Knowledge of cytology results affects the performance of colposcopy: a crossover study

Eva Lalande
University of Geneva

Holly Clarke (✉ hollyisabellaclarke@gmail.com)
University Hospitals of Geneva

Manuela Undurraga
University Hospitals of Geneva

Vu Quoc Huy Nguyen
Hue University of Medicine and Pharmacy

Cyril Jaksic
Geneva University Hospitals, University of Geneva

Frederic Goffin
University of Liege

Marc Arbyn
Belgian Cancer Centre

Jose Jeronimo
National Cancer Institute

Jean-Christophe Tille
Geneva University Hospitals

Essia Saiji
Geneva University Hospitals

Pierre Vassilakos
Geneva Foundation for Medical Education and Research

Patrick Petignat
University Hospitals of Geneva

Abstract

Objective – To determine whether knowledge of cytology affects the colposcopist's diagnostic accuracy in the identification of cervical intraepithelial neoplasia grade 2 and worse (≥ CIN2).

Method – In this cross-over study, healthcare professionals interpreted colposcopy images from 80 patient cases with known histological diagnoses. For each case, 2 images taken with a colposcope were provided (native and after acetic acid application). Inclusion criteria consisted of women with a transformation zone type 1 or 2, who had both a cytological and histological diagnosis. Cases were distributed across two online surveys, one including and one omitting the cytology. A wash-out period of six weeks between surveys was implemented. Colposcopists were asked to give their diagnosis for each case as < CIN2 or ≥ CIN2 on both assessments. Statistical analysis was conducted to compare the two interpretations.

Results – Knowledge of cytology significantly improved the sensitivity when interpreting colposcopic images, from 51.1% [95%CI: 39.3 to 62.8] to 63.7% [95%CI: 52.1 to 73.9] and improved the specificity from 63.5% [95%CI: 52.3 to 73.5] to 76.6% [95%CI: 67.2 to 84.0]. Sensitivity was higher by 38.6% when a high-grade cytology (ASC-H, HSIL, AGC) was communicated compared to a low-grade cytology (inflammation, ASC-US, LSIL). Specificity was higher by 31% when a low-grade cytology was communicated compared to a high-grade.

Conclusion – Our data suggests that knowledge of cytology increases sensitivity and specificity for diagnosis of ≥ CIN2 lesions at colposcopy. Association between cytology and histology may have contributed to the findings.

Introduction

Cervical cancer affects a large number of women worldwide, and represents the fourth most frequent cancer diagnosed in this population (1,2). In recent years, the incidence of cervical cancer in high-income countries has significantly declined, mainly due to effective prevention through vaccination, screening, diagnosis and treatment of pre-cancerous lesions (1). Cytological screening contributes to early diagnosis of cervical precancerous lesions. When combined with colposcopy for women with an abnormal screen, it has been shown to be an effective standard for ≥ CIN2 diagnosis (3).

The colposcopy exam includes the observation of the native cervix as well as the cervix after application of 3–5% acetic acid solution to determine the presence of acetowhite lesions. Colposcopy allows localization of the lesion(s), evaluation of the lesion(s) severity, and facilitates directed biopsy for diagnosis. Results from this exam determine whether patients require biopsy, or if they can be managed conservatively with follow-up. In countries with screening programs, gynecologists may carry out colposcopies in diverse settings such as primary care, regional and tertiary hospitals. Some perform exams sporadically whilst others see large volumes, frequently in colposcopy clinics. Therefore, there is likely to be a great variability in the experience and training of colposcopists (4). The diagnostic

performance of colposcopy depends on the experience of the observers, and their skill in recognizing the acetowhitening of the epithelium after acetic acid application (thickness, color, border irregularity). Inconsistencies in performance for colposcopy have been demonstrated in the literature (5,6) particularly for the detection of high-grade abnormalities (7). Reported sensitivity varies from 58–99% (8–13) while specificity ranges from 23–93% (8–13) depending also on the grade of the lesions. This range of values demonstrates the inherent subjectivity of this method, limited by the clinician's capacity to distinguish lesions, appreciate their characteristics (6) and differentiate precancerous from benign appearances, leading in some cases to a misdiagnosis. To overcome the weakness of colposcopy, investigators have suggested systematically performing cervical biopsy even if the cervix appears normal. One study demonstrated that the sensitivity for detecting ≥ CIN2 increased from 61% (95%CI: 55–67) in a single biopsy to 86% (95%CI: 80–90) with two biopsies and to 96% (95%CI: 91–99) with three biopsies (14).

