HHS Public Access

Author manuscript

Eur J Gastroenterol Hepatol. Author manuscript; available in PMC 2016 May 01.

Published in final edited form as:

Eur J Gastroenterol Hepatol. 2015 May ; 27(5): 550–556. doi:10.1097/MEG.0000000000000321.

Prevalence and correlates of HCV monoinfection, HIV and HCV coinfection among persons who inject drugs in Vietnam

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Abstract

Background—Vietnam bears a high burden of HCV and HIV infection among persons who inject drugs (PWID). The high prevalence of HCV and HIV occur in a context of stigma and limited prevention interventions for PWID.

Objectives—This study aims to estimate the prevalence of HCV, HIV and HIV/HCV coinfection among PWID, and also to explore their associations with lifetime injection behaviors.

Methods—A total of 1434 PWID were recruited in Thai Nguyen Province, in Vietnam, between 2005 and 2007. Participants responded to a structured questionnaire and provided blood samples at baseline. A cross-sectional analysis of data collected at baseline was conducted. Factors associated with HCV monoinfection and, HIV/HCV coinfection were evaluated using multinomial logistic regression.

Results—The prevalence of HIV and HCV were 35.1% and 88.8% respectively and the prevalence of HIV/HCV coinfection, HCV monoinfection were 34.8%and 53.9%, respectively. After adjusting for confounders in multivariate analysis, ever reusing a syringe and a needle was significantly associated with HIV monoinfection (AOR, 3.13; 95% CI, 1.99-4.94), and HIV/HCV coinfection (AOR, 3.34; 95% CI, 2.02-5.51). Ever sharing diazepam or novocaine was also significantly associated with HIV monoinfection (AOR, 2.14; 95% CI, 1.38-3.32) and HIV/HCV coinfection (AOR, 2.47; 95% CI, 1.57-3.90).

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Conflicts of interest There are no conflicts of interest for this study.

Conclusion—Our findings demonstrated a high burden of HIV and HCV infection among PWID in Vietnam. Lifetime injection behaviors, including sharing diazepam or novocaine, may account for the high prevalence of HIV and HCV. Improving prevention and ensuring access to care remains critically important for this vulnerable population.

Keywords

hepatitis c; hiv; coinfection; persons who inject drugs; diazepam; novocaine

Introduction

Hepatitis C virus (HCV) and human immunodeficiency virus (HIV) significantly affect the morbidity and mortality of infected individuals globally [1-3]. Although HCV and HIV are both bloodborne pathogens that share similar modes of transmission, the transmission efficiency of each virus varies[4]. HCV is more than 10 times as infectious as HIV through percutaneous blood exposures and the prevalence of HCV infection among HIV infected PWID is almost 90% [5]. The majority of HIV/HCV-coinfected persons are former or current long-term PWID[6].

Located in close proximity to the “Golden Triangle” region (Laos, Myanmar and Thailand), one of Asia’s main opium-producing areas, Vietnam has a large population of PWID, approximately 200,000 persons [7,8], and a high prevalence of HIV, HCV and HIV/HCV coinfection [9]. National HIV prevalence in Vietnam among PWID was approximately 30% from 2007 to 2012[10], varying by region, from 13.5% to 64%[11]. The prevalence of HCV in PWID has been reported to be as high as 74.1% in 2003[12]. Research suggests that HCV is acquired relatively early after initiation to injection, and mean time between first injection and first positive HCV test was 1.2 to 2 years[13]. Similarly, a higher risk of HIV was observed in early course of injection among PWID [14].

Percutaneous exposures cause most HCV infections[15]. Shared use of syringe and drug preparation equipment can expose PWID to infectious blood and increase likelihood of HCV and HIV infection [16]. Specific patterns of injection behaviors that increase transmission of HCV and HIV in regions need to be explored. In urban areas of Vietnam, psychoactive substances, called “Western medicine” have become popular among young PWID in the urban areas of Vietnam[8]. These substances, such as diazepam and novocaine, may be used to amplify, augment or extend the positive psychoactive effects of heroin[17], or to forestall onset of heroin withdrawal [13]. The context in which PWID abuse these substances and the impact injecting these drugs has on the transmission of HIV and HCV are unknown.

