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Review Article

Lymph node biopsy in resource-limited breast cancer systems: a scoping review of non-nuclear mapping, implementation and outcomes

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ABSTRACT

This study aimed to map non-nuclear sentinel lymph node biopsy techniques for breast cancer in resource-limited systems and synthesise implementation requirements and outcomes. Scoping review following Joanna Briggs Institute guidance and PRISMA-ScR. Setting: Services meeting a service-level definition of resource limitation; low- or middle-income country location alone was insufficient. Information sources: PubMed, Europe PMC and backward citation searching. Subjects: Clinical studies, implementation reports, surveys, reviews and guidelines on axillary staging. Outcome measures: Identification, false-negative performance, morbidity, axillary dissection avoided, cost, barriers and training. The merged database exports contained 2,301 records; 1,252 unique records were screened and 36 evidence sources included. Methylene blue (MB) programmes reported 85.7%–100% identification, with a 13% false-negative rate in one meta-analysis. Fluorescein plus MB achieved 82%–100% identification with false-negative rates of 6.3%–8.7%. Indocyanine green series achieved 95.7%–100% identification but required near-infrared equipment. Gentian violet achieved 97.5% identification in a small cohort. Ethiopian programmes achieved 100% identification; one avoided axillary dissection in 80%. North African data showed less lymphoedema after sentinel biopsy than dissection (3.8% versus 23.0%). Constraints were nuclear medicine, pathology, supply, training and follow-up. Non-nuclear sentinel node biopsy appears feasible in resource-limited services when introduced as a governed pathway rather than dye substitution. MB was the lowest-cost/lowest-infrastructure option identified; fluorescein plus MB adds redundancy, while indocyanine green suits services able to support reusable imaging. Evidence is insufficient to establish oncological equivalence. Prospective implementation studies with audited recurrence, morbidity and cost are required.

Keywords: Breast cancer, Sentinel lymph node biopsy, Resource-limited settings, Methylene blue, Implementation science

INTRODUCTION

Breast cancer accounted for an estimated 2.3 million new diagnoses in 2022 and is now the most commonly diagnosed cancer in women. Its burden is rising across Sub Saharan Africa and South Asia, where population growth, epidemiological transition and uneven access to early diagnosis increase the number of women presenting to services that cannot deliver the full surgical pathway. In Sub Saharan Africa, advanced stage presentation is common and materially reduces the pool eligible for de-escalation, but it does not remove the obligation to provide accurate, low morbidity axillary staging for women who do present with clinically node-negative disease.[1,2]

Sentinel lymph node biopsy, or SLNB, replaced routine axillary lymph node dissection, or ALND, for clinically

node-negative early breast cancer because it preserves staging information while reducing arm morbidity. Randomised evidence established equivalent survival after sentinel node resection in node negative disease and better quality of life than standard axillary treatment.[3,4] The implementation gap is therefore not uncertainty about whether SLNB is beneficial. It is the failure of a complex service to reach patients when radiopharmaceuticals, gamma probes, pathology workflows and trained teams are unavailable.

This gap is large. In an eleven country survey, 67% of surgeons working in resource-limited settings reported no access to SLNB and 60% lacked immunohistochemistry.[5] Resource-stratified frameworks recognise that safe care must be matched to available diagnostic, surgical, pathology and radiotherapy capacity, yet adoption of high-income country recommendations without those linked services can produce incomplete or unsafe care.[6] A radioisotope is only one component of the problem: a low-cost dye cannot compensate for poor patient selection, absent pathology, no rescue plan after failed mapping, or unreliable follow-up.

A scoping review was selected because the evidence spans validation cohorts, implementation case series, surveys, training interventions, technology studies, guidelines and landmark trials, with substantial heterogeneity that precludes a single pooled effect estimate. The review follows PRISMA-ScR and contemporary scoping review guidance.[7,8] Its objectives were to map non-nuclear tracers, infrastructure, barriers, training and outcomes; determine which combinations are scalable; and propose a staged implementation model for resource-limited breast cancer systems. The question is timely because isotope supply remains fragile, affordable fluorescence is maturing, and virtual training has expanded since the pandemic. To our knowledge, this is the first scoping review centred specifically on non-nuclear mapping as a health system intervention rather than a tracer accuracy question. It links technical performance to the pathology, adjuvant treatment and surveillance functions required for meaningful de-escalation.

METHODS

Protocol and reporting

An a priori protocol defined the population, concept and context, eligibility criteria, search, charting fields and narrative synthesis. The protocol was not externally registered. Reporting follows the PRISMA-ScR checklist, which is provided in Appendix II.

Eligibility criteria

The population was adults with breast cancer undergoing or being considered for SLNB, principally those with clinically node-negative early-stage disease. The concept comprised non-nuclear mapping, locally adapted nuclear pathways, infrastructure, cost, training, implementation barriers and clinical outcomes. The context was operationalised at service level. A study was considered resource-limited when the report documented at least one SLNB-relevant constraint, such as absent or unstable nuclear medicine or gamma-probe access, limited pathology capacity, tracer or device affordability or supply constraints, training or case-volume limitations, or unreliable follow-up, or when investigators explicitly described the service as resource-limited. Low- or middle-income country location alone was not sufficient. Borderline tertiary-centre reports were included only when an explicit SLNB-relevant constraint or resource adaptation was described. Landmark axillary trials and resource-stratified guidance were eligible as contextual evidence only when they directly informed omission of ALND or service design; they were not used to infer feasibility in resource-limited services. Primary clinical studies, systematic reviews, implementation reports, surveys, training evaluations and guidelines were included. Laboratory or animal studies, non-breast cancers, purely diagnostic imaging studies, reports without extractable implementation relevance, and non-English reports were excluded. No starting date was imposed. Evidence available through 24 August 2026 was considered.

Information sources and search strategy

PubMed and Europe PMC were searched on 24 August 2026. The electronic strategy combined controlled vocabulary and title or abstract terms for breast cancer and sentinel node biopsy with a third enrichment block covering named tracers, resource-setting terms and implementation concepts. Embase, Scopus/Web of Science and Cochrane databases were not searched. Because the enrichment block can miss SLNB reports whose titles or abstracts do not state a tracer, implementation issue or resource constraint, resource setting was assessed again at full-text eligibility and backward citation searching plus targeted journal-site searching was used to identify regional reports. The review should therefore be interpreted as a focused evidence map rather than an exhaustive bibliographic census. The complete reproducible strategy and source counts are in Appendix I.

Selection process

Records were deduplicated by DOI and normalised title. One reviewer screened titles and abstracts, retrieved potentially eligible reports, applied the eligibility criteria at full text and charted included studies. A second independent reviewer was not available; duplicate screening and duplicate charting were therefore not performed. Reasons for full-text exclusion were recorded in mutually exclusive categories. Selection is summarised in Figure 1.

