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# Syndromic and laboratory diagnosis of sexually transmitted infection: a comparative study in China

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## Summary

The rate of sexually transmitted infections (STIs) has soared in China. Yet, there is no universal consensus about the accuracy of the syndromic approach to STI management. This study aims to compare the syndromic approach with laboratory tests. A randomly selected sample of market vendors in eastern China ($n$ = 4510) was recruited and assessed for the five most common STIs (*Chlamydia trachomatis* infection, gonorrhoea, genital herpes [herpes simplex type 2, HSV-2] syphilis and trichomoniasis [female only]). Symptom-based assessments made by physicians were compared with laboratory tests. Laboratory test results were used as the gold standard for the comparisons. The overall sensitivity of physician symptom-based assessment was about 10%; sensitivity was lower for males (1.6%) than for females (17.2%). The sensitivity of physician assessments for those who reported STI symptoms was relatively higher (36.7%) than for those who reported no symptoms (5.1%). More than half (54.37%) of the participants were diagnosed with STI of trichomoniasis. For the other four types of STIs, physicians correctly identified only <10% of the positive cases. The study detected a low sensitivity of STI diagnosis made by physicians in an Eastern city of China. The failure in the detection of asymptomatic patients remains one of the limitations of the syndromic approach.

### Keywords

STD; syndromic approach; China

## INTRODUCTION

Sexually transmitted infections (STIs), including human immunodeficiency virus (HIV), are imposing an increasing burden not only on public health but also on the world's economies, especially those of developing countries. According to an estimate by the World Health Organization (WHO), nearly a million people acquire STI, including HIV, every day.[1] All these infections cause 17% of economic losses for developing countries, which is a significant

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burden.[1] Failure to diagnose and treat STIs at an early stage may result in serious complications and sequelae and an increase in medical cost.[2,3] In order to respond to the need of STI prevention and treatment, especially in countries with limited resources, the syndromic diagnostic approach based on treatment of symptoms without laboratory confirmation was recommended by WHO.[4] This syndromic approach remains the key component of the most recent WHO guidelines.[3] Rather than relying on aetiological laboratory diagnosis, which requires relatively sophisticated laboratories, the syndromic approach is based on the identification of consistent groups of symptoms and easily recognized signs,[3] which is more practical and feasible for resource-limited settings. A study by Bosu (1999) has identified several advantages of the syndromic approach, including the simplicity of its implementation, rapid diagnosis and treatment, savings on the cost of laboratory tests, broader coverage and lower requirements for existing health systems.[5] Several studies have also demonstrated the efficacy of the syndromic approach.[5–8]

On the other hand, the syndromic approach has been criticized because it relies on symptoms, physical signs and the physician's subjective judgement, all of which are sometimes non-specific, inaccurate or even misleading. Furthermore, the approach does not address asymptomatic STIs. Although there is no universal consensus about the effectiveness of this approach, high clinically assessed cure rates have been achieved in Abidjan (91%) and Mwanza (96–98%).[2,9] A 100% correct treatment rate based on patient-reported symptoms has also been reported in China.[6] However, some studies suggest a poor sensitivity for detecting chlamydial and gonococcal infections among women.[10,11] Therefore, the sensitivity of syndromic management may vary depending upon gender, risk group and organism.[5,8]

To address this issue, we investigated STI assessments with a population of market vendors in Fuzhou, China.[12] We assessed the sensitivity of the syndromic approach in diagnosing five laboratory-confirmed STIs, *Chlamydia trachomatis*, gonorrhoea, HSV-2, syphilis and trichomoniasis (female only).

## MATERIALS AND METHODS

### Study background and population selection

This study is part of a National Institute for Mental Health (NIMH) Collaborative HIV/STD Prevention Trial conducted with five populations at risk for HIV and STDs in China, India, Peru, Russia and Zimbabwe.[13] The study phases consist of an ethnographic study, pilot studies, an epidemiological study and a randomized controlled trial. The current study focused on findings from the epidemiological data collected at baseline.

This study was conducted in food markets in an eastern coastal city in China. Participants for this study were recruited from 40 local food markets. Market selection was based on the size and geographic location of the markets. Market vendors aged 18–49 years from the selected markets were invited to participate in the study.

### Data collection

Agreements were obtained from the gatekeepers, government officials and market managers prior to data collection. Market vendors were informed of the study purpose and the type of recruitment activities. After the administration of informed consent, study participants were transported by van to the Institute of Health Education of the Centers for Disease Control and Prevention (CDC) to participate in a questionnaire survey, medical assessment and the collection of biological specimens. All participants were paid 20 Yuan (US$2.50) in cash for their participation. The study was approved by both the UCLA and China CDC IRB.

**Collecting biological data—**Venous blood samples were collected to test for syphilis, HSV-2 and HIV. For *C. trachomatis* infection and gonorrhoea testing, vaginal swabs and urine specimens were collected for women and men, respectively. Trichomoniasis testing was performed for women only.

