HSV

The psychosocial impact of serological herpes simplex type 2 testing in an urban HIV clinic


Background/objectives: Herpes simplex virus type 2 (HSV-2) is a common infection among HIV infected people. HSV type specific serologies permit the diagnosis of previously unrecognised HSV-2 infection. While substantial psychosocial morbidity has been associated with a clinical diagnosis of genital herpes, the burden associated with a serological diagnosis of HSV-2 is unclear. This study prospectively measured the psychosocial response to a new serological HSV-2 diagnosis in patients receiving care at an urban HIV clinic.

Methods: At entry, sera were tested for HSV-1 and HSV-2 antibodies by western blot. Participants completed a 90 item psychosocial and life quality questionnaire at enrolment, and at 2 weeks, 3 months, and 6 months after receiving test results.

Results: Of 248 HIV infected participants, 172 (69.4%) were HSV-2 seropositive and 116 (67.4%) seropositive people did not have a previous history of genital herpes. After correction for multiple comparisons, no statistically significant differences were detected on the psychosocial and life quality scales between those who received a new HSV-2 serological diagnosis compared with those who were HSV-2 seropositive with a history of genital herpes, or those who tested HSV-2 seronegative. Additionally, no significant changes in scores were observed during follow up.

Conclusions: HSV-2 was a common but often unrecognised infection in this urban HIV clinic and participants coped well with a positive HSV-2 result. Concerns about psychosocial burden should not deter serological testing for HSV-2. Given the epidemiological and clinical interaction between HSV-2 and HIV, these data support routine HSV-2 testing of HIV infected people.
characteristics, medical and sexual histories, and a 90 item psychosocial and life quality scale. Participants were provided with HSV-2 test results by phone approximately 2 weeks after enrolment. Those patients who tested HSV-2 seropositive were provided with information about genital herpes and counselled about the natural history of infection and risk of transmission to partners. The psychosocial questionnaires and interim sexual histories were again completed at 2 weeks, 3 months, and 6 months after test results were given. The University of Washington institutional review board approved the study protocol.

Quality of life and psychosocial scales
Self administered questionnaires were used to measure the emotional, social/occupational, and relationship burdens associated with a new HSV-2 serological diagnosis (see table 1 for examples). Internal reliability, assessed using Cronbach’s alpha, was calculated from the baseline life quality questionnaire before scoring of the individual psychosocial subscales. Since each item is correlated with the construct of the scale, person level mean substitution was used to estimate missing responses (<10% of the data were excluded (with exception to the Profile of Mood States and Herpes Related Quality of Life, for which two missing values were allowed).

Profile of Mood States
Psychological distress was measured through the Profile of Mood States Brief (POMS) questionnaire that contained 30 items from the original 65 item scale.18 Participants were asked how they had been feeling during the past week and each characteristic—for example, tense, sad, or lonely, was rated on a 5 point scale ranging from 0 (not at all) to 4 (extremely). The mood scales included tension-anxiety, depression-dejection, anger-hostility, vigour-activity, fatigue-inertia, and confusion-bewilderment. A composite score, total mood disturbance, was calculated by summing each of the individual scores for tension, depression, anxiety, fatigue, and confusion, with vigour scores subtracted.19 Cronbach’s alpha was 0.86 for tension-anxiety, 0.88 for depression-dejection, 0.86 for anger-hostility, 0.87 for vigour-activity, 0.90 for fatigue-inertia, and 0.70 for confusion-bewilderment.

Herpes Related Quality of Life (HRQoL)
Among HSV-2 seropositive participants, the impact of genital herpes on health related quality of life was measured by 25 herpes specific questions, scored on a 4 point scale as previously described.20 The HRQoL was only administered to HSV-2 seropositive participants during post-test visits. A higher score indicated greater quality of life. Cronbach’s alpha for this scale at the 2 week visit was 0.92.

