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Validation and feasibility of patient self-sampling of HPV for cervical cancer screening

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IRB Minimal Risk Protocol Template

Note: If this study establishes a human specimen repository (biobank) for research purposes, do not use this template. Use the Mayo Clinic Human Specimen Repository Protocol Template found on the IRB home page under Forms and Procedures at http://intranet.mayo.edu/charlie/irb/

First-time Use: Use this template to describe your study for a new IRB submission.

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2. Save an electronic copy of this protocol for future revisions.
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1. Open your study in IRBe. Click on the study 'Documents' tab and select the most recent version of the protocol. Save it to your files.
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General Study Information

Principal Investigator: Kathy MacLaughlin, MD

Study Title: Validation and feasibility of patient self-sampling of HPV for cervical cancer screening

Protocol version number and date: Version 5 on 11/17/2023

Research Question and Aims

Hypothesis: Patient self-sampling for vaginal HPV infection using the Evalyn collection swab device will generate comparable results (defined as sensitivity of ≥90%; specificity of ≥95%) to the gold standard of a clinician-collected cervical sample for HPV testing.

Aims, purpose, or objectives: Primary aim is to validate a patient self-sampling vaginal collection kit and laboratory testing for the detection of HPV infection. Secondary aim is to assess the patient perspective on acceptability and feasibility of a self-sampling approach to cervical cancer screening through a survey of study enrollees.
Phase 2 aims: Validate a patient self-sampling vaginal collection kit that is mailed to the patient, collected at home, mailed back to Mayo Clinic for HPV testing and compared with HPV test results from a clinician-collected cervical sample. Assess the patient perspective on acceptability and feasibility of a self-sampling approach to cervical cancer screening at home through a survey of study enrollees.
Note: Phase 1 (original IRB submission) involved study subject self-collection conducted on the Mayo Clinic campus and compared with a clinician-collected specimen with transport of both specimens within Mayo campus to the Mayo lab.

Phase 3 Aim - Stability testing: Mayo Virology Lab will conduct time-based pre-processing stability testing and temperature extremes stability testing of Evalyn brush samples to ensure that time-delay in receipt and processing of Evalyn brush samples and exposure to hot and cold temperatures will not impact the HPV test results.

Background (*Include relevant experience, gaps in current knowledge, preliminary data, etc*.):

Cervical cancer is preventable through screening and treatment of pre-cancers yet estimates from the American Cancer Society (ACS) predict 14,100 cervical cancer cases and 4,280 deaths in the US in 2022, which occur most often in never or under-screened women. (1) Data from National Health Information Survey (NHIS) illustrate a concerning trend with a decline in screening rates from 2000 (86.5%) to 2018 (81.1%). (2, 3) Cervical cancer screening rates may be even lower as NHIS results are based on self-reported data which have been shown to over-estimate actual rates. (4) Only 64.6% of screening-eligible women in Olmsted County were up to date with cervical cancer screening using data from confirmed diagnosis and billing codes (5) falling well below the Healthy People 2030 goal of 84.3%. (6) Disparities in screening are associated with sociodemographic factors including race and ethnicity, household income, education, sexual orientation and geography. (6) As well, marked declines in cervical cancer screening were noted early in the COVID-19 pandemic. Compared with one year prior, screening rates among women aged 30-65 years in Kaiser Permanente of Southern California dropped 82% during the first 3 months of the pandemic and remained 24% lower in the 3 months after lifting of a stay-at-home order. (7)

Lack of health insurance or a primary care provider are often the most significant roadblocks to cervical cancer screening completion (8) though these factors are less likely to be barriers for screening eligible women receiving primary care in Mayo Clinic Rochester. Instead, previously identified barriers that may be applicable to our population include time challenges related to work or childcare schedules (9) and inconvenient appointment times (10), discomfort with past gynecologic exams (9) or having multiple medical co-morbidities. (11) As recommended by the Community Preventive Services Task Force, effective interventions to increase uptake of cervical cancer screening incorporate multiple components addressing broader categories of increasing community demand, community access and clinician delivery of cervical cancer screening along with addressing structural barriers. (12)