HIV and HCV coinfection complicates clinical care for patients, and increases the probability of morbidity and mortality as compared to monoinfection. HIV infection facilitates hepatic fibrosis in HCV infected patients, and HCV triples the chance of liver-associated toxicity from antiretroviral therapy (ART) [18], making it more difficult for doctors to optimize treatment strategy. Furthermore, HIV/HCV coinfection places a significant burden on the HIV/AIDS care delivery system. Despite greater associated morbidity and mortality and higher health care costs, HIV/HCV coinfection has received far

less health investment than HIV alone, and data on how to specifically target this high-risk population for the provision of effective prevention and treatment are scarce[15].

In this study, we estimated the prevalence of HIV,HCV, and HIV/HCV coinfection, explored their associations with lifetime injection behaviors, and compared correlates of HCV monoinfection and HIV/HCV coinfection in a population of PWID living in northeast Vietnam.

Methods

Study population

Out-of-treatment PWID were recruited by trained outreach workers, many of whom were former PWID, to participate in a cluster randomized controlled trial of a peer educator, network-oriented behavioral intervention to decrease HIV risk among PWID. The study was conducted between 2005 and 2007 in Thai Nguyen Province which borders China, is 50 miles from Hanoi, the capital of Vietnam, and has a tradition of opium cultivation and use.

We analyzed data collected during screening phase of the main HIV intervention trial. To be eligible for screening, participants must be (1) 18-45 years of age, (2) have injected in the past 6 months. To be eligible for trial enrollment, the index participants were required to (1) be at least 18 years of age, (2) have injected at least once a week in the past 3 months, and (3) have HIV negative antibody test results within 30 days prior to randomization, and (4) be willing to identify and recruit at least one eligible network member. Network members had to (1) be at least 18 years of age, (2) have injected drugs with or had sexual intercourse with their index participant in the past 3 months, (3) interact at least once a week with index. Network members were not required to be HIV negative. Eligible networks (index and associated network members) were randomized to either the intervention arm or the control arm (1:1 ratio). Details of this trial are presented elsewhere [19]. The research protocol was reviewed and approved by the Johns Hopkins Bloomberg School of Public Health IRB and Thai Nguyen Center for Preventive Medicine IRB.

Data collection

A total of 1434 consenting PWID underwent a baseline behavioral assessment interview and also received HIV and HCV antibody testing at baseline. The surveys were administered face-to-face, using a structured questionnaire. The survey asked about socio-demographic characteristics and, lifetime injection behaviors of interest including ever shared a needle, ever reused a needle and a syringe, ever shared diazepam (ever drawn diazepam from the same ampoule with other people) and ever shared novocaine (ever drawn novocaine from the same ampoule with other people), and other injection related variables such as duration of injection drug use. Having a tattoo and number of sexual partners in lifetime were also assessed.

HIV serostatus was determined by using double HIV enzyme-linked immunosorbent assay (ELISA) (Abbott Murex Biotech Ltd, Kent, England and BioRad Laboratories, Marnes-la-Coquette, France); reactive samples were confirmed by Western Blot method (BioRad Laboratories). To determine HCV serostatus, specimens were measured for HCV antibody

using a second generation ELISA (Ortho Clinical Diagnostics 100 Indigo Creek Drive Rochester, New York, USA).

The primary outcomes of interest were HCV monoinfection (defined as HCV antibody positivity alone), and HIV/HCV coinfection (defined as being positive for both HIV and HCV antibody testing). Lifetime injection behaviors were our primary variables of interest, including ever shared a needle, ever reused a syringe and a needle, ever shared diazepam, ever shared novocaine, and ever shared diazepam or novocaine.

Statistical analysis

Frequency distributions by prevalent HIV and HCV serostatus (no HIV or HCV infection, HCV monoinfection and HIV/HCV coinfection) were calculated to present a profile of sample characteristics.

