Supplemental Table S1. Patient variables analyzed in included articles

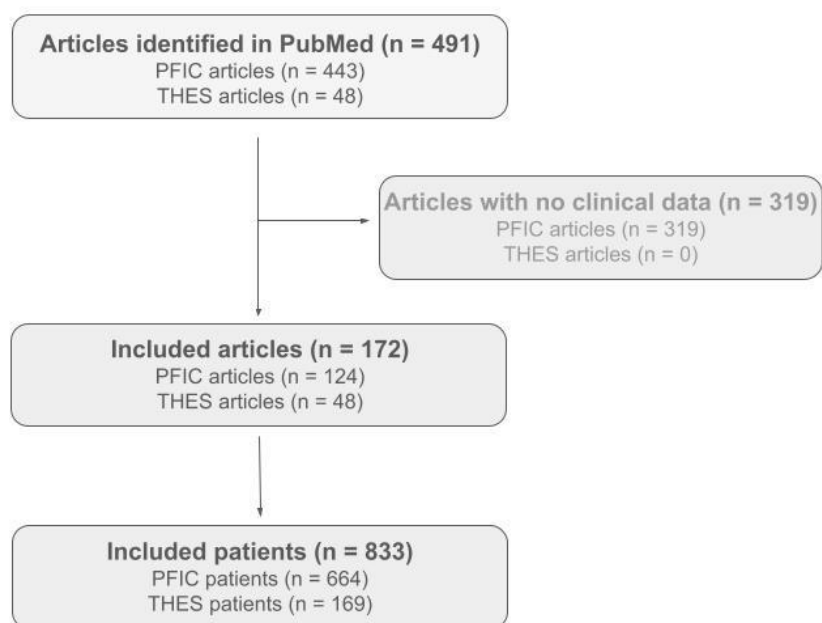| Category	Variable	Details
Neonatal	Consanguinity	Yes/no
	Gestational age at birth	In weeks of gestation and dichotomized as preterm (< 40 weeks) or term (≥ 40 weeks)
	Size at birth	Weight, length and head circumference in kg/cm and in percentiles and standard scores.
	Sex	Female or male.
Disease progression	Age at first symptoms	In months (defined as 30.4 days).
	Age at molecular diagnosis	In years (defined as 365 days).
	Age at last follow-up	In years (defined as 365 days).
	Status at last follow-up	Alive or dead, with age at death if reported.
Growth	Size at last follow-up	Weight, height and head circumference in kg/cm and in percentiles and standard scores.
Symptoms	Phenotypic abnormalities	As HPO (*5*) terms (*https://hpo.jax.org*) with age of onset if reported.
Genetics	Gene	HGNC-approved symbol (*https://www.genenames.org/*)
	Variants	HGVS codes (*https://hgvs-nomenclature.org/*) based on mRNA and protein sequences.

HPO, Human Phenotype Ontology; AST, aspartate transaminase; ALT, alanine transaminase; GGT, gamma-glutamyltransferase; HGNC, HUGO Gene Nomenclature Committee; HGVS, Human Genome Variation Society.

Supplemental Table S2. Number of included articles, patients and data points and data completeness[a] for the studied diseases.

Disease	Articles	Patients	Data points	Completeness[a]
PFIC1	26	86	290	64.9%
PFIC2	30	159	561	69.1%
PFIC3	23	147	497	66.0%
PFIC4	19	66	167	47.2%
PFIC5	4	9	45	100%
PFIC6	1	3	15	100%
PFIC7	4	27	135	100%
PFIC8	3	12	60	100%
PFIC9	2	10	50	100%
PFIC10	11	144	622	86.4%
PFIC11	1	1	5	100%
THES1	19	107	184	86.3%
THES2	29	62	233	72.4%

PFIC, progressive familial intrahepatic cholestasis, THES, trichohepatoenteric syndrome.

