Original Article

Polysubstance Use Among the Homeless In Germany

A Nationwide, Cross-Sectional Multicenter Study

Fabian Heinrich*[1], Jakob Manthey*[1], Birgit Wulff, Franziska Stallbaum, Katharina Dost, Wiebke Graf, Veronika Kowalski, Anna Brennecke, André Hajek, Hans-Helmut König, Klaus Püschel, Benjamin Ondruschka*[2], Stefanie Iwersen-Bergmann*[2]

*[1] Joint first authors

*[2] Joint last authors

Institute of Legal Medicine, University Medical Center Hamburg-Eppendorf, Hamburg: Fabian Heinrich, MD, MSc; Birgit Wulff, MD; Katharina Dost, DMD; Wiebke Graf, MD; Veronika Kowalski, MD; Anna Brennecke, MD; Klaus Püschel, MD; Benjamin Ondruschka, MD; Stefanie Iwersen-Bergmann, PhD

Department of Medical Statistics, London School of Hygiene and Tropical Medicine, London, UK: Fabian Heinrich, MD, MSc

Centre for Data and Statistical Science for Health, London School of Hygiene and Tropical Medicine, London, UK: Fabian Heinrich, MD, MSc

Center for Interdisciplinary Addiction Research (ZIS), Department of Psychiatry and Psychotherapy, University Medical Center Hamburg-Eppendorf, Hamburg: Jakob Manthey, PhD

Department of Psychiatry, Medical Faculty, University of Leipzig: Jakob Manthey, PhD

First Department of Medicine, University Medical Center Hamburg-Eppendorf, Hamburg: Franziska Stallbaum, MD

Department of Health Economics and Health Services Research, University Medical Center Hamburg-Eppendorf, Hamburg: André Hajek, PhD; Hans-Helmut König, MD

Summary

Background: The number of people experiencing homelessness (PEH) in Germany reached 440 000 in 2024, double the total from 2022. Representative data on substance use among PEH is largely lacking. In this study, we estimate the prevalence of substance use among PEH and identify subgroups at risk of polysubstance use.

Methods: A cross-sectional study of 674 PEH was conducted in four German metropolitan areas in 2021. All PEH were interviewed and provided blood samples in homeless support facilities. Toxicological analysis of serum samples revealed the presence of 22 substances, which were grouped as alcohol, central nervous system (CNS) stimulants, narcotic analgesics, and cannabis. Polysubstance use was defined as the detection of substances belonging to at least two of these groups.

Results: The toxicological analyses revealed that 35% of PEH had no recent substance use (95% confidence interval [31; 39]), while 34% had recently engaged in polysubstance use ([30; 38]). Alcohol was the most prevalent substance (39% [35; 43]), followed by CNS stimulants (30% [27; 34]), cannabis (28% [24; 32]), and narcotic analgesics (18% [15; 21]). Polysubstance use was linked to younger age, prior incarceration, current tobacco use, and geographical location.

Conclusion: In Germany today, the number of PEH is growing, substance availability is widespread, and drug-related deaths are on the rise. It is, therefore, vitally important to continue monitoring the situation and to provide targeted support to those who need it.

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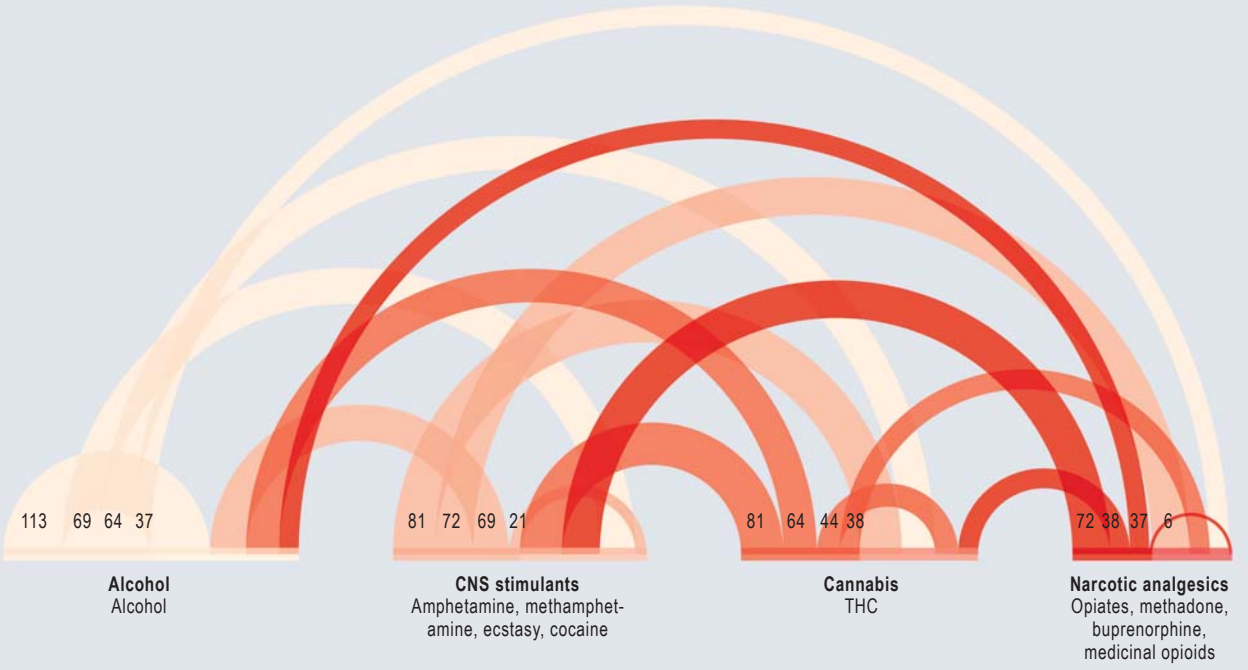
There are currently about 1 300 000 homeless persons (persons experiencing homelessness, PEH) in Europe (1), with around three in four of them suffering from mental disorders (2). Among PEH, disorders caused by alcohol and illegal substance use are the most common psychiatric conditions (2), and illegal substance-related deaths are widespread (3). Data from Denmark and Canada indicate that the standardized all-cause mortality rate among PEH is 3 to 12 times greater than that in the general population (4). Among individuals with previous substance-related hospitalization for the principal cause of death, PEH were seven times more likely to die from illegal substance use, but not alcohol use, than the general population (3).

Although substance use is known to be an integral factor in homelessness and the continuation of homelessness (5), little research into substance consumption in this vulnerable sector of the population has been conducted. Given the lack of a systematic review on the prevalence of substance use among PEH, we reviewed the literature and found only three population-based studies on PEH from different parts of France, Spain, and Canada. In all three countries, PEH were recruited from three major cities, with settings classified as roofless and houseless according to the European Typology on Homelessness and Housing Exclusion (ETHOS) (6). The Canadian study also included PEH from inadequate settings, as defined by ETHOS (e.g., mobile homes or temporary structures). The French study stated the prevalence of tobacco, alcohol, and cannabis use among PEH as 40%, 30%, and 10%, respectively (7), while the Spanish (8) and Canadian (9) studies documented only the prevalence of problematic substance use. In-depth information on the distribution of illicit substance use was not reported in any of these studies. No previous population-based study determined substance use through toxicological analysis.

Figure 1



An arc plot illustrating co-use patterns across four substance classes. Each wedge on the x-axis signifies a substance class, with its width representing the total number of users. The arcs depict substance combinations: their color corresponds to the initial class, and their thickness indicates the frequency of occurrence. Arcs within a single class show intraclass combinations. The numbers below each arc indicate the number of users of that specific combination of substances.
CNS, Central nervous system; co-use, collaborative use; THC, tetrahydrocannabinol

In Germany, official figures reported 262 000 PEH in 2022, with 178 000 persons registered in emergency accommodation (10). Between 2022 and 2024, the number of persons living in such shelters more than doubled to 440,000 (11). Increasing numbers of PEH have also been observed in other European countries, such as Ireland (1). Furthermore, mortality as a direct consequence of illicit substance use in Germany has almost doubled in the past decade, reaching 2137 deaths in 2024 (12). Polysubstance use, mainly in the form of heroin or other opioids mixed with other substances, was a common cause of death (13), suggesting that this is a widespread and hazardous practice.

The current study aims to provide detailed information about substance and polysubstance use among PEH in Germany in the period July to September 2021. Using a population-based approach and relying on self-reporting and toxicological data, this study provides a comprehensive overview of the use of specific substances and their combination and explores risk factors for polysubstance use.

