

1 **Title**

2 Using life course charts to assess and compare trajectories of amphetamine type stimulant consumption in
3 different user groups – a cross-sectional study

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46

47 **Abstract**

48 **Background:**

49 Amphetamine-type stimulants (ATS) are the second most commonly used illicit drugs globally, and in Europe.
50 However, there is limited understanding of what shapes patterns of ATS use over the life course. The ATTUNE
51 project “Understanding Pathways to Stimulant Use: a mixed methods examination of the individual, social and
52 cultural factors shaping illicit stimulant use across Europe” aims to fill this gap. Here we report initial findings
53 from the life course chart exercise conducted as part of qualitative interviews with ATS users and nonusers.

54 **Methods:**

55 279 in-depth qualitative interviews were conducted with five ATS user groups (current and former dependent
56 users/-current and former frequent users/ non-frequent users) and one group of exposed non-ATS users were
57 conducted in five European countries (Germany, United Kingdom, Poland, Netherlands and Czech Republic).
58 As part of the interviews, we used life course charts to capture key life events and substance use histories. Life
59 events were categorised as either positive, neutral or negative, and associated data were analysed
60 systematically to identify differences between user groups. We applied statistical analysis of variance (ANOVA)
61 and analysis of covariance (ANCOVA) to test for group differences.

62 **Results:**

63 Out of 3,547 life events documented, 1,523 life events were categorised as neutral, 1,005 life events as positive
64 and 1,019 life events as negative. Current and formerly dependent ATS users showed more negative life events
65 for the entire life course after age adjustment. Although some group differences could be attributed to the
66 individuals’ life course prior to first ATS use, most negative life events were associated with periods of ATS
67 usage. A detailed analysis of the specific life domains reveal that dominantly the social environment were
68 affected by the negative life events.

69 **Conclusions:**

70 For non- dependent, frequent and non-frequent ATS users negative life events from the period of ATS use do
71 not become obvious in our analysed data. Besides preventing a pathway into ATS dependency, the aim of an

72 intervention should be to reduce the harm by for example drug testing which offers also the opportunity for
73 interventions to prevent developing a substance use dependency.

74 For the group of dependent ATS user our study suggests holistic, tailored interventions and specialist
75 treatment services are needed, as a single, simple intervention is unlikely to cover all the life domains affected.

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77

78 **Keywords**

79 Life course charts, amphetamine type stimulant, life events, adults, life course approach,

80

81 **Background**

82 Amphetamine-type stimulants (ATS) refers to a range of drugs including amphetamine, methamphetamine,
83 3,4-methylenedioxy-methylamphetamin (MDMA and ecstasy), fenethylamine, ephedrine and prescribed drugs
84 containing methylphenidate (e.g. "Ritalin®"). According to the United Nations Office on Drugs and Crime
85 (UNODC) (1), ATS use is rising rapidly, with seizures of ATS having doubled in the five years prior to 2015 (191
86 tons in 2015). The UNODC estimated that there were 37 million users of amphetamines and 22 million users
87 of ecstasy worldwide in 2015 (1), making ATS the second most commonly used illicit drugs after cannabis (1).
88 In Europe, as in other parts of the world, a number of different indicators reveal widespread use of
89 amphetamines and ecstasy (2). The EU drugs agency (European Monitoring Centre for Drugs and Drug
90 Addiction - EMCDDA) in association with the Sewage Analysis CORe group Europe (SCORE), analysed urinary
91 biomarkers in the wastewater of 56 European cities to explore drug taking habits for amphetamine,
92 methamphetamine and MDMA (3). The highest level of amphetamine detected in wastewater were found in
93 cities in the north and east of Europe, while methamphetamine levels were highest in cities in the Czech
94 Republic, Slovakia, Eastern Germany and Finland. Belgium, Germany and the Netherlands also reported the
95 highest levels of MDMA use. According to the EMCDDA, among Europeans aged 15-34, the 12-month
96 prevalence of amphetamine use was highest in the Netherlands, at 3.6% (4). Amphetamine use prevalence
97 was also high in Finland (2.4%), Germany (1.9%), and Czech Republic (1.7%). For the same age group, the 12-
98 month prevalence for MDMA was significantly higher. Again, the highest MDMA 12-month prevalence was
99 found in the Netherlands (7.4%), with high rates of 12-month use also found in Ireland (4.4%), Czech Republic
100 (4.1%), Bulgaria (3.1%) and the United Kingdom (2.6%).

