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EVALUATION OF QUALITY ASSURANCE STRATEGIES FOR IMMUNOHISTOCHEMISTRY TESTING IN BREAST CANCER: A LITERATURE REVIEW

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ABSTRACT

Relevance: *External quality assessment (EQA) programs should be used alongside the technique to achieve accurate and reliable results when performing Immunohistochemistry (IHC) tests and diagnostics. Ensuring the accuracy of tumor biomarker tests is critically important in precision medicine since individualized treatment plans are now common in oncology.*

The study aimed to *systematically review evidence related to EQA in reducing inter-laboratory discrepancies and interpretative concordance variability in human epidermal growth factor receptor 2 (HER2) IHC testing for breast cancer and to identify current challenges and future directions.*

Methods: *This study's systematic literature search revealed 306 records, of which 25 full-text articles were included in the final analysis. The review followed the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020).*

Results: *Recent studies suggest that EQA programs greatly improve the agreement and accuracy of HER2 IHC testing done in several laboratories. Global standards ensure standardized, reliable, and consistent HER2 testing procedures throughout the process. Moreover, new approaches like digital pathology, algorithms, and messenger RNA (mRNA)-based tests hold great potential for improving the consistency of results and reducing judgment errors in manual reviews.*

Conclusion: *Implementing EQA programs has reduced variation in results from HER2 IHC across different laboratories. With the introduction of the HER2-low classification, testing methods are moving from subjective approaches to using various forms of data to improve the test's importance to doctors. Participation in EQA enhances the efficiency of testing HER2 receptors, with the same results in several places worldwide. Having a team of experts improves the diagnosis and repeatability of breast cancer.*

Keywords: *Immunohistochemistry (IHC), External Quality Assessment (EQA), Breast Cancer, HER2, Quality Control (QC).*

Introduction: Breast cancer's diverse biological characteristics remain a serious challenge despite new developments in screening, diagnostics, and therapies. Ensuring an accurate evaluation of HER2 status is vital for treatment strategy selection. IHC testing is commonly used as the initial method for assessing HER2 status due to its widespread availability, low cost, and rapid turnaround time. However, its diagnostic accuracy can be affected by variability in antibody selection, staining protocols, and pathologists' subjective interpretation of it. The mentioned variability can misjudge the HER2 status of some cancer cells, leading to faulty treatment decisions. EQA programs have been adopted and standardized across countries to help hospitals stay consistent in testing and diagnoses [1, 2].

Using the quality control case in HER2 IHC scoring for breast cancer, we present a systematic review that summarizes authoritative international quality assessment initiatives, associated standards, and the documented impact of EQA programs on enhancing inter-laboratory reproducibility and diagnostic consistency.

The study aimed to systematically review evidence related to EQA in reducing inter-laboratory discrepancies and interpretative concordance variability in HER2 IHC testing for breast cancer and to identify current challenges and future directions.

Materials and Methods: This research conducted a systematic review of 306 records. Following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines, the study assessed quality control measures in immunohistochemistry laboratories for HER2 testing in breast cancer on a global scale [3]. The exclusion criteria included studies not related to breast cancer (n=65), those not focusing on EQA (n=50), studies lacking sufficient methodological details (n=18), publications published before 2020 (n=4), and non-English language articles (n=3). We selected 25 full-text articles for final analysis.

Search Strategy: A thorough search was conducted within PubMed, Scopus, Web of Science, and Google Scholar databases for the literature released between 2020 and 2025. The search applied such terms as "immunohistochemistry" or "IHC" with "quality assessment," "quality assurance," or "quality control," in addition to the terms "breast cancer" and "HER2". In addition, manual citation searches were done, and Rayyan was used to manage references and complete the research.

Study Selection Process: The review followed a clear workflow to ensure robust findings closely aligned with quality control in breast cancer immunohistochemistry testing, as illustrated in Figure 1.

Results:

1. The Present Condition of Quality Control Research in Breast Cancer Immunohistochemistry (IHC)

This study conducts a systematic search and analysis of 25 research articles published between the years 2020

and 2025 in order to provide a quantitative overview and academic summary of the current research landscape on quality control of HER2 IHC analysis.

1.1. Publication Trends Over the Last Five Years

According to bibliometric analysis, the number of publications on EQA of HER2 IHC testing in breast cancer has shown an overall increasing trend despite some fluctuations (Figure 2). In 2023, the number of publications reached its highest point. This upward trajectory may be strongly associated with the growing clinical recognition of the role of HER2-low subtypes in guiding targeted treatment decisions. Notably, the timing of this increase aligns with the release of updated guidelines from two major international bodies — the American Society of Clinical Oncology/College of American Pathologists (ASCO/CAP) and the European Society for Medical Oncology (ESMO) [1, 4]. As of April 2025, four studies have been published, meaning that research activity in this area continues to be strong. It is expected that the total number of publications for the year will remain at a relatively high level.

