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Review Article

Reporting Completeness of Biliary Atresia Organoid Studies: A Scoping Review and Structured Audit

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Abstract

Background and Aims: Biliary atresia (BA) is the leading cause of pediatric obstructive cholestasis and a major indication for liver transplantation in infants. Organoid models are increasingly used to investigate BA pathogenesis and therapeutic responses, but incomplete methodological and clinical reporting may limit cross-study comparison and translational interpretation. This study aimed to map the landscape of BA-related organoid research, identify major reporting gaps, and propose Biliary Atresia Minimum Reporting Standard (BA-MRS) as a preliminary framework for improving reporting completeness. ***Methods:*** PubMed, Scopus, and Web of Science Core Collection were searched on March 8, 2026, in accordance with the PRISMA-ScR (Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews) and the 2024 Joanna Briggs Institute (JBI) Manual for Evidence Synthesis. Reporting completeness was assessed using a 36-item BA-MRS across six domains, scored as fully reported, partially reported, not reported, or not applicable. ***Results:*** Twenty-six studies published between 2020 and 2026 were included. Fibrosis and epithelial–mesenchymal transition were the most frequently studied themes, whereas only one study linked organoid findings to post-Kasai outcomes. BA case/model definition, ethics approval, and differentiation protocols were fully reported in all applicable studies (100%). In contrast, contamination monitoring (3.8%), core biliary function assays (34.6%), and clinical outcome linkage (26.3%) were poorly reported. Culture System and Sample Acquisition showed the lowest domain-level fully reported rates (58.1% and 63.2%, respectively). ***Conclusions:*** BA organoid research has progressed beyond early model development, but reporting remains insufficient for robust comparison, reproducibility, and clinically meaningful interpretation. BA-MRS may serve as a preliminary framework for improving standardized reporting in future studies.

Keywords: Biliary atresia; Organoids; Kasai portoenterostomy; Cholangiocytes; Reporting completeness; Reproducibility; Scoping review; Translational hepatology.

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Introduction

Biliary atresia (BA) is the leading cause of obstructive cholestasis in infancy[1,2] and is characterized by progressive fibro-obliterative injury of the extrahepatic bile ducts.[2,3] Untreated BA progresses to cirrhosis and liver failure, often requiring liver transplantation.[1,2] Kasai portoenterostomy (KPE) remains the only initial surgical treatment,[2,4] and earlier surgery is generally associated with better jaundice clearance and native liver survival (NLS).[4–6] Even within the usual "early" window, however, outcomes vary widely, with many children later developing cholangitis, fibrosis, portal hypertension, and eventually requiring liver transplantation.[7,8] This heterogeneity suggests that BA is not simply a mechanical obstruction but a broader disease process involving epithelial injury, barrier dysfunction, inflammation, and altered repair responses.[2,3]

Organoid technology now provides a useful platform for studying these processes.[9,10] BA-relevant organoids include patient-derived biliary or liver organoids, animal model-derived organoids, and human pluripotent stem cell (hPSC)-derived cholangiocyte-like systems, including induced pluripotent stem cell (iPSC)-derived models.[11] These models retain key biliary features in vitro and have been used to investigate polarity, lumen formation, cilia-related phenotypes, barrier integrity, transport function, injury responses, fibrosis-related signaling, infection models, drug response, and multi-omic profiling.[9,11–14] As the field expands, the main question is no longer whether BA-relevant organoids can be established but whether published studies can be compared, reproduced, and interpreted in a clinically meaningful way.

This question is important because reporting heterogeneity is already recognized as a barrier to reproducibility across the broader organoid literature.[15,16] In BA, incomplete reporting has additional consequences. The interpretation of organoid findings depends on clinical and biological context, including surgical timing, disease subtype, post-KPE course, and the anatomical source of the sampled tissue.[1,2,14] When

sample handling, culture conditions, characterization, and functional validation are incompletely described, cross-study comparison becomes difficult, and the relationship between organoid phenotypes and post-KPE heterogeneity remains unclear. For a field that ultimately aims to inform mechanistic stratification and therapeutic development, this is a translational problem as well as a methodological one.[15,16]

The literature is also heterogeneous in model source, intended application, and depth of characterization, making a scoping review appropriate for mapping the field and identifying reporting gaps.[17] We therefore conducted a scoping review guided by the PRISMA-ScR (Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews)[17,18] of published BA-related organoid studies, combining evidence mapping with a structured reporting audit of 36 BA-specific items across six domains. A second aim was to derive a preliminary disease-specific reporting framework, the Biliary Atresia Minimum Reporting Standard (BA-MRS), from the observed evidence landscape and reporting gaps. BA-MRS is proposed as an evidence-informed working framework rather than a guideline or consensus standard and requires future external and Delphi-based validation.[19,20]

Methods

Protocol, design, and eligibility

This scoping review was prospectively registered on the Open Science Framework (OSF; DOI: 10.17605/OSF.IO/3Z6KU) and conducted in accordance with PRISMA-ScR and the 2024 Joanna Briggs Institute (JBI) Manual.[17,18] The review addressed two linked questions: how completely BA organoid studies report disease context, sample acquisition, culture conditions, characterization, functional validation, and design traceability; and which reporting items are needed to support clearer linkage between organoid findings and clinically relevant post-KPE outcomes, such as jaundice clearance, cholangitis, and NLS.

Eligible studies were peer-reviewed full-text reports with original data on three-dimensional biliary or cholangiocyte organoid models relevant to BA. This included organoids derived from BA patient tissue, BA animal models, hPSC/iPSC-derived cholangiocyte-like systems used to model BA-relevant mechanisms, and non-BA biliary organoids exposed to BA-relevant injury stimuli. Methodological papers and case series were eligible if they contained original organoid data. Studies were excluded if they did not use a three-dimensional organoid system, had no clear BA relevance, lacked sufficient information to determine model relevance, were non-original publications, or were conference abstracts, posters, preprints without full-text counterparts, or reports that could not be charted. Selected non-BA biliary organoid and methodological papers were used only to inform item development and conceptual framing; they were not included in the audited evidence set.

Search, study selection, and data charting

A systematic search of PubMed, Scopus, and Web of Science Core Collection was performed on March 8, 2026, without language, date, or study design restrictions. Search terms combined BA and organoid concepts; full strategies for all databases are provided in Supplementary File 1. Records were deduplicated in Zotero and screened in two stages by two reviewers independently. Title and abstract screening was intentionally broad because the literature was sparse and focused. Potentially eligible reports underwent full-text review, and disagreements were resolved by discussion or third-reviewer adjudication. The selection process is shown in Supplementary Figure 1.

Data were charted using an a priori form piloted on three studies. Charting covered six modules: basic study characteristics; BA disease definition and comparator context; sample acquisition and preanalytical handling; culture system; phenotypic characterization and validation; and clinically linked information. Reviewers recorded supporting quotations and page references for subjective fields to improve consistency during adjudication. Two reviewers charted studies independently. Insufficient methodological detail after eligibility confirmation was treated as a reporting deficit rather than an exclusion criterion. Of the 26 included studies, one was published in Chinese and was charted and harmonized by Chinese-English bilingual reviewers using the same process as for English-language articles.

Reporting audit and BA-MRS framework development

The reporting audit used a 36-item checklist. After completion of the audit, the items were provisionally classified as 27 Core items and 9 Optional items. Each item was rated independently by two reviewers as fully reported (√), partially reported (△), not reported (×), or not applicable (NA). "Fully reported" indicated sufficient detail for reproducibility or clinical interpretation; "partially reported" indicated that the item was mentioned but key information was missing; "not reported" indicated omission in the full text. NA was reserved for structurally inapplicable items, such as surgical timing in hPSC-based modeling studies or patient clinical outcomes in purely animal-based systems. NA values were excluded from denominators when reporting coverage rates. Item-specific thresholds are provided in Supplementary Table 1. This audit assessed reporting completeness only and was not designed as an appraisal of methodological quality, risk of bias, or certainty of evidence.

For evidence mapping, studies were summarized descriptively by publication year, country or region, species category, model source, and primary research theme. No meta-analysis or inferential statistical testing was performed. Findings were presented using counts, percentages, and descriptive comparisons, with visual outputs including an evidence gap matrix (Fig. 1), a domain-level reporting plot (Fig. 2), an item-level ranking plot (Fig. 3), and a study-by-item heatmap (Fig. 4).

The BA-MRS item pool was developed through a staged, evidence-informed process. First, a provisional 38-item candidate pool was assembled from the evidence map, the a priori charting modules, general reporting guidance, and organoid-related methodological literature, including Animal Research: Reporting of In Vivo Experiments (ARRIVE) 2.0, STAR Methods, Biospecimen Reporting for Improved Study Quality (BRISQ), and Minimum Information for Publication of Quantitative Real-Time PCR Experiments (MIQE) 2.0.[15,19–24] Second, candidate items were piloted during charting and audit calibration. Items were retained when they captured BA-specific clinical context, organoid culture traceability, phenotypic or functional characterization, or design transparency relevant to reproducibility or clinical interpretation. Overlapping items were merged when they assessed the same reporting construct, items were split when one field contained distinct clinical or laboratory concepts, and items were removed when they could not be scored reproducibly or were already covered by another item. This process yielded the final 36-item checklist.