101 A number of previous studies have focussed on increasing our understanding of which factors influence the
102 initiation of amphetamine use (5, 6), and in particular, the transition into methamphetamine (7-11) or ecstasy
103 (12, 13) consumption. Research to date suggests that a range of individual, social and environmental factors
104 affect ATS initiation. These include personality traits, with some evidence to suggest that hedonism, shaped
105 by curiosity about the ATS effects, sensation seeking and propensity for experimentation, can contribute to
106 initiation of ATS use (5, 11-13). Furthermore, self-management or coping with mental health problems and

107 trauma have also been identified as a common reason for initiating ATS, especially for methamphetamine
108 users (5-8, 10, 12). Carbone-Lopez et al's qualitative study of the experiences of female methamphetamine
109 users living in a Missouri prison, found that the majority had experienced critical adverse events in childhood
110 (9). Family dysfunction (parental mental health problems, domestic violence), experiences of physical or sexual
111 violence often triggered the transition into the use of methamphetamines for these women. Studies also
112 suggests that prior to ATS initiation, most users have tried other substances, including alcohol, tobacco and
113 marijuana, at a relatively early age (12-14 years) (9, 11, 13). Social factors also play a key part in influencing
114 ATS initiation; in particular, having friends and/or intimate partners who are already using ATS (6, 7, 9, 10, 12)
115 and/or pressure amongst close peers (9). Previous research also highlights functional use of ATS, where
116 consumption is motivated by the desire to increase energy levels to manage the pressures of work, family or
117 life in general (10).

118 However, whilst several studies have been published exploring factors shaping initiation, there is less available
119 evidence about what affects the subsequent development of ATS consumption over time (14). A recent review
120 of qualitative literature exploring the individual, social and environmental influences on ATS use concluded
121 that a variety of interrelated factors affected key turning points in drug use trajectories (14). Both the initiation
122 and continued use of ATS were associated with family, friends, and social networks, were linked to individual
123 and social stressors, as well as ongoing health problems and critical life events. Specifically, three major factors
124 have been identified as motivating the continued use of ATS: perceived functionality for stress management,
125 boosting sexual pleasure, clubbing, reduced insecurity in social situations. (9, 15-19); critical life events such
126 as unemployment, death of a close person, separation from close persons, domestic violence (6, 10, 20); and
127 withdrawal effects (21-23). Yet there remains a limited understanding of how ATS use trajectories may vary
128 between different groups of users, and the ways, which circumstances lead to more controlled or more
129 problematic consumption patterns.

130 The European study "Understanding Pathways to Stimulant Use: a mixed methods examination of the
131 individual, social and cultural factors shaping illicit stimulant use across Europe" (ATTUNE) seeks to respond
132 to this evidence gap by exploring and comparing the different substance use pathways of five specific ATS

133 user and one non-ATS user groups. Research institutions from Germany, the United Kingdom (UK), Poland, the
134 Netherlands and the Czech Republic formed a consortium to examine interactions between potential
135 influencing factors and the trajectories of the ATS use in all five countries. The research study is the first of its
136 kind as it applies qualitative and quantitative methods to generate an in-depth, contextualised understanding
137 of ATS use over the life course(24).

138 In this paper, we report on the analysis of life course charts completed as part of semi-structured qualitative
139 interviews with ATS users and non-users across Europe. The aim of this paper was to identify life events
140 associated with the individuals' substance use trajectory.

141

142 **Methods**

143 ATTUNE is a cross-sectional mixed-methods study which seeks to explore the dynamics and trajectories of
144 different ATS use patterns in Europe. In addition to systematic reviews of the existing qualitative and the
145 qualitative literature on ATS use, ATTUNE comprises two key components. First, in-depth semi-structured
146 interviews with ATS users and non-users to explore experiences with ATS over the life course and to identify
147 key turning points in their consumption patterns. Second, structured questionnaire administered by computer
148 tablet to a larger sample of users and non-users to validate and generalise the qualitative interview findings.
149 The semi-structured interviews employed two topic guides: one for ATS users and one for non-ATS users who
150 were exposed to ATS (defined as having been present when family or friends took ATS but did not consume
151 themselves and have never taken ATS during their entire life course). The topic guides covered aspects of
152 initiation, continuation, increase and decrease of ATS consumption. As part of these interviews, life course
153 charts were used to help provide a chronological structure for discussions about ATS use over time, and to
154 capture more detailed data on participants' living environment, health conditions, social functioning, life
155 events and broader lifestyle. The life course charts were used here with the very specific intention of providing
156 a more systematic means of recording valuable contextual data. Here we report exclusively on findings from
157 analysis of the life course data.

