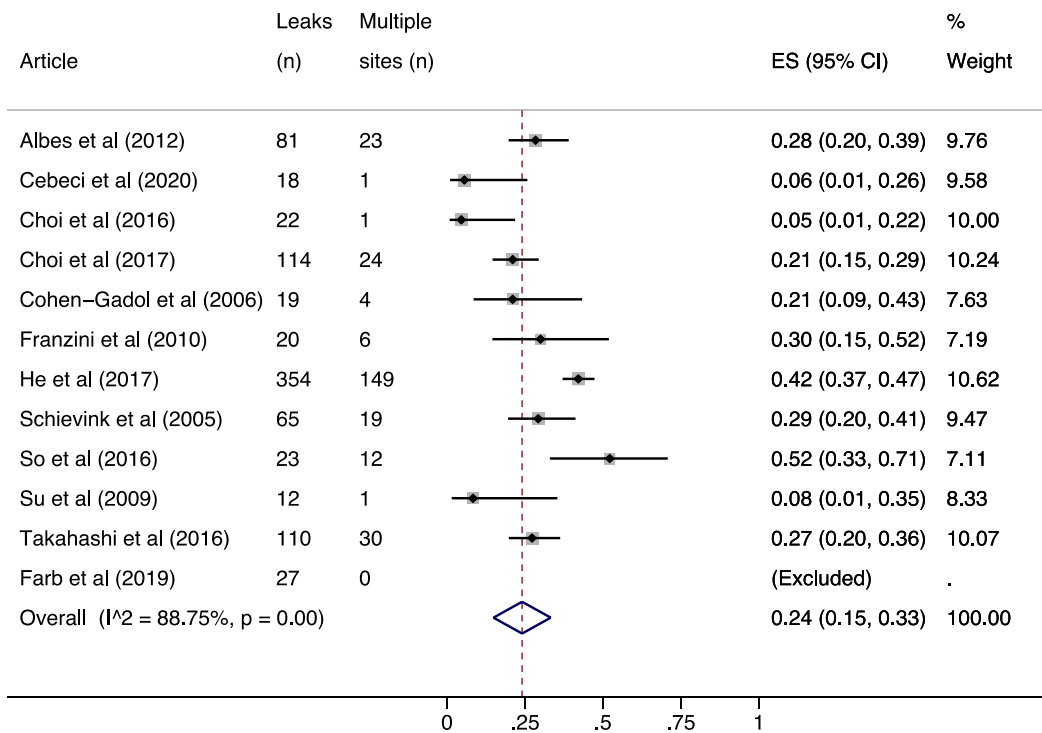
eFigure 17e. Meta-analysis of proportions of leak location (lumbar)



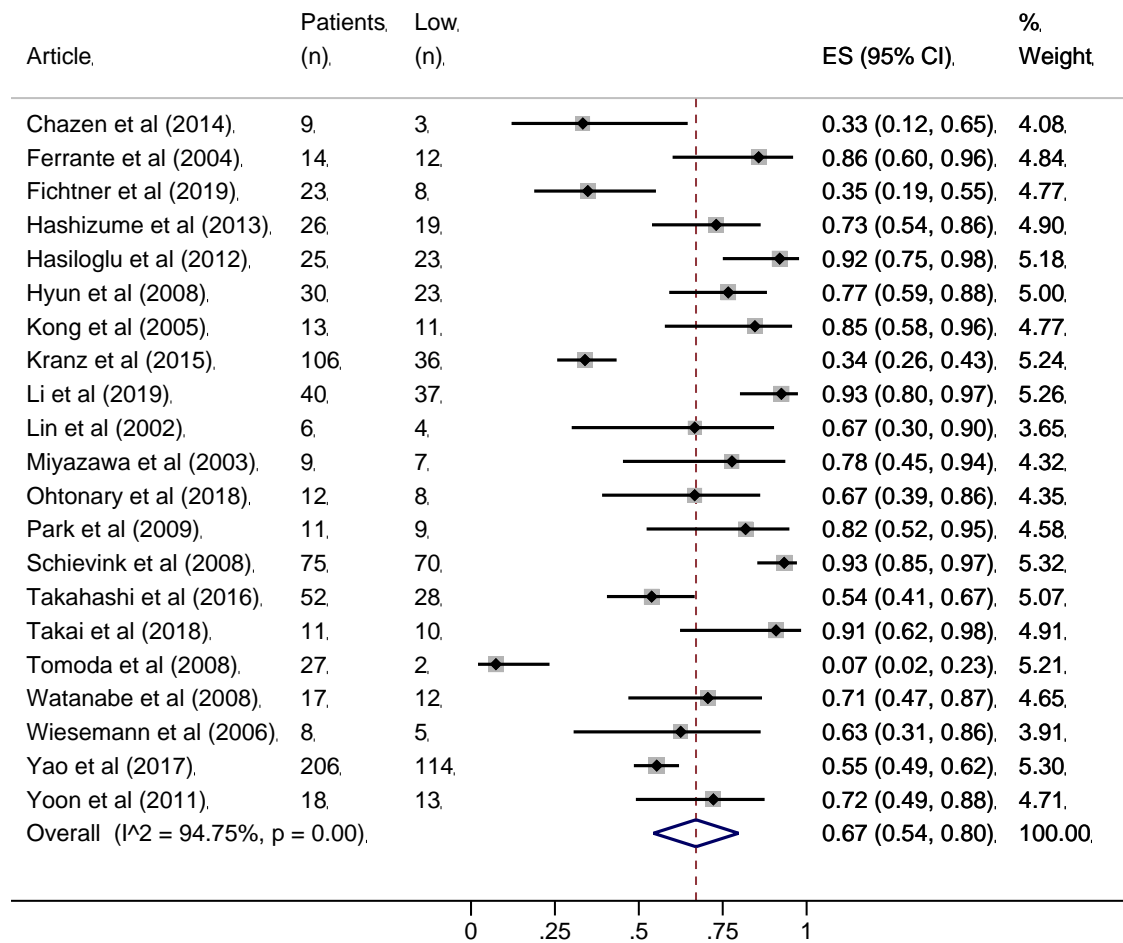
eFigure 17f. Meta-analysis of proportions of leak location (sacral)