Sexual relationships: present and future satisfaction
Twelve questions pertaining to current sexual satisfaction were included and participants utilised a 7 point scale. A total score was calculated; a higher score indicated decreased current sexual satisfaction. Cronbach’s alpha for present sexual satisfaction at the 2 week visit was 0.83.

The sexual optimism scale of the Multidimensional Sexual Self Concept Questionnaire (MSSCQ) was utilised to measure anticipated future sexual satisfaction.22 Sexual optimism is defined as the expectation that the future sexual aspects of one’s life will be positive and rewarding. The values of individual responses (range of 0–4) were averaged and a higher score suggested greater optimism.

Ways of coping
Six scales, derived from the ways of coping,22 including distancing, self controlling, seeking social support, and escape avoidance, were assessed. Participants were asked to respond to each item on a 4 point scale, to indicate the frequency with which each strategy was used (0 = not at all, 3 = most of the time) in 3 months before the study visit. Results are presented as the mean response for each item and higher values indicate a greater tendency to use that coping strategy. Since six different scales were to assess ways of coping, the significance level for these comparisons was revised with a Bonferroni correction. The significance level was considered $p/6 = 0.0083$.

Health Belief Model—perceived severity subscale
The Health Belief Model (HBM) seeks to identify cognitive factors predisposing people to voluntarily engage in preventive health behaviours or seek services for morbid conditions.23 The perceived severity component of the HBM defines the individual’s assessment of consequences of contracting a disease/condition or leaving the condition untreated. Perceived severity is an important psychological construct that underlies several theories in health behaviour and is postulated to be a primary determinant of how people view and respond to any given health threat.24–26 The level of perceived severity may be an important determinant of the magnitude of the action.27

Participants were asked to rate 13 situations that may be considered stressful on a 5 point scale (1 = not at all traumatic, 5 = extremely traumatic), including involvement in a car accident, the death of a close friend, or a chronic disease diagnosis as well as genital herpes. The results are
reported as the mean response of all participants to each item.

Laboratory methods
At enrolment, sera were tested for HSV-1 and HSV-2 antibodies by western blot.28

Statistical analysis
Sample size
We hypothesised that participants with a new serological diagnosis of HSV-2 will initially experience psychosocial distress, but that adjustment will occur within 6 months. To calculate the sample size, estimated mean differences and variances were obtained from a study by Patel et al, which measured the increase in quality of life associated with suppressive antiviral therapy.29 These investigators scored the HRQoL on a scale of 0 to 60, whereas ours was scored on a 100 point scale. Therefore, the mean difference and variances used for the calculations were scaled accordingly. Assuming \( \alpha = 0.05 \) and \( \beta = 0.10 \), it was estimated that 77 participants with a new serological diagnosis of HSV-2 must be followed to detect a difference of 5 and 26 to detect a difference of 10 on the HRQoL.

Psychosocial scales
Current literature suggests the psychosocial repercussions of a new serological HSV-2 diagnosis may be transitory.17 Therefore, statistical tests were chosen to detect early changes in summary scores which may resolve. Each psychosocial scale was analysed separately using generalised estimating equations (GEE) with an identity link (for normally distributed outcomes). These models account for the correlation of measures taken on the same subject and are appropriate when assessing measures that are assessed repeatedly over time. Differences in scores over time and between participants with different HSV-2 history/status were assessed simultaneously using GEE. HSV-2 history/status was summarised in three categories: “HSV-2 negative,” “HSV-2 positive, no previous history,” and “HSV-2 positive, previous history.” In scores where a baseline measure was obtained before HSV-2 testing, both linear and quadratic time effects were examined. Where only post-notification measures were obtained (2 weeks, 3 months, and 6 months) only linear time effects were assessed. Sex and race were also entered into secondary models. No interactions with gender or race could be considered, since most participants were male and white. The only interaction terms examined were those of HSV-2 history/status and time, where time could be expressed linearly (numerically) and quadratically (squared).

GEE models were performed on summary scores within each scale, with the intention of performing additional, separate modelling of subscales should overall significance be found. Since the different “ways of coping” had no appropriate summary measure, each of these was examined separately.