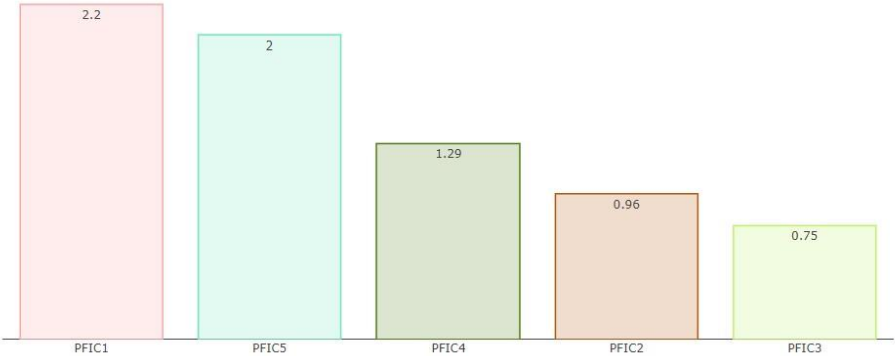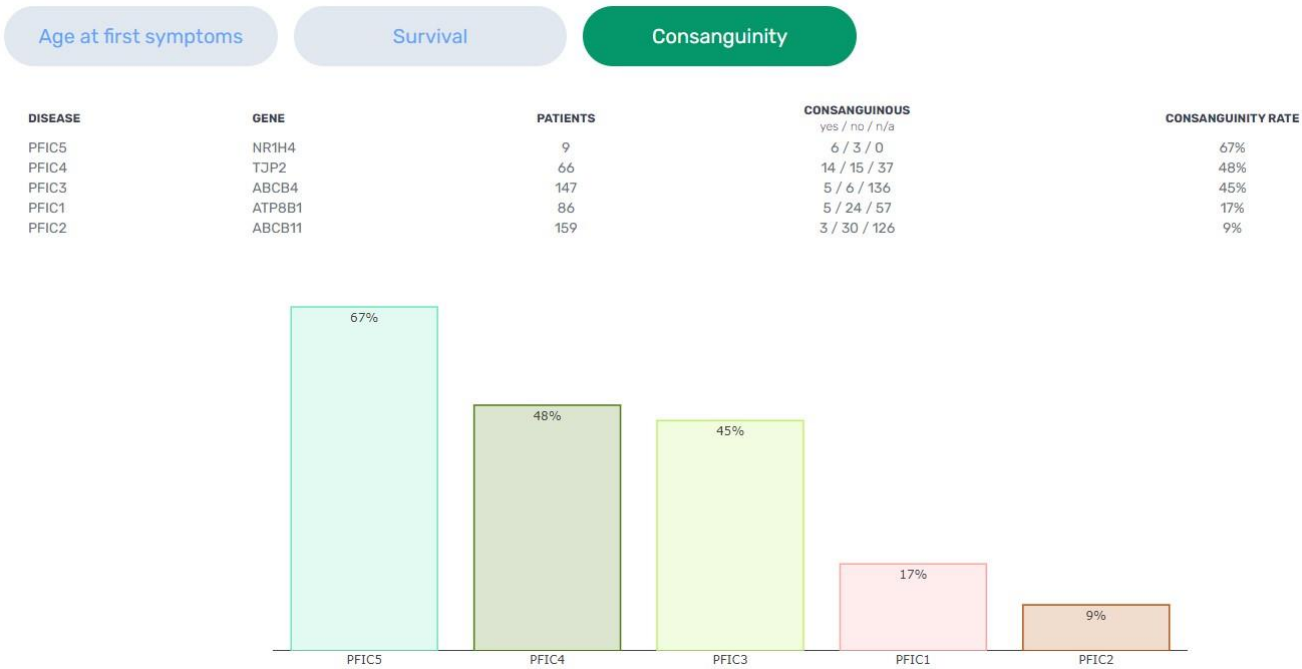[a]Proportion of currently studied variables reported in included articles.
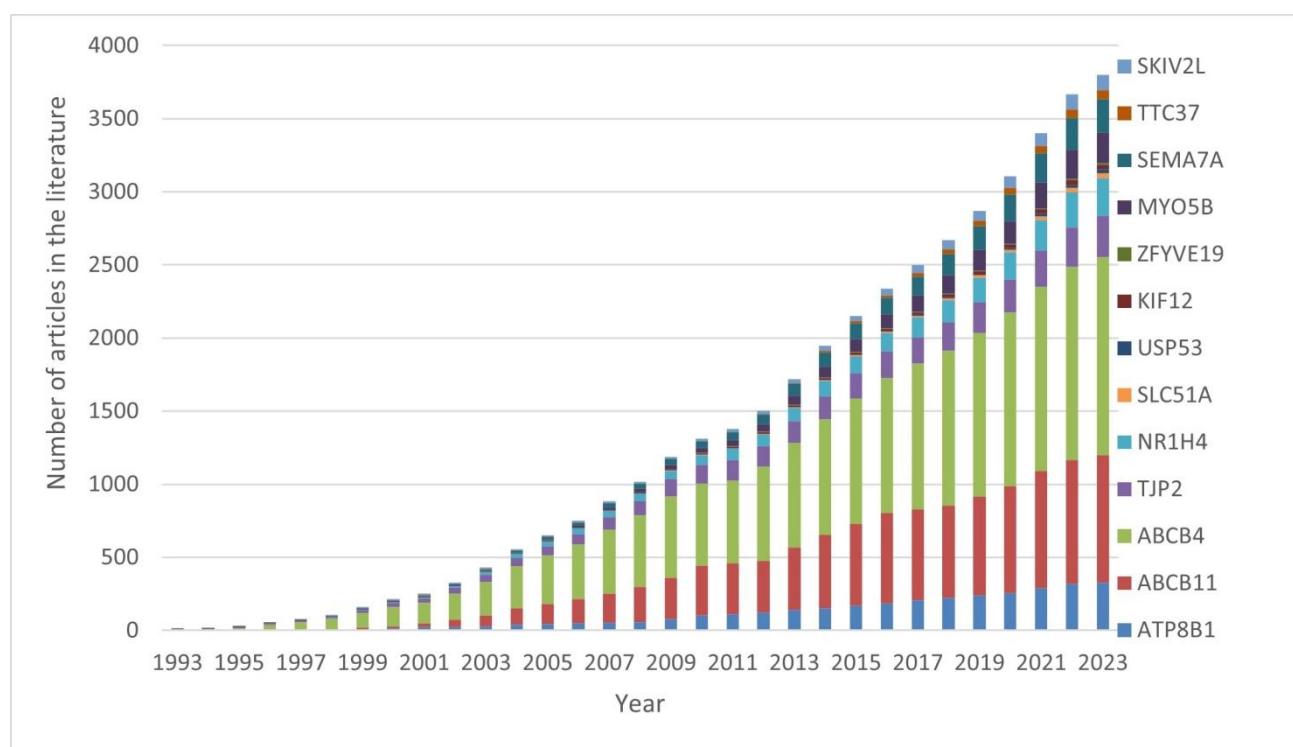
Supplemental Figure S1. Flowchart of the study.