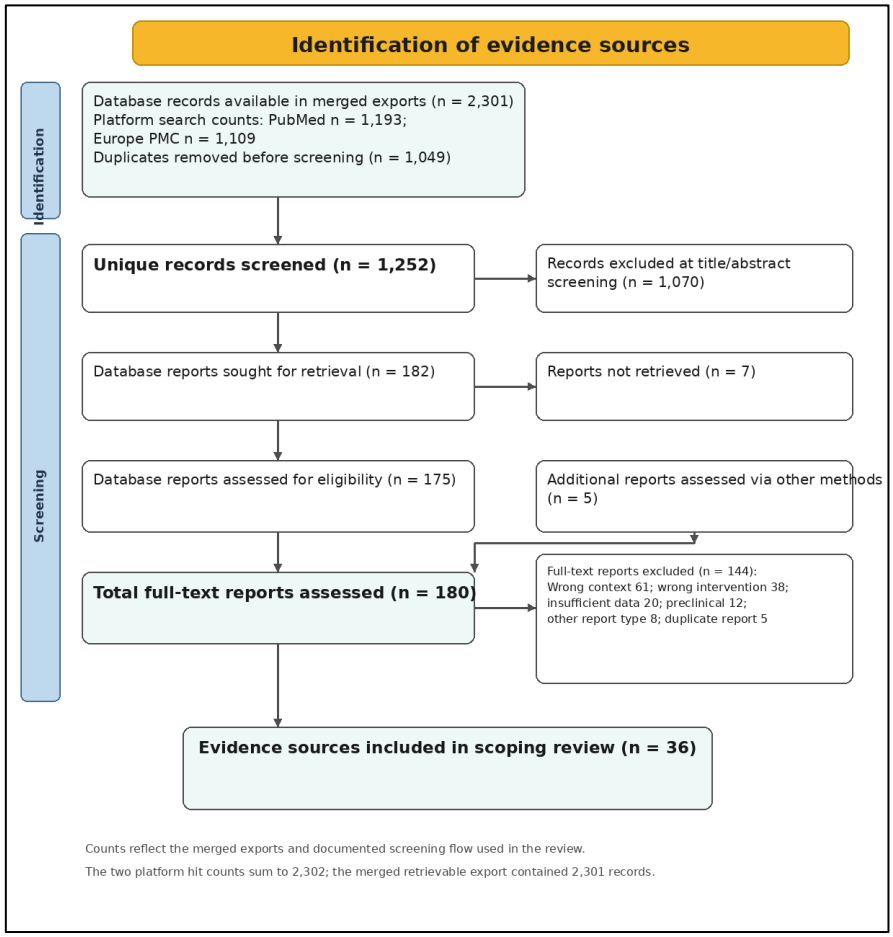


Figure 1: PRISMA-ScR flow diagram. The merged database exports contained 2,301 records; 1,252 unique records were screened, 180 full-text reports were assessed (including five located through other methods), and 36 evidence sources were included.

Data charting

A piloted charting form captured country, setting, design, sample, clinical eligibility, tracer and injection method, comparator, identification rate, nodes retrieved, sensitivity, false-negative rate, complications, ALND avoided, follow-up, infrastructure, cost, training and implementation determinants. Numerical data were checked against the article abstract or full report. Where denominators differed between enrolled, mapped and analysable cohorts, the study denominator was retained and stated. Currency figures are reported as stated by investigators, with approximate United States dollar equivalents only where the source provided them. No inflation adjustment was attempted, so costs describe local affordability at the study time rather than present universal prices.

Critical appraisal and synthesis

Formal risk of bias appraisal was not performed because the purpose was to map evidence and implementation requirements rather than estimate a treatment effect. Evidence maturity was nevertheless made explicit by separating randomised or completion ALND validation studies from retrospective cohorts, training surveys, preclinical technology reports and a preprint. Results were synthesised descriptively across five domains: mapping performance; infrastructure and cost; barriers and facilitators; training; and clinical outcomes. Between study comparisons are interpretive because case mix, injection technique, neoadjuvant exposure, pathological reference standards and definitions differed.

RESULTS

Selection and evidence profile

The merged database exports contained 2,301 records. After 1,049 duplicates were removed, 1,252 unique records were screened and 1,070 were excluded at title/abstract screening. Of 182 database reports sought for retrieval, seven were not retrieved and 175 were assessed in full text. Five additional reports entered full-text assessment through other methods, giving 180 full-text reports assessed; 144 were excluded and 36 evidence sources were included (Figure 1). Table I lists all 36 included evidence sources (references 3-6 and 9-40). References 1-2 provide background epidemiology and

references 7-8 provide reporting and methodological guidance and are not counted among the 36 included sources. The included evidence comprised clinical validation studies and programme series, two technology development reports, one training evaluation, an international service survey, systematic reviews, resource frameworks and landmark axillary trials. India generated most country-specific reports, while Sub-Saharan African evidence came from Ethiopia, Nigeria, Kenya and South Africa (Figure 2).

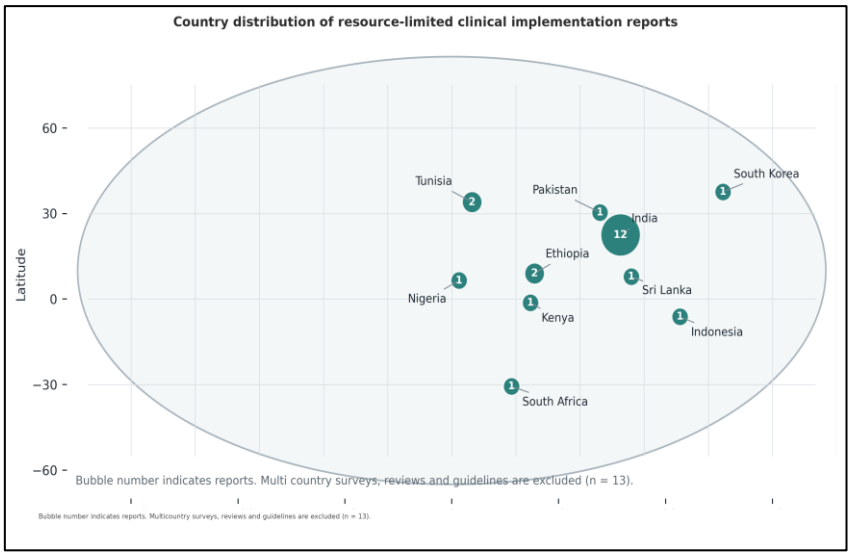


Figure 2: Country distribution of resource-limited clinical implementation reports. Bubble numbers show report counts. Multicountry surveys, systematic reviews, guidelines and landmark trials are excluded from the map.

Methylene blue and programme feasibility

Methylene blue (MB) was the most frequently represented low-infrastructure technique in the included evidence and can use existing theatre instruments with an inexpensive, widely stocked dye. Across 18 studies, a meta-analysis estimated 91% identification but a 13% false-negative rate, above conventional acceptability thresholds.[9] This pooled result is a necessary counterweight to selected programme estimates of 78% to 98% identification and 3% to 10% false-negative performance. High rates in experienced units should not be treated as proof that dye alone is intrinsically equivalent to dual mapping.