Core versus Optional classification was then determined

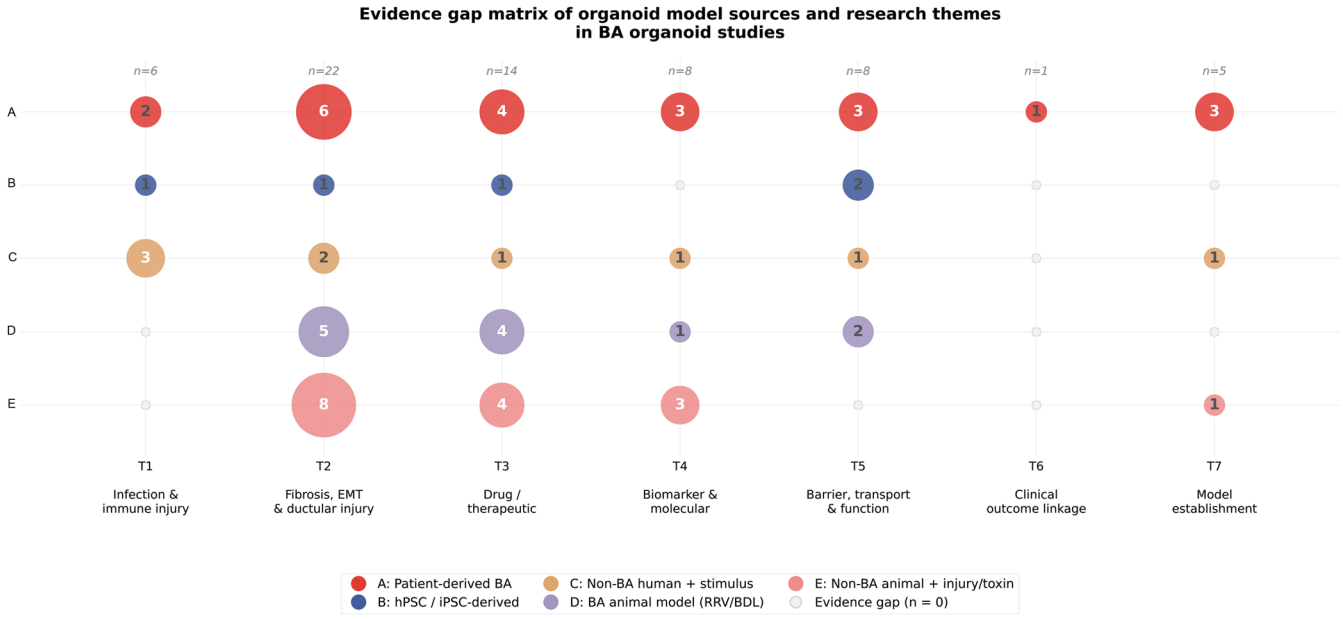

Fig. 1. Evidence gap matrix of organoid model sources and research themes in BA organoid studies. Each cell shows the number of studies addressing a given combination of organoid model type (rows) and research theme (columns). Studies contributing to multiple categories were counted in each applicable cell; empty cells represent evidence gaps. BA, biliary atresia; EMT, epithelial–mesenchymal transition; hPSC, human pluripotent stem cell.

after completion of the audit using prespecified considerations: relevance to post-KPE clinical interpretation, expected impact on reproducibility or translational use, applicability across major model types, and observed reporting performance. Items were classified as Core when they represented a minimum reporting expectation for interpretable or reproducible BA organoid studies within the relevant model context, even if current reporting was poor. Items were classified as Optional when they were clinically or methodologically informative but inherently context-dependent, not applicable to several model types, or premature to require across the field. Disagreements during scoring or classification were resolved by reviewer discussion and, when needed, third-reviewer adjudication. The item-level classification rationale is summarized in Table 1.[1,2,4,10,11,13,25–38]

Results

Study selection and characteristics of the evidence base

The database search identified 145 records: 43 from Pub-

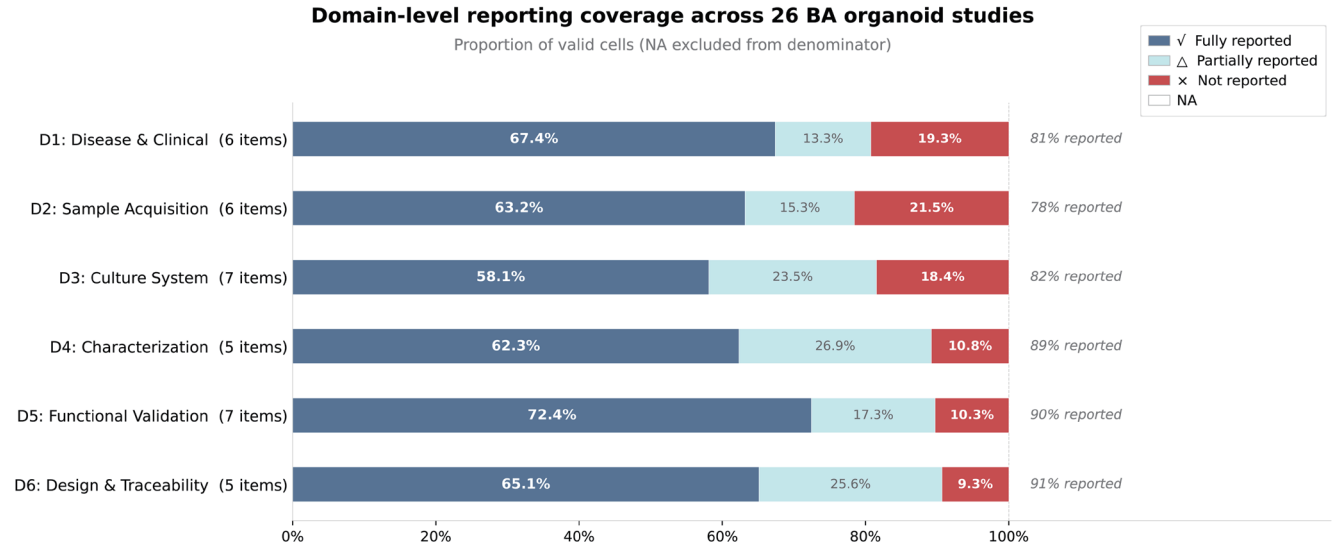

Fig. 2. Domain-level reporting coverage across six BA-MRS domains. Horizontal stacked bar chart showing the proportion of valid audit cells scored as fully reported (√), partially reported (△), or not reported (×) for each BA-MRS domain across 26 included studies. Percentages within each segment denote the proportion of valid cells; annotations to the right show the combined acceptable reporting rate (√ + △). Items scored as NA were excluded from the denominator. BA-MRS, Biliary Atresia Minimum Reporting Standard; NA, not applicable.

