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Exploring group differences in the response to a sexual risk reduction intervention to prevent hepatitis C virus reinfection in HIV-infected MSM: A mixed-methods study

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Exploring group differences in the response to a sexual risk reduction intervention to prevent hepatitis C virus re-infection in HIV-infected MSM: A mixed-methods study

Abstract (max 200 words) (198)

To prevent hepatitis C virus (HCV) reinfection, within the *Swiss HCVree Trial*, a preventive risk reduction intervention was implemented alongside curative treatment. Formative qualitative research identified three response patterns to the intervention. This mixed-methods study's aim was to cross-validate group differences in a) the content of sexual risk reduction goals set during intervention and b) the extent of their behavioural change in condomless anal intercourse with non-steady partners (nsCAI), sexualised and intravenous drug use at start and six-month post-intervention. Qualitative thematic analysis was used to summarize goal setting domains. Quantitative descriptive analysis was used to evaluate group differences based on assumptions of the group descriptions. Results largely confirmed assumptions on inter-group response differences in goal setting and behaviour: as expected group 1 *Avoid risks* showed the lowest HCV risk profile with changes in nsCAI. Group 2 *Minimize-risks* and Group 3 *Accept-risks* showed unchanged nsCAI. Group 3 had the highest HCV risk profile. Differences in their goal preferences (1: condom use; 2 reduction blood exposure; 3 safer dating) highlight diversity in attitudes to behavioural change. Our results improve understanding of variability in intervention responses such as changes in attitudes and behaviour. This provides evidence for intervention tailoring and outcome measurement.

Trial registration number: NCT02785666

Keywords: Homosexuality, Male; hepatitis C; HIV Infections; Sex Counselling; Harm Reduction

Introduction

The recent availability and broad implementation of well-tolerated hepatitis C virus (HCV) treatment have resulted in high cure rates (Braun et al., 2020; European Association for the Study of the Liver (EASL), 2020). However, eradication efforts have been accompanied by growing numbers of reinfections. The highest-risk population is HIV-diagnosed men-who-have-sex-with-men (MSM) showing a 52% increase, resulting in the incidence of new cases increasing from 5.93 to 9.02/100 person years between 2014 and 2018 (Berenguer et al., 2019; Ingiliz et al., 2019). This is a serious public health challenge. It emphasises the need for combined prevention strategies that include interventions to reduce sexual- and drug-use-related risk taking in this population (Lockart et al., 2019; Nijmeijer et al., 2019).

Sexual HCV transmission plays a major role in reinfection via associated risk behaviours including condomless anal intercourse, receptive fisting, group sex, and sexualized drug use (SDU) including injection drug use (IDU) (Berenguer et al., 2019; Chan et al., 2016; Danta & Rodger, 2011; Ghisla et al., 2016; Schmidt et al., 2011). While sound evidence supports sexual risk reduction interventions for HIV prevention in MSM (Crepaz et al., 2015; Higa et al., 2013; Johnson et al., 2008), few evidence-based interventions are either available or under development to reduce HCV risk (Prinsenberg et al., 2020).

In 2016/17, the *Swiss HCVree Trial* tested a multi-component HCV prevention program targeting HIV/HCV co-infected MSM. Its participants were recruited from the *Swiss HIV Cohort Study* (SHCS) sample (Swiss HIV Cohort Study et al., 2010). All received direct-acting antivirals (DAAs). Additionally, those who reported condomless anal intercourse with non-steady partners (nsCAI) over the previous year were invited to participate in a newly developed theory-based HCV risk reduction intervention (D. L. Braun et al., 2019).

Participants received four individual counselling sessions, each delivered by a trained nurse and supported by an eHealth tool. The first of these focused on exploring the participant's emotions and values regarding their sexuality and drug use, the second on perceived benefits/disadvantages of their current sexual behaviour, the third on setting individual behaviour change goals compatible with their preferences and confidence that they could achieve those goals, and the fourth on goal implementation and reinforcement (Nicca et al., 2017).

In order to understand how to further adapt this behavioural intervention for effective intervention scale-up, we extended the quantitative outcome evaluation in a pre-post design with a qualitative study of participants' experiences with and responses to the program. This qualitative evaluation was conducted in a purposefully selected subsample of 17 of the original intervention's 51 participants. The purpose was to have a sample that represented variation in key characteristics (e.g., various ages, years since HCV/HIV diagnosis, treated in different clinics etc.) of the intervention group (Künzler-Heule et al., 2021). We found three distinct response patterns in participants regarding the study program: group 1 *Avoid risks*: get rid of HCV for life; group 2 *Minimize risks*: live as long as possible without HCV; and group 3 *Accept risks*: live with the risk of HCV. These patterns reflect differences in how various MSM perceived life with HCV, how they experienced DAAs treatment, how they used the intervention and how they dealt with their vulnerability to reinfection (table 1).
[Insert table 1 here]

To evaluate these groups' potential for further adaptation and planning of behavioural interventions, especially for group-specific tailoring, the overall aim of this convergent mixed-methods study was to cross-validate group differences regarding a) the content of the sexual risk reduction goals set in the third intervention session and b) the extent of participants' behavioural change regarding nsCAI, sexualised drug use (SDU) and

intravenous drug use (IDU) first at the start of the study (t0), and after a three-month course of DAAs treatment and counselling, followed by a three-month post-intervention period (t6) (total: 6 months).