With recognition that persistent high-risk human papillomavirus (HPV) infection causes cervical cancer and with development and FDA-approval of clinician-collected HPV screening tests, a paradigm shift in cervical cancer screening method from cytology-based (Pap) testing to an emphasis on HPV-based testing has occurred (13) as illustrated by the U.S. Preventive Services Task Force endorsement of primary HPV screening in 2018 (14) and ACS's preferential recommendation for primary HPV screening in 2020. (15) This evolution in screening strategy has led to a unique application of HPV screening that addresses community access and barriers to screening by involving patients in self-collection of a vaginal specimen at home (or other settings) for HPV testing. High levels of concordance have been observed between patient-collected vaginal and clinician-collected cervical samples for HPV results in multiple studies. (16) (17) In a meta-analyses of 56 test accuracy studies and 25 randomized trials, vaginal specimens collected by patient self-sampling were as sensitive as clinician-collected samples when specimens were processed on a PCR-based test platform for detecting CIN2+ or CIN3+ (pooled ratio 0.99, 95% confidence interval 0.97 to 1.02). (18) Offering at home self-sampling has been shown to increase screening uptake in under-screened women in Canada and Europe. (19, 20)

Acceptance of HPV test self-collection among diverse groups of women in low-resource settings has been observed in pilot studies performed in Appalachian Kentucky (21), with Somali immigrants in Minnesota (22), Latina and Haitian women in Miami (23), and Black women in the Mississippi Delta (24) with different test collection settings including homes, clinics and a church. Less is known about patient acceptance of self-sampling among women in higher resource settings such as the Mayo Clinic Rochester, though most women agreed that self-sampling would be more convenient, easier and less painful than clinician-collected screening in a survey conducted across Minnesota. (25) As part of this study, we will conduct a survey of accrued subjects after they have collected the self-sampled specimen to assess acceptability and feasibility of this screening method. The survey questions are based on a theoretical framework of acceptability (TFA) questionnaire designed to be adapted and applied to assess any healthcare intervention. (26)
For this study, patients will use the Evalyn brush (Rovers Medical Devices, Lekstraat, The Netherlands) for self-collection, a device that is well-studied and currently offered as an in-home vaginal self-sampling screening option through the national cervical cancer screening program of the Netherlands. (27) Design of the device resolves practical sampling issues by incorporating insertion indicator wings and "click sounds" so patients' insert to the appropriate depth and perform adequate brush rotation. The Evalyn brush device is manufactured, packaged, and marketed by Rovers Medical Devices B.V. in Oss, the Netherlands. The Evalyn brush device is an FDA-cleared device with 510(k) status and will be used according to its cleared indication. Testing for HPV will be performed in the clinical virology lab at Mayo Clinic (Rochester, MN) on the Roche Cobas 4800 platform for phase 1 and 6800/8800 platform for phase 2, using a polymerase chain reaction-assay (PCR) that is FDA-approved for clinician-collected HPV testing, however not approved for self-collected HPV testing. In multiple studies evaluating the performance of the Evalyn brush on the Roche Cobas HPV PCR assay, strong concordance was noted between self- vs clinician-collected results (28) (29) and the self-sampled specimen test sensitivity was high/non-inferior when compared to the gold standard of a clinician-collected cervical specimens. (30, 31)

To move forward with future Mayo Clinic-led pragmatic interventional trials aimed at improving cervical cancer screening uptake through the option of patient self-sampling, a collection device for HPV screening must be validated in a Mayo Clinic lab. The goal of our proposed study is to validate such a tool and assess the feasibility of this screening approach from the perspective of the study enrollees.

References

1. American Cancer Society. Key Statistics for Cervical Cancer. 2021 [cited 2021 January 19]. Available from: https://www.cancer.org/cancer/cervical-cancer/about/key-statistics.html.
2. Watson M, Benard V, King J, Crawford A, Saraiya M. National assessment of HPV and Pap tests: Changes in cervical cancer screening, National Health Interview Survey. Prev Med. 2017;100:243-7.
3. National Cancer Institute. Cancer Trends Progress Report. 2020 [cited 2021 February 9]. Available from: https://progressreport.cancer.gov/detection/cervical_cancer.
4. Howard M, Agarwal G, Lytwyn A. Accuracy of self-reports of Pap and mammography screening compared to medical record: a meta-analysis. Cancer Causes Control. 2009;20(1):1-13.
5. MacLaughlin KL, Jacobson RM, Radecki Breitkopf C, Wilson PM, Jacobson DJ, Fan C, et al. Trends Over Time in Pap and Pap-HPV Cotesting for Cervical Cancer Screening. J Womens Health (Larchmt). 2019;28(2):244-9.

