



# Risk Factors for Hepatitis C in HIV positive MSM

## A Preliminary Analysis of a Case Control Study

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### Background:

Increasing numbers of infections with the hepatitis C virus (HCV) in HIV positive men who have sex with men (MSM) have been reported by European clinicians at least since the year 2001 [1-4]. There is no doubt that HCV infections arise from direct blood contacts, as taking place amongst injecting drug users who exchange needles or during blood transfusions (in Germany, mandatory HCV antibody screening of donated blood was introduced in 1991).

However, the role of sexual routes of HCV transmission is still unclear and controversial [5-10]. Major longitudinal studies, both with serodiscordant heterosexual couples [11-14] and HIV-negative MSM [15-16], failed to come up with clear indications for an epidemiologically relevant sexual transmission. This appears surprising since sexual transmission of HCV would be biologically plausible due to the presence of the virus in body fluids involved in sexual intercourse [17-19].

Therefore, the aim of this study is to explore social, behavioural/sexual, clinical (such as ulcerative STIs like lymphogranuloma venereum [20]) or nosocomial risk factors [21] for hepatitis C in HIV positive MSM.

The role of the compromised immune system in relation to contagiousness and susceptibility is largely unclear [2, 22-23] but cannot be investigated by this type of study. However, the guiding hypothesis of this epidemiological approach is that HIV infection is a significant co-factor for a subsequent HCV infection among sexually active MSM.

### Results:

So far, 22 cases and 44 controls could be included for preliminary evaluation. In bivariate analyses (tables 1 and 2), significant risk factors were (1) consumption of nasally administered drugs like cocaine or speed (OR=10.5), (2) history of major surgery (OR=9.1), (3) group sex (OR=7.7), (4) a history of >5 episodes of unprotected anal intercourse (UAI) within the past year (OR=7.5), (5) bleeding anal injuries from any sort of sexual intercourse (OR=7.1), (6) "fisting" (OR=5.9), or (7) use of sildenafil or comparable inhibitors of phosphodiesterase-5 (OR=4.1).

In a logistic regression, nasally administered drugs and bleeding anal injuries remained in the model (Fig. 1).

Table 1: Bivariate analysis (KABaSTI main questionnaire)

	Cases n (%)	Controls n (%)	OR	95% confidence interval
<b>persons</b>	22 (31.3)	44 (67.7)		
<b>age group</b>				
<30 years	2 (9.1)	5 (11.4)	1	
30-44 years	16 (72.7)	33 (75.0)	1.21	0.21 - 6.94
>45 years	4 (18.2)	6 (13.6)	1.67	0.21 - 13.22
<b>city size</b>				
< 1 million	0 (0.0)	14 (31.3)	*	(Fisher's exact test: n. s.)
≥ 1 million	21 (100.0)	28 (66.7)	*	
<b>education</b>				
< 12 years	9 (40.9)	21 (48.8)	1	
≥ 12 years	13 (59.1)	22 (51.2)	1.38	0.49 - 3.90
<b># of sexual partners</b>				
≤10	7 (31.8)	23 (53.1)	1	
>10	15 (68.2)	20 (46.5)	2.46	0.84 - 7.25
<b>any UAI*</b>				
No	8 (40.0)	30 (68.3)	1	
Yes	12 (60.0)	6 (16.7)	7.5	2.14 - 26.24
<b>insertive anal intercourse</b>				
never - sporadic	9 (40.9)	22 (50.4)	1	
often - always	13 (59.1)	17 (43.6)	1.87	0.65 - 5.41
<b>receptive anal intercourse</b>				
never - sporadic	9 (40.9)	24 (54.5)	1	
often - always	13 (59.1)	15 (38.3)	2.31	0.79 - 6.71
<b>S/M or "fisting"</b>				
never - sporadic	15 (68.2)	33 (84.6)	1	
often - always	7 (31.8)	6 (15.4)	2.36	0.74 - 8.20

Figure 1: Odds Ratios from bi- and multivariate analyses

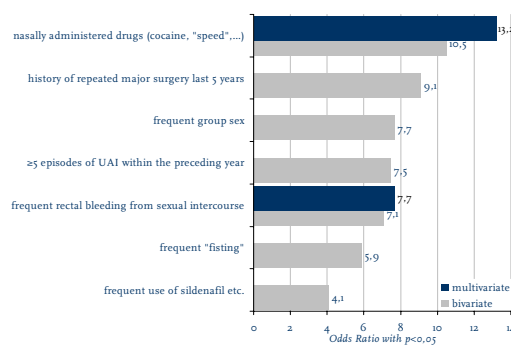


Table 2: Bivariate analysis (Hepatitis C additional questionnaire)

