

# **Burden and Treatment of Achondroplasia: A Systematic Literature Review**

## **Supplementary Appendices**

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## Contents

<b>SUPPLEMENTARY APPENDIX 1</b> .....	<b>3</b>
<b>SUPPLEMENTARY APPENDIX 2</b> .....	<b>6</b>
Supplementary Table 1. Inclusion criteria for the SLR .....	3
Supplementary Table 2. Clinical efficacy and safety search terms for MEDLINE, MEDLINE In-Process, MEDLINE Daily and MEDLINE Epub Ahead of Print (via Ovid) .....	6
Supplementary Table 3. Economic evaluation, HRQoL/utility and cost/resource use search terms for MEDLINE, MEDLINE In-Process, MEDLINE Daily and MEDLINE Epub Ahead of Print (via Ovid) .....	7
Supplementary Table 4. Clinical efficacy and safety search terms for Embase (via Ovid).....	9
Supplementary Table 5. Economic evaluation, HRQoL/utility and cost/resource use search terms for Embase (via Ovid) .....	11
Supplementary Table 6. Search terms for Cochrane Library databases: CDSR and CENTRAL (via Wiley) .	13
Supplementary Table 7. Search terms for DARE (via the University of York CRD platform) .....	13
Supplementary Table 8. Search terms for the NHS-EED and HTAD (via the University of York CRD platform) .....	13
Supplementary Table 9. Search terms for the HTAD (via the INAHTA platform) .....	14
Supplementary Table 10. Search terms for non-English databases and clinical trial registries .....	14
Supplementary Table 11. Search strategies for hand-searching of relevant congresses .....	15
Supplementary Table 12. Search strategies for hand-searching of HTA body and economic websites .....	17
Supplementary Table 13. Search terms for clinical guideline repositories .....	21

**SUPPLEMENTARY APPENDIX 1**

Eligibility Criteria

**Supplementary Table 1. Inclusion criteria for the SLR**

Burden and Treatment of Achondroplasia SLR – Supplementary Appendices

Category	Economic evaluations	Patient and caregiver HRQoL	Cost and resource use	Clinical efficacy and safety
<b>Population</b>	<ul style="list-style-type: none"> <li>Paediatric or adult patients with achondroplasia or any other form of short stature*, or their caregivers**</li> </ul> <p><i>* For patient/caregiver HRQoL, data specifically for achondroplasia were subsequently prioritised over other short stature conditions in a deviation from the protocol</i>  <i>** Caregiver quality of life was included from the point of the SLR update onwards, however, records identified in the original SLR searches were re-reviewed in order to ensure all relevant data on caregiver quality of life were captured.</i></p>			<ul style="list-style-type: none"> <li>Paediatric patients (aged &lt;18 years) with achondroplasia</li> <li>Patients with active or "open" growth plates</li> <li>Mixed populations if results for paediatric patients with achondroplasia were reported separately</li> </ul>
<b>Intervention/comparators</b>	<ul style="list-style-type: none"> <li>Any or none</li> </ul>			<ul style="list-style-type: none"> <li>CNP analogues</li> <li>Growth hormone therapies</li> <li>FGFR3 inhibitors</li> <li>SoC or placebo</li> <li>Surgical limb lengthening</li> </ul>
<b>Outcomes</b>	<ul style="list-style-type: none"> <li>ICERs</li> <li>Cost per clinical outcome</li> <li>Total QALYs</li> <li>Total DALYs</li> <li>Total LYGs</li> <li>Total costs</li> <li>Incremental costs and QALYs/DALYs</li> </ul>	<p>Any QoL data related to treatment options and their adverse events, if measured by a formal validated tool or instrument, including but not limited to:</p> <ul style="list-style-type: none"> <li>SF-36</li> <li>PedsQL</li> <li>QoLISSY</li> <li>WeeFIM</li> <li>EQ-5D</li> <li>Standard gamble</li> <li>Time trade-off</li> </ul> <p>Caregiver QoL</p>	<p>Both direct and indirect cost/resource use:</p> <p><b>Direct costs</b>, including:</p> <ul style="list-style-type: none"> <li>Drug cost</li> <li>Administration cost</li> <li>Hospitalisation cost</li> </ul> <p><b>Indirect costs</b>, including:</p> <ul style="list-style-type: none"> <li>Productivity loss</li> <li>Home adaptation</li> <li>Travel costs</li> </ul> <p><b>Resource use</b>, including:</p> <ul style="list-style-type: none"> <li>Surgery</li> <li>Imaging (e.g. MRI/x-ray)</li> <li>GP/hospital consultations</li> <li>Blood/insulin tests</li> </ul>	<p>Efficacy outcomes, including:</p> <ul style="list-style-type: none"> <li>Change in height</li> <li>Growth velocity</li> <li>Upper:lower body segment ratio, or other body proportion ratios</li> <li>Height Z scores</li> <li>MRI imaging</li> <li>FAH</li> <li>Bone age</li> <li>Bone mineral density</li> <li>IGF-1 levels</li> </ul> <p>Safety outcomes, including but not limited to:</p> <ul style="list-style-type: none"> <li>AEs</li> <li>Treatment-related AEs</li> <li>Serious AEs</li> <li>Deaths</li> <li>Discontinuation due to AEs</li> <li>Discontinuation due to treatment-related AEs</li> <li>Bone morphology/quality-related changes</li> </ul>

Burden and Treatment of Achondroplasia SLR – Supplementary Appendices

Category	Economic evaluations	Patient and caregiver HRQoL	Cost and resource use	Clinical efficacy and safety
<b>Study design</b>	Any of the following analysis types: <ul style="list-style-type: none"> <li>• Cost-utility</li> <li>• Cost-effectiveness</li> <li>• Cost-consequence</li> <li>• Cost-benefit</li> <li>• Cost-minimisation</li> </ul>	Any original research study		<ul style="list-style-type: none"> <li>• Any RCTs</li> <li>• Interventional non-RCTs, such as controlled (but not randomised) clinical trials and single arm clinical trials</li> <li>• Observational studies</li> </ul>
<b>Other considerations</b>	<ul style="list-style-type: none"> <li>• Original research studies</li> <li>• Congress abstracts published in or after 2018</li> <li>• Human subjects</li> <li>• Any language</li> <li>• Any country</li> </ul>			

**Abbreviations:** AE, adverse event; CNP, C-type natriuretic peptide; DALY, Disability-adjusted life year; EQ-5D, EuroQol five dimensions five levels; FAH, final adult height; FGFR3, fibroblast growth factor receptor 3 gene; GP, general practitioner; HRQoL, health-related quality of life; HTA, health technology assessment; ICER, incremental cost-effectiveness ratio; IGF-1, insulin-like growth factor-1; LYG, life years gained; MRI, magnetic resonance imaging; NA, not applicable; PedsQL, Pediatric Quality of Life Inventory; QALY, quality-adjusted life-year; QoL, quality of life; QoLISSY, Quality of Life of Short Stature Youth; RCT, randomised clinical trial; SF-36, 36-Item Short Form Survey; SLR, systematic literature review; SoC, standard of care; WeeFIM, Pediatric Functional Independence Measure.