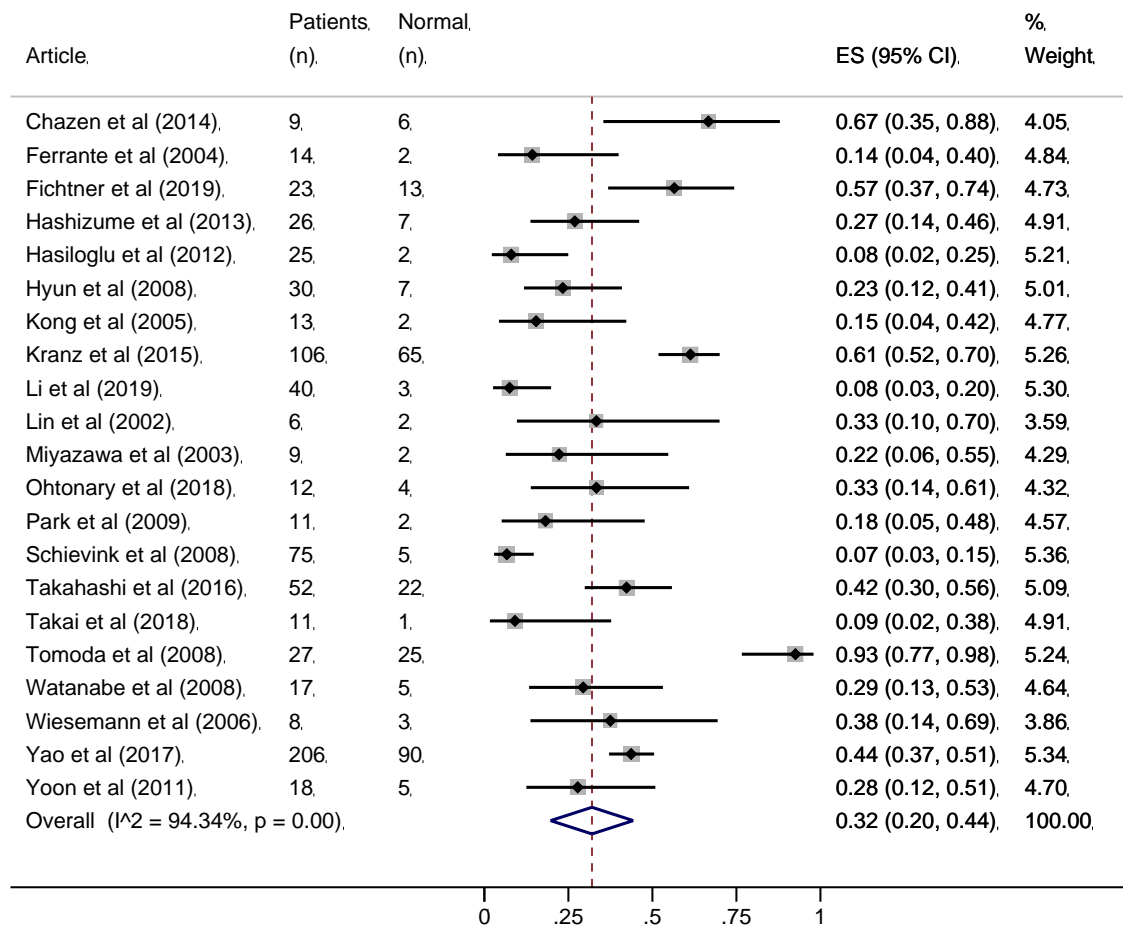
eFigure 17g. Meta-analysis of proportions of leak location (multiple)



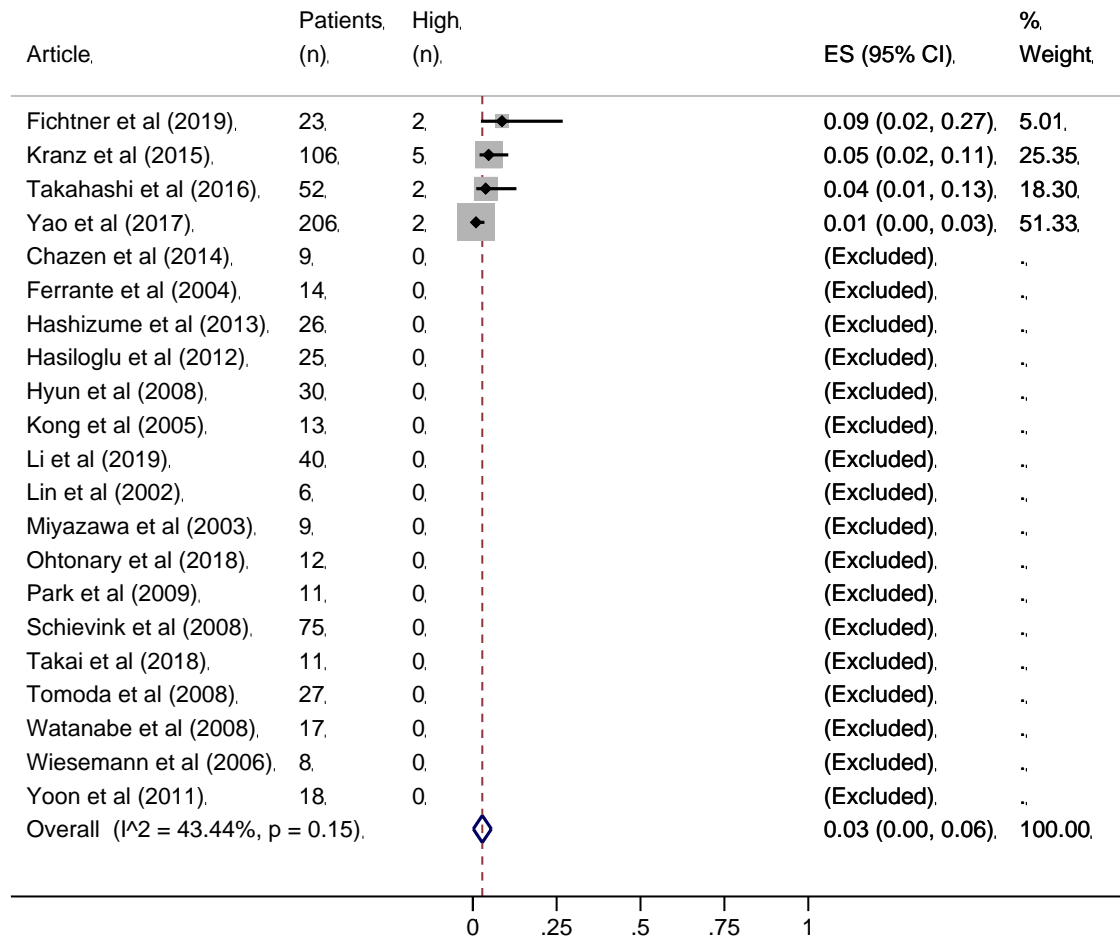
eFigure 18a. Meta-analysis of proportions of lumbar puncture opening pressure (low)