RESULTS
The median age of the 248 participants was 40 years (range 22–66); 211 (85.1%) were male and 166 (66.9%) were white (table 2). An annual household income of less than $15 000 was reported by 161 (64.9%) and 173 (69.7%) had publicly funded health care. Overall, 145 (62.2%) had had an AIDS diagnosis. Characteristics of the study population were...
American participants rated their summary quality of life \( (p = 0.28) \). No interaction terms were found to demonstrate differ over time \( (p = 0.63) \) or by history of HSV-2 positivity. Only subjects positive for HSV-2 completed the Herpes tension, and vigour) were not examined individually. Since no associations were found to correspond to the total mood disturbance with either sex or race. The total mood disturbance score was not found to be associated with time (linear, \( p = 0.29 \); quadratic, \( p = 0.25 \)) or with HSV-2 history/status when comparing those with a history of HSV-2 with either those with a new diagnosis or those seronegative for HSV-2 \( (p = 0.049) \) and those with a history of HSV-2 \( (p = 0.49) \), and no interactions were detected.

### Psychosocial scale outcomes

#### Profile of mood states

The total mood disturbance score was not found to be associated with time (linear, \( p = 0.29 \); quadratic, \( p = 0.25 \)) or with HSV-2 history/status when comparing those with a history of HSV-2 with either those with a new diagnosis or those seronegative for HSV-2 \( (p = 0.47 \) and \( p = 0.72 \), respectively) (table 3). No statistically significant associations were found for total mood disturbance with either sex or race. Since no associations were found to correspond to the total mood score, subscales (anger, fatigue, confusion, depression, tension, and vigour) were not examined individually.

#### Herpes Related Quality of Life (HRQoL)

Only subjects positive for HSV-2 completed the Herpes Related Quality of Life surveys. Scores were not found to differ over time \( (p = 0.63) \) or by history of HSV-2 positivity \( (p = 0.28) \). No interaction terms were found to demonstrate statistical significance. In secondary analysis, African American participants rated their summary quality of life score, on average, 7 points below white people and others \( (p = 0.0087) \), independent of time and history of HSV-2.

### Sexual relationships: present and future satisfaction

Sexual satisfaction was not found to differ over the course of follow up (for linear trend, \( p = 0.76 \); for quadratic trend, \( p = 0.84 \)) or when comparing participants with previous history of HSV-2 with either newly diagnosed subjects \( (p = 0.40) \) or HSV-2 negative participants \( (p = 0.97) \). No interaction was found with time and HSV-2 history/status. Sex and race trends were not found to be statistically significant \( (p = 0.90 \) and \( p = 0.19 \), respectively).

The MSSQ was also completely only by participants positive for HSV-2. No statistically significant differences were found over time \( (p = 0.10) \) or by history of HSV-2 positivity \( (p = 0.49) \), and no interactions were detected. Neither gender \( (p = 0.32) \) nor race \( (p = 0.92) \) were significantly associated with this summary score.

### Ways of coping

Seeking social support as a way of coping decreased over the course of follow up for subjects with a new diagnosis of HSV-2 \( (p = 0.018 \) for linear trend), but was not found to change for other subgroups. Among subjects with a new diagnosis of HSV-2, the mean score decreased from 1.4 at baseline to 1.0 at the 6 month visit. The significance level reported is that of the interaction term of HSV-2 newly diagnosed with time (linear) relative to HSV negative subjects. Use of alcohol was found to initially decrease, then increase (convex shape) slightly over follow up, \( (p = 0.019 \) and \( p = 0.018 \) for linear and quadratic time trends, respectively). This effect was found to be independent of HSV-2 antibody or history. In addition, the change is so small \( (\pm 0.1) \) as to not be clinically meaningful. Lastly, using sex to cope was slightly lower at all time points both for those with a new HSV diagnosis \( (0.12 \) lower, \( p = 0.049 \)) and those with a history of HSV-2 \( (0.14 \) lower, \( p = 0.043 \)) relative to HSV negative subjects. The differences, however, were small, and after adjusting for multiple comparisons, none of the trends observed in ways of coping