Colposcopy is generally conducted with knowledge of the cytology results, but it is still unclear if the sensitivity and specificity of colposcopy is significantly impacted when interpreted in the presence of the cytological result. Alongside cytology, colposcopy may also be influenced by the knowledge of other results or demographic parameters such as HPV status, age or prior histopathology (15).

Our study aim was to determine whether knowledge of cytology influences the colposcopic diagnosis of ≥ CIN2 lesions.

Method

Case Selection – A total of 80 cases were collected from a cohort of women already recruited to a study entitled 'Use of a smartphone-based Artificial Intelligence classifier as an adjunct to colposcopy for identifying cervical pre-cancer and cancer: Proof of concept' (study number 2020 – 00868) Fig. 1. Patients were consented for this aforementioned study at the colposcopy clinic, gynecologic division of the University Hospital of Geneva, between June 2021 and June 2022, and all patients signed an informed consent. Inclusion criteria were women (i) aged 18–75, (ii) having a transformation zone type 1 or 2 and having (iii) a cytology result (iv) histopathology result and (v) colposcope images of sufficient quality for use. All cases addressed in our colposcopy setting that fulfilled inclusion criteria were considered in a chronological manner.

Case Interpretation – The study relied on specialists in colposcopy analyzing two images for each of the 80 cases, one native and one after acetic acid application. The interpretation was recorded in the form of a JotForm web-based survey. The same images were analyzed twice on two separate sessions with at least a six-week interval between the two sessions. In one of the sessions the images without cytology were analysed, while in another session the images were complemented by the cytological status. No other information such as HPV status or age was provided. Each participant was asked to categorize the image as "<CIN2" (< cervical intra-epithelial neoplasia grade 2) or "≥CIN 2". Overall, the study involved 40 patients with < CIN2 histopathology results, and 40 patients with ≥ CIN2 histopathology but participants were unaware of the ratio of positive and negative cases.

Colposcopists and Interpretation Rounds – A web-based Lime-survey link was distributed to multiple gynecology departments, inviting colposcopists to enroll and participate in the study. Initially, 71 participants enlisted, and ultimately, 38 of them completed both surveys and were divided into groups A and B. In keeping with the crossover design, group A received the survey without the cytology result, and then the survey with the cytology result six weeks later. Group B received the surveys in the opposite order. The participants were not aware of each other's responses. A 6-week washout period was chosen as in the literature this has been demonstrated to confer a reduced rate of residuary recall, thus minimizing risks associated with intra-observer studies (16). Empirically, multiple studies assessing whole-slide imaging (WSI) in pathology have used a minimum of 3 weeks as a washout period in their method (17,18).

Reference Standard – The histological assessment of biopsy constituted the reference standard diagnosis. Patients with a ≥ CIN2 diagnosis based on biopsy underwent confirmation of the diagnosis through cone biopsy. Colposcopy-directed biopsies from all suspicious areas on examination had been undertaken for all women with histology that was revealed to be < CIN2. <CIN2 patients also had a colposcopy follow-up visit at 6 months with cytology +/-biopsy if lesions were seen. During the colposcopy examination, native images of the cervix and images after application of acetic acid were taken. All patient data was gathered retrospectively.

Cytological and Histological Interpretation – The cytological results were classified according to the Bethesda system 2015 (19). Namely: negative for intraepithelial lesions or malignancy; atypical squamous cells of undetermined significance (ASC-US); atypical squamous cells of undetermined significance that cannot exclude high-grade squamous intraepithelial lesions (ASC-H); low-grade squamous intraepithelial lesions (LSIL); and high-grade squamous intraepithelial lesions (HSIL). Cervical biopsy specimens were interpreted using the WHO classification of Tumors 2020, which describes: low grade dysplasia (CIN1); and high-grade dysplasia including moderate (CIN2) and severe (CIN3) dysplasia (20).

Statistical Method – Sample size calculation: We expected the sensitivity of colposcopy in isolation to be around 60% to detect high grade lesions. Few articles have evaluated the sensitivity of colposcopy alone, therefore an approximate average of values mentioned in available literature on colposcopy was used (8–13). A simulation study was conducted to assess the smallest improvement in sensitivity with the cytology for which the statistical power was 90% with the above-mentioned sample size. The simulation study was generated under a two-sided risk alpha of 5% and crossed random effects (standard deviation of 0.40). Ultimately, with the planed sample size, the power is 90% or more to detect an absolute difference in sensitivity of 7% or more (60% for colposcopy in isolation versus 67% for colposcopy and cytology). The power calculation was similar for specificity.