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Age at first symptoms

DISEASE	GENE	PATIENTS	BOYS / GIRLS	SEX RATIO
PFIC1	ATP8B1	86	44 / 20	2.2
PFIC5	NR1H4	9	6 / 3	2
PFIC4	TJP2	66	9 / 7	1.29
PFIC2	ABCB11	159	64 / 67	0.96
PFIC3	ABCB4	147	53 / 71	0.75

Supplemental Figure S2. Screenshot of PytheasDB output for the comparison of ages at first symptoms for PFIC1–5. The bars are color-coded by disease: PFIC1 in salmon, PFIC5 in light green, PFIC4 in olive green, PFIC2 in tan and PFIC3 in yellow-green.

Age at first symptoms		Survival		Consanguinity		

DISEASE	GENE	PATIENTS	CONSANGUINOUS yes / no / n/a	CONSANGUINITY RATE
PFIC5	NR1H4	9	6 / 3 / 0	67%
PFIC4	TJP2	66	14 / 15 / 37	48%
PFIC3	ABCB4	147	5 / 6 / 136	45%
PFIC1	ATP8B1	86	5 / 24 / 57	17%
PFIC2	ABCB11	159	3 / 30 / 126	9%

Supplemental Figure S3. Screenshot of PytheasDB output for the comparison of consanguinity rates between patients with PFIC1–5. The bars are color-coded by disease: PFIC1 in salmon, PFIC5 in light green, PFIC4 in olive green, PFIC2 in tan and PFIC3 in yellow-green.

Supplemental Figure S4. Stacked bar chart of the cumulative number of articles in the literature by calendar year and by studied gene.