In the univariate analysis, we estimated unadjusted odds ratios of HCV monoinfection or HIV/HCV coinfection for each demographic variable as compared with reference group (no HIV or HCV infection). This was done to facilitate the model-building in multivariate analysis. Variables with a p-value of 0.05 were entered into a multivariate model and automatically chosen by backwards stepwise selection procedure in combination with likelihood tests (2-sides, $P<0.05$). Predetermined variables (including age, number of sexual partners in lifetime) were locked into models regardless of statistical significance considering known risk factors for HIV and HCV infections based on previous studies [9, 16, 20-22]. Demographic characteristics and risk behaviors identified through this procedure were used as the basic variables in multivariate analysis. To compare the independent association of each lifetime injection behavior of interest (ever shared a needle, ever reused a needle and a syringe, ever shared diazepam and ever shared novocaine), eight models were constructed while controlling for basic variables (Table 2). We used multinomial logistic regression models to simultaneously explore correlates of HCV monoinfection and HIV/HCV coinfection.

Possible interactions in final models based on prior knowledge were examined such as being in a stable relationship and reusing a syringe and needle. Variance inflation factors (VIF) were calculated to determine potential collinearity among independent variables. A ratio of 1:10 at least for the number of explanatory variables versus sample size was applied to account for the risk of overfitting. The model fit was addressed using Hosmer-Lemeshow (H-L) goodness-of-fit test due to the large number of unique covariate patterns in our models. All data analyses were performed using Stata statistical software version 12.0 (Stata Corp LP, Texas).

Results

Description of the study population

A total of 1434 individuals completed the baseline study visit. The median age was 31 years (interquartile range [IQR]:27-36). Participants were mostly male (96%). Thirty-two percent, were in a stable relationship (defined as currently married or living with a partner), about

half (47%) had completed high school, and most (71%) had an either full-time or part-time job. About half (52%) had ever had a tattoo (Table 1).

Most PWID were frequent injectors, with 95% injecting drugs at least 2 to 3 days per week in the past three months. They also had a relatively long history of injection drug use with 95% injecting for more than 2 years. Thirty-four percent reported a history of drug treatment. Twenty-eight percent had ever shared a needle in their lifetime, and 83% reported that they had reused a needle and a syringe in their lifetime. Almost half had shared diazepam or novocaine in their lifetime (12% shared diazepam, and 46% shared novocaine). Most participants (44%) had 2 to 5 sexual partners in their lifetime, 32% had had more than five sexual partners, and 18% had one or no sexual partner in their lifetime (Table 1).

Prevalence of HIV and HCV

Among all participants, 88.8% were infected with HCV and 35.1% were infected with HIV. The prevalence of HCV monoinfection was 53.9% and the prevalence of HIV/HCV coinfection was 34.8%. Almost all (99%) HIV-infected PWID were also coinfected with HCV. Only 39% of individuals with HCV were also diagnosed with HIV. Prevalence of HCV monoinfection was higher among persons who had injected for more than two years as compared with those who had injected for less than two years (87% vs 59%). Participants who had injected for more than two years had a higher prevalence of HIV/HCV coinfection than those who had injected for less than two years (82% vs 24%).

Correlates for HCV monoinfection

In univariate analysis, being older, male, ever having a tattoo, having 2 to 5 sexual partners in lifetime, injecting for more than two years, injecting drugs at least 2-3 days per week in the past three months, a history of drug treatment and lifetime injection behaviors (ever reused a needle and a syringe, ever shared diazepam and ever shared novocaine) were significantly associated with higher odds of HCV monoinfection ($P<0.05$). Ever sharing a needle was not significantly associated with HCV monoinfection. Those who were currently in a stable relationship or employed were less likely to have HCV monoinfection (Table 1).

In multivariate analysis, models (2,4 and 5) revealed that ever reused a syringe and a needle (AOR, 3.23; 95%CI, 2.10-4.98), ever shared novocaine (AOR, 2.40; 95%CI, 1.57-3.69) and ever shared diazepam or novocaine (AOR, 2.32; 95%CI,1.52-3.52) were all significantly associated with higher odds of HCV monoinfection. Ever shared diazepam or novocaine drugs remained significant after controlling for potential confounders (model 6 and 7). In the final model 8, AOR of ever shared diazepam or novocaine was 2.14 (95% CI, 1.38-3.32) and AOR of ever reused a syringe and a needle was 3.13 (95% CI, 1.99-4.94). Ever shared a needle was not statistically significant with AOR 0.65(95% CI, 0.40-1.05) (Table 2).