Statistical Analyses – We used mixed effects logistic regression models with two crossed random effects on the intercept: one random effect models the between-readers variability, and one random effect models the between-cases variability. We expect that the sensitivity varied across readers but also across

cases as some cases may be more difficult to interpret than others. Statistical analyses were conducted with software R (R Core Team (2022)).

Results

Patient Characteristics – We included a total number of 80 patients who were referred to our colposcopy clinic. The principal reason for referral was an abnormal pap smear. The mean age of the women included at the time of colposcopy was 33.4 years (standard deviation 7.3 years). Twenty-two women (27.5%) were aged under 30, and 58 (72.5%) were aged over 30. For the 40 patients classified as "<CIN2", 13 had a normal histology result, 12 had inflammation or metaplasia, and 15 had a CIN1 histology result. Amongst the 40 patients classified as "≥CIN2", 9 had a CIN2 histology result, 28 had a CIN3 histology result, and 3 had AIS cytology result. Regarding the cytology, 18 had normal or inflammation results, 10 had ASC-US, 18 had LSIL, 15 had ASC-H, 15 had HSIL, 1 had an AGC result and 3 had an AIS result.

Colposcopist Characteristics – The average experience in colposcopy of the participants was 10.9 years with a standard deviation of 9.5 years, and range of 1 to 35 years. Overall, 37,8% (n = 14) of colposcopists performed less than 50 colposcopies per year, and 63,2% (n = 24) performed more than 50 colposcopies per year. The washout period between the two rounds was 9.4 weeks on average.

Diagnostic Performance: With Cytology versus Without Cytology – The overall sensitivity of colposcopy without cytology was 51.1% [95%CI: 39.3 to 62.8], and 63.7% [95%CI: 52.1 to 73.9] with knowledge of cytology. The presence of cytology increased the chance of correctly identifying a patient as positive with an odds ratio (OR) of 1.68 [95%CI: 1.42 to 1.99]. The overall specificity of colposcopy without cytology was 63.5% [95%CI: 52.3 to 73.5], and 76.7% [95%CI: 67.2 to 84.0] with knowledge of cytology. Knowing the cytological result increased the chance of correctly identifying a patient as negative with an OR of 1.88 [95%CI: 1.57 to 2.24]. This is illustrated in Fig. 2 which represents the overall sensitivity and specificity of each colposcopist in both assessments of the cases.

Participant's Experience Associated with Performance – For colposcopists who performed fewer than 50 colposcopies per year, the sensitivity was 55.9% [95%CI: 44.0 to 67.1] without cytology and 66.8% [95%CI: 55.5 to 76.5] with cytology. Having the cytological result available increased the likelihood of correctly identifying a patient as positive, with an OR of 1.59 [95%CI: 1.21 to 2.08]. In this subgroup, the specificity without cytology was 52.1% [95%CI: 41.1 to 62.6], which improved to 72.7% [95%CI: 63.2 to 80.5] with cytology. The presence of cytology increased the chance of correctly identifying a patient as negative, with an OR of 2.45 [95%CI: 1.86 to 3.22]. For colposcopists who performed more than 50 colposcopies per year, the sensitivity without cytology was 48.4% [95%CI: 33.6 to 63.6], and 62.7% [95%CI: 47.5 to 75.8] with cytology. In this group, the inclusion of cytology increased the likelihood of correctly identifying a patient as positive, with an OR of 1.79 [95%CI: 1.44 to 2.23]. The specificity without cytology was 71.9% [95%CI: 57.6 to 82.8], and 80.1% [95%CI: 68.0 to 88.4] with knowledge of cytology. Having the cytological result available increased the chance of correctly identifying a patient as negative, with an OR of 1.57 [95%CI: 1.24 to 1.99].