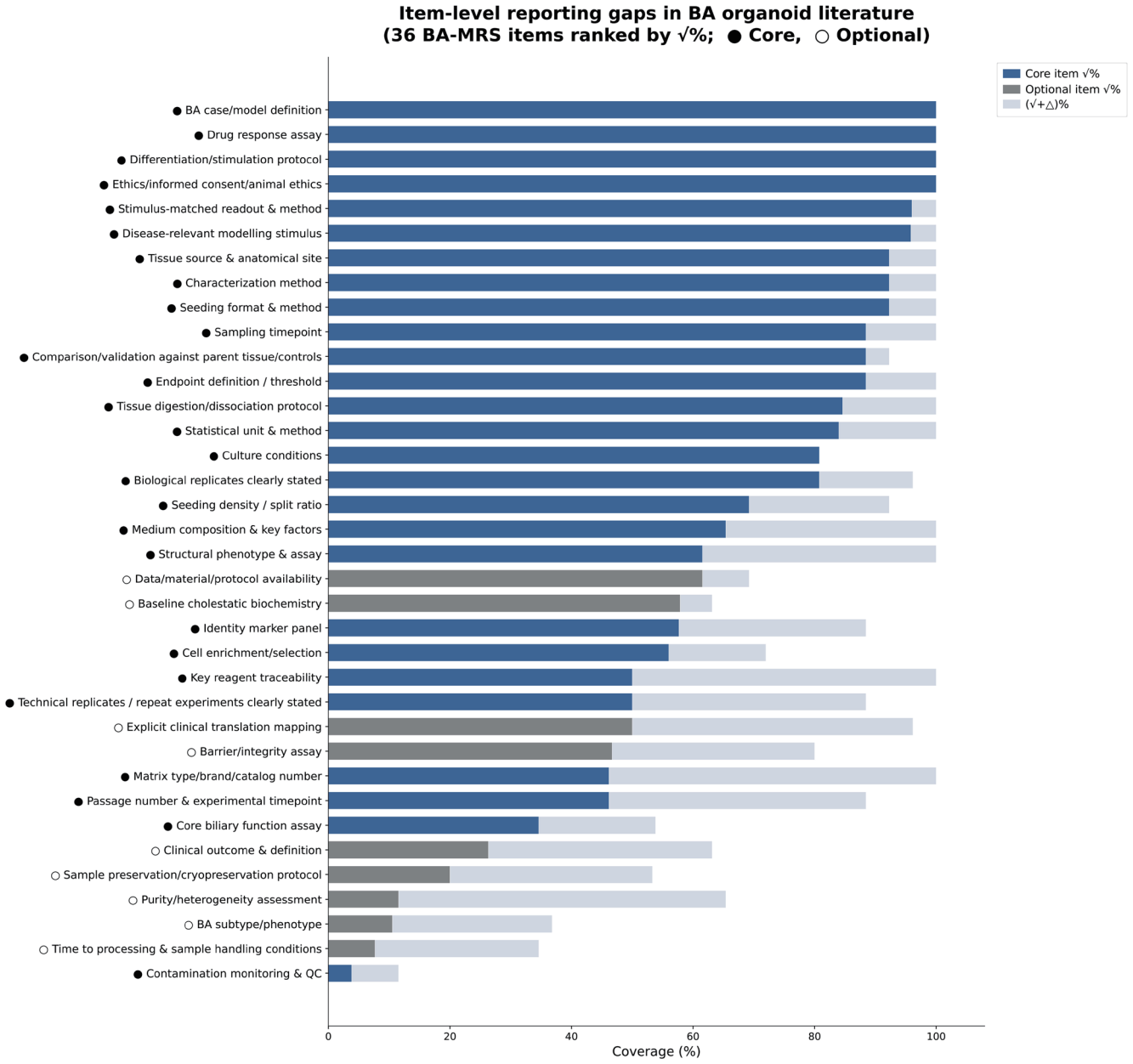

Fig. 3. Item-level reporting gaps across 36 BA-MRS items ranked by fully reported rate. Horizontal bar chart displaying the fully reported rate (√%) for each of the 36 BA-MRS items across 26 studies, ranked from highest to lowest. Dark blue bars denote Core items (•); dark gray bars denote Optional items (○). Light gray background bars represent the combined acceptable reporting rate (√ + △)%. NA items were excluded from the denominator. BA-MRS, Biliary Atresia Minimum Reporting Standard; NA, not applicable; QC, quality control.

Med, 44 from Scopus, and 58 from Web of Science Core Collection. After removal of 80 duplicates, 65 records underwent screening. Fourteen conference abstracts could not be retrieved as chartable full texts. Of the 51 full-text reports assessed for eligibility, 25 were excluded: 16 reviews or editorials, 7 reports without BA relevance, and 2 studies without an organoid model. Twenty-six studies were included in the scoping review and reporting audit.

The included studies were published between 2020 and 2026, with most appearing in 2024–2026 (Supplementary Fig. 2A). Geographically, the literature was concentrated in China and cross-regional collaborations: 13 studies were cross-regional collaborations, 8 originated from Chinese mainland, 2 from Hong Kong/Macao, and 1 each came from the USA, Japan, and the Netherlands (Supplementary Fig. 2B). In this review, "cross-regional" refers to studies with author affiliations, study materials, datasets, or collaborative teams spanning more than one geographic region, including collaborations involving Chinese mainland, Hong Kong/Macao, and/or international partners. By species composition, 11 studies involved humans only, 13 combined human and animal evidence, and 2 were mouse-only studies (Supplementary Fig. 2C). Twenty-five studies were published in English, and one was published in Chinese (Wang 2021[39]). Detailed study-level

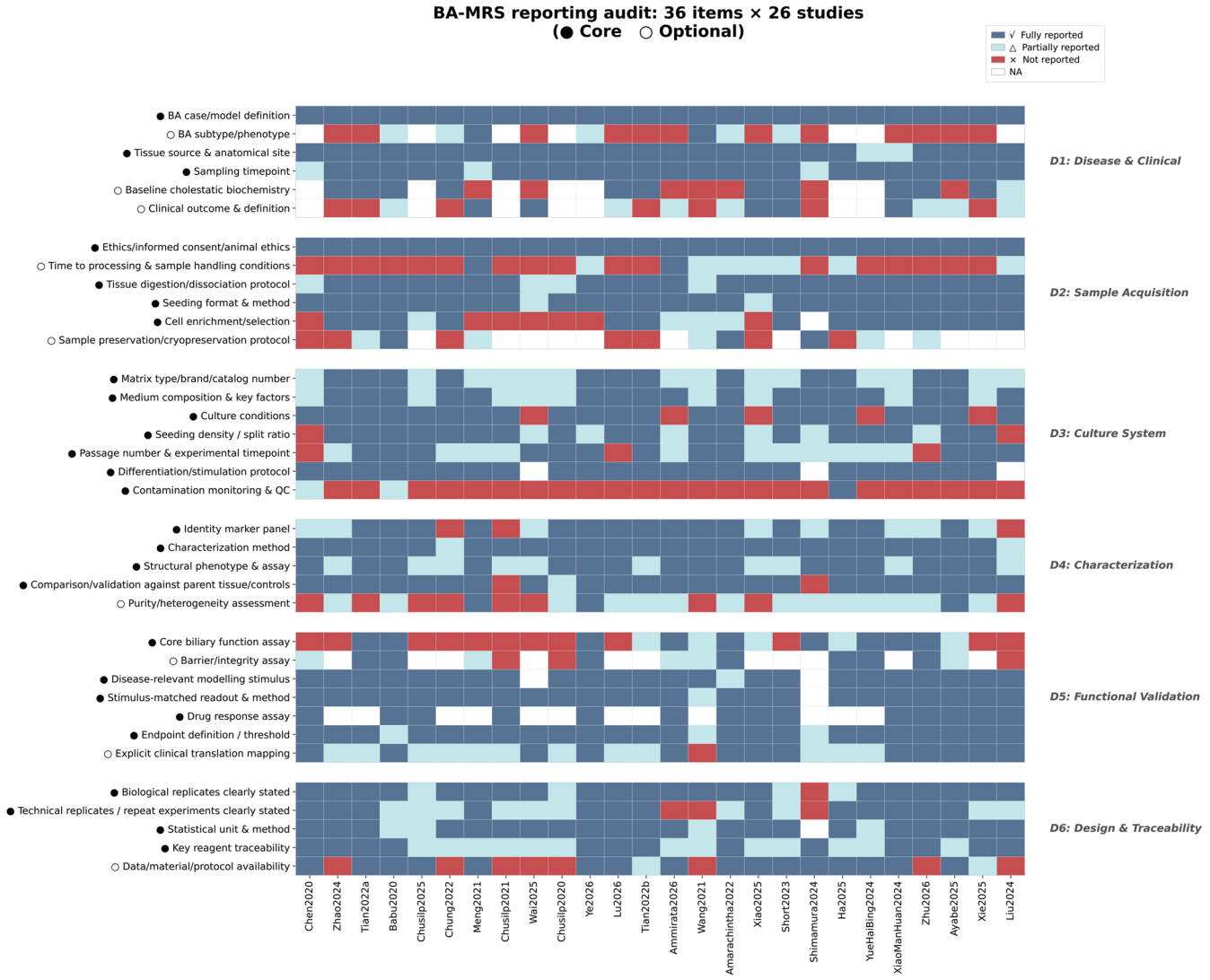

Fig. 4. BA-MRS reporting audit heatmap: 36 items and 26 studies. Cell-level heatmap depicting the four-level audit score for each of the 36 BA-MRS items (rows) across 26 studies (columns). Colors: steel blue, fully reported (√); light blue, partially reported (△); coral red, not reported (×); white, NA. Items are grouped by domain (D1 to D6) and prefixed with • (Core) or ○ (Optional). BA-MRS, Biliary Atresia Minimum Reporting Standard; NA, not applicable; QC, quality control.

characteristics are summarized in Table 2.[12–14,39–61]

Model sources were heterogeneous. Human studies most often used wedge liver biopsy or portal plate remnant tissue obtained at KPE, with choledochal cyst or hepatoblastoma-adjacent tissue commonly used as controls. Other approaches included hPSC/iPSC-derived cholangiocyte-like organoids, BA animal models, and non-BA biliary organoids exposed to BA-relevant injury stimuli. Among animal models, the neonatal mouse model induced by rhesus rotavirus was the most frequently used,[62] with additional studies using bile duct ligation mouse models or zebrafish models. Primary aims included disease modeling, infection- or toxin-related injury, fibrosis and epithelial–mesenchymal transition (EMT), therapeutic evaluation, biomarker investigation, and transcriptomic or multi-omic characterization. Common analytical approaches included immunofluorescence, quantitative reverse-transcription polymerase chain reaction (qRT-PCR), Western blotting, transport or swelling assays, bulk and single-cell RNA sequencing, and barrier-related readouts such as transepithelial electrical resistance (TEER) and fluorescein isothiocyanate–dextran 4 kDa (FD4) permeability assays.

Evidence gap matrix

The evidence gap matrix showed an uneven field structure across model sources and research themes (Fig. 1). Patient-derived BA organoids were the most versatile model class and contributed to all seven research themes. Fibrosis, EMT, and ductular injury represented the densest part of the literature, accounting for 22 study-theme entries, followed by drug or therapeutic evaluation (n = 14). hPSC/iPSC-derived models were represented by only two studies, Ye 2026[13] and Ha 2025,[56] indicating that this model category remains comparatively sparse. In contrast, themes requiring direct clinical anchoring were sparse. The weakest area was linkage to clinical outcomes after KPE. Only one study (Wai 2025[14]) explicitly related organoid findings to NLS or timing of transplantation. No animal-derived, hPSC-derived, or stimulus-treated non-BA models addressed clinical endpoints.