Methods

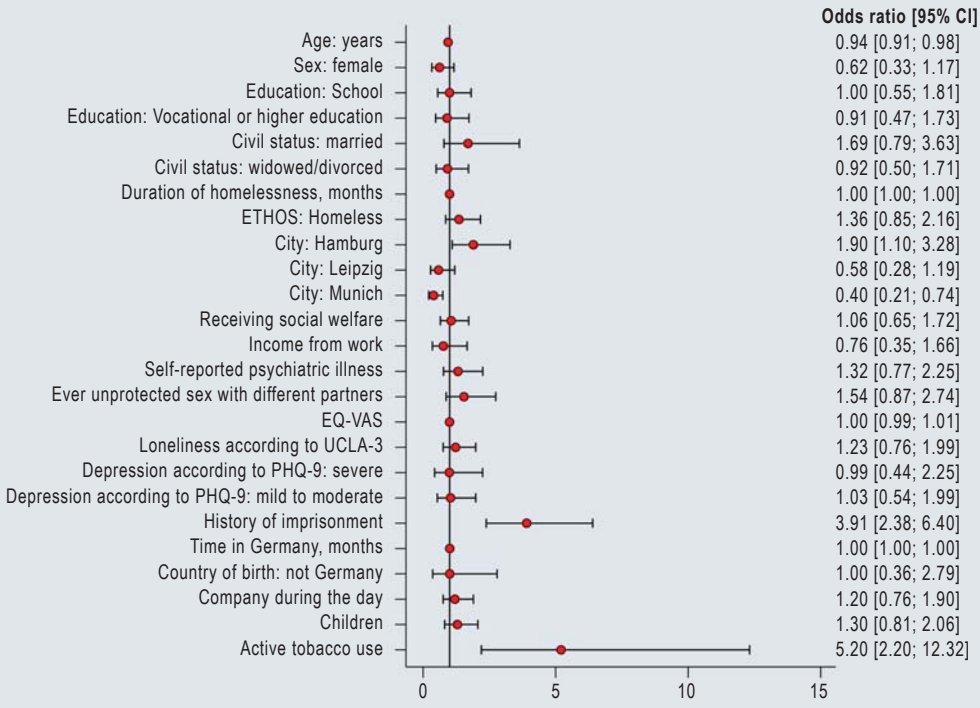
Study design

This was a national cross-sectional study in four German metropolitan areas: Hamburg, Frankfurt am Main (including Mainz and Wiesbaden), Leipzig (including Halle an der Saale), and Munich (including Augsburg). The National Survey on the Psychiatric and Somatic Health of Homeless Individuals (NAPSHI) was conducted between July and September 2021 (14). This study was designed in adherence to the Declaration of Helsinki and approved by the ethics committee of the Hamburg Medical Association (application number PV7333). Reporting followed the STROBE guidelines (Strengthening the Reporting of Observational Studies in Epidemiology). Details of the recruitment process can be found in *eSupplement Material 1*. Data on the homeless support landscape were obtained through an online survey of homeless support facilities *(eSupplement Material 2)*.

Primary outcome: Polysubstance use

The primary outcome, the prevalence of polysubstance use, was examined by means of toxicological analyses (see *eSupplement Material 3* for details). Polysubstance use was defined as the use of substances from at least two groups, comprising alcohol, central nervous system (CNS) stimulants, narcotic analgesics, and cannabis Details of each see substance group examined can be found in *eSupplement Table 1*. Single substances were identified as positive when testing for the substance or its metabolite yielded a positive result. Substance groups were identified as positive when at least one substance or metabolite was positive and negative when all substances and metabolites were negative. For some PEH, individual substance group measurements were missing when insufficient samples were available to measure the remaining substances. These missing measurements were assumed missing at random (n = 37). Polysubstance use was determined only for complete cases.

Figure 2



Odds ratios and 95% confidence intervals from pooled multivariable logistic regression, after substantive-model compatible multiple imputations with 50 imputation data sets and 1000 iterations between the imputations. The imputations of the dependent variable were deleted (n = 583).
95% CI, 95% Confidence interval; EQ-VAS, EuroQol Visual Analogue Scale; ETHOS, European Typology of Homelessness and Housing Exclusion; UCLA-3, University of California. Los Angeles. Loneliness Scale; PHQ-9, Patient Health Questionnaire-9

Secondary outcome: Single substance use

As secondary outcome, the prevalence of use of the following substances was determined from blood samples and self-reports: alcohol (blood alcohol and desialotransferrin [carbohydrate-deficient transferrin, CDT]), amphetamine, methamphetamine, cocaine, MDMA (3,4-methylenedioxymethylamphetamine, "ecstasy"), opiates, medicinal opioids, substitution opioids, and cannabis. The questionnaire used to assess self-reported substance use is shown in *eSupplement Material 4*.

Exposure

Self-reported sociodemographic characteristics, somatic and psychiatric health status, and geography constitute exposures of interest. No effect modification was assumed.

Bias

Selection bias was avoided by the multicenter recruitment in homeless support facilities. To minimize barriers to participation in the study, questionnaire-based interviews were offered so that illiterate persons could also take part. The questionnaires were available in several languages, and a translator was called upon when necessary. Self-report bias was addressed by performing objective toxicological measurements. Multiple imputation was used to handle missing data.

Statistical analysis

The sample for analysis included all PEH eligible for study enrolment. The methods used for statistical analysis can be found in *eSupplement Material 5*.

Graphical illustration

GraphPad Prism (Version 10.2.3 [347]; GraphPad Software, CA, USA) and Adobe Illustrator 2024 (Version 28.5; Adobe, CA, USA) were used for graphical illustration.

Results

In total, 674 PEH were enrolled from four metropolitan areas in Germany: 213 from Hamburg, 108 from Leipzig, 154 from Frankfurt, and 199 from Munich. The mean age was 44 years (standard deviation [SD] 12), with an 18% proportion of women (n = 118). The PEH were recruited from settings classified as rooflessness (sleeping rough, without any form of shelter; 57%, n = 353) and houselessness (sleeping in temporary shelters or institutions; 43%, n = 262). *Table 1, eSupplement Table 2*, and *eSupplement Table 3* contain further information on housing status and sample characteristics.

Primary outcome: Polysubstance use

The primary outcome was evaluated among PEH with complete toxicological data (n = 583). No substantial differences from PEH with incomplete toxicological analysis were observed *(eSupplement Table 3)*. In one third of the

Table 1

Description of the sample of PEH in Germany by sex (n = 674); 25 PEH did not report their sex.

		Male N = 531 mean (SD) and number (%)	Female N = 118 mean (SD) and number (%)	Total N = 674 mean (SD) and number (%)
● Sociodemographics				
Age, years		43.7 (12.3%)	42.5 (11.5%)	43.5 (12.2%)
Age range, years		18–80	18–79	18–80
Educational attainment	– No qualification – High school – Vocational or higher education	86 (17.0%) 232 (45.9%) 187 (37.0%)	26 (22.6%) 54 (47.0%) 35 (30.4%)	113 (18.1%) 287 (46.0%) 224 (35.9%)
Marital status	– Single – Married – Widowed/divorced	362 (70.3%) 59 (11.5%) 94 (18.3%)	55 (50.9%) 15 (13.9%) 38 (35.2%)	420 (67.0%) 74 (11.8%) 133 (21.2%)
● Characteristics of homelessness				
Duration of homelessness*1, months		18.0 (5.0–48.0)	12.5 (3.0–60.0)	18.0 (5.0–48.0)
European Typology of Homelessness*2	– Roofless – Houseless	291 (58.8%) 204 (41.2%)	57 (50.9%) 55 (49.1%)	353 (57.4%) 262 (42.6%)
Social welfare		224 (44.1%)	62 (53.9%)	287 (45.8%)
Financial income from work		56 (11.4%)	16 (15.0%)	73 (12.1%)
● Psychiatric health status				
Self-reported psychiatric illness		109 (20.8%)	39 (33.3%)	149 (22.7%)
Quality of life according to EQ-VAS*1		75.0 (50.0–90.0)	75.0 (50.0–85.0)	75.0 (50.0–90.0)
Loneliness according to UCLA-3		208 (40.7%)	54 (47.8%)	264 (41.7%)
Anxiety disorder according to GAD-2		131 (25.7%)	40 (25.1%)	171 (27.1%)
Depression according to PHQ-9	– None – Mild to moderate – Moderately severe to severe	90 (18.2%) 282 (57.1%) 122 (24.7%)	13 (11.8%) 57 (51.8%) 40 (36.4%)	104 (17.0%) 345 (56.4%) 163 (26.6%)
● Risk factors				
History of imprisonment		292 (58.2%)	43 (37.4%)	339 (54.2%)
Ever unprotected sex with different partners		98 (21.9%)	18 (18.2%)	118 (21.3%)

*1 Median (IQR) is presented wherever the data are not normally distributed.
*2 Defined according to the categories of the European Typology of Homelessness
EQ-VAS, EuroQol Visual Analogue Scale; GAD-2, Generalized Anxiety Disorder-2; IQR, interquartile range; PEH, people experiencing homelessness; PHQ-9, Patient Health Questionnaire-9; SD, standard deviation; UCLA-3, University of California, Los Angeles, Loneliness Scale

PEH, no recent substance use was detected (n = 201; 34.5% [95% confidence interval [30.6; 38.5]). Conversely, two thirds of the PEH (n = 382; 65.6% [61.5; 69.4]) had recently used one of the four substance groups examined. In every third PEH (n = 198; 34.0% [30.1; 38.0]), polysubstance use was identified (≥ 2 substance groups; male 36% vs female 28%). Among PEH who had recently used any substance, a median of two substance groups were consumed (interquartile range [IQR] 1 to 4). As shown in *Figure 1*, the most common two-way combinations of substance groups were alcohol with CNS stimulants, alcohol with cannabis, CNS stimulants with cannabis, and CNS stimulants with narcotic analgesics. Distinct patterns of substance group use can be found in *eSupplement Table 4*.

After controlling for other sociodemographic and health variables, polysubstance use was significantly associated with age, history of incarceration, active tobacco use, and geography *(Figure 2)*. If all PEH had reported having been in prison, the proportion of polysubstance use would have been 39%. In contrast, if none of the PEH had been in prison, the proportion of polysubstance use in this sample would have been 14%. Results from the complete case analysis are shown in *eSupplement Table 5*. Only about half of the surveyed sites allow PEH to use substances on their premises (illegal substance use: 13%; alcohol use: 23%).

