

Systematic literature review to assess the cost and resource use associated with spinal muscular atrophy (SMA) management

Pharmacoeconomics: Online resource materials

Systematic literature review to assess the cost and resource use associated with spinal muscular atrophy (SMA) management

Noman Paracha¹, Pollyanna Hudson², Stephen Mitchell² and C. Simone Sutherland^{1*}

1. F. Hoffmann-La Roche Ltd, Basel, Switzerland.
2. Mtech Access Limited, Bicester, Oxfordshire, United Kingdom.

***Corresponding author**

Contact email address: simone.sutherland@roche.com

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Online Resource Table 1. Supplementary Sources

Supplementary Sources
<ul style="list-style-type: none">• Reference lists of included studies
<ul style="list-style-type: none">• Conference proceedings (2017–2021):<ul style="list-style-type: none">– American Academy of Neurology (AAN)– European Academy of Neurology (EAN)– The World Muscle Society (WMS)– Cure SMA
<ul style="list-style-type: none">• HTA agencies were searched to identify relevant, previous regulatory submissions in this indication:<ul style="list-style-type: none">– National Institute for Health and Care Excellence (NICE)– Scottish Medicines Consortium (SMC)– Haute Autorité de Santé (HAS)– Institute for Clinical and Economic Review (ICER)– Institute for Quality and Efficiency in Health Care (IQWiG)– Canadian Agency for Drugs and Technologies in Health (CADTH)– Pharmaceutical Benefits Advisory Committee (PBAC)
<ul style="list-style-type: none">• Additional sources/websites:<ul style="list-style-type: none">– Research Papers in Economics (RePEc): http://repec.org/– Mapi Research Trust: https://mapi-trust.org/– International Network of Agencies for Health Technology Assessment (INAHTA): http://www.inahta.org/– TreatSMA: https://www.treatsma.uk/– Spinal Muscular Atrophy UK: https://smauk.org.uk/– Muscular Dystrophy UK: https://www.muscular dystrophyuk.org/

Abbreviations: *HTA* health technology assessment, *SMA* spinal muscular atrophy.

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Online Resource Table 2. Search strategy

Search term number	Search terms	Original search, # (Accessed 28 August 2019)	Update search, # (Accessed 29 July 2021)
Embase: 1974 to 28 August 2019 (original search) / 28 July 2021 (update search)			
1	spinal muscular atrophy/	6693	8059
2	myodystroph*.mp.	194	208
3	exp muscular dystrophy/	41621	45678
4	(musc* adj2 (dystroph* or atroph*)).mp.	80411	90420
5	(kugelberg adj2 (syndrome or disease)).mp.	387	559
6	exp Kugelberg Welander disease/	320	492
7	exp Werdnig Hoffmann disease/	714	1046
8	Werdnig Hoffmann.mp.	828	1163
9	exp amyotrophic lateral sclerosis/	35535	40821
10	amyotrophic lateral sclerosis.mp.	39494	45435
11	(Lou Gehrig* adj2 (syndrome or disease)).mp.	228	247
12	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11	122541	138410
13	Socioeconomics/	134094	146742
14	Cost benefit analysis/	81972	87576
15	Cost effectiveness analysis/	144742	160648
16	Cost of illness/	18488	20026
17	Cost control/	66054	70906
18	Economic aspect/	110473	115777
19	Financial management/	110882	115475
20	Health care cost/	182184	199872
21	Health care financing/	13116	13487
22	Health economics/	32150	33555
23	Hospital cost/	20500	22746
24	(fiscal or financial or finance or funding).tw.	180418	226886