Correlates for HIV/HCV coinfection

Univariate analysis of HIV/HCV coinfection found that being male, ever having a tattoo, having 2 to 5 sexual partners in lifetime, having injected for more than two years, injecting drugs at least 2-3 days per week in the past three months, a history of drug treatment and all lifetime injection behaviors (ever shared a needle, ever reused a needle and a syringe, ever

shared diazepam, ever shared novocaine) were significantly associated with higher odds of HCV/HCV coinfection. Individuals in a stable relationship or employed had a relatively lower likelihood of HCV/HCV coinfection compared to those who were not in a stable relationship or who were unemployed.

Multivariate analysis found that in the first five models, ever shared a needle (AOR, 1.59; 95% CI, 1.00-2.52) , ever reused a syringe and a needle (AOR, 3.94; 95% CI, 2.45-6.34), ever shared diazepam (AOR, 3.83; 95% CI, 1.60-9.19), ever shared novocaine (AOR, 2.69; 95%CI, 1.72-4.19) and ever shared diazepam or novocaine (AOR, 2.90; 95%CI, 1.88-5.50) were all significantly associated with higher odds of HIV/HCV coinfection. Ever shared diazepam or novocaine remained significant after controlling for ever shared a needle (model 6) and ever reused a syringe and a needle (model 7). In the final model (model 8), AOR of ever shared diazepam or novocaine was 2.47 (95% CI, 1.57-3.90) and AOR of ever reused a syringe and a needle was 3.34 (95% CI, 2.02-5.51). Ever shared a needle was not statistically significant with AOR 0.96 (95% CI, 0.58-1.58).

Discussion

In this study, we observed a high prevalence of HCV monoinfection, and HIV/HCV coinfection among hard-to-reach PWID in Vietnam. These data provides important information on the burden of disease in a high-risk and vulnerable population, which is critical for health resource allocation in the provision of effective treatment and prevention interventions in low-income countries. In the new era of HCV treatment, patients with HCV identified by this study could be potentially treated through oral direct antiviral agents with less adverse effects, less treatment duration, and higher efficacy[23] which would further reduce the risk of HCV transmission[24].

In our research, we found that PWID who had ever shared diazepam or novocaine and those who had ever reused a syringe and a needle, were more likely to have HCV monoinfection and HIV/HCV coinfection. These effects are independent of demographic characteristics and known risk factors, and remain of consistent magnitude and significance across all separate models. Of note, there is no substantial difference of correlates for HCV monoinfection and HIV/HCV coinfection. The only difference is that the magnitude of risk for HIV/HCV is slightly higher than HCV monoinfection as people with HIV/HCV coinfection may be exposed to those unsafe injection behaviors to a greater extent.

Both diazepam and novocaine are commonly injected in combination with heroin among PWID in certain parts of the world [17, 25]. One study reported that, in addition to heroin, persons who used drugs were also exposed to a number of other substances in their lifetime in Vietnam, including novocaine(91.6%) and diazepam(24.0%)[26], which were higher than our findings that overall 46% used novocaine and 12% used diazepam. Studies also found that PWID may use diazepam or novocaine to augment a suboptimal dose heroin when they were unable to obtain their full usual dose of heroin. These drugs may also be used to overcome the side effects of heroin withdrawal, and to avoid risk of police arrest since diazepam and novocaine are significantly cheaper than heroin, and readily and legally purchased without prescription in pharmacies [26]. PWID who use diazepam or novocaine

might be at particularly high risk, perhaps because they lack money or are in drug withdrawal. This may prompt them to adopt risky injection practices that are not usually practiced in routine injection [27].

Of note, a history of sharing a needle did not increase the likelihood of HIV and HCV infection in our study. A possible explanation for this is that the measures of sharing may not capture the risk dynamics of injection [28]. We do not know whether individuals followed someone else's injection or passed a needle to others, both of which are associated with different risks of HIV and HCV infection. This analysis also revealed that having multiple sexual partners was associated with lower odds of HIV and HCV infection. This may reflect network stability or less frequent drug use among these individuals as has been previously observed [29, 30].