158 Ethical approval for data collection and use was secured in five of the six participating countries, in the
159 Netherlands an ethical approval was not required. All participants received an information leaflet about the
160 study, informed consent was then obtained and anonymity and confidentiality protected. The interviews were
161 audio recorded and transcribed in full. Trained and experienced fieldworkers implemented the interviews that
162 lasted between 60 to 90 minutes. Participants also received a small incentive after the interview, by way of
163 thanks for their time.

164

165 **Life course charts**

166 Life course charts have been used previously in qualitative research as means of contextualising individual
167 semi-structured interviews (25). In the substance use field, life course charts are used to assess the intensity
168 of drug use at critical time points in a participants' history; and to observe possible associations between
169 critical life events and changes in the drug use trajectory. One particular study with substance using
170 adolescents found that life course charts enhanced the memory of the respondents to recall their drug career
171 and significant life events in a chronological order (26-28). A review of the use of calendar or timeline
172 instruments demonstrated that these types of instruments contributed to improved data quality as they
173 helped respondents relate specific events and dates to different behaviours and consequences (27).

174 Timeline instruments have the structure of a chart, with rows referring to the person's life in years and
175 columns representing different aspects of life (life domains) and substance use, which can vary by study (26,
176 27). For this research, a life course chart was developed which reflected the overarching study objectives (see
177 Appendix 1). This study used the following time data related to defined periods in an individual participants'
178 life course: until the age of 13, age 14-16, age 17-19, age 20-25, age 26-30, age 31-39, age 40-49 and age 50+.
179 The chart included two separate sections, one referring to substance use and one referring to life events. The
180 section on substances covered the use of different ATS, cannabis, cocaine, opiates and alcohol. The drug use
181 pattern was recorded for each time period by asking users to identify how frequently particular substances
182 were used out of the following five options: no use; use less than monthly; monthly use; weekly use or (almost)
183 daily use. Where the frequency of use varied significantly within one time period, the most frequent use was

184 entered into the life chart. The life event section included 11 different domains, including family history,
185 education, friends, health and illness, involvement with the criminal justice system, substance use treatment,
186 and leisure.

187 The life course chart was implemented as part of the semi-structured, face-to-face interviews with ATS users
188 and non-users. Whilst the life course chart provided interviewers with structured prompts to motivate the
189 interviewer to ask for details of specific live events, the instrument itself was administered iteratively, to
190 reflect the fact that certain life events may not have been experienced by some respondents, or were not felt
191 to be especially significant. For each of the specific time periods and associated life domains, only one
192 significant life event could be recorded. Where two key life events were reported for the same life domain
193 and time period, the more critical negative life event was noted.

194

195 **Sampling criteria and recruitment**

196 To be eligible for inclusion, the first consumption or exposure to ATS needed to have been at least five years
197 before the interview took place. Further inclusion criteria were that individuals should be: 18 years or older;
198 have no opioid dependency in their lifetime (with five exceptions for the UK sample); resident in one of the
199 five countries; and able to participate in the interview. The inclusion criteria was reviewed with each individual
200 via a standardised screening checklist and only eligible individuals were interviewed.

201 To ensure variation in ATS pathways and trajectories, we targeted five predefined groups of ATS users, and a
202 further group of non-users. Eligible interview participants were allocated to one of the study groups,
203 depending on their consumption pattern, their ATS dependency level and current state of use (figure 1).
204 Dependency was measured with the Severity of Dependence Scale (SDS), which is a 5-item questionnaire that
205 provides a score indicating the severity of dependence on amphetamines (29). An ATS related SDS greater
206 than four was approximated as dependency. Former ATS users (defined as not having used ATS in the last 12
207 months) were asked to fill in the SDS for the phase when their ATS use was the most intense in their life.
208 Current ATS users related the SDS to the last 12 months and if this result was negative, the SDS was
209 administered again to relate to the most intensive phase.