6. Office of Disease Prevention and Health Promotion. Healthy People 2020: Cancer Objectives. 2020 [cited 2021 February 9]. Available from: https://www.healthypeople.gov/2020/topics-objectives/topic/cancer/objectives.
7. Miller MJ, Xu L, Qin J, Hahn EE, Ngo-Metzger Q, Mittman B, et al. Impact of COVID-19 on Cervical Cancer Screening Rates Among Women Aged 21-65 Years in a Large Integrated Health Care System - Southern California, January 1-September 30, 2019, and January 1-September 30, 2020. MMWR Morb Mortal Wkly Rep. 2021;70(4):109-13.
8. White A, Thompson TD, White MC, Sabatino SA, de Moor J, Doria-Rose PV, et al. Cancer Screening Test Use - United States, 2015. MMWR Morb Mortal Wkly Rep. 2017;66(8):201-6.
9. Oscarsson MG, Benzein EG, Wijma BE. Reasons for non-attendance at cervical screening as reported by non-attendees in Sweden. J Psychosom Obstet Gynaecol. 2008;29(1):23-31.
10. Waller J, Bartoszek M, Marlow L, Wardle J. Barriers to cervical cancer screening attendance in England: a population-based survey. J Med Screen. 2009;16(4):199-204.
11. Crawford A, Benard V, King J, Thomas CC. Understanding Barriers to Cervical Cancer Screening in Women With Access to Care, Behavioral Risk Factor Surveillance System, 2014. Prev Chronic Dis. 2016;13:E154.
12. Community Preventive Services Task Force. Increasing Cervical Cancer Screening: Multicomponent Interventions. 2016 [January 19, 2021]. Available from: https://www.thecommunityguide.org/sites/default/files/assets/Cancer-Screening-Multicomponent-Cervical.pdf.
13. Tota JE, Bentley J, Blake J, Coutlee F, Duggan MA, Ferenczy A, et al. Introduction of molecular HPV testing as the primary technology in cervical cancer screening: Acting on evidence to change the current paradigm. Prev Med. 2017;98:5-14.
14. USPSTF Task Force, Curry SJ, Krist AH, Owens DK, Barry MJ, Caughey AB, et al. Screening for Cervical Cancer: US Preventive Services Task Force Recommendation Statement. JAMA. 2018;320(7):674-86.
15. Fontham ETH, Wolf AMD, Church TR, Etzioni R, Flowers CR, Herzig A, et al. Cervical cancer screening for individuals at average risk: 2020 guideline update from the American Cancer Society. CA Cancer J Clin. 2020.
16. Petignat P, Faltin DL, Bruchim I, Tramer MR, Franco EL, Coutlee F. Are self-collected samples comparable to physician-collected cervical specimens for human papillomavirus DNA testing? A systematic review and meta-analysis. Gynecol Oncol. 2007;105(2):530-5.
17. Arbyn M, Castle PE, Schiffman M, Wentzensen N, Heckman-Stoddard B, Sahasrabuddhe VV. Meta-analysis of agreement/concordance statistics in studies comparing self- vs clinician-collected samples for HPV testing in cervical cancer screening. Int J Cancer. 2022.
18. Arbyn M, Smith SB, Temin S, Sultana F, Castle P, Collaboration on S-S, et al. Detecting cervical precancer and reaching underscreened women by using HPV testing on self samples: updated meta-analyses. BMJ. 2018;363:k4823.
19. Racey CS, Gesink DC, Burchell AN, Trivers S, Wong T, Rebbapragada A. Randomized Intervention of Self-Collected Sampling for Human Papillomavirus Testing in Under-Screened Rural Women: Uptake of Screening and Acceptability. J Womens Health (Larchmt). 2016;25(5):489-97.
20. Racey CS, Withrow DR, Gesink D. Self-collected HPV testing improves participation in cervical cancer screening: a systematic review and meta-analysis. Can J Public Health. 2013;104(2):e159-66.
21. Vanderpool RC, Jones MG, Stradtman LR, Smith JS, Crosby RA. Self-collecting a cervico-vaginal specimen for cervical cancer screening: an exploratory study of acceptability among medically underserved women in rural Appalachia. Gynecol Oncol. 2014;132 Suppl 1:S21-5.