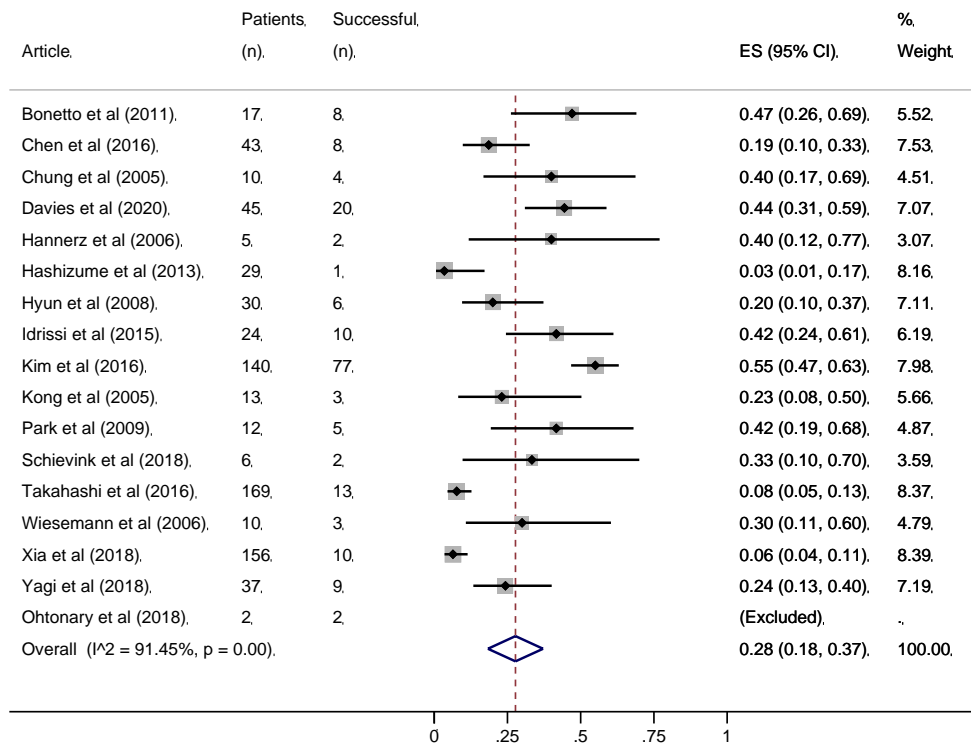
eFigure 18b. Meta-analysis of proportions of lumbar puncture opening pressure (normal)



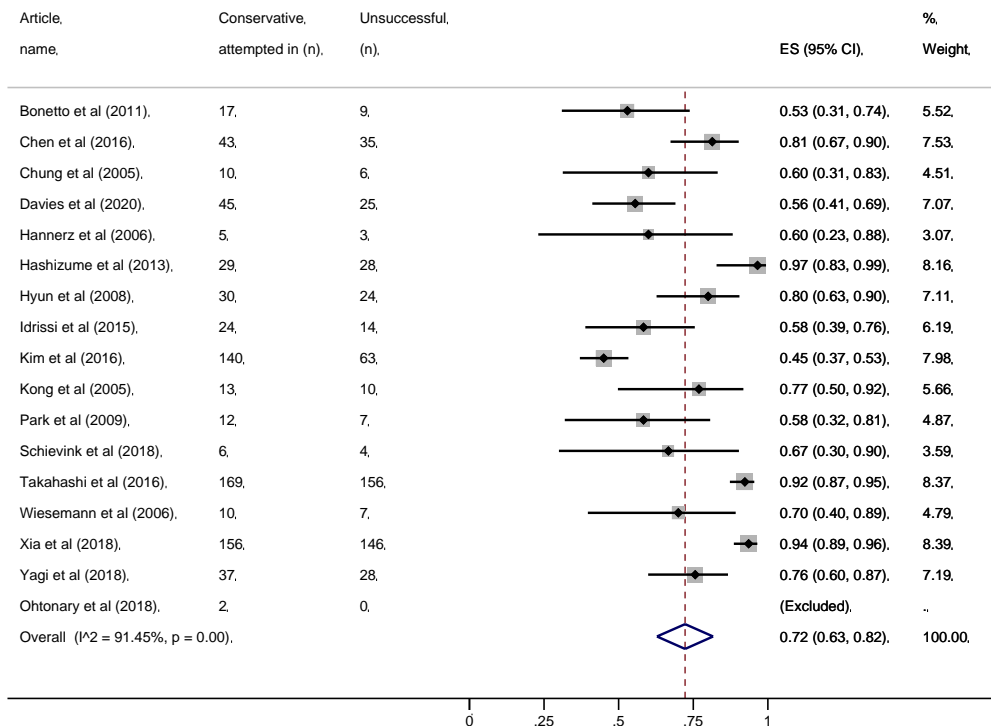