Secondary outcome: Single substance use (blood-based)

Overall, alcohol was the single most frequently used substance, followed by cannabis, cocaine, amphetamines and methadone *(Table 2)*. The *eSupplement Figure* shows the serum concentrations of the respective substances and metabolites among PEH testing positive for substance use. Blood alcohol concentrations (median 1.2‰, IQR 0.5–2.0) and CDT concentrations (median 4.70%, IQR 3.00–8.60) were very high.

Secondary outcome: Single substance use (self-reported)

About 40% of PEH reported consuming more than seven glasses of alcohol per week. More than 40% exceeded

Table 2

Positive toxicological tests for substances and substance groups in PEH in Germany by sex (n = 674); 25 PEH did not report their sex.

	Male N = 531 number (%)	Female N = 118 number (%)	Total N = 674 ,umber (%)
● **CNS stimulants**	150 (30.7%)	32 (32.3%)	185 (30.2%)
Amphetamine	64 (13.1%)	10 (10.1%)	74 (12.1%)
Methamphetamine	39 (8.0%)	6 (6.1%)	47 (7.7%)
Cocaine	77 (15.7%)	20 (20.2%)	98 (16.0%)
Ecstasy	3 (0.6%)	2 (2.0%)	5 (0.8%)
● **Alcohol**	198 (41.1%)	26 (27.1%)	234 (38.9%)
Acute alcohol use	152 (31.3%)	20 (20.2%)	180 (29.6%)
Chronic alcohol use	161 (33.3%)	14 (14.6%)	183 (30.3%)
● **Narcotic analgesics**	87 (17.8%)	19 (19.2%)	107 (17.5%)
Opiates	47 (9.6%)	10 (10.1%)	57 (9.3%)
– Heroin*1	33 (6.7%)	8 (8.1%)	41 (6.7%)
– Morphine*2	6 (1.2%)	0 (0.0%)	6 (1.0%)
Methadone	53 (10.8%)	14 (14.1%)	67 (10.9%)
Buprenorphine	8 (1.6%)	2 (2.0%)	11 (1.8%)
Medicinal opioids	8 (1.6%)	0 (0.0%)	8 (1.3%)
– Tramadol	1 (0.2%)	0 (0.0%)	1 (0.2%)
– Tilidine	2 (0.4%)	0 (0.0%)	2 (0.3%)
– Fentanyl	2 (0.4%)	0 (0.0%)	2 (0.3%)
– Tapentadol	2 (0.4%)	0 (0.0%)	2 (0.3%)
– Oxycodone	1 (0.2%)	0 (0.0%)	1 (0.2%)
– Hydromorphone	0 (0.0%)	0 (0.0%)	0 (0.0%)
– Hydrocodone	0 (0.0%)	0 (0.0%)	0 (0.0%)
– Sufentanil	0 (0.0%)	0 (0.0%)	0 (0.0%)
– Alfentanil	0 (0.0%)	0 (0.0%)	0 (0.0%)
– Piritramide	1 (0.2%)	0 (0.0%)	1 (0.2%)
– Pethidine	0 (0.0%)	0 (0.0%)	0 (0.0%)
– Dextromethorphan	0 (0.0%)	0 (0.0%)	0 (0.0%)
● **Cannabis**	145 (30.1%)	15 (15.6%)	167 (27.8%)

*1 Heroin is rapidly metabolized to monoacetylmorphine and morphine. Codeine, as an ingredient of raw opium, is routinely detectable after heroin. Heroin was considered positive only when monoacetylmorphine, morphine, and codeine were detected.
*2 Morphine was considered positive when morphine or morphine and codeine were detected.
CNS, Central nervous system; PEH, people experiencing homelessness

sex-specific thresholds for heavy episodic alcohol consumption on a daily to weekly basis *(Table 3)*. Every sixth PEH stated they used substances intravenously, with the majority of PEH having done so for many years. Every second PEH stated they had used illegal substances in the past year. The substances mostly concerned were cannabis, cocaine, and street opiates.

Discussion

Among 674 PEH from four metropolitan areas in Germany, two thirds had recently used alcohol, cannabis, or illegal substances. One third of the PEH were found to have recently used substances from at least two groups, most commonly alcohol together with CNS stimulants or alcohol and cannabis. Among PEH with documented substance use, polysubstance use appears to be a common practice.

This is the first population-based study to estimate the prevalence of substance use by means of toxicological measurements in a large, heterogeneous sample of PEH. At first sight, the high prevalence of substance use among PEH is not surprising and corresponds to previous studies (2). However, our findings add a critical dimension: a tripartition of PEH into abstainers, single-substance users, and polysubstance users. Considerable heterogeneity of substance use can be observed among PEH: one third did not test positive for any substance, while another third tested positive for two or more substances. Very high blood levels of alcohol and CDT, together with a high proportion of PEH engaging in heavy episodic drinking on a daily or weekly basis, indicate severe chronic alcohol use. The high rates of cardiovascular and liver problems observed in this population (14) may be caused by regular alcohol intake over a long period (15). Nevertheless, it needs to be stressed that a considerable number of PEH do not use any substances. In fact, the proportion of abstainers may be similar to that in the general population or even larger (16). In 2021, three out of ten adults in Germany reported that they had not consumed alcohol in the previous month. There are no data on the use of other substances remains unclear (16). With both abstainers and heavy users represented among PEH, shared spaces may be difficult to

Table 3

Self-reported substance use by sex (n = 674); 25 PEH did not report their sex.

		Male N = 531 mean (SD) and number (%)	Female N = 118 mean (SD) and number (%)	Total N = 674 mean (SD) and number (%)
● Alcohol				
Alcohol > 7 glasses*/week		217 (42.9%)	22 (19.5 %)	243 (38.8%)
Time since starting to consume alcohol >7 glasses*/week, years		15.0 (5.0–25.0)	10.0 (2.0–20.0)	15.0 (4.0–25.0)
Past year: Alcohol ♂ > 5 glasses*/day and ♀ > 4 glasses*/day	– Never – 1–2 times – Monthly – Weekly – Daily	162 (31.8%) 52 (10.2%) 65 (12.7%) 64 (12.5%) 167 (32.7%)	50 (43.5%) 14 (12.2%) 16 (13.9%) 13 (11.3%) 22 (19.1%)	213 (33.6%) 67 (10.6%) 83 (13.1%) 81 (12.8%) 189 (29.9%)
● Substances				
Intravenous substance use		73 (14.3%)	20 (17.7%)	94 (14.9%)
Duration of intravenous substance use, months		84.0 (20.0–288.0)	114.0 (19.0–324.0)	87.0 (20.0–300.0)
● Substance use				
Past year: use of illegal substances	– Never – 1–2 times – Monthly – Weekly – Daily	279 (56.9%) 20 (4.1%) 44 (9.0%) 40 (8.2%) 107 (21.8%)	64 (58.2%) 2 (1.8%) 6 (5.5%) 7 (6.4%) 31 (28.2%)	350 (57.5%) 22 (3.6%) 50 (8.2%) 48 (7.9%) 139 (22.8%)
Cannabis use		168 (32.7%)	23 (20.2%)	193 (30.3%)
Cocaine use		85 (16.6%)	24 (21.1%)	110 (17.3%)
Use of stimulants (“uppers”, e.g., Ritalin, Concerta, Dexedrine, Adderall, diet tablets)		9 (1.8%)	4 (3.5%)	13 (2.0%)
Use of amphetamines or methamphetamines (e.g., speed, crystal, ice)		70 (13.6%)	11 (9.6%)	81 (12.7%)
Use of sedatives or sleeping pills (“downers”, e.g., Valium, Xanax, Rohypnol, GHB)		12 (2.3%)	8 (7.0%)	20 (3.1%)
Use of hallucinogens (e.g., LSD, acid, mushrooms, PCP, special K, ecstasy)		30 (5.8%)	7 (6.1%)	37 (5.8%)
Use of street opiates (e.g., heroin, opium)		78 (15.2%)	20 (17.5%)	98 (15.4%)
Use of medicinal opioids (e.g., fentanyl, oxycodone, Vicodin, hydrocodone, methadone)		41 (8.0%)	13 (11.4%)	54 (8.5%)

*One glass = 330 ml.
GHB, Gamma-hydroxybutyric acid; ice, street name for methamphetamine; LSD, lysergic acid diethylamide; PCP, phencyclidine; PEH, persons experiencing homelessness; special K, street name for ketamine

establish. In most of the facilities surveyed, use of alcohol or illegal substances is not allowed, creating a barrier to heavy users but potentially creating a safe environment for abstainers. By acknowledging the differential needs of PEH, services can be tailored to meet the specific requirements of different subgroups. Essentially, this means housing programs that presuppose recovery from substance use problems (17); such programs have shown promising health impacts (18).

A number of studies have revealed that incarceration constitutes a major, partly avoidable risk factor for continued homelessness (19) and health consequences (20). The study presented here shows, in addition, that previous imprisonment is a strong predictor of current polysubstance use. In our sample, 54% of PEH reported having been imprisoned at some point in their lives. Imprisonment can result from criminal offenses or non-payment of administrative fines. In Germany, a substitute custodial sentence can be imposed for non-payment of administrative fines (e.g., as a result of not paying transport fares). Such sentences disproportionately affects socioeconomically disadvantaged persons, including PEH and those with substance use problems (21).

Several limitations of this study need to be acknowledged. First, it is difficult to establish true representativeness. As there is no register of either facilities or PEH, we cannot rule out possible selection biases due to non-response. This is further limited by the lack of response rates in our and many other studies on PEH. Many studies on PEH underrepresent women (22), and we may not be an exception in this regard (the proportion of women in our study is 18%; official estimates range around 35%) (10). Yet, considering various forms of homelessness in four regions, our sample of PEH is believed to be approximately representative of PEH in Germany in 2021. Second, serum samples were employed for toxicological analyses using highly sensitive measurement techniques. Blood measurements generally limit the detection window to about 24 to 48 hours before enrolment, contingent on substance and frequency of use. This constraint precludes the direct extrapolation of our findings to long-term patterns of substance use.