In Enugu, 24 of 28 patients had a sentinel node identified, giving 85.7% identification, 90.9% sensitivity and a 9.1% false-negative rate; identification improved from 78.6% in the first half of cases to 92.9% in the second.[10] Indian and Indonesian cohorts reported identification of 95.9% and 97.6%, respectively.[11,12] In Addis Ababa, all 20 patients had one to six nodes retrieved and 30% contained metastases, but all underwent completion ALND because frozen section and reliable adjuvant pathways were constrained.[13] At St Paul's Hospital, all 40 cases mapped successfully and 32 women, or 80%, avoided ALND after negative pathology.[14] These two Ethiopian experiences show that technical success and therapeutic de-escalation are different implementation outcomes.

The Kenyan series reported 31 positive SLNBs among 129 women and a 5.1% regional recurrence rate among 79 followed beyond two years, while adjuvant treatment completion was incomplete.[15] In South Africa, replacing the nuclear pathway with superparamagnetic iron oxide increased the proportion of eligible women receiving SLNB from 42% to 53%, but required a proprietary magnetometer.[16] A Tunisian comparison found lymphoedema after SLNB in 3.8% versus 23.0% after ALND, with lower early pain and a shorter hospital stay.[17] Thus access, morbidity and downstream treatment are at least as important as node detection.

Technique performance and cost

An Indian randomised study reported identification of 97.4% with methylene blue plus radioisotope and a 2.6% false-negative proportion, while a roughly 10 mL methylene blue vial cost about INR 15.[18] Dye availability does not eliminate quality requirements. Deep parenchymal or peritumoral injection should be favoured over intradermal delivery when feasible because superficial methylene blue can cause skin staining or necrosis. Each programme needs a predefined failed mapping plan and an initial validation phase. Table II and Figure 3 compare the principal non-nuclear options.

Table 1: Characteristics and implementation findings.

Ref.	Source	Country or context	Design and sample	Mapping or system	Key finding	Implementation interpretation
3	Krag et al, 2010	Multicentre	Randomised trial, n = 5,611	Radiocolloid with or without blue dye	SLNB alone and SLNB plus ALND had equivalent overall survival in sentinel negative disease.	Foundation for replacing routine ALND.
4	Mansel et al, 2006	United Kingdom	Randomised trial, n = 1,031	Standard SLNB versus axillary treatment	Less arm morbidity and better quality of life with sentinel node management.	Defines the patient centred benefit.
5	Yadav et al, 2022	Eleven countries	Surgeon survey, n = 199	Service capability survey	67% of resource-limited respondents lacked SLNB; 60% lacked immunohistochemistry.	Shows coupled diagnostic and treatment gaps.
6	El Saghir et al, 2018	Global	Resource framework review	WHO, BHGI, NCCN and ASCO frameworks	Resource tiers link recommendations to diagnostic and treatment capacity.	Supports adaptation by service level.
9	Li et al, 2018	Multiple countries	Systematic review, 18 studies	Methylene blue alone	Pooled identification 91%; false-negative rate 13%.	Detection acceptable; false-negative performance cautions against unvalidated use.
10	Okoye and Ezeome, 2022	Nigeria	Prospective validation, n = 28	Methylene blue; completion ALND	Identification 85.7%; false-negative rate 9.1%; later cases identified 92.9%.	Demonstrates feasibility and a learning effect.
11	Devarakonda et al, 2021	India	Retrospective cohort, n = 172	Methylene blue alone	Identification 95.9%; no reported axillary recurrence at mean 26.7 months.	Large dye only programme with short follow-up.
12	Hermansyah et al, 2021	Indonesia	Cross sectional validation, n = 60	Methylene blue; completion ALND	Identification 97.6%; sensitivity 91.7%; NPV 96.7%.	Supports single dye validation outside India.
13	Bekele et al, 2024	Ethiopia	Prospective feasibility, n = 20	Methylene blue; completion ALND	Identification 100%; one to six nodes; 30% metastatic.	Technical success did not avoid ALND because downstream capacity was limited.
14	Suga et al, 2026	Ethiopia	Implementation cohort, n = 40	Methylene blue with pathology pathway	Identification 100%; 32 patients, 80%, avoided ALND.	Shows pathway maturation from validation to therapeutic de-escalation.
15	Brand et al, 2018	Kenya	Retrospective cohort, n = 129	Radioisotope, blue dye or both	24% sentinel positive; regional recurrence 5.1% among 79 followed beyond two years.	Adjuvant treatment completion and surveillance affect safety.
16	Yousef et al, 2023	South Africa	Before and after cohort	Nuclear mapping versus Sentimag	Eligible patients receiving SLNB increased from 42% to 53%.	Non-nuclear equipment improved access but required capital.

Continued.

Ref.	Source	Country or context	Design and sample	Mapping or system	Key finding	Implementation interpretation
17	Belkhodja et al, 2026	Tunisia	Retrospective comparison, n = 64	SLNB versus ALND	Lymphoedema 3.8% versus 23.0%; less pain; shorter stay; detection 89%.	Direct regional morbidity benefit.
18	Seenu et al, 2019	India	Randomised trial, n = 237	Methylene blue or patent blue plus radioisotope	Identification 97.4% versus 96.6%; MB cost about INR 15 per vial.	Validates the lowest cost dye within dual mapping.
19	Valiveru et al, 2020	India	Prospective validation, n = 65	Fluorescein, methylene blue and radiocolloid	Fluorescein plus MB identification 95.4%; false-negative rate 6.3%.	Low capital dual dye alternative.
20	Khadka et al, 2022	India	Randomised trial, n = 130	Fluorescein plus MB versus technetium plus MB	Identification 89.0% versus 90.9%; non inferior; lower cost.	Best direct randomised fluorescein comparison.
21	Chavda et al, 2022	India	Prospective validation, n = 58	Fluorescein plus MB; completion ALND	Identification 96.7% before and 82% after neoadjuvant treatment; false-negative 7.4% and 8.7%.	Post treatment mapping needs further validation.
22	Sethi et al, 2024	India	Prospective study, n = 60	Fluorescein plus MB	Identification 100%; false-negative rate 7.1%; accuracy 98.3%.	Promising but single-centre.
23	Gupta et al, 2026	India	Prospective cohort, n = 50	Fluorescein with handheld ultraviolet light	Detection and sensitivity 96%; specificity 98%; false-negative rate 4.2%.	Requires multicentre replication.
24	Suhani et al, 2023	India	Randomised trial, n = 70	ICG plus MB versus radioisotope plus MB	Identification 100% versus 91.4%; ICG arm cost more with equipment.	Technical performance does not ensure affordability.
25	Agrawal et al, 2020	India	Comparative cohort, n = 207	ICG plus MB versus radioisotope plus MB	Identification 97% versus 95%; isotope availability declined markedly.	ICG can protect continuity during isotope shortages.
26	Somashekhar et al, 2020	India	Prospective comparison, n = 100	ICG versus radiocolloid plus MB	Identification 96% versus 94%; false-negative rate 3.1% versus 6.2%.	High performance with reusable imaging.
27	Hidar et al, 2021	Tunisia	Retrospective cohort, n = 47	ICG, some with blue dye	Identification 95.7%; no axillary recurrence at mean 29.2 months.	North African feasibility; short follow-up.
28	Sugie et al, 2017	Multiple countries	Meta analysis, 12 studies; n = 1,736	ICG versus radioisotope	No significant overall detection difference; heterogeneous studies.	Supports ICG performance, not local cost transfer.
29	Mooghal et al, 2026	Pakistan	Retrospective cohort, n = 40	Gentian violet plus radioisotope	Identification 97.5%; false-negative rate 2.5%; no short term complications.	Exploratory; not standalone validation.
30	Park et al, 2021	South Korea	Device development	Photoacoustic finder	Integrated solid state laser and transparent ultrasound detector.	Technical platform preceding clinical feasibility.
31	Han et al, 2025	South Korea	Prospective cross-	Photoacoustic finder	Detection 87%; sensitivity 0.81;	Proof of concept, not an independent