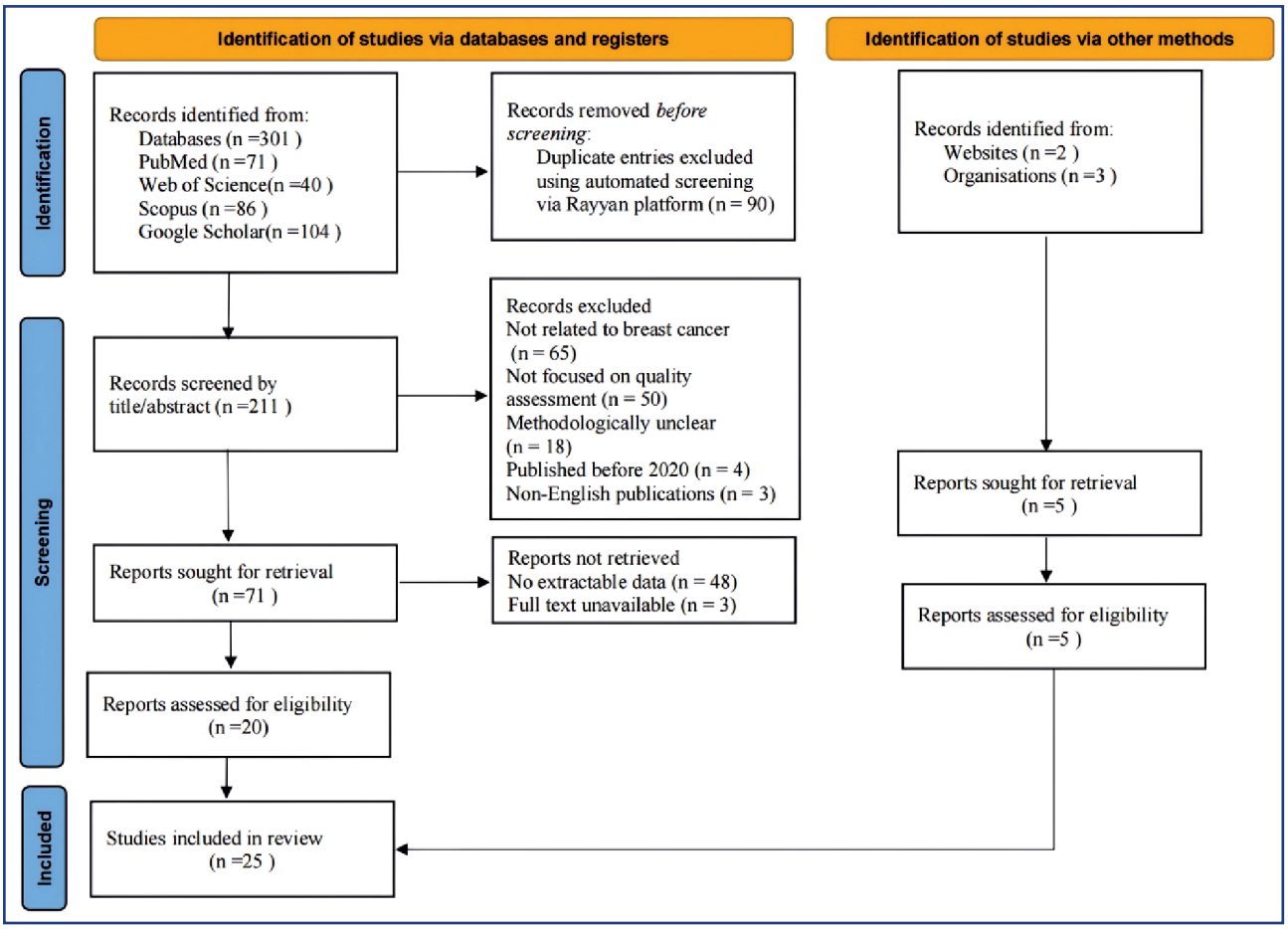

Figure 1 – PRISMA flow diagram of HER2 IHC EQA review

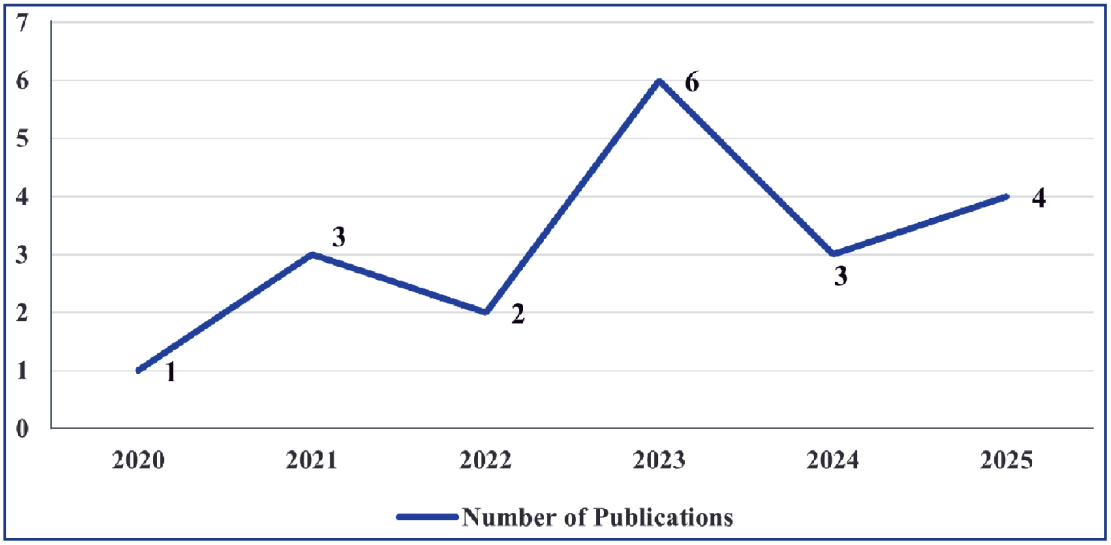

Figure 2 – Annual number of publications on EQA of HER2 IHC testing in breast cancer (2020-2025)

