

Are Tampons Credible Devices for Human Papillomavirus (HPV) Testing as a Means to Detect

Cervical Lesions and Cancer:

A Systematic Review & Technical Optimisation Study

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OBJECTIVE

Systematic Review

 To conduct a systematic review and meta-analysis on the technical accuracy and acceptability of self-inserted tampons to detect HPV-associated cervical disease.

Technical Optimisation Study

- To measure the liquid absorbency of tampons provided by Daye.
- To assess the level of liquid recovery from tampons using 20mL and 50mL syringes.
- To assess the feasibility and sensitivity of detecting HPV mRNA in tampons using simulated material.
- To determine the optimal pre-analytical processes for recovering HPV from tampons.

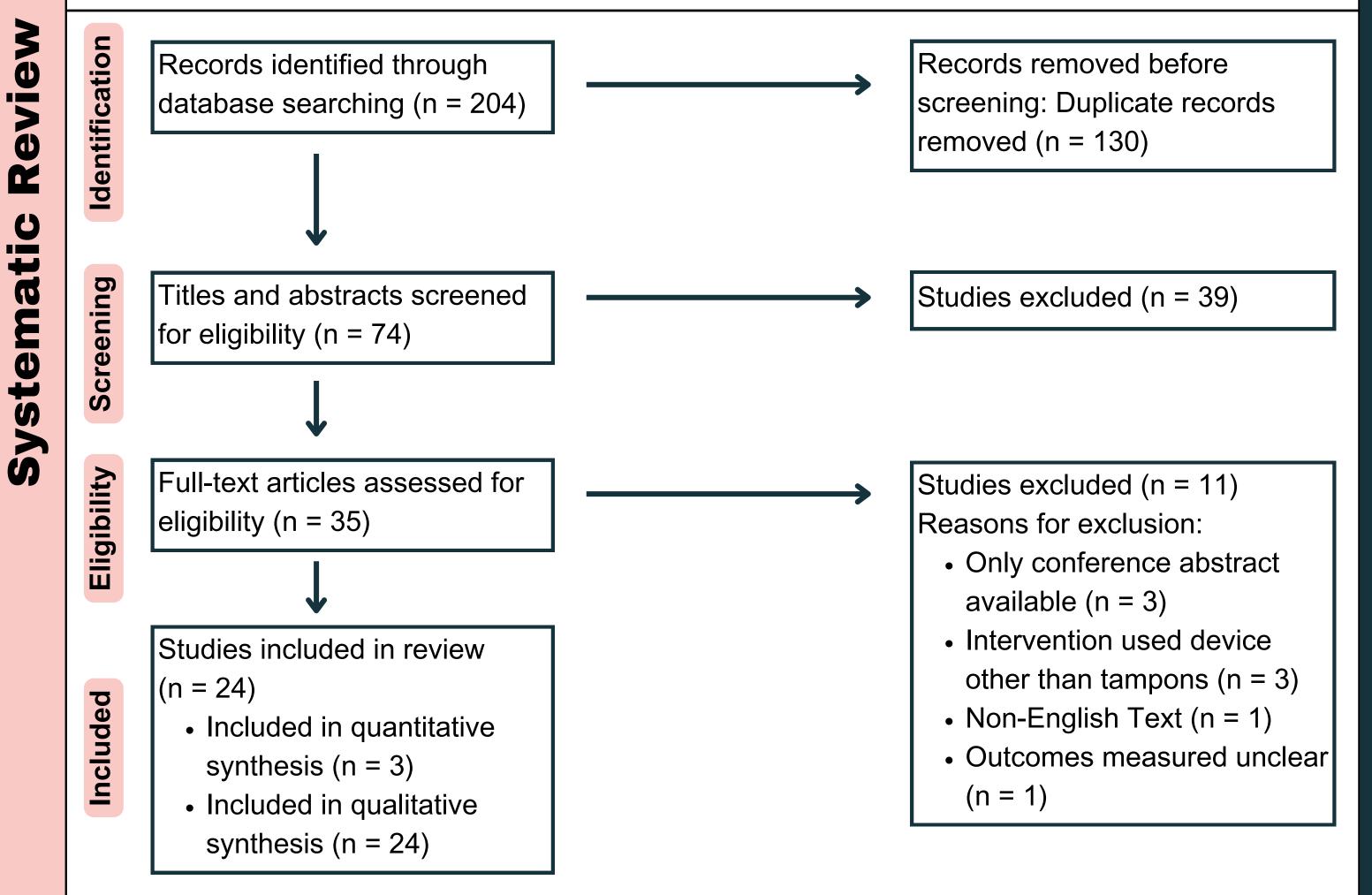
METHODOLOGY

The systematic review was underlined based on a protocol on PROSPERO.