22. Sewali B, Okuyemi KS, Askhir A, Belinson J, Vogel RI, Joseph A, et al. Cervical cancer screening with clinic-based Pap test versus home HPV test among Somali immigrant women in Minnesota: a pilot randomized controlled trial. Cancer Med. 2015;4(4):620-31.
23. Ilangovan K, Kobetz E, Koru-Sengul T, Marcus EN, Rodriguez B, Alonzo Y, et al. Acceptability and Feasibility of Human Papilloma Virus Self-Sampling for Cervical Cancer Screening. J Womens Health (Larchmt). 2016;25(9):944-51.
24. Crosby RA, Hagensee ME, Fisher R, Stradtman LR, Collins T. Self-collected vaginal swabs for HPV screening: An exploratory study of rural Black Mississippi women. Prev Med Rep. 2017;7:227-31.
25. Zhu X, MacLaughlin KL, Fan C, Jacobson DJ, Jenkins GD, Jacobson RM, et al. Awareness of HPV Testing and Acceptability of Self-sampling for Cervical Cancer Screening Among Women in Minnesota. J Gen Intern Med. 2021.
26. Sekhon M, Cartwright M, Francis JJ. Development of a theory-informed questionnaire to assess the acceptability of healthcare interventions. BMC Health Serv Res. 2022;22(1):279.
27. Environment NIfPHat. Cervical Cancer Population Screening: Self-Sampling Kit 2022 [cited 2022 April 2]. Available from: https://www.rivm.nl/bevolkingsonderzoek-baarmoederhalskanker/zelfafnameset.
28. Ketelaars PJW, Bosgraaf RP, Siebers AG, Massuger L, van der Linden JC, Wauters CAP, et al. High-risk human papillomavirus detection in self-sampling compared to physician-taken smear in a responder population of the Dutch cervical screening: Results of the VERA study. Prev Med. 2017;101:96-101.
29. Tranberg M, Jensen JS, Bech BH, Blaakaer J, Svanholm H, Andersen B. Good concordance of HPV detection between cervico-vaginal self-samples and general practitioner-collected samples using the Cobas 4800 HPV DNA test. BMC Infect Dis. 2018;18(1):348.
30. Ornskov D, Jochumsen K, Steiner PH, Grunnet IM, Lykkebo AW, Waldstrom M. Clinical performance and acceptability of self-collected vaginal and urine samples compared with clinician-taken cervical samples for HPV testing among women referred for colposcopy. A cross-sectional study. BMJ Open. 2021;11(3):e041512.
31. Leinonen MK, Schee K, Jonassen CM, Lie AK, Nystrand CF, Rangberg A, et al. Safety and acceptability of human papillomavirus testing of self-collected specimens: A methodologic study of the impact of collection devices and HPV assays on sensitivity for cervical cancer and high-grade lesions. J Clin Virol. 2018;99-100:22-30.

Study Design and Methods

Methods: *Describe in lay terms, completely detailing the research activities that will be conducted by Mayo Clinic staff under this protocol.*

Identification of potential subjects: Appointment lists for Gynecology and ICS Colposcopy Clinics and Gynecology Clinic will be reviewed by study coordinator and/or PI/Co-I to identify potential subjects ages 25-65 yo. Two groups of patients will be enrolled, those undergoing cervical colposcopy due to prior abnormal results (speculum exam required) and those with a cervix who will be receiving a speculum exam as part of their gynecologic care. Review of electronic medical record will be done to apply inclusion and exclusion criteria.
Pre-appointment consent: Study coordinator will contact potential subjects as identified on the schedule to describe the study, assess interest, and obtain consent using IRB-approved written consent sent electronically

through secure email using the PTRAX system. For patients not comfortable with that approach, study team member will provide in-person written consent option on day of clinic.

