Additional file 3: Table S3. Summary of published screening studies based primarily on medical chart review and bioinformatics/data mining

Cohort (reference)	Study population	Design / observation period	Centres / countries	Screening method(s)	Patients identified, n/N (%)*
Yerushalmi et al. 2002 [50]	Neonates with jaundice/cholestasis N = 40	Retrospective, observational / 2 years	Single centre / US	Medical chart review *NPC1/NPC2* sequencing† Other laboratory tests‡	Patients: 3 (7.5%)
Verity et al. 2010 [52]	Children (<16 years) with suspected early-onset cognitive impairment N = 2,636	Prospective surveillance / 12 years	Multicentre / UK	Clinical case surveillance reporting	Patients: 38 (1.4%)
Hegarty et al. 2015 [51]	Patients <5 years old with acute liver failure N = 127	Retrospective observational / 10 years	Single centre / UK	Clinical, laboratory, and outcome data	Patients: 3 (2.4%)
Wassif et al. 2016 [14]	Subjects (all ages) included in 4 large, sequencing projects N = 17,754 chromosomes	Retrospective genetic database / No period specified	Multicentre / International	Historical *NPC1/NPC2* sequencing (*WES*)	Patients: 0 (0%) (1 in 89,229††)
Winstone et al. 2017 [53]	Children aged < 16 years with progressive intellectual and neurological deterioration N = 3,979	Retrospective cross-sectional national surveillance 18 years	Multicentre / UK	Clinical case surveillance reporting	Patients: 53 (1.3%)
Corry 2014 [54]	UK ethnic subjects with suspected autosomal recessive conditions N = >13,000	Retrospective analysis of regional and national patient registries 3 years	Multicentre / UK	Clinical case surveillance reporting	NR

**n/N (%), number of cases detected per cohort or study over total number of subjects in cohort/study (% based on n/N); †Sanger sequencing; ‡other laboratory tests including, but not limited to filipin staining, cholesterol esterification assay, liver/skin biopsy and electron microscopy; ††Calculated frequency of pathogenic NPC1/NPC2 variants; IEM, inborn error of metabolism; WES, whole-exome sequencing.*