All in all, these trends evidence the ongoing global focus on HER2 IHC testing standardization, increased concordance of scoring, and the establishment of strong EQA programs. This increased awareness is sparked not only because of the newly defined HER2-low category used in enhanced therapeutic selection for breast cancer but also because of the importance of precision pathology in making individualized treatment options both accessible and effective.

1.2. Geographic Dispersion of Publications

As illustrated in Figure 3, In terms of single-country studies, the United States provided four publications, reflecting its dominant role in HER2 testing validation and establishing associated regulations. China independently contributed two studies, reflecting an ongoing national-level commitment to proficiency testing and diagnostic standardization. Likewise, Denmark, Australia, and the Netherlands contributed two studies, reflecting their respective engagement in HER2-related quality assurance. Italy contributed to one study. However, most of the investigations in this review emerged from international collaborative multinational studies, with six studies classified as multinationals, representing the largest proportion of all identified. This finding demonstrates the growing dependence on international cooperation around the quality assurance of HER2 IHC testing and a significant need for harmonized international standards. International collaborative studies often aim to improve scoring concordance, share methodology, and collaboratively advance clinical practice guidelines.

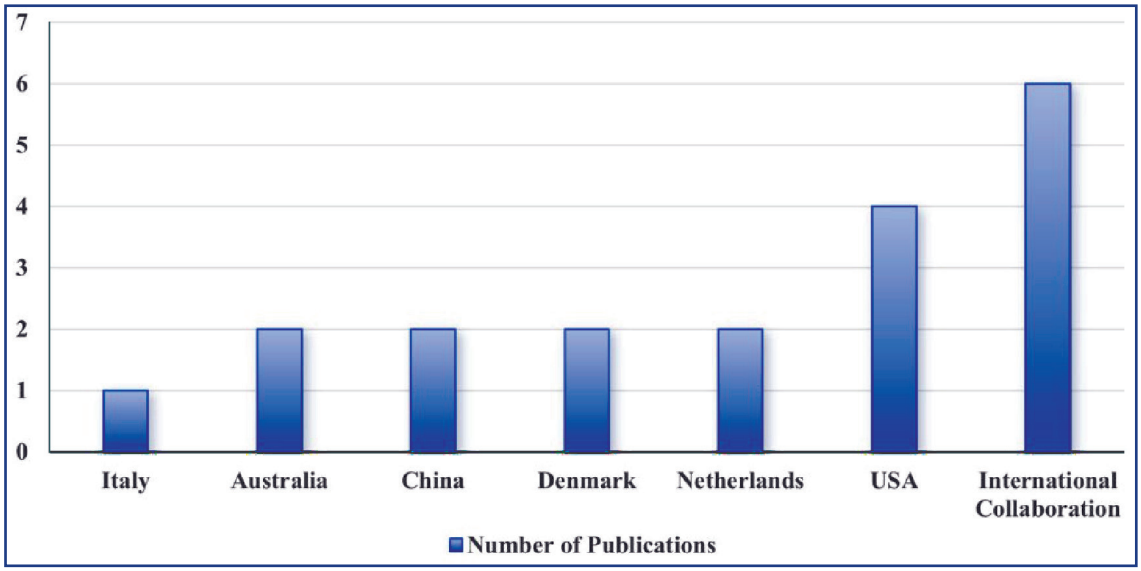

Figure 3 – Distribution of cited publications by country/international collaboration

1.3. Distribution of Research Themes

As depicted in Figure 4, the literature reviewed comprises diverse research topics about HER2 testing in breast cancer. The three areas addressed most frequently were interobserver agreement and reproducibility, HER2-low subtyping and management, and the utilization of artificial intelligence and digital pathology, with 21% of the literature comprising each area (n=4 per category).

In total, 16% of studies (n=3) explored molecular diagnostics and proficiency testing on the following components: fluorescence in situ hybridization (FISH) confirmation in IHC 2+ cases, inter-laboratory reproducibility of mRNA detection assays, and an increased need to establish concordance between IHC and molecular-level assays in borderline cases. Two studies (11%) focused on quality assurance and EQA systems, including themes such as EQA program design, pathologists' interpretive performance, and laboratory compliance analysis. These findings indicate an actionable pathway towards standardization of HER2 testing workflows and ultimately improving diagnostic quality overall.