**SUPPLEMENTARY APPENDIX 2**Electronic Database Search Terms**Supplementary Table 2. Clinical efficacy and safety search terms for MEDLINE, MEDLINE In-Process, MEDLINE Daily and MEDLINE Epub Ahead of Print (via Ovid)**

Group	#	Searches	Results (11.09.20)	Results (10.06.21)	
<b>Achondroplasia</b>	1	exp achondroplasia/	2292	2339	
	2	(achondroplas\$ or FGFR3\$ or FGFR-3\$ or Fibroblast Growth Factor Receptor 3).ti,ab,kf.	4267	4479	
	3	1 or 2	5100	5320	
<b>RCTs</b>	4	randomized controlled trials as topic/	135997	144602	
	5	randomized controlled trial/	512759	533070	
	6	random allocation/	103565	105440	
	7	double blind method/	159695	164865	
	8	single blind method/	28994	30314	
	9	clinical trial/	524656	529237	
	10	clinical trial, phase i.pt.	20761	21716	
	11	clinical trial, phase ii.pt.	33381	34984	
	12	clinical trial, phase iii.pt.	17197	18502	
	13	clinical trial, phase iv.pt.	1947	2112	
	14	controlled clinical trial.pt.	93834	94201	
	15	randomized controlled trial.pt.	512759	533070	
	16	multicenter study.pt.	278747	295979	
	17	clinical trial.pt.	524656	529237	
	18	exp clinical trials as topic/	345552	358461	
	19	controlled clinical trial/	93834	94201	
	20	multicenter study/	278747	295979	
	21	(clinical adj trial\$).ti,ab,kf.	381905	410496	
	22	((singl\$ or doubl\$ or treb\$ or tripl\$) adj (blind\$3 or mask\$3)).ti,ab,kf.	174360	180756	
	23	placebos/	35071	35518	
	24	placebo\$.ti,ab,kf.	218533	226678	
	25	(allocat\$ adj2 random\$).ti,ab,kf.	35525	37796	
	26	Randomi?ed adj2 trial\$.ti,ab,kf.	327471	354421	
	27	rct.ti,ab,kf.	23704	26307	
	28	or/4-27	1743054	1824665	
	<b>Non-RCTs/ observational studies</b>	29	exp Epidemiologic studies/	2530938	2688798
		30	exp Case Control studies/	1101734	1181597
		31	exp Cohort Studies/	2028376	2148359
32		Case control.ti,ab,kf.	128055	135392	
33		(cohort adj (study or studies)).ti,ab,kf.	215089	241484	
34		cohort analy\$.ti,ab,kf.	9018	9942	
35		(follow up adj (study or studies)).ti,ab,kf.	51201	52972	
36		(observational adj (study or studies)).ti,ab,kf.	110703	124088	
37		Longitudinal\$.ti,ab,kf.	268941	289124	
38		retrospective\$.ti,ab,kf.	757585	828215	
39		Cross sectional.ti,ab,kf.	362274	400362	
40		Cross-sectional studies/	336408	369992	
41		exp Longitudinal Studies/	137289	146130	

## Burden and Treatment of Achondroplasia SLR – Supplementary Appendices

Group	#	Searches	Results (11.09.20)	Results (10.06.21)
	42	exp Follow-Up Studies/	646691	663944
	43	exp Prospective Studies/	547767	578536
	44	exp Retrospective Studies/	837290	904830
	45	(Prospective adj (study or studies)).ti,ab,kf.	177332	185958
	46	(evaluation adj (study or studies)).ti,ab,kf.	5894	6335
	47	(epidemiologic adj (study or studies)).ti,ab,kf.	26833	27498
	48	(( or Single arm) adj3 (study or studies or trial\$)).ti,ab,kf.	5585	6463
	49	(Open-label adj (trial\$ or stud\$)).ti,ab,kf.	11432	12015
	50	Non-blinded stud\$.ti,ab,kf.	132	132
	51	(chart adj3 review).ti,ab,kf.	40514	43478
	52	or/29-51	3231774	3442969
	<b>Exclusion terms</b>	53	exp animals/ not exp humans/	4732434
54		(comment or editorial).pt.	1239544	1304305
55		historical article/	360019	363956
56		or/53-55	6261662	6435645
<b>Combined</b>	57	3 and (28 or 52)	757	823
	58	57 not 56	736	799
	59	Remove duplicates from 58	<b>733</b>	<b>797</b>

**Database:** Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily 1946 to September 09, 2020 (original SLR) and June 09, 2021 (SLR update).

### Supplementary Table 3. Economic evaluation, HRQoL/utility and cost/resource

use search terms for MEDLINE, MEDLINE In-Process, MEDLINE Daily and

MEDLINE Epub Ahead of Print (via Ovid)

Group	#	Searches	Results (27.08.20)	Results (10.06.21)
Achondroplasia	1	exp achondroplasia/ or exp dwarfism/	16150	16458
	2	(achondroplas\$ or FGFR3\$ or FGFR-3\$ or Fibroblast Growth Factor Receptor 3 or dwarfism*).ti,ab,kf.	9033	9393
	3	1 or 2	20716	21303
Economic Evaluations	4	Cost-benefit analysis/	81537	84855
	5	"Costs and cost analysis"/	48792	49626
	6	Economics/	27220	27335
	7	(cost\$ adj (effective\$ or utilit\$ or consequence\$ or benefit\$ or minimi\$)).ti,ab,kf.	149951	160344
	8	(economic evaluation\$ or economic analysis or life year\$ gained or ICER or QALY\$ or DALY\$ or quality adjusted or adjusted life year\$ or disability adjusted life or qald\$ or qale\$ or qtime\$).ti,ab,kf.	35113	38024
	9	Quality-adjusted life years/	12378	13336
	10	Value of life/	5711	5749
	11	or/4-10	272881	286015
	12	(health utilit\$ or health state\$1 or illness state\$1 or HSUV or HSUVs or health state\$ value\$ or health state\$ preference\$ or utility assessment\$ or utility measure\$ or preference based or utility based).ti,ab,kf.	9794	10545
	13	((index adj3 wellbeing) or (quality adj3 wellbeing) or qwb).ti,ab,kf.	767	850

Burden and Treatment of Achondroplasia SLR – Supplementary Appendices

Group	#	Searches	Results (27.08.20)	Results (10.06.21)
	14	(multiattribute\$ or multi attribute\$).ti,ab.	886	971
	15	utility.ab. /freq=2	17804	19303
	16	(utilities or disutilit\$).ti,ab,kf.	7575	8139
	17	(euro qual or euro qual5d or euro qol5d or eq-5d or eq5-d or eq5d or eq 5d or euroqual or euroqol or euro qol or euroqual5d or euroqol5d or eq-sdq or eqsdq).ti,ab,kf.	11403	12787
	18	(short form\$ or shortform\$).ti,ab.	33930	36610
	19	(sf36\$ or sf 36\$ or sf thirtysix or sf thirty six).ti,ab,kf.	22380	23546
	20	(sf6 or sf 6 or sf6d or sf 6d or sf six D or sfsixD or sf six or sfsix or sf8 or sf 8 or sf eight or sfeight).ti,ab,kf.	3328	3496
	21	(sf12 or sf 12 or sf twelve or sftwelve).ti,ab,kf.	4836	5250
	22	(sf16 or sf 16 or sf sixteen or sfsixteen).ti,ab,kf.	30	30
	23	(sf20 or sf 20 or sf twenty or sftwenty).ti,ab,kf.	337	343
	24	(15D or 15-D or 15 dimension).ti,ab,kf.	5302	5577
	25	visual analog\$ scale\$.ti,ab,kf.	56168	60883
	26	(standard gamble\$ or sg).ti,ab,kf.	10931	11820
	27	(time trade off\$1 or time tradeoff\$1 or tto or timetradeoff\$1).ti,ab,kf.	1928	2032
	28	(health\$1 year\$1 equivalent\$1 or hye or hyes).ti,ab,kf.	78	83
	29	(hui or hui1 or hui2 or hui3 or rosser).ti,ab,kf.	1643	1759
	30	*quality of life/ and (quality of life or qol or hrqol).ti,ab,kf.	73519	79795
	31	quality of life/ and ((quality of life or qol) adj3 (improv\$ or chang\$)).ti,ab,kf.	27745	30653
	32	quality of life/ and ((quality of life or qol or hrqol) adj (score\$1 or measure\$1)).ti,ab,kf.	13952	15007
	33	quality of life/ and health-related quality of life.ti,ab,kf.	32330	35434
	34	quality of life/ and ec.fs.	10119	10572
	35	quality of life/ and (health adj3 status).ti,ab,kf.	9071	9731
	36	((qol or hrqol or quality of life).ti,kf. or *quality of life/) and ((qol or hrqol\$ or quality of life) adj2 (increas\$ or decrease\$ or improv\$ or declin\$ or reduc\$ or high\$ or low\$ or effect or effects or worse or score or scores or change\$1 or impact\$1 or impacted or deteriorat\$)).ab.	38348	42283
	37	(brief pain inventory or BPI\$ or patient health questionnaire\$ or PHQ\$ or (generalized anxiety disorder\$ adj2 questionnaire) or GAD\$ or PedsQL or Peds-QL or Pediatric Quality of Life Inventory or Quality of Life of Short Stature Youth or QoLISSY or adolescent pediatric pain tool or adolescent paediatric pain tool or APPT or weefim or functional independence measure).ti,ab,kf.	63326	68022
	38	or/12-37	300104	324832
Healthcare Cost and Resource Use	39	Cost allocation/	2004	2008
	40	Cost control/	21509	21585
	41	Cost savings/	11882	12226
	42	Cost of illness/	27401	28910