In this study, qualitative thematic analysis was used to categorize individual goals into domain summaries. For the purpose of analysis, these summaries indicate participants' choices between goal-setting strategies regarding sexual risk reduction. Regarding our 17-person purposeful sample, which we used to differentiate the response patterns, quantitative descriptive analysis was used to explore how representative that sample was compared with the overall participant sample. Then, based on the descriptions of the three response groups our T0 and T6 measurements allowed us to evaluate inter-group differences in relation to three assumptions: a. that group 1 *Avoid-risks* would show low levels of nsCAI and SDU at t0, maintained at t6; b. that group 2 *Minimize-risks* would show high levels of nsCAI and SDU at t0, but lower levels of SDU at t6; and c. that group 3 *Accept-risks* would show high levels of nsCAI and SDU both at t0 and at t6.

Materials & Methods

To cross-validate inter-group differences, we applied a convergent mixed-methods approach. For this type of design, qualitative and quantitative data are collected concurrently, analysed separately, then merged for comparison (Creswell & Plano Clark, 2011) (see figure 1).

[Insert figure 1 here]

We used all available qualitative and quantitative data from MSM who had participated in both *Swiss HCVree Trial's* interventions (D. L. Braun et al., 2019), *i.e.,* DAAs medical treatment plus sexual risk reduction counselling (n=51). Two arguments support including the data of all 51 of these men in the beginning of the study. First, regarding the formulation of domain summaries, their inclusion allowed us to pursue more goals. Second, it

allowed us to reinvestigate the purposive subsample of previously analysed participants (n=17) that had resulted in the differentiation of the three groups. After each analysis, the data were merged to test our assumptions.

For all seven study sites, we obtained ethical approval from the relevant cantonal ethics committees and written informed consent from all study participants.

Qualitative data collection and analysis

The behaviour-change goals participants had set in their third counselling sessions were used as qualitative data. In collaboration with a nurse, each participant had set at least one goal he felt motivated to achieve. Activities necessary to achieve these goals were also defined (Michie et al., 2013). Following the session, two copies of these goals were printed—one for the participant, the other for inclusion in the study documentation.

All forms with hand-written goals were analysed via thematic analysis. This approach facilitated systematic categorization of individual goals into domain summaries that reflected broader strategies of sexual risk reduction goal-setting (V. Braun et al., 2019). To compare inter-group differences, we additionally counted the individual goals assigned to each domain.

Quantitative data collection and analysis

At t0 (before HCV treatment start) and t6 (follow-up planned for testing sustained viral response, at least 6 or 7 months after first dose of HCV treatment according to guidelines (European Association for the Study of the Liver (EASL), 2020), participants completed a sexual and drug use behaviour questionnaire. Items asked about anal intercourse with non-steady partners (nsCAI), condom use, fisting, use of stimulant drugs (cocaine, methamphetamine, ketamine, or mephedrone), SDU (use of γ-butyrolactone/γ-hydroxybutyric acid [GHB/GBL], cocaine, methamphetamine, ketamine, or mephedrone

during sex), and IDU over the previous 6 months (yes/no). They also completed two validated questionnaires: one on attitudes towards condom use (via 13 items using a 5-point Likert scale) (1 = "I don't agree" to 5= "I completely agree") (DeHart & Birkimer, 1997); and one on condom use self-efficacy, measured via five items on a 10-point visual scale (0= "I cannot"; 10= "I am sure that I can") (Rotheram-Borus et al., 1997). Socio-demographics and clinical data were assessed via the standard *SHCS*/clinical records questionnaire.

Available data were descriptively analysed using medians and interquartile ranges (IQRs) for non-normally distributed data, with frequencies (percentages) used for categorical data and pre-post analysed outcomes, *i.e.,* nsCAI, fisting, use of stimulant drugs, SDU and IDU. We used Chi-square tests for categorical and Mann-Whitney U tests for continuous variables. However, considering our small sample sizes and measured values, no statistical tests were used to assess significant changes between t0 and t6.

Data integration

After qualitative or quantitative analysis of each data set, results were merged for comparison (Fetters et al., 2013). To cross-validate the three group assumptions, we focused on the participant subsample (n=17) upon whose qualitative evaluation data we based our three response patterns. To test our assumptions, after examining these participants' comparability with the remaining 33 who had completed at least one questionnaire (missing n=1), we complemented the three groups with all available results—socio-demographic characteristics, sexual behaviour, drug use behaviour. For inter-group comparison, we added results for determinants of the outcome behaviours and goal-setting.

Results

Strategies for sexual risk reduction - Qualitative results

Individual goals were provided by 47 participants (92%). These were categorized into six domains reflecting broader sexual risk reduction strategies: *1) planning for safer dating; 2) preparing and using tools to reduce blood exposure; 3) improving my social and personal life; 4) using condoms consistently; 5) disclosing HCV to my sexual partners;* and *6) reducing sexualized drug use* as described in table 2. Two participants (4%) had set single goals, 21 (45%) two goals and 24 (51%) three goals (total goals: 116). Seven goals were not categorized because they occurred only once, *e.g.,* getting tested regularly for STIs, or continuously seeking new information about HCV.

[Insert table 2 here]

Representativeness of interviewed MSM - Quantitative results

Of the 51 men who received the counselling intervention and DAAs, fifty (98%) reported on their sexual and drug use behaviour at baseline (t0); 48 (94%) reported at t6. Comparison of baseline data between the 17 MSM interviewed to determine the three group patterns (table 1) and the remaining 33 showed that they are similar in terms of median and percentages (table 3).