210

211 Figure 1: Operationalisation of the study groups

Group 1: Currently ATS dependent (CDU)	Group 2: Formerly ATS dependent users (FDU)	Group 3: Currently frequent, non-dependent ATS users (CFU)	Group 4: Formerly frequent, non-ATS dependent users (FFU)	Group 5: Non-frequent ATS users (currently and formerly) (NFU)	Group 6: Exposed non-ATS users (ENU)
SDS positive (last 12 months)	SDS positive (any time except last 12 months)	SDS negative lifetime	SDS negative lifetime	SDS negative lifetime	SDS not applicable
≥ 10 ATS consumption days within past 12 months	≥ 10 ATS consumption days within a year except past 12 months	≥ 10 ATS consumption days within past 12 months	≥ 10 ATS consumption days within a year except past 12 months	< 10 ATS consumption days within any given 12 months	Exposed to ATS without ATS consumption

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213 We aimed to purposively sample five participants per study group in the Czech Republic and 10 participants
 214 per group in the other four countries. Participants were recruited into the study using a number of recruitment
 215 strategies, including advertising the study by flyer, poster and social media, via contacts with drug and health
 216 services, and by interviewees who shared the study link in their network (snowball sampling). The interviewees
 217 were asked how they learnt about the study and more than half of them (51%) were informed by friend or
 218 family members. Almost a quarter of participants were recruited by staff of drug treatment services (24%), a
 219 smaller number responded to the flyer and posters (16%), and the remaining interviewees heard about the
 220 study in social media or by researchers.

221 In total, 279 eligible participants across five countries participated in the interviews. However, the target
 222 sample for each study group could not be realised in all countries (table 1). While in Group 2 (FDU - formerly
 223 ATS dependent users) the recruitment target was exceeded, Group 4 (FFU - formerly frequent ATS users)
 224 proved difficult to access, especially in Germany and Poland.

225 The interviews were performed by national experienced expert teams. All interviewers were familiarised with
 226 the interview materials prior to data collection, all guidance materials utilised and translated into the national
 227 languages where applicable. The Czech partner engaged three well experienced qualitative researchers, two
 228 on post PHD employment; in Germany the team comprised of three post PHD and two senior researchers; in
 229 the Netherlands experts comprised two persons with experiences in qualitative interviewing, one with MSc

230 and one PHD; in Poland the team was led by an assistant professor (15 interviews) supported by one
 231 experienced university researcher, two experienced external interviewers and two well trained university co-
 232 workers. For the UK all interviewers were experienced in qualitative interviewing (two post PHD and one MSc)
 233 and completed the National Institute for Health Research Good Clinical Practice training.

234

235 Table 1: Sample size by country and study group

	Group 1: Currently ATS dependent (CDU)	Group 2: Formerly ATS dependent users (FDU)	Group 3: Currently frequent, non- dependent ATS users (CFU)	Group 4: Formerly frequent, non-ATS dependent users (FFU)	Group 5: Non- frequent ATS users (currently and formerly) (NFU)	Group 6: Exposed non-ATS users (ENU)	Total
Germany	9	17	12	6	9	7	60
United Kingdom	12	14	9	11	11	11	68
Poland	10	10	12	5	15	9	61
The Netherlands	10	10	10	10	10	10	60
Czech Republic	6	5	5	5	4	5	30
Total	47	56	48	37	49	42	279

236

237 **Characteristics of the participants**

238 41.2% of the participants were female, and the mean age of all participants was 31 years (table 2). On average,
 239 exposure and use of ATS occurred when participants were 18 years old. More than a third of participants had
 240 at some point, been in contact with drug treatment services (39.4%), in particular those from group 1
 241 (currently dependent) and group 2 (formerly dependent). SDS screening scores confirmed that participants in
 242 group 1 (currently dependent) and group 2 (formerly dependent) were severely dependent, with a SDS score
 243 of 7.2 and 7.3 respectively (30). Overall, 33.9% of the sample had ever used ATS (almost) daily, 43.7% of the
 244 ATS users consumed (almost) daily or at least weekly amphetamines within the given time periods, but with
 245 huge differences among the groups. Daily or weekly amphetamine use was highest in group 1 (currently
 246 dependent) at 80.9%, and lowest in group 5 (non-frequent) at 22.4%. In groups 1 (currently dependent) and 2
 247 (formerly dependent) 21.3% and 30.4% took methamphetamines frequently, but no one from group 5 (non-

248 frequent). Daily or weekly MDMA use was evidence in around 30% of the ATS users, but again, group 5 (non-
249 frequent) had the lowest rate of frequent MDMA use.

250 In all ATS user groups more than 90% reported lifetime cannabis use, even in group 6 (non-ATS users, at almost
251 80%). More than half of all respondents reported lifetime cocaine use, with the prevalence highest in the
252 group 4 (former frequent) and lowest in the group 6 (non-ATS users) at 83.8% versus 4.8%. With regard to
253 alcohol consumption, around 40% of the sample reporting having ever drunk alcohol on a daily basis, rising to
254 around half of respondents from the two ATS dependent groups.