eFigure 18c. Meta-analysis of proportions of lumbar puncture opening pressure (high)



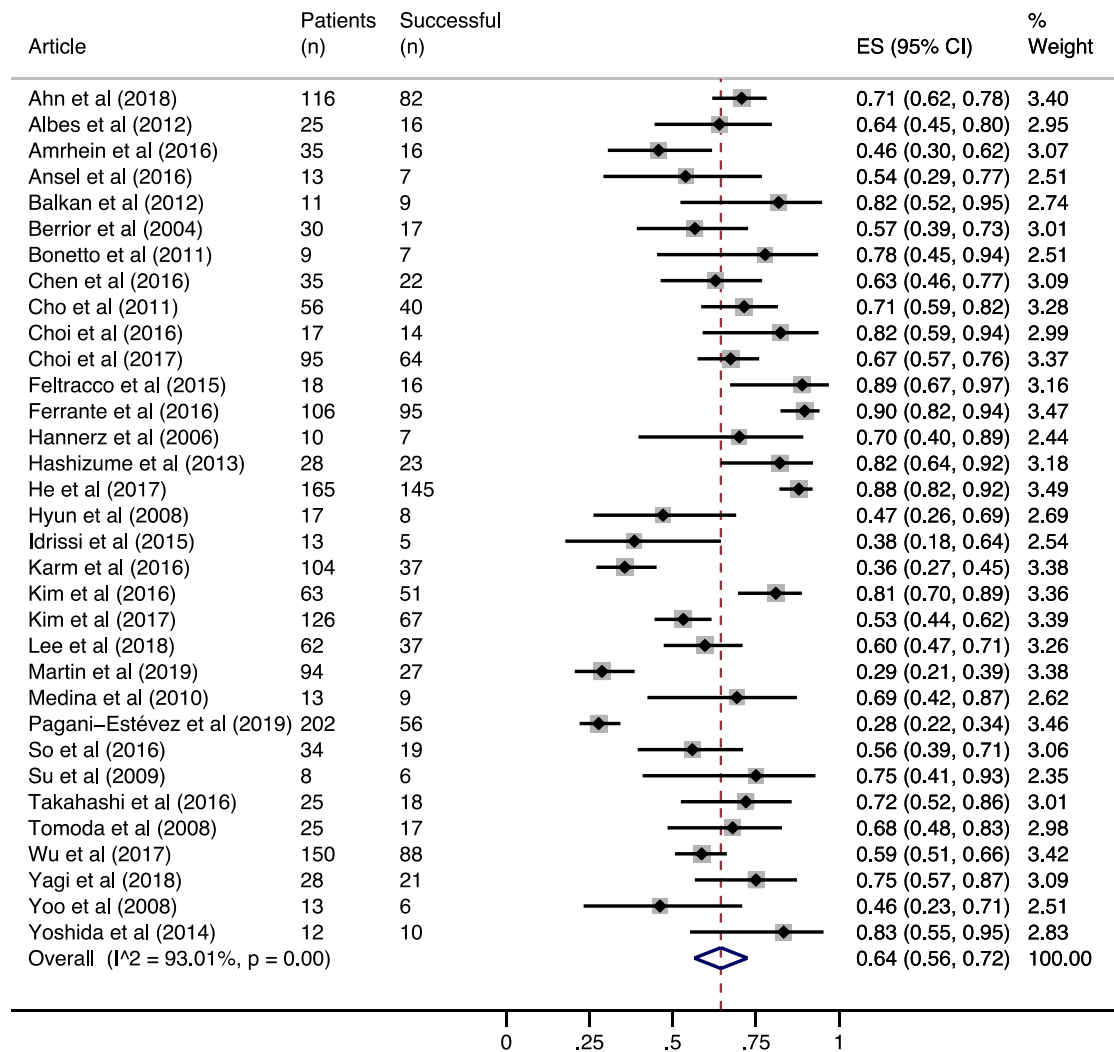
eFigure 19a. Meta-analysis of proportions of successful conservative treatment