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25	Cost minimisation analysis/	3392	3665
26	(cost adj estimate\$).mp.	3206	3711
27	(cost adj variable\$).mp.	242	285
28	(unit adj cost\$).mp.	4229	4883
29	((indirect or direct or employe*) adj2 (cost* or resource* or benefit*)).mp.	30009	34755
30	or/13-29	891041	995877
31	12 and 30	1518	1845
32	limit 31 to yr="2019 -Current"	–	421
Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Daily and Versions(R): 1946 to 28 August 2019 (original search) / 28 July 2021 (update search)			
1	exp Muscular Atrophy, Spinal/	4723	5495
2	myodystroph*.mp.	201	204
3	exp Muscular Dystrophies/	25700	27697
4	(musc* adj2 (dystroph* or atroph*)).mp.	52147	57553
5	(kugelberg adj2 (syndrome or disease)).mp.	146	151
6	exp "Spinal Muscular Atrophies of Childhood"/	1227	1432
7	Werdnig Hoffmann.mp.	303	310
8	exp Amyotrophic Lateral Sclerosis/	17805	20287
9	amyotrophic lateral sclerosis.mp.	25726	29704
10	(Lou Gehrig* adj2 (syndrome or disease)).mp.	201	227
11	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10	80598	90071
12	Economics/	27068	27350
13	cost analysis/	47537	49795
14	Cost allocation/	1998	2008
15	Cost-benefit analysis/	77546	85558
16	Cost control/	21384	21594
17	Cost savings/	11332	12283
18	Cost of illness/	25544	29184
19	Cost sharing/	2447	2615

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20	deductibles/	1720	1786
21	coinsurance/	1720	1786
22	Medical savings accounts/	530	543
23	Health care costs/	37431	41722
24	Direct service costs/	1171	1204
25	Drug costs/	15454	16698
26	Employer health costs/	1088	1094
27	Hospital costs/	10482	11549
28	Health expenditures/	19096	21658
29	Capital expenditures/	1987	1997
30	Value of life/	5653	5755
31	exp economics, hospital/	23785	25225
32	exp economics, medical/	14116	14269
33	Economics, nursing/	3989	4005
34	Economics, pharmaceutical/	2883	3005
35	exp fees/	29842	30811
36	exp charges/	29842	30811
37	exp budgets/	13549	13861
38	(low adj cost).mp.	51799	67440
39	(high adj cost).mp.	13399	16301
40	(health?care adj cost\$).mp.	10484	13375
41	(fiscal or funding or financial or finance).tw.	137682	163232
42	(cost adj estimate\$).mp.	2145	2451
43	(cost adj variable).mp.	43	47
44	(unit adj cost\$).mp.	2381	2740
45	(economic\$ or pharmacoeconomic\$ or price\$ or pricing).tw.	279311	336596
46	((indirect or direct or employe*) adj2 (cost* or resource* or benefit*)).mp.	28788	31724
47	or/12-46	698929	809702
48	11 and 47	675	851

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49	limit 48 to yr="2019 -Current"	–	226
	EBM Reviews - Cochrane Database of Systematic Reviews 2005 to 21 August 2019, EBM Reviews - ACP Journal Club 1991 to July 2019, EBM Reviews - Database of Abstracts of Reviews of Effects 1st Quarter 2016, EBM Reviews - Cochrane Clinical Answers August 2019, EBM Reviews - Cochrane Central Register of Controlled Trials July 2019, EBM Reviews - Cochrane Methodology Register 3rd Quarter 2012, EBM Reviews - Health Technology Assessment 4th Quarter 2016, EBM Reviews - NHS Economic Evaluation Database 1st Quarter 2016:		
1	exp Muscular Atrophy, Spinal/	72	97
2	myodystroph*.mp. [mp=ti, ab, tx, kw, ct, ot, sh, hw]	2	3
3	exp Muscular Dystrophies/	396	476
4	(musc* adj2 (dystroph* or atroph*)).mp. [mp=ti, ab, tx, kw, ct, ot, sh, hw]	2296	2861
5	(kugelberg adj2 (syndrome or disease)).mp. [mp=ti, ab, tx, kw, ct, ot, sh, hw]	17	24
6	exp "Spinal Muscular Atrophies of Childhood"/	24	28
7	Werdnig Hoffmann.mp.	15	18
8	exp Amyotrophic Lateral Sclerosis/	492	595
9	amyotrophic lateral sclerosis.mp.	1288	1546
10	(Lou Gehrig* adj2 (syndrome or disease)).mp. [mp=ti, ab, tx, kw, ct, ot, sh, hw]	29	32
11	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10	3578	4393
12	Economics/	66	68
13	cost analysis/	3909	3978
14	Cost allocation/	16	16
15	Cost-benefit analysis/	18757	19542
16	Cost control/	285	289
17	Cost savings/	1031	1066
18	Cost of illness/	1393	1453
19	Cost sharing/	24	28
20	deductibles/	23	24
21	coinsurance/	23	24