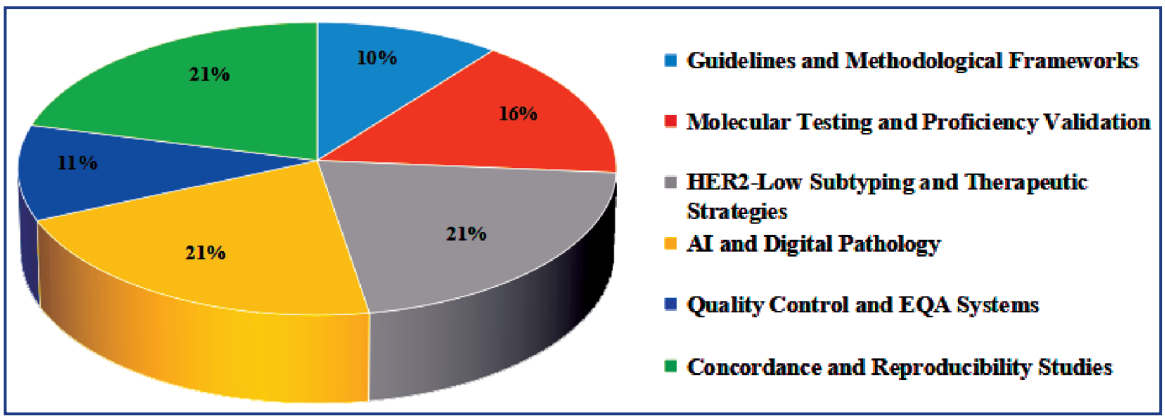

Figure 4 – Research focus distribution in HER2 IHC EQA studies

In conclusion, the diversity found in Figure 4 indicates the obstacles and challenges faced when performing HER2 testing in an HER2-low setting. Even though targeted therapeutic options continue to be developed, limitations in clinically applying HER2-low as a biomarker arise due to consistent scoring concordance, reproducibility of the assay, and variability of methods. As a result, enhancing the precision and reliability of IHC-scored will continue to be an important area of focus and direction in active HER2 research.

1.4. HER2 IHC testing scoring concordance

Due to more individualized treatment of breast cancer, there has been increasing scrutiny on the issue of concordance in HER2 IHC scoring, especially for classification and treatment decisions around the "HER2-low" subtype. HER2-low tumors are primarily defined as those with an IHC score of 1+ or 2+ and a negative FISH result and may now benefit from targeted therapies such as trastuzumab deruxtecan (T-DXd). However, substantial inter-laboratory and inter-observer variability, particularly in distinguishing IHC 0 from 1+, remains a major challenge to accurate patient stratification.

Multiple multicenter scoring studies have supported this trend. In a study of 18 breast pathology experts conducted in the United States by Robbins et al., the overall concordance rate for HER2 IHC 0 was only 25%. The concordance for 1+ and 2+ was similarly low, with a Fleiss' κ coefficient of only 0.49, indicating poor reliability of the current scoring system for interpreting HER2-low cases [5]. This conclusion was further supported by a consensus study conducted in the United Kingdom and Ireland. In this study, 16 experienced pathologists independently reviewed 50 digitized HER2 IHC slides. The participants agreed upon only about 6% of the evaluated cases. Notably, overall agreement increased to 86% when scores were dichotomized into 0 versus non-0, suggesting that score aggregation strategies may help reduce inter-observer variability [6].

Simultaneously, data from the real world also demonstrated variability in HER2 scoring at the laboratory level. A population-based cohort study using a national registry in Denmark with 50,714 breast cancer cases showed differences of 25.5 percentage points in the classification of HER2-low tumors by laboratory. The testing laboratory was identified as an independent variable associated with HER2 0 versus HER2-low from the multivariate regression, providing evidence that there was still low laboratory concordance with HER2 0 and HER2-low concordance even under standardized testing conditions [2].

The National Cancer Center of China has embarked on a proficiency testing (PT) program designed in practice to assess the consistency of HER2 scoring in three categories: 0, 1+, and 2+ (FISH-negative). The concordance rate for HER2 0 was 78.1%, while for HER2 2+, some institutions scored less than 59%, demonstrating systematic biases in scoring. The PT program, conducted using ISO/IEC 17043 quality criteria, exemplifies the variation in scoring methods and the importance of training and subsequent feedback in scoring concordance [7].

By contrast, an Australian study offers an encouraging example of improving interpretive concordance. The research group implemented a HER2-low-specific scoring protocol, which was validated based on two scoring rounds against a cohort of 64 HER2-negative breast cancer samples. Their results included a reported accuracy rate of 89.58% and Cohen's κ coefficient of 0.81, denoting "excellent agreement." This study provides all-important evidence that targeted training and scoring workflow optimization can improve reproducibility regarding the interpretation of HER2-low [8].

Comprehensive descriptions of the previous studies are provided in Table 1. The table represents a summary of the HER2 scoring studies, methodological characteristics of the studies, and scoring concordance results. As well as different dimensions of evidence to support scoring consistency and quality control in HER2 immunohistochemistry.

