

**Table S1: Baseline characteristics by HSV-1 and HSV-2 DNA detection**

Variable	Level	Overall (N=251) % (n/N)	HSV-1 (N=24) % (n/N)	No HSV-1 (N=227) % (n/N)	P value	HSV-2 (N=14) % (n/N)	No HSV-2 (N=237) % (n/N)	P value
Age (years)	Median (IQR)	23 (21 - 27)	22 (20 - 24)	23 (21 - 27)	0.265	24 (22 - 27)	23 (21 - 27)	0.547
Age category (years)	Less than 25	64.9 (163)	79.2 (19)	63.4 (144)		57.1 (8)	65.4 (155)	
	25 and over	35.1 (88)	20.8 (5)	36.6 (83)	0.176	42.9 (6)	34.6 (82)	0.570
The highest level of education	Primary education	0.4 (1/247)	4.5 (1/22)	0		0	0.4 (1/233)	
	Secondary education	72.9 (180/247)	63.6 (14/22)	73.8 (166/225)	0.059	100.0 (14)	71.2 (166/233)	0.053
	Tertiary education	26.7 (66/247)	31.8 (7/22)	26.2 (59/225)		0	28.3 (66/233)	
Reason for presentation	STI symptoms	88.4 (222)	87.5 (21)	88.5 (201)		100.0 (14)	87.8 (208)	
	No symptoms	8.0 (20)	8.3 (2)	7.9 (18)	0.773	0	8.4 (20)	
	Other	3.6 (9)	4.2 (1)	3.5 (8)		0	3.4 (9)	0.771
Median number of sex partners in last two months	Median (IQR)	1 (1 - 2)	1 (1 - 2)	1 (1 - 2)	0.106	1 (1 - 2)	1 (1 - 2)	1.000
Sex partners in the last two months	None	1.2 (3)	0	1.3 (3)		0	1.3 (3)	
	1 partner	68.1 (171)	54.2 (13)	69.6 (158)	0.218	71.4 (10)	67.9 (161)	1.000
	> 1 partner	30.7 (77)	45.8 (11)	29.1 (66)		28.6 (4)	30.8 (73)	
Gender(s) of sex partner(s)	Men	98.4 (247)	95.8 (23)	98.7 (224)		100.0 (14)	98.3 (233)	1.000
	Both	1.6 (4)	4.2 (1)	1.3 (3)	0.333	0	1.7 (4)	
Type of sex (Anal)	Yes	4.8 (12)	4.2 (1)	4.8 (11)	1.000	7.1 (1)	4.6 (11)	0.506
Type of sex (Oral)	Yes	28.7 (72)	37.5 (9)	27.8 (63)	0.345	21.4 (3)	29.1 (69)	0.763
Contraceptive use	Yes	35.9 (90)	37.5 (9)	35.7 (81)		42.9 (6)	35.4 (84)	
	No	64.1 (161)	62.5 (15)	64.3 (146)	0.827	57.1 (8)	64.6 (153)	0.577
Type of contraceptive	Condom only	7.8 (7/90)	22.2 (2/9)	6.2 (5/81)		0	8.3 (7/84)	
	Oral pill	11.1 (10/90)	0	12.3 (10/81)	0.382	33.3 (2)	9.5 (8/84)	
	Progesterone injections	58.9 (53/90)	66.7 (6/9)	58.0 (47/81)		66.7 (4)	58.3 (49/84)	0.323
	Subdermal implant	20.0 (18/90)	11.1 (1/9)	21.0 (17/81)		0	21.4 (18/84)	
	IUD	2.2 (2/90)	0	2.5 (2/81)		0	2.4 (2/84)	
Genital examination	Abnormal	48.2 (121)	50.0 (12)	48.0 (109)	1.000	50.0 (7)	48.1 (114)	1.000
	Normal	51.8 (130)	50.0 (12)	52.0 (118)		50.0 (7)	51.9 (123)	
Any STI (CT/TV/NG)	Yes	20.3 (51)	0	22.5 (51)		14.3 (2)	20.7 (49)	
	No	79.7 (200)	100.0 (24)	77.5 (176)	0.006	85.7 (12)	79.3 (188)	0.741
BV by Nugent Score	Median (IQR)	5 (3 - 7)	4.5 (3 - 7)	5 (3-7)	0.275	6.5 (3 - 7)	5 (3 - 7)	0.636
BV by Nugent Score	Normal (0 - 3)	30.7 (77)	37.5 (9)	30.0 (68)		35.7 (5)	30.4 (72)	
	Subclinical (4 - 6)	35.1 (88)	29.2 (7)	35.7 (81)	0.716	14.3 (2)	36.3 (86)	
	BV (7-10)	34.3 (86)	33.3 (8)	34.4 (78)		50.0 (7)	33.3 (79)	0.200

IQR; interquartile range, IUD; intrauterine device, CT; *Chlamydia trachomatis*; NG; *Neisseria gonorrhoea*, TV; *Trichomonas vaginalis*