[Insert table 3 here]

Cross-validating our assumptions and differences in goal-setting - Mixed-methods results

Our assumption for group 1 A*void-risks* (low levels of nsCAI and SDU at t0 (maintained at t6)) was confirmed (table 4). Although men in this group had reported nsCAI during the previous year (an inclusion criterion for the counselling part of the *Swiss HCVree Trial*), they reported no nsCAI (0) levels at baseline. Their scores regarding self-efficacy and attitudes towards condom use were consistent with these reports—the highest of the three groups.

Overall, both at baseline and six months later, they also showed the lowest HCV risk profiles. Many of these participants had been living for many years with HIV (median 20.7 years, IQR 9.2–21.8) and HCV (median 5.8 years, IQR 1.5–9.5). Of the three groups, only this one set goals in line with the *using condoms consistently* domain (4/5).

Our assumption for group 2 *Minimize-risks* (high nsCAI and SDU levels at t0, but reduced SDU at t6) was partially confirmed. They reported unchanged levels of nsCAI (6/8) and stable self-efficacy scores at both t0 and t6. The assumption that they would show a reduction in SDU at t6 was not confirmed. Compared to group 1 A*void-risks*, group 2 *Minimize-risks* MSM had been living with diagnosed HCV for a much shorter time (median 1.6 years, IQR 1.1–2.3). Regarding goal-setting, they favoured risk reduction in domains other than condom use. This group set most goals in the domains of *preparing and using tools to reduce blood exposure* (7/8) and *planning for safer dating* (6/8).

The assumptions for group 3 *Accept-risks* (high nsCAI and SDU levels at t0 and t6) were confirmed. Overall, both at baseline and six months later, this group also showed the highest HCV risk profile. No change was measured regarding nsCAI or SDU (4/4). These men had been living for a rather long time with HIV (median 14.7 years, IQR 11.7–16) but shorter periods with HCV (median 1.5 years, IQR 1.2-2). Of this group's four members, two had already been re-infected at least once after successful treatment before this trial. Compared to the other groups, these men's few goals fell mostly in the domains of *planning for safer dating* (3/4) and *disclosing HCV to my sexual partners* (2/4).

[Insert table 4 here]

Discussion

With this convergent mixed-methods study, we explored differences between three participant groups (with group allocation based on their responses to the intervention) regarding their goal-setting content and behavioural change from baseline to six months later.

Our assumptions regarding behaviour change were almost confirmed. Overall, while the achieved behavioural changes matched the range of goals set and represented the pre-defined groups well, changes were not measurable regarding the pre-defined quantitative outcomes. However, findings contribute to the needed evidence-base on tailored sexual risk reduction interventions that correspond to the needs of groups affected (Kurth et al., 2011).

Interestingly, group 1 *Avoid-risks*, which maintained its low t0 levels of nsCAI and SDU, was the only group with goals in the domain of *using condoms consistently*. This fits with their pre-post behaviour-change outcomes, which included low nsCAI reports and a lower risk profile regarding other high-risk practices, *e.g.,* receptive fisting or SDU. This means that despite the decreasing popularity of condom use in HIV-infected MSM (Champenois et al., 2018; Kouyos et al., 2015), some of this group's members still consider it necessary. Baseline measurements immediately before the first session showed no observable nsCAI, indicating that between study screening/inclusion, these MSM had started changing their behaviour. This unexpected result is reflected in their high scores (the highest of the three groups, including at baseline) regarding both positive condom attitudes and self-efficacy to negotiate condom use. As identified by Nöstlinger et al. (2015), both of these may exert mediating effects on behaviour change.

Our assumption for group 2 M*inimize-risks* was only partially confirmed: as expected, high nsCAI levels persisted; however, SDU did not decrease. Viewed alongside this group's goals, these results become more comprehensible. Few of this group's members hoped to reduce their SDU; however, a large majority had chosen at least one goal within the domain of *preparing and using tools to reduce blood exposure*. Considering that both the eHealth tool and the nurses encouraged these men to reflect on their own sexual practices, particularly regarding blood and mucosal trauma, this preference indicates intentions to adopt effective risk reduction strategies. This supports developing “blood awareness” to reduce HCV

transmission (Schmidt et al., 2016; Schmidt et al., 2011). Unfortunately, none of our outcomes focused on reducing behaviours that risk blood contact (beginning with practices that commonly cause bleeding) or practising safer drug use. Bridging this gap will require revision and development of our outcome measures.

Group 3 A*ccept-risks* showed no behavioural change, thereby confirming our assumption (high levels of nsCAI and SDU at both t0 and t6). This group's goal-setting fell predominantly within the domain of *planning for safer dating*, *e.g.,* "Have no sex with men I don't know" or "Leave my mobile phone at home to avoid spontaneous dates through social media." These goals illustrate that MSM acknowledge that geosocial networking applications represent a sexual risk in themselves. This observation is congruent with findings linking MSM's use of such platforms with increased higher-risk activities (Holloway et al., 2015); however, a more recent cross-sectional study could not identify a link between dating app use and STI outcomes (DeVost et al., 2018). While such correlations were beyond this study's scope, our results both emphasize the popularity of dating apps and highlight the challenges they pose for MSM trying to reduce long-term sexual risk behaviour.