Association between Colposcopic Diagnosis and Histology and Cytology Grades – In Table 1, sensitivity and specificity were assessed in histological sub-groups. Specificity for detection of benign appearances of the cervix was increased by 12.8% when cytology was known. Specificity for detection of CIN1 was increased by 13.8% when cytology was known. For the detection of CIN2 lesions, sensitivity was increased by 17.7% and for the detection of CIN3 lesions sensitivity was increased by 7.7%. Sensitivity and specificity were also analysed in cytological sub-groups, presented in Table 2. The cytology information communicated to the colposcopists was binarised into 'benign/borderline' (normal, inflammation, ASC-US, LSIL) and 'high-grade' (ASC-H, HSIL, AGC, AIS). Sensitivity when cytology was reported as high-grade was 75.5% [95%CI: 63.3 to 84.6] compared to 36.9% [95%CI: 21.0 to 56.3] when cytology was reported benign. A high-grade cytology increased the chance of correctly identifying a patient as positive by an OR of 5.25 [95%CI: 2.11 to 13.12]. Specificity when cytology was reported as benign was 81.5% [95%CI: 72.7 to 88.0] compared to 50.5% [95%CI: 28.0 to 72.8] when cytology was reported as high-grade. A benign cytology increased the chance of correctly identifying a patient as negative by an OR of 4.33 [95%CI: 1.54 to 12.14].

Table 1
Specificity in patient identified benign/borderline and CIN1 by histology and sensitivity in patient identified CIN2 and CIN3 by histology in each condition (with and without cytology).

		Without cytology	With cytology	OR [95%CI]
Specificity	Benign	0.651 [0.512 to 0.769]	0.779 [0.663 to 0.863]	1.88 [1.50 to 2.37]
	CIN1	0.610 [0.450 to 0.749]	0.748 [0.607 to 0.850]	1.90 [1.43 to 2.52]
Sensitivity	CIN2	0.206 [0.098 to 0.381]	0.383 [0.209 to 0.593]	2.40 [1.64 to 3.50]
	CIN3	0.621 [0.501 to 0.727]	0.698 [0.586 to 0.791]	1.41 [1.16 to 1.72]

CIN1: cervical intraepithelial neoplasia grade 1; CIN2: cervical intraepithelial neoplasia grade 2; CIN3: cervical intraepithelial neoplasia grade 3; OR: odds ratio

Table 2
Sensitivity and specificity for patients identified as benign vs high-grade by the cytology.

		Without cytology	With cytology	OR [95%CI]
Patients with a benign/borderline cytology	Sensitivity	0.598 [0.403 to 0.766]	0.369 [0.210 to 0.563]	0.39 [0.29 to 0.54]
	Specificity	0.636 [0.515 to 0.742]	0.815 [0.727 to 0.880]	2.53 [2.06 to 3.10]
Patients with a high-grade cytology	Sensitivity	0.474 [0.336 to 0.616]	0.755 [0.633 to 0.846]	3.41 [2.75 to 4.24]
	Specificity	0.621 [0.384 to 0.811]	0.505 [0.280 to 0.728]	0.62 [0.42 to 0.92]

OR: odds ratio

Discussion

Our study was designed to evaluate to what extent knowledge of cytology results affects interpretation of colposcopy. Our main finding supports that a known cytology influences the colposcopist's diagnosis. Our study showed an improvement in sensitivity for ≥ CIN2 detection when cytology was available (51.1% vs 63.7%). Information offered by cytology, particularly in the case of women with a high-grade result, may make the colposcopist more attentive to possible cervical abnormalities that would have otherwise been overlooked. This allows disease that would be missed to be correctly identified and may therefore reduce morbidity and mortality by facilitating disease treatment at an early stage. Equally, a benign or borderline cytology increased the chances of correctly identify a patient as negative. The improved specificity demonstrated in this study (63.5% vs 76.6%) has important implications, namely reducing the chances of women having unnecessary cervical biopsy and prolonged follow-up which may be associated with discomfort, emotional distress, and extra financial costs.

Since the initial cytology had contributed to the diagnostic outcome (< CIN2 and ≥ CIN2), some level of inflation of the contrast between colposcopy interpretation with and without knowledge of cytology cannot be excluded.

The principal strength of our study is the large number of colposcopists who took part, increasing statistical power to elucidate the effect of cytology on the overall performance of colposcopy. Additionally, the use of a crossover design to account for individual variation and possible confounding factors strengthens the validity of the results. Finally, the use of a logistic regression mixed model to calculate sensitivities and specificities also enhances the statistical rigour. A relative weakness of this study is that static images were used which does not completely reflect the process of colposcopy. Static images do not convey the ability of the colposcopist to manipulate the cervix in order to visualise the entire squamocolumnar junction, to identify lesions that may be partially hidden inside the os. Another important difference is that when evaluating static images, the interpreter loses the potential to assess the dynamic acetowhite character of cervical tissue. The dynamic nature of acetowhite changes have been proposed as an important factor in determining the likelihood of ≥ CIN2 pathology (21). Despite this, studies have shown that sensitivity of diagnosing ≥ CIN2 can be very high even when using solely static images (22).

