**Supporting information**

**Supplemental congress searches**

* + American Association for the Study of Liver Disease
	+ European Association for the Study of the Liver
	+ Digestive Disease Week
	+ International Society for Pharmacoeconomics and Outcomes Research (ISPOR) US congress
	+ ISPOR European congress
	+ North American Society for Pediatric Gastroenterology, Hepatology and Nutrition
	+ European Society for Paediatric Gastroenterology, Hepatology and Nutrition
	+ World Congress of Pediatric Gastroenterology, Hepatology and Nutrition
	+ Studies of Pediatric Liver Transplantation (SPLIT) Annual Meeting
	+ American Transplant Congress
	+ International Pediatric Transplant Association

**Supplementary methods**

**Table 1**

**a) Eligibility criteria for epidemiological SR.**

|  |  |  |
| --- | --- | --- |
|  | **Inclusion criteria** | **Exclusion criteria** |
| Population | Patients with ALGS (adults or children)Carriers of ALGS (adults or children) | Animal/*in vitro* |
| Interventions | Not considered | N/A |
| Study design | Epidemiological study, retrospective medical case reports, studies reporting clinical features of ALGS  | Studies enrolling <15 patients with ALGS |
| Outcomes | Prevalence (any time frame)Incidence (any time frame)Disease natural history | All other outcomes including: clinical outcomes, treatment preferences, risk factors |
| Publication type | Primary data  | Editorial, letter, systematic reviewa, meta-analysisa, reviewa |
| aRelevant reviews and meta-analyses were ordered and bibliographic references were reviewed for additional relevant studies. ALGS, Alagille syndrome, N/A, not applicable; SR, systematic review. |

**b) Eligibility criteria for HRQoL.**

|  |  |  |
| --- | --- | --- |
|  | **Inclusion criteria** | **Exclusion criteria** |
| Population | Patients with ALGS (adults or children) | Animal/*in vitro* |
| Interventions | Any approved or experimental therapy or no treatment | N/A |
| Study design | Prospective or retrospective trialObservational study | Case study |
| Outcomes | Utilities (using any elicitation method) or preference weight* Including disutility associated with adverse events

Mapping studiesGeneric and disease-specific HRQoL questionnaires, for example, EQ-5D, SF-6D, SF-12, SF-36, VAS, PedsQL, itching severity scales  | All other outcomes including: clinical outcomes, treatment preferences, risk factors |
| Publication type | Primary data | Editorial, letter, systematic reviewa, meta-analysisa, reviewa |
| aRelevant reviews and meta-analyses were ordered and bibliographic references were reviewed for additional relevant studies. ALGS, Alagille syndrome; EQ-5D, 5- dimension EuroQol questionnaire; HRQoL, health-related quality of life; N/A, not applicable; PedsQL, Pediatric Quality of Life Inventory; SF-6D, 6-dimension Short-Form Health Survey; SF-12, 12-item Short-Form Health Survey; SF-36, 36-item Short-Form Health Survey; VAS, visual analogue scale.  |

**c) Eligibility criteria for economic evaluation and resource use studies.**

|  |  |  |
| --- | --- | --- |
|  | **Inclusion criteria** | **Exclusion criteria** |
| Population | Patients with ALGS (adults or children) | Animal/*in vitro* |
| Interventions | Any approved or experimental therapy or no treatment | N/A |
| Study design | * Prospective or retrospective study
* Observational study
* Economic evaluation
 | Case study |
| Outcomes | * ICERs
* QALYs
* Direct costs (total or disaggregated costs) associated with ALGS
	+ Individual costs to include hospitalization, pharmaceutical and labor costs
* Indirect costs associated with sick leave, disability, etc.
 | * + All other outcomes including: clinical outcomes, treatment preferences, risk factors
 |
| Publication type | Primary data | Editorial, letter, systematic reviewa, meta-analysisa, reviewa |
| aRelevant reviews and meta-analyses were ordered and bibliographic references were reviewed for additional relevant studies.ALGS, Alagille syndrome; ICER, incremental cost-effectiveness ratio; N/A, not applicable; QALY, quality-adjusted life-year. |