In conclusion, our findings show that polysubstance use was identified in around one third of PEH—in addition to a multitude of other environmental and social risk factors. Within this already vulnerable population, those engaging in polysubstance use may represent the subgroup at greatest risk, given their elevated rates of incarceration. Against the backdrop of a growing PEH population (10), wide availability of legal and illegal substances (23), and escalating rates of illicit substance overdose deaths in Germany (12), continued monitoring and targeted support of those in need appear especially warranted.

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Conflict of interest statement
KP, FH, and BO received support for manuscript compilation from the Volkswagen Foundation. JM's institution received funding from the German Federal Ministry of Health JM himself has received consultation fees from the AOK and the WHO, as well as fees for presentations on the topic of substance use from the BAS, the DHS, the Friedrich Ebert Foundation, the Voluntary Welfare League of Sachsen–Anhalt, and the Therapy Store (Therapieladen e. V.). Travel costs were paid by the charitable foundation of Hanover Medical School. The remaining authors declare that no conflict of interest exists.

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Corresponding author
Fabian Heinrich, MD, MSc
fa.heinrich@uke.de

Supplementary material
Complete list of full references, eFigure, eSupplement:
www.aerzteblatt-international.de/m2025.0132

Supplementary material to accompany the article

Polysubstance Use Among the Homeless In Germany

A Nationwide, Cross-Sectional Multicenter Study

Fabian Heinrich*[1], Jakob Manthey*[1], Birgit Wulff, Franziska Stallbaum, Katharina Dost, Wiebke Graf, Veronika Kowalski, Anna Brennecke, André Hajek, Hans-Helmut König, Klaus Püschel, Benjamin Ondruschka*[2], Stefanie Iwersen-Bergmann*[2]

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Complete list of full references

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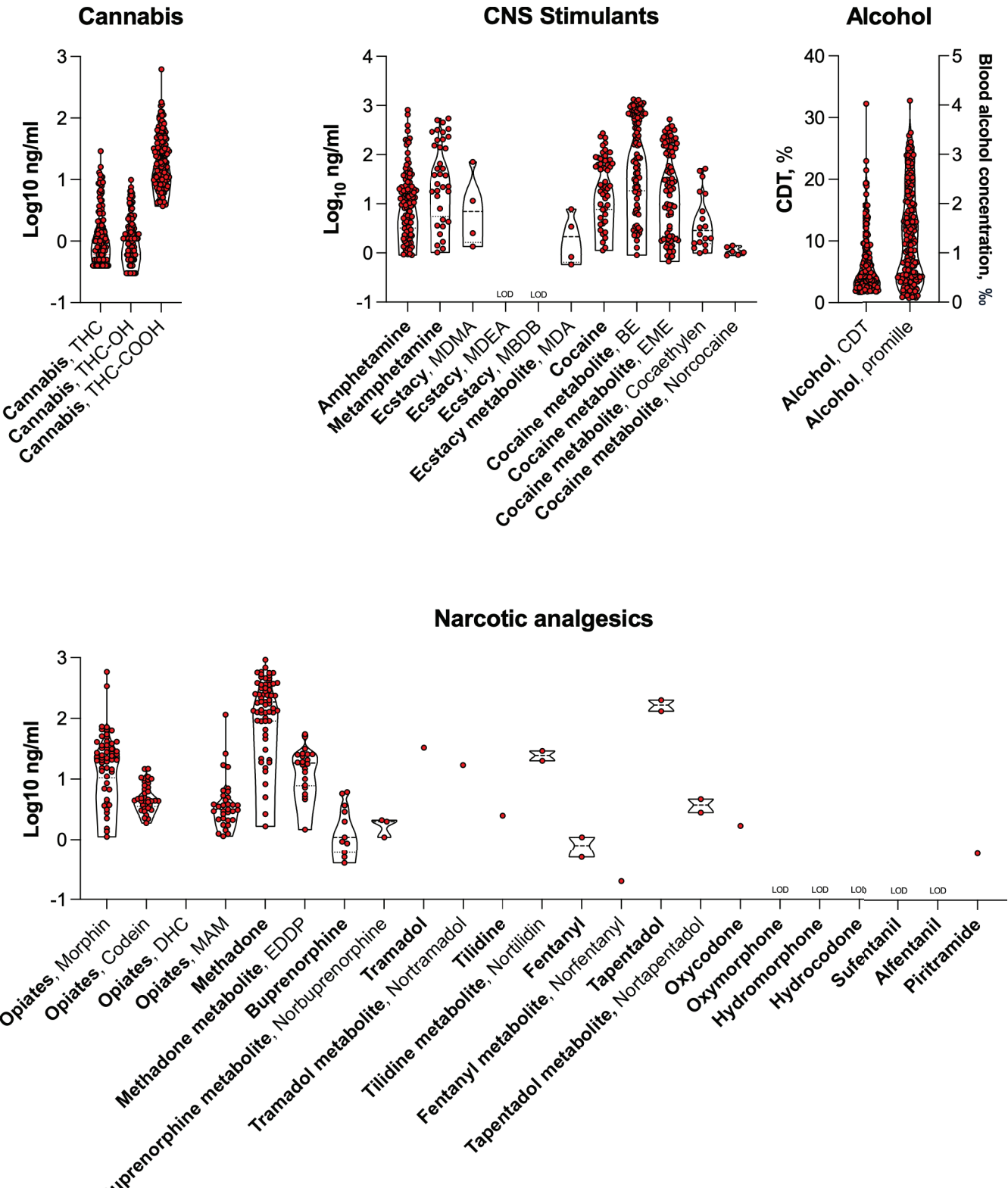
Supplementary Figure 1. Truncated violin plots of individual substances and metabolites according to substance group. Active and inactive metabolite concentrations are shown on the log10 scale, with the mean $\log_{10}$ concentration corresponding to the geometric mean on the linear scale. Cocaethylene is a metabolite of cocaine that forms in the presence of alcohol. Values for positive individuals above the LOD are shown, with the LOQ remaining unconsidered for this illustration.



Abbreviations: LOD, lower limit of detection; LOQ, lower limit of quantification; THC, Δ9-Tetrahydrocannabinol; THC-OH, 11-hydroxy-THC; THC-COOH, THC-carboxylic acid; CNS, Central nervous system; MDMA, Methylenedioxymethamphetamine; MDEA, Methylenedioxyethylamphetamine; MBDB, Benzodioxolylmethylbutanamine; MDA, Methylenedioxyamphetamine; BE, Benzoylecgonine; EME, Ecgoninemethylester; CDT, Carbohydrate-deficient transferrin; DHC, Dihydrocodeine; MAM, Monoacetylmorphine; EDDP, Ethylidenedimethyldiphenylpyrrolidine.

Polysubstance use in homeless individuals in Germany: a nationwide cross-sectional multicentre study

Authors: Fabian Heinrich[1,2,3*], Jakob Manthey[4,5*], Birgit Wulff[1], Franziska Bertram[6], Katharina Dost[1], Wiebke Graf[1], Veronika Kowalski[1], Anna Brennecke[1], André Hajek[7], Hans-Helmut König[7], Benjamin Ondruschka[1*], Stefanie Iwersen-Bergmann[1*]

[*]These authors equally contributed to this article.

Supplementary Material

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Supplementary Table 1. Mother substances and metabolites are shown to depict the definition of substances and substance groups.

Substance group	Active substance/Metabolite	LOD (ng/ml)	LOQ (ng/ml)
Cannabis			
	Δ9-Tetrahydrocannabinol (THC)	0.12	0.39
	11-hydroxy-THC (THC-OH)	0.09	0.27
	THC-carboxylic acid (THC-COOH)	1.00	2.30
CNS Stimulants			
Cocaine	Cocaine	0.34	1.10
	Benzoylecgonine (BE)	0.28	0.89
	Ecgoninemethylester (EME)	0.20	0.66
	Norcocaine	0.25	0.80
	Cocaethylene	0.30	0.99
Methamphetamine	Methamphetamine	0.31	0.97
Amphetamine	Amphetamine	0.26	1.06
Ecstasy	Methylenedioxymethamphetamine (MDMA)	0.21	0.69
	Methylenedioxyamphetamine (MDA)	0.15	0.97
	Methylenedioxyethylamphetamine (MDEA)	0.13	0.69
Opioids			
Heroin	6-Monoacetylmorphine (MAM)	0.37	1.10
Morphine	Morphine	0.34	1.06
Codeine	Codeine	0.47	1.40
Dihydrocodeine	Dihydrocodeine (DHC)	0.40	1.40
Methadone	Methadone	0.52	1.50
	Ethylidenedimethyldiphenylpyrrolidine (EDDP)	0.38	1.10
Buprenorphine	Buprenorphine	0.30	1.10
	Norbuprenorphine	0.30	0.80
Medicinal opioids			
Alfentanil	Alfentanil	0.60	1.90
Fentanyl	Fentanyl	0.20	0.50
	Norfentanyl	0.20	0.50
Hydrocodone	Hydrocodone	1.30	4.70
Hydromorphone	Hydromorphone	0.50	1.20
Piritramide	Piritramide	0.10	0.60
Sufentanil	Sufentanil	0.30	1.20
Tapentadol	Tapentadol	2.50	5.90
	N-Desmethyltapentadol	0.50	2.50
Oxycodone	Oxycodone	0.40	1.70
Tilidine	Tilidine	1.80	7.10
	Nortilidine	2.30	8.60
Tramadol	Tramadol	9.70	25.00
	O-Desmethyltramadol	7.80	24.00
Alcohol			
Alcohol	Ethanol (ETOH)	0.01%	0.01%
	Carbohydrate-deficient transferrin (CDT)	..	1.7%

Abbreviations: LOD, limit of detection; LOQ, limit of quantification, CNS, central nervous system; NA, not applicable.