255

256 Table 2: Characteristics of the interviewees by study group

	Group 1: Currently ATS dependent (CDU)	Group 2: Formerly ATS dependent users (FDU)	Group 3: Currently frequent, non- dependent ATS users (CFU)	Group 4: Formerly frequent, non-ATS dependent users (FFU)	Group 5: Non- frequent ATS users (currently and formerly) (NFU)	Group 6: Exposed non-ATS users (ENU)	Total
N	47	56	48	37	49	42	279
Female	46.8%	44.6%	25.0%	45.9%	40.8%	45.2%	41.2%
Mean age (SD)	32.2 (7.7)	33.6 (8.6)	29.3 (6.8)	32.6 (9.5)	31.0 (7.6)	28.8 (6.8)	31.3 (8.0)
Mean age of onset/exposure ATS use (SD)	16.6 (2.2)	17.6 (4.7)	18.6 (4.0)	17.0 (4.3)	18.8 (3.8)	17.6 (3.4)	17.7 (3.9)
Mean duration of ATS use/exposition in years (SD)	15.5 (8.0)	12.5 (6.8)	10.7 (5.3)	9.9 (6.8)	8.5 (6.5)	11.2 (6.1)	11.5 (6.9)
Ever contact with drug service	68.1%	78.6%	25.0%	29.7%	22.4%	0.0%	39.4%
SDS ATS score (SD)	7.2 (2.8)	7.3 (3.4)	1.9 (1.6)	2.2 (1.8)	0.3 (1.2)	0.0 (0.0)	3.3 (3.8)
(almost) Daily ATS use	74.5%	70.9%	20.8%	22.2%	4.1%	0.0%	33.9%
Daily/weekly amphetamine use	80.9%	71.4%	45.8%	29.7%	22.4%	0.0%	43.7%
Daily/weekly methamphetamine use	21.3%	30.4%	6.3%	10.8%	0.0%	0.0%	12.2%
Daily/weekly MDMA use	44.7%	50.0%	37.5%	35.1%	10.2%	0.0%	30.5%
Ever used cannabis	91.5%	96.4%	91.7%	94.6%	91.8%	78.6%	91.0%
Ever used cocaine	66.0%	62.5%	60.4%	83.8%	51.0%	4.8%	54.8%
Ever daily alcohol use	48.9%	51.8%	27.1%	40.5%	42.9%	28.6%	40.5%

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260 **Analysis**

261 A total of 3,547 life events were documented in the life course charts for the 279 interviewees, each of which
 262 referred to the respective time period when the event occurred. The life events were extracted from the life

263 course charts, multiple same responses aggregated to a single entry and disconnected from any interviewee
 264 information. In order to analyse the life events, experienced researchers based in the respective national
 265 research institutions normatively rated each event either as positive, negative or neutral, where neutral means
 266 that the life event could not be rated as positive nor negative because according to the normative judgement
 267 of the national experts it was neither positive nor negative. As such, the meaning attributed to each event
 268 could reflect the cultural importance of certain life events in relation to each national fieldsite, for example,
 269 marriage (positive in Poland), living with a partner (neutral in UK, positive in other countries), and university
 270 degree (positive in Germany, neutral in UK). Figure 2 shows examples for the ratings in the defined 11 life
 271 domains. None of the interviewees ascribed any positive life event in the categories illness or criminal justice
 272 system.

273

274 Figure 2: Examples for ratings of the life events according to the life domain

Life domain	Positive	Negative	Neutral
Parents / family	Caring, supportive parents	Divorce of parents, parental alcohol dependence, domestic violence	Being adopted, in general good family relationships
School	Completed post-compulsory, Graduation, certification	Excluded from school, bullying, not completed school	Completed school
Education /work	Started University, regular / proper work	Unemployment, stressful job, dealing drugs	Temporary employment, full-time employment
Friends	Good social network, drug-free friends, having best friends	No friends, social isolation, drug using/ dealing friends	Partying or clubbing with friends
Romantic partner	New romantic relationship, marriage, stable partnership	Drug using partner, divorce, separation, domestic violence	Being single, divorce, multiple sex partners
Living	Having own flat, with own family /children	Homeless, kicked-out of home, assisted living	Alone, with parents, with boyfriend, in hostel
Illness		Mental health problems, self-harm, physical injuries	Diagnosed with Attention deficit hyperactivity disorder, physical recovery in hospital
Criminal justice system		Imprisonment, conviction, arrests	Drug-related crime, occasional / minor offenses
Treatment	Detoxification, outpatient drug treatment, psychotherapy, psychiatry	In hospital, in psychiatry	Detoxification, psychiatry, rehabilitation
Religion /spirituality	Yoga, meditation	Strong aversion to faith and church	Catholic upbringing, atheist