**Epidemiology/clinical features search strategies**

Embase, date assessed: 13 May 2015

|  |  |  |
| --- | --- | --- |
| [**# ▲**](https://ovidsp.tx.ovid.com/sp-3.15.1b/ovidweb.cgi?&S=NMDCFPMOIMDDMKHKNCKKCDOBINJFAA00&Sort+Sets=descending) | **Searches** | **Results** |
| 1 | exp Alagille syndrome/ | 1214 |
| 2 | (Alagille\* adj2 syndrome$).mp. | 1309 |
| 3 | algs.mp. | 66 |
| 4 | Arteriohepatic dysplasia.mp. | 127 |
| 5 | 1 or 2 or 3 or 4 | 1355 |
| 6 | exp epidemiology/ or exp genetic epidemiology/ | 2208938 |
| 7 | epidemiolog\*.mp. | 557908 |
| 8 | Prevalence.mp. or exp prevalence/ | 669581 |
| 9 | exp familial incidence/ or exp incidence/ or incidence.mp. | 828104 |
| 10 | exp history/ | 324659 |
| 11 | (natural or disease).mp. | 6451232 |
| 12 | 10 and 11 | 41684 |
| 13 | natural history.mp. | 49298 |
| 14 | 6 or 7 or 8 or 9 or 12 or 13 | 3028965 |
| 15 | 5 and 14 | 217 |
| **16** | **limit 15 to human** | **200** |

MEDLINE® date assessed: 13 May 2015

|  |  |  |
| --- | --- | --- |
|  | **Searches** | **Results** |
| 1 | exp Alagille Syndrome/ | 513 |
| 2 | (Alagille\* adj2 syndrome$).mp. | 764 |
| 3 | algs.mp. | 50 |
| 4 | Arteriohepatic dysplasia.mp. | 108 |
| 5 | 1 or 2 or 3 or 4 | 828 |
| 6 | exp Epidemiology/ | 22302 |
| 7 | genetic epidemiology.mp. | 1635 |
| 8 | epidemiolog\*.mp. | 355123 |
| 9 | Prevalence.mp. or exp Prevalence/ | 482392 |
| 10 | incidence.mp. or exp Incidence/ | 629610 |
| 11 | familial incidence.mp. | 574 |
| 12 | exp Natural History/ | 648 |
| 13 | natural history.mp. | 38542 |
| 14 | 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 | 1334748 |
| 15 | 5 and 14 | 50 |
| **16** | **limit 15 to humans** | **47** |

