Economic and Humanistic Burden of Cerebral Vasospasm and Its Related Complications after Aneurysmal Subarachnoid Hemorrhage: a Systematic Literature Review

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Supplementary Material

Table S1. Embase and Medline search strategies (searched via Embase.com)

No.	Query
#1	'subarachnoid hemorrhage'/exp
#2	(subarachnoid NEXT/2 (hemorrhage OR haemorrhage)):ti,ab
#3	'intracranial aneurysm'/exp
#4	'intracranial aneurysm':ti,ab OR 'aneurysm':ti,ab OR 'aneurysmal':ti,ab OR 'brain infarction':ti,ab OR 'brain ischemia':ti,ab OR 'cerebral infarction':ti,ab OR 'cerebral ischemia':ti,ab
#5	(#1 OR #2) AND (#3 OR #4)
#6	'aneurysmal subarachnoid hemorrhage':ti,ab OR 'aneurysmal subarachnoid haemorrhage':ti,ab
#7	#5 OR #6
#8	'vasospasm':ti,ab OR 'brain vasospasm':ti,ab
#9	#7 OR #8
#10	'health care cost'/exp OR 'drug cost'/exp OR 'cost of illness'/exp OR 'hospital cost'/exp OR 'pharmacoeconomics'/exp OR 'treatment cost*':ti,ab OR 'direct cost*':ti,ab OR 'direct medical cost*':ti,ab OR 'nonmedical cost*':ti,ab OR 'non-medical cost*':ti,ab OR 'total cost*':ti,ab OR 'cost per patient treated':ti,ab OR 'budget impact':ti,ab OR 'cost burden':ti,ab OR 'societal cost*':ti,ab OR 'administrative cost*':ti,ab OR 'travel cost*':ti,ab OR 'travel time':ti,ab OR 'disease cost':ti,ab OR 'cost of drugs':ti,ab
#11	'indirect cost*':ti,ab OR 'disability':ti,ab OR 'functional status':ti,ab OR 'physical function':ti,ab OR 'impairment':ti,ab OR 'disabilities':ti,ab OR 'productivity':ti,ab OR 'employment':ti,ab OR 'retirement':ti,ab OR 'work disability':ti,ab OR 'absenteeism':ti,ab OR 'presenteeism':ti,ab OR 'sick leave':ti,ab OR 'sick day':ti,ab OR 'worktime loss':ti,ab OR 'opportunity loss':ti,ab OR 'job performance':ti,ab OR ((work NEAR/2 loss):ti,ab)
#12	'healthcare resource*':ti,ab OR 'medical resource*':ti,ab OR 'healthcare resource use':ti,ab OR 'health resource consumption':ti,ab OR 'health care consumption':ti,ab OR 'medical resource consumption':ti,ab OR 'hospital admission*':ti,ab OR 'icu admission*':ti,ab OR 'emergency department visit*':ti,ab OR 'emergency room visit*':ti,ab OR 'er visit*':ti,ab OR 'ed visit*':ti,ab OR 'inpatient visit*':ti,ab OR 'outpatient visit*':ti,ab OR 'specialist visit*':ti,ab OR 'unscheduled doctor visit*':ti,ab OR 'unscheduled physician visit*':ti,ab OR 'general practitioner visit*':ti,ab OR 'hospitalization':ti,ab OR 'health care utilization'/exp OR 'hospitalization'/exp OR 'length of stay':ti,ab OR 'discharge*':ti,ab OR 'readmission':ti,ab
#13	'quality adjusted life year*':ti,ab OR 'qaly':ti,ab OR 'qalys':ti,ab
#14	'cost utility analysis'/exp OR 'cost minimization analysis'/exp OR 'economic evaluation'/exp OR 'cost benefit analysis'/exp OR 'cost effectiveness analysis'/exp OR 'cost-consequence':ti,ab OR 'cost-minimisation':ti,ab OR 'cost minimisation':ti,ab OR 'cost-minimization':ti,ab OR 'cost minimization':ti,ab OR 'cost effectiveness':ti,ab OR 'icer':ti,ab OR 'incremental cost effectiveness ratio':ti,ab OR ('cost effectiveness':ti,ab AND ratio:ti,ab) OR 'incremental cost-effectiveness ratio':ti,ab
#15	#10 OR #11 OR #12 OR #13 OR #14
#16	'quality of life'/exp OR 'qol':ti,ab OR 'quality of life':ti,ab OR 'hrql':ti,ab OR 'hrqol':ti,ab OR 'hr qol':ti,ab OR 'hql':ti,ab OR 'hqol':ti,ab OR 'h qol':ti,ab OR 'quality adjusted life year*':ti,ab OR 'quality adjusted life':ti,ab OR 'qaly*':ti,ab OR 'disability adjusted life year*':ti,ab OR 'disability adjusted life':ti,ab OR 'daly*':ti,ab OR 'patient reported outcome*':ti,ab OR 'satisfaction':ti,ab OR 'preference*':ti,ab OR 'activities of daily living':ti,ab OR 'adl':ti,ab OR 'assessment of quality of life':ti,ab OR 'aqol':ti,ab OR 'quality of well being scale':ti,ab OR 'sf36':ti,ab OR 'sf 36':ti,ab OR 'short form 36':ti,ab OR 'shortform 36':ti,ab OR 'sf thirtysix':ti,ab OR 'sf thirty six':ti,ab OR 'shortform thirtysix':ti,ab OR 'shortform thirty six':ti,ab OR 'short form thirtysix':ti,ab OR 'short form thirty six':ti,ab OR 'sf6':ti,ab OR 'sf 6':ti,ab OR 'short form 6':ti,ab OR 'shortform 6':ti,ab OR 'sf six':ti,ab OR 'sfsix':ti,ab OR 'shortform six':ti,ab OR 'short form six':ti,ab OR 'sf6d':ti,ab