Considering that cytology results are typically available at the point of colposcopy in high income settings worldwide, there is very little literature examining how cytology influences the colposcopist, and therefore to what extent it is beneficial to know the cytology result during colposcopy. One notable study showed, like us, that ≥ CIN2 lesions were more frequently missed when the referral PAP was negative (15). However, after analysis, the investigators concluded that this was because these lesions were smaller at colposcopy, and that referral PAP result had no influence when this was taken into account. Our study did not evaluate the effect of the size of the lesion during colposcopy. This study added to

existing literature suggesting that, as a tool in isolation, examination of cervical appearances after acetic acid application may have relatively poor sensitivity (23). Our reported sensitivity of 51% for the detection of ≥ CIN2 implies that there are nearly equal numbers of true positives and false negatives, and therefore colposcopy alone likely represents an insufficient measure when determining whether there is significant pathology present.

An interesting result generated by this study was that healthcare professionals with greater recent experience (> 50 colposcopies per year) had a worse sensitivity for the detection of ≥ CIN2 (48.4% without cytology and 62.7% with cytology) than their colleagues undertaking fewer colposcopies (55.9% without cytology and 66.8% with cytology). They did, however, record a superior specificity. This is consistent with other literature in the field which reports that increasing colposcopic experience does not always equate to better sensitivity for the diagnosis of ≥ CIN2 at colposcopy (24). A different interpretation of this could be that senior healthcare workers - who have greater overall experience - may do fewer colposcopies each year than their junior counterparts, as they have more responsibilities outside of the direct clinical environment.

In cervical cytology, also a rather subjective diagnostic activity, the cytologist's pre-knowledge of HPV status has been reported to influence its accuracy (25). With screening based on HPV test results becoming commonplace, the role of HPV testing in colposcopy, and its sensitivity and specificity in detecting ≥ CIN2 lesions should be investigated. The effect of knowing HPV-status on the overall performance of colposcopy will require investigation and could be conducted in a format similar to this study.

Conclusions

In conclusion, our findings support that knowledge of cytology results significantly influences the interpretation of colposcopy, leading to improved sensitivity for detecting ≥ CIN2 lesions. In cases of high-grade results, colposcopist performance is improved to a greater degree. This may be attributed to the association between cytology and colposcopy results.

Declarations

Ethics approval and consent to participate: Participants were retrospectively taken from a cohort of patients recruited to the study: 'Use of a smartphone-based Artificial Intelligence classifier as an adjunct to colposcopy for identifying cervical pre-cancer and cancer: Proof of concept' (study number 2020-00868). The study was approved by the Ethics committee: Cantonal Commission for Research Ethics, Geneva.

Consent for publication: Not applicable.

Availability of data and materials: The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Authors' contributions:

Conception and design: PP, HC, EL, PV

Creation of Jotform web survey: HC, EL

Organization and/or dissemination of Jotform web surveys: EL, HN, FG, MA, JJ

Cytological and histological analysis: JC-T, ES

Statistical analysis: CJ

Interpretation of results, writing and review of final manuscript: EL, HC, MU, HN, CJ, FG, MA, JJ, JC-T, ES, PV, PP

References

1. WHO, Cervical cancer [Internet]. who.int. 2022. https://www.who.int/news-room/fact-sheets/detail/cervical-cancer. Accessed 12 Mar 2023

2. Arbyn M, Weiderpass E, Bruni L, de Sanjosé S, Saraiya M, Ferlay J, et al. Estimates of incidence and mortality of cervical cancer in 2018: A worldwide analysis. The Lancet Global Health. 2020;8(2). doi:10.1016/s2214-109x(19)30482-6

3. Dickinson JA, Stankiewicz A, Popadiuk C, Pogany L, Onysko J, Miller AB. Reduced cervical cancer incidence and mortality in Canada: National data from 1932 to 2006. BMC Public Health. 2012;12(1). doi:10.1186/1471-2458-12-992

4. Moss EL, Redman CWE, Arbyn M, Dollery E, Petry KU, Nieminen P, et al. Colposcopy training and assessment across the member countries of the European Federation for Colposcopy. European Journal of Obstetrics and Gynecology and Reproductive Biology. 2015;188:124–8. doi:10.1016/j.ejogrb.2015.03.012

5. Wesley R, Sankaranarayanan R, Mathew B, Chandralekha B, Aysha Beegum A, Amma N, et al. Evaluation of visual inspection as a screening test for cervical cancer. British Journal of Cancer. 1997;75(3):436–40. doi:10.1038/bjc.1997.72