Table 1. BA-MRS: Proposed minimum reporting framework for biliary atresia organoid studies

Item	Description	Level	√%	(√+△)%	Clinical relevance to BA outcomes	Classification rationale
Domain 1: Disease & Clinical Context (6 items)						
D1_01	BA case/model definition	Core	100.0	100.0	Confirmation of BA status or equivalent modeling context is necessary for interpretable linkage between organoid phenotypes and BA-relevant clinical outcomes	Designated Core because BA identity is the foundational inclusion criterion; without it, no downstream organoid result can be interpreted in a BA-specific context
D1_02	BA subtype/ phenotype (e.g., BASM, CMV-associated)	Optional	10.5	36.8	Different BA subtypes may be associated with variation in post-Kasai jaundice clearance and cholangitis risk[2,25,26]; reporting supports stratified interpretation of organoid findings	Designated Optional because coverage was very low (√ 10.5%) and many studies used animal models where clinical subtyping is inapplicable (NA = 7); enforcing Core would penalize the majority of current literature without clear gain in reproducibility
D1_03	Tissue source & anatomical site	Core	92.3	100.0	Anatomical origin (portal plate remnant, intrahepatic or extrahepatic duct) may influence cholangiocyte lineage features and repair-related phenotypes relevant to BA outcome interpretation	Designated Core because tissue origin directly determines cholangiocyte lineage and phenotype, making it essential for any cross-study comparison
D1_04	Sampling timepoint (age at surgery/model day)	Core	88.5	100.0	Age at KPE is an established prognostic factor in BA[1,4] and supports comparison of organoid findings across clinically distinct cohorts	Designated Core because age at KPE is among the strongest established prognostic factors in BA,[27] and omitting it removes a key clinical covariate from organoid–outcome mapping
D1_05	Baseline cholestatic biochemistry (TB/DB or GGT; ≥1 reported)	Optional	57.9	63.2	Baseline TB/DB and GGT provide context on cholestasis severity and biliary injury burden,[28–30] supporting clinical–organoid correlation analyses	Designated Optional because baseline biochemistry provides useful clinical context but is not universally reportable—animal models and non-patient studies inherently lack these data, and forcing Core would exclude a substantial proportion of otherwise well-conducted studies
D1_06	Clinical outcome & definition (clearance/cholangitis/NLS/LT)	Optional	26.3	63.2	Explicit outcome definitions help determine whether organoid readouts can be interpreted consistently in relation to clinical endpoints	Designated Optional because the majority of current BA organoid studies are mechanistically oriented rather than clinically anchored; requiring explicit outcome definitions as Core would be premature given the field's translational maturity
Domain 2: Sample Acquisition & Processing (6 items)						
D2_01	Ethics/informed consent/animal ethics approval	Core	100.0	100.0	Ethical compliance and sample traceability support responsible linkage between organoid data and associated clinical information	Designated Core as a publication prerequisite; ethics approval is universally required by journals and institutions

(continued)

Table 1. *(continued)*

Item	Description	Level	√%	(√+△)%	Clinical relevance to BA outcomes	Classification rationale
D2_02	Time to processing & sample handling conditions	Optional	7.7	34.6	Ischemia time may affect cell viability and downstream functional readouts,[31] and incomplete reporting limits assessment of pre-analytical variation	Designated Optional at this stage because this item is most directly applicable to patient-derived tissue studies and no field-specific threshold for allowable warm or cold ischemia time has been established for pediatric hepatobiliary organoid work. Nevertheless, reporting the time interval and handling conditions is strongly encouraged and should be revisited in future consensus refinement
D2_03	Tissue digestion/dissociation protocol	Core	84.6	100.0	Dissociation method may influence cell yield and stress responses, which can affect organoid phenotypes and cross-study comparability	Designated Core because enzyme type, concentration, and duration are the minimum parameters another laboratory needs to reproduce the dissociation step
D2_04	Seeding format (single-cell/fragment) & method	Core	92.3	100.0	Input format may affect establishment success and structural maturation, supporting interpretation of downstream functional readouts	Designated Core because seeding format (single-cell vs. fragment) determines organoid formation mode and directly affects downstream morphological and functional readouts
D2_05	Cell enrichment/selection (e.g., $EpCAM^+$)	Core	56.0	72.0	Enrichment strategy may alter purity and heterogeneity, which can influence the interpretation of organoid-based comparisons across BA cohorts	Designated Core because whether enrichment was performed (or explicitly omitted) is essential for interpreting purity-dependent results; stating "no enrichment" also satisfies the criterion
D2_06	Sample preservation/cryopreservation protocol	Optional	20.0	53.3	Cryopreservation conditions may influence downstream functional stability and are relevant to multicenter or longitudinal study design	Designated Optional because 11 of 26 studies were scored NA (fresh tissue only, no cryopreservation involved), making this a conditional item with limited universal applicability
Domain 3: Culture System (7 items)						
D3_01	Matrix type/brand/catalogue number	Core	46.2	100.0	Matrix type and lot may affect differentiation and barrier-related phenotypes; incomplete reporting limits cross-study reproducibility and interpretation	Designated Core because Matrigel lot-to-lot variability is a widely recognized source of organoid heterogeneity,[32] and reporting at least the brand and catalogue number is the minimum needed for procurement-level reproducibility
D3_02	Medium composition & key factors	Core	65.4	100.0	Key growth factors shape cholangiocyte maturation and transport-related phenotypes, supporting interpretation of BA-relevant functional assays	Designated Core because the culture medium recipe is the single most critical parameter for another group attempting to replicate the organoid system
D3_03	Culture environment (temperature/CO_2 environment)	Core	80.8	80.8	Culture temperature and the CO_2/incubator environment are basic conditions for interpreting organoid growth, phenotype, and stimulus-response experiments	Designated Core because routine incubation conditions affect comparability across BA organoid models. Exact CO_2 percentage was not treated as mandatory for full reporting when standard CO_2 incubation or routine organoid culture temperature was otherwise adequately described; O_2 reporting was not required because atmospheric oxygen is the default condition and is rarely stated explicitly

(continued)

Table 1. *(continued)*

Item	Description	Level	√%	(√+△)%	Clinical relevance to BA outcomes	Classification rationale
D3_04	Seeding density/split ratio	Core	69.2	92.3	Seeding density may influence growth kinetics and structural maturity, which can affect consistency of downstream readouts	Designated Core because seeding density directly affects organoid size, confluence timing, and assay-to-assay variability within the same study
D3_05	Passage number & experimental timepoint	Core	46.2	88.5	Passage number and assay timing may contribute to phenotypic drift; reporting supports reproducible comparison across studies	Designated Core because passage number is a known driver of phenotypic drift in organoids, and omitting it makes it impossible to judge whether results were obtained from early- or late-passage cultures
D3_06	Differentiation/ stimulation protocol (if used)	Core	100.0	100.0	Differentiation conditions help define whether BA-relevant injury pathways are being modelled and therefore support interpretation of disease-related responses	Designated Core because all 23 applicable studies reported their differentiation protocol in full, confirming both feasibility and field consensus
D3_07	Contamination monitoring & QC (e.g., mycoplasma)	Core	3.8	11.5	Contamination can compromise experimental reliability[33,34]; documenting monitoring procedures supports confidence in mechanistic and functional findings	Designated Core despite the lowest coverage in the entire framework (√ 3.8%) because mycoplasma and other occult contamination can compromise transcriptomic, functional, and drug-sensitivity readouts in cell-culture and patient-derived organoid systems[33,34]; the threshold was set at simply stating whether testing was performed
Domain 4: Characterization (5 items)						
D4_01	Identity marker panel (minimum set)	Core	57.7	88.5	Minimum marker panels confirm cholangiocyte lineage identity, supporting the relevance of the model to biliary biology in BA	Designated Core because without a minimum marker panel confirming cholangiocyte identity, the model cannot be distinguished from hepatocyte or other epithelial organoids
D4_02	Characterization method (IF/qPCR/flow cytometry, etc.)	Core	92.3	100.0	Method transparency supports independent verification of cholangiocyte identity and maturity and facilitates comparison across studies	Designated Core because the method by which identity was established (IF, qPCR, FACS) must be transparent for independent verification
D4_03	Structural phenotype & assay (polarity/ lumen/cilia/TJ)	Core	61.5	100.0	Polarity, tight junctions, and cilia are linked to barrier-related and ductal phenotypes that may be relevant to BA pathobiology and post-Kasai outcomes[35–37]	Designated Core because structural features such as polarity, lumen formation, and cilia are the morphological hallmarks that distinguish biliary from hepatic organoids and underpin barrier and transport assays
D4_04	Comparison/ validation against parent tissue/controls	Core	88.5	92.3	Comparison with parental tissue supports model fidelity and helps contextualize whether observed phenotypes are plausibly BA relevant	Designated Core because comparison with parent tissue or appropriate controls is the minimum validation needed to assess model fidelity; the criterion was broadened to accept comparison with disease controls
D4_05	Purity/heterogeneity assessment	Optional	11.5	65.4	Heterogeneity can confound functional readouts; reporting supports interpretation of whether observed differences reflect biology or mixed cell states	Designated Optional because quantitative purity assessment (e.g., FACS-based % $CK19^{+}$) is methodologically demanding and not yet standard practice in the BA organoid field (√ 11.5%); requiring it as Core would be premature, though qualitative acknowledgment of heterogeneity is strongly encouraged

