**Supplementary Results**

**Table 1** | Summary of studies exploring the epidemiology/clinical features of ALGS

| Reference, country [sites] | Objectivea | Design (study period) | Population (n) | Data of interest |
| --- | --- | --- | --- | --- |
| *Incidence studies* | | | | |
| Danks *et al.,* 1977 [8]  Australia  [sites NR] | To report aetiological factors in babies with biliary atresia or neonatal hepatitis | Prospective study of children born in the state of Victoria (1963–1974; 11.5 years) | * Live births (n = 790 385) * Extrahepatic biliary atresia (n = 55) * Intrahepatic biliary atresia (ALGS) (n = 11) * Neonatal hepatitis (n = 105) | Incidence of ALGS |
| Leonard *et al.,* 2014 [9]  [country and sites NR] | To outline the clinical utility of genetic testing for ALGS | N/A | N/A | A calculation of the incidence of ALGS based on reported literature |
| *Clinical features of ALGS* | | | | |
| Alagille *et al.*, 1987 [10]  France  [1 site] | To assess the clinical characteristics of patients with PILBD | Retrospective analysis of patient records (1960–1985; 25 years) | * Patients with PILBD (n = 80) | Major and minor clinical features of ALGS, survival |
| Deprettere *et al.*, 1987 [11]  UK  [NR] | To assess variability of hepatic features and frequency of associated abnormalities in patients with syndromic PILBD | Retrospective analysis of patients identified by liver biopsies (1973–1983; 10 years) | * Children with PILBD and major clinical features (cardiovascular, vertebral, characteristic facies or embryotoxon, excluding other specific causes of intrahepatic cholestasis) of ALGS (n = 27) | Major and minor clinical features of ALGS, survival |
| Emerick *et al.*, 1999 [12]  USA  [3 sites] | To determine the frequency of clinical manifestations and to correlate the clinical findings with outcome | Retrospective analysis of gastroenterology records (1974–1997; 23 years) | Paediatric patients with ALGS (n = 92) comprising unrelated probands (n = 83) and significantly affected family members (n = 9) | Major and minor clinical features of ALGS, survival, LT, PEBD |
| Hoffenberg *et al.*, 1995 [13]  USA  [3 sites] | To determine the outcome of syndromic PILBD in patients with ALGS with onset of cholestasis in infancy | Retrospective review of the records of patients with ALGS with PILBD (1983–1994; 11 years) | * Unrelated children with ALGS and PILBD (n = 26) | Major and minor clinical features of ALGS, survival, LT |
| Kamath *et al.,* 2004 [15]  USA  [1 site] | To determine the prevalence of  non-cardiovascular anomalies and events in a cohort of individuals  with ALGS | Retrospective analysis of patient records (NR) (1992–2002, 10 years) | * Children with diagnosis of ALGS or a mutation in *JAG1*(n = 268) | Vascular anomalies |
| Kamath *et al.*, 2012a [16]  USA, Canada  [16 sites] | To determine LT outcomes | Retrospective review of the SPLIT database (1995–2009; 14 years) | * Children with ALGS who had undergone LT (n = 91) * Age-matched control patients with biliary atresia who had undergone LT (n = 236) | Survival, ALGS-specific pre‑transplant characteristics, indications for LT, PEBD |
| Kamath *et al.,* 2012b [14]  USA  [sites NR] | To describe and characterize renal involvement in a large cohort of *JAG1* mutation-positive individuals | Retrospective analysis of patient records (NR) | * *JAG1* mutation-positive individuals with renal involvement (n = 187) | Renal abnormalities |
| Lykavieris *et al.*, 2001 [18]  France  [1 site] | To evaluate the effect of the liver condition on mortality, morbidity and long-term outcomes | Retrospective analysis of patient records (1960–2000; 40 years) | * Children with ALGS and liver involvement (n = 163) | Major and minor clinical features of ALGS, survival, LT, PEBD |
| Lykavieris *et al.*, 2003 [17] France  [1 site] | To assess the incidence and sites of bleeding (excluding intracranial bleeding) and the potential contribution of bleeding to morbidity | Retrospective analysis of patient records (1960–2000; 40 years) | * Children with ALGS and severe haemorrhagic complications, without biological signs of liver failure (n = 38) | Bleeding episodes, types of bleeding, haemorrhagic complications, heart defects, vascular complications, cardiovascular manifestations, LT |
| Narula *et al.*, 2006 [19]  UK  [1 site] | To review the incidence of visual loss and intracranial hypertension | Retrospective analysis of patient records (1989–2004; 15 years) | * Children with ALGS who had undergone an ophthalmic examination (n = 41 of whom met the diagnostic criteria) | Visual problems, clinical characteristics at presentation, LT |
| Nischal *et al.*, 1997 [20]  UK  [1 site] | To perform full ocular examinations to detect optic disc drusen (abnormal deposits) | Cross-sectional (NR) | * Unrelated children with ALGS (n = 20) * Unrelated children with non-ALGS-related cholestatic jaundice (n = 8) | Visual problems |
| Quiros-Tejeira *et al.*, 1999 [21]  USA  [2 sites] | To assess the long-term clinical course of ALGS | Retrospective analysis of patient records (1976–1997 and 1980–1997; 22 years) | * Children with ALGS and cholestasis (n = 43) | Major and minor clinical features of ALGS, survival, LT |
| Subramaniam *et al.*, 2011 [22]  UK  [1 site] | To assess the frequency of clinical, radiological and histological features at presentation | Retrospective analysis of patient records (1980–2005; 25 years) | * Children with ALGS (n = 117) | Major and minor clinical features of ALGS, survival |

aOnly objectives relevant to the systematic review study questions have been extracted.

A1ATD, alpha-1-antitrypsin deficiency; ALGS, Alagille syndrome; *JAG1*, Jagged 1; LT, liver transplantation; N/A, not applicable; NR, not reported; PEBD, partial external biliary diversion; PFIC, progressive intrahepatic cholestasis; PILBD, paucity of interlobular bile ducts; SPLIT, Studies of Pediatric Liver Transplantation.

**Supplementary Figure legends**

**Figure S1** | PRISMA diagram of included and excluded studies in the epidemiology and natural history systematic review

Figure footnotes: ALGS, Alagille syndrome; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

**Figure S2** | PRISMA diagram of included and excluded studies in the HRQoL systematic review

Figure footnotes: ALGS, Alagille syndrome; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.