Supplementary Table 2. People experiencing homelessness (PEH) are categorised based on the European Typology of Homelessness and Housing Exclusion and sex.

	Male Number (%) N=531	**Female** Number (%) N=118	**Total** Number (%) N=674
People living rough, category 1	211 (42.6)	42 (37.5)	254 (41.3)
People in emergency accommodations, category 2	80 (16.2)	15 (13.4)	99 (16.1)
People in accommodation for the homeless, category 3	188 (38.0)	34 (30.4)	225 (36.6)
People in women shelters, category 4	12 (2.4)	20 (17.9)	32 (5.2)
People in accommodation for immigrants, category 5	1 (0.2)	1 (0.9)	2 (0.3)
People due to be released from institutions, category 6	3 (0.6)	0 (0.0)	3 (0.5)

Supplementary Table 3. Baseline characteristics and self-reported substance use for individuals with complete and partial toxicological analysis and individuals without blood for toxicological analysis.

	Complete toxicological analysis N=583 Mean (SD) and number (%)	**Partial toxicological analysis** N=37 Mean (SD) and number (%)	**No toxicological analysis** N=54 Mean (SD) and number (%)	**Total** N=674 Mean (SD) and number (%)
Age, years	43.6 (12.4)	43.5 (9.7)	41.9 (11.4)	43.5 (12.2)
Sex				
Male	467 (83.4%)	29 (80.6%)	35 (66.0%)	531 (81.8%)
Female	93 (16.6%)	7 (19.4%)	18 (34.0%)	118 (18.2%)
Educational attainment				
No degree	98 (18.2%)	6 (16.7%)	9 (17.6%)	113 (18.1%)
School education	247 (46.0%)	19 (52.8%)	21 (41.2%)	287 (46.0%)
Vocational and higher education	192 (35.8%)	11 (30.6%)	21 (41.2%)	224 (35.9%)
Marital status				
Single	359 (66.4%)	26 (74.3%)	35 (68.6%)	420 (67.0%)
Married	67 (12.4%)	2 (5.7%)	5 (9.8%)	74 (11.8%)
Widowed/divorced	115 (21.3%)	7 (20.0%)	11 (21.6%)	133 (21.2%)
Characteristics of homelessness				
Time of homelessness[a], months	18.0 (5.0-48.0)	24.0 (6.0-60.0)	12.0 (3.5-48.0)	18.0 (5.0-48.0)
European Typology of Homelessness				
Roofless	308 (57.8%)	20 (55.6%)	25 (54.3%)	353 (57.4%)
Houseless	225 (42.2%)	16 (44.4%)	21 (45.7%)	262 (42.6%)
Social welfare	241 (44.5%)	17 (47.2%)	29 (58.0%)	287 (45.8%)
Financial income from work	62 (11.9%)	2 (6.2%)	9 (18.4%)	73 (12.1%)
Psychiatric health status				
SR Psychiatric disease	121 (21.3%)	13 (35.1%)	15 (29.4%)	149 (22.7%)
Quality of life according to EQ-VAS[a]	75.0 (50.0-90.0)	75.0 (50.0-80.0)	70.0 (50.0-90.0)	75.0 (50.0-90.0)
Loneliness according to UCLA-3	228 (41.6%)	20 (55.6%)	16 (32.7%)	264 (41.7%)
Anxiety disorder according to GAD-2	145 (26.7%)	11 (29.7%)	15 (30.0%)	171 (27.1%)
Depression according to PHQ-9				
None	91 (17.3%)	6 (16.2%)	7 (14.6%)	104 (17.0%)
Mild to moderate	303 (57.5%)	19 (51.4%)	23 (47.9%)	345 (56.4%)
Medium to severe	133 (25.2%)	12 (32.4%)	18 (37.5%)	163 (26.6%)
Risk factors				
History of prison	290 (53.6%)	23 (63.9%)	26 (54.2%)	339 (54.2%)
Ever unprotected sex with different partners	106 (22.0%)	6 (17.6%)	6 (15.8%)	118 (21.3%)
Self-reported substance use				
Alcohol				
Alcohol >7 glasses[b]/week	219 (40.3%)	9 (25.7%)	15 (30.6%)	243 (38.8%)
Time since alcohol >7 glasses[b]/week[a], years	15.0 (5.0-25.0)	7.5 (2.0-15.5)	15.0 (3.0-25.0)	15.0 (4.0-25.0)
Recent year: Alcohol ♂ >5 glasses[b]/day and ♀ >4 glasses[b]/day				
Never	183 (33.2%)	13 (36.1%)	17 (37.8%)	213 (33.6%)
1-2 times	54 (9.8%)	9 (25.0%)	4 (8.9%)	67 (10.6%)
Monthly	73 (13.2%)	4 (11.1%)	6 (13.3%)	83 (13.1%)
Weekly	72 (13.0%)	3 (8.3%)	6 (13.3%)	81 (12.8%)
Daily	170 (30.8%)	7 (19.4%)	12 (26.7%)	189 (29.9%)
IV substance use				
IV substance use	70 (12.8%)	7 (19.4%)	17 (35.4%)	94 (14.9%)

Time IV substance use[a], months	120.0 (20.0-294.0)	72.0 (18.0-336.0)	84.0 (24.0-120.0)	87.0 (20.0-300.0)
Substance use				
Recent year: use of illegal substances				
Never	311 (59.1%)	13 (36.1%)	26 (55.3%)	350 (57.5%)
1-2 times	20 (3.8%)	2 (5.6%)	0 (0.0%)	22 (3.6%)
Monthly	45 (8.6%)	2 (5.6%)	3 (6.4%)	50 (8.2%)
Weekly	38 (7.2%)	8 (22.2%)	2 (4.3%)	48 (7.9%)
Daily	112 (21.3%)	11 (30.6%)	16 (34.0%)	139 (22.8%)
Cannabis use	167 (30.4%)	15 (40.5%)	11 (22.4%)	193 (30.3%)
Cocaine use	88 (16.0%)	13 (35.1%)	9 (18.4%)	110 (17.3%)
Stimulants use (upper, e.g., Ritalin, Concerta, Dexedrine, Adderall, Diet tablets)	11 (2.0%)	0 (0.0%)	2 (4.1%)	13 (2.0%)
Amphetamine or methamphetamine use (e.g., Speed, Crystal, ICE)	67 (12.2%)	6 (16.2%)	8 (16.3%)	81 (12.7%)
Sedatives or sleeping pills use (downer, e.g., Valium, Xanax, Rohypnol, GHB)	16 (2.9%)	1 (2.7%)	3 (6.1%)	20 (3.1%)
Hallucinogen use (e.g., LSD, Acid, Mushrooms, PCP, Special K, Ecstasy)	35 (6.4%)	1 (2.7%)	1 (2.0%)	37 (5.8%)
Street opiate use (e.g., Heroin, Opium)	76 (13.8%)	11 (29.7%)	11 (22.4%)	98 (15.4%)
Medical opioids use (e.g., Fentanyl, Oxycodone, Vicodin, Hydrocodone, Methadone)	43 (7.8%)	5 (13.5%)	6 (12.2%)	54 (8.5%)

[a]Median (IQR) is presented where approximate normality was substantially violated. [b]One glass was defined as 330 ml. **Abbreviations:** SD, standard deviation; BMI, body mass index; SR, self-reported; HIV, human immunodeficiency virus; EQ-VAS, EuroQol Visual Analogue Scale; UCLA-3, University of California, Los Angeles, Loneliness Scale; GAD-2, Generalized Anxiety Disorder-2; PHQ-9, Patient Health Questionnaire-9; IV, intravenous; GHB, gamma-hydroxybutyric acid; LSD, Lysergic acid diethylamide; PCP, Phencyclidine.

Supplementary Table 4. Patterns of substance use, defined as combinations of substance groupings determined using toxicological analyses overall and by sex (n=649).

	Male N=531 Number (%)	**Female** N=118 Number (%)	**Total** N=674 Number (%)
None	150 (32.1%)	42 (45.2%)	201 (34.5%)
Alcohol	93 (19.9%)	13 (14.0%)	113 (19.4%)
Cannabis	38 (8.1%)	4 (4.3%)	44 (7.5%)
CNS Stimulants and Cannabis	25 (5.4%)	4 (4.3%)	30 (5.1%)
Cannabis and Alcohol	25 (5.4%)	2 (2.2%)	29 (5.0%)
CNS Stimulants and Narcotic analgesic	22 (4.7%)	7 (7.5%)	29 (5.0%)
CNS Stimulants and Alcohol	21 (4.5%)	3 (3.2%)	24 (4.1%)
CNS Stimulants and Alcohol and Cannabis	21 (4.5%)	1 (1.1%)	23 (3.9%)
CNS Stimulants	14 (3.0%)	7 (7.5%)	21 (3.6%)
CNS Stimulants and Cannabis and Narcotic analgesic	17 (3.6%)	3 (3.2%)	21 (3.6%)
CNS Stimulants and Alcohol and Narcotic analgesic	11 (2.4%)	4 (4.3%)	15 (2.6%)
Narcotic analgesic and Alcohol	9 (1.9%)	1 (1.1%)	10 (1.7%)
CNS Stimulants and Alcohol and Cannabis and Narcotic analgesic	6 (1.3%)	1 (1.1%)	7 (1.2%)
Narcotic analgesic	5 (1.1%)	1 (1.1%)	6 (1.0%)
Narcotic analgesic and Cannabis	5 (1.1%)	0 (0.0%)	5 (0.9%)
Narcotic analgesic and Alcohol and Cannabis	5 (1.1%)	0 (0.0%)	5 (0.9%)

Note. Patterns of different substances used simultaneously were determined in cases with complete toxicological analysis and sorted by the frequency of overall occurrence. **Abbreviations:** CNS, central nervous system.