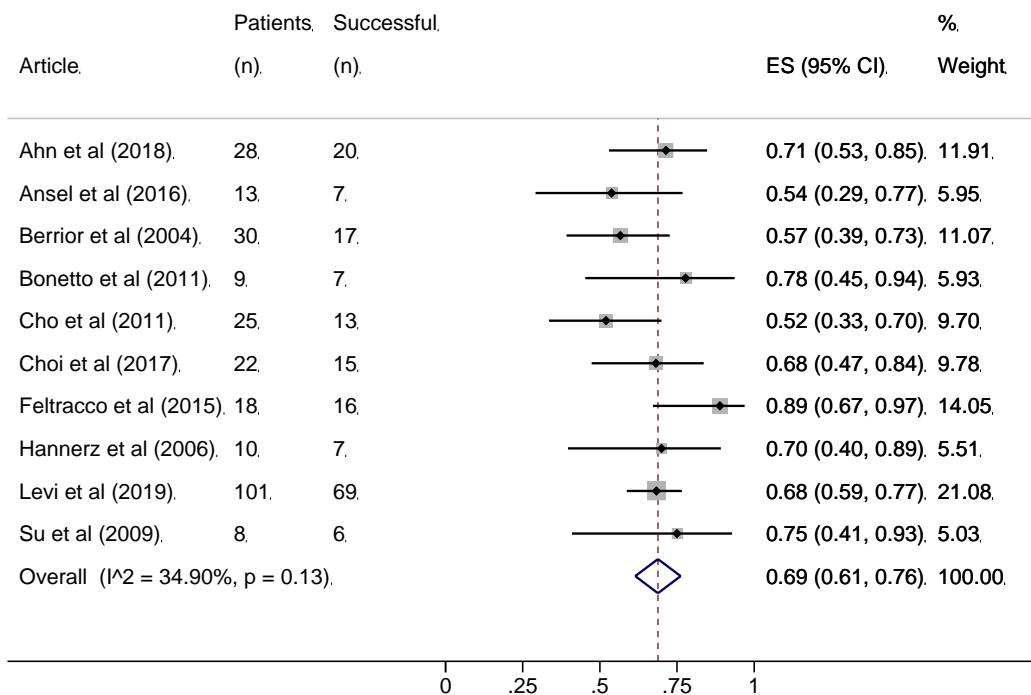
eFigure 19b. Meta-analysis of proportions of unsuccessful conservative treatment



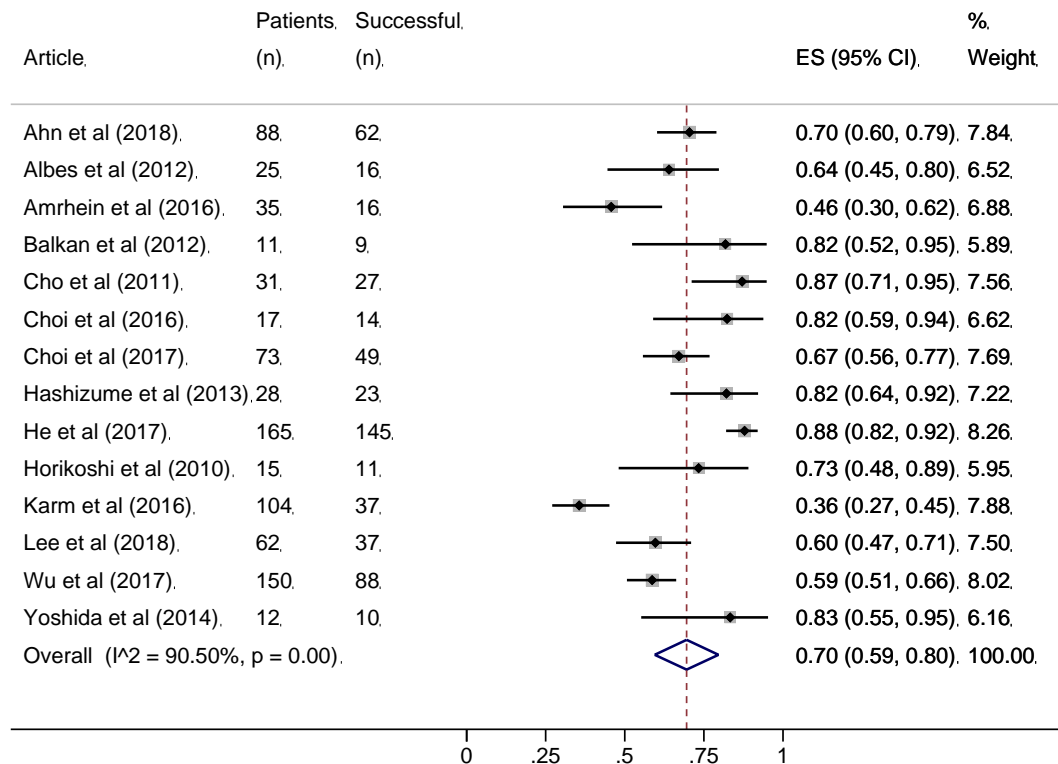
eFigure 20a. Meta-analysis of proportions of successful first EBP