Table 1 – Overview of concordance studies in HER2 IHC testing for breast cancer

Study / Project	Study Type	Sample Size	Key Findings
Robbins et al. (USA)	Multi-institutional scoring concordance study	170 biopsy specimens	Overall concordance for HER2 0 was only 25%; low agreement for 1+ and 2+; Fleiss' κ=0.49
Zaakouk et al. (UK/ Ireland)	Expert consensus scoring study	50 digital slides	Absolute concordance was achieved in only 6% of cases and increased to 86% when grouped as 0 vs. non-0
Nielsen et al. (Denmark)	Nationwide registry study	50,714 breast cancer cases	The proportion of HER2-low cases ranged from 46.3% to 71.8% across different pathology departments (P<0.0001, relative difference 0.55); the pathology department was a significant independent factor influencing HER2 scoring (P<0.0001).
Xue et al. (China)	National proficiency testing program	HER2 slides from 173 institutions	Concordance for HER2 0 was 78.1%; some labs showed <59% accuracy for 2+ scoring
Farshid et al. (Australia)	HER2-low focused scoring system validation	64 HER2-negative breast cancer cases	Achieved 89.58% mean accuracy for HER2-low vs non-low classification; Cohen's κ=0.81, indicating excellent interobserver concordance

In summary, the interpretation of HER2 IHC scores within the HER2-low range, specifically 0 to 1+, continues to be a real challenge that has shown considerable variability across countries, laboratories, and observers. Improving agreement on the score will require establishing a standardized assessment system using HER2-low as a case example, internationally harmonized interpretive frameworks, and implementation of digital pathology, external proficiency testing programs, and artificial intelligence-assisted tools. Several approaches shall be applied simultaneously to improve the reliability, standardization, and clinical utility of HER2-low breast cancer classification.

2. Quality Assessment Programs for Immunohistochemistry Testing in Breast Cancer

As precision medicine continues to advance and breast cancer treatments become more individualized, the accuracy and reproducibility of HER2 testing have become increasingly critical. Standardized EQA systems are essential to ensure diagnostic reliability and support clin-

ical decision-making. Growing concern about inter-laboratory variability in testing has prompted international organizations to actively promote the quality of HER2 testing through EQA initiatives. Table 2 summarizes key global EQA providers and their specific focus in assessing the quality of HER2 testing.

Table 2 – The functions of global EQA organizations in quality assessment of HER2 IHC testing

EQA Organization	Description
College of American Pathologists (CAP) [9]	CAP is the number one major proficiency testing body and laboratory accreditation agency in the U.S. Its Immunohistochemistry Proficiency Testing Program (CAP IHC PT) is a proficiency test that tests for necessary breast cancer biomarkers such as HER2, ER, and PR to enhance inter-laboratory agreement and analytical accuracy.
Nordic Immunohistochemical Quality Control (NordiQC) [10]	NordiQC offers EQA programs for several predictive biomarkers (HER2, ER, PR, and Ki-67). It evaluates staining outcomes and concordance, providing technical evaluation to standardize and enhance diagnostic precision.
UK National External Quality Assessment Service for Immunocytochemistry (UK NEQAS ICC) [11]	UK NEQAS ICC provides EQA schemes for IHC and ISH, emphasizing the inter-laboratory achievability of consensus in HER2 biomarker analysis, achieved through standardized scoring and feedback.

Notes: CAP=College of American Pathologists; NordiQC=Nordic Immunohistochemical Quality Control; UK NEQAS ICC= UK National External Quality Assessment Service for Immunocytochemistry.

These initiatives have significantly contributed to the global standardization of HER2 IHC testing and the reduction of inter-laboratory variability, thereby improving diagnostic accuracy and reinforcing the reliability of treatment decisions in breast cancer care. As a whole, EQA organizations have become essential features of HER2 testing quality assurance.

Multiple reputable global guidelines in HER2 IHC testing for breast cancer have created organized frameworks for testing, validation, and quality assurance (Table 3). Specifically, the joint guidelines from the American Society of Clinical Oncology (ASCO) and College of CAP from 2007, 2013, 2018, and 2023 established standardized interpretation criteria for HER2 IHC and in situ hybridization (ISH) assays. These guidelines utilize evidence-based recommendations to guide testing methodology, scoring, and interpretations [1, 12].

Furthermore, the International Organization for Standardization (ISO) 15189:2022 specifies the requirements for a quality management system and technical competency for medical laboratories established by the ISO and provides a fundamental basis for their validity, reliability, and comparability of test results [13]. A complete revision of earlier versions has made ISO 17043:2023 a pillar for the organization's standardization, implementation, and evaluation of proficiency testing schemes. It sets sounder technical requirements and procedures for risk management, statistical data analysis, and results reporting for EQA programs to ensure their scientific soundness, impartiality, transparency, and practicality [14]. Together, these standards and guidelines provide an internationally accepted framework for quality control for HER2 assays in breast cancer biology, giving standardized referential and institutional acceptances for laboratory quality control.

Table 3 – International Guidelines and Standards for Quality Assurance of HER2 IHC Testing in Breast Cancer

Program	Description
ASCO/CAP HER2 Testing Guideline [12]	Developed by ASCO and CAP. This guideline identifies HER2 IHC and ISH testing and interpretation standards, scoring systems, and laboratory accreditation requirements. It is the world's most authoritative guideline for HER2 testing.
ISO 15189:2022	Developed by the ISO, this standard provides requirements for the quality and competence of medical labs. It is relevant to laboratories doing HER2 testing for reliability and quality control.
ISO 17043:2023	ISO also released this standard, which describes the general requirements for proficiency testing providers. It sets standards for the development, implementation, and evaluation of the outcome of EQA programs, maintaining scientific validity, fairness, and transparency in the process.

