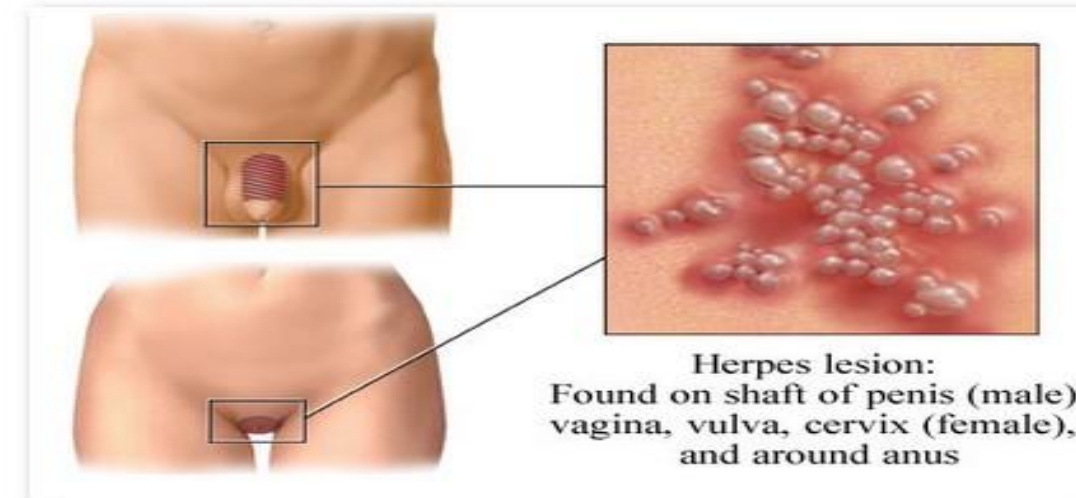


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Introduction

Herpes Simplex Virus (HSV) is a chronic, life-long viral infection that affects millions of people in the U.S. There are two types of the virus, HSV-1 and HSV-2, and either can cause herpes labialis or “fever blisters” near the mouth as well as genital herpes. Consequences of HSV infection include recurrent outbreaks of painful lesions, as well as an increased risk of acquiring HIV.



The ability to diagnose HSV is limited. In most cases, health care providers make the diagnosis by visual inspection and clinical judgment. Currently available tests, such as the HSV culture and polymerase chain reaction (PCR) are expensive and time-consuming. Blood tests can also be used to document past exposure, but do not help diagnosis when a patient presents with new lesions. Timely treatment is critical as it can speed healing of the lesions and prevent transmission to others.

New diagnostic tools for HSV are urgently needed. The ideal diagnostic device would be a point-of-care (POC) device that has reasonable sensitivity (>85%) and high specificity (>95%) compared to culture, which is the current clinical gold standard. However, all new devices must also be compared to PCR as this is the research gold standard. POC testing for HSV would reduce patient cost and allow for immediate diagnosis and treatment.

This study was conducted to evaluate the performance of a prototype POC device to detect HSV compared to PCR.

Aims and Hypotheses

Aim 1: (women) To establish the accuracy of a POC device to detect HSV from a direct swab of a **vulvar** lesion compared to a research gold standard (PCR).

Hypothesis 1.1: Used on a vulvar swab, the POC HSV device will have at least 80% sensitivity and 95% specificity to detect HSV-1 or HSV-2, compared to PCR.

Aim 2: (men) To establish the accuracy of a POC device to detect HSV from a direct swab of a **genital** lesion compared to a research gold standard (PCR).

Hypothesis 2.1: Used on a genital swab, the POC HSV device will have at least 80% sensitivity and 95% specificity to detect HSV-1 or HSV-2, compared to PCR.

Aim 3: (men and women) To establish the accuracy of a POC device to detect HSV from a direct swab of an **oral** lesion compared to a research gold standard (PCR).

Hypothesis 3.1: Used on an oral swab, the POC HSV device will have at least 80% sensitivity and 95% specificity to detect HSV-1 or HSV-2, compared to PCR.