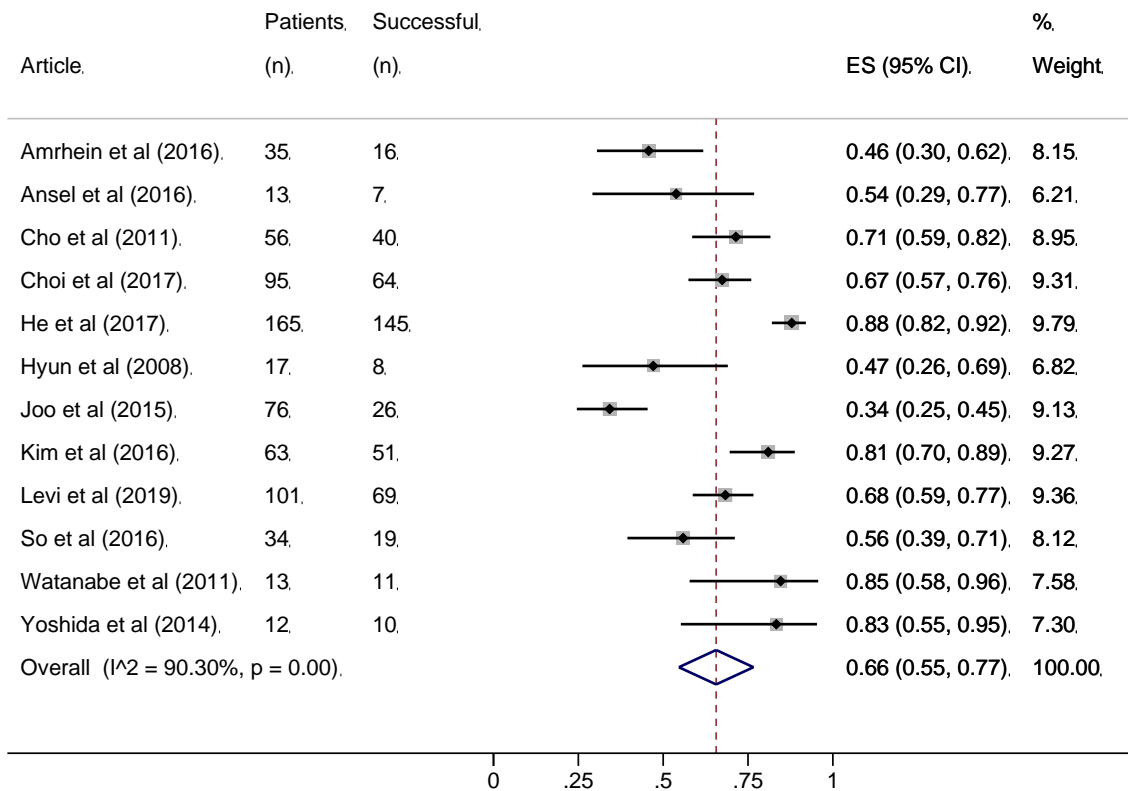
eFigure 20b. Meta-analysis of proportions of successful nontargeted EBP



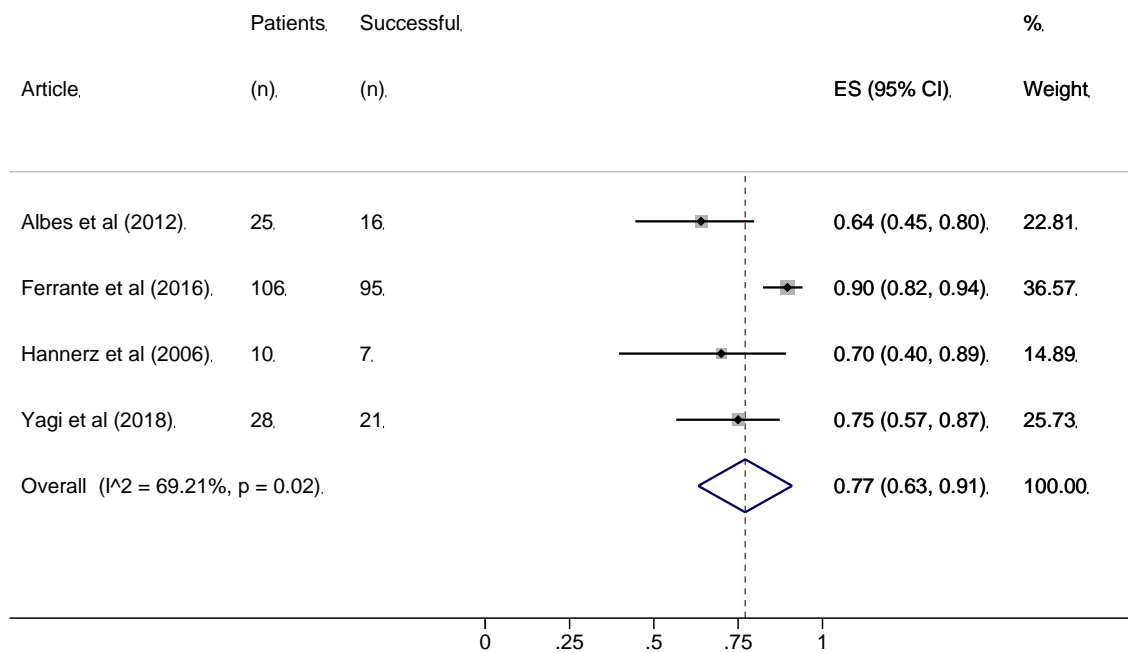
eFigure 20c. Meta-analysis of proportions of successful targeted EBP