Process flow for subject self-collected and clinician-collected specimens: Subject will check in at the Gynecology desk and be roomed per usual practice. Study coordinator will meet with subject next and provide a bag containing a study card from Biospecimen Accessioning and Processing (BAP) and a labeled self-sampling Evalyn brush kit, along with printed instructions on how to use the Evalyn brush to collect the vaginal sample. The device will be labeled with patient identifiers. Subject will be directed to a private room to collect the vaginal specimen. Subject will be in or return to exam room and give specimen container to study coordinator. Study coordinator will leave the labeled clinician-collection kit (endocervical brush, spatula and ThinPrep specimen container in the exam room. The clinician providing the care for that appointment will then enter the room and will conduct a speculum exam, collecting a cervical specimen using the clinician-collection kit material describe above before performing the remainder of the visit. The clinician collection will be completed before the colposcopy or other reason for the visit.

Patient survey: After the subject has finished the self-collection and returned to the exam room, the study coordinator will give the subject an iPad to complete the REDCap electronic acceptability and feasibility survey in the exam room. iPad will be left in exam room for the study coordinator to collect directly after the visit. In the event that the electronic survey does not work (ex. technical issues), a paper copy of the survey will be provided to the subject to complete. If for any reason the subject is not able to complete the survey on site during the clinic visit, the study coordinator (or designated team member) may call the subject to complete the survey by phone.

Specimen pathway and processing (partnering with BAP/RLIMS): After visit is complete, the study coordinator or clinical staff will place the labeled subject-collected and clinician-collected specimens into a bag with the study card and leave it in the bin where Central Clinic Lab (CCL) specimens are placed for routine/non-study Gynecology appointments. The paired specimens will be sent from the Gyn Clinic (via General Service delivery) to the BAP group. BAP will accession the specimens, enter them into Soft and into the RLIMS system for tracking. The specimens will then be submitted to the Mayo Virology lab for HPV molecular testing by a commercially available (FDA-approved for clinician collected) testing platform (Roche Cobas HPV). The results will be collected by BAP and periodic reports will be issued for the study team.

Test result management: Through the written informed consent process, subjects will be informed that the primary HPV tests performed as part of this study (by patient vaginal self-sampling and provider cervical sampling) are not a replacement for recommended routine cervical cancer screening or for surveillance (recommended followup of abnormal Pap, HPV, colposcopy biopsy or precancer treatment). Because vaginal HPV testing of a self-collected sample is not FDA-approved, those results will not be reported to the accrued subject or to the Gynecology healthcare provider performing the clinician-collection of a cervical sample. The informed consent will note that subjects should continue with any screening procedures or testing as recommended by their healthcare provider.

The HPV test results of the clinician-collected research cervical sample will not be reported to the accrued subjects or to the clinician who collected the sample. This is because previously obtained HPV test results from clinical encounters should guide management, not research study results. As well, there is no reason to repeat an HPV test sooner than clinically indicated, whether that is for screening or surveillance after abnormal cervical

cytology, HPV, colposcopy biopsy or LEEP procedure. If patient is due for a clinical specimen collection the day of the visit in which self-sampling and clinician research-sampling will be done, that will be collected and that result will be part of the medical record and will guide management.

For a situation in which only a self-collected sample is obtained in absence of a clinician-collected research sample, the self-sample will be sent to the BAP lab and then onto the Virology lab as per the usual method.

In the event that the clinician-collected research cervical swab is not completed or is otherwise not useable (examples include but are not limited to: damaged in transport, has insufficient cellular material for testing, is not located due to loss in transport), the study team may access the patient's Epic medical record to look for a clinician-collected cervical swab done for clinical purposes (for HPV testing) within one week before or after the date of the patient self-collected vaginal specimen. In these instances, the participant will not be called back in to provide another sample.

Identification of subject demographics: The study will identify sociodemographics of accrued subjects through review of electronic medical record (age, race/ethnicity, insurance status, education, BMI, gravidity and parity, menstrual status, geography of residence/Rural-Urban Commuting Area codes/RUCA, SDOH profile from Epic including tobacco history, transportation needs, financial resource strain of the subjects) for use in the data analysis of the HPV test results and subject survey results.

Subject remuneration: Accrued study subjects who complete the vaginal self-sampling with the Evalyn brush, the clinician-collected cervical sampling and the electronic survey will receive $50 in remuneration. Payment will be prorated for those unable to complete the whole study as outlined in the consent form.