	OR 'sf 6d':ti,ab OR 'short form 6d':ti,ab OR 'shortform 6d':ti,ab OR 'sf six d':ti,ab OR 'sfsixd':ti,ab OR 'shortform six d':ti,ab OR 'short form six d':ti,ab OR 'sf12':ti,ab OR 'sf 12':ti,ab OR 'short form 12':ti,ab OR 'shortform 12':ti,ab OR 'sf twelve':ti,ab OR 'sftwelve':ti,ab OR 'shortform twelve':ti,ab OR 'short form twelve':ti,ab OR 'sf20':ti,ab OR 'sf 20':ti,ab OR 'short form 20':ti,ab OR 'shortform 20':ti,ab OR 'sf twenty':ti,ab OR 'sftwenty':ti,ab OR 'shortform twenty':ti,ab OR 'short form twenty':ti,ab OR 'eq 5d':ti,ab OR 'eq5d':ti,ab OR 'euroqol':ti,ab OR 'euro qol':ti,ab OR 'health status':ti,ab OR 'hye':ti,ab OR 'hyes':ti,ab OR 'health* year* equivalent*':ti,ab OR 'the oxford participation and activities questionnaire':ti,ab OR 'ox-paq':ti,ab OR 'stroke specific quality of life scale':ti,ab OR 'ss-qol':ti,ab
#17	'psychological well-being'/exp OR ('utilit*':ti,ab AND 'health':ti,ab) OR ('utilit*':ti,ab AND 'scor*':ti,ab) OR ('utilit*':ti,ab AND 'valu*':ti,ab) OR ('disutilit*':ti,ab AND 'health':ti,ab) OR ('disutilit*':ti,ab AND 'scor*':ti,ab) OR ('disutilit*':ti,ab AND 'valu*':ti,ab) OR 'utilit*':ti,ab OR 'disutilit*':ti,ab OR 'standard gamble':ti,ab OR 'time trade off':ti,ab OR 'time tradeoff':ti,ab OR 'tto':ti,ab OR 'visual analog scale':ti,ab OR 'visual analogue scale':ti,ab OR 'vas':ti,ab OR 'discrete choice experiment':ti,ab OR '15d':ti,ab OR 'health utilities index':ti,ab OR 'hui':ti,ab OR 'hui1':ti,ab OR 'hui2':ti,ab OR 'hui3':ti,ab OR 'rosser index':ti,ab OR 'rosser':ti,ab OR 'quality of wellbeing':ti,ab OR (('quality' NEAR/2 'wellbeing'):ti,ab) OR 'qwb':ti,ab
#18	#16 OR #17
#19	#9 AND #15
#20	#9 AND #18
#21	#19 OR #20
#22	#21 NOT ('animal'/de NOT 'human'/de)
#23	#22 NOT ([conference abstract]/lim OR [conference paper]/lim OR [conference review]/lim OR [editorial]/lim OR [erratum]/lim OR [letter]/lim OR [note]/lim)
#24	#23 NOT 'case report'
#25	#24 NOT (review:it NOT ((systematic:ti,ab OR meta:ti,ab) AND analy*:ti,ab OR ((indirect:ti,ab OR mixed:ti,ab) AND 'treatment comparison':ti,ab)))