Burden of illness search strategies

Embase, date assessed: 13 May 2015

|  |  |  |
| --- | --- | --- |
|  | **Searches** | **Results** |
| 1 | exp Alagille syndrome/ | 1214 |
| 2 | (Alagille\* adj2 syndrome$).mp. | 1309 |
| 3 | algs.mp. | 66 |
| 4 | Arteriohepatic dysplasia.mp. | 127 |
| 5 | 1 or 2 or 3 or 4 | 1355 |
| 6 | exp "quality of life"/ | 299346 |
| 7 | (qol or HRQoL or HRQL).mp. | 53685 |
| 8 | quality of life.mp. | 344337 |
| 9 | (Humanistic adj2 burden).mp. | 110 |
| 10 | health status.mp. or exp Health Status/ | 174469 |
| 11 | (Utilit\* or disutilit\*).mp. | 177742 |
| 12 | (EQ5D or EQ 5D or EuroQoL).mp. | 8543 |
| 13 | (health state\* or HSUV).mp. | 6494 |
| 14 | patient preference.mp. or exp Patient Preference/ | 9778 |
| 15 | (health utility index or health utility index or HUI2 or HUI3 or HUI 2 or HUI 3).mp. | 631 |
| 16 | (medical outcome study or short-form or shortform or mos-sf or sf12 or sf 12 or sf36 or sf 36 or sf6d or sf 6d or RAND36 or RAND12 or RAND 36 or RAND 12).mp. | 45046 |
| 17 | ((quality of well being or quality of wellbeing or QWB) and (question\* or utilit\* or survey)).mp. | 290 |
| 18 | (Time Trade Off or Standard Gamble or rating$ scale).mp. | 137960 |
| 19 | ((mapping or crosswalk\*) and utilit\*).mp. | 3368 |
| 20 | exp Health Assessment Questionnaire/ or exp questionnaire/ or questionnaire.mp. | 556874 |
| 21 | patient report\* outcome$.mp. | 8989 |
| 22 | PedsQL.mp. | 1363 |
| 23 | exp visual analog scale/ or VAS.mp. or visual analog\* scale$.mp. | 81808 |
| 24 | Pruritus.mp. or exp pruritus/ | 67837 |
| 25 | Itch\*.mp. | 16952 |
| 26 | exp Medication compliance/ | 8024 |
| 27 | (Medication adj2 (adher\* or complian\*)).mp. | 17529 |
| 28 | exp body image/ | 16005 |
| 29 | exp personal appearance/ | 512 |
| 30 | (((personal or physical) adj appearance) and (feeling$ or perception or opinion$)).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] | 485 |
| 31 | 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 | 1367525 |
| 32 | exp Economics, Hospital/ or exp Economics/ or exp Economics, Nursing/ or economics.mp. or exp Economics, Medical/ | 789244 |
| 33 | exp "Costs and Cost Analysis"/ or (Costs and Cost Analysis).mp. | 271588 |
| 34 | cost of illness.mp. or exp "Cost of Illness"/ | 16248 |
| 35 | cost control.mp. or exp "Cost Control"/ | 52708 |
| 36 | drug costs.mp. or exp Drug Costs/ | 61751 |
| 37 | cost$.mp. | 720060 |
| 38 | hospital charges.mp. or exp Hospital Charges/ | 5325 |
| 39 | health care costs.mp. or exp Health Care Costs/ | 221289 |
| 40 | (resource adj2 (use\* or utili\* or allocat\*)).mp. | 38188 |
| 41 | Cost-Benefit Analysis.mp. or exp Cost-Benefit Analysis/ | 69463 |
| 42 | economic\*.mp. | 518517 |
| 43 | cost minimi?ation.mp. | 3236 |
| 44 | economic evaluation.mp. | 14931 |
| 45 | cost utility.mp. | 7414 |
| 46 | exp Economics, Pharmaceutical/ | 173356 |
| 47 | exp Models, Statistical/ or exp Markov Chains/ | 168890 |
| 48 | Markov model.mp. | 8178 |
| 49 | decision trees.mp. or exp Decision Trees/ | 7409 |
| 50 | exp Models, Theoretical/ | 68886 |
| 51 | Quality-Adjusted Life Years.mp. or exp Quality-Adjusted Life Years/ | 15071 |
| 52 | QALY.mp. | 8424 |
| 53 | (Life Years Gained or LYG).mp. | 1446 |
| 54 | (incremental cost effectiveness ratio or icer).mp. | 6200 |
| 55 | (cost effective\* or cost utilit\* or CEA or CUA).mp. | 192087 |
| 56 | budget impact.mp. | 1466 |
| 57 | (economic adj2 burden).mp. | 8232 |
| 58 | exp health insurance/ | 195184 |
| 59 | Medical claims.mp. | 1337 |
| 60 | exp Medicare/ or medicare.mp. | 63824 |
| 61 | exp Medicaid/ or medicaid.mp. | 36507 |
| 62 | 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 | 1531855 |
| **63** | **5 and (31 or 62)** | **177** |