Leisure	Travelling, playing music, sport	Boredom, social isolation, drug use, always staying at home	Clubbing, festivals, raves
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276 For each person, we calculated the cumulated sum of negative, positive and neutral life events at different
 277 points in time for all life domains together, as well as the sum for negative life events for every single life
 278 domain. An empty cell in the life course chart for life events was counted for the sum scores as zero. The sums
 279 of life events serve in our models as the dependent variable. For the analysis of the life events in the entire
 280 life course, we applied an age adjusted factorial ANCOVA, with the independent variables study group and
 281 country. For the analysis of life events while using ATS we calculated a duration adjusted ANCOVA in which for
 282 group 6 (non-ATS users), here we determined the duration from age at first ATS exposition to the current age.
 283 For comparing the six groups (independent variable), we computed univariate analysis of analysis of variance
 284 (ANOVA) and analysis of covariance (ANCOVA) in SPSS (31) and chose partial ETA squared as an indicator of
 285 the effect size, where 0.01 is considered a small, 0.06 a medium and 0.14 a large effect (32). A p value of < 0.05
 286 was employed to state statistical significance.

287 This data analysis was largely explorative, but the following hypotheses were guiding some parts of the
 288 analysis:

- 289 1. Dependent ATS users will show more negative life events in total
- 290 2. Dependent ATS users will show more negative life events before the onset of ATS use
- 291 3. Dependent ATS users will show more negative life events from the time period using ATS

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296 **Results**

297 Overall, 1,523 life events rated as neutral, 1,005 life events as positive and 1,019 life events as negative.

298 We did not observe any statistically significant differences between males and females in an age adjusted
299 ANCOVA for the total positive life events (male: 1.7(SD=2.2), female: 1.9 (SD=2.2)), total neutral life events
300 (male: 2.5 (SD=3.3), female: 3.0 (SD=3.3)) and total negative life events (male: 1.6 (SD=1.8), female: 2.0
301 (SD=2.4)). Only the combined sum of positive, neutral and negative life events (male: 5.8 (SD=4.6), female: 6.9
302 (SD=5.3)) showed statistically significant group differences ($F(1,276) = 3.92, p = 0.049$).

303 A two-way age adjusted ANCOVA was conducted to compare the main effects of the independent variables
304 study group and country and the interaction effects between study group and country on the sum of all four
305 categories of documented life events. The average sum of all documented life events did not differ significantly
306 between the groups, ranging from 13.6 in group 2 (formerly dependent) to 11.4 in group 3 (currently frequent).
307 No significant differences were observed for the neutral life events, which ranged from 6.7 in group 6 to 4.5
308 in group 3 (table 3). The average number of positive life events per person was lowest for group 1 (currently
309 dependent), with 2.1 documented positive life events in the entire life course, and highest among group 3
310 (currently frequent) and group 4 (formerly frequent) at 4.0. However, despite these group differences, the
311 ANCOVA, adjusted for age failed to show statistical significance.

312 Both dependent ATS user groups (CDU & FDU) report considerably more negative life events than the other
313 four groups. The dependent users (CDU & FDU) appear on the upper end of cumulated negative life events
314 whereas the frequent users and the non-frequent users (CFU & FFU&NFU) are in the middle and the exposed
315 non-ATS users (ENU) showed the lowest number. The age adjusted ANCOVA showed a statistically significant
316 difference between groups ($F(5,248) = 9.89, p = 0.000$).The group effect is large ($\eta_p^2=0.17$).

317 The country effects were statistical significant for all four scores of life events: positive life events ($F(4,248) =$
318 $33.57, p = 0.000, \eta_p^2=0.35$); neutral life events ($F(4,248) = 28.13, p = 0.000, \eta_p^2=0.31$); negative life events
319 ($F(4,248) = 2.80, p = 0.026, \eta_p^2=0.04$); all life events ($F(4,248) = 9.78, p = 0.000, \eta_p^2=0.14$).

320 The interaction effect between study group and country did not become significant for any of the four life
321 event scores: positive life events ($F(20,248) = 1.58, p = 0.058, \eta_p^2=0.113$); neutral life events ($F(20,248) = 1.25,$
322 $p = 0.212, \eta_p^2=0.092$); negative life events ($F(20,248) = 0.81, p = 0.697, \eta_p^2=0.062$); all life events ($F(20,248)$
323 $= 1.333, p = 0.159, \eta_p^2=0.097$).