6. Massad LS, Collins YC. Strength of correlations between colposcopic impression and biopsy histology. Gynecologic Oncology. 2003;89(3):424–8. doi:10.1016/s0090-8258(03)00082-9

7. Numnum TM, Kirby TO, Leath CA, Huh WK, Alvarez RD, Straughn JM. A prospective evaluation of "See and treat" in women with Hsil pap smear results: Is this an appropriate strategy? Journal of Lower Genital Tract Disease. 2005;9(1):2–6. doi:10.1097/00128360-200501000-00002

8. NICE, Adjunctive colposcopy technologies for assessing suspected cervical abnormalities: the DYSIS colposcope with DYSISmap and the ZedScan Guidance [Internet]. nice.org. 2018. https://www.nice.org.uk/guidance/dg32/chapter/4-Evidence. Accessed 26 Dec 2023

9. Sellors JW, Sankaranarayanan R, Colposcopy and treatment of cervical intraepithelial neoplasia: a beginners' manual [Internet]. iarc.fr. 2023. https://screening.iarc.fr/colpochap.php?lang=1&chap=7.php. Accessed 15 Feb 2023

10. Barut MU, Kale A, Kuyumcuoğlu U, Bozkurt M, Ağaçayak E, Özekinci S, et al. Analysis of sensitivity, specificity, and positive and negative predictive values of smear and colposcopy in diagnosis of premalignant and malignant cervical lesions. Medical Science Monitor. 2015;21:3860–7. doi:10.12659/msm.895227

11. Fachetti-Machado G, Figueiredo-Alves RR, Moreira MA. Performance of conventional cytology and colposcopy for the diagnosis of cervical squamous and glandular Neoplasias. Revista Brasileira de Ginecologia e Obstetrícia / RBGO Gynecology and Obstetrics. 2018;40(07):410–6. doi:10.1055/s-0038-1666995

12. Singh V, Sehgal A, Luthra UK. Screening for cervical cancer by direct inspection. BMJ. 1992;304(6826):534–5. doi:10.1136/bmj.304.6826.534

13. Mitchell M. Colposcopy for the diagnosis of squamous intraepithelial lesions: A meta-analysis. Obstetrics & Gynecology. 1998;91(4):626–31. doi:10.1016/s0029-7844(98)00006-4

14. Wentzensen N, Walker J, Smith K, Gold MA, Zuna R, Massad LS, et al. A prospective study of risk-based colposcopy demonstrates improved detection of cervical precancers. American Journal of Obstetrics and Gynecology. 2018;218(6). doi:10.1016/j.ajog.2018.02.009

15. Pretorius RG, Belinson JL, Zhang WH, Burchette RJ, Elson P, Qiao YL. The colposcopic impression. Is it influenced by the colposcopist's knowledge of the findings on the referral Papanicolaou smear. Journal of Reproductive Medicine. 2001;46(8):724–8.

16. Campbell WS, Talmon GA, Foster KW, Baker JJ, Smith LM, Hinrichs SH. Visual Memory Effects on Intraoperator Study Design: Determining a Minimum Time Gap Between Case Reviews to Reduce Recall Bias. American Jounal of Clinical Pathology. 2015;143(3):412–8. doi.org/10.1309/ajcpuc3tyms3qobm

17. Nielsen PS, Lindebjerg J, Rasmussen J, Starklint H, Waldstrøm M, Nielsen B. Virtual microscopy: An evaluation of its validity and diagnostic performance in routine histologic diagnosis of skin tumors.

Human Pathology. 2010;41(12):1770–6. doi:10.1016/j.humpath.2010.05.015

18. Jukić DM, Drogowski LM, Martina J, Parwani AV. Clinical examination and validation of primary diagnosis in anatomic pathology using whole slide digital images. Archives of Pathology & Laboratory Medicine. 2011;135(3):372–8. doi:10.5858/2009-0678-oa.1

19. Nayar R, Wilbur DC. The Bethesda System for reporting cervical cytology: Definitions, criteria, and explanatory notes. Cham: Springer; 2015.