## Burden and Treatment of Achondroplasia SLR – Supplementary Appendices

Group	#	Searches	Results (27.08.20)	Results (10.06.21)
	43	Cost sharing/	2535	2609
	44	"Deductibles and coinsurance"/	1754	1783
	45	Medical savings accounts/	536	542
	46	Health care costs/	39780	41418
	47	Direct service costs/	1191	1204
	48	Drug costs/	16151	16618
	49	Employer health costs/	1092	1094
	50	Hospital costs/	11115	11497
	51	Health expenditures/	20379	21457
	52	Capital expenditures/	1990	1997
	53	exp economics, Hospital/	24627	25137
	54	exp economics, Medical/	14214	14262
	55	Economics, nursing/	3999	4004
	56	Economics, pharmaceutical/	2950	2994
	57	exp Budgets/	13733	13832
	58	Financial management/	16565	16686
	59	exp "Fees and charges"/	30366	30732
	60	(low adj cost).mp.	59665	66237
	61	(high adj cost).mp.	14889	16092
	62	(health?care adj cost\$).mp.	11888	13163
	63	(fiscal or funding or financial or finance).ti,ab,kf.	151063	163542
	64	(cost adj estimate\$).mp.	2308	2428
	65	(cost adj variable\$).mp.	165	172
	66	(unit adj cost\$).mp.	2544	2709
	67	(economic\$ or pharmacoeconomic\$ or price\$ or pricing).ti,ab,kf.	326903	354043
	68	((resource\$ or healthcare\$ or service\$) adj3 (use\$ or utilis\$ or utiliz\$ or consume\$ or consuming or consumption\$)).ti,ab,kf.	105427	114689
	69	((patient\$ or caregiver\$ or carer\$ or social\$ or society\$ or family\$ or work\$) adj2 (burden\$ or productiv\$)).ti,ab,kf.	19989	22307
	70	("length of stay" or utili?ation or "economic burden" or "cost-of-illness" or nursing cost\$ or physician cost\$ or physician visit\$ or "out of pocket").ti,ab,kf.	278374	300997
	71	(absenteeism or presenteeism or employment or unemployment).ti,ab,kf. or exp presenteeism/ or exp absenteeism/ or exp unemployment/ or exp employment/	143016	150515
	72	or/39-71	1083883	1161986
Exclusion Terms	73	exp animals/ not exp humans/	4728766	4839817
	74	(comment or editorial).pt.	1236733	1304305
	75	historical article/	359840	363956
	76	or/73-75	6255066	6435645
Combination	77	3 and (11 or 38 or 72)	388	406
	78	77 not 76	343	359
	79	remove duplicates from 78	<b>342</b>	<b>359</b>

**Database:** Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily 1946 to August 26, 2020 (original SLR) and June 09, 2021 (SLR update).

### Supplementary Table 4. Clinical efficacy and safety search terms for Embase

(via Ovid)

Group	#	Searches	Results (11.09.20)	Results (10.06.21)
<b>Achondroplasia</b>	1	exp achondroplasia/	2894	2995

Burden and Treatment of Achondroplasia SLR – Supplementary Appendices

Group	#	Searches	Results (11.09.20)	Results (10.06.21)
	2	(achondroplas\$ or FGFR3\$ or FGFR-3\$ or Fibroblast Growth Factor Receptor 3).ti,ab,kw.	6388	6782
	3	1 or 2	7319	7723
<b>RCTs</b>	4	"randomized controlled trial (topic)"/	185806	204657
	5	randomized controlled trial/	619164	660463
	6	clinical trial/	982734	1004644
	7	exp "clinical trial (topic)"/	331586	358413
	8	controlled clinical trial/	464566	463504
	9	multicenter study/	261302	289842
	10	exp randomization/	88082	91209
	11	single blind procedure/	40106	42848
	12	double blind procedure/	175711	184677
	13	crossover procedure/	64301	67159
	14	placebo/	354584	367187
	15	phase 1 clinical trial/ or phase 2 clinical trial/ or phase 3 clinical trial/ or phase 4 clinical trial/	163567	177381
	16	(clinical adj trial\$).ti,ab,kw.	552787	593881
	17	((singl\$ or doubl\$ or treb\$ or tripl\$) adj (blind\$3 or mask\$3)).ti,ab,kw.	241816	251909
	18	placebo\$.ti,ab,kw.	313159	327424
	19	(allocat\$ adj2 random\$).ti,ab,kw.	44144	46926
	20	Randomi?ed adj2 trial\$.ti,ab,kw.	444685	480799
	21	rct.ti,ab,kw.	40375	44514
	22	or/4-21	2410758	2545054
<b>Non-RCTs/ observational studies</b>	23	exp epidemiology/	3476935	3721562
	24	exp case control study/	178215	191151
	25	exp cohort analysis/	612312	715015
	26	Case control.ti,ab,kw.	167969	178104
	27	(cohort adj (study or studies)).ti,ab,kw.	315243	353125
	28	cohort analy\$.ti,ab,kw.	13435	14884
	29	(follow up adj (study or studies)).ti,ab,kw.	67254	69731
	30	(observational adj (study or studies)).ti,ab,kw.	173447	193742
	31	Longitudinal\$.ti,ab,kw.	364428	392597
	32	retrospective\$.ti,ab,kw.	1260054	1374677
	33	Cross sectional.ti,ab,kw.	475608	526652
	34	cross-sectional study/	365032	414755
	35	exp longitudinal study/	143824	156632
	36	exp follow-up/	1579374	1694159
	37	exp prospective study/	624575	689678
	38	exp retrospective study/	958644	1085903
	39	exp observational study/	206530	235440
	40	(Prospective adj (study or studies)).ti,ab,kw.	266255	280587
	41	(evaluation adj (study or studies)).ti,ab,kw.	8386	8907
	42	(epidemiologic adj (study or studies)).ti,ab,kw.	34151	35116
	43	((single arm or Single arm) adj3 (study or studies or trial\$)).ti,ab,kw.	11814	13406
	44	(Open-label adj (trial\$ or stud\$)).ti,ab,kw.	19720	20948
	45	Non-blinded stud\$.ti,ab,kw.	193	196
	46	(chart adj3 review).ti,ab,kw.	83290	90646
	47	or/23-46	6552508	7034296
<b>Exclusion terms</b>	48	("conference abstract" or "conference review").pt.	3864200	4116930
	49	limit 48 to yr="1974-2017" <sup>a</sup>	3030273	3802372
	50	exp animals/ not exp humans/	4674232	4793230

Burden and Treatment of Achondroplasia SLR – Supplementary Appendices

Group	#	Searches	Results (11.09.20)	Results (10.06.21)
	51	editorial.pt.	665035	693297
	52	historical article/	1	1
	53	or/49-52	8079724	8914014
<b>Combined</b>	54	3 and (22 or 47)	2027	2219
	55	54 not 53	1438	1344
	56	Remove duplicates from 55	<b>1404</b>	<b>1326</b>

<sup>a</sup> limit 48 to yr="1974-2019" was used in the SLR update. **Database:** Embase 1974 to 2020 September 10 (original SLR) and 2021 June 09 (SLR update).