Sexualized drug use (chemsex) was common and persistent across all three groups. A recent systematic review found a 3-29% prevalence of chemsex in MSM from high-income countries (Maxwell et al., 2019). In Switzerland, while various studies indicate regular SDU among roughly 10% of MSM (Weber et al., 2019), *SHCS* data indicate a prevalence nearly 40% higher among HIV-diagnosed MSM (Hampel et al., 2019). Among HCV-coinfected MSM, our measured SDU levels suggest a strong association between SDU and HCV infection. However, the SHCS data may actually reflect underreporting in its clinical interviews format, which is more prone to social acceptability bias than the self-completed forms we used (Schroder et al., 2003).

As noted, many of our study's MSM set goals regarding SDU. More concretely, they worked in the two domains: *reducing sexualized drug use* and *preparing and using tools to reduce blood exposure*. While the first of these involves reducing drug use, the second includes *safe(r)* drug use. It is well established that successful strategies for safe drug use generally integrate "blood awareness" components, *i.e*., they teach people to minimize the risk of blood-borne infection entailed, *e.g.,* by shared snorting or injection paraphernalia (Chan et al., 2016; Hagan et al., 2015; N. K. Martin et al., 2016; T. Martin et al., 2018; Schmidt & Bremer, 2016). Our findings highlights the importance not only working on the reduction of SDU in MSM, but also of discussing *safer* drug use with them. Further, our results show that, while behaviour changes clearly occurred, our instruments lacked the sensitivity to measure those changes.

Currently, this inability to measure lower-risk drug use exposes a limitation of our study design. Other limitations also warrant mentioning. First, generalisability – the *Swiss HCVree Trial* - was conducted within the framework of the SHCS and included only MSM who receive regular care from specialised healthcare professionals in SHCS centres. Second the lack of power due to the limited sample size of this study. In this context, the number of participants was given by the population of HCV/HIV co-infected MSM and determined by the feasibility of providing a complex intervention. However, the combined use of quantitative and qualitative data allowed us to identify three distinct response patterns, leading to consistent findings. Third our results also identified weaknesses in the current questionnaire design—especially regarding "blood awareness" and related behaviours—implying a need to implement a range of items reflecting the variety of HCV exposure- and/or risk-reduction strategies.

Conclusion

Our results confirm MSM's response patterns to an HCV risk reduction intervention addressing various transmission-related behavioural and contextual risk factors. Based on formative research, we differentiated the participants into three main groups. Differences between these groups were especially evident regarding goal-setting choices. Variance in goal-setting and response to intervention helps to explain MSM's support needs and indicate their levels of motivation toward behavioural changes. While one group took up goals related to blood awareness, others focussed on safer dating or increased condom use.

This study only measured and explained behavioural changes towards condom use. To address a wider range of behavioural changes, future prevention programs should adapt their outcome measures to allow more sensitive measurement. This will require instruments and/or variables designed to indicate subtle changes in low-level SDU and other strategies MSM employ for HCV prevention.

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Disclosure statement

No potential conflict of interest was reported by the author(s).

Availability of data

The individual level datasets generated and/or analysed during the current study are not publicly available because open access to all SHCS data is currently not possible. These data are too dense and comprehensive to preserve patient privacy in patients with HIV infection. Free access to the data would be incompatible both with the SHCS informed consent policy and with preserving patient privacy. Investigators with requests for selected data should send a proposal to the corresponding author. The provision of data will be considered by the study team and the Scientific Board of the SHCS.

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References

Berenguer, J., Gil-Martin, A., Jarrin, I., Montes, M. L., Dominguez, L., Aldamiz-Echevarria, T., Tellez, M. J., Santos, I., Troya, J., Losa, J. E., Serrano, R., De Guzman, M. T., Calvo, M. J., Gonzalez-Garcia, J. J., & Madrid-CoRe Study, G. (2019). Reinfection by hepatitis C virus following effective all-oral direct-acting antiviral drug therapy in HIV/hepatitis C virus coinfected individuals. *AIDS*, *33*(4), 685-689. https://doi.org/10.1097/QAD.0000000000002103

Braun, D. L., Hampel, B., Kouyos, R., Nguyen, H., Shah, C., Flepp, M., Stockle, M., Conen, A., Beguelin, C., Kunzler-Heule, P., Nicca, D., Schmid, P., Delaloye, J., Rougemont, M., Bernasconi, E., Rauch, A., Gunthard, H. F., Boni, J., & Fehr, J. S. (2019). High Cure Rates With Grazoprevir-Elbasvir With or Without Ribavirin Guided by Genotypic Resistance Testing Among Human Immunodeficiency Virus/Hepatitis C Virus-coinfected Men Who Have Sex With Men. *Clin Infect Dis*, *68*(4), 569-576. https://doi.org/10.1093/cid/ciy547

Braun, D. L., Hampel, B., Ledergerber, B., Grube, C., Nguyen, H., Kunzler-Heule, P., Shah, C., Salazar-Vizcaya, L., Conen, A., Flepp, M., Stockle, M., Beguelin, C., Schmid, P., Rougemont, M., Delaloye, J., Bernasconi, E., Nicca, D., Boni, J., Rauch, A., Kouyos, R. D., Gunthard, H. F., & Fehr, J. S. (2020). A treatment as prevention trial to eliminate hepatitis C among men who have sex with men living with HIV in the Swiss HIV Cohort Study. *Clin Infect Dis*. https://doi.org/10.1093/cid/ciaa1124

Braun, V., Clarke, V., Hayfield, N., & Terry, G. (2019). Thematic Analysis. In P. Liamputtong (Ed.), *Handbook of Research Methods in Health Social Sciences* (pp. 844-858). Springer Nature. https://doi.org/10.1007/978-981-10-5251-4_103

Champenois, K., Seng, R., Persoz, A., Essat, A., Gaud, C., Laureillard, D., Robineau, O., Duvivier, C., Yazdanpanah, Y., Goujard, C., Meyer, L., & group, A. P. c. s. (2018).