Continued.

Ref.	Source	Country or context	Design and sample	Mapping or system	Key finding	Implementation interpretation
			sectional, n = 121; 375 nodes	on excised nodes	specificity 0.63 against dual mapping.	clinical pathway.
32	Yadav et al, 2026	International virtual	Training evaluation, 75 pre and 66 post	Seven hour BRIDGE course	At least 85% reported greater confidence; 96% intended to adopt a technique.	Measures intention, not competence or outcomes.
33	Yadav et al, 2026	India	Prospective learning curve, n = 100	Fluorescein plus MB	Identification reached 92% after case 20; false-negative rate below 7%.	Supports proctored case based credentialing.
34	Bandaranayake et al, 2026	Sri Lanka	Retrospective preprint, n = 115	Methylene blue alone	Identification 98.3%; no isolated axillary recurrence among 75 negative cases at mean 36.3 months.	Encouraging, but not peer reviewed and loss to follow-up occurred.
35	Ratnagiri et al, 2025	India	Mixed cancer cohort, n = 70	SPECT CT, lymphoscintigraphy and MB	Localisation 100%; operative time improved; axillary recurrence 6.5% in breast cases.	Team redesign can partly bypass gamma probe scarcity.
36	Buccimazza, 2011	South Africa	Implementation commentary	Programme implementation	Emphasised team training, validation and local quality assurance.	Early regional pathway model.
37	Anderson et al, 2008	Global	Consensus guideline	BHGI resource tiers	Links early detection, diagnosis and treatment to available resources.	Foundation for staged adoption.
38	Park et al, 2025	Global	ASCO guideline	Contemporary axillary staging	Defines selected groups for SLNB omission and management after positive nodes.	Requires imaging, biology, radiotherapy and follow-up assumptions.
39	Giuliano et al, 2017	United States	Randomised trial follow-up, n = 856	ALND versus no ALND after one or two positive nodes	Ten year survival non inferior without ALND in eligible breast conserving therapy.	Reduces surgery only when trial cointerventions apply.
40	Bartels et al, 2023	Europe	Randomised trial follow-up, n = 1,425 sentinel positive	Axillary radiotherapy versus ALND	Comparable control; less lymphoedema after radiotherapy.	Relevant where radiotherapy is reliably available.

Table 1 contains all 36 evidence sources included in the scoping review (Refs 3-6 and 9-40). Refs 1-2 provide background epidemiology and Refs 7-8 provide reporting/methodological guidance and are not counted among the 36 included sources. Landmark trials and resource-stratified guidelines in Table I are contextual evidence only and were not used to infer feasibility in resource-limited services. ALND, axillary lymph node dissection; BHGI, Breast Health Global Initiative; ICG, indocyanine green; MB, methylene blue; NACT, neoadjuvant chemotherapy; NPV, negative predictive value; SLNB, sentinel lymph node biopsy.

Table 2: Comparison of non-nuclear mapping techniques.

Technique	Evidence base	Identification	False negative rate	Infrastructure	Reported cost	Advantages	Limitations and learning
Methylene blue	Meta analysis plus African and Asian validation cohorts	85.7% to 100%; pooled 91%	2.6% to 13%	Standard theatre; dye, syringe and pathology	About INR 15 per 10 mL vial in one Indian study	Lowest-cost/lowest-infrastructure option identified in this review; widely available; visible	Single channel mapping; staining and rare tissue injury; validate locally
Fluorescein alone	Prospective Indian cohorts	92% to 96%	About 4.2% to 10%	Blue or ultraviolet torch; light control	Low consumable cost; local torch cost	Bright signal; no nuclear medicine	Definitions and light sources differ; operator must recognise fluorescence
Methylene blue plus fluorescein	Randomised and completion ALND validation	82% after NACT to 100%	6.3% to 8.7%	Two dyes and validated blue light source	INR 2,000, about US$23, in one programme; INR 2,543 per successful case in one trial	Two visual channels; inexpensive redundancy	Lower post NACT identification; dye supply and torch quality must be controlled
ICG alone	Prospective cohorts and meta-analysis	95.7% to 96% in selected regional series	3.1% in one completion ALND study	Near infrared camera, sterile drape and maintenance	Dye modest; camera capital high and variable	Real time lymphatic anatomy; no radiation	Capital, maintenance and failure contingency; rapid lymphatic transit
Methylene blue plus ICG	Randomised and comparative Indian studies	97% to 100%	Not reported in the included direct comparative cohorts	Near infrared camera plus standard dye setup	Can cost more when capital is included	Redundant visible and fluorescent channels	Equipment training and procurement burden
Gentian violet	One small radioisotope validated cohort	97.5%	2.5%	Standard theatre; locally approved dye and pathology	Described as low-cost; no transferable microcost	Visible and inexpensive	Regulatory and tissue safety review required; no standalone validation
Photoacoustic finder	Device report and one ex vivo clinical feasibility study	87% of excised sentinel nodes	Not established	Prototype laser and ultrasound detector; blue dye	No market price	Radiation free instrumented detection	Sensitivity 0.81 and specificity 0.63; in vivo workflow and cost unproven
Superparamagnetic iron oxide	South African before and after programme	Access outcome rather than direct identification comparison	Not reported in included programme	Magnetometer, magnetic tracer and non-ferrous instruments	Capital and proprietary consumables	No isotope scheduling; reusable detector	MRI artefact and capital dependence; not a dye technique