MEDLINE®, date assessed: 13 May 2015

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| **[# ▲](https://ovidsp.tx.ovid.com/sp-3.15.1b/ovidweb.cgi?&S=HGADFPCONIDDMKPENCKKOHOBJGCGAA00&Sort+Sets=descending)** | **Searches** | **Results** |
| 1 | exp Alagille syndrome/ | 513 |
| 2 | (Alagille\* adj2 syndrome$).mp. | 764 |
| 3 | algs.mp. | 50 |
| 4 | Arteriohepatic dysplasia.mp. | 108 |
| 5 | 1 or 2 or 3 or 4 | 828 |
| 6 | Quality of life.mp. or exp "Quality of Life"/ | 213430 |
| 7 | (qol or HRQOL or HRQL).mp. | 32118 |
| 8 | (humanistic adj2 burden).mp. | 49 |
| 9 | health status.mp. or exp Health Status/ | 151541 |
| 10 | (utilit\* or disutilit\*).mp. | 133755 |
| 11 | (EQ5D or EQ 5D or EuroQoL).mp. | 4852 |
| 12 | (health state\* or HSUV).mp. | 4154 |
| 13 | patient preference.mp. or exp Patient Preference/ | 6011 |
| 14 | (health utility index or HUI2 or HUI3 or HUI 2 or HUI 3).mp. | 451 |
| 15 | (medical outcome study or short-form or shortform or mos-sf or sf12 or sf 12 or sf36 or sf 36 or sf6d or sf 6d or RAND36 or RAND12 or RAND 36 or RAND 12).mp. | 29400 |
| 16 | ((quality of well being or quality of wellbeing or QWB) and (question\* or utilit\* or survey)).mp. | 247 |
| 17 | (Time Trade Off or Standard Gamble or rating$ scale).mp. | 35049 |
| 18 | ((mapping or crosswalk\*) and utilit\*).mp. | 3532 |
| 19 | exp Questionnaires/ or Health Assessment Questionnaire.mp. | 331150 |
| 20 | patient report\* outcome$.mp. | 5090 |
| 21 | PedsQL.mp. | 767 |
| 22 | exp visual analog scale/ or VAS.mp. or visual analog\* scale$.mp. | 49635 |
| 23 | Pruritus.mp. or exp pruritus/ | 18081 |
| 24 | Itch\*.mp. | 9964 |
| 25 | exp Medication adherence/ | 9058 |
| 26 | (Medication adj2 (adher\* or complian\*)).mp. | 14491 |
| 27 | exp body image/ | 13447 |
| 28 | (((personal or physical) adj appearance) and (feeling$ or perception or opinion$)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] | 309 |
| 29 | 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 | 858183 |
| 30 | exp Economics, Hospital/ or exp Economics/ or exp Economics, Nursing/ or economics.mp. or exp Economics, Medical/ | 512387 |
| 31 | exp "Costs and Cost Analysis"/ or (Costs and Cost Analysis).mp. | 188263 |
| 32 | cost of illness.mp. or exp "Cost of Illness"/ | 19461 |
| 33 | cost control.mp. or exp "Cost Control"/ | 30186 |
| 34 | drug costs.mp. or exp Drug Costs/ | 14055 |
| 35 | cost$.mp. | 474509 |
| 36 | hospital charges.mp. or exp Hospital Charges/ | 4008 |
| 37 | health care costs.mp. or exp Health Care Costs/ | 55168 |
| 38 | (resource adj2 (use\* or utili\* or allocat\*)).mp. | 24298 |
| 39 | Cost-Benefit Analysis.mp. or exp Cost-Benefit Analysis/ | 63549 |
| 40 | economic\*.mp. | 229421 |
| 41 | cost minimi?ation.mp. | 915 |
| 42 | economic evaluation.mp. | 5820 |
| 43 | cost utility.mp. | 2811 |
| 44 | exp Economics, Pharmaceutical/ | 2572 |
| 45 | exp Markov Chains/ or exp Models, Statistical/ or exp Models, Theoretical/ | 1355458 |
| 46 | markov model.mp. | 4684 |
| 47 | decision trees.mp. or exp Decision Trees/ | 9724 |
| 48 | Quality-Adjusted Life Years.mp. or exp Quality-Adjusted Life Years/ | 9441 |
| 49 | QALY.mp. | 4842 |
| 50 | (Life Years Gained or LYG).mp. | 877 |
| 51 | (incremental cost effectiveness ratio or icer).mp. | 3513 |
| 52 | (cost effective\* or cost utilit\* or CEA or CUA).mp. | 103885 |
| 53 | budget impact.mp. | 490 |
| 54 | (economic adj2 burden).mp. | 5203 |
| 55 | exp Insurance, Health/ | 125876 |
| 56 | Medical claims.mp. | 738 |
| 57 | exp Medicare/ or medicare.mp. | 52911 |
| 58 | exp Medicaid/ or medicaid.mp. | 36498 |
| 59 | 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 | 2224981 |
| **60** | **5 and (29 or 59)** | **101** |