Recent trends in sexual behaviours among MSM followed since primary HIV-1 infection. *AIDS*. https://doi.org/10.1097/QAD.0000000000001916

Chan, D. P., Sun, H. Y., Wong, H. T., Lee, S. S., & Hung, C. C. (2016). Sexually acquired hepatitis C virus infection: a review. *Int J Infect Dis*, *49*, 47-58. https://doi.org/10.1016/j.ijid.2016.05.030

Crepaz, N., Baack, B. N., Higa, D. H., & Mullins, M. M. (2015). Effects of integrated interventions on transmission risk and care continuum outcomes in persons living with HIV: meta-analysis, 1996-2014. *AIDS*, *29*(18), 2371-2383. https://doi.org/10.1097/QAD.0000000000000879

Creswell, J. W., & Plano Clark, V. L. (2011). *Desiging and conducting mixed methods reserach* (2 ed.). SAGE Publications.

Danta, M., & Rodger, A. J. (2011). Transmission of HCV in HIV-positive populations. *Curr Opin HIV AIDS*, *6*(6), 451-458. https://doi.org/10.1097/COH.0b013e32834b4974

DeHart, D., & Birkimer, J. (1997). Trying to practice safer sex: Development of the sexual risks scale. *The Journal of Sex Research 34*(1), 11-25. https://doi.org/10.1080/00224499709551860

DeVost, M. A., Beymer, M. R., Weiss, R. E., Shover, C. L., & Bolan, R. K. (2018). App-Based Sexual Partner Seeking and Sexually Transmitted Infection Outcomes: A Cross-Sectional Study of HIV-Negative Men Who Have Sex With Men Attending a Sexually Transmitted Infection Clinic in Los Angeles, California. *Sex Transm Dis*, *45*(6), 394-399. https://doi.org/10.1097/OLQ.0000000000000770

European Association for the Study of the Liver. (2020). EASL recommendations on treatment of hepatitis C: Final update of the series(). *J Hepatol*. https://doi.org/10.1016/j.jhep.2020.08.018

Fetters, M. D., Curry, L. A., & Creswell, J. W. (2013). Achieving integration in mixed methods designs-principles and practices. *Health Serv Res*, *48*(6 Pt 2), 2134-2156. https://doi.org/10.1111/1475-6773.12117

Ghisla, V., Scherrer, A. U., Nicca, D., Braun, D. L., & Fehr, J. S. (2016). Incidence of hepatitis C in HIV positive and negative men who have sex with men 2000-2016: a systematic review and meta-analysis. *Infection*. https://doi.org/10.1007/s15010-016-0975-y

Hagan, H., Jordan, A. E., Neurer, J., & Cleland, C. M. (2015). Incidence of sexually transmitted hepatitis C virus infection in HIV-positive men who have sex with men. *AIDS*, *29*(17), 2335-2345. https://doi.org/10.1097/QAD.0000000000000834

Hampel, B., Kusejko, K., Kouyos, R. D., Boni, J., Flepp, M., Stockle, M., Conen, A., Beguelin, C., Kunzler-Heule, P., Nicca, D., Schmidt, A. J., Nguyen, H., Delaloye, J., Rougemont, M., Bernasconi, E., Rauch, A., Gunthard, H. F., Braun, D. L., Fehr, J., & Swiss, H. I. V. C. S. g. (2019). Chemsex drugs on the rise: a longitudinal analysis of the Swiss HIV Cohort Study from 2007 to 2017. *HIV Med*. https://doi.org/10.1111/hiv.12821

Higa, D. H., Crepaz, N., Marshall, K. J., Kay, L., Vosburgh, H. W., Spikes, P., Lyles, C. M., & Purcell, D. W. (2013). A systematic review to identify challenges of demonstrating efficacy of HIV behavioral interventions for gay, bisexual, and other men who have sex with men (MSM). *AIDS Behav*, *17*(4), 1231-1244. https://doi.org/10.1007/s10461-013-0418-z

Holloway, I. W., Pulsipher, C. A., Gibbs, J., Barman-Adhikari, A., & Rice, E. (2015). Network Influences on the Sexual Risk Behaviors of Gay, Bisexual and Other Men Who Have Sex with Men Using Geosocial Networking Applications. *AIDS Behav*, *19 Suppl 2*, 112-122. https://doi.org/10.1007/s10461-014-0989-3

Ingiliz, P., Wehmeyer, M. H., Boesecke, C., Schulze Zur Wiesch, J., Schewe, K., Lutz, T., Baumgarten, A., Simon, K. G., Hueppe, D., Rockstroh, J. K., Mauss, S., Christensen, S., group, N. s., & group, G. s. (2019). Reinfection with the hepatitis C virus in men who have sex with men after successful treatment with direct-acting antivirals in Germany: Current incidence rates compared with rates during the interferon era. *Clin Infect Dis*. https://doi.org/10.1093/cid/ciz949

Johnson, W. D., Diaz, R. M., Flanders, W. D., Goodman, M., Hill, A. N., Holtgrave, D., Malow, R., & McClellan, W. M. (2008). Behavioral interventions to reduce risk for sexual transmission of HIV among men who have sex with men. *Cochrane Database Syst Rev*(3), CD001230. https://doi.org/10.1002/14651858.CD001230.pub2