Table 3: Barrier, facilitator and accountability matrix

Barriers	Clinical consequence	Minimum countermeasure	Accountability indicator	Implementation phase
No nuclear medicine or isotope interruptions	Eligible women default to ALND	Choose MB plus fluorescein or supported ICG; retain a failed mapping plan	Eligible patients offered SLNB; identification; conversion to ALND	Readiness and validation
Limited pathology and 60% lacking immunohistochemistry	Nodes may be misclassified and biology unknown	Standardise slicing and permanent section; referral pathology; documented turnaround	Turnaround; inadequate specimens; amended reports	Readiness
High tracer or device cost	Low uptake despite nominal availability	Local microcosting; pooled procurement; capital depreciation and maintenance budget	Cost per eligible patient and per successful map	Readiness and scale
Tracer stock interruption	Cancelled or downgraded surgery	Two approved tracers; minimum stock; batch and expiry dashboard	Stockout days; cancelled procedures	Service assurance
Insufficient surgeon experience	Failed mapping or high false-negative performance	Theory, simulation, proctoring and consecutive case validation	Identification by case sequence; nodal yield; retraining events	Validation
No frozen section	Second operation may be needed	Permanent section with a preagreed staged axillary plan; counsel patients	Reoperation and time to completion	Pathway design
Late presentation	Fewer clinically node-negative patients	Earlier diagnosis pathway and axillary ultrasound selection	Stage distribution; proportion eligible	System wide
Unreliable radiotherapy	Unsafe transfer of Z0011 or AMAROS rules	Use only nodal de-escalation pathways whose cointerventions are deliverable	Radiotherapy completion; protocol deviations	Governance
Loss to follow-up	Axillary recurrence and morbidity remain invisible	Registry, telephone follow-up, patient navigation and regional linkage	Follow up completeness at one, three and five years	Service assurance
Weak multidisciplinary coordination	Delays, specimen errors and unclear responsibility	Named pathway lead; preoperative huddle; written standard operating procedure	Cancellations; specimen discrepancies; result acknowledgement	All phases
Virtual training mistaken for credentialing	Confidence without competence	Use virtual teaching as prerequisite; certify observed performance	Proctored cases and competency sign off	Training

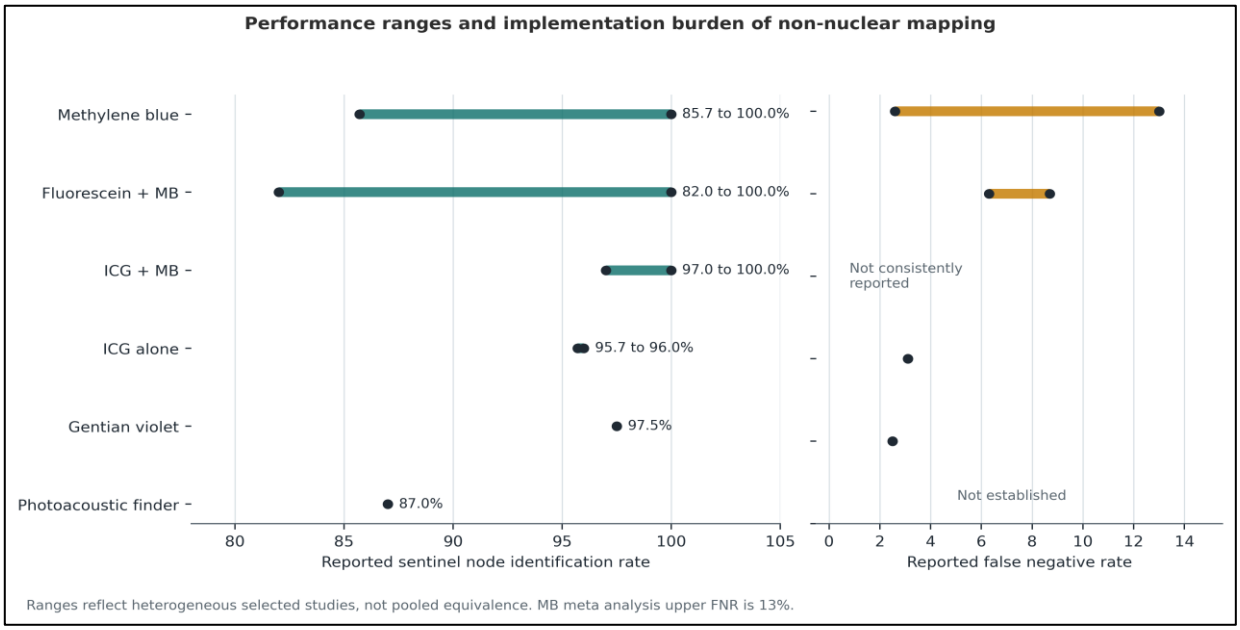


Figure 3: Reported performance ranges for non-nuclear mapping. Ranges are descriptive across heterogeneous studies and should not be interpreted as pooled equivalence. The methylene blue upper false-negative estimate is from a meta-analysis.

Fluorescein provides visible fluorescence using an inexpensive blue or ultraviolet light source. In a 65 patient validation study, fluorescein plus methylene blue identified nodes in 95.4% with a 6.3% false-negative rate, comparable with 97% and 6.3% for radioisotope plus methylene blue.[19] A 130 patient randomised trial found identification of 89.0% versus 90.9%, establishing non inferiority within its prespecified margin; this corrects the occasionally repeated 84.6% estimate.[20] A further validation cohort reported 96.7% identification and 7.4% false-negative results before chemotherapy, but only 82% identification after neoadjuvant treatment.[21] Other prospective reports found 100% identification with a 7.1% false-negative rate and, separately, 96% detection, 96% sensitivity, 98% specificity and a 4.2% false-negative rate.[22,23] A practical cost estimate for fluorescein, light source and methylene blue was INR 2,000, about US$23, although one randomized cost analysis reported INR 2,543 per successful procedure. These programme specific figures should not be transferred between health systems without local microcosting.

Indocyanine green, or ICG, offers real-time lymphatic visualisation without nuclear medicine. An Indian randomised trial found 100% identification with ICG plus methylene blue versus 91.4% with radioisotope plus methylene blue, but the ICG arm cost more when camera capital was included.[24] A 207 patient comparison reported 97% identification with ICG plus methylene blue and 95% with radioisotope plus methylene blue, against a background decline in isotope availability.[25] In a 100 patient prospective study, ICG alone identified 96% of nodes and had a 3.1% false-negative rate, while the dual dye comparator identified 94% with a 6.2% false-negative rate.[26] A Tunisian series achieved 95.7% identification and observed no axillary recurrence at 29.2 months.[27] Meta analytic evidence found no material detection difference between ICG and radioisotope, but heterogeneity was substantial.[28] ICG therefore shifts rather than removes infrastructure: it avoids radioactive procurement but requires a maintained near infrared camera, trained staff, sterile draping and contingency for equipment failure.