Process flow for phase 2 includes the same identification and enrollment procedures, however the study team will need to ensure remote enrollment is complete before mailing an Evalyn brush self-sampling kit (including instructions for collection, labels for specimen container and bag, BAP lab form and pre-metered return mailing envelope) to their home. The kit will be mailed out prior to their clinic appointment and study subjects will be instructed to collect the sample at home and mail it back prior to the clinic appointment. On the day of the clinic appointment, a study team member will provide the subject with the electronic survey via iPad to be completed at the visit (if self-collected sample was done at home prior to the visit).

Specimen pathway and processing (partnering with BAP/RLIMS): The study subject-collected vaginal specimen will be mailed back via USPS to BAP and from that point forward, the specimen pathway and processing is unchanged in phase 2. For the clinician-collected cervical specimen, the specimen pathway and processing is unchanged in phase 2.

In the event that the subject has not enrolled remotely, they may still enroll and participate in the study if willing and able to enroll on site at the appointment, have a self-collection kit mailed to their home,collect the Evalyn brush sample at home on days 7-21 post-clinic appointment, mail the specimen back in as directed, and complete the survey by email or phone.

If the study subject has enrolled but does not collect the vaginal self-swab at home before the clinic appointment and wishes to complete the study, they may complete the Evalyn brush self-collection at home on days 7-21 post-Gynecology or Colposcopy appointment, mail it back and complete the survey by email or phone.

Added Lab evaluation for specimen stability:

Time-based stability testing: One HPV-positive study subject will be enrolled to collect 3 Evalyn Brush vaginal samples at their clinic visit. Those samples will be processed by the Mayo Virology lab following the same process outlined earlier in the Methods section for phase 1 and phase 2. However, processing will be performed at approximately 24 hours, 48 hours and 5 days after collection to determine how long after collection the Evalyn brush samples are stable prior to processing.

Temperature extremes stability testing: Four study subjects will be enrolled, two HPV-positive study subjects and two HPV-negative study subjects. Each study subject will collect 2 Evalyn Brush vaginal samples at their clinic visit. One sample from each of the study subjects' collections will be tested for HPV without temperature extreme stability testing. In order to assess for potential extreme temperature impact on sample and analyte stability during transportation from the home to the laboratory for mailed test kits, the second sample will be evaluated by the Food and Drug Administration (FDA) winter or summer temperature cycling profiles (1 HPV-positive swab for summer profile, 1 HPV-positive swab for winter profile, 1 HPV-negative swab for summer profile, 1 HPV-negative swab for winter profile) Samples will be tested following completion of the temperature cycling and qualitative results compared to results acquired following initial testing.
The process for identifying potential study subjects for the specimen stability aim component of the study will be identical to the process outlined in Methods for phase 1 and phase 2, other than there will be review of past cervical HPV test results to ensure 3 HPV-positive and 2 HPV-negative study subjects are included. The pre-appointment consent process will be identical to that outlined in Methods for phase 1 and phase 2, other than a new consent form will be created to reflect the specimen stability evaluation details outlined here.

Study subjects enrolled for the specimen stability aim will NOT have a clinician-collected cervical research sample nor will they be given the survey.

Remuneration: Accrued subjects who complete the required number of self-sampling collections (2 - 3), will receive $50 in remuneration.

Subject Information

Target accrual is the proposed total number of subjects to be included in this study at Mayo Clinic. A "Subject" may include medical records, images, or specimens generated at Mayo Clinic and/or received from external sources.

Target accrual: Up to 250

Subject population (children, adults, groups): Adults aged 25-65 years old.

Inclusion Criteria:

- Appointment at Mayo Clinic Rochester in Gynecology Colposcopy Clinic or ICS (integrated community specialty) Colposcopy Clinic (will always include a speculum exam).

- Appointment at Mayo Clinic Rochester in Gynecology Clinic for indication that will already include a speculum exam (e.g., cervical cancer screening or IUD insertion).

Exclusion Criteria:

- Excluded if self-reported as currently menstruating, pregnant, or within 3 months following pregnancy.

- Excluded if no cervix (history of total hysterectomy).

- Excluded if moderate to heavy vaginal bleeding on the day of the visit.

- Excluded if reason for visit in Gynecology Clinic is abnormal vaginal discharge.

- Exclude patients who are on Gynecology Colposcopy Clinic for LEEP (loop electrosurgical excision procedure).