Kouyos, R. D., Hasse, B., Calmy, A., Cavassini, M., Furrer, H., Stockle, M., Vernazza, P. L., Bernasconi, E., Weber, R., Gunthard, H. F., Swiss, H. I. V. C. S., Aubert, V., Battegay, M., Bernasconi, E., Boni, J., Bucher, H. C., Burton-Jeangros, C., Calmy, A., Cavassini, M., Dollenmaier, G., Egger, M., Elzi, L., Fehr, J., Fellay, J., Furrer, H., Fux, C. A., Gorgievski, M., Gunthard, H., Haerry, D., Hasse, B., Hirsch, H. H., Hoffmann, M., Hosli, I., Kahlert, C., Kaiser, L., Keiser, O., Klimkait, T., Kouyos, R., Kovari, H., Ledergerber, B., Martinetti, G., de Tejada, B. M., Metzner, K., Muller, N., Nadal, D., Nicca, D., Pantaleo, G., Rauch, A., Regenass, S., Rickenbach, M., Rudin, C., Schoni-Affolter, F., Schmid, P., Schupbach, J., Speck, R., Tarr, P., Trkola, A., Vernazza, P., Weber, R., & Yerly, S. (2015). Increases in Condomless Sex in the Swiss HIV Cohort Study. *Open Forum Infect Dis*, *2*(2), ofv077. https://doi.org/10.1093/ofid/ofv077

Künzler-Heule, P., Fierz, K., Schmidt, A. J., Rasi, M., Bogdanovic, J., Kocher, A., Engberg, S., Battegay, M., Nöstlinger, C., Lehner, A., Kouyos, R., Schmid, P., Braun, D., Fehr, J., & Nicca, D. (2021). Response to a sexual risk reduction intervention provided in

combination with hepatitis C treatment by HIV/HCV co-infected men who have sex with men: a reflexive thematic analysis. *BMC Infectious Diseases*, *21*. https://doi.org/10.1186/s12879-021-06003-z

Kurth, A. E., Celum, C., Baeten, J. M., Vermund, S. H., & Wasserheit, J. N. (2011). Combination HIV prevention: significance, challenges, and opportunities. *Curr HIV/AIDS Rep*, *8*(1), 62-72. https://doi.org/10.1007/s11904-010-0063-3

Lockart, I., Matthews, G. V., & Danta, M. (2019). Sexually transmitted hepatitis C infection: the evolving epidemic in HIV-positive and HIV-negative MSM. *Curr Opin Infect Dis*, *32*(1), 31-37. https://doi.org/10.1097/QCO.0000000000000515

Martin, N. K., Thornton, A., Hickman, M., Sabin, C., Nelson, M., Cooke, G. S., Martin, T. C., Delpech, V., Ruf, M., Price, H., Azad, Y., Thomson, E. C., & Vickerman, P. (2016). Can Hepatitis C Virus (HCV) Direct-Acting Antiviral Treatment as Prevention Reverse the HCV Epidemic Among Men Who Have Sex With Men in the United Kingdom? Epidemiological and Modeling Insights. *Clin Infect Dis*, *62*(9), 1072-1080. https://doi.org/10.1093/cid/ciw075

Martin, T., Rauch, A., Salazar-Vizcaya, L., & Martin, N. (2018). Understanding and Addressing Hepatitis C Virus Reinfection Among Men Who Have Sex with Men. *Infect Dis Clin North Am*, *32*(2), 395-405. https://doi.org/10.1016/j.idc.2018.02.004

Maxwell, S., Shahmanesh, M., & Gafos, M. (2019). Chemsex behaviours among men who have sex with men: A systematic review of the literature. *Int J Drug Policy*, *63*, 74-89. https://doi.org/10.1016/j.drugpo.2018.11.014

Michie, S., Richardson, M., Johnston, M., Abraham, C., Francis, J., Hardeman, W., Eccles, M. P., Cane, J., & Wood, C. E. (2013). The behavior change technique taxonomy (v1) of 93 hierarchically clustered techniques: building an international consensus for the

reporting of behavior change interventions. *Ann Behav Med*, *46*(1), 81-95. https://doi.org/10.1007/s12160-013-9486-6

Nicca, D., Fierz, K., Nöstlinger, C., Künzler-Heule, P., Langewitz, W., Schmidt, A. J., Hampel, B., Stöckle, M., Béguelin, C., Delaloye, J., Schmid, P., Flepp, M., Braun, D., Fehr, J., & (SHCS), a. t. S. H. C. S. (2017, 25.-27.10.2017). *Doing the impossible: An e-health assisted counseling intervention to reduce risk in HCV-reinfection in men who have sex with men*. 16th Euroepean AIDS Conference, Milan, Italy.