**Supplementary Table 5. Economic evaluation, HRQoL/utility and cost/resource use search terms for Embase (via Ovid)**

Group	#	Searches	Results (27.08.20)	Results (10.06.21)
<b>Achondroplasia</b>	1	exp achondroplasia/ or exp dwarfism/	7536	7701
	2	(achondroplas\$ or FGFR3\$ or FGFR-3\$ or Fibroblast Growth Factor Receptor 3 or dwarfism*).ti,ab,kw.	10912	11445
	3	1 or 2	14065	14638
<b>Economic Evaluations</b>	4	Cost benefit analysis/ or exp economic evaluation/ or cost effectiveness analysis/ or cost minimization analysis/ or cost benefit/	307773	319723
	5	Economics/ or health economics/ or socioeconomics/ or economic aspect/ or pharmacoeconomics/	498023	510407
	6	(cost\$ adj (effective\$ or utilit\$ or consequence\$ or benefit\$ or minimi\$)).ti,ab,kw.	208752	222988
	7	(economic evaluation\$ or economic analysis or life year\$ gained or ICER or QALY\$ or DALY\$ or quality adjusted or adjusted life year\$ or disability adjusted life or qald\$ or qale\$ or qtime\$).ti,ab,kw.	54323	58613
	8	Quality adjusted life year/	26911	29060
	9	or/4-8	840936	872599
<b>Health-Related Quality of Life</b>	10	(health utilit\$ or health state\$1 or illness state\$1 or HSUV or HSUVs or health state\$ value\$ or health state\$ preference\$ or utility assessment\$ or utility measure\$ or preference based or utility based).ti,ab,kw.	16441	17701
	11	((index adj3 wellbeing) or (quality adj3 wellbeing) or qwb).ti,ab,kw.	1213	1349
	12	(multiattribute\$ or multi attribute\$).ti,ab.	1132	1221
	13	utility.ab. /freq=2	27785	30109
	14	(utilities or disutilit\$).ti,ab,kw.	12472	13420
	15	(euro qual or euro qual5d or euro qol5d or eq-5d or eq5-d or eq5d or eq 5d or euroqual or euroqol or euro qol or euroqual5d or euroqol5d or eq-sdq or eqsdq).ti,ab,kw.	21143	23607
	16	(short form\$ or shortform\$).ti,ab.	46255	50116
	17	(sf36\$ or sf 36\$ or sf thirtysix or sf thirty six).ti,ab,kw.	38415	40579
	18	(sf6 or sf 6 or sf6d or sf 6d or sf six D or sfsixD or sf six or sfsix or sf8 or sf 8 or sf eight or sfeight).ti,ab,kw.	4577	4828
	19	(sf12 or sf 12 or sf twelve or sftwelve).ti,ab,kw.	8305	8949
	20	(sf16 or sf 16 or sf sixteen or sfsixteen).ti,ab,kw.	54	56
21	(sf20 or sf 20 or sf twenty or sftwenty).ti,ab,kw.	345	352	

Burden and Treatment of Achondroplasia SLR – Supplementary Appendices

Group	#	Searches	Results (27.08.20)	Results (10.06.21)
	22	(15D or 15-D or 15 dimension).ti,ab,kw.	6692	6996
	23	visual analog\$ scale\$.ti,ab,kw.	80089	86717
	24	(standard gamble\$ or sg).ti,ab,kw.	16341	17558
	25	(time trade off\$1 or time tradeoff\$1 or tto or timetradeoff\$1).ti,ab,kw.	2827	2996
	26	(health\$1 year\$1 equivalent\$1 or hye or hyes).ti,ab,kw.	154	162
	27	(hui or hui1 or hui2 or hui3 or rosser).ti,ab,kw.	2466	2658
	28	*quality of life/ and (quality of life or qol or hrqol).ti,ab,kw.	98367	106533
	29	quality of life/ and ((quality of life or qol) adj3 (improv\$ or chang\$)).ti,ab.	76938	83099
	30	quality of life/ and ((quality of life or qol or hrqol) adj (score\$1 or measure\$1)).ti,ab,kw.	29915	32121
	31	quality of life/ and health-related quality of life.ti,ab,kw.	59054	64114
	32	quality of life/ and (health adj3 status).ti,ab,kw.	16371	17574
	33	((qol or hrqol or quality of life).ti. or *quality of life/) and ((qol or hrqol\$ or quality of life) adj2 (increas\$ or decrease\$ or improv\$ or declin\$ or reduc\$ or high\$ or low\$ or effect or effects or worse or score or scores or change\$1 or impact\$1 or impacted or deteriorat\$)).ab.	50970	55301
	34	(brief pain inventory or BPI\$ or patient health questionnaire\$ or PHQ\$ or (generalized anxiety disorder\$ adj2 questionnaire) or GAD\$ or PedsQL or Peds-QL or Pediatric Quality of Life Inventory or Quality of Life of Short Stature Youth or QoLISSY or adolescent pediatric pain tool or adolescent paediatric pain tool or APPT or weefim or functional independence measure).ti,ab,kw.	96568	104115
	35	or/10-34	470636	507722
	Healthcare Cost and Resource Use	36	Cost control/	68645
37		Cost of illness/	19285	19908
38		Health care cost/	190528	198654
39		Drug cost/	77613	79860
40		Hospital cost/	21600	22585
41		exp Budget/	29294	30550
42		Financial management/	113339	115171
43		health care financing/	13310	13472
44		exp Fee/	40171	40981
45		(low adj cost).mp.	67323	74988
46		(high adj cost).mp.	19477	21180
47		(health?care adj cost\$.mp.	20758	22908
48		(fiscal or funding or financial or finance).ti,ab,kw.	202567	222888
49		(cost adj estimate\$.mp.	3451	3685
50		(cost adj variable\$.mp.	266	281
51		(unit adj cost\$.mp.	4534	4829
52		(economic\$ or pharmacoeconomic\$ or price\$ or pricing).ti,ab,kw.	402434	434957
53		((resource\$ or healthcare\$ or service\$) adj3 (use\$ or utilis\$ or utiliz\$ or consume\$ or consuming or consumption\$)).ti,ab,kw.	147742	160939
54		((patient\$ or caregiver\$ or carer\$ or social\$ or society\$ or family\$ or work\$) adj2 (burden\$ or productiv\$)).ti,ab,kw.	33522	37338
55		("length of stay" or utili?ation or "economic burden" or "cost-of-illness" or nursing cost\$ or physician cost\$ or physician visit\$ or "out of pocket").ti,ab,kw.	404402	438913

## Burden and Treatment of Achondroplasia SLR – Supplementary Appendices

Group	#	Searches	Results (27.08.20)	Results (10.06.21)
	56	(absenteeism or presenteeism or employment or unemployment).ti,ab,kw. or exp presenteeism/ or exp absenteeism/ or exp unemployment/ or exp employment/	147396	157144
	57	or/36-56	1543616	1654805
<b>Exclusion</b>	58	("conference abstract" or "conference review").pt.	3859319	4116930
	59	limit 58 to yr="1974-2017"	3030273	3802372
	60	exp animal/ not exp human/	4669553	4793230
	61	(comment or editorial).pt.	663975	693297
	62	historical period/	673	736
	63	or/59-62	8074505	8914580
<b>Combination</b>	64	3 and (9 or 35 or 57)	382	414
	65	64 not 63	252	241
	66	remove duplicates from 65	<b>251</b>	<b>241</b>

Embase 1974 to 2020 August 27 (original SLR) and 2021 June 09 (SLR update).