Table S2. Cochrane search strategy

ID	Search
#1	MeSH descriptor: [Subarachnoid Hemorrhage] explode all trees
#2	(subarachnoid NEXT/2 (hemorrhage OR haemorrhage)):ti,ab
#3	MeSH descriptor: [Intracranial Aneurysm] explode all trees
#4	('intracranial aneurysm' OR 'aneurysm' OR 'aneurysmal' OR 'brain infarction' OR 'brain ischemia' OR 'cerebral infarction' OR 'cerebral ischemia'):ti,ab
#5	(#1 OR #2) AND (#3 OR #4)
#6	('aneurysmal subarachnoid hemorrhage' OR 'aneurysmal subarachnoid haemorrhage'):ti,ab
#7	#5 OR #6
#8	('vasospasm' OR 'brain vasospasm'):ti,ab
#9	#7 OR #8
#10	(conference OR 'conference paper'):pt
#11	review:pt
#12	((systematic OR meta) AND analy* OR ((indirect OR mixed) AND 'treatment comparison')):ti,ab
#13	#11 NOT #12
#14	#9 NOT (#10 OR #13)

Table S3. Summary of data extraction variables

Study objective	As stated in the publication	
Study characteristics	Author, year Design (e.g. randomized, observational, survey) Randomization & blinding methods (if RCTs) Selection criteria and study design for non-RCTs Baseline stratification Years of study conduct	Follow up duration Country Key inclusion/exclusion criteria Study phase Sample size
Patient characteristics	Age Sex Race/ethnicity Body weight, BMI Comorbidities	Morbidity score on admission Days between admission and treatment Treatment modality (coiling, clipping)
Medication	Drugs (such as prophylactic "triple-H" therapy, clazosentan, and intraarterial papaverine calcium channel blockers, milrinone, tirilazad, fasudil, cilostazol, albumin, eicosapentaenoic acid, erythropoietin, corticosteroids, minocycline, deferoxamine, intrathecal thrombolytics)	
Study outcomes	<u>Economic</u> Direct costs Indirect costs (such as loss of productivity, sickness, early retirement, provision of community health and social services) Economic model results (including, CEA, CUA, BIA, CMA): (e.g. ICER, LYG, cost per QALY) Resource use (such as rescue therapy, re-admission, length of hospital stay [ICU, main wards], discharge status after hospitalization, rehabilitation)	<u>Health-related quality of life/Humanistic</u> Utility, disutility scores Health-related quality of life measures (disease specific and generic) Care giver burden

Table S4. Study characteristics of the 42 studies included in the Systematic Literature Review