Search and screening strategy via MeSH terms was done based on the PICOS framework using SyRf.

Key findings from screened studies were extracted and assessed for risk of bias using QUADAS-2.

Statistical analysis was completed using the Meta-DiSc software.



80% glycerol stock solution was prepared from 100% glycerol solution.

Daye tampons were inserted in 4 50mL-falcon tubes containing different volumes of 5mL, 10mL, 15mL, and 20mL of 80% glycerol solution respectively.

The tampons were incubated at room temperature for 30 minutes.

The absorbency of the tampons was measured by calculating the remaining volume left in the falcon tubes.

The steps were repeated using 20mL and 50mL syringes to extract the 80% glycerol solution from the tampons.

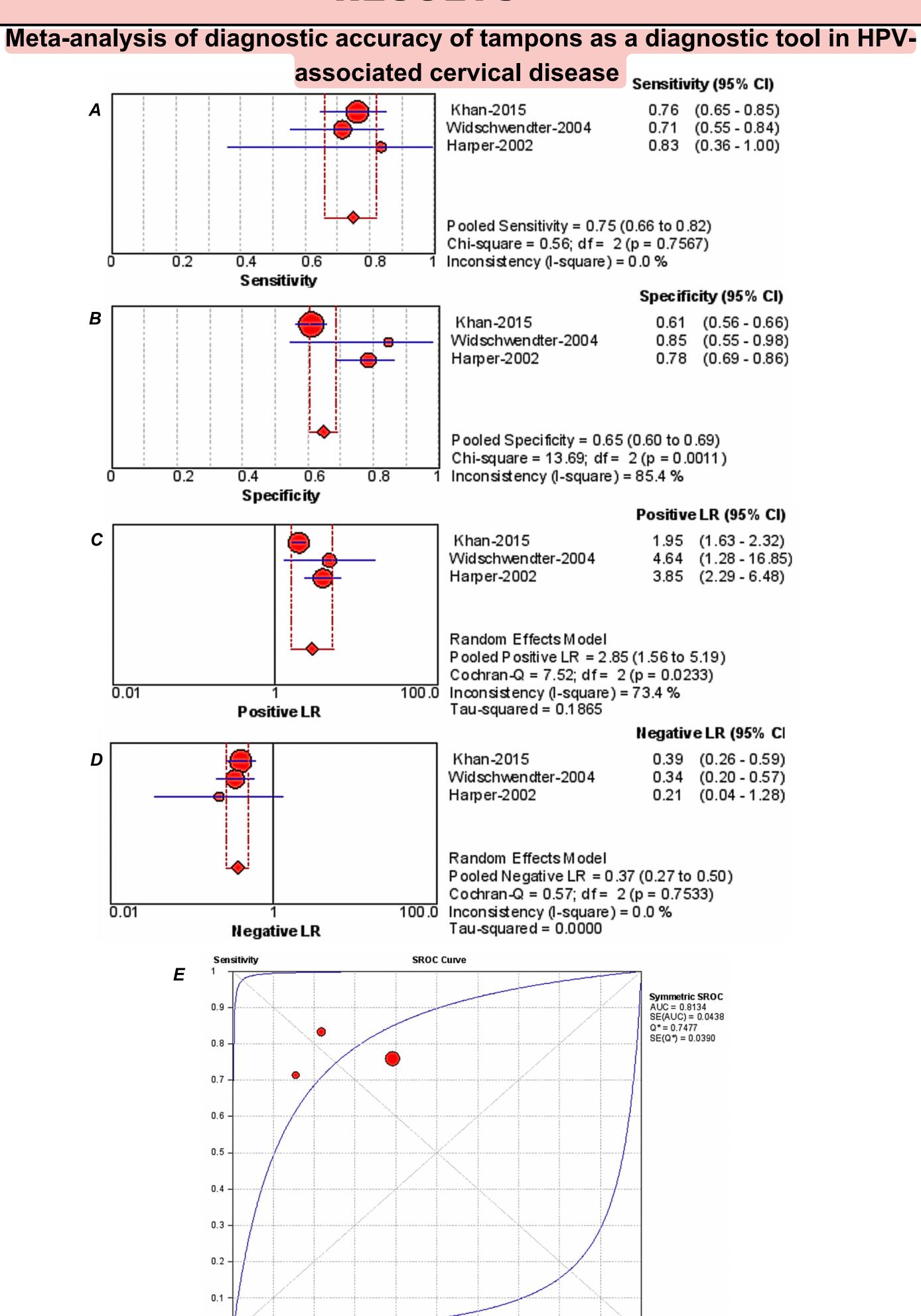
Pre-analytical Experiment to Recover HPV from Tampons 1 2 80% glycerol & SiHa cell lines 40ml (30ml 80% glycerol + 10ml distilled water) 10°(v) 10°(v) 10°(v) 10°(v) 10°(v) 10°(s) 10°(s)