Gentian violet and photoacoustic detection remain developmental. In 40 patients, gentian violet plus radioisotope identified 97.5% of sentinel nodes with a reported 2.5% false-negative rate and no short-term complications.[29] Because the study was small, retrospective and radioisotope validated, gentian violet cannot yet be recommended as a standalone tracer. A handheld photoacoustic finder combines blue dye with optical excitation and ultrasound detection.[30] In a prospective cross-sectional study it detected 87% of excised sentinel nodes, compared with 85% for a gamma probe and 73% for visual inspection, but sensitivity was 0.81 and specificity 0.63 against dual mapping.[31] Ex vivo node assessment is proof of concept, not evidence for unsupervised clinical replacement.

Infrastructure, barriers and training

A minimum service requires reliable clinical and axillary ultrasound selection, sterile dye preparation, theatre lighting or a validated fluorescence device, specimen orientation, trained histopathology, a result communication pathway and longitudinal surveillance.

Frozen section is helpful but not essential if a safe staged plan exists. Immunohistochemistry should be available for tumour biology, but routine cytokeratin staining of every sentinel node is not a prerequisite. Dyes need secure procurement, batch tracking and storage according to the manufacturer; most avoid the radiopharmaceutical cold chain, but ICG and fluorescein remain vulnerable to stock interruption and expired consumables.

The recurring barriers were high technology cost, isotope and tracer shortages, absent nuclear medicine, limited pathology, late presentation, insufficient case volume, no proctored training and weak follow-up. These are coupled constraints. For example, introducing mapping without adjuvant radiotherapy can invalidate treatment strategies that rely on breast irradiation, while introducing frozen section without reliable staffing may delay operations and waste specimens. Table III converts these barriers into measurable countermeasures.

Training evidence was limited. The BRIDGE course delivered seven hours of virtual teaching on resource adapted breast surgery, including methylene blue and a fluorescein torch. Among 66 post course respondents, at least 85% reported improved confidence across domains and 96% planned to adopt at least one technique, but competence and patient outcomes were not measured.[32] In a 100 case single surgeon series using fluorescein plus methylene blue, identification reached 92% after case 20 and the false-negative rate remained below 7%.[33] Virtual teaching should therefore prepare teams, not credential them. A sustainable pathway combines theory, a skills laboratory, proctored consecutive cases, validation against an audited reference standard, and service dashboards (Supplementary Figure 1). Oncoplastic breast surgery workshops can host this practical component because they already bring multidisciplinary teams together.

Clinical outcomes and evidence maturity

The strongest immediate benefit was avoidance of ALND and its morbidity. The St Paul's cohort avoided ALND in 80%, and the Tunisian comparison showed an absolute 19.2 percentage point reduction in lymphoedema. Indian, Indonesian and Tunisian cohorts reported no axillary recurrence during relatively short follow-up, but sample sizes and surveillance completeness limit oncological inference. A Sri Lankan retrospective preprint reported 98.3% identification in 115 analysable patients, no isolated axillary recurrence among 75 sentinel negative women over a mean 36.3 months, and an estimated tracer cost near US$0.50.[34] It is labelled as a preprint because peer review could alter those estimates. Another Indian programme achieved 100% localisation without a handheld gamma probe by coordinating SPECT CT, lymphoscintigraphy and methylene blue, but its mixed cancer cohort and 6.5% axillary recurrence signal underline the importance of disease specific audit.[35] Supplementary Figure 2 summarises selected programme outcomes.

DISCUSSION

Summary and interpretation

This review found that non-nuclear SLNB is feasible in selected resource-limited services, but the evidence does not establish oncological equivalence of non-nuclear pathways across settings or justify replacing routine ALND without local validation and dependable downstream care. MB was the lowest-cost/lowest-infrastructure option identified in this review and had the broadest regional evidence, but its pooled false-negative rate remains the principal caution. Fluorescein plus MB offers redundancy for little consumable cost and an observable learning curve. ICG performs well and provides real-time anatomy, but camera purchase, maintenance and sterile integration can make it less affordable than its label suggests. Gentian violet and photoacoustic detection are promising research options, not current service standards.

Identification rate is a technical process measure, not a surrogate for oncological safety. A service may achieve high node identification while still having an unacceptable false-negative rate or unreliable downstream pathology, adjuvant treatment or follow-up. Claims about safe de-escalation therefore require evidence on false-negative performance, regional recurrence, morbidity, treatment completion and surveillance. These outcomes were inconsistently reported and were usually based on small cohorts with short follow-up in the included literature.

The implementation unit is the pathway. Earlier South African experience emphasised multidisciplinary planning, validation and local ownership rather than isolated technical transfer.[36] At minimum, a programme must answer five questions before the first independent case: who is eligible; what happens if no node maps; how will nodes be processed and results communicated; when can ALND be omitted; and how will axillary recurrence and arm morbidity be detected? A tracer should be selected only after these questions are resolved.

Resource-stratified care

Resource-stratified frameworks from the Breast Health Global Initiative, WHO scenarios and the NCCN Framework are better interpreted as sequencing tools than permission for a lower standard.[37] At a basic level, clinically node-negative patients may still receive ALND when pathology, safe mapping or follow-up is absent. At a limited level, methylene blue or fluorescein dual dye can be introduced with permanent section pathology and a planned second operation when needed. At an enhanced level, ICG or magnetic tracers, frozen section and structured survivorship surveillance become realistic.

ASCO guidance defines which contemporary patients may omit SLNB or further axillary treatment, but those recommendations assume accurate imaging, tumour biology, radiotherapy and follow-up that cannot be taken for granted.[38]

Z0011 showed no survival detriment from omitting ALND in selected women with one or two positive sentinel nodes receiving breast conserving therapy and whole breast irradiation.[39] AMAROS showed that axillary radiotherapy provides comparable control with less lymphoedema than ALND for sentinel node positive disease.[40] These trials can reduce surgical burden only where their cointerventions are reproducible. Applying the nodal rule while omitting radiotherapy, systemic treatment or follow-up is not adaptation; it is partial adoption with uncertain oncological safety.

Authors' proposed implementation framework

The framework below is a synthesis-derived proposal intended to support local planning; it has not been prospectively validated as a guideline. A hub-and-spoke model may be practical. A regional hub can provide pathology oversight, trainer accreditation, camera or magnetic device maintenance, procurement and outcome analysis, while district or provincial units perform carefully selected dye-guided cases. The first phase should establish baseline ALND volume, morbidity and pathway failures. The second should use proctored consecutive cases with completion ALND or another defensible reference standard during the learning phase. The authors propose 20–30 consecutive proctored validation cases as a pragmatic starting range; the lower bound is informed by the learning-curve report in which identification reached 92% after case 20[33]. The full 20–30 range is not a validated universal requirement. Likewise, an identification rate of at least 90% is presented only as a pragmatic local audit trigger, not as a surrogate for oncological safety or a universal credentialing standard. Programmes should predefine local criteria that also include acceptable false-negative performance, a failed-mapping plan, pathology reliability and follow-up. Subsequent spread should occur through trained teams rather than individual enthusiasts.