### Supplementary Table 6. Search terms for Cochrane Library databases: CDSR and CENTRAL (via Wiley)

Group	#	Searches	Results (11.09.20)	Results (10.06.21)
<b>Achondroplasia</b>	1	[mh "achondroplasia"]	8	11
	2	(achondroplas* OR FGFR3* OR FGFR NEXT 3* OR "Fibroblast Growth Factor Receptor 3"):ti,ab,kw	81	100
	3	#1 OR #2	81	100
<b>Combined</b>	4	#3 in Trials	<b>81</b>	<b>100</b>
	5	#3 in Cochrane Reviews and Cochrane Protocols	<b>0</b>	<b>0</b>

### Supplementary Table 7. Search terms for DARE (via the University of York CRD platform)

Group	#	Searches	Results (11.09.20)
<b>Achondroplasia</b>	1	(MeSH DESCRIPTOR achondroplasia EXPLODE ALL TREES)	4
	2	(achondroplas* or FGFR3* or FGFR-3* or Fibroblast Growth Factor Receptor 3)	7
	3	(#1 or #2) in DARE	<b>1</b>

### Supplementary Table 8. Search terms for the NHS-EED and HTAD (via the University of York CRD platform)

Group	#	Searches	Results (27.08.20)
<b>Achondroplasia</b>	1	(MeSH DESCRIPTOR achondroplasia EXPLODE ALL TREES) or (MeSH DESCRIPTOR dwarfism EXPLODE ALL TREES)	21
	2	(achondroplas* or FGFR3* or FGFR-3* or Fibroblast Growth Factor Receptor 3 or dwarfism*)	16
	3	(#1 or #2) in NHS EED, HTAD	<b>17</b>

**Supplementary Table 9. Search terms for the HTAD (via the INAHTA platform)**

Group	#	Searches	Results (10.06.21)
Achondroplasia	1	"Achondroplasia"[mhe] or "dwarfism"[mhe]	5
	2	achondroplas*	5
	3	FGFR3* or "FGFR-3*" or "FGFR 3" or "Fibroblast Growth Factor Receptor 3"	0
	4	dwarfism*	1
Combination	5	#1 or #2 or #3 or #4	7

Supplementary Database Search Terms**Supplementary Table 10. Search terms for non-English databases and clinical trial registries**

Database	Group	#	Searches	Results (Original SLR)	Results (SLR update)
VHL (via <a href="https://bvshalud.org">https://bvshalud.org</a> )	Achondroplasia	1	tw:(achondroplasia) OR tw:(achondroplasia) <i>Filter out MEDLINE hits</i>	145	NA
LiSSa (via <a href="https://www.lissa.fr/dc/#env=lissa">https://www.lissa.fr/dc/#env=lissa</a> )	Achondroplasia	1	(achondroplasia.tl) OU (achondroplasia.mc)	136	137
Ichushi Web	Achondroplasia	1	軟骨無形成症/TH	2044	NA
		2	軟骨無形成症/TA or FGFR3/TA or FGFR-3/TA	846	NA
		3	#1 or #2	2275	NA
	Exclusion	4	動物/TH not ヒト/TH	341967	NA
		5	(#3) and (CK=動物)	242	NA
		6	#4 or #5	342131	NA
		7	#3 not #6	2031	NA
		8	(#7) and (LA=日本語)	1819	NA
		9	#8 and (AB=Y or FT=Y)	804	NA
CrescNet (via <a href="https://crescnet.org">https://crescnet.org</a> )	Achondroplasia	1	<i>Publications listed under "Wissenschaft" tab were searched</i>	NA	35
ClinicalTrials.gov	Achondroplasia	1	Achondroplasia	23	25
		2	FGFR3 Gene Mutation	11	12
EU Clinical Trials	Achondroplasia	1	Achondroplasia	NA	11
		2	FGFR3 Gene Mutation	NA	9
European Medicines Agency (EMA) clinical data portal	Achondroplasia	1	Achondroplasia	NA	0
		2	FGFR3	NA	3
Arzneimittel Informationssystem (AMIS)	Achondroplasia	1	achondroplasia	NA	0
		2	achondroplasia	NA	4
		3	FGFR3	NA	4

**Abbreviations:** AMIS, Arzneimittel Informationssystem; EMA, European Medicines Agency; EU-CTR, EU Clinical Trials Register; ICTRP, International Clinical Trials Registry Platform (ICTRP).

**Supplementary Table 11. Search strategies for hand-searching of relevant congresses**

Conference	Link	Search strategy	Total hits	Relevant hits
<p>The International Society for Pharmacoeconomics and Outcomes Research (ISPOR) Annual International and European Meetings</p> <ul style="list-style-type: none"> <li>• ISPOR International 2021</li> <li>• ISPOR International 2020</li> <li>• ISPOR International 2019</li> <li>• ISPOR International 2018</li> <li>• ISPOR Europe 2020</li> <li>• ISPOR Europe 2019</li> <li>• ISPOR Europe 2018</li> </ul>	<p>2020, 2019 and 2018:  <a href="https://www.ispor.org/heor-resources/presentations-database/search">https://www.ispor.org/heor-resources/presentations-database/search</a></p>	<p>2021, 2020, 2019 and 2018:                      Under Conference, click on each congress in turn.                      Enter in the keyword search bar:</p> <ul style="list-style-type: none"> <li>• achondroplas* OR FGFR3* OR FGFR-3* OR "Fibroblast Growth Factor Receptor 3" OR dwarfism*</li> </ul>	<ul style="list-style-type: none"> <li>• ISPOR International 2021: 1</li> <li>• ISPOR International 2020: 0</li> <li>• ISPOR International 2019: 0</li> <li>• ISPOR International 2018: 0</li> <li>• ISPOR Europe 2020: 0</li> <li>• ISPOR Europe 2019: 0</li> <li>• ISPOR Europe 2018: 0</li> </ul>	<ul style="list-style-type: none"> <li>• ISPOR International 2021: 1</li> <li>• ISPOR International 2020: 0</li> <li>• ISPOR International 2019: 0</li> <li>• ISPOR International 2018: 0</li> <li>• ISPOR Europe 2020: 0</li> <li>• ISPOR Europe 2019: 0</li> <li>• ISPOR Europe 2018: 0</li> </ul>
<p>Endocrine Society Conference (ENDO)</p> <ul style="list-style-type: none"> <li>• ENDO 2021</li> <li>• ENDO 2020</li> <li>• ENDO 2019</li> </ul>	<p>2021:  <a href="https://academic.oup.com/jes/issue/5/Supplement_1">https://academic.oup.com/jes/issue/5/Supplement_1</a>                      2020:  <a href="https://academic.oup.com/jes/issue/4/Supplement_1?page=3#1062435-5832293">https://academic.oup.com/jes/issue/4/Supplement_1?page=3#1062435-5832293</a>                      2019:  <a href="https://academic.oup.com/jes/issue/3/Supplement_1#:~:text=ENDO%202019%20Abstracts%20%2D%20101st%20Annual.%2C%202019%20%E2%80%93%20New%20">https://academic.oup.com/jes/issue/3/Supplement_1#:~:text=ENDO%202019%20Abstracts%20%2D%20101st%20Annual.%2C%202019%20%E2%80%93%20New%</a></p>	<p>2021, 2020, 2019: In the search bar in the top right select the dropdown for "This issue" and search the phrase:                      achondroplas* OR FGFR3* OR FGFR-3* OR "Fibroblast Growth Factor Receptor 3" OR dwarfism*</p>	<ul style="list-style-type: none"> <li>• 2021: 5</li> <li>• 2020: 6</li> <li>• 2019: 7</li> </ul>	<ul style="list-style-type: none"> <li>• 2021: 1</li> <li>• 2020: 1</li> <li>• 2019: 0</li> </ul>