Supplementary Table 5. Odds ratios and 95% confidence intervals from multivariable logistic regression pooled after multiple imputations using 50 imputation datasets and 1000 iterations between imputations. Imputed outcome data were dropped after the imputation (n=583).

	Odds ratio	95% Confidence interval	P-value
Age, years	0.94	0.91 to 0.98	<0.001
Sex (Ref: Male)			
Female	0.62	0.33 to 1.17	0.14
Education (Ref: None)			
School education	1.00	0.55 to 1.81	0.99
Vocational or higher education	0.91	0.47 to 1.73	0.77
Marital status (Ref: Single)			
Married	1.69	0.79 to 3.63	0.18
Widowed/divorced	0.92	0.50 to 1.71	0.80
Time of homelessness, months	1.00	0.996 to 1.003	0.86
Houselessness according to ETHOS (Ref: Rooflessness)	1.36	0.85 to 2.16	0.20
Social welfare (Ref: None)	1.06	0.65 to 1.72	0.82
Income from work (Ref: None)	0.76	0.35 to 1.66	0.50
Psychiatric disease	1.32	0.77 to 2.25	0.31
Ever unprotected sex with different partners	1.54	0.87 to 2.74	0.14
EQ-VAS	1.00	0.99 to 1.01	0.47
Loneliness according to ULCA-3	1.23	0.76 to 1.99	0.41
Depression according to PHQ-9 (Ref: None)			
Mild to moderate	1.03	0.54 to 1.99	0.92
Medium to severe	0.99	0.44 to 2.25	0.98
History of imprisonment (Ref: None)	3.91	2.38 to 6.40	<0.001
Time in Germany, months	1.00	0.998 to 1.004	0.29
Country of birth (Ref: Germany)			
Abroad	1.00	0.36 to 2.79	0.99
Company during the day (Ref: None)	1.20	0.76 to 1.90	0.44
Children (Ref: None)	1.30	0.81 to 2.06	0.27
Active tobacco use (Ref: None)	5.20	2.20 to 12.32	<0.001
City (Ref: Frankfurt)			<0.001[1]
Hamburg	1.90	1.10 to 3.28	0.02
Leipzig	0.58	0.28 to 1.19	0.14
Munich	0.40	0.21 to 0.74	0.004

[a]Multivariable Wald test. **Abbreviations:** ETHOS, European Typology of Homelessness and Housing Exclusion; EQ-VAS, EuroQol Visual Analogue Scale; UCLA-3, University of California, Los Angeles, Loneliness Scale; PHQ-9, Patient Health Questionnaire-9.

Supplementary Table 6. Odds ratios and 95% confidence intervals from multivariable logistic regression complete-case analysis without substantive model-compatible multiple imputation (n=331).

	Odds ratio	95% Confidence interval	P-value
Age, years	0.96	0.92 to 0.997	0.04
Sex (Ref: Male)			
Female	0.80	0.35 to 1.80	0.58
Education (Ref: None)			
School education	1.35	0.63 to 2.89	0.45
Vocational or higher education	0.76	0.33 to 1.74	0.52
Marital status (Ref: Single)			
Married	1.23	0.43 to 3.51	0.69
Widowed/divorced	0.90	0.39 to 2.05	0.80
Time of homelessness, months	1.00	0.99 to 1.01	0.96
Houselessness according to ETHOS (Ref: Rooflessness)	0.99	0.55 to 1.81	0.98
Social welfare (Ref: None)	0.96	0.51 to 1.82	0.90
Income from work (Ref: None)	0.71	0.26 to 1.97	0.51
Psychiatric disease	1.48	0.72 to 3.02	0.29
Ever unprotected sex with different partners	1.30	0.66 to 2.58	0.45
EQ-VAS	0.99	0.98 to 1.01	0.25
Loneliness according to ULCA-3	1.42	0.76 to 2.65	0.27
Depression according to PHQ-9 (Ref: None)			
Mild to moderate	0.96	0.40 to 2.29	0.92
Medium to severe	0.62	0.20 to 1.89	0.40
History of imprisonment (Ref: None)	5.51	2.87 to 10.58	<0.001
Time in Germany, months	1.00	0.995 to 1.002	0.57
Country of birth (Ref: Germany)			
Abroad	0.64	0.16 to 2.49	0.52
Company during the day (Ref: None)	1.48	0.80 to 2.71	0.21
Children (Ref: None)	1.40	0.77 to 2.54	0.26
Active tobacco use (Ref: None)	6.63	2.26 to 19.41	0.001
City (Ref: Frankfurt)			
Hamburg	1.68	0.81 to 3.51	0.16
Leipzig	0.67	0.26 to 1.77	0.42
Munich	0.28	0.12 to 0.69	0.01

Abbreviations: ETHOS, European Typology of Homelessness and Housing Exclusion; EQ-VAS, EuroQol Visual Analogue Scale; UCLA-3, University of California, Los Angeles, Loneliness Scale; PHQ-9, Patient Health Questionnaire-9.

Supplementary Figure 1. Truncated violin plots of individual substances and metabolites according to substance group. Active and inactive metabolite concentrations are shown on the $\log_{10}$ scale, with the mean $\log_{10}$ concentration corresponding to the geometric mean on the linear scale. Cocaethylene is a metabolite of cocaine that forms in the presence of alcohol. Values for positive individuals above the LOD are shown, with the LOQ remaining unconsidered for this illustration.

Abbreviations: LOD, lower limit of detection; LOQ, lower limit of quantification; THC, Δ9-Tetrahydrocannabinol; THC-OH, 11-hydroxy-THC; THC-COOH, THC-carboxylic acid; CNS, Central nervous system; MDMA, Methylenedioxymethamphetamine; MDEA, Methylenedioxyethylamphetamine; MBDB, Benzodioxolylmethylbutanamine; MDA, Methylenedioxyamphetamine; BE, Benzoylecgonine; EME, Ecgoninemethylester; CDT, Carbohydrate-deficient transferrin; DHC, Dihydrocodeine; MAM, Monoacetylmorphine; EDDP, Ethylidenedimethyldiphenylpyrrolidine.

Supplementary Material 1. Details on the recruitment process.

Recruitment took place in forty homeless support facilities. Facilities received study information and materials for advertisement two weeks before study enrolment. A study team comprising medical students and doctors visited each study site. No response rates were evaluated. Inclusion criteria were the lack of permanent residence (> seven days), age > 18 years, and the capacity to provide informed consent. Pregnant individuals were not included in the study. The enrolment of PEH according to the European Typology of Homelessness and Housing Exclusion (ETHOS) is shown in Supplementary Table 1 (1). Written informed consent was obtained. An allowance of 10€ per hour was offered for compensation.

Data on sociodemographic, somatic and psychiatric health conditions were collected using questionnaire-based interviews. Interviews were conducted by trained medical personnel. An excerpt of the study questionnaire relevant to this study can be found in Supplementary Material 2. Extensive methodological descriptions of the study are published elsewhere (2). Trained medical professionals took venous blood samples, which were centrifuged, stored, and transported to the University Medical Center Hamburg-Eppendorf at 4°C. Toxicological analyses of serum samples were analysed at the accredited laboratory of the Department of Forensic Toxicology and Alcohology, Institute of Legal Medicine, University Medical Center Hamburg-Eppendorf, Hamburg, Germany. Details on the immunoassays and liquid chromatography with tandem mass spectrometry conducted can be found in Supplementary Material 5.

Supplementary Material 2. Methods of the online survey of homeless support facilities.

In 2022, an online survey was sent to the designated contact person of participating homelessness assistance facilities. Participation was voluntary, and the survey requested information about the organisation, staff, access requirements, and support services. Two reminders were sent to the facilities, followed by telephone interviews if no feedback was received after two weeks.

Supplementary Material 3. Details on toxicological analyses performed at the accredited laboratory at the Forensic Toxicology and Alcohololology, Institute of Legal Medicine, University Medical Center Hamburg-Eppendorf.

Immunoassays
Blood alcohol concentrations (BAC) were measured enzymatically (DRI®-Ethanol-Assay, Thermo Fisher Scientific, California, USA). Cannabinoids were pretested using a standard immunoassay screening test (CEDIA DAU, CEDIA® Multi-Level THC-Assay, Thermo Fisher Scientific) on a clinical-chemical automatic analyser (AU 480, Beckmann Coulter, California, USA). Carbohydrate-deficient transferrin (CDT) was analysed by high-performance liquid chromatography using a commercially available, fully validated, and IVD-CE-labelled kit (CDT in blood ClinRep© Komplettkit CDT im Serum - HPLC, Recipe, München, Germany).