### Table 3 Profile of Mood States, by HSV-2 serostatus and study visit

<table>
<thead>
<tr>
<th></th>
<th>Mean score (SD)†</th>
<th>Baseline</th>
<th>2 weeks</th>
<th>3 months</th>
<th>6 months</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HSV-2 positive, no previous history</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anger-hostility</td>
<td>6.1 (4.9)</td>
<td>5.7 (5.0)</td>
<td>6.2 (5.1)</td>
<td>5.7 (5.3)</td>
<td></td>
</tr>
<tr>
<td>Fatigue-inertia</td>
<td>8.4 (5.3)</td>
<td>7.6 (5.5)</td>
<td>8.8 (5.4)</td>
<td>8.1 (5.7)</td>
<td></td>
</tr>
<tr>
<td>Vigour-activity</td>
<td>8.4 (4.4)</td>
<td>8.3 (4.9)</td>
<td>7.5 (5.3)</td>
<td>8.0 (4.4)</td>
<td></td>
</tr>
<tr>
<td>Depression-dejection</td>
<td>6.4 (5.4)</td>
<td>6.2 (5.5)</td>
<td>6.4 (5.5)</td>
<td>6.2 (5.6)</td>
<td></td>
</tr>
<tr>
<td>Confusion-bewilderment</td>
<td>6.6 (4.0)</td>
<td>6.5 (4.3)</td>
<td>6.9 (3.9)</td>
<td>6.6 (4.1)</td>
<td></td>
</tr>
<tr>
<td>Tension-anxiety</td>
<td>6.8 (5.1)</td>
<td>6.2 (4.9)</td>
<td>6.6 (4.7)</td>
<td>6.0 (5.0)</td>
<td></td>
</tr>
<tr>
<td>Mood disturbance</td>
<td>26.0 (22.9)</td>
<td>24.0 (24.0)</td>
<td>27.3 (23.3)</td>
<td>24.3 (24.6)</td>
<td></td>
</tr>
<tr>
<td><strong>HSV-2 positive, previous history</strong></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Anger-hostility</td>
<td>6.0 (4.5)</td>
<td>5.8 (4.9)</td>
<td>5.7 (5.0)</td>
<td>5.7 (4.4)</td>
<td></td>
</tr>
<tr>
<td>Fatigue-inertia</td>
<td>9.7 (4.9)</td>
<td>8.7 (5.0)</td>
<td>8.8 (5.1)</td>
<td>8.5 (5.0)</td>
<td></td>
</tr>
<tr>
<td>Vigour-activity</td>
<td>7.1 (4.4)</td>
<td>8.2 (5.1)</td>
<td>8.1 (4.9)</td>
<td>7.2 (4.5)</td>
<td></td>
</tr>
<tr>
<td>Depression-dejection</td>
<td>6.8 (5.7)</td>
<td>6.2 (5.1)</td>
<td>6.0 (5.0)</td>
<td>5.6 (4.2)</td>
<td></td>
</tr>
<tr>
<td>Confusion-bewilderment</td>
<td>7.4 (4.1)</td>
<td>7.1 (4.2)</td>
<td>6.7 (3.9)</td>
<td>6.3 (3.5)</td>
<td></td>
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<tr>
<td>Tension-anxiety</td>
<td>7.2 (5.4)</td>
<td>6.4 (5.0)</td>
<td>7.0 (5.2)</td>
<td>6.9 (5.1)</td>
<td></td>
</tr>
<tr>
<td>Mood disturbance</td>
<td>30.3 (21.0)</td>
<td>26.1 (21.5)</td>
<td>26.2 (23.2)</td>
<td>24.9 (18.0)</td>
<td></td>
</tr>
<tr>
<td><strong>HSV-2 negative</strong></td>
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<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Anger-hostility</td>
<td>5.4 (4.2)</td>
<td>5.5 (4.4)</td>
<td>6.0 (4.6)</td>
<td>5.6 (3.8)</td>
<td></td>
</tr>
<tr>
<td>Fatigue-inertia</td>
<td>8.2 (5.3)</td>
<td>8.6 (5.5)</td>
<td>92.5 (3.5)</td>
<td>8.4 (4.7)</td>
<td></td>
</tr>
<tr>
<td>Vigour-activity</td>
<td>8.5 (4.6)</td>
<td>8.3 (4.9)</td>
<td>7.6 (4.7)</td>
<td>7.9 (4.4)</td>
<td></td>
</tr>
<tr>
<td>Depression-dejection</td>
<td>5.2 (4.7)</td>
<td>5.3 (4.9)</td>
<td>5.7 (4.7)</td>
<td>5.3 (4.0)</td>
<td></td>
</tr>
<tr>
<td>Confusion-bewilderment</td>
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<td>6.1 (4.2)</td>
<td>7.0 (3.7)</td>
<td>6.6 (3.6)</td>
<td></td>
</tr>
<tr>
<td>Tension-anxiety</td>
<td>6.4 (4.5)</td>
<td>7.0 (5.1)</td>
<td>6.8 (4.5)</td>
<td>6.7 (4.3)</td>
<td></td>
</tr>
<tr>
<td>Mood disturbance</td>
<td>22.6 (22.0)</td>
<td>24.7 (24.2)</td>
<td>26.5 (21.2)</td>
<td>24.5 (19.2)</td>
<td></td>
</tr>
</tbody>
</table>