20. WHO Classification of Tumours Editorial Board WHO. Female Genital Tumours WHO Classification of Tumours, 5th Edition, Volume 4 [Internet]. who.int. 2020. https://publications.iarc.fr/Book-And-Report-Series/Who-Classification-Of-Tumours/Female-Genital-Tumours-2020. Accessed Jun 7 2023

21. Gutiérrez-Fragoso K, Acosta-Mesa HG, Cruz-Ramírez N, Hernández-Jiménez R. Optimization of classification strategies of acetowhite temporal patterns towards improving diagnostic performance of Colposcopy. Computational and Mathematical Methods in Medicine. 2017;2017:1–10. doi:10.1155/2017/5989105

22. Liu AH, Gold MA, Schiffman M, Smith KM, Zuna RE, Dunn ST, et al. Comparison of colposcopic impression based on live colposcopy and evaluation of Static Digital Images. Journal of Lower Genital Tract Disease. 2016;20(2):154–61. doi:10.1097/lgt.0000000000000194

23. Sarian LO, Derchain SF, Naud P, Roteli-Martins C, Longatto-Filho A, Tatti S, et al. Evaluation of visual inspection with acetic acid (via), Lugol's iodine (Vili), cervical cytology and HPV testing as cervical screening tools in Latin America: This report refers to partial results from the LAMS (Latin American screening) study. Journal of Medical Screening. 2005;12(3):142–9. doi:10.1258/0969141054855328

24. Bekkers RL, van de Nieuwenhof HP, Neesham DE, Hendriks JH, Tan J, Quinn MA. Does experience in colposcopy improve identification of high grade abnormalities? Obstetrical & Gynecological Survey. 2009;64(2):97–8. doi:10.1097/01.ogx.0000343913.30802.6f

25. Benoy IH, Vanden Broeck D, Ruymbeke MJ, Sahebali S, Arbyn M, Bogers JJ, et al. Prior knowledge of HPV status improves detection of CIN2+ by cytology screening. American Journal of Obstetrics and Gynecology. 2011;205(6). doi:10.1016/j.ajog.2011.06.101
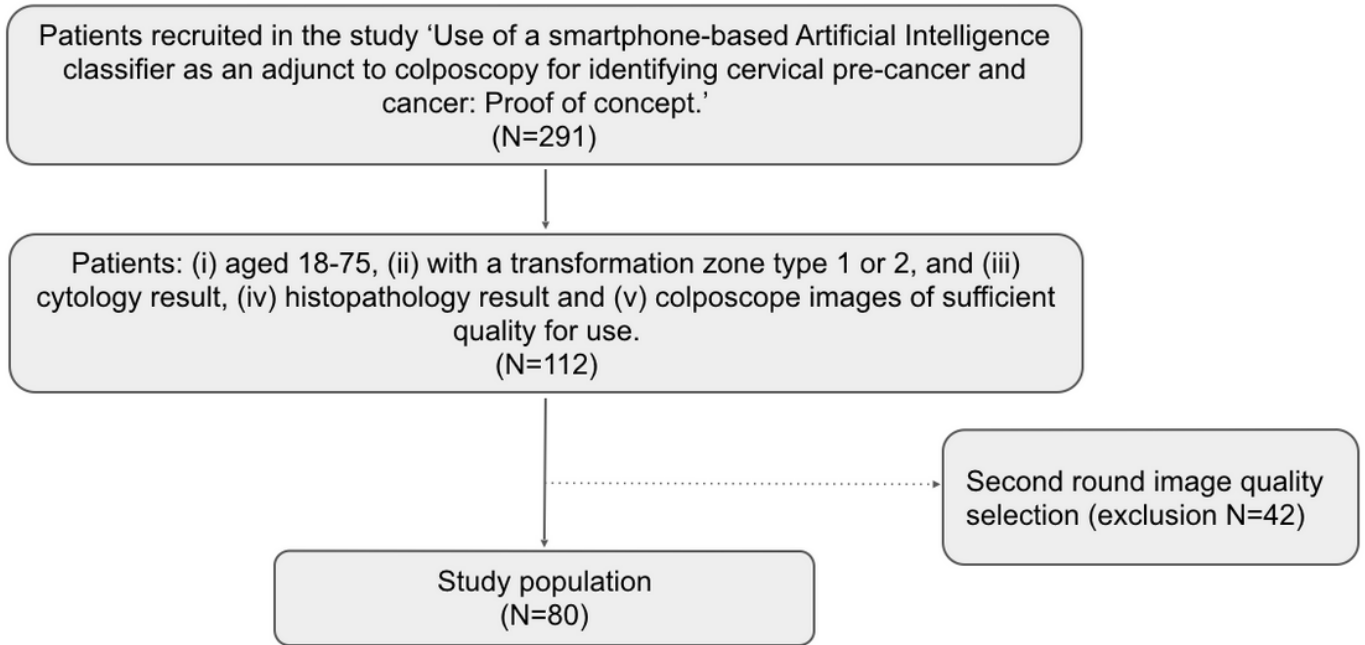
Figures