Author (Date) Study ID	Country	Data sources	No. of centers	Study design	No. pts	Clearly defined pts criteria/ Consecutive recruitment	Data collection years	% of pts with VSP [a]
Clinical trials								
Raval et al. (2021) [30]	USA	-	1	RCT	33	Yes/ Yes	2015–2017	Unspecified
Ren et al. (2019) [31]	China	-	1	RCT	86	Yes /Yes	2017–2019	13.79%–41.38%
Mahajan et al. (2014) [28]	India	-	1	RCT	66	Yes/ Yes	NR (over 2-year period)	25%–26.5%
Senbokuya et al. (2013) [33]	Japan	UMIN000004347	7	RCT	109	Yes/ Yes	2009–2010	13%
Macdonald et al. (2012) [27] CONSCIOUS-1	Austria, Canada, Finland, France, Germany, Israel, Italy, Sweden, Switzerland, UK, USA	NCT00111085	52	Post hoc RCT	409	Yes/ Yes	2005–2006	58.67%
Rivero-Arias et al. (2009) [32] ISAT	UK	ISRCTN49866681	42	Post hoc RCT	1,644	Yes/ Yes	1997–2002	25.2%
Fountas et al. (2008) [26]	USA	-	-	RCT	74	Yes/ Yes	1999–2001	32%–41.6%
Zwienenberg-Lee et al. (2008) [34]	USA, Canada, Netherlands	National Institutes of Health–funded study	10	RCT	170	Yes/ Yes	2000–2005	54.1%–56.5% [b]
Prevedello et al. (2006) [29]	Brazil	Hospital Nossa Senhora das Gracas	1	Non-RCT	72	Yes/ NR	2000–2004	47.9%–58.3%
Observational studies								
Chatrath et al. (2020) [41]	USA	University of Virginia	1	RLC	206	Yes/ Yes	2011–2018	Unspecified

Author (Date) Study ID	Country	Data sources	No. of centers	Study design	No. pts	Clearly defined pts criteria/ Consecutive recruitment	Data collection years	% of pts with VSP [a]
Hoffman et al. (2020) [46]	USA	NRD	Multicenter	RLC	8,346	Yes/ Unclear	2010–2014	3.2%–4.0%
Sokolowski et al. (2021) [56]	USA	-	1	RLC	195	Yes /Yes	2011–2018	11%–57.1% [c]
Strickland et al. (2020) [59]	USA	Tertiary referral UH and safety net CH	2	RCC	131	Yes/Unclear	2010–2015	31%–32.9% [c]
Wilde et al. (2020) [63]	USA	Value Data Driven Outcome Database and medical records	-	RCC	198	Yes/Unclear	2001–2017	16.7%–18.2% [d]
Chotai et al. (2021) [42]	USA	NIS database	1	RCC	5,353	Yes/Yes	2012–2015	19%
Rumalla et al. (2018) [52]	USA	NRD	-	RLC	12,777	Yes/ Yes	2013–2013	2.7%
Abulhasan et al. (2018) [35]	Canada	Hospital registry and ICU database	1	RLC	419	Yes/ Yes	2010–2016	24.2%
Alaraj et al. (2017) [36]	USA	Department of Neurosurgery, University of Illinois at Chicago	1	RCC	174	Yes/ Yes	2011–2014	25.9%
Drazin et al. (2015) [44]	USA	Cedars Sinai Medical Center	1	RCC	107	Yes/Yes	-	32.3%–58%
Kreiter et al. (2013) [48]	USA	Columbia University Subarachnoid Hemorrhage Outcomes Project	1	PLC	534	Yes/Yes	1996–2001	14%
Khatri et al. (2011) [47]	USA	NIS database	-	RCC	74,356	Yes/Unclear	2005–2007	Unspecified
Chou et al. (2010) [43]	USA	Duke University Medical Center database	1	RCC	198	Yes/Yes	1999–2004	61.3% [b]