(continued)

Table 1. *(continued)*

Item	Description	Level	√%	(√+△)%	Clinical relevance to BA outcomes	Classification rationale
Domain 5: Functional Validation (7 items)						
D5_01	Core biliary function assay (transport/ CFTR/bile acid)	Core	34.6	53.8	Bile acid transport, CFTR, and related assays provide functionally relevant readouts for cholestasis-related interpretation in BA models[11]	Designated Core because at least one biliary-specific function assay (e.g., Rho123 transport, CFTR-dependent swelling) is necessary to confirm that the organoid is functionally biliary, not merely marker-positive[10]
D5_02	Barrier/integrity assay	Optional	46.7	80.0	Barrier integrity assays may inform interpretation of cholangitis-related vulnerability and epithelial dysfunction in BA models[13]	Designated Optional because 11 of 26 studies were scored NA (no barrier-related claims made); the item is only relevant to studies that specifically investigate epithelial integrity, making universal enforcement inappropriate
D5_03	Disease-relevant modeling stimulus (inflammation/ toxin/virus)	Core	95.8	100.0	Explicit BA-relevant stimuli help explain organoid responses in relation to inflammatory, fibrotic, or cholangitic mechanisms	Designated Core because disease modeling is the central purpose of BA organoid research, and 95.8% of applicable studies already reported their stimulus in full
D5_04	Stimulus-matched readout & method	Core	96.0	100.0	Transparent pairing of stimuli, readouts, and methods facilitates cross-study comparison and more consistent interpretation of BA-relevant responses	Designated Core because a stimulus without a matched readout constitutes an incomplete experiment; high existing compliance (96.0%) confirms feasibility
D5_05	Drug response assay (if therapeutic claim made)	Core	100.0	100.0	When therapeutic claims are made, drug-response data support interpretation of potential translational relevance	Designated Core (conditional) because all 14 studies that performed drug screening reported it fully; the item is NA for studies without therapeutic claims and thus imposes no burden on non-applicable studies
D5_06	Endpoint definition/threshold	Core	88.5	100.0	Defined thresholds or response criteria improve comparability and support clearer linkage between *in vitro* findings and clinically interpretable outcomes	Designated Core because without a defined threshold for what constitutes a "response" or "positive" result, findings are not verifiable or comparable across studies
D5_07	Explicit clinical translation mapping	Optional	50.0	96.2	Explicit mapping of *in vitro* readouts to clearance, cholangitis, NLS, or KPE-age stratification supports potential use in clinically oriented study design	Designated Optional because explicit mapping of *in vitro* readouts to clinical endpoints (e.g., jaundice clearance, NLS) requires clinical outcome data that most current studies lack; forcing Core would penalize mechanistic studies that do not intend direct clinical translation
Domain 6: Design & Traceability (5 items)						
D6_01	Biological replicates (donor n) clearly stated	Core	80.8	96.2	Donor n informs statistical power and the stability of subgroup analyses relevant to BA outcome interpretation	Designated Core because donor n is the minimum information needed to judge statistical power and generalizability

(continued)

Table 1. *(continued)*

Item	Description	Level	√%	(√+△)%	Clinical relevance to BA outcomes	Classification rationale
D6_02	Technical replicates/repeat experiments clearly stated	Core	50.0	88.5	Technical replication affects confidence in observed differences and supports more robust interpretation of functional readouts	Designated Core because distinguishing biological from technical replicates is essential to prevent pseudoreplication, a known issue in organoid studies[38]
D6_03	Statistical unit & method (donor as unit, etc.)	Core	84.0	100.0	Clear statistical units (for example, donor-level analysis) reduce pseudoreplication and support credible cross-study interpretation	Designated Core because specifying the statistical unit (donor vs. organoid vs. well) is necessary to evaluate whether reported p-values are valid
D6_04	Key reagent traceability (catalogue/lot number)	Core	50.0	100.0	Reagent traceability supports cross-laboratory reproducibility and verification of BA-relevant findings	Designated Core because catalogue numbers are the most direct way for another laboratory to procure identical reagents; the threshold was set at ≥3 key reagents
D6_05	Data/material/protocol availability	Optional	61.5	69.2	Data sharing supports external validation and pooled analyses, which may facilitate multicenter evidence generation in BA organoid research	Designated Optional because open data sharing is not yet standard practice in the BA organoid field, and many studies without omics data have no dataset to deposit; encouraging a statement of availability is appropriate without making it a compliance requirement

36 items across 6 domains (27 Core + 9 Optional). NA excluded from denominator; applicable denominators varied by item; √% = fully reported; (√+△)% = fully + partially reported. BA, biliary atresia; BA-MRS, Biliary Atresia Minimum Reporting Standard; BASM, biliary atresia splenic malformation; CFTR, cystic fibrosis transmembrane conductance regulator; CK19, cytokeratin 19; CMV, cytomegalovirus; EpCAM, epithelial cell adhesion molecule; FACS, fluorescence-activated cell sorting; GGT, gamma-glutamyl transferase; IF, immunofluorescence; KPE, Kasai portoenterostomy; LT, liver transplantation; NA, not applicable; NLS, native liver survival; QC, quality control; qPCR, quantitative polymerase chain reaction; TB/DB, total/direct bilirubin; TJ, tight junction.

This pattern suggests a structural imbalance rather than a simple absence of studies. The field has been productive in generating mechanistic and intervention-oriented models but much less successful in embedding organoid work within clinically interpretable trajectories. The imbalance is especially important in BA, where age at KPE, disease subtype, tissue origin, and postoperative course are central to outcome interpretation.[1,2,4,6,25]

Reporting audit

Domain-level coverage: At the domain level, acceptable reporting rates (√+△) ranged from 78% to 91% (Fig. 2). Design & Traceability ranked highest (91%), followed by Functional Validation (90%), Characterization (89%), Culture System (82%), Disease & Clinical Context (81%), and Sample Acquisition & Processing (78%). Fully reported rates (√) showed a similar but more discriminating pattern: Functional Validation ranked highest (72.4%), followed by Disease & Clinical Context (67.4%), Design & Traceability (65.1%), Sample Acquisition & Processing (63.2%), Characterization (62.3%), and Culture System (58.1%). Taken together, these results indicate that the weakest reporting domains were Sample Acquisition & Processing and Culture System, particularly when stricter "fully reported" thresholds were applied.

Item-level gaps: Item-level ranking further clarified this pattern (Fig. 3). Near-complete or complete reporting was observed for BA case/model definition (D1_01, 100%), ethics/informed consent/animal ethics (D2_01, 100%), differentiation or stimulation protocol when applicable (D3_06, 100%; applicable n = 23), drug-response assay when applicable (D5_05, 100%; applicable n = 14), stimulus-matched readout and method (D5_04, 96.0%), and disease-relevant modeling stimulus (D5_03, 95.8%). These high-coverage items show that most studies clearly stated what model they used, the broad intervention logic, and the immediate experimental readout.

By contrast, the lowest-performing items were contamination monitoring and quality control (D3_07; √ 3.8%, [√+△] 11.5%), time to processing and sample handling (D2_02; 7.7%, 34.6%), BA subtype or phenotype (D1_02; 10.5%, 36.8%), purity or heterogeneity assessment (D4_05; 11.5%, 65.4%), and sample preservation or cryopreservation protocol (D2_06; 20.0%, 53.3%). Culture System showed the widest internal spread: differentiation or stimulation protocol (D3_06) achieved full reporting in all applicable studies, whereas matrix type/brand/catalogue number (D3_01) and passage number/experimental timepoint (D3_05) were fully reported in only 46.2% of studies. In Disease & Clinical Context, disease definition, tissue source, and sampling timepoint were generally well reported, but baseline cholestatic biochemistry (D1_05; applicable n = 19, √ 57.9%, [√+△] 63.2%) and clinical outcome definition (D1_06, 26.3%) were much less consistent.