Burden and Treatment of Achondroplasia SLR – Supplementary Appendices

Conference	Link	Search strategy	Total hits	Relevant hits
	<a href="#">20Orleans%2C%20Louisiana</a>			
European Society for Paediatric Endocrinology (ESPE) <ul style="list-style-type: none"> <li>• ESPE 2019</li> <li>• ESPE 2018</li> </ul>	2019/2018: <a href="https://abstracts.eurospe.org/search">https://abstracts.eurospe.org/search</a>	In the keyword textbox enter: achondroplas* OR FGFR3* OR FGFR-3* OR "Fibroblast Growth Factor Receptor 3" OR dwarfism* Event series: ESPE Annual Meeting Volume or conference: ESPE2019/ESPE 2018 in turn Click apply. Sift the records giving >20% match	<ul style="list-style-type: none"> <li>• 2019: 38</li> <li>• 2018: 2</li> </ul>	<ul style="list-style-type: none"> <li>• 2019: 0</li> <li>• 2018: 0</li> </ul>
International Conference on Children's Bone Health (ICCBH) <ul style="list-style-type: none"> <li>• ICCBH 2019</li> </ul>	2019: Abstract book, saved to server	Use the ctrl+f function to identify each term in turn: 1. achondroplasia 2. FGFR 3. Fibroblast Growth Factor Receptor 4. dwarfism Highlight each term once in each abstract it is present in; use a new highlighting colour for each search term; only review abstracts containing the search term; use the comment function to identify hit number of each search term (number of highlighted words)	<ul style="list-style-type: none"> <li>• 2019: 28</li> </ul>	<ul style="list-style-type: none"> <li>• 2019: 0</li> </ul>
Annual Clinical Genetics Meeting (ACGM) <ul style="list-style-type: none"> <li>• ACGM 2021</li> <li>• ACGM 2020</li> <li>• ACGM 2019</li> </ul>	2021: <a href="https://acmg.plaion.com/Web/User/AbsSearch?ACCOUNT=ACMG&amp;CONF=AM21&amp;ssoOverride=OFF&amp;USERPID=PUBLIC&amp;standalone=YES">https://acmg.plaion.com/Web/User/AbsSearch?ACCOUNT=ACMG&amp;CONF=AM21&amp;ssoOverride=OFF&amp;USERPID=PUBLIC&amp;standalone=YES</a>  2020: <a href="https://www.acmgmeeting.net/acmg2020/Public/Content.aspx?ID=3366&amp;sortMenu=110000">https://www.acmgmeeting.net/acmg2020/Public/Content.aspx?ID=3366&amp;sortMenu=110000</a>  2019: <a href="https://acmg.expoplanner.com/index.cfm?do=expomap.sesResults&amp;search_type=abstract">https://acmg.expoplanner.com/index.cfm?do=expomap.sesResults&amp;search_type=abstract</a>	2021, 2020: In the keyword box, enter the following in turn: 1. achondroplasia 2. FGFR 3. Fibroblast Growth Factor Receptor 4. dwarfism  2020: Under abstract type, select "Poster presentations only". In the keyword box, enter the following in turn: 1. achondroplasia 2. FGFR3 3. Fibroblast Growth Factor Receptor 4. dwarfism	<ul style="list-style-type: none"> <li>• 2021: 9</li> <li>• 2020: 3</li> <li>• 2019: 20</li> </ul>	<ul style="list-style-type: none"> <li>• 2021: 1</li> <li>• 2020: 0</li> <li>• 2019: 0</li> </ul>



Conference	Link	Search strategy	Total hits	Relevant hits
	<a href="#">s&amp;event_id=13&amp;ID=3331</a>			

**Abbreviations:** ACGM, Annual Clinical Genetics Meeting; ENDO, Endocrine Society Conference; ESPE, European Society for Paediatric Endocrinology; FGFR3, Fibroblast growth factor receptor 3; ICCBH, International Conference on Children's Bone Health; ISPOR, International Society for Pharmacoeconomics and Outcomes Research.

**Supplementary Table 12. Search strategies for hand-searching of HTA body and economic websites**

HTA Body	Link	Search strategy	Total hits Original SLR (SLR Update)	Relevant hits Original SLR (SLR Update)
National Centre for Pharmacoeconomics (NCPE)	<a href="http://www.ncpe.ie/">http://www.ncpe.ie/</a>	In the search bar at the top right, search the following: 1. achondroplasia 2. dwarfism 3. short stature 4. FGFR3 5. fibroblast growth factor receptor Screen the interventions against the list of relevant interventions in the eligibility table. For each relevant intervention, select these and review the "Summary" document (where available) for relevance. If no summary document is available, use the information given on the screen (these will therefore always be excluded).	achondroplasia : 0 (0) dwarfism: 0 (0) short stature: 0 (0) FGFR3: 0 (0) fibroblast growth factor receptor: 0 (0)	achondroplasia: 0 (0) dwarfism: 0 (0) short stature: 0 (0) FGFR3: 0 (0) fibroblast growth factor receptor: 0 (0)
National Institute for Health and Care Excellence (NICE)	<a href="https://www.nice.org.uk/">https://www.nice.org.uk/</a>	In the search bar, search the following: 1. "achondroplasia" OR "dwarfism" OR "short stature" OR "FGFR3" OR "fibroblast growth factor receptor" Under the "Filter results by..." on the left-hand side of the screen, check the following 2 boxes only: "Guidance" and "NICE Advice".  Screen the titles of the results for relevance. For relevant results, click these and look for the "History" tab on the right-hand side of the screen. Download the "Final Appraisal Document" and "Committee papers" for each result. Within the "Committee papers" document, double click the "Submission from manufacturer" document and screen this for relevance.	achondroplasia : 2 (3) dwarfism: 0 (0) short stature: 2 (0) FGFR3: 2 (0) fibroblast growth factor receptor: 0 (0)	achondroplasia: 0 (0) dwarfism: 0 (0) short stature: 0 (0) FGFR3: 0 (0) fibroblast growth factor receptor: 0 (0)
Haute Autorité de Santé (HAS)	<a href="http://www.has-sante.fr/portail/jcms/fc_1250_026/fr/evaluation-medico-">www.has-sante.fr/portail/jcms/fc_1250_026/fr/evaluation-medico-</a>	In the search bar in the centre of the homepage, search the following: 1. achondroplasie 2. nanisme 3. "petite taille" 4. FGFR3	'Les recommandations et guides' filter: achondroplasia : 0 (0) Nanisme: 4 (4)	'Les recommandations et guides' filter: achondroplasia: 0 (0) Nanisme: 0 (0)