There are several limitations to our study. First, the generalizability of the study's findings is limited to PWID in northern areas in Vietnam. In addition, we were not able to determine causality since the cross-sectional design precluded temporality of our variables of interest. Third, there may have been some residual underreporting of lifetime injection or other risk behaviors since participants may have provided what they perceived to be socially desirable responses. However, the proportion of subjects who reported ever shared a needle was 28% in our findings, which is consistent with ranges 27%-49% from previous studies [16, 31, 32]. Finally, we defined HCV monoinfection as HCV antibody positivity alone. The antibody test for diagnosis of HCV infection, reflects exposure experience rather than the status of chronic infection as approximately 15%-20% HCV-exposed persons may spontaneously clear the virus [20]. Therefore, it is possible that our study may have overestimated the true prevalence of chronic HCV infection.

Our study makes clear the tremendous burden of disease faced by PWID in Vietnam. PWID continue to engage in high risk sharing behaviors and are adopting new behaviors such as sharing diazepam or novocaine that appears to be associated with even higher risk. The advent of a cure for HCV as well as effective treatment for HIV offers real promise for this highly marginalized and vulnerable population. Future interventions should target the specific needs of this population by both addressing prevention of infection and transmission as well as developing mechanisms for enhancing access to care.

Acknowledgements

The authors would like to thank José Miguel Flores,PhD and Detian Deng, PhD from Johns Hopkins Bloomberg of Public Health who had provided assistance in statistical analysis.

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Table 1

Baseline Characteristics among 1434 PWID in Vietnam, 2005-2007

	Entire Cohort (n=1434)	No HIV or HCV (n=157)	HCV Mono[a] (n=773)	Odds Ratio[c] (95% CI)	HIV/HCV Co[b] (n=499)	Odds Ratio[d] (95% CI)
Age						
Median (interquartile range)	31(27-36)	30(23-36)	32(28-37)	1.06(1.03-1.09)	30(27-34)	1.02(0.99-1.05)
Gender						
Female	59(4.11)	28(17.83)	14(1.81)	Reference	16(3.21)	Reference
Male	1375(95.89)	129(82.17)	759(98.19)	11.77(6.03-2.95)	483(96.79)	6.55(3.44-12.48)
In a stable relationship						
No	972(67.78)	83(52.87)	519(67.14)	Reference	367(73.55)	Reference
Yes	462(32.22)	74(47.13)	254(32.86)	0.55(0.39-0.78)	132(26.45)	0.40(0.28-0.58)
High school completed						
No	762(53.14)	83(52.87)	393(50.84)	Reference	283(56.71)	Reference
Yes	672(46.86)	74(47.13)	380(49.16)	1.08(0.77-1.53)	216(43.29)	0.86(0.60-1.23)
Employment status						
No	420(29.49)	34(22.52)	226(29.35)	Reference	157(31.53)	Reference
Yes	1004(70.51)	117(77.48)	544(70.65)	0.70(0.46-1.06)	341(68.47)	0.63(0.41-0.97)
Ever had a tattoo						
No	691(48.19)	112(71.34)	375(48.51)	Reference	202(40.48)	Reference
Yes	743(51.81)	45(28.66)	398(51.49)	2.64(1.82-3.84)	297(59.52)	3.66(2.48-5.40)
Injecting >= 2 years						
No	69(4.93)	25(18.94)	36(4.69)	Reference	8(1.61)	Reference
Yes	1330(95.07)	107(81.06)	731(95.31)	4.74(2.74-8.22)	488(98.39)	14.25(6.26-32.46)
Injected drugs at least 2-3 days per week						
No	67(4.79)	15(11.54)	37(4.81)	Reference	15(3.02)	Reference
Yes	1333(95.21)	115(88.46)	733(95.19)	2.58(1.37-4.86)	481(96.98)	4.18(1.99-8.80)
Ever had been in drug treatment						
No	923(65.69)	111(83.46)	467(60.57)	Reference	342(68.81)	Reference
Yes	482(34.31)	22(16.54)	304(39.43)	3.28(2.03-5.30)	155(31.19)	2.29(1.39-3.75)
Sexual partners in lifetime						
<=1	267(18.62)	38(24.20)	133(17.21)	Reference	95(19.04)	Reference
2-5	632(44.07)	53(33.76)	347(44.89)	1.87(1.18-2.97)	228(45.69)	1.72(1.06-2.78)
>=5	464(32.36)	53(33.76)	254(32.86)	1.37(0.86-2.18)	157(31.46)	1.18(0.73-1.93)
Unknown	71(4.95)	13(8.28)	39(5.05)	0.86(0.42-1.77)	19(3.81)	0.58(0.26-1.30)
Lifetime Injection Behaviors						
Ever shared a needle						
No	1004(71.61)	99(75.00)	579(75.19)	Reference	323(65.12)	Reference
Yes	398(28.39)	33(25.00)	191(24.81)	0.99(0.65-1.52)	173(34.88)	1.61(1.04-2.48)
Ever reused a syringe and a needle						
No	232(16.55)	54(40.91)	114(14.81)	Reference	63(12.70)	Reference