324

325

326 Table 3: In the entire life course: mean number and standard deviation (SD) of life events by groups –two-way

327 ANCOVA (group and country), age adjusted

	Group 1: Currently ATS dependent (CDU)	Group 2: Formerly ATS dependent users (FDU)	Group 3: Currently frequent, non- dependent ATS users (CFU)	Group 4: Formerly frequent, non-ATS dependent users (FFU)	Group 5: Non- frequent ATS users (currently and formerly) (NFU)	Group 6: Exposed non- ATS users (ENU)	Total	F (5, 248)	p	η_p^2
Positive life events (SD)	2.1 (2.4)	3.9 (3.7)	4.0 (3.7)	4.0 (4.1)	3.7 (5.3)	3.9 (4.4)	3.6 (4.0)	2.19	0.056	0.04
Neutral life events (SD)	5.4 (4.8)	4.5 (4.0)	4.8 (5.1)	6.3 (5.7)	5.6 (5.6)	6.7 (6.0)	5.5 (5.2)	0.97	0.436	0.19
Negative life events (SD)	5.3 (2.9)	5.2 (3.2)	2.7 (2.9)	3.3 (2.5)	2.9 (2.1)	2.1 (2.1)	3.7 (2.9)	9.89	0.000	0.17
All life events (SD)	12.8 (5.9)	13.6 (6.1)	11.4 (7.2)	13.6 (9.7)	12.2 (9.2)	12.7 (7.5)	12.7 (7.6)	0.22	0.955	0.04

328

329 In order to investigate negative life events in more depth, the group differences were analysed for each of the

330 life domains in respect of the cumulated sum of negative life events. Highest mean sums for negative life

331 events are reported for the dependent user groups with 1.16 (formerly dependent) and 1.15 (currently

332 dependent) in the domain parents/family. For the domains parents/family, friends, romantic partner and

333 illness, we found that dependent ATS user groups showed higher sums of negative life events over the entire

334 life course in comparison to the four other groups. The ANCOVA, age adjusted, demonstrates statistically

335 significant group differences with low to medium effect sizes (table 4). Group differences for other life

336 domains, such as criminal justice system and leisure, fell just short of reaching statistical significance.

337

338 Table 4: In the entire life course by life domains: mean number and standard deviation of negative life events

339 by groups and life domain - ANCOVA, age adjusted

Life domain	Group 1: Currently ATS dependent (CDU)	Group 2: Formerly ATS dependent users (FDU)	Group 3: Currently frequent, non- dependent ATS users (CFU)	Group 4: Formerly frequent, non-ATS dependent users (FFU)	Group 5: Non- frequent ATS users (currently and formerly) (NFU)	Group 6: Exposed non-ATS users (ENU)	Total	F (5, 272)	p	η_p^2
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Parents / family (SD)	1.15 (1.10)	1.16 (1.11)	0.71 (1.17)	0.81 (0.91)	0.55 (0.84)	0.76 (1.05)	0.87 (1.06)	2,84	0,016	0,05
School	0.15 (0.36)	0.23 (0.43)	0.06 (0.24)	0.11 (0.39)	0.22 (0.55)	0.10 (0.30)	0.15 (0.40)	1,83	0,106	0,03
Education /work	0.23 (0.48)	0.32 (0.47)	0.10 (0.31)	0.19 (0.46)	0.22 (0.47)	0.10 (0.30)	0.20 (0.43)	1,38	0,233	0,03
Friends	0.83 (1.32)	0.55 (0.83)	0.29 (0.54)	0.32 (0.58)	0.39 (0.70)	0.24 (0.58)	0.45 (0.83)	3,12	0,009	0,05
Romantic partner	0.36 (0.79)	0.39 (0.68)	0.19 (0.49)	0.11 (0.31)	0.06 (0.24)	0.07 (0.26)	0.21 (0.54)	4,17	0,001	0,07
Living	0.53 (0.80)	0.48 (0.69)	0.17 (0.43)	0.38 (0.76)	0.45 (0.79)	0.29 (0.92)	0.39 (0.74)	1,20	0,309	0,02
Illness	1.02 (1.15)	1.14 (1.31)	0.73 (1.27)	0.68 (0.88)	0.51 (0.87)	0.45 (0.74)	0.77 (1.10)	3,11	0,010	0,05
Criminal justice system	0.77 (1.11)	0.64 (1.02)	0.27 (0.96)	0.54 (1.14)	0.35 (0.78)	0.12 (0.33)	0.46 (0.95)	2,22	0,053	0,04
Treatment	0.04 (0.20)	0.02 (0.13)	0.02 (0.14)	0.08 (0.28)	0.02 (0.14)	0.00 (0.00)	0.03 (0.17)	1,08	0,373	0,02
Religion /spirituality	0.04 (0.29)	0.00 (0.00)	0.04 (0.20)	0.03 (0.16)	0.04 (0.20)	0.02 (0.15)	0.03 (0.19)	0,39	0,854	0,01
Leisure	0.15 (0.62)	0.23 (0.63)	0.08 (0.28)	0.08 (0.28)	0.04 (0.20)	0.00 (0.00)	0.10 (0.42)	1,92	0,090	0,03