Figure 1

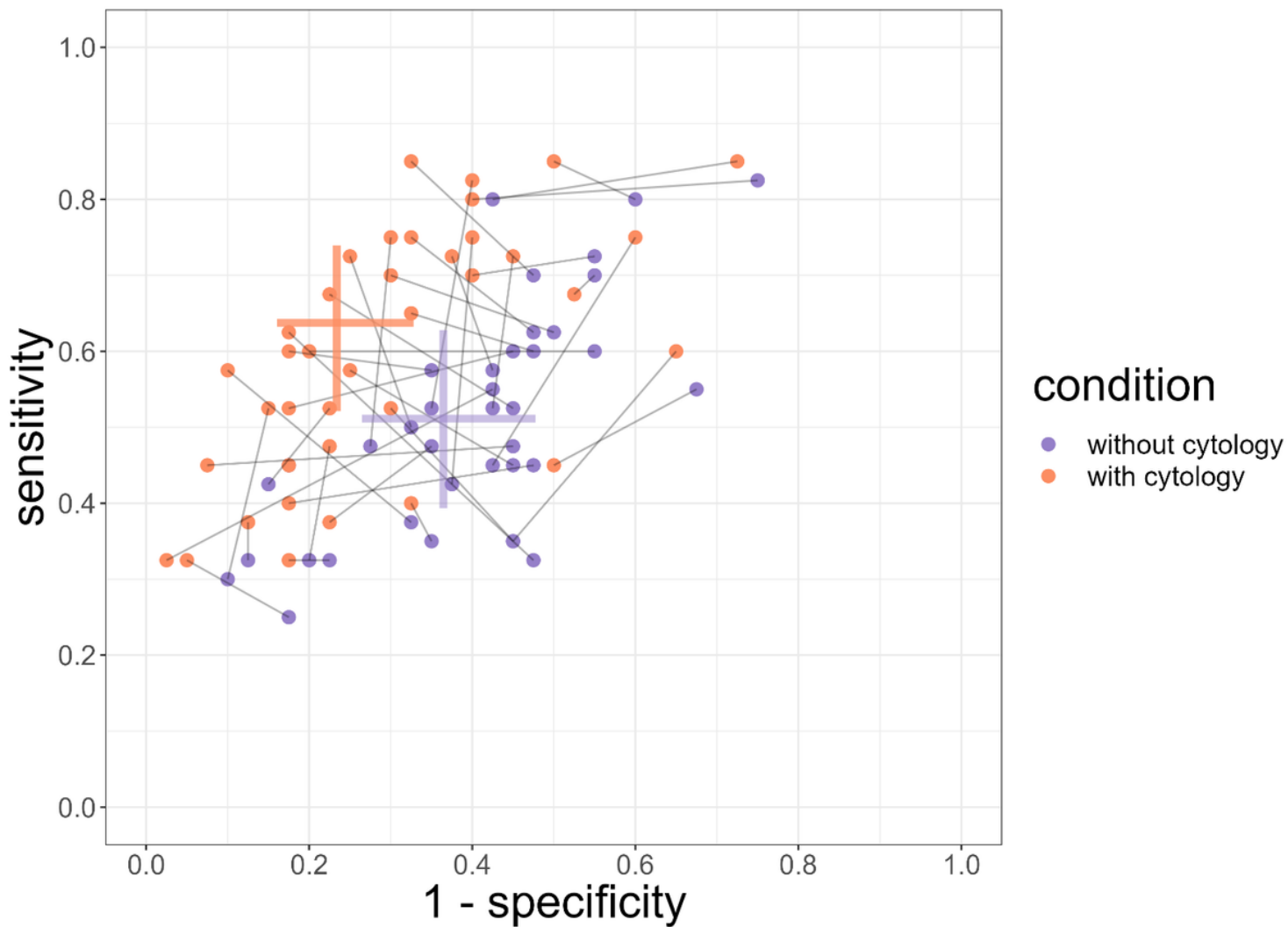Flowchart of participants recruited for the online surveys.

Figure 2

Sensitivity and 1-specificity per rater, with (orange circles) and without (purple circles) cytology. The horizontal (respectively vertical) lines represent the 95% confidence intervals of the overall sensitivities and specificities with and without cytology.