Liquid chromatography with tandem mass spectrometry
All solvents and reagents for sample preparation were obtained from Merck Schuchard (Hohenbrunn, Germany) and were of analytical grade. Solvents and chemicals for LC-MS/MS analysis were of the specified LC/MS grade (Chromasolv®) and were purchased from Fluka (Munich, Germany). Stock solutions for THC, THC-OH, and THC-COOH were purchased from Ceriliant (Sigma-Aldrich, Steinheim). Stock solutions of all other certified standards and deuterated standards were purchased from LGC (Luckenwalde, Germany). Quality control samples for the tested substances were purchased from ACQ Science GmbH (Rottenburg-Hailfingen, Germany). All methods have been validated according to the Society of Toxicological and Forensic Chemistry guidelines and have been applied in routine diagnostics for several years (3). Regular external quality control is performed by periodic proficiency testing. Limits of detection (LODs) and limits of quantification (LOQs) for all substances and metabolites are depicted in Supplementary Table 1. All substances and metabolites exceeding the LOD were called positive. Substances were defined as positive where the active substance and/ or metabolites were detected.

Details on determining all relevant substances using liquid chromatography with tandem mass spectrometry
Basic substances (amphetamine, methamphetamine, methylenedioxymethamphetamine (MDMA), methylendioxyamphetamine (MDA), methylenedioxyethylamphetamine (MDEA) cocaine, benzoylecgonine, methylecgonine, norcocaine, morphine, 6-acetylmorphine (MAM), codeine, dihydrocodeine, methadone and EDDP) were determined as follows: A 0.05 ml aliquot of the serum sample was spiked with 5 µl of the deuterated internal standard solution (0.1 ng/µl), followed by protein precipitation with 250 µl ice-cold acetonitrile. After being shaken and centrifuged, 100 µl of the supernatant was diluted with 500 µl of water. The resulting solution was analysed via LC-MS/MS (Waters Acquity® UPLC with a C18 Waters Acquity BEH, 1.7 µm, 2.1 x 50 mm column at 40 °C). The injection volume of the sample was 10 µl, the flow rate at 0.5 ml/min, and the binary gradient was as follows: 0-3.0 min: 100% A, 3.0-4.0 min 10% A 90% B, 4.1-5.5 min 100% A. Mobile phase A consisted of 90% 10 mM ammonium bicarbonate in water (pH 9) and 10% methanol, mobile phase B was 100% methanol. A Waters Xevo® TQ-XS triple quadrupole mass analyser operating in multiple reaction monitoring modes was used for detection (Waters, Milford, USA).

Δ9-tetrahydrocannabinol (THC) concentrations and its main metabolites (THC-carboxylic acid (THC–COOH) and 11-hydroxy-THC (THC-OH)) were determined as follows: A 0.4 ml aliquot of the serum sample was spiked with 4 µl of the deuterated internal standard solution (1 ng/µl). After being shaken and centrifuged, the supernatant was applied to a preconditioned C18 Column (Agilent) and the substances were cleaned up by solid-phase extraction (SPE). The cartridges were subsequently washed with 1.0 ml of water, 1.0 ml of acetic acid 0.25 M, and 1.0 ml of water and then allowed to dry for 5 min at maximum vacuum. After the addition of 0.1 ml n-hexane and another 5 min drying, the analytes were extracted from the columns with 0.5 ml of acetone. After the addition of 0.5 ml chlorbutane, the extract was evaporated to dryness under a gentle stream of nitrogen. The residue was resolved with 0.2 ml of methanol (LC-MS-Grade) and 0.1 ml of water (LC-MS-Grade), and the resulting solution was analysed via LC-MS/MS (same column and LC-MS/MS as above). The injection volume of the sample was 10 µl, the flow rate at 0.3 ml/min, and the binary gradient was as follows: 0-4.5 min 45 % A / 55 % B throughout 4.5 min, then increased to 100 % mobile phase B at 6min held for 0.5 min after which the initial conditions were instantaneously reinstated until 8 min. Mobile phase A consisted of 1% formic acid in water, and mobile phase B was 1% formic acid in methanol.

Medicinal opioids, comprising alfentanil, buprenorphine, dextromethorphan, fentanyl, hydrocodone, hydromorphone, oxycodone, oxymorphone, pethidine, piritramide, sufentanil, tapentadol, tilidine, and tramadol, were determined as described elsewhere (4).

Supplementary Material 4. Excerpt of the study questionnaire in the German language.

Anamnese und körperliche Untersuchung (im Interview)

Körpergewicht, kg	
Körpergröße, cm	
RR, mmHg	
Puls, pro minute	
Temperatur (Ohr), °C	

Hat Ihnen ein Arzt gesagt, dass sie an einer der folgenden Krankheiten leiden?

Herzinfarkt, Herzinsuffizienz oder andere Herzkrankheiten	O nein	O ja
Bluthochdruck	O nein	O ja
Hohe Cholesterinwerte	O nein	O ja
Schlaganfall oder Durchblutungsstörung des Gehirns	O nein	O ja
Diabetes oder hohe Blutzuckerwerte	O nein	O ja
Chronische Erkrankungen der Lunge (Bronchitis, Lungenemphysem)	O nein	O ja
Krebs (bösartige Tumore, Leukämien, Lymphdrüsenkrebs)	O nein	O ja
Alzheimer, Demenz, Gedächtnisstörungen	O nein	O ja
Seelische Probleme (Angststörung, Psychische Probleme)	O nein	O ja
Leberzirrhose, Leberschaden	O nein	O ja
HIV, AIDS	O nein	O ja
Tuberkulose	O nein	O ja

Fragebogen für ALLE Teilnehmer: Fragen zur Person

Geschlecht: O männlich O weiblich

Alter: _____Jahre, geboren im Jahr _____

Haben Sie im letzten Jahr schonmal an dieser Studie teilgenommen? O nein O ja

Wie ist ihr Familienstand?

- O Verheiratet, zusammenlebend
- O Verheiratet, dauerhaft getrennt lebend
- O Single
- O Verwitwet
- O Geschieden

Was ist ihr höchster Bildungsabschluss?

- O (noch) kein Abschluss
- O Gymnasial-, Hauptschul- oder Realschulabschluss
- O beruflicher Ausbildungsabschluss (Geselle, Meister, Techniker)
- O Fachhochschul- oder Universitätsabschluss

Haben Sie ein Haustier?

- O nein
- O ja, einen Hund
- O ja, etwas anderes_____

Haben Sie Kinder?

- O nein
- O ja, ich habe _____ Kinder.

Seit wie vielen Monaten sind Sie obdachlos? Seit_____ Monaten

Was ist der wichtigste Grund weshalb Sie noch immer obdachlos sind?

- O Unzureichendes Einkommen
- O Mangel an geeignetem/angemessenem Wohnraum
- O Mangel an Arbeit/Beschäftigung
- O Abhängigkeit(en) von Alkohol und/oder Drogen
- O Familiäre oder häusliche Instabilität
- O Psychischer Gesundheitszustand
- O Andere

Bekommen Sie Geld von der Sozialhilfe? O nein O ja

Haben Sie eine Arbeit für die Sie Geld bekommen? O nein O ja
Wurden Sie in Deutschland geboren? O nein O ja

Beantworten Sie folgende Fragen nur wenn sie NICHT in Deutschland geboren wurden

Wie viele Monate leben Sie in Deutschland? _____Monate

In welchem Land wurden Sie geboren? _____

Fragebogen für ALLE Teilnehmer: Tagesablauf und Risikoverhalten

Ich schlafe meist….

O im öffentlichen Raum (Straße, Brücke, Verschläge, Zelte)
O In Notschlafstellen oder Wärmestuben
O In Übergangswohnheimen
O In Asylstellen und Herbergen
O In Übergangswohnungen
O In Frauenhäusern
O In Hotels, Hostels und Herbergen (befristet)
O In Quartieren für Arbeitsmigranten
O In Krankenhäusern, Heilanstalten, Jugendheimen oder Gefängnissen

Ich teile mir ein Zimmer/Schlafplatz meist mit _____ anderen Leuten

Tagsüber bin ich die meiste Zeit:

O alleine
O mit einer Person zusammen
O mit einer kleinen Gruppe zusammen
O mit verschiedenen Personen zusammen

Ich habe Sex mit verschiedenen Partnern, ohne ein Kondom zu benutzen

O überhaupt nicht
O selten
O manchmal
O häufig

Ich habe schon einmal im Gefängnis eingesessen O nein O ja

Ich spritze mir Drogen in die Adern O nein O ja
Wenn ja, seit wie vielen Monaten? _____

Ich bin in einem Substitutionsprogramm (z.B. Methadon) O nein O ja

Ich rauche (Tabak/Marihuana/anderes) O nein O ja
Wenn sie rauchen, wie viele Zigaretten pro Tag rauchen Sie? _____
Wenn Sie rauchen, seit wie vielen Jahren rauchen Sie? _____

Ich trinke mehr als 7 Gläser Alkohol pro Woche? O nein O ja
Wenn ja, seit wie vielen Jahren trinken Sie diese Menge Alkohol? Seit_____Jahren

Im letzten Jahr, wie oft haben Sie die folgenden Dinge konsumiert?