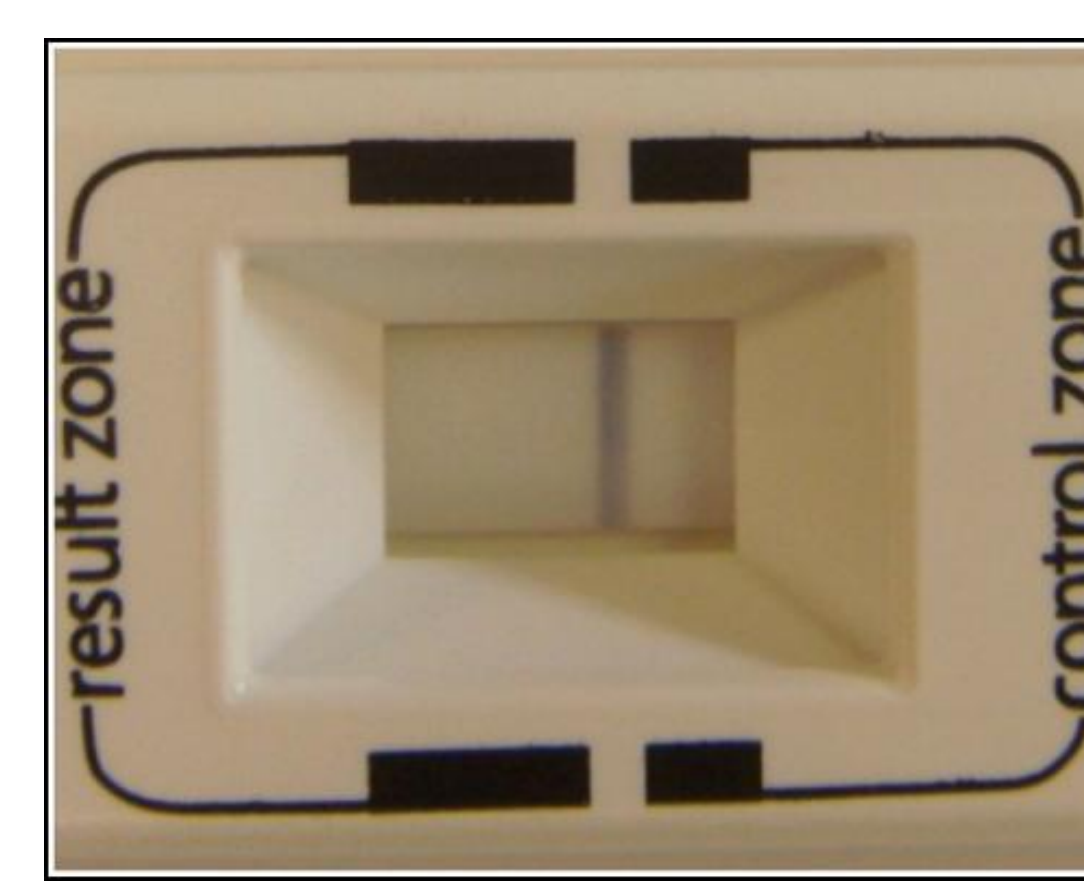
Methods

Men and women were recruited through Cincinnati Children’s Hospital Medical Center (CCHMC) using flyers as well as email invitations. Recruitment was open to patients, staff, and the community. Interested individuals were contacted and completed a phone screening form to determine eligibility. If eligible, a study visit was scheduled.

- Inclusion:** Men and women, ≥16 and <80 years of age, who report either a history of oral or genital herpes or who have an oral or genital lesion suspicious for herpes. Must be willing to have swab samples taken from the lesion (or site of a prior lesion) and attend up to three visits.
- Exclusions:** Unable to comprehend written and verbal instructions in English. Visits with asymptomatic sample collection cannot occur if participants have a lesion or symptoms consistent with a herpes outbreak.
- Participants completed three visits: consent obtained and demographic and herpes history information collected (visit 1); asymptomatic visit when lesion not present (visit 2); and symptomatic visit when lesion present (visit 3). Participants could combine visit 1 with visit 2 or 3.
- At the visits, 2 clinician-obtained swabs from the lesion or, for asymptomatic participants, from the site of the usual lesion, were obtained. One was tested with the POC device at the bedside. One was tested with PCR for HSV-1 and HSV-2. The used device was submitted for POC testing in the laboratory. Bedside and laboratory testers were blinded to PCR results.
- Agreement between bedside POC and PCR and laboratory POC and PCR was calculated.



Positive Result



Negative Result

Results

Twenty-nine participants were recruited. There were 26 women and 3 men.