Heatmap patterns and preliminary BA-MRS classification: The audit heatmap (Fig. 4) showed that more recent studies tended to contain more fully reported items in Disease & Clinical Context and Functional Validation, but under-reporting remained concentrated in specific rows. Contamination monitoring and quality control (QC; D3_07) was predominantly not reported across the matrix; only Ha 2025[56] was fully reported for this item, whereas Chen 2020[40] and Babu 2020[43] were partially reported. NA values clustered in a few context-dependent items, especially drug-response assay (D5_05; 12 NA), sample preservation/cryopreservation (D2_06; 11 NA), and barrier/integrity assay (D5_02; 11 NA), reinforcing the importance of interpreting coverage

Table 2. Characteristics of the 26 included BA organoid studies

Study	Journal	Country	Species	Organoid source	BA-relevant model	n (BA/Ctrl)	Primary aim	Core assays
Chen2020[40]	mBio	Netherlands	Human	Fetal/adult liver & bile duct tissue (non-BA donors)	Rotavirus infection of normal biliary organoids	N/A/7 batches	Demonstrate rotavirus lifecycle in human biliary organoids as BA-relevant infection model	qRT-PCR, IF, TEM, flow cytometry, CFTR functional assay (FIS)
Zhao2024[41]	Int J Biochem Cell Biol	China	Human + Mouse	Mouse liver EpCAM$^+$ cells; human plasma & liver biopsies	Clinical BA (human specimens) + BDL mouse model	139 (plasma); 3 (IF)/50 (plasma); 4 (WB)	Investigate NTS as diagnostic biomarker and its role in BA cholestasis via NTSR1 signaling	ELISA, IF/IHC, organoid morphology, WB, qRT-PCR
Tian2022a[42]	Clin Transl Gastroenterol	China	Human + Mouse + Zebrafish	Mouse liver EpCAM$^+$ cells; human plasma & liver tissue	Clinical BA (human) + Aβ-treated mouse organoids	34 (plasma); 5 (liver)/22 (plasma); 5 (CC)	Investigate beta-amyloid roles in BA pathogenesis and effects on liver organoid growth/metabolism	Organoid morphology, Seahorse OCR, WB, qRT-PCR, R123 permeability
Babu2020[43]	J Hepatol	Cross-regional	Human + Mouse	Liver wedge biopsy at Kasai (BA) or surgery (controls)	Patient-derived BA organoids + RRV mouse model	14 (organoids); 46 (tissue)/15 (organoids)	Identify beta-amyloid deposition as pathobiological feature of BA; characterize BA organoids	IF, TEM, Thioflavin-T, CFTR/MDR1 functional assays, scRNA-seq
Chusilp2025[44]	Stem Cells Transl Med	Cross-regional	Human + Mouse	Neonatal mouse intrahepatic bile duct fragments	TGF-β1-induced biliary EMT model	N/A/N/A	Establish TGF-β1-induced biliary EMT model; assess anti-fibrotic effect of hAFSCs	RT-qPCR, IF (EMT markers), WB, organoid morphology
Chung2022[45]	Curr Issues Mol Biol	Cross-regional	Human	Liver wedge biopsy at Kasai (BA) or surgery (controls)	Clinical BA organoids + Poly I:C-treated non-BA organoids	2/5	Create BA-like organoids by Poly I:C treatment; compare with native BA organoid transcriptome	Organoid morphology, Organoid-derived monolayer, RNA-seq
Meng2021[46]	Front Pediatr	China	Human	Liver wedge biopsy at Kasai (BA); para-HB tissue (controls)	Patient-derived BA organoids + KPN co-culture	3 (RNA-seq); 23 (qPCR)/5	Characterize post-Kasai gut microbiome; model KPN-induced cholangiocyte injury	16S rDNA sequencing, RNA-seq, ELISA, IF, organoid–bacteria co-culture
Chusilp2021[47]	J Pediatr Surg	Cross-regional	Human + Mouse	Neonatal mouse intrahepatic bile duct organoids	APAP-injury cholangiocyte model + hAFSC co-culture	N/A/N/A	Assess whether hAFSCs attenuate cholangiocyte apoptosis and fibrogenic cytokine expression	IF (cleaved caspase-3, Ki67), RT-qPCR, Transwell co-culture
Wai2025[14]	J Pediatr Surg	Cross-regional	Human	Liver biopsy at KPE and post-KPE (BA); CC/HB biopsy (controls)	Patient-derived BA organoids (at-KPE & post-KPE)	21 (23 specimens)/9	Investigate whether organoid transcriptomes at KPE predict NLS vs. liver transplant	Bulk RNA-seq (Smart-seq), organoid morphology

(continued)

Table 2. *(continued)*

Study	Journal	Country	Species	Organoid source	BA-relevant model	n (BA/Ctrl)	Primary aim	Core assays
Chusilp2020[48]	Pediatr Surg Int	Cross-regional	Mouse	Neonatal mouse intrahepatic bile duct fragments	APAP injury model in mouse ductal organoids	N/A/N/A	Develop injured cholangiocyte organoid model; evaluate fibrogenic cytokines and apoptosis	RT-qPCR, IF (cleaved caspase-3), organoid morphology
Ye2026[13]	Nat Commun	Cross-regional	Human (iPSC-derived)	hiPSC-derived CLC organoids; BA/non-BA liver biopsies for validation	HCMV-infected iPSC-CLC organoids as BA model	29 (biopsies)/18 (CC biopsies)	Establish HCMV infection model in hiPSC-CLC organoids; characterize barrier disruption and EMT	IF, bulk RNA-seq, scRNA-seq, TEER, FD4 permeability, WB
Lu2026[49]	Dig Dis Sci	China	Human	Liver tissue at KPE (BA); CC tissue (controls); $EpCAM^+$ isolation	Patient-derived BA cholangiocyte organoids	47 (tissue); 8 (organoids)/11 (tissue); 3 (organoids)	Identify CASC15 as upregulated lncRNA in BA organoids; evaluate CASC15/HNRNPU-IGFBP3 axis	Smart-seq, qRT-PCR, CCK-8, EdU, Transwell, WB
Tian2022b[50]	Cell Death Dis	China	Human + Mouse + Zebrafish	Mouse liver $EpCAM^+$ cells; human plasma & liver tissue	Clinical BA (human) + D-2-HG-treated mouse organoids	46 (plasma)/22 (plasma)	Investigate D-2-HG metabolic regulation in BA cholestasis via TET activity modulation	Metabolomics, Seahorse OCR, TET activity assay, IF/IHC, qRT-PCR
Ammirata2026[51]	Biomolecules	Cross-regional	Human + Mouse	Liver/biliary tissue at KPE (BA); FFPE sections; murine models	Patient-derived cholangiocyte organoids + murine cholangiopathy models	2 (organoids)/≥2 (organoids)	Characterize ESRP1 expression in cholangiopathies; assess as marker distinguishing BA from PSC/PBC	qRT-PCR, WB, IHC, organoid culture, scRNA-seq (public data)
Wang2021[39]	Chin J Pediatr Surg	China	Human	Extrahepatic biliary epithelium at Kasai (BA) or cyst excision (CC)	Patient-derived extrahepatic cholangiocyte organoids	4/4	Establish patient-derived primary extrahepatic cholangiocyte organoid culture from BA children	Organoid morphology, H&E, IF (CK7/CK19/CFTR), WB
Amarachintha2022[52]	Hepatology	Cross-regional	Human	Liver biopsy at Kasai or transplant (BA); non-BA cholestasis & healthy controls	Patient-derived biliary organoids (BA vs. disease vs. normal controls)	20/9	Uncover epithelial developmental delay and barrier dysfunction in BA organoids; test EGF+FGF2 rescue	IF (ZO-1, F-actin, β-catenin, CK7, CFTR), CFTR functional assay, R123 permeability, qRT-PCR
Xiao2025[53]	Hepatology	Cross-regional	Human + Mouse	Liver tissue at Kasai (BA); CC/HB tissue (controls); RRV mouse model	Patient-derived BA organoids + RRV mouse + multi-omics	14/9	Define pathogenic cholangiocyte niche in BA; identify TNFSF12–TNFRSF12A as therapeutic target	10x scRNA-seq, Stereo-seq spatial transcriptomics, multiplex IHC, organoid drug response
Short2023[54]	Hepatology	Cross-regional	Human + Mouse	Mouse liver $EpCAM^+$ cells (WT & Prom1 KO); human RNA-seq (GEO)	rmTWEAK-treated mouse HPC organoids + RRV mouse *in vivo*	4–9/group (*in vivo*)/4–9/group (saline)	Investigate TWEAK/FN14-driven profibrogenic ductular reaction in $Prom1^+$ hepatic progenitor cells	Organoid growth/morphology, IF, qRT-PCR, RNA-seq (GEO secondary)

(continued)