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22	Medical savings accounts/	0	1
23	Health care costs/	4862	5040
24	Direct service costs/	196	198
25	Drug costs/	1805	1843
26	Employer health costs/	18	18
27	Hospital costs/	1536	1577
28	Health expenditures/	366	402
29	Capital expenditures/	6	6
30	Value of life/	148	148
31	exp economics, hospital/	1804	1855
32	exp economics, medical/	103	104
33	Economics, nursing/	20	20
34	Economics, pharmaceutical/	237	239
35	exp fees/	513	522
36	exp charges/	513	522
37	exp budgets/	73	73
38	(low adj cost).mp.	4242	5456
39	(high adj cost).mp.	1350	1623
40	(health?care adj cost\$).mp.	2197	2807
41	(fiscal or funding or financial or finance).tw.	42777	48407
42	(cost adj estimate\$).mp.	2547	2612
43	(cost adj variable).mp.	10	11
44	(unit adj cost\$).mp.	5488	5633
45	(economic\$ or pharmacoeconomic\$ or price\$ or pricing).tw.	42008	47381
46	((indirect or direct or employe*) adj2 (cost* or resource* or benefit*)).mp. [mp=ti, ab, tx, kw, ct, ot, sh, hw]	11871	12558
47	or/12-46	85613	98519
48	11 and 47	247	277
49	limit 48 to yr="2019 -Current" [Limit not valid in DARE; records were retained]	-	63

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EconLit 1886 to 22 August 2019 (original search) / 22 July 2021 (update search)			
1	amyotrophic lateral sclerosis.mp.	3	3
2	((spin* or musc*) adj2 (dystroph* or atroph*)).mp.	4	6
3	1 or 2	7	9
4	limit 3 to yr="2019 -Current"	–	2

Abbreviations: *ACP* American College of Physicians, *DARE* Database of Abstracts of Reviews of Effects, *EBM* Evidence-Based Medicine, *NHS* National Health Service.

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Online Resource Table 3. PICO Criteria and SLR Search Parameters

Category	Details
Population	<ul style="list-style-type: none"> • Indication: Type 1, 2, 3 and/or 4 SMA, Kugelberg–Welander disease or Werdnig–Hoffmann disease, regardless of age of onset and severity • Myodystrophia, muscular dystrophy and amyotrophic lateral sclerosis
Intervention	<ul style="list-style-type: none"> • Not applicable
Comparator	<ul style="list-style-type: none"> • Not applicable
Outcomes	<ul style="list-style-type: none"> • Direct costs (including medical and non-medical) • Indirect costs (including caregiver-related costs) • Healthcare resource use • Cost drivers
Study designs	<ul style="list-style-type: none"> • Economic evaluations reporting original cost data • Cost analyses • Cost/burden of illness studies • Randomised and non-randomised controlled trials • Observational and real-world evidence (e.g., registries, surveys)
Language	<ul style="list-style-type: none"> • No restriction
Country	<ul style="list-style-type: none"> • No restriction
Date of publication	<ul style="list-style-type: none"> • No restriction

Abbreviations: *PICO* population, interventions, comparators, outcomes, *SLR* systematic literature review, *SMA* spinal muscular atrophy.

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Online Resource Table 4. Resource use reported within identified articles (n=40)

Reported resource use (number of publications)	Publications
Requirement for respiratory support (n=30)	[1-30]
Length of stay in hospital (n=19)	[1, 3, 4, 8, 9, 17-19, 22-32]
Number of hospital admissions (n=24)	[2-5, 7-9, 11, 17-19, 22-30, 32-35]
Requirement for nutritional support (n=18)	[3, 4, 6, 7, 9-11, 14, 17, 18, 20, 21, 26-30, 36]
Outpatient or specialist visits (n=20)	[2, 4, 7, 9, 18-21, 23-30, 32-34, 37]
Medication (non-DMT) resource use (n=15)	[2, 4, 7, 9, 13, 20, 22, 25-29, 32-34]
Patients requiring carers (n=16)	[7, 9, 20-23, 25, 26, 29, 30, 33, 34, 36-39]
Patients requiring physiotherapy (n=9)	[4, 9, 11, 20, 23, 25, 26, 29, 40]
Use of assistive devices or medical aids such as care aids or adapted beds (n=14)	[7, 9, 19-23, 26, 28-30, 33, 34, 36]

Abbreviation: *DMT* disease-modifying therapy.