	Entire Cohort (n=1434)	No HIV or HCV (n=157)	HCV Mono[a] (n=773)	Odds Ratio[c] (95% CI)	HIV/HCV Co[b] (n=499)	Odds Ratio[d] (95% CI)
Yes	1170(83.45)	78(59.09)	656(85.19)	3.98(2.67-5.94)	433(87.30)	4.76(3.07-7.36)
Ever shared diazepam						
No	1232(87.87)	126(95.45)	692(89.87)	Reference	411(82.86)	Reference
Yes	170(12.13)	6(4.55)	78(10.13)	2.37(1.01-5.55)	85(17.14)	4.34(1.85-10.18)
Ever shared novocaine						
No	762(54.35)	97(73.48)	417(54.16)	Reference	248(50.00)	Reference
Yes	640(45.65)	35(26.52)	353(45.84)	2.34(1.55-3.54)	248(50.00)	2.77(1.81-4.24)
Ever shared diazepam or novocaine						
No	717(51.14)	94(71.21)	400(51.95)	Reference	223(44.96)	Reference
Yes	685(48.86)	38(28.79)	370(48.05)	2.29(1.53-3.42)	273(55.04)	3.03(2.00-4.59)

[a] HCV monoinfection;

[b] HIV/HCV coinfection;

[c] comparing HCV monoinfection with no HIV or HCV infection;

[d] comparing HIV/HCV coinfection with no HIV or HCV infection .

Table 2

els of HCV Monoinfection, HIV/HCV Coinfection among 1434 PWID in Vietnam, 2005-2007