†Higher score indicates elevated mood state.

*Correlation of mood disturbance with HSV-2 positivity is slightly over follow up, \( (p = 0.019 \) and \( p = 0.018 \) for linear and quadratic trend, respectively). This effect was found to be independent of HSV-2 antibody or history. In addition, the change is so small \( (\pm 0.1) \) as to not be clinically meaningful. Lastly, using sex to cope was slightly lower at all time points both for those with a new HSV diagnosis \( (0.12 \) lower, \( p = 0.049 \)) and those with a history of HSV-2 \( (0.14 \) lower, \( p = 0.043 \)) relative to HSV negative subjects. The differences, however, were small, and after adjusting for multiple comparisons, none of the trends observed in ways of coping
scores were significant (Bonferroni corrected α for six subscales = 0.0083) (table 4).

Health belief model, perceived severity subscale
Trauma associated with receiving a new HSV-2 diagnosis (mean 2.9) in this population was similar to that associated with involvement in a car accident without hospitalisation (mean 2.7), receiving a poor work evaluation (mean 2.8) or finding out that you have high blood pressure (mean 2.9) (fig 1). The loss of a job (mean 3.2), a HIV/AIDS (mean 3.6), prostate/breast cancer (mean 3.6), or diabetes diagnosis (mean 3.6), being robbed (mean 3.7), ending a relationship (mean 3.9), and the death of a close friend (mean 4.2) were ranked as more traumatic than a new herpes diagnosis. Items ranked as less traumatic included moving to a new house or apartment (mean 2.2), or committing a minor violation of the law (mean 2.5). The overall rank of these items did not vary by sex, race, or HSV-2 status (data not shown).

DISCUSSION
Our prospective study found no evidence of psychosocial morbidity associated with a new serological diagnosis of HSV-2 in HIV infected participants. Among the scales used to measure the emotional, social, and relationship burden associated with HSV-2, no differences were detected between those who received a new HSV-2 serological diagnosis, those
who tested HSV-2 seropositive but had a history of genital herpes, and those who tested HSV-2 seronegative. One of the scales showed a decrease in social support seeking behaviour among those with new diagnosis, but it did not reach statistical significance after correction for multiple comparisons. Additionally, no significant changes were observed over the course of the 6 month follow up period. In relation to other events that may be perceived as stressful, a new genital herpes diagnosis was ranked as only somewhat traumatic. While different scales were used, these findings are in general agreement with the other studies addressing the psychosocial sequelae associated with a new HSV-2 serological diagnosis in people attending an STD clinic\textsuperscript{15,29} and in a qualitative study in people attending a variety of healthcare facilities.\textsuperscript{17} Lack of statistically significant results raises the issue of adequate power. A priori, we calculated that 77 people with a new HSV-2 serological diagnosis were needed to detect a paired difference of 5 points on the HRQoL scale with 90% power; we enrolled 116. Differences found between groups based on HSV-2 serology and history of genital herpes never exceeded 3 points, a figure that appears not to be clinically relevant. Similarly, the observed effect size was small on other scales, lending support to the conclusion that there is no true difference between the groups and no differences were noted in longitudinal follow up.