**Chlamydia and gonorrhoea were tested using polymerase chain reaction—**The MRL Diagnostics HSV-2 IgG test (Focus Technologies, CA, USA) was used to identify specimens with positive HSV-2 antibody. Syphilis testing was performed by rapid plasma reagin and confirmed using the *Treponema pallidum* particle agglutination test. Vaginal swabs were cultured for *Trichomonas vaginalis* using the InPouch *T. vaginalis* test. In this study, STI status was defined as a test positive result for chlamydia, gonorrhoea, syphilis, trichomoniasis or HSV-2 following standardized laboratory protocols.

**Collecting medical assessment data—**The medical assessment was conducted in a private room. A total of six physicians trained in STI diagnosis participated in the assessment. The physicians asked questions about the participants' current health and STI symptoms such as genital discharge, urination pain and genital sores. Then, the physicians performed a medical examination for every participant. Particular attention was given to signs of inflammation of the genital organ, characteristics of genital discharge and presence of ulcers. An STI was diagnosed by physicians based on their perception of the syndromes and signs from the medical examination.

**Collecting demographic data—**The computer-assisted personal interview was developed to collect participants' demographic information. Five demographic variables were employed in this study: age, gender, marital status, education and self-reported discretionary income per month.

### Data analysis

All analyses were performed using SAS statistical software version 9.1.3 (SAS Inc., Cary, NC, USA). First, descriptive analyses were performed to determine the prevalence of self-reported STI symptoms, physician-diagnosed STIs and laboratory-determined STIs. Secondly, self-reported STI symptoms and physician-diagnosed STI were compared with STI laboratory results. Sensitivity and specificity were calculated. Thirdly, we calculated the number and proportion of STI cases correctly identified by physicians for each of the five tested STIs (chlamydia, gonorrhoea, syphilis, trichomoniasis or HSV-2).

## RESULTS

A total of 4510 market vendors participated in the study. Table 1 summarizes the characteristics of the study population. Among all the participants, 52.7% were women, 82.4% were currently married or lived with a partner and 12.9% had an education level of high school and above. About 73.4% of the sample reported having discretionary money of 500 Yuan per month or less. About 10.7% of the study sample reported STI symptoms such as genital discharge, urination pain and genital sores. Of the study sample, physicians identified 151 people (3.46%) who had symptoms and/or physical signs indicative of STI, of whom 139 (90.1%) were male. However, the laboratory results identified 16.5% of the study participants who had at least one STI.

Table 2 summarizes the sensitivity and specificity of physician diagnosis and self-reported symptoms. The sensitivity of physician assessment was very low, only about 10%. In other words, physicians identified only 10% of the real infection cases, and the sensitivity was lower for males (1.6%) than in females (17.2%). The specificity was high (>95%) for both males and

females. About half of the physician-diagnosed STI cases were actually false-positive according to the laboratory results. The positive predictive value (PPV) for physician diagnosis was only 0.497. The sensitivity of physician assessment for subjects who reported STI symptoms was relatively higher (36.7%) than for those who reported no symptoms (5.1%). For those who reported STI symptoms, however, physician diagnosis had a low specificity, only 80.6%.

Among the participants who had STI based on the laboratory testing, only 123 (16.6%) reported with symptoms. More females (22.9%) reported with symptoms than males (3.7%). Of all those who reported STI symptoms, approximately one-fourth (25.6%) really had STI according to the laboratory results.

Table 3 includes the number and proportion of STI cases identified by physicians for each type of STIs. More than half (54.37%) of the participants were diagnosed with STI of trichomoniasis and this was the highest proportion among all five STIs. For chlamydia, gonorrhoea, HSV and syphilis, physicians identified only >10% of the real infections. Among the laboratory-determined positive cases across all five STIs, physicians accurately identified more cases in females than in males.

## DISCUSSION

This study showed that the syndromic approach might not be a very effective way to identify STI patients. The performance of the algorithm in predicting these infections was unacceptably poor. The application of the syndromic approach showed no advantage over a random guess. These findings are similar to the study of Ronsmans *et al.*,[11] which revealed that the algorithm had a sensitivity of only 9% in detecting chlamydial infection in low-risk Turkish women. Because the syndromic approach is based on self-reported symptoms and physicians' examination for visible signs, it fails to detect the asymptomatic STI patients, especially when the sample is a general population. In our study, only 3% of males and 23% of females were symptomatic; this exemplifies the challenge faced by the syndromic approach. The failure in the detection of asymptomatic patients remains to be one of the limitations of the syndromic approach.

Over-diagnosis and over-treatment are also major disadvantages of the syndromic approach. In this study, half of the physician-diagnosed STI cases actually did not have STI according to the laboratory results. The low PPV may result in erroneous diagnosis of some healthy participants as having a serious STI. Moreover, these false-positive cases would be over-treated with unnecessary antibiotics, which can cause potential side-effects and drug resistance.