Author (Date) Study ID	Country	Data sources	No. of centers	Study design	No. pts	Clearly defined pts criteria/ Consecutive recruitment	Data collection years	% of pts with VSP [a]
Springer et al. (2009) [58]	USA	Columbia University Subarachnoid Hemorrhage Outcomes Project	1	PLC	232	-/Unclear	1996–2002	Unspecified
Frontera et al. (2009) [11]		Columbia University Subarachnoid Hemorrhage Outcomes Project	1	PLC	580	-/Yes	1996-2002	16%-45%
Zaidat et al. (2009) [65]	USA	-	1	RCC	216	Yes/Yes	1999–2005	35%–55% [b]
Badjatia et al. (2005) [39]	USA	-	1	RCC	352	Yes/Unclear	1995–2002	29.2%
Suarez et al. (2004) [60]	USA	University Hospitals of Cleveland	1	RCC	140	Yes/Yes	1998–2000	23.5%
Yundt et al. (1996) [64]	USA	Barnes Hospital	1	RCC	112	Yes/Yes	1993–1994	12.5%–51.9%
Alay et al. (2020) [37]	Turkey	Ankara Numune Education & Research Hospital	1	RCC	143	Yes/ Unclear	During 2013	16%–26%
Harris et al. (2021) [45]	UK	Havering and Redbridge University Hospital NHS Trust, Queen's Hospital, Romford, UK	1	RLC	137	Yes/ Yes	2012–2018	27.5%–47.4%
Sousa et al. (2019) [57]	Portugal	Santa Maria University Hospital	1	Cross-sectional	14	Yes/ Yes	2004–2006	21.3%
Ali et al. (2018) [38]	Turkey	Istanbul Medical Faculty, Istanbul	1	PLC	82	Yes/ Yes	2013–2015	84%
Bercker et al. (2018) [40]	Germany	University Hospital of Leipzig	1	RCC	276	Yes/ Yes	2009–2014	17.2%–33.9%

Author (Date) Study ID	Country	Data sources	No. of centers	Study design	No. pts	Clearly defined pts criteria/ Consecutive recruitment	Data collection years	% of pts with VSP [a]
Sakr et al. (2016) [53]	Germany	Friedrich-Schiller university hospital surgical ICU	1	RCC	142	Yes/ Yes	2004–2010	65.5%
Vetkas et al. (2013) [24]	Estonia	Department of Neurology and Neurosurgery, University of Tartu	1	RLC	114	Yes/ Yes	2001–2010	24%
Szmuda et al. (2013) [61]	Poland	Neurosurgery Department, Medical University of Gdansk	1	RCC	206	Yes/Unclear	1997–2006	7.8% [e]
Taylor et al. (2011) [62]	UK	15 bedded tertiary referral unit, National Hospital for Neurology and Neurosurgery, London	1	RLC	47	Yes/ Yes	2004–2008	38%
Soehle et al. (2007) [55]	UK	Unclear	1	PLC	29	Yes/ Unclear	NR	Unspecified
Scharbrodt et al. (2009) [54]	Germany	NR	1	RLC	128	Yes/ Yes	1995–2003	25%
Niskanen et al. (2004) [50]	Finland	Kuopio University Hospital	1	RCC	171	Yes/ Unclear	1997–2000	5.8%–5.9%
Morgan et al. (2000) [49]	Australia	Royal North Shore Hospital	1	RLC	200	Yes/ Yes	1992–1998	42.5%
Ogden et al. (1994) [51]	New Zealand	Auckland Hospital	1	PLC	89	Yes/ Yes	1988–1991	24.7%

[a] If % unspecified, VSP data was available, but the number of VSP patients was not reported. [b] Transcranial Doppler VSP. [c] Clinical VSP. [d] Mild to severe. [e] Reported as delayed cerebral ischemia.

Abbreviations: aSAH, aneurysmal subarachnoid hemorrhage; CH, county hospital; CONSCIOUS-1, Clazosentan to Overcome Neurological Ischemia and Infarction Occurring After Subarachnoid Hemorrhage; ISAT, International Subarachnoid Aneurysm Trial; NIS, Nationwide Inpatient Sample; No., number; NRD, Nationwide Readmissions Database; PLC, prospective longitudinal cohort; pts, patients; RCC, retrospective case control; RCT, randomized controlled trial; RLC, retrospective longitudinal cohort; UH, university hospital; VSP, cerebral vasospasm.

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