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Liquid-based cytology in cervical cancer screening: A systematic review and meta-analysis

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Corresponding author:
Tobias Vogelmann

tv@link-care.de

Author Affiliation:
LinkCare GmbH.

Böhmer, G; Stolte, C; Vogelmann, T; Schubert, T; Ikenberg, H.

ADMINISTRATIVE INFORMATION

Support - Hologic.

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - Gerd Böhmer received honoraria from Hologic and Roche. Claudia Stolte received honoraria from Hologic. Tobias Vogelmann and Tino Schubert are oweners and employees of LinkCare, which received Honoria from Hologic and BD. Hans Ikenberg has received contributions for speaking engagements and travels as well as support for research projects from BD, Hologic, Otto Bock, Qiagen and Roche Diagnostics.

INPLASY registration number: INPLASY202560028

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 7 June 2025 and was last updated on 7 June 2025.

INTRODUCTION

Review question / Objective The objective of this systematic review and meta-analysis was to systematically assess the diagnostic accuracy of LBC compared to conventional Pap cytology in the detection of cervical precancerous and cancerous lesions.A systematic literature search was conducted in PubMed and the Cochrane Library. Comparative studies assessing LBC and conventional Pap cytology in primary CC screening were included. Outcomes included unsatisfactory sample rate, abnormal histology-confirmed cytology detection rate (ADR) CIN2+ lesions (cervical intraepithelial neoplasia), SCC (squamous cell carcinoma), and glandular abnormalities. Random-effects models were used to estimate risk ratios (RR). A two sided p-value of 0.05 was used to determine statistical significance.

Rationale Despite these technological improvements, there is ongoing debate regarding the comparative diagnostic accuracy of LBC versus conventional Pap cytology. Some studies suggest that LBC may be superior in detecting cervical precancerous and cancerous lesions, while others report comparable or even lower performance than the traditional method. Furthermore, differences in study design, population characteristics, and cytological interpretation criteria have contributed to variability in reported outcomes. These inconsistencies highlight the need for a rigorous, evidence-based evaluation of the relative diagnostic accuracy of LBC and Pap testing.

Condition being studied Cervical cancer.

METHODS

Search strategy ("cervix"[All Fields] OR "cervical"[All Fields] OR "cin"[All Fields]) OR Cervix Uteri [MESH] OR Vaginal Smears [MESH]
("monolayer"[All Fields] OR "thin layer"[All Fields] OR "liquid-based"[All Fields] OR "Thin-Prep"[All Fields] OR "Thinprep"[All Fields] OR "CytoRich"[All Fields] OR Cyto-Rich [All Fields] OR "Autocyte"[All Fields] OR "SurePath"[All Fields] OR "PreservCyt"[All Fields]) AND
("conventional"[All Fields] OR "conventionals"[All Fields] OR "smear"[All Fields] OR "smear s"[All Fields] OR "smears"[All Fields] OR "PAP"[All Fields]) OR Vaginal Smears [MESH] AND
((("diagnosis"[MeSH Terms] OR "diagnosis"[All Fields] OR "diagnostic"[All Fields] OR "diagnostics"[All Fields]) AND ("management"[All Fields] OR "organization and administration"[MeSH Terms] OR "disease management"[MeSH Terms] OR "performance"[All Fields] OR "accuracy"[All Fields] OR "yield"[All Fields])) OR ("sensitivity and specificity"[MeSH Terms] OR "sensitivity"[All Fields] OR "specificity"[All Fields]) OR ("true positive"[All Fields] OR "true negative"[All Fields] OR "false positive"[All Fields] OR "false negative"[All Fields]) OR ("positive predictive value"[All Fields] OR "negative predictive value"[All Fields]) OR ("area under curve"[MeSH Terms] OR "AUC"[All Fields]) OR "ROC"[All Fields] OR concordance [All Fields] OR satisfactory [All Fields] OR unsatisfactory [All Fields] OR adequacy [All Fields] OR adequate [All Fields] OR inadequate [All Fields] OR
("mortality"[MeSH Terms] OR "mortality"[All Fields] OR "mortalities"[All Fields] OR "mortality"[MeSH Subheading] OR ("death"[MeSH Terms] OR "death"[All Fields] OR "died"[All Fields]) OR ("death"[MeSH Terms] OR "death"[All Fields] OR "dead"[All Fields]) OR ("death"[MeSH Terms] OR "death"[All Fields] OR "deceased"[All Fields] OR "deceased s"[All Fields]) OR ("epidemiology"[MeSH Subheading] OR "epidemiology"[All Fields] OR "morbidity"[All Fields] OR "morbidity"[MeSH Terms] OR "morbid"[All Fields] OR "morbidities"[All Fields] OR "morbids"[All Fields]) OR ("quality of life"[MeSH Terms] OR ("quality"[All Fields] AND "life"[All Fields]) OR "quality of life"[All Fields]) OR "QoL"[All Fields] OR ("hrqols"[All Fields] OR "quality of life"[MeSH Terms] OR ("quality"[All Fields] AND "life"[All Fields]) OR "quality of life"[All Fields] OR "hrqol"[All Fields])).