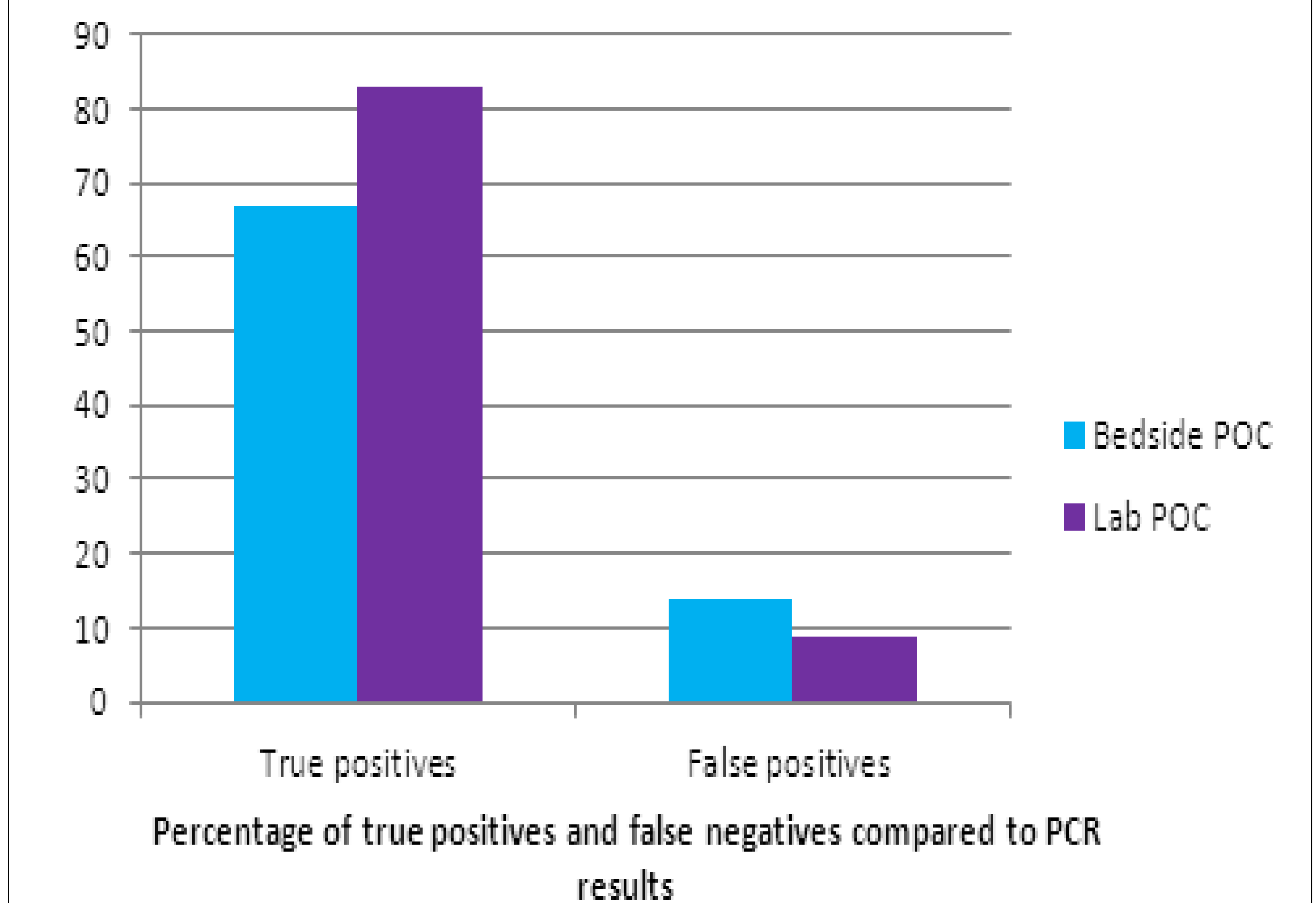
- Of the 29 participants:
 - 18 participants completed asymptomatic visits only
 - 6 participants completed symptomatic visits only
 - 5 participants completed both visits (symptomatic and asymptomatic visit)
 - Total asymptomatic swabs: 23**
 - Total symptomatic swabs (lesion): 11**
- Oral lesions were reported by 27 participants, and only 1 participant had an acute genital outbreak.
- PCR was positive for 7 out of 11 (64%) swabs from lesions, and negative for 23 swabs without lesions (100%).
- Three participants with lesions greater than 7 days old who were using antivirals were PCR and POC negative. Four bedside POC and two laboratory POC tests were invalid.

Accuracy

- Bedside POC
 - Sensitivity:** detected 4 out of 6 (67%) PCR-positive lesions
 - false positive for 3 out of 21 (14%) of PCR-negative no-lesions (**Specificity: 86%**)
- Laboratory POC
 - Sensitivity:** detected 5 out of 6 (83%) PCR-positive lesions
 - false positive for 2 out of 22 (9%) PCR-negative no-lesions (**Specificity: 91%**)

Agreement between POC and PCR

- Bedside POC
 - Moderate
 - kappa=0.51
- Laboratory POC
 - Good
 - kappa=0.71



Conclusions

- In this small pilot sample, the POC HSV device shows promise but seemed to perform better in the laboratory than at the bedside.
- More testing with a larger sample is needed to determine the long-term efficacy of the POC HSV device.

Implications for Programs, Policy, and/or Research

- Sensitive POC tests are needed for HSV1 and HSV2 screening, and highly specific POC tests could hasten diagnosis in symptomatic women.
- Preclinical studies can inform the design of large clinical trials.
- It is difficult to recruit individuals with acute HSV outbreaks for whom the device would be most useful.
- Comparisons of bedside and laboratory performance can lead to device enhancements early in product development.

Acknowledgements

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