Notes: ASCO/CAP = American Society of Clinical Oncology / College of American Pathologists; ISO=International Organization for Standardization

In conclusion, internationally recognized guidelines and standards provide the technical support and evaluation criteria for HER2 testing. EQA systems support ongoing improvements in quality through localized operationalization. These guidelines, standards, and EQA systems establish the foundation for quality assurance in HER2 testing for breast cancer as part of the precision medicine paradigm.

3. The challenges of external quality assurance for breast cancer testing with immunohistochemistry

Despite the presence of relatively well-established EQA systems to support HER2 IHC testing, an issue remains with inter-laboratory variability, driven by different technical issues and subjective interpretative factors involved at every stage of the testing process. Laboratory-based variability in interpreting HER2 IHC testing is a significant problem, and a variety of pre-analytical and analytical factors, including inconsistent tissue processing, variability from staining platforms, antibody sensitivity, antibody clone selection, non-specific background staining, variations in protocols, and subjective interpretation influences this variability. Addressing the contribution of these issues to variability is fundamental to improving the accuracy and reproducibility of HER2 testing.

Table 4 provides key procedural steps and recommendations for HER2 IHC testing in the pre-analytical, analytical, and post-analytical settings to aid this targeted intervention framework. Each of these procedural steps aims to help optimize and standardize aspects of laboratory quality control.

Studies have underscored considerable inter-platform variability concerning staining intensity and staining reproducibility when assessing the efficacy of various automated IHC staining platforms for HER2 assessment. Jiang et al. established that the combined use of standardized cell lines and algorithm-based real-time monitoring can

detect the relative level of staining variability attributed to the instrument and counterbalance for potential slot position effects. This methodology supports routinized evaluation and maintenance, which ultimately enhances the consistency and reliability of staining [15]. In addition, different staining protocols (NordiQC, Protocol 1, and Protocol 2) influence HER2 IHC results, especially when examining HER2-low cases. In particular, great differences were observed in the NordiQC compared to the other staining protocols, emphasizing the importance of standardizing staining protocols in limiting pre-analytical variables among laboratories [16].

Table 4 – Crucial processing steps and best practice recommendations for each phase of HER2 IHC testing [1, 12]

Phase	Critical Steps	Recommendations
Pre-analytical	Biopsy/Surgical Excision, Tissue Fixation, Processing, Paraffin Embedding, Sectioning	Cold ischemic time should be less than 1 hour. Transporting at a controlled temperature is advised. To ensure antigenicity, tissue samples should be fixed in 10 % (neutral buffered formalin) for 6-72 hours. Laboratories should make use of internal quality control and EQA programs. Paraffin sections should not be greater than 5 μm thick, and sections stored longer than 6 weeks should be avoided to avoid antigen degradation.
Analytical	Antibody Selection, Staining Platform, Antigen Retrieval, Tissue Controls, Interpretation, Recognition of Aberrant Expression and Unusual Staining Patterns	Apply FDA-approved IHC antibody clones, PATHWAY anti-HER-2 /neu (4B5), or HercepTest pharmDx. Use validated automated staining platforms such as Ventana BenchMark and Dako Omnis. Apply standardized protocols of antigen retrieval. Every staining run must include adequate low-level and high-level positive and negative controls. ASCO/CAP criteria must be referred to, especially when dividing IHC scores 0 vs. 1+. Pay particular attention to the staining heterogeneity and aberrant patterns that need re-evaluation.
Post-analytical	SOP Adherence, Pathologist Training, Report Annotation (e.g., IHC 0 vs. 1+ distinction), Reference Materials for Varying HER2 Expression Levels	All HER2 testing procedures have to conform to institutional SOPs. The continuous training of pathologists and credentialing should be sustained. IHC results and interpretation notes should be kept in the patient's clinical record. Reports should specify the differences between the weak IHC 0 and the weak plus (IHC +) cases, including HER2-negative (the IHC 0, 1+, and equivocal 2+/ISH−). The verification of detection sensitivity should involve reference materials for 1+ expression.

The choice of antibody clones and their compatibility with staining platforms is an important factor influencing the correct identification of HER2-low expression. In a comparison study, Hempenius et al. found that the 4B5 antibody had a higher agreement and lower background staining in samples in the HER2-low category when used with the OptiView detection system; therefore, this approach should be considered a better option for detecting this expression category [17]. These observations continue to highlight the importance of optimized matching of antibody clones and staining platforms in improving the accuracy of HER2-low detection and inter-laboratory reproducibility of HER2 IHC testing.

Furthermore, Fernandez et al., leveraging data from the CAP proficiency testing program and a multi-institutional scoring dataset provided by Yale, observed low concordance in HER2 IHC scoring (0 and 1+) at only 26%, compared to a higher concordance of 58% in 3+ cases [18]. These results illustrate greater subjectivity and less reproducibility in the HER2-low scoring range, warranting improved and standardized interpretive guidelines and targeted training in that interval that creates diagnostic ambiguity for more consistent diagnostics.