Participant or population Women in primary cervical carcinoma screening (no restriction regarding age or country).

Intervention Thin layer cytology (no restrictions regarding manufacturer).

Comparator Conventional cytology (smear test, PAP).

Study designs to be included Comparative studies (randomised/non-randomised, prospective and retrospective).

Eligibility criteria n/a.

Information sources PubMed, Cochrance Library.

Main outcome(s) Unsatisfactory sample rate, abnormal histology-confirmed cytology detection rate (ADR) CIN2+ lesions (cervical intraepithelial neoplasia), SCC (squamous cell carcinoma), and glandular abnormalities.

Additional outcome(s) n/a.

Data management A standardized data extraction form was used to collect information on study characteristics, population details, diagnostic methods, outcome measures, and key results. The extracted data were cross-checked for accuracy and consistency.

Quality assessment / Risk of bias analysis The Risk of Bias (RoB) and applicability was evaluated by two reviewers independently using the Quality Assessment of Diagnostic Accuracy Studies (QUADAS)-2 too.

Strategy of data synthesis Meta-analyses were performed to estimate pooled measures of the outcomes.
Heterogeneity across studies was assessed using the I^2 statistic, which quantifies the proportion of variability due to true differences rather than chance. An I^2 value above 50% was considered indicative of substantial heterogeneity, and values above 75% were classified as high heterogeneity. When substantial heterogeneity was observed, random effect models were used to calculate pooled effects, otherwise, a fixed effect model was used.

Subgroup analysis Subgroup analyses were conducted to evaluate variations in diagnostic performance based on cytology classification thresholds (e.g., ASCUS+, LSIL+, HSIL+),). These subgroup analyses were pre-specified in the study protocol, except for additional exploratory analyses performed post hoc to investigate specific discrepancies in results.

Subgroup analyses were conducted specifically for FDA-approved liquid-based cytology tests, including ThinPrep® (Hologic, Inc.) and BD SurePath™ (Becton, Dickinson and Company), to evaluate potential variations in diagnostic performance. These subgroup analyses focused solely on manufacturer-specific comparisons and were pre-specified in the study protocol.

Sensitivity analysis n/a.

Language restriction English, German.

Country(ies) involved Germany.

Other relevant information n/a.

Keywords Cervical cancer; liquid-based cytology; Pap smear; abnormal histology; CIN2+; SCC; glandular abnormalities; meta-analysis.

Contributions of each author

Author 1 - Gerd Böhmer - Gerd Boehmer interpretated the data and corrected the draft and final manuscript.
Email: boehmer@izd-hannover.de
Author 2 - Claudia Stolte - Claudia Stolte interpretated the data and corrected the draft and final manuscript.
Email: stolte@izd-hannover.de
Author 3 - Tobias Vogelmann - Tobias Vogelmann performed the meta analysis and drafted the manuscript.
Email: tv@link-care.de
Author 4 - Tino Schubert - Tino Schubert performed the meta analysis and finalized the manuscript.
Email: ts@link-care.de
Author 5 - Hans Ikenberg - Hans Ikenberg interpreted the data and corrected the manuscript.