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Online Resource Table 5. Quality assessment of full-text publications included in this systematic literature review (original search)

Quality considerations	[3]	[4]	[5]	[6]	[7]	[9]	[10]	[14]	[15]	[20]	[34]	[36]	[39]
1. Was a clear definition of the illness given?	YES	YES	YES	YES	YES	YES	YES	YES	NO	YES	YES	YES	YES
2. Were epidemiological sources carefully described?	YES	YES	NO	YES	YES	YES	YES	YES	NO	YES	YES	NO	YES
3. Were costs sufficiently disaggregated?	NO	YES	NO	NO	YES	NO	-	-	-	YES	YES	-	NO
4. Were activity data sources carefully described?	YES	YES	YES	YES	YES	-	NO	NO	NO	YES	YES	NO	NO
5. Were activity data appropriately assessed?	Partially	Partially	Partially	Partially	YES	YES	NO	NO	NO	Partially	Partially	NO	NO
6. Were the sources of all cost values analytically described?	YES	YES	YES	YES	YES	YES	-	-	-	YES	YES	-	-
7. Were unit costs appropriately valued?	YES	YES	YES	YES	YES	-	-	-	-	YES	YES	-	-
8. Were the methods adopted carefully explained?	YES	YES	YES	YES	YES	-	-	-	-	YES	YES	-	-
9. Were costs discounted?	NO	NO	NO	NO	NO	-	-	-	-	NO	YES	-	-
10. Was the presentation of study results consistent with the methodology of study?	YES	YES	YES	YES	YES	-	YES	YES	YES	YES	YES	YES	YES
11. Were the major assumptions tested in a sensitivity analysis?	YES	YES	NO	NO	YES	YES	NO	NO	NO	NO	NO	NO	NO

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Overall quality	✓✓	✓✓✓	✓✓	✓✓	✓✓✓	✓	✓	✓	-	✓✓	✓✓✓	-	✓
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✓ 3–5 quality considerations; ✓✓ 6–8 quality considerations; ✓✓✓ 9–11 quality considerations, where quality considerations refer to “yes” responses only; partially indicates insufficient information for a “yes” response, – not applicable

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Online Resource Table 6. Quality assessment of full-text publications included in this systematic literature review (update search)

Quality considerations	[22]	[23]	[24]	[25]	[26]	[27]	[28]	[29]	[33]	[41]	[42]
1. Was a clear definition of the illness given?	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES
2. Were epidemiological sources carefully described?	YES	YES	YES	YES	YES	YES	YES	YES	YES	NO	YES
3. Were costs sufficiently disaggregated?	NO	NO	NO	YES	YES	–	YES	Partially	YES	YES	–
4. Were activity data sources carefully described?	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES
5. Were activity data appropriately assessed?	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES
6. Were the sources of all cost values analytically described?	NO	YES	YES	YES	YES	–	NO	YES	NO	YES	–
7. Were unit costs appropriately valued?	Unclear	YES	Unclear	YES	YES	–	Unclear	YES	Unclear	YES	–
8. Were the methods adopted carefully explained?	Partially	YES	YES	YES	YES	Partially	Partially	YES	Partially	Partially	YES
9. Were costs discounted?	Unclear	Unclear	Unclear	Unclear	Unclear	–	Unclear	Unclear	Unclear	Unclear	–
10. Was the presentation of study results consistent with the methodology of study?	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES
11. Were the major assumptions tested in a sensitivity analysis?	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO
Overall quality	✓	✓✓	✓✓	✓✓✓	✓✓✓	✓	✓✓	✓✓	✓✓	✓✓	✓✓

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✓ 3–5 quality considerations; ✓✓ 6–8 quality considerations; ✓✓✓ 9–11 quality considerations, where quality considerations refer to “yes” responses only; partially indicates insufficient information for a “yes” response,
– not applicable

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