Hepatitis C questionnaire	Cases n (%)	Controls n (%)	OR	95% confidence interval
<b>last CD4 count</b>				
>200/µl	15 (68.2)	27 (61.0)	1	
250-200/µl	3 (13.6)	7 (15.9)	0.77	0.17 - 3.43
<200/µl	1 (5.3)	2 (6.5)	0.90	0.08 - 10.77
<b>blood transfusion</b>				
no	21 (95.5)	39 (89.1)	1	
yes	1 (4.5)	2 (4.9)	0.93	0.79 - 10.85
<b>major surgery</b>				
no / once	15 (68.2)	39 (89.1)	1	
(since the year 2000)	7 (31.8)	2 (4.9)	9.10	1.70 - 48.85
<b>major dental treatment</b>				
no	21 (95.5)	35 (84.4)	1	
yes	1 (4.5)	6 (14.6)	0.28	0.31 - 2.47
<b>endoscopy</b>				
no / once	13 (59.1)	27 (67.5)	1	
repeatedly	9 (40.9)	13 (32.5)	1.44	0.49 - 4.22
<b>acupuncture</b>				
no / once	19 (86.4)	37 (90.2)	1	
repeatedly	3 (13.6)	4 (9.8)	1.46	0.30 - 7.20
<b>living in HCV-pos. person</b>				
yes	20 (90.9)	38 (95.0)	1	
no	2 (9.1)	2 (5.0)	1.90	0.25 - 14.52
<b>UAI* w HCV-pos. partner</b>				
yes	14 (63.6)	38 (97.4)	1	
no	2 (9.1)	2 (5.0)	5.43	0.46 - 64.66
<b>tattoo</b>				
no / once	21 (95.5)	35 (84.4)	1	
repeatedly	1 (4.5)	6 (14.6)	0.28	0.03 - 2.47
<b>body piercing</b>				
no / once	19 (86.4)	38 (97.4)	1	
repeatedly	3 (13.6)	3 (7.3)	2.78	0.84 - 9.12

### Discussion:

Despite relative small numbers of cases and controls, the results from bivariate analyses show that unprotected anal intercourse (UAI) *per se* does not sufficiently explain HCV transmission among HIV positive MSM. However, the possibility of HCV coinfection is frequently used to encourage HIV positive MSM to consistently use condoms, and condom use seems to be the predominant focus in HCV prevention messages for MSM. We fear that in this narrow perspective, other and possible more effective HCV prevention messages could be neglected.

Non-IDU-related transmission of HCV in MSM seems to take place in sexual contexts involving more factors than unprotected anal intercourse alone. 46% of cases (vs. 10% of controls) report that when having sex, it is frequently or always in a group sex situation. 27% of cases (vs. 5% of controls) report frequent rectal bleeding while having sex. Anal insertion of sex toys or forearms easily leads to bleeding; the risk of small rectal injuries is also high if anal intercourse of any kind is temporally extended by use of sildenafil or similar prescription drugs. Use of drugs like cocaine or amphetamines implies two distinct possible transmission risks: non-intended (direct) ulcerative effects on nasal or rectal mucosa, bearing a risk of blood borne transmission through shared and contaminated drug equipment, sex toys, or lubricants; on the other hand the intended (indirect) mucosa damaging effect of triggering sexual desire or feelings of invulnerability. Cognitive impairment or reduced algesia are not uncommon under the influence of party drugs. Direct immunological effects of party drugs, being especially common in HIV positive MSM, are currently discussed [26]. Serotyping among HIV positive MSM might further enhance the risk of HCV transmission by increasing situational HCV prevalence.

Interestingly, while social practices like body piercing or tattoos were not associated with HCV infection, cases were more likely than controls to report "major surgery" since the year 2000 (32% vs. 5%). This could especially be applicable to HIV-positive MSM, who due to the nature of HIV infection, spend more time in hospitals than other men their age, or usually enter the operation theatres last on the list. We did not ask which type of operations our participants had undergone. As the "major surgery" variable clustered with the sex-associated variable, we suggest that the operations could be related to sexual intercourse, such as circumcision, anal condyloma, or even rectal proctectomy - serving as a proxy for certain sexual practices rather than for nosocomial safety. However, bias due to place of diagnosis cannot be ruled out - it is possible that the HCV was first diagnosed at time of operation - and the cross-sectional design of our study does not allow causal inferences. Large cohort studies on HIV positive MSM should therefore survey participants' history of surgery and hospital admission.

### Conclusions:

There is evidence that in HIV positive MSM, a complex interaction between sexual practices and associated behaviour like consumption of cocaine or amphetamines are relevant risk factors for HCV transmission.

Especially in risk factor analyses in MSM populations, sexual practices have to be surveyed in detail, instead of focussing on unprotected anal intercourse only. Prevention efforts are needed to communicate sexual or sex-associated routes of transmission for HCV that can not be prevented by condoms alone.

However, it is notable that despite high standards of hygiene in German hospitals, cases were more likely than controls to report nosocomial exposures. More cases and controls are needed to provide adequate power and precision.

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### Methods:

In 2006, the Robert Koch Institute conducted a case control study embedded in a survey on knowledge, attitudes and behaviour in German MSM as to STIs (KABaSTI-study [24]). Into this cross sectional study, we embedded a case control study. Participants were recruited between September 2006 and January 2007.

Cases consisted of HIV/HCV coinfecting MSM without history of injecting drug use (IDU), as the sharing of related equipment is the leading risk factor for infections with HCV in industrialized countries. All cases were recruited from an ongoing clinical study (on treatment of HIV/HCV coinfection) at the University of Bonn, where they had been referred to from other medical sites in Germany (HIV clinics, private practices etc.).

HIV positive MSM without HCV infection, matched for age group, served as controls. For each case, two controls were recruited from the respective referring medical sites. They were *not* necessarily tested for HCV antibodies before inclusion, to reduce selection bias. However, known HCV positive MSM or HIV negative MSM were *not* considered as possible controls. Participants' HCV negative serostatus was confirmed by an automated chemiluminescent microparticle immunoassay (CMIA, ARCHITECT anti-HCV) from dried blood specimens [25].

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