## Burden and Treatment of Achondroplasia SLR – Supplementary Appendices

HTA Body	Link	Search strategy	Total hits Original SLR (SLR Update)	Relevant hits Original SLR (SLR Update)
	<a href="#">economie</a>	<p>5. "récepteur du facteur de croissance des fibroblastes"</p> <p>Select 'Les recommandations et guides' from dropdown menu to the right of the search bar.</p> <p>Repeat this method, this time selecting 'Médicaments' from the dropdown menu.</p>	<p>"petite taille": 197 (213)</p> <p>FGFR3: 0 (1)</p> <p>"récepteur du facteur de croissance des fibroblastes": 0 (0)</p> <p>'Médicaments' filter:</p> <p>achondroplasia: 0 (0)</p> <p>nanisme: 9 (9)</p> <p>"petite taille": 59 (74)</p> <p>FGFR3: 0 (0)</p> <p>"récepteur du facteur de croissance des fibroblastes": 3 (0)</p>	<p>"petite taille": 0 (0)</p> <p>FGFR3: 0 (0)</p> <p>"récepteur du facteur de croissance des fibroblastes": 0 (0)</p> <p>'Médicaments' filter:</p> <p>achondroplasia: 0 (0)</p> <p>nanisme: 0 (0)</p> <p>"petite taille": 0 (0)</p> <p>FGFR3: 0 (0)</p> <p>"récepteur du facteur de croissance des fibroblastes": 0 (0)</p>
Ministerio de Sanidad, Consumo y Bienestar Social (MSCBS)	<a href="https://redets.sanidad.gob.es/productos/buscarProductos.do?metodo=buscaTipos&amp;d-6893580-s=3&amp;d-6893580-p=1&amp;tipo=1&amp;d-6893580-o=1">https://redets.sanidad.gob.es/productos/buscarProductos.do?metodo=buscaTipos&amp;d-6893580-s=3&amp;d-6893580-p=1&amp;tipo=1&amp;d-6893580-o=1</a>	<p>In the Excel file of all records from the website (S:\Clients\BioMarin\BMN-EVDUK-ACP-01a (HTA SLRs for Achondroplasia)\3. Economic SLR\3. Searches\Hand Searches\BioMarin Vosortide Supplementary Searches_MSCBS.xls), Ctrl+F to search for the following:</p> <ol style="list-style-type: none"> <li>1. acondroplasia</li> <li>2. enanismo</li> <li>3. estatura baja</li> <li>4. FGFR3</li> <li>5. "receptor del factor de crecimiento de fibroblastos"</li> </ol> <ul style="list-style-type: none"> <li>• From the website, download the PDF of any relevant records.</li> </ul>	<p>acondroplasia: 0</p> <p>Enanismo: 0</p> <p>estatura baja: 0</p> <p>FGFR3: 0</p> <p>"receptor del factor de crecimiento de fibroblastos": 0</p>	<p>acondroplasia: 0</p> <p>Enanismo: 0</p> <p>estatura baja: 0</p> <p>FGFR3: 0</p> <p>"receptor del factor de crecimiento de fibroblastos": 0</p>
Comissão Nacional de Incorporação de Tecnologias no SUS (CONITEC)	<a href="http://conitec.gov.br/">http://conitec.gov.br/</a>	<p>In the search bar at the top right, search the following:</p> <ol style="list-style-type: none"> <li>1. acondroplasia</li> <li>2. nanismo</li> <li>3. "baixa estatura"</li> <li>4. FGFR3</li> <li>5. "receptor de fator de crescimento de fibroblasto"</li> </ol>	<p>acondroplasia: 0</p> <p>nanismo: 0</p> <p>"baixa estatura": 5</p> <p>FGFR3: 0</p> <p>"receptor de fator de crescimento de fibroblasto": 0</p>	<p>acondroplasia: 0</p> <p>nanismo: 0</p> <p>"baixa estatura": 0</p> <p>FGFR3: 0</p> <p>"receptor de fator de crescimento de fibroblasto": 0</p>

## Burden and Treatment of Achondroplasia SLR – Supplementary Appendices

HTA Body	Link	Search strategy	Total hits Original SLR (SLR Update)	Relevant hits Original SLR (SLR Update)
				de fibroblasto": 0
Instituto de Evaluación Tecnológica en Salud (IETS)	<a href="http://www.iets.org.co/">http://www.iets.org.co/</a>	In the search bar at the top right, search the following: 1. acondroplasia 2. enanismo 3. estatura baja 4. FGFR3 5. "receptor del factor de crecimiento de fibroblastos"	acondroplasia: 0 enanismo: 0 estatura baja: 0 FGFR3: 0 "receptor del factor de crecimiento de fibroblastos": 0	acondroplasia: 0 enanismo: 0 estatura baja: 0 FGFR3: 0 "receptor del factor de crecimiento de fibroblastos": 0
Agenzia Nazionale per i Servizi Sanitari Regionali (AGENAS)	<a href="https://www.agenas.gov.it/">https://www.agenas.gov.it/</a>	In the search bar at the top right, search the following: 1. acondroplasia 2. nanismo 3. "bassa statura" 4. FGFR3 5. "recettore del fattore di crescita dei fibroblasti"	acondroplasia: (0) nanismo: (0) "bassa statura": (0) FGFR3: (0) "recettore del fattore di crescita dei fibroblasti": (0)	acondroplasia: (0) nanismo: (0) "bassa statura": (0) FGFR3: (0) "recettore del fattore di crescita dei fibroblasti": (0)
Agenize Italiana del Farmaco (AIFA)	<a href="https://www.aifa.gov.it/">https://www.aifa.gov.it/</a>	In the search bar at the top right, search the following: 1. acondroplasia 2. nanismo 3. "bassa statura" 4. FGFR3 5. "recettore del fattore di crescita dei fibroblasti"	acondroplasia: (5) nanismo: (0) "bassa statura": (14) FGFR3: (0) "recettore del fattore di crescita dei fibroblasti": (0)	acondroplasia: (0) nanismo: (0) "bassa statura": (0) FGFR3: (0) "recettore del fattore di crescita dei fibroblasti": (0)
Institute for Quality and Efficiency in Health Care (IQWiG)	<a href="https://www.iqwig.de/">https://www.iqwig.de/</a>	In the search bar, search the following: 1. achondroplasie 2. zwergwuchs 3. kleinwuchs 4. FGFR3 5. "Fibroblasten-Wachstumsfaktor-Rezeptor"	achondroplasie : (0) zwergwuchs: (0) kleinwuchs: (2) FGFR3: (0) "Fibroblasten-Wachstumsfaktor-Rezeptor": (0)	achondroplasie: (0) zwergwuchs: (0) kleinwuchs: (0) FGFR3: (0) "Fibroblasten-Wachstumsfaktor-Rezeptor": (0)
Gemeinsamer	<a href="https://www.g-ba.de/">https://www.g-ba.de/</a>	In the search bar at the top right, search the following: 1. achondroplasie	achondroplasie : (1)	achondroplasie: (1)