Audit should use denominators that expose implementation failure: the proportion of eligible patients offered SLNB; identification rate; number of sentinel nodes; conversion to ALND; nodal positivity; pathology turnaround; reoperation; seroma, infection, pain and lymphoedema; adjuvant treatment completion; loss to follow-up; and regional recurrence. Identification alone can look excellent while most eligible women never reach the procedure. Patient reported arm function and financial toxicity should be added because avoiding ALND has value only if savings and morbidity reduction reach patients.

Infrastructure and policy implications

Policy makers should fund SLNB as a bundled service rather than a dye line item. Procurement contracts should cover at least two approved tracers, light source or camera maintenance, emergency drugs for hypersensitivity, pathology consumables and data capture. Shared equipment can improve utilisation, but a camera that circulates between hospitals without scheduled maintenance or sterile accessories is not reliable capacity. Cold chain planning is essential for radiocolloid where retained; non-nuclear dyes simplify logistics but still need storage monitoring and predictable national registration.

Training should be competency-based. Short virtual courses are efficient for theory and can support tele-mentoring, case selection meetings and video review, especially where travel is expensive. They should be followed by simulation, direct proctoring and outcome-based credentialing. Regional oncoplastic workshops are a natural platform for injection practice, axillary anatomy, troubleshooting and specimen handling. Tele mentoring can extend expert reach, but connectivity, consent, data governance and the ability to intervene after a failed map must be designed in advance.

Limitations

The review is limited by heterogeneous designs, small single-centre cohorts, inconsistent outcome definitions and short follow-up. Completion ALND, the best available validation reference in many studies, exposes participants to the morbidity the programme seeks to avoid and was not uniformly used. Formal quality appraisal and meta-analysis were outside the scoping objective. One reviewer performed screening and charting and no duplicate review was available, increasing the risk of selection or extraction error. The bibliographic search was limited to PubMed and Europe PMC and English-language reports; Embase, Scopus/Web of Science and Cochrane were not searched. In addition, the third search block required a tracer, implementation or resource-related term, which may have missed relevant SLNB studies that did not signal resource constraints in titles or abstracts. Although the revised eligibility criteria use a service-level operational definition, heterogeneity between settings remains. Publication bias probably favours successful programmes, several estimates came from motivated specialist centres, and evidence from Francophone Africa, much of South Asia and rural services was sparse. The Sri Lankan report was a preprint and the newest gentian violet, fluorescein and photoacoustic reports require replication. High identification rates and technical feasibility should therefore not be interpreted as evidence of long-term oncological equivalence.

Future directions

Research should move from single-tracer accuracy to prospective implementation science. Priorities include multicentre validation of methylene blue plus fluorescein; pragmatic comparison with ICG where a reusable camera is already present; microcosting that includes capital depreciation, pathology, reoperation and patient travel; and registries with at least five years of axillary recurrence and patient-reported arm outcomes. Clustered studies should test hub-and-spoke training, tele-mentoring and procurement. Equity analyses should assess rural and neoadjuvant populations. Photoacoustic devices require in vivo workflow, clinically meaningful specificity and independent cost validation before scale-up.

CONCLUSIONS

Non-nuclear SLNB is feasible in selected resource-limited services, but current evidence does not establish oncological equivalence. MB was the lowest-cost/lowest-infrastructure option identified in this review; fluorescein plus MB may add redundancy, and ICG suits services with sustainable imaging. Safe adoption requires reliable pathology, local validation, failed-mapping plans and longitudinal audit. Longer-term multicentre outcomes are required before broad de-escalation.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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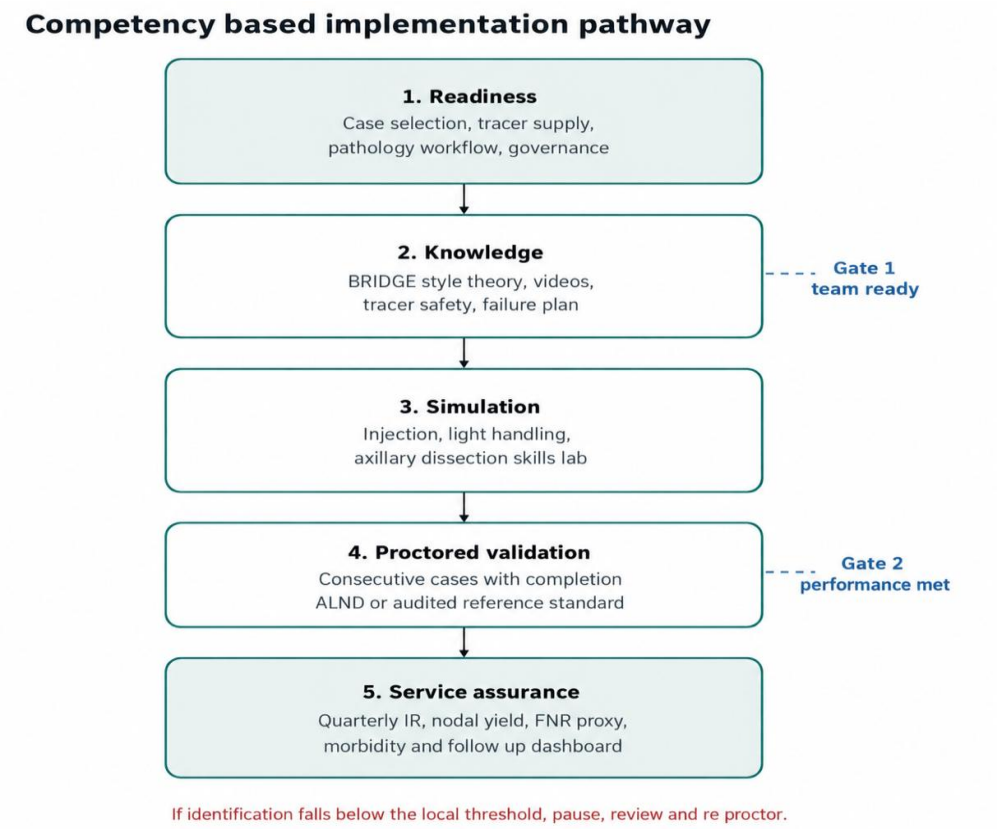
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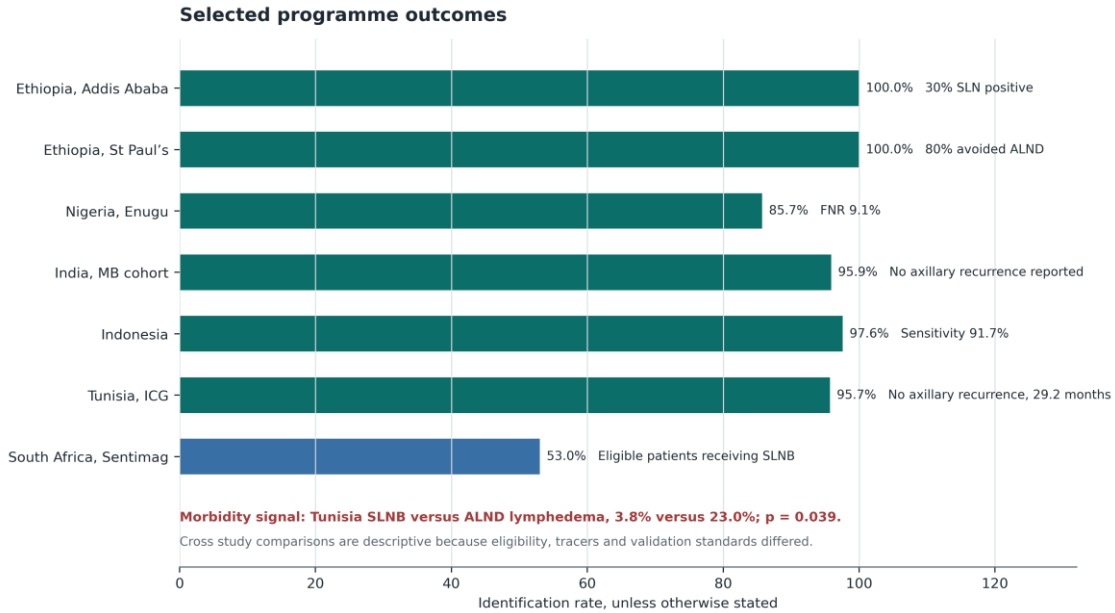
APPENDIX