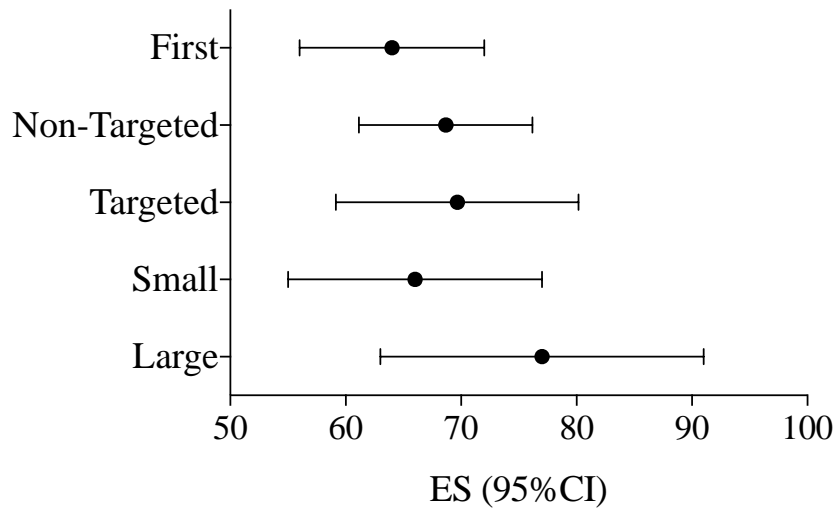
eFigure 20d. Meta-analysis of proportions of successful small EBP



eFigure 20e. Meta-analysis of proportions of successful large EBP



eFigure 21. Epidural Blood Patches (EBPs) outcomes. Pooled estimates of proportions (95% CI) of successful EBP treatment stratified by EBP technique (non-targeted/targeted, small/large)



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