In conclusion, there continues to be meaningful inter-laboratory variability for HER2 IHC testing regarding the interpretation of staining, antibody choice, and execution of protocols, which can be a significant barrier to diagnostic accuracy. Incorporating digital pathology and enhanced laboratory accreditation may represent meaningful deliveries toward the standardization of testing pathways. The prospect of artificial intelligence (AI)-based automated scoring systems represents a significant pathway to deliver the quality of HER2 assessment as an essential of precision oncology.

Discussion: With the advancement of precision medicine, the drawbacks of traditional single-modality HER2 testing, that is, its ability to accurately diagnose and reproducibly detect HER2 status, have garnered increasing interest in the subtype of breast cancer setting. In response to a growing interest in providing more reliable diagnosis, recently, there has been a transition toward a more integrated approach, in which digital technologies, artificial intelligence, and multi-omics are increasingly incorporated into testing [19, 20].

Utilizing AI and digital image analysis (DIA) within the HER2 testing workflow mitigates many intrinsic limitations of conventional manual test scoring. An AI-based scoring system will be trained on large datasets of well-annotated histopathological images. The system can quantitatively measure both membrane staining intensity and the proportion of tumor cells that exhibit positive staining. The AI systems have a particular advantage in resolving interpretative issues in the HER2 0 vs 1+ scoring range. Several studies demonstrated the clinical value of these tools. Sode et al. demonstrated that DIA improved interpretative concordance in HER2-low cases, especially in interpreting IHC 0 vs. 1+, which often has high uncertainty [21]. Likewise, Glass et al. constructed a quality control tool using machine learning that identified inter-laboratory differences in scoring HER2. The tool improved HER2 assessment reproducibility and diagnostic accuracy, even when assessing sub-category classifications such as <2+, 2+, and 3+ cross-laboratory [22].

Currently, complementary molecular assays have become valuable options to enhance the accuracy of determining HER2 status in equivocal or inconsistent results with IHC or FISH. For example, reverse transcription-quantitative polymerase chain reaction (RT-qPCR) allows for accurate quantification of HER2 mRNA expression and shows promise as a complementary tool in intermediate or otherwise uncertain cases. HER2 mRNA levels evaluated by RT-qPCR were almost perfectly concordant with the results of IHC in the study by Caselli et al. [23]. This suggests that RT-qPCR represents a viable test for confirming HER2 status, specifically in cases with intermediate results with IHC.

At the same time, the EQA framework for assessing HER2 testing is also at a tipping point of improvement. Most EQA programs historically have been based on cases with well-defined HER2-positive or HER2-negative testing [24]. More recently, studies have recommended that EQA programs begin to include cases scored as 0, 1+, and 2+ with defined interpretation criteria, specifically with borderline cases. Also, new techniques, including AI-assisted interpretation and mRNA-based assays, should have incremental inclusion into the EQA structure to help pave the way for a multimodal quality assessment system for testing HER2 (i.e., for genomic, transcriptomic, and proteomic quality assessments). For example, the EQA structure that Badrick et al. suggested includes how molecular diagnostics fit into pathology quality assurance and outlines a pathway to develop quality HER2-low testing standards [20].

Global standardization of HER2 testing will require coordinated collaboration at an international level. Significant variances exist across and within countries in HER2 testing guidelines, antibody clone selection); scoring criteria, and implementation of EQA programs [25]. Developing a comprehensive global standardized HER2 testing framework allows for the comparability of results across diagnostic platforms and the recognizability of data amongst laboratories. Such a framework would be increasingly important in reducing diagnostic variances from regional practices. Creating this comprehensive framework would improve diagnostic accuracy and patient accessibility for receiving appropriate treatment for breast cancer across the globe.

In conclusion, the assessment of HER2 IHC quality is moving from subjective, single-method, and experience-based approaches to objective, integrated, and evidence-based assessments. Integrating digital pathology, laboratory accreditation, and AI-based automated scoring represents new standardization approaches to HER2 testing within a move to precision oncology.

Conclusion: EQA has become a critical quality assurance component in HER2 testing and is developing into an internationally recognized framework. Beyond evaluating test results, it provides critical feedback on staining, interpretation, and workflow, enhancing inter-laboratory consistency. The classification of HER2-low introduces new demands, requiring alignment with updated guidelines.

As international collaboration increases, laboratory participation in EQA programs will encourage us to establish a uniform and highly comparable quality assurance framework for immunohistochemical testing; we will be able to provide the most reliable and reproducible diagnostic pathology support for patients with breast cancer.

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АҢДАТПА

СҮТ БЕЗІ ОБЫРЫ КЕЗІНДЕ ИММУНОГИСТОХИМИЯЛЫҚ ЗЕРТТЕУЛЕРДІҢ САПАСЫН ҚАМТАМАСЫЗ ЕТУ СТРАТЕГИЯЛАРЫН БАҒАЛАУ: ӘДЕБИЕТКЕ ШОЛУ

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Өзектілігі: *Сапаның сыртқы бақылау бағдарламалары (EQA) иммуногистохимиялық (ИГХ) тесттер мен диагностикалық зерттеулерді орындау кезінде нақты және сенімді нәтижелерге қол жеткізу үшін әдістемемен қатар қолданылуы тиіс. Ісік биомаркерлерін анықтау дәлдігін қамтамасыз ету дәл медицинада өте маңызды, өйткені онкологияда жекелендірілген емдеу әдістері кеңінен қолданыла бастады.*