Burden and Treatment of Achondroplasia SLR – Supplementary Appendices

HTA Body	Link	Search strategy	Total hits Original SLR (SLR Update)	Relevant hits Original SLR (SLR Update)
Bundesausschuss (G-BA)		<p>2. zwergwuchs 3. kleinwuchs 4. FGFR3 5. "Fibroblasten-Wachstumsfaktor-Rezeptor" Filtered by "Nutzenbewertungsverfahren" ("benefit assessment procedures")</p>	<p>zwergwuchs: (2) kleinwuchs: (28) FGFR3: (16) "Fibroblasten-Wachstumsfaktor-Rezeptor": (33)</p>	<p>zwergwuchs: (1) kleinwuchs: (3) FGFR3: (0) "Fibroblasten-Wachstumsfaktor-Rezeptor": (1)</p>
The Cost-Effectiveness Analysis (CEA) Registry, managed by Tufts Medical Center	<a href="http://healthconometrics.tuftsmedicalcenter.org/cear4/SearchingtheCEARegistry.aspx">http://healthconometrics.tuftsmedicalcenter.org/cear4/SearchingtheCEARegistry.aspx</a>	<p>Click on the yellow box titled 'View the CEA Registry'. In the search bar, paste in the first search term in the list below, with 'Methods' selected and hit search. 1. achondroplasia 2. dwarfism 3. "short stature" 4. FGFR3 5. "fibroblast growth factor receptor" Cross reference all results against the title/abstract review tracker. For any articles that were not captured in the title/abstract review, screen the abstract against the title/abstract eligibility flowchart. For any relevant at this stage, search for and download any freely available full text articles (using the full text searching process document in the Evidence Development Manual). Record any full texts behind paywalls. Repeat the above for each term with 'Ratios' selected and then with 'Utility Weights' selected.</p>	0 (0)	0 (0)
The University of Sheffield Health Utilities Database (SchARRHU D)	<a href="http://www.scharrhudd.org/">http://www.scharrhudd.org/</a>	<p>Select "search" in the menu at the top. In the first search bar, search for the following (in Abstract [AB]): 1. achondroplasia 2. dwarfism 3. "short stature" 4. FGFR3 5. "fibroblast growth factor receptor" Cross reference all results against the title/abstract review tracker. For any articles that were not captured in the title/abstract review, screen the abstract against the title/abstract eligibility flowchart. For any relevant at this stage, search for and download any freely available full-text articles. Record any full texts behind paywalls.</p>	0 (0)	0 (0)

HTA Body	Link	Search strategy	Total hits Original SLR (SLR Update)	Relevant hits Original SLR (SLR Update)
The EQ-5D Publications Database	<a href="http://eq-5dpublications.euroqol.org/?noheader=true">http://eq-5dpublications.euroqol.org/?noheader=true</a>	<p>Ensure the advanced search is presented. In the “type” dropdown, select “abstract” and in the “abstract” box enter the following:</p> <ol style="list-style-type: none"> <li>1. "achondroplasia" OR "dwarfism" OR "short stature" OR "FGFR3" OR "fibroblast growth factor receptor"</li> </ol> <p>Click the [+] button to the right of the abstract. This will add a new search line. In this search line in the “type” dropdown, select “And” in the operator box and “abstract” in the Type box. Search the following in the “abstract” box:</p> <ol style="list-style-type: none"> <li>2. Cost</li> </ol> <p>Cross reference all results against the title/abstract review tracker. For any articles that were not captured in the title/abstract review, screen the abstract against the title/abstract eligibility flowchart. For any relevant at this stage, search for and download any freely available full-text articles (using the full-text searching process document in the Evidence Development Manual). Record any full texts behind paywalls.</p> <p>Once the results of "achondroplasia" OR "dwarfism" OR "short stature" OR "FGFR3" OR "fibroblast growth factor receptor" AND cost have been searched, delete “cost” from the abstract box and replace it with the following terms one by one:</p> <ol style="list-style-type: none"> <li>3. Economic</li> <li>4. Utility</li> <li>5. Utilities</li> <li>6. Quality of life</li> <li>7. Resource</li> </ol>	3 (0)	0 (0)

**Abbreviations:** AB, abstract; AGENAS, Agenzia Nazionale per i Servizi Sanitari Regionali; AIFA, Agenzia Italiana del Farmaco; CEA, Cost-effectiveness analysis; CONETIC, Comissão Nacional de Incorporação de Tecnologias no SUS; FGFR3, fibroblast growth factor receptor 3 gene; EQ-5D, EuroQol-5 Dimension Questionnaire; G-BA, Gemeinsamer Bundesausschuss; HAS, Haute Autorité de Santé; HTA, Health Technology Assessment; IETS, Instituto de Evaluación Tecnológica en Salud; IQWiG, Institute for Quality and Efficiency in Health Care; MSCBS, Ministerio de Sanidad, Consumo y Bienestar Social; NCPE, National Centre for Pharmacoeconomics; NICE, National Institute for Health and Care Excellence; SchARRHUD, School of Health and Related Research Health Utilities Database.

## Guidelines

**Supplementary Table 13. Search terms for clinical guideline repositories**

Source	Link	Search Strategy (18.06.21)
The Guidelines International Network (GIN) International Guideline Library	<a href="https://guidelines.euroqol.com/">https://guidelines.euroqol.com/</a>	<p>Use the search bar to search for each key word in turn:</p> <ol style="list-style-type: none"> <li>1. achondroplasia: 0 hits</li> </ol>

## Burden and Treatment of Achondroplasia SLR – Supplementary Appendices

Source	Link	Search Strategy (18.06.21)
		2. FGFR: 0 hits 3. Fibroblast Growth Factor Receptor: 0 hits 4. dwarfism: 0 hits
Evidence Search, maintained by the UK NHS	<a href="https://www.evidence.nhs.uk/">https://www.evidence.nhs.uk/</a>	Search each key word in turn, filtering the 'Evidence type' to 'Guidance'.  1. achondroplasia: 8 hits 2. FGFR: 3 hits 3. Fibroblast Growth Factor Receptor: 47 hits 4. dwarfism: 4 hits
GuidelineCentral.com app	<a href="https://www.guidelinecentral.com/summaries/">https://www.guidelinecentral.com/summaries/</a>	Navigate to the search tab and then search each key word in turn, filtering to 'title'.  1. achondroplasia: 0 hits 2. FGFR: 0 hits 3. Fibroblast Growth Factor Receptor: 0 hits 4. dwarfism: 0 hits
Das Portal der Wissenschaftlichen Medizin (AWMF)	<a href="https://www.awmf.org/leitlinieNAktuelle-leitlinien.html#FA">https://www.awmf.org/leitlinieNAktuelle-leitlinien.html#FA</a>	Search for each key word in turn:  1. achondroplasie: 6 hits 2. FGFR: 9 hits 3. Fibroblasten-Wachstumsfaktor-Rezeptor: 0 hits 4. zwergrwuchs: 0 hits
The National Agency for Regional Health Services (AGENAS)	<a href="https://www.agenas.gov.it/">https://www.agenas.gov.it/</a>	Search for each key word in turn:  1. acondroplasia: 0 hits 2. FGFR: 0 hits 3. Recettore del fattore di crescita dei fibroblasti: 0 hits 4. nanismo: 0 hits
Haute Autorité de Santé (HAS)	<a href="https://www.has-sante.fr/">https://www.has-sante.fr/</a>	Search for each key word in turn filtering for 'les recommandations et guides'. Record results for 'practice guidelines and other guides'.  1. achondroplasie: 0 hits 2. FGFR: 0 hits 3. Récepteur du facteur de croissance des fibroblastes: 1 hit 4. nanisme: 1 hit
PubMed	<a href="https://pubmed.ncbi.nlm.nih.gov/">https://pubmed.ncbi.nlm.nih.gov/</a>	("guideline"[Publication Type] OR "clinical guideline"[Publication Type] OR "practice guideline"[Publication Type]) AND (achondroplasia OR "short stature" OR dwarfism): 40 hits
Google	<a href="https://www.google.co.uk/">https://www.google.co.uk/</a>	Review the first 50 results using the following search strings: <ul style="list-style-type: none"> <li>• ("guideline" AND "achondroplasia")</li> <li>• ("guideline" AND "short stature" OR "dwarfism")</li> </ul> ("best practice*" OR "guideline*") AND ("achondroplasia" OR "skeletal dysplasias")

**Abbreviations:** AGENAS, Agenzia Nazionale per i Servizi Sanitari Regionali; AWMF, Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften; GIN, Guidelines International Network; HAS, Haute Autorité de Santé.