Nijmeijer, B. M., Koopsen, J., Schinkel, J., Prins, M., & Geijtenbeek, T. B. (2019). Sexually transmitted hepatitis C virus infections: current trends, and recent advances in understanding the spread in men who have sex with men. *J Int AIDS Soc*, *22 Suppl 6*, e25348. https://doi.org/10.1002/jia2.25348

Nöstlinger, C., Platteau, T., Bogner, J., Buyze, J., Dec-Pietrowska, J., Dias, S., Helps, J., Kocsis, A., Mueller, M., Rojas, D., Stanekova, D., van Lankveld, J., Colebunders, R., & Eurosupport Study Group. (2015). Computer-assisted Intervention for Safer Sex in HIV-Positive Men Having Sex with Men: Findings of a European Randomized Multi-Center Trial. *J Acquir Immune Defic Syndr*. https://doi.org/10.1097/QAI.0000000000000882

Prinsenberg, T., Zantkuijl, P., Zuilhof, W., Davidovich, U., Schinkel, J., Prins, M., & van der Valk, M. (2020). Design and Implementation of a Multilevel Intervention to Reduce Hepatitis C Transmission Among Men Who Have Sex With Men in Amsterdam: Co-Creation and Usability Study. *JMIR Form Res*, *4*(9), e19100. https://doi.org/10.2196/19100

Rotheram-Borus, M. J., Murphy, D. A., & Coleman, C. L. (1997). Risk Acts, Health Care, and Medical Adherence Among HIV+ Youths in Care over Time. *AIDS Behav*, *1*(1), 43–52. https://doi.org/10.1023/A:1026213905034

Schmidt, A. J., Bourne, A., Weatherburn, P., Reid, D., Marcus, U., Hickson, F., & Network, E. (2016). Illicit drug use among gay and bisexual men in 44 cities: Findings from the European MSM Internet Survey (EMIS). *Int J Drug Policy*, *38*, 4-12. https://doi.org/10.1016/j.drugpo.2016.09.007

Schmidt, A. J., & Bremer, V. (2016). Response to the calculation of population attributable fractions (PAFs) of risk factors for hepatitis C transmission. *AIDS*, *30*(10), 1683-1684. https://doi.org/10.1097/QAD.0000000000001090

Schmidt, A. J., Rockstroh, J. K., Vogel, M., An der Heiden, M., Baillot, A., Krznaric, I., & Radun, D. (2011). Trouble with bleeding: risk factors for acute hepatitis C among HIV-positive gay men from Germany--a case-control study. *PLoS One*, *6*(3), e17781. https://doi.org/10.1371/journal.pone.0017781

Schroder, K. E., Carey, M. P., & Vanable, P. A. (2003). Methodological challenges in research on sexual risk behavior: II. Accuracy of self-reports. *Ann Behav Med*, *26*(2), 104-123. https://doi.org/10.1207/S15324796ABM2602_03

Swiss HIV Cohort Study, Schoeni-Affolter, F., Ledergerber, B., Rickenbach, M., Rudin, C., Gunthard, H. F., Telenti, A., Furrer, H., Yerly, S., & Francioli, P. (2010). Cohort profile: the Swiss HIV Cohort study. *Int J Epidemiol*, *39*(5), 1179-1189. https://doi.org/10.1093/ije/dyp321

Weber, P., Gredig, D., Lehner, A., & Nideröst, S. (2019). European MSM Internet Survey (EMIS-2017) Länderbericht für die Schweiz.

Table 1: Short description of the three patterns of sense-making work

No	Response patterns	Description
1	Avoid risks: get rid of HCV	• HCV is serious, being cured by DAAs is a unique opportunity • Behavioural change initiated prior to the intervention • Intervention helped to maintain behavioural changes • Re-infection must be prevented
2	Minimize risks: live as long as possible without HCV	• HCV is a problem but manageable via DAAs • No thoughts about behavioural changes prior to the intervention • Intervention helped them learn about behavioural changes and to decide what was feasible • Re-infection might happen but could be treated again
3	Accept risks: live with the risk of HCV	• HCV is socially limiting but manageable via DAAs • In men's view, feasible behavioural changes had already been implemented prior to the intervention • Intervention helped to reflect on the difficulties of other behavioural changes • Re-infection will happen, but re-treatment is easy

Table 2: Six identified broader HCV risk reduction strategies

Domain summary	Examples of original quotes to illustrate the meaning	n=116 goals in 47 MSM n (%)
Planning for safer dating	"I leave my mobile phone at home to avoid spontaneous dates through social media." "I leave relevant chatrooms." "We define and implement the rules of the game together in advance of sex."	30 (26)
Preparing and using tools to reduce blood exposure	"I create my personal (happy) box with my toys and lubricant." "I insist my partners take clean gloves when I get fisted." "I organise my personal snorting tubes."	26 (22)
Improving my social and personal life	"I look for sustainable leisure activities at the weekends outside sexual encounters." "I am going to the gym 3–5 times a week for a better body-feeling and loving my body again."	16 (14)
Using condoms consistently	"I will behave safely, meaning take condoms with me and use them with no discussion." "I will have safer sex with occasional partners also oral."	13 (11)
Disclosing HCV to my sexual partners	"I talk with potential sex partners about HCV" "I ask a potential sexual partner if he is HCV positive or negative"	12 (9)
Reducing sexualized drug use	"I say no for drug use" "I will be having sex without hard drugs for one month. "	12 (9)

Table 3. Comparison of socio-demographics, sexual behaviour, psychological constructs and goal-setting themes among interviewed and non-interviewed participants