Appendix I



Supplementary Figure 1: Competency-based implementation pathway.

Two gates separate team readiness from independent practice and require re-proctoring when performance deteriorates. The pathway is an author-proposed implementation framework rather than a validated credentialing guideline.



Supplementary Figure 2: Selected programme outcomes.

The South African bar represents the proportion of eligible patients receiving SLNB after Sentimag introduction, not an identification rate.

Appendix II

Reproducible search strategy

Search date: 24 August 2026. No start date was applied. Language was restricted to English during eligibility assessment.

PubMed

("Breast Neoplasms"[Mesh] OR "breast cancer"[tiab]) AND ("sentinel lymph node biopsy"[tiab] OR "sentinel node biopsy"[tiab] OR "sentinel lymph node mapping"[tiab]) AND ("methylene blue"[tiab] OR fluorescein[tiab] OR "gentian violet"[tiab] OR "indocyanine green"[tiab] OR ICG[tiab] OR photoacoustic[tiab] OR "low resource"[tiab] OR "resource limited"[tiab] OR "resource constrained"[tiab] OR "developing country"[tiab] OR Africa[tiab] OR Ethiopia[tiab] OR Nigeria[tiab] OR Kenya[tiab] OR Ghana[tiab] OR Egypt[tiab] OR Morocco[tiab] OR Tunisia[tiab] OR India[tiab] OR Pakistan[tiab] OR Bangladesh[tiab] OR "Sri Lanka"[tiab] OR Nepal[tiab] OR Indonesia[tiab] OR implementation[tiab] OR feasibility[tiab] OR training[tiab] OR "learning curve"[tiab] OR cost[tiab] OR barriers[tiab] OR infrastructure[tiab])

Records returned: 1,193.

Europe PMC

TITLE_ABS:"breast cancer" AND (TITLE_ABS:"sentinel lymph node biopsy" OR TITLE_ABS:"sentinel node biopsy" OR TITLE_ABS:"sentinel lymph node mapping") AND (TITLE_ABS:"methylene blue" OR TITLE_ABS:fluorescein OR TITLE_ABS:"gentian violet" OR TITLE_ABS:"indocyanine green" OR TITLE_ABS:ICG OR TITLE_ABS:photoacoustic OR TITLE_ABS:"low resource" OR TITLE_ABS:"resource limited" OR TITLE_ABS:"resource constrained" OR TITLE_ABS:implementation OR TITLE_ABS:feasibility OR TITLE_ABS:training OR TITLE_ABS:"learning curve" OR TITLE_ABS:cost OR TITLE_ABS:barriers OR TITLE_ABS:infrastructure) AND FIRST_PDATE:[1900-01-01 TO 2026-08-24]

Records returned: 1,109.

Other methods

Reference lists of included reports and relevant journal websites were searched for regional studies and implementation guidance. Five reports entered full text assessment through these methods.

Deduplication and screening

The platform search counts sum to 2,302, while 2,301 records were present in the merged retrievable exports used for deduplication and screening. Deduplication by DOI or normalised title removed 1,049 records, leaving 1,252 unique records for title and abstract screening. Of these, 1,070 were excluded at title/abstract screening and 182 database reports were sought for retrieval. Seven were not retrieved, leaving 175 database reports assessed in full text. Five additional reports identified through other methods entered full-text assessment, giving 180 full-text reports assessed. A total of 144 full-text reports were excluded (wrong context, 61; wrong intervention, 38; insufficient data, 20; preclinical, 12; other report type, 8; duplicate report, 5), and 36 evidence sources were included.

Appendix III

PRISMA-ScR checklist.

The checklist follows the 20 essential and two optional PRISMA-ScR reporting items. Page locations refer to this revised blinded manuscript.

Item	Section	PRISMA-ScR requirement	Reported on
1	Title	Identify the report as a scoping review.	p. 1
2	Structured summary	Provide a structured summary of background, objectives, eligibility, sources, charting, results and conclusions.	pp. 1-2
3	Rationale	Describe the rationale in relation to existing knowledge and explain why a scoping review approach was used.	pp. 3-4
4	Objectives	State the questions and objectives with population, concept and context elements.	p. 4
5	Protocol and registration	Indicate whether a protocol exists and provide registration information.	p. 4
6	Eligibility criteria	Specify characteristics and eligibility, with rationale.	pp. 4-5
7	Information sources	Describe all information sources and the last search date.	p. 5
8	Search	Present the full electronic strategy so it can be repeated.	p. 29
9	Selection of evidence	State the selection process.	p. 5
10	Data charting	Describe charting methods and calibration.	pp. 5-6
11	Data items	List and define charted variables and assumptions.	pp. 5-6
12	Critical appraisal	If performed, explain why, how and how it informed synthesis.	p. 6
13	Synthesis	Describe handling and summary of charted data.	p. 6
14	Selection results	Report screened, assessed and included sources with reasons and a flow diagram.	p. 6 and Figure 1, p. 19
15	Source characteristics	Present characteristics of each source and citations.	pp. 6-11 and Table I, pp. 24-26
16	Critical appraisal within sources	If performed, present appraisal results.	p. 6 (not performed)
17	Results of individual sources	Present relevant charted data for included sources.	pp. 7-11 and Tables I-II, pp. 24-27
18	Synthesis of results	Summarise and relate results to objectives.	pp. 7-15 and Tables II-III, pp. 27-28
19	Summary of evidence	Summarise main results, concepts and implications.	pp. 11-15
20	Limitations	Discuss limitations of the scoping review process.	p. 14
21	Conclusions	Provide a general interpretation and potential implications.	p. 15
22	Funding	Describe sources of funding for included evidence and the review.	p. 1