Adjusted Odds Ratio (95% Confidence Interval)															
Model 1		Model 2		Model 3		Model 4		Model 5		Model 6		Model 7		Model 8	
	HIV/HCV Co[b]	HCV Mono[a]	HIV/HCV Co[b]	HCV Mono[a]	HIV/HCV Co[b]	HCV Mono[a]	HIV/HCV Co[b]	HCV Mono[a]	HIV/HCV Co[b]	HCV Mono[a]	HIV/HCV Co[b]	HCV Mono[a]	HIV/HCV Co[b]	HCV Mono[a]	HIV/HCV Co[b]
)	0.99 (0.96-1.03)	1.02 (0.99-1.06)	0.98 (0.94-1.02)	1.04 (1.01-1.07)	0.99 (0.96-1.03)	1.04 (1.01-1.08)	1.00 (0.96-1.03)	1.04 (1.01-1.08)	1.00 (0.96-1.03)	1.04 (1.01-1.08)	1.00 (0.96-1.04)	1.03 (1.00-1.07)	0.99 (0.95-1.02)	1.03 (1.00-1.07)	0.99 (0.95-1.02)
)	0.36 (0.23-0.57)	0.47 (0.31-0.74)	0.37 (0.23-0.59)	0.48 (0.31-0.74)	0.38 (0.24-0.60)	0.44 (0.28-0.69)	0.34 (0.21-0.55)	0.45 (0.29-0.70)	0.34 (0.22-0.55)	0.45 (0.29-0.69)	0.35 (0.22-0.55)	0.46 (0.29-0.71)	0.35 (0.22-0.57)	0.46 (0.29-0.71)	0.36 (0.22-0.57)
)	2.46 (1.61-3.75)	1.65 (1.10-2.49)	2.37 (1.54-3.64)	1.70 (1.14-2.55)	2.44 (1.59-3.73)	1.60 (1.06-2.40)	2.29 (1.49-3.52)	1.61 (1.07-2.42)	2.30 (1.50-3.53)	1.61 (1.07-2.43)	2.28 (1.49-3.51)	1.58 (1.04-2.38)	2.24 (1.45-3.45)	1.58 (1.04-2.38)	2.22 (1.44-3.43)
)	14.30 (5.78-35.39)	3.05 (1.64-5.66)	12.32 (4.90-30.97)	3.56 (1.95-6.48)	14.30 (5.77-35.45)	3.44 (1.88-6.31)	14.01 (5.64-34.82)	3.35 (1.83-6.15)	13.36 (5.37-33.24)	3.40 (1.85-6.24)	13.14 (5.28-32.71)	2.90 (1.55-5.41)	11.34 (4.49-28.63)	2.96 (1.58-5.34)	11.41 (4.52-28.78)
)	0.76 (0.41-1.41)	0.81 (0.44-1.49)	0.65 (0.35-1.22)	0.98 (0.54-1.77)	0.79 (0.43-1.47)	0.92 (0.51-1.67)	0.74 (0.40-1.38)	0.93 (0.51-1.68)	0.74 (0.40-1.39)	0.93 (0.51-1.70)	0.73 (0.39-1.36)	0.80 (0.43-1.47)	0.63 (0.34-1.20)	0.80 (0.44-1.48)	0.63 (0.33-1.19)
)	0.41 (0.22-0.78)	0.53 (0.29-0.97)	0.38 (0.20-0.72)	0.61 (0.34-1.11)	0.43 (0.23-0.80)	0.55 (0.30-1.00)	0.40 (0.21-0.75)	0.56 (0.30-1.02)	0.39 (0.21-0.74)	0.57 (0.31-1.05)	0.38 (0.20-0.71)	0.49 (0.26-0.90)	0.34 (0.18-0.65)	0.51 (0.28-0.96)	0.34 (0.18-0.65)
)	0.20 (0.08-0.52)	0.46 (0.19-1.41)	0.22 (0.08-0.59)	0.44 (0.18-1.04)	0.22 (0.08-0.56)	0.39 (0.16-0.94)	0.19 (0.07-0.49)	0.40 (0.17-0.95)	0.19 (0.07-0.49)	0.40 (0.17-0.96)	0.19 (0.07-0.49)	0.44 (0.18-1.08)	0.21 (0.08-0.56)	0.45 (0.18-1.11)	0.21 (0.08-0.56)
)	1.59 (1.00-2.52)	…	…	…	…	…	…	…	…	0.84 (0.53-1.34)	1.26 (0.78-2.03)	…	…	0.65 (0.40-1.05)	0.96 (0.58-1.58)
	…	3.23 (2.10-4.98)	3.94 (2.45-6.34)	…	…	…	…	…	…	…	…	2.84 (1.83-4.41)	3.31 (2.04-5.38)	3.13 (1.99-4.94)	3.34 (2.02-5.51)
	…	…	…	2.20 (0.92-5.23)	3.83 (1.60-9.19)	…	…	…	…	…	…	…	…	…	…
	…	…	…	…	…	2.40 (1.57-3.69)	2.69 (1.72-4.19)	…	…	…	…	…	…	…	…
	…	…	…	…	…	…	…	2.32 (1.52-3.52)	2.90 (1.88-5.50)	2.40 (1.56-3.67)	2.78 (1.78-4.34)	1.99 (1.30-3.05)	2.46 (1.57-3.84)	2.14 (1.38-3.32)	2.47 (1.57-3.90)

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uxen (diazepam) from the same ampoule with other people";

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