The figure describes the pre-analytical processes to assess the feasibility and sensitivity of detecting HPV mRNA in tampons using simulated material.

- 1.80% glycerol solution and SiHa cell lines were prepared.
- 2. A serial dilution of glycerol and SiHa cell suspension was performed.
- 3. Daye tampons were inserted into each of the falcon tubes containing different suspension concentrations and incubated for 30 minutes. The tampons were removed and stored in specimen bags for 24 hours at room temperature.
- 4. The tampons were placed into their respective specimen pots and added PreservCyt before syringing and vortexing them.
- 5. Aliquots from each specimen pot were tested using APTIMA HPV assay.

RESULTS

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The figure illustrates the diagnostic accuracy forest plots for the studies included in the meta-analysis and used tampons as a diagnostic tool in HPV-associated cervical disease.

3 studies were pooled in a meta-analysis of the diagnostic accuracy of tampons in HPV-associated cervical diseases. **[A]** The sensitivity of the studies was 75% (95% CI: 66% - 82%). **[B]** The specificity was 65% (95% CI: 60% - 69%). **[C&D]** The random effect was used to pool positive and negative likelihood ratios and their results were 2.85 (95% CI 1.56 - 5.19) and 0.37 (95% CI 0.27 - 0.50). **[E]** The summary receiver operating characteristic (SROC) plot displays the SROC curve in blue lines along with standard error (SE). The Q* marks where the SROC curve intersects the diagonal, where sensitivity equals specificity. The red dots plotted on the sensitivity versus 1-specificity axes represent each study with the dot size indicating the study's sample size.

Daye tampons absorb approximately 5ml to 10ml of 80% glycerol solution.

A minimum volume of 15mL of 80% glycerol solution addition is required to provide a remaining yield of solution for testing after 30 minutes of incubation.

The yield of fluid captured from Daye tampons using a 20mL syringe ranges from 12% to 30% of the original volume.

An average of 10% increment in yield of the glycerol solution is obtained from tampons extraction using 50mL syringes compared to 20mL syringes.

A larger suspension yield can be extracted via syringes compared to vortexing while minimising spillage during extraction from tampons.

HPV at starting concentration(s) of 10³ copies/ml of HPV 16 are detectable on

tampons using an mRNA-based test.

The sensitivity of HPV detection on tampons at the concentrations used did

CONCLUSION

not appear affected by the pre-analytical processing step.

Systematic Review

- Tampons show promising diagnostic accuracy for HPV-related cervical disease, especially among populations with limited cervical screening access.
- There is a shortage of research on self-testing tampons in populations where cervical disease was defined by histology which warrants further investigation.

Technical Optimisation Study

- The maximum absorbance of Daye tampons is 10 ml of glycerol suspension; using a larger syringe may enhance the sample yield.
- Serially diluted samples extracted via both syringing and vortexing successfully recover HPV from tampons, indicating the sensitivity of HPV detection is not affected by the pre-analytical processes at the concentrations used.