Table 2. *(continued)*

Study	Journal	Country	Species	Organoid source	BA-relevant model	n (BA/Ctrl)	Primary aim	Core assays
Shimamura2024[55]	Cytotechnology	Japan	Human	Extrahepatic bile duct tissue at Kasai (gallbladder/portal area)	BA patient-derived cholangiocyte culture (2D, 3D, immortalized)	NR/N/A	Establish stable 2D/3D cholangiocyte culture from BA extrahepatic bile duct tissue	IHC (CK7/CK19/SOX9/MUC1/EpCAM), RT-qPCR, SV40T+hTERT immortalization
Ha2025[56]	eBioMedicine	Cross-regional	Human (iPSC) + Mouse	hPSC-derived CLC organoids (CRISPR ADD3 KO); mouse liver EpCAM$^+$ cells	ADD3 KO iPSC-CLC organoids + RRV mouse BA model	N/A (iPSC model)/WT iPSC controls	Elucidate how ADD3 loss impairs bile duct development, ciliogenesis, and barrier function	IF (ZO-1, claudins, cilia markers), TEER, FD4 permeability, TEM, RNA-seq
YueHaiBing2024[57]	Toxins	China (HK)	Human	Liver biopsy from non-BA pediatric patients (HB/CC)	Biliatresone-treated non-BA organoids as BA-like model	N/A/7	Validate biliatresone as BA mechanism in human organoids; assess cilia and hepatocyte transdifferentiation	Organoid growth, H&E, IF (HNF4A/CK19/SOX9/acetylated α-tubulin), SEM
XiaoManHuan2024[58]	eBioMedicine	China	Human	BA liver/blood at HPE; HB controls; HB-derived biliary organoids	MAIT cell–organoid co-culture system (organoids from non-BA tissue)	47/41	Investigate liver MAIT cell functions in BA ductular reaction via amphiregulin signaling	ssGSEA, flow cytometry, ELISA, IF, Transwell co-culture, organoid morphology
Zhu2026[59]	Cell Mol Gastroenterol Hepatol	China	Human + Mouse	Liver tissue at KPE (BA); CC controls; EpCAM$^+$ organoids; RRV mouse	Patient-derived BA cholangiocyte organoids + RRV mouse organoids	51 (tissue); 3 (organoids)/16 (CC tissue); 3 (organoids)	Investigate EP300/YAP1-SERPINE1 signaling in BA ductular reaction and fibrosis	RT-qPCR, WB, IHC, ChIP-qPCR, CUT&Tag, organoid drug response
Ayabe2025[12]	Nat Commun	USA	Human + Mouse	Liver biopsy at Kasai/transplant (BA); normal donors; HUVECs + MSCs	Patient-derived multilineage biliary organoids (MBOs: cholangiocytes + endothelial + mesenchymal)	9/6	Investigate TGF-β-driven EMT and epithelial–mesenchymal crosstalk in BA using tri-culture MBOs	Whole-mount IF, 3D confocal, Alcian blue, RNA-seq, scRNA-seq, organoid drug response
Xie2025[60]	Lab Invest	Cross-regional	Human + Mouse	Human liver biopsies (BA/CC); mouse liver EpCAM$^+$ cells (RRV model)	Clinical BA tissue + mouse CLC organoids (RRV + pharmacological)	32/16 (CC)	Investigate Hippo-YAP1 signaling in intrahepatic biliary repair and oxidative stress in BA	qRT-PCR, WB, IHC, organoid morphology, RNA-seq, ROS assay
Liu2024[61]	Pediatr Surg Int	China (HK)	Mouse	BALB/c neonatal mouse liver (RRV-induced BA model)	RRV mouse BA organoids ± prednisolone treatment	12/12	Evaluate anti-fibrotic effect of prednisolone in RRV-BA model using animal and organoid approaches	H&E, Sirius Red, IHC (α-SMA), RNA-seq, organoid morphology

APAP, acetaminophen; BA, biliary atresia; BDL, bile duct ligation; CC, choledochal cyst; CCK-8, Cell Counting Kit-8; CFTR, cystic fibrosis transmembrane conductance regulator; CLC, cholangiocyte-like cell; EMT, epithelial–mesenchymal transition; ELISA, enzyme-linked immunosorbent assay; EpCAM, epithelial cell adhesion molecule; FD4, fluorescein isothiocyanate–dextran 4 kDa; FIS, forskolin-induced swelling; hAFSC, human amniotic fluid stem cell; HB, hepatoblastoma; HCMV, human cytomegalovirus; H&E, hematoxylin and eosin; HPC, hepatic progenitor cell; HPE, hepatoportoenterostomy; IF, immunofluorescence; IHC, immunohistochemistry; iPSC, induced pluripotent stem cell; KPE, Kasai portoenterostomy; MBO, multilineage biliary organoid; MDR1, multidrug resistance protein 1; NLS, native liver survival; NR, not reported; qRT-PCR, quantitative reverse-transcription polymerase chain reaction; R123, rhodamine 123; RNA-seq, RNA sequencing; ROS, reactive oxygen species; RRV, rhesus rotavirus; RT-qPCR, reverse-transcription quantitative polymerase chain reaction; scRNA-seq, single-cell RNA sequencing; SEM, scanning electron microscopy; TEER, transepithelial electrical resistance; TEM, transmission electron microscopy; WB, western blot.

alongside item applicability.

Species category also affected the visual pattern. Human-only studies had more clinically applicable cells in Domain 1 and therefore more opportunities to report disease context and outcomes. Human + Animal studies showed descriptively better coverage for disease-relevant modeling stimulus (D5_03) and drug-response assay (D5_05). The mouse-only subgroup was too small (n = 2) for meaningful comparison.

Based on the audit and the framework-development process, the 36 BA-MRS items were provisionally classified as 27 Core and 9 Optional items (Table 1). Every domain contained at least one Core item, and all seven items in the Culture System domain were classified as Core. Optional items were concentrated in context-dependent areas such as subtype definition, baseline cholestatic biochemistry, outcome linkage, cryopreservation, and data or material availability. The gap between fully reported and acceptable reporting rates was informative: for example, matrix description (D3_01) and passage number/experimental timepoint (D3_05) were often mentioned but not with enough detail to support procurement-level reproducibility or interpretation of passage-related drift.

Discussion

This study provides, to our knowledge, the first disease-specific evidence map and structured reporting audit of BA organoid research. Three broad conclusions emerge. First, the evidence base has moved beyond simple proof-of-concept model establishment. Studies published from 2020 to 2026 increasingly address mechanistic questions, injury pathways, and therapeutic evaluation. Second, this expansion has been uneven. Fibrosis, EMT, and ductular injury dominate the literature, whereas direct linkage to post-KPE clinical outcomes is rare. Third, the main reporting deficits are no longer in stating the broad model identity but in documenting the details needed for reproducibility, cross-study comparison, and clinical interpretation. These observations align with reporting concerns raised in the wider organoid literature.[15,16]

These points are important because BA is a clinically heterogeneous disease in which KPE outcomes are strongly influenced by disease subtype, surgical timing, and postoperative trajectory.[1,2,6] A literature built mainly around mechanistic plausibility but with inconsistent clinical and methodological anchoring is difficult to translate into cumulative knowledge. In other words, the field now has enough studies to expose its reporting weaknesses clearly.

The audit identified four linked reporting gaps. The first is inadequate clinical anchoring of heterogeneous model sources. BA-relevant organoid studies now include patient-derived tissue, hPSC-derived biliary systems, animal model-derived organoids, and injury-stimulated non-BA organoids. This diversity is valuable, but it requires stronger context if findings are to be interpreted across studies. BA subtype or phenotype (D1_02) and baseline cholestatic biochemistry (D1_05) were among the weakest clinical items. Without these anchors, many studies can be labelled "BA-relevant" while still representing clinically distinct settings that are difficult to compare directly.[3,25,63]

The second gap is insufficient pre-analytical and culture traceability. Time to processing, sample handling, matrix specification, passage number, and especially contamination monitoring were inconsistently reported. The pattern is notable: disease-relevant stimulation protocols were usually described well, but baseline conditions required for reproducibility were not. This imbalance matters because pre-analytical handling and culture drift can influence establishment success, phenotype stability, and downstream readouts. Matrix-related reporting was particularly uneven despite the known importance of matrix composition and procurement-level specification in organoid culture systems.[32] Contamination monitoring and QC deserve particular attention because D3_07 had the lowest fully reported rate in the entire audit (3.8%). This gap is not only a low-prevalence reporting issue. Mycoplasma contamination has been detected in public cell-culture transcriptomic datasets,[33] and unrecognized contamination may confound molecular profiles, growth behavior, stress responses, and assay readouts. Although direct evidence in BA or cholangiocyte organoids remains limited, findings from patient-derived organoid systems indicate that mycoplasma contamination can alter drug-sensitivity readouts,[34] further supporting routine contamination monitoring in organoid-based translational studies. In BA models, such effects could be especially problematic because many key readouts, including epithelial barrier integrity, cholangiocyte differentiation, EMT-related signatures, and drug-response assays, are sensitive to culture state and cellular stress. As organoid work becomes more comparative and multicenter, omissions in processing time, matrix specification, passage number, and contamination/QC reporting may therefore create tangible methodological and clinical-interpretive consequences: apparent differences between BA and control organoids, or between treatment conditions, may reflect uncontrolled culture artifacts rather than disease-relevant biology.[15,16]

The third gap is incomplete functional validation. Core biliary function assays were fully reported in only 34.6% of studies (D5_01), despite their central relevance to cholestatic disease biology.[1–3] Several studies created biologically plausible BA models, but documentation of functionally interpretable cholangiocyte phenotypes remained inconsistent. Importantly, D5_01 should not be interpreted as a single mandatory assay for all BA organoid studies. The most appropriate functional readout depends on the primary research aim. Drawing on established hepatobiliary physiology,[64,65] organoid functional readouts can be grouped along three axes relevant to post-KPE interpretation: bile excretory capacity—reflected by cystic fibrosis transmembrane conductance regulator- or multidrug resistance protein 1-dependent assays, such as forskolin-induced swelling—which may contextualize jaundice clearance trajectories[52,66]; epithelial barrier integrity—approximated by TEER and FD4 permeability measurements—which may inform interpretation of cholangitis susceptibility[67]; and repair/fibrosis-related responses—captured through EMT and niche-related readouts—which may relate to progressive ductular injury and long-term NLS.[12,53] These links are biologically plausible rather than validated surrogate relationships, but they illustrate why functional detail matters for translational interpretation. Future Delphi or consensus refinement of BA-MRS should consider annotating or subdividing D5_01 by major research aim, such as bile-excretory function for transport studies, barrier integrity for infection or injury models, and repair/fibrosis signatures for EMT-focused work.