Konsum von Alkohol im letzten Jahr (Männer: mehr als 5 Gläser am Tag, Frauen: mehr als 4 Gläser am Tag)

O Nie
O ein oder zweimal im Jahr
O Monatlich
O Wöchentlich
O Täglich, oder nahezu täglich

Konsum von Tabak im letzten Jahr (Rauchen, Schnupfen, Kauen)

O Nie
O ein oder zweimal im Jahr
O Monatlich
O Wöchentlich
O Täglich, oder nahezu täglich

Konsum von verschreibungspflichtigen Tabletten die mir nicht verschrieben wurden
- O Nie
- O ein oder zweimal im Jahr
- O Monatlich
- O Wöchentlich
- O Täglich, oder nahezu täglich

Konsum von illegalen Drogen im letzten Jahr
- O Nie
- O ein oder zweimal im Jahr
- O Monatlich
- O Wöchentlich
- O Täglich, oder nahezu täglich

Wenn Sie illegale Drogen nehmen, welche nehmen Sie?
- O Cannabis
- O Cocain
- O Stimulanzien (“upper“ Ritalin, Concerta, Dexedrin, Adderall, Diättabletten)
- O Methamphetamin / Amphetamin (Speed, crystal, ice, …)
- O Sedativa oder Schlafmittel (“downer” Valium, Xanax, Rohypnol, GHB…)
- O Halluzinogene (LSD, Acid, Pilze, PCP, Special K, Ecstasy)
- O Straßen Opiate (Heroin, Opium, etc.)
- O Medizinische Opioide (Fentanyl, Oxycodon, Vicodin, Hydrocodon, Methadon)

Fragen zur psychischen Gesundheit und Gesundheitsversorgung

Haben Sie eine Gesundheitskarte einer gesetzlichen Krankenversicherung?
- O Ja
- O Nein
- O Weiß nicht

Haben Sie in den letzten 12 Monaten Ärzte aufgesucht?
- O Ja.
- O Nein
- O Weiß nicht

Waren Sie in den letzten 12 Monaten in einem Krankenhaus in Behandlung?
- O Ja.
- O Nein
- O Weiß nicht

Wie häufig vermissen Sie Gesellschaft?
- O selten oder nie
- O manchmal
- O häufig

Wie häufig haben Sie das Gefühl, am Rande zu stehen?
- O selten oder nie
- O manchmal
- O häufig

Wie häufig fühlen sie sich isoliert von anderen?
- O selten oder nie
- O manchmal
- O häufig

Wie oft fühlten Sie sich im Verlauf der letzten 2 Wochen durch die folgenden Beschwerden beeinträchtigt?

Nervosität, Ängstlichkeit oder Anspannung
- O überhaupt nicht
- O an manchen Tagen
- O an mehr als der Hälfte der Tage
- O beinahe jeden Tag

Nicht in der Lage zu sein, Sorgen zu stoppen oder zu kontrollieren
- O überhaupt nicht

O an manchen Tagen
O an mehr als der Hälfte der Tage
O beinahe jeden Tag

Wenig Interesse oder Freude an Ihren Tätigkeiten
O überhaupt nicht
O an manchen Tagen
O an mehr als der Hälfte der Tage
O beinahe jeden Tag

Niedergeschlagenheit, Schwermut oder Hoffnungslosigkeit
O überhaupt nicht
O an manchen Tagen
O an mehr als der Hälfte der Tage
O beinahe jeden Tag

Schwierigkeiten ein- oder durchzuschlafen oder vermehrter Schlaf
O überhaupt nicht
O an manchen Tagen
O an mehr als der Hälfte der Tage
O beinahe jeden Tag

Müdigkeit oder Gefühl, keine Energie zu haben
O überhaupt nicht
O an manchen Tagen
O an mehr als der Hälfte der Tage
O beinahe jeden Tag

Verminderter Appetit oder übermäßiges Bedürfnis zu essen
O überhaupt nicht
O an manchen Tagen
O an mehr als der Hälfte der Tage
O beinahe jeden Tag selten oder nie

Schlechte Meinung von sich selbst, Gefühl ein Versager zu sein oder die Familie enttäuscht zu haben
O überhaupt nicht
O an manchen Tagen
O an mehr als der Hälfte der Tage
O beinahe jeden Tag selten oder nie

Schwierigkeiten, sich auf etwas zu konzentrieren, z.B. beim Zeitungslesen oder Fernsehen
O überhaupt nicht
O an manchen Tagen
O an mehr als der Hälfte der Tage
O beinahe jeden Tag selten oder nie

Waren ihre Bewegungen oder Sprache so verlangsamt, dass es auch anderen auffallen würden? Oder waren Sie im Gegenteil „zappelig“ oder ruhelos und hatten dadurch einen stärkeren Bewegungsdrang als sonst?
O überhaupt nicht
O an manchen Tagen
O an mehr als der Hälfte der Tage
O beinahe jeden Tag

Gedanken, dass sie lieber tot wären oder sich Leid zufügen möchten
O überhaupt nicht
O an manchen Tagen
O an mehr als der Hälfte der Tage
O beinahe jeden Tag

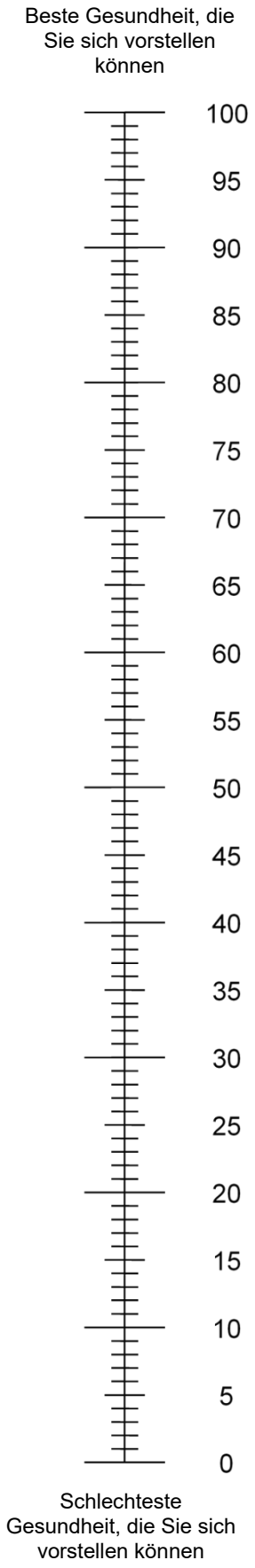
Nun möchte ich Sie gern bitten, mir zu sagen, wie gut oder schlecht Ihre Gesundheit HEUTE ist.

Ich möchte, dass Sie versuchen, sich eine Skala vorzustellen, die wie ein Thermometer aussieht.

Die beste Gesundheit, die Sie sich vorstellen können, ist mit der Zahl 100 (Einhundert) am oberen Ende der Skala gekennzeichnet, und die schlechteste Gesundheit, die Sie sich vorstellen können, ist am unteren Ende mit der Zahl 0 (Null) gekennzeichnet.

Ich möchte nun, dass Sie mir sagen, wo auf der Skala Sie Ihre Gesundheit HEUTE ansiedeln würden.

GESUNDHEIT DES BEFRAGTEN HEUTE = ☐



Supplementary Material 5. Methods of statistical analysis.

Categorical variables were summarised as numbers (%). Exact binomial 95% confidence intervals were calculated. Continuous variables were summarised as the mean (SD) and median (IQR), as appropriate; inspection for approximate normality was done using Q-Q plots. The proportion of missingness was inspected for each variable.

Substantive model compatible multiple imputation
Proportions of missing data for the substantive model were inspected. Substantive model-compatible multiple imputation (SMCMI) was employed to deal with missing values, assuming missingness at random. For SMCMI, variables in the substantive model were included, and regression with stepwise elimination of covariates was used to determine strong predictors of missingness and the underlying values. Stepwise elimination of covariables was based on multivariable Wald tests with a significance level of 0.05. Variables predictive of missingness and the underlying values were included as auxiliary variables. Substantive model-compatible multiple imputation was done in R Studio (Version 2024.04.1+748; Posit Software, MA, USA). The following packages were used: `haven`, `jomo`, and `finalfit`. Fifty imputations with 1,000 iterations between imputations were utilised for multiple imputations with full conditional specification, and 1,000 iterations were used for burn-in. Summary statistics of observed and imputed values were inspected and compared to summary statistics of combined values. After SMCMI, imputed outcome data were omitted to prevent bias from incorrectly specified imputation models (5).

Substantive model
A generalised linear mixed model with binomial outcome distribution and its canonical link function was used. Polysubstance use [0/1] was included as the dependent variable. The independent variables were *a priori*-specified potential risk factors for polysubstance use, identified based on clinical knowledge. Age [continuous], sex [binary: male, female], education [categorical: none, school education, vocational or higher education], marital status [categorical: single, married, widowed or divorced], time of homelessness [continuous], ETHOS housing status [binary: roofless, houseless], social welfare [categorical: no, yes], income from work [categorical: no, yes], psychiatric disease [categorical: no, yes], ever unprotected sex with different partners [categorical: no, yes], EQ-VAS [continuous], loneliness according to UCLA-3 [categorical: no, yes], depression according to PHQ-9 [categorical: none, mild to moderate, medium to severe], history of imprisonment [categorical: no, yes], time in Germany [continuous], country of birth [categorical: Germany, Abroad], company during the day [categorical: no, yes], children [categorical: no, yes], active tobacco use [categorical: no, yes], and the city of enrolment [categorical: Frankfurt am Main, Hamburg, Leipzig, Munich] were included as model independent variables. A linear functional form of continuous variables was assumed. Pooled estimates were derived using Rubin's rule (6). Model fit was examined using index plots to investigate potentially influential values and Pearson's residuals to investigate potential model misspecification on a random subset of 5 imputation datasets. Multivariable Wald tests were derived assuming proportionality of the between-imputation and within-imputation variance (7). G-computation was used to predict covariate-specific values from the model.

A p-value of 0.05 was set for all statistical tests. Statistical analysis was conducted in STATA/MP 18.5 (StataCorp, TX, USA).

Supplementary Material 6. AI-assisted technologies in scientific writing

AI-assisted technologies in scientific writing were used to improve the readability and language of the work with human oversight and control (Grammarly, CA, USA). The results were carefully reviewed and edited.

Supplementary References

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