Among the five STIs, we found that the syndromic approach identified more cases of trichomoniasis than chlamydia, gonorrhea, HSV and syphilis. Liu *et al.*[6] found the sensitivity and specificity of a syndromic approach to be fairly high for gonorrhea but very low for chlamydia. These results suggest that the syndromic approach may be more effective for some diseases than for others.

Interestingly, females in this study reported more symptoms than males, which is inconsistent with the previous studies.[14] The greater reporting of symptoms among women found in this study may be due to a higher sensitivity to personal health and symptoms in women than in men. Alternatively, an explanation for lower reporting in women – as found in the study by Van Dam *et al.*[14] – could be that the societal stigma towards female STI resulted in a tendency to under-report symptoms. In this study, the project staff maintained a neutral attitude towards STI and a non-critical demeanour towards participants such that the female participants would become more comfortable and report their symptoms more openly.

Historically, the syndromic approach has been regarded as a simple and effective approach for STI control, particularly in resource-poor settings where laboratory assessments are not available. However, the utilization of a syndromic approach should be specific to the setting, with consideration of different populations, STI epidemics, disease types and capacity of health-care workers. In order to assess the effectiveness of the syndromic approach, it is necessary to carry out regular evaluations of the accuracy of diagnoses and patient satisfaction. At the same time, cheaper and more effective laboratory approaches for STI diagnosis are required to ensure quality of care in STI clinics in resource-poor settings.

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## Table 1

Description of study sample

| | Number | % |
|---|---|---|
| **Gender** | | |
| Male | 2132 | 47.28 |
| Female | 2378 | 52.72 |
| **Age** | | |
| 25 or younger | 862 | 19.11 |
| 26–30 | 718 | 15.93 |
| 31–35 | 907 | 20.12 |
| 36 or older | 2023 | 44.84 |
| **Marital status** | | |
| Married/live with partner | 3717 | 82.43 |
| Never married/single | 740 | 16.4 |
| Widowed/separated/divorced | 53 | 1.18 |
| **Education** | | |
| No schooling | 379 | 8.39 |
| Primary school | 1667 | 36.99 |
| Junior high | 1882 | 41.74 |
| High school | 557 | 12.34 |
| College and higher | 25 | 0.55 |
| **Discretionary money (Yuan) per month** | | |
| ≤200 | 1597 | 35.41 |
| 201–500 | 1714 | 38.01 |
| 501–1000 | 907 | 20.1 |
| ≥1000 | 292 | 6.48 |
| Self-reported symptoms of STI | 480 | 10.72 |
| Physician-diagnosed STI | 151 | 3.46 |
| Laboratory-diagnosed STI | 743 | 16.49 |

STI = sexually transmitted infection

**Table 2**

Comparing sexually transmitted infection laboratory results to physician diagnosis and self-reported symptoms

| | | Laboratory result | | |
|---|---|---|---|---|
| | | + | – | |
| | *Physician diagnosis* | | | |
| All | + | 75 | 76 | SE = 0.103 |
| | – | 650 | 3558 | SP = 0.979 |
| Male | + | 4 | 8 | SE = 0.016 |
| | – | 239 | 1878 | SP = 0.996 |
| Female | + | 71 | 68 | SE = 0.172 |
| | – | 411 | 1680 | SP = 0.961 |
| For those who | + | 44 | 66 | SE = 0.367 |
| reported symptoms | – | 76 | 274 | SP = 0.806 |
| For those who did | + | 31 | 10 | SE = 0.051 |
| not report symptoms | – | 574 | 3277 | SP = 0.997 |
| | *Self-reported symptoms* | | | |
| All | + | 123 | 357 | SE = 0.166 |
| | – | 616 | 3378 | SP = 0.904 |
| Male | + | 9 | 28 | SE = 0.037 |
| | – | 234 | 1856 | SP = 0.985 |
| Female | + | 114 | 329 | SE = 0.229 |
| | – | 382 | 1522 | SP = 0.822 |

SE = sensitivity; SP = specificity

**Table 3**

Number and proportion of physician-diagnosed positive sexually transmitted infection by disease

| | **Chlamydia** | | **Gonorrhoea** | | **HSV** | | **Syphilis** | | **Trichomoniasis** |
|---|---|---|---|---|---|---|---|---|---|
| No. of lab-positives | 387 | | 42 | | 281 | | 57 | | 103 |
| No. diagnosed by physician (%) | 30 (7.75) | | 4 (9.52) | | 22 (7.83) | | 5 (8.77) | | 56 (54.37) |
| Gender | M | F | M | F | M | F | M | F | F only |
| No. of lab-positives | 135 | 252 | 12 | 30 | 98 | 183 | 26 | 31 | 103 |
| No. diagnosed by physician (%) | 3 (2.22) | 27 (10.71) | 0 (0.00) | 4 (13.33) | 1 (1.02) | 21 (11.48) | 0 (0.00) | 5 (16.13) | 56 (54.37) |