- Exclude if any use of over-the-counter or prescription vaginal cream for vaginal infection or prescription vaginal estrogen cream for at least two days before using the Evalyn Brush.
  (Vaginal contraceptives, condoms and water-based lubricants can be used as normal.)

Biospecimens

Collection of blood samples. When multiple groups are involved copy and paste the appropriate section below for example repeat section b when drawing blood from children and adults with cancer.

a. **From healthy, non-pregnant, adult subjects who weigh at least 110 pounds**. For a minimal risk application, the amount of blood drawn from these subjects may not exceed 550ml in an 8 week period and collection may not occur more frequently than 2 times per week.
   Volume per blood draw: _____ml
   Frequency of blood draw (e.g., single draw, time(s) per week, per year, etc.) _____

b. **From other adults and children considering age, weight, and health of subject.** For a minimal risk application, the amount of blood drawn from these subjects may not exceed the lesser of 50 ml or 3 ml per kg in an 8-week period, and collection may not occur more frequently than 2 times per week.
   Volume per blood draw: _____ml
   Frequency of blood draw (e.g., single draw, time(s) per week, per year, etc.) _____

Prospective collection of biological specimens other than blood: Enrolled subjects will self-collect a vaginal swab that will be tested for HPV. The clinician conducting the Gynecology Clinic or Colposcopy Clinic visit will collect a cervical primary HPV sample.

Review of medical records, images, specimens

Check all that apply (data includes medical records, images, specimens).

☐ Only data that exists before the IRB submission date will be collected.

Date Range for Specimens and/or Review of Medical Records:
Examples: *01/01/1999 through 12/31/2015*, or all records through *mm/dd/yyyy*.

Note: The Date Range must include the period for collection of baseline data, as well as follow-up data, if applicable.

X The study involves data that exist at the time of IRB submission **and** data that will be generated after IRB submission. Include this activity in the Methods section.

- The study will identify sociodemographics of accrued subjects (including, but not limited to age, race/ethnicity, insurance status, education, BMI, gravidity and parity, menstrual status, SDOH profile from Epic including tobacco history, transportation needs, financial resource strain) of the subjects).
- The study will include an electronic survey of accrued subjects
- The study will generate data on subjects' self-collected vaginal swab HPV results and paired clinician-collected cervical swab HPV results.

☐ The study will use data that have been collected under another IRB protocol. Include in the Methods section and enter the IRB number from which the research material will be obtained. *When appropriate, note when subjects have provided consent for future use of their data and/or specimens as described in this protocol*.

Enter one IRB number per line, add more lines as needed

☐ Data ☐ Specimens ☐ Data & Specimens _____

☐ Data ☐ Specimens ☐ Data & Specimens _____

☐ Data ☐ Specimens ☐ Data & Specimens _____

Data Analysis

Power analyses may not be appropriate if this is a feasibility or pilot study, but end-point analysis plans are always appropriate even if only exploratory. Provide all information requested below or provide justification if not including all of the information.

Power Statement

1. For the HPV self-sampling validation component of the study, we will assess sensitivity and specificity of a patient-collected vaginal swab to detect HPV infection compared with the gold standard of a clinician-collected cervical swab. We estimate that HPV infection prevalence in the Colposcopy Clinic population is 60%. Using a target sensitivity of $\geq$ 0.9 to define validity, a minimum sample size of 74 patients for each separate phase (1 & 2) is required.

Data Analysis Plan

1. Sensitivity and specificity analyses of paired patient samples (patient-collected vaginal swab compared with gold standard of clinician-collected cervical swab) for detection of HPV infection.

2. Descriptive, bivariate, and multivariate analyses of acceptability/feasibility of patient self-sampling for cervical cancer screening and associations with patient sociodemographic characteristics.

3. For stability testing component of study, we will analyze concordance of multiple self-collected Evalyn brush HPV results within the same study subject.

Endpoints

1. Primary: Sensitivity and specificity of patient-collected vaginal swab to detect HPV infection compared with gold standard of clinician-collected cervical swab.

2. Secondary: Patient perspectives on acceptability and feasibility of HPV self-sampling for cervical cancer screening by sociodemographic characteristics.

3. Tertiary: Time-based and temperature extreme stability testing results.