Зерттеу мақсаты *– сапаның сыртқы бағалау бағдарламаларының сүт безі обыры кезінде адам эпидермалдық өсу факторының 2-типті рецепторын (HER2) анықтауға арналған иммуногистохимиялық (ИГХ) тестілеудегі зертханалар арасындағы айырмашылықтар мен интерпретациялық өзгергіштікті төмендетудегі рөлін жүйелі түрде шолу, сондай-ақ қазіргі қиындықтар мен болашақ даму бағыттарын анықтау.*

Әдістері: *Бұл зерттеу аясында жүргізілген жүйелі әдебиеттерді шолу барысында 306 жарияланым анықталып, оның ішінде 25 толық мәтінді мақала соңғы талдауға енгізілді. Шолу жүйелі шолулар мен метаанализдерге арналған PRISMA 2020 нұсқаулығына сәйкес жүргізілді.*

Нәтижелері: *Соңғы зерттеулер сапаның сыртқы бағалау бағдарламалары HER2 ИГХ тестілеуінің дәлдігі мен сәйкестігін әртүрлі зертханаларда айтарлықтай жақсартатынын көрсетіп отыр. Ғаламдық стандарттар HER2 тестілеуінің барлық кезеңдерінде стандартталған, сенімді және үйлесімді процедураларды қамтамасыз етеді. Сонымен қатар, цифрлық патология, алгоритмдер және мРНҚ (мессенджер РНҚ) негізіндегі тесттер сияқты жаңа әдістер нәтижелердің бірізділігін арттырып, қолмен жүргізілетін сараптамаларда қателіктерді азайтуға зор мүмкіндік береді.*

Қорытынды: *Сапаның сыртқы бақылау бағдарламаларын енгізу HER2 ИГХ нәтижелерінің әртүрлі зертханалар арасындағы айырмашылықтарын азайтты. HER2-low санаттамасының енгізілуімен тестілеу әдістері субъективті тәсілдерден деректердің әртүрлі түрлерін қолдануға қарай ауысып жатыр, бұл дәрігерлер үшін тесттің клиникалық маңызын арттырады. Сапаның сыртқы бақылау бағдарламаларына қатысу HER2 рецепторларын тестілеу тиімділігін арттырып, әлемнің әртүрлі бөліктерінде бірдей нәтижелер алуға мүмкіндік береді. Сарапшылар тобының болуы сүт безі обырын диагностикалау мен нәтижелердің қайталануын жақсартады.*

Түйінді сөздер: *иммуногистохимия, сыртқы сапаны бағалау (EQA), сүт безі обыры, HER2, сапаны бақылау (QC).*

АННОТАЦИЯ

ОЦЕНКА СТРАТЕГИЙ ОБЕСПЕЧЕНИЯ КАЧЕСТВА ИММУНОГИСТОХИМИЧЕСКОГО ТЕСТИРОВАНИЯ ПРИ РАКЕ МОЛОЧНОЙ ЖЕЛЕЗЫ: ОБЗОР ЛИТЕРАТУРЫ

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Актуальность: *При проведении иммуногистохимических (ИГХ) тестов и диагностических исследований для достижения точных и надёжных результатов помимо методики проведения исследований следует также применять программы внешнего контроля*

качества (EQA). Обеспечение точности тестов на опухолевые биомаркеры имеет критически важное значение в прецизионной медицине, поскольку индивидуализированные схемы лечения стали обычной практикой в онкологии.

***Цель исследования** – провести систематический обзор данных, касающихся роли внешней оценки качества в снижении межлабораторных расхождений и вариабельности интерпретации при иммуногистохимическом определении рецептора эпидермального фактора роста человека 2-го типа (HER2) при раке молочной железы, а также выявить текущие проблемы и возможные направления развития.*

***Методы:** Систематический обзор литературы в рамках данного исследования выявил 306 публикаций, из которых 25 полнотекстовых статей были включены в окончательный анализ. Обзор проводился в соответствии с руководством по предпочтительным элементам отчётности для систематических обзоров и метаанализов (PRISMA 2020)*

***Результаты:** Последние исследования показывают, что программы внешней оценки качества значительно повышают согласованность и точность ИГХ-тестирования HER2, проводимого в различных лабораториях. Глобальные стандарты обеспечивают стандартизированные, надёжные и последовательные процедуры тестирования HER2 на всех этапах. Кроме того, новые подходы, такие как цифровая патология, алгоритмы и тесты на основе мРНК (мессенджер РНК), обладают большим потенциалом для повышения согласованности результатов и снижения ошибок при ручной интерпретации.*

***Заключение:** Внедрение программ внешнего контроля качества позволило снизить расхождение результатов HER2 ИГХ между различными лабораториями. С введением классификации HER2-low методы тестирования переходят от субъективных подходов к использованию различных видов данных, что повышает клиническую значимость теста для врачей. Участие в программах внешнего контроля качества повышает эффективность тестирования рецепторов HER2, обеспечивая воспроизводимые результаты в разных частях мира. Наличие команды экспертов улучшает точность диагностики и повторяемость результатов при раке молочной железы.*

***Ключевые слова:** иммуногистохимия, внешняя оценка качества (EQA), рак молочной железы, HER2, контроль качества (QC).*

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