The results of this study are striking when compared with the published literature documenting the psychological distress experienced by those with a new clinical diagnosis of genital herpes.\textsuperscript{12} The discrepancy may be partially explained by the frequency and severity of symptoms experienced by those with a clinical versus serological diagnosis of genital herpes. A clinical diagnosis of genital herpes is predicated upon a first episode of genital lesions, which may be a severe illness in a young, otherwise healthy person. Most participants with symptomatic HSV-2 adjust to the diagnosis, although recurrences have been shown to impair this process.\textsuperscript{12,25} In contrast, prevalent cases of HSV-2 infection first detected by serological tests are more likely to be characterised by milder disease. Before testing, these participants were not bothered by genital herpes symptoms, and had little reason to anticipate that they will be in the future. These findings highlight the role of severe clinical illness in determining the subsequent psychosocial function among person with HSV-2 infection.

Another potential explanation of our null results may be linked to the clinical context and social milieu in which this study was performed. Living with HIV infection is inherently stressful, in addition to the poverty, illicit drug use, and mental illness that are often pervasive within this group. As such, it is possible that the scales utilised were not able to detect anxiety attributable to an HSV-2 diagnosis beyond the appreciable level of stress that is already experienced by members of this cohort. Future studies may explore this issue by examining the impact of a serological diagnosis of genital herpes on otherwise healthy people.

Because our observations were made in the context of a research protocol, the consent process and the counselling attendant to the HSV testing were probably more informative than occurs in the course of routine clinical care. This may also have diminished the observed effect of serological testing and allayed anxiety about a positive HSV-2 result to some extent.

Our data recapitulate that HSV-2 is an extremely prevalent and mostly unrecognised infection among HIV seropositive people. The majority (69.4%) of this cohort had antibodies to HSV-2, and two thirds of these were not aware of their infection before study entry. Given the high prevalence in this group, even a modest fraction of people experiencing recurrent disease translates into substantial morbidity. From a public health standpoint, the high prevalence of HSV-2 among this group of sexually active people has implications for HIV transmission, as HSV-2 has been shown to reactivate more frequently among immunocompromised individuals, potentially rendering them contagious for both infections. This study demonstrates that HSV-2 testing among HIV seropositive participants is acceptable, and not associated with negative psychosocial consequences. As concern for the psychosocial impact of HSV serological testing has been cited as the major deterrent from the routine introduction of such tests into clinical care,\textsuperscript{19} this study should be reassuring, suggesting that those with HIV infection will adequately cope with the knowledge of having HSV-2 infection.

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Contributors

JLM, data collection, data analysis, and manuscript preparation; RAC, acquisition of the study funds, selection of the assessment instruments and design the final questionnaire, and manuscript preparation; WHW, acquisition of study funds, study design, data analysis, and manuscript preparation; DC, data management, manuscript preparation; RA-M, study design, supervision of HSV serological testing, and manuscript preparation; AM, statistical analysis, manuscript preparation; RDH, data collection, study implementation, manuscript preparation; RDC, acquisition of study funds, selection of the assessment instruments and design of the final questionnaire, data analysis and manuscript preparation; AW, acquisition of study funds, study design, selection, and assessment of study instruments, data analysis, and manuscript preparation.

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HSV-2 testing in HIV patients

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