Table S2: Associations between cytokine concentrations and HSV-2 DNA detection

Cytokine	$\beta$ coefficient	Lower (95% CI)	Upper (95% CI)	P value	FDR p value
IL-1 $\alpha$	0.28	-0.25	0.81	0.300	0.599
IL-1 $\beta$	0.44	-0.23	1.12	0.197	0.499
IL-6	0.24	-0.19	0.67	0.272	0.593
IL-12p40	0.72	-0.16	1.60	0.107	0.499
IL-12p70	0.22	-0.45	0.89	0.514	0.663
IL-18	0.60	0.01	1.18	<b>0.045</b>	0.499
MIF	0.36	-0.19	0.92	0.195	0.499
TNF- $\alpha$	0.18	-0.21	0.57	0.368	0.610
TNF- $\beta$	0.41	-0.20	1.01	0.187	0.499
TRAIL	0.46	-0.42	1.34	0.305	0.599
CTACK	-1.02	-1.77	-0.26	<b>0.009</b>	0.412
EOTAXIN	0.08	-0.77	0.93	0.852	0.870
GRO- $\alpha$	0.26	-0.54	1.05	0.525	0.663
IL-8	0.17	-0.41	0.75	0.564	0.695
IL-16	0.62	-0.23	1.47	0.150	0.499
IP-10	0.74	-0.06	1.53	0.070	0.499
MCP-1	0.08	-0.50	0.66	0.780	0.832
MCP-3	0.77	-0.18	1.72	0.114	0.499
MIG	0.50	-0.03	1.02	0.063	0.499
MIP-1 $\alpha$	0.11	-0.57	0.80	0.744	0.814
MIP-1 $\beta$	0.19	-0.50	0.89	0.586	0.703
RANTES	0.29	-0.55	1.13	0.496	0.663
IFN- $\alpha$ 2	0.36	-0.40	1.13	0.350	0.610
SDF-1 $\alpha$	0.18	-0.14	0.50	0.271	0.593
$\beta$ -NGF	0.70	-0.18	1.58	0.119	0.499
FGF BASIC	-0.15	-0.89	0.59	0.688	0.786
G-CSF	0.10	-0.50	0.70	0.746	0.814
GM-CSF	0.22	-0.38	0.83	0.468	0.661
HGF	0.23	-0.39	0.85	0.464	0.661
IL-3	0.54	-0.19	1.27	0.146	0.499
IL-7	0.35	-0.18	0.89	0.193	0.499
IL-9	0.32	-0.16	0.81	0.193	0.499
LIF	0.40	-0.11	0.91	0.128	0.499
M-CSF	0.34	-0.11	0.78	0.135	0.499
PDGF- $\beta\beta$	0.09	-0.65	0.82	0.821	0.856
SCF	0.54	-0.51	1.58	0.312	0.599
SCGF- $\beta$	-0.19	-0.61	0.24	0.386	0.616
VEGF	0.43	-0.16	1.01	0.160	0.499
IFN- $\gamma$	-0.39	-1.01	0.24	0.224	0.537
IL-2	-0.36	-1.20	0.48	0.398	0.616
IL-4	0.28	-0.33	0.88	0.367	0.610
IL-5	0.29	-0.46	1.03	0.447	0.661
IL-13	-0.19	-1.11	0.73	0.679	0.786
IL-15	0.35	-0.36	1.06	0.328	0.606
IL-17A	0.05	-0.92	1.03	0.914	0.915
IL-2R $\alpha$	0.64	-0.06	1.34	0.072	0.499
IL-10	0.19	-0.38	0.75	0.521	0.663
IL-1RA	0.66	-0.09	1.42	0.084	0.499

$\beta$ -coefficients and corresponding P-values were determined using linear regression. <sup>1</sup>Multivariable regression models were adjusted for Nugent's score, sexually transmitted infections, number of sexual partners in the last two months, and genital examination. Significant P-values ( $P<0.05$ ) are indicated by

shading and significance after FDR adjustment is indicated by (\*). Abbreviations: interleukin (IL)-1 $\beta$ , IL-1RA, IL-2, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL10, IL-12p70, IL-12p40, IL-16, IL-18, IL-1 $\alpha$ , IL-2R $\alpha$ , IL-3, IL-13, IL-15, IL-17, basic fibroblast growth factor (FGF), cutaneous T-cell attraction chemokine (CTACK), eotaxin, granulocyte colony stimulating fact (G-CSF), granulocyte macrophage colony stimulating factor (GM-CSF), growth regulated (GRO)- $\alpha$ , hepatocyte growth factor (HGF), interferon (INF)- $\gamma$ , IFN- $\alpha$ 2, interferon gamma induced protein (IP)-10, leukaemia inhibitory factor (LIF), monocyte chemotactic protein (MCP)-1, MCP-3, macrophage colony-stimulating factor (M-CSF), monokine induced by gamma-Interferon (MIG), macrophage migration inhibitory factor (MIF), macrophage inflammatory protein (MIP)-1 $\alpha$ , MIP-1 $\beta$ , nerve growth factor (NGF)- $\beta$ , platelet derived growth factor (PDGF)- $\beta\beta$ , regulated upon activation normal T cell expressed and presumably secreted (RANTES), stem cell factor (SCF), stem Cell Growth Factor (SCGF)- $\beta$ , stromal derived factor (SDF)-1 $\alpha$ , tumour necrosis factor (TNF)- $\alpha$ , TNF- $\beta$ , TNF-related apoptosis inducing ligand (TRAIL), vascular endothelial growth factor (VEGF).