The fourth gap is weak linkage to clinical outcomes. Clinical outcome definition (D1_06) was poorly reported, and the evidence map showed that only one study explicitly connected organoid data to post-KPE outcomes.[14] This is not simply an under-reporting problem; it also reflects study design. Clinical endpoints are still not routinely built into BA organoid protocols. The same caution applies to drug-response studies. Current organoid drug screening in BA is better viewed as a tool for pathway prioritization, mechanistic subtyping, and translational readiness than as evidence for immediate treatment personalization.[68]

These four gaps interact. The clinical meaning of a report-

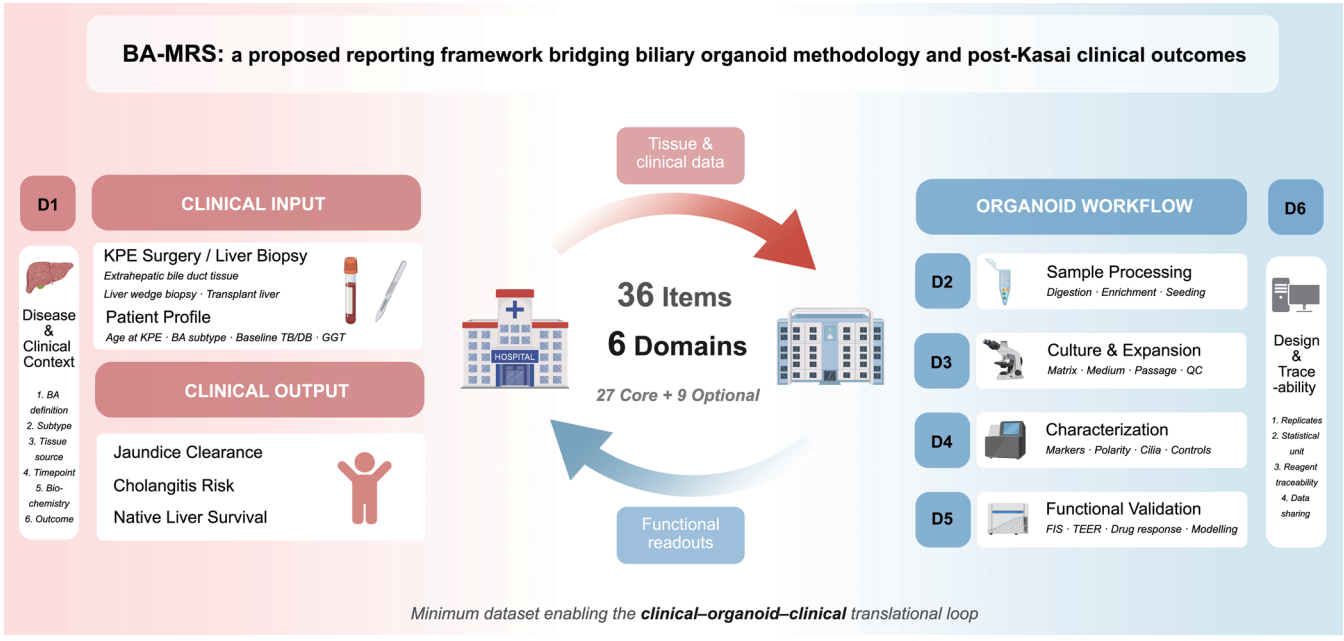

Fig. 5. BA-MRS: a proposed reporting framework bridging biliary organoid methodology and post-Kasai clinical outcomes. This figure shows the bidirectional data flow between clinical and laboratory settings. The left panel shows clinical information, including sample source, blood-based biomarkers, and clinical outcomes. Through the clinical-to-organoid-to-clinical pathway, these data may further inform clinical practice. For animal model-only studies, D1 clinical items were scored as not applicable (NA), whereas the organoid workflow (D2–D6) remains applicable. The BA-MRS comprises 36 items across 6 domains and is proposed here as a preliminary disease-specific reporting framework. BA, biliary atresia; BA-MRS, Biliary Atresia Minimum Reporting Standard; FIS, forskolin-induced swelling; GGT, gamma-glutamyl transferase; KPE, Kasai portoenterostomy; NLS, native liver survival; QC, quality control; TB/DB, total/direct bilirubin; TEER, transepithelial electrical resistance.

ed organoid phenotype depends simultaneously on who the sample came from, how it was handled, how the phenotype was functionally validated, and whether any postoperative outcome context was available. Addressing only one gap in isolation is therefore unlikely to solve the main interpretive problem.

The BA-MRS was developed to address this combined problem. As summarized in Figure 5 and Table 1, it contains 36 items across six domains, with 27 Core and 9 Optional items, and is intended as a disease-specific reporting framework for BA organoid studies rather than a quality-scoring tool or consensus guideline. Its purpose is to improve reproducibility, comparability, and, where applicable, the clinical interpretability of organoid findings. In this context, "Core" should be read as a prospective minimum reporting expectation for future studies within the relevant model context, not as a description of what most published studies currently report. This distinction is important for items such as contamination monitoring/QC, where current uptake is very low but the consequences for experimental interpretation are substantial.

BA-MRS does not replace broader frameworks. ARRIVE 2.0 addresses animal experiments,[21] BRISQ addresses preanalytical biospecimen variables,[23] and MIQE 2.0 addresses qPCR reporting.[24] In organoid-focused work, Marsee *et al*. proposed nomenclature and characterization principles for liver organoids,[15] and the 2023 International Society for Stem Cell Research standards addressed stem cell-derived models more broadly.[69] BA-MRS complements rather than replaces these tools by adding three disease-specific dimensions. First, it incorporates clinical context items—BA subtype, baseline cholestatic biochemistry, and post-KPE outcome definitions—that are absent from general-purpose frameworks.[15,21,23,69] Second, its Core/Optional structure acknowledges that not all items apply equally across patient-derived, animal-derived, and hPSC-derived models. Third, it can function prospectively during study design, not only retrospectively during manuscript preparation.

The framework should nevertheless be interpreted cautiously. The same research team developed and applied BA-MRS, so external validation is essential. The Core/Optional distinction reflects team-level judgment guided by prespecified considerations rather than formal consensus methodology.[20] Item generation was iterative and evidence-informed but was not based on a formal content-analysis or stakeholder-consensus process.[19] Finally, BA-MRS scores what is reported, not what was actually done or how well it was done. For these reasons, BA-MRS should be viewed as a working, translation-oriented framework that requires independent testing and future Delphi refinement involving pediatric surgery, hepatology, pathology, organoid methodology, and biostatistics.[70]

This study has several limitations. First, it is a reporting-completeness audit, not an appraisal of study validity, treatment effect, or risk of bias. Second, "not reported" should not be interpreted as "not performed," although absent reporting remains unusable for reproducibility and translational interpretation.[19,71] Third, the search was limited to PubMed, Scopus, and Web of Science and did not include Embase or systematic reference-list scanning, so some relevant studies may have been missed. Fourth, the 26 included studies were heterogeneous in model type, research question, and evidence level, so coverage rates should be interpreted as indicators of current field patterns rather than fixed quality benchmarks.

Even with these limitations, the present review establishes a useful baseline for the field. Near-term priorities include routine reporting of contamination monitoring and pre-analytical handling; clearer definition of BA subtype, baseline biochemistry, and postoperative outcomes in patient-derived studies; inclusion of at least one aim-appropriate biliary

functional assay where appropriate; and prospective study designs that link organoid phenotypes to post-KPE clinical trajectories. These steps would strengthen not only manuscript quality but also the ability of BA organoid research to accumulate into a clinically interpretable evidence base.

Conclusions

This scoping review and structured reporting audit of 26 BA organoid studies shows that the field is advancing beyond model establishment but remains limited by inconsistent reporting. The main deficits concern clinical anchoring of heterogeneous models, pre-analytical and culture traceability, functional validation, and linkage to post-KPE outcomes. Together, these gaps weaken reproducibility, cross-study comparison, and translational interpretation. The BA-MRS, comprising 27 Core and 9 Optional items across six domains, is proposed as an evidence-informed starting framework for study design and reporting in this area. External validation and Delphi-based consensus development are the next steps toward a more cumulative and clinically interpretable BA organoid literature.

Supporting information

Supplementary material for this article is available at https://doi.org/10.14218/JCTH.2026.00352.

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Conflict of interest

The authors have no conflict of interests related to this publication.

Author contributions

Study conception and design (JH, GL), literature search, study selection, data charting, reporting audit (GL, DW, SL, KH, YG, YaZ, YoZ, JL), analysis and interpretation (GL, DS), drafting of the manuscript (GL), and critical revision of the manuscript (JH, DS). All authors read and approved the final manuscript.

Ethical statement

Not applicable. This study was a scoping review of published literature and did not involve human participants, human tissues, animal experiments, or identifiable personal data.

Data sharing statement

All data generated or analyzed during this study are included in this published article and its supplementary information files.

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