Characteristics	**Non-interviewed n=33**		**Interviewed n=17**		**p§**
Socio-demographics					
Age, median (IQR)	44 (34–50)		44 (41–53)		1.000
Skin colour white, n (%)	26 (79)		16 (94)		0.646
Post-secondary education, n (%)	15 (45)		8 (47)		1.000
Years since HIV diagnosis, median (IQR)	8.6 (5.9–13.5)		10.9 (6.5–17.3)		0.762
Years since HCV diagnosis, median (IQR)	1.7 (0.7–4.9)		1.6 (1.2–4.1)		0.836
Sexual behaviour	**t0**	**t6**	**t0**	**t6**	
Any nsAI	22 (67)		13 (76)		0.946
		19 (58)		13 (76)	0.710
Any nsCAI, n (%)	18 (55)		11 (65)		0.914
		13 (39)		11 (65)	0.468
Any fisting, n (%)	10 (30)		4 (24)		0.952
		9 (27)		4 (24)	1.000
Drug use behaviour					
Any stimulant drug use*, n (%)	20 (61)		11 (65)		1.000
		17 (52)		9 (53)	1.000
Any sexualised drug use#, n (%)	20 (61)		11 (65)		1.000
		17 (52)		11 (65)	0.825
Any injection drug use, n (%)	10 (30)		2 (12)		0.412
		7 (21)		3 (18)	1.000
Determinants of the outcome behaviours					
Positive attitudes towards condoms, median (IQR)	39 (31–48)		34 (23–39)		0.351
		40 (33–47)		36 (25–41)	0.231
Self-efficacy in condom-use, median (IQR)	28 (20–40)		30 (14–41)		0.963
		28 (25–44)		38 (31–45)	0.28

Individual goal-setting±			
Planning for safer dating	20 (25)	10 (27)	
Preparing and using tools to reduce blood exposure	18 (23)	8 (22)	
Improving my social and personal life	9 (11)	7 (19)	
			.492
Using condoms consistently	9 (11)	4 (11)	
Disclosing HCV to my sexual partners	9 (11)	3 (8)	
			.892
Reducing sexualised drug use	9 (11)	3 (8)	
			.892

nsAI, anal intercourse with non-steady partners; nsCAI, condomless anal intercourse with non-steady partners; IQR, interquartile range

§ Chi-square tests for categorical and Mann-Whitney U tests for continuous variables

* stimulant drugs: cocaine, methamphetamine, ketamine, or mephedrone

sexualised drug use: use γ-butyrolactone/γ-hydroxybutyric acid (GHB/GBL), cocaine, methamphetamine, ketamine, or mephedrone during sex

± Multiple goals were possible, every man set between 1 and 3 goals

Table 4. Comparing socio-demographics, sexual and drug use behaviour, psychological constructs and goal-setting themes across three sense-making groups

	Group 1 **Avoid risks: get rid of HCV for life** **N=5**	**Group 2** **Minimize risks: live as long as possible without HCV** **N=8**	**Group 3** **Accept risks: live with the risk of HCV** **N=4**
Socio-demographics, clinical data			
Age, median (IQR)	44 (38–51)	43 (41–52)	49 (42–53)
Skin colour white, n (%)	5 (100)	7 (87.5)	4 (100)
Post-secondary education, n (%)	5 (100)	2 (25)	2 (50)
HIV years since diagnosis, median (IQR)	20.7 (9.2–21.8)	9.3 (5.4–11.5)	14.7 (11.7–16)
HCV years since diagnosis, median (IQR)	5.8 (1.5–9.5)	1.6 (1.1–2.3)	1.5 (1.3–2)
Treatment for HCV re-infection, n (%)	0	2 (25)	2 (50)

Sexual behaviour	**t0**	**t6**	**t0**	**t6**	**t0**	**t6**
Any nsAI, n (%)	3 (60)	3 (60)	6 (75)	6 (75)	4 (100)	4 (100)
Any nsCAI, n (%)	0	1 (20)	6 (75)	6 (75)	3 (75)	4 (100)
Any Fisting, n (%)	1 (20)	0	2 (25)	2 (25)	1 (25)	2 (50)
Drug use behaviours						
Any stimulant drug use*, n (%)	1 (20)	2 (40)	3 (37.5)	3 (37.5)	4 (100)	4 (100)
Any sexualised drug use#, n (%)	2 (40)	2 (40)	5 (62.5)	5 (62.5)	4 (100)	4 (100)
Any injection drug use, n (%)	1 (20)	0	1 (12.5)	1 (12.5)	0	2 (50)
Psychosocial constructs						
Self-efficacy condom-use, median (IQR)	39 (38–47)	51 (40–58)	35 (27–37)	36 (30–37)	23 (20–24)	20 (15–22)
Positive attitudes regarding condoms, median (IQR)	47 (40–47)	45 (38–49)	29 (15–40)	37 (29–41)	10 (7–16)	30 (28–33)
Goal-setting themes±						
Planning for safer dating, n (%)	1 (20)		6 (75)		3 (75)	
Preparing and using tools to reduce my blood exposure, n (%)	0		7 (87.5)		1 (25)	
Improving my social and personal life, n (%)	3 (60)		3 (37.5)		1 (25)	
Disclosing HCV to my sexual partners, n (%)	1 (20)		0		2 (50)	
Reducing my sexualised drug use, n (%)	1 (20)		1 (12.5)		1 (25)	
Using condoms consistently, n (%)	4 (80)		0		0	

nsAI, anal intercourse with non-steady partners; nsCAI, condomless anal intercourse with non-steady partners; IQR, interquartile range

*stimulant drugs: cocaine, methamphetamine, ketamine, or mephedrone

#sexualised drug use: sexualised use of γ-butyrolactone/γ-hydroxybutyric acid (GHB/GBL), cocaine, methamphetamine, ketamine, or mephedrone

±Multiple themes were possible, every man set between 1 and 3 goals

[b]One participant took a sexual break, i.e. he had no sex with steady or non-steady partners in the previous 6 months