340

341 The sum of all life events occurring until the first ATS use or exposition did not show group differences.
342 However, there were significant differences between groups for the number of positive, neutral and negative
343 life events (table 5). Neutral life events were higher in the exposed non-ATS user group (ENU) and fewest in
344 the currently dependent ATS user group (CDU). The ANOVA demonstrated statistically significant differences
345 between both groups ($F(5,273) = 3.29, p = 0.007$). The positive life events revealed a similar trend for the
346 groups ($F(5,273) = 2.27, p = 0.048$). The combined sum of negative life events occurring before first use or
347 exposition to ATS were highest for the two dependent groups, lower for the non-dependent user groups, and
348 lowest of all for the non-users ($F(5,273) = 2.37, p = 0.039$). However the group size effects on the observed
349 differences in positive, neutral and negative life events are small.

350

351 Table 5: Until the first ATS use/exposure: mean number and standard deviation (SD) of life events, ANOVA

	Group 1: Currently ATS	Group 2: Formerly ATS dependent	Group 3: Currently frequent, non-	Group 4: Formerly frequent, non-ATS	Group 5: Non- frequent ATS users	Group 6: Exposed non-ATS	Total	F (5, 273)	p	η_p^2
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	dependent (CDU)	users (FDU)	dependent ATS users (CFU)	dependent users (FFU)	(currently and formerly) (NFU)	users (ENU)				
Positive life events (SD)	0.40 (0.88)	1.07 (1.74)	1.38 (1.61)	1.19 (2.42)	1.67 (3.15)	1.60 (2.12)	1.21 (2.11)	2.27	0.048	0.040
Neutral life events (SD)	1.55 (1.53)	1.38 (1.67)	2.13 (2.77)	2.62 (2.88)	2.94 (3.72)	3.17 (3.75)	2.24 (2.87)	3.29	0.007	0.057
Negative life events (SD)	1.96 (1.88)	2.05 (1.73)	1.42 (2.02)	1.65 (1.72)	1.33 (1.39)	1.07 (1.39)	1.60 (1.73)	2.37	0.039	0.042
All life events (SD)	3.91 (3.05)	4.50 (3.26)	4.92 (4.12)	5.46 (5.65)	5.94 (6.27)	5.83 (4.96)	5.05 (4.65)	1.39	0.228	0.025

352

353 The duration of ATS use for the five user groups and the exposure to ATS for the non-ATS user group (ENU)
354 showed group differences (table 2). Therefore, we applied an ANCOVA adjusted by the duration of ATS use to
355 test for group differences with regard to life events in the time between the onset and desistance of ATS use
356 (table 6)

357 The reported sum of all life events while using ATS differs significantly between groups, ranging from 4.2
358 (SD=4.6) in group 5 (non-frequent) to 8.8 (SD=5.1) in group 1 (currently dependent). The number of neutral
359 life events also differ significantly. The positive life events showed no group effects. The negative life events
360 while using ATS are comparably low in the four non-dependent groups, but up to 3.7 times higher for the two
361 dependent groups (CDU&FDU). The lowest number of negative life events we found among group 5 (NFU)
362 with 0.9 while using ATS and the highest in group 1 (CDU) with 3.3. The duration adjusted ANCOVA showed
363 statistically significant differences between the groups ($F(5,272) = 13.16, p = 0.000$). The partial ETA squared
364 demonstrated a large size effect ($\eta_p^2=0.20$).

365

366 Table 6: Continued ATS use: Mean number and standard deviation (SD) of life events by groups, ANCOVA,
367 duration adjusted

	Group 1: Currently ATS dependent (CDU)	Group 2: Formerly ATS dependent users (FDU)	Group 3: Currently frequent, non- dependent ATS users (CFU)	Group 4: Formerly frequent, non-ATS dependent users (FFU)	Group 5: Non- frequent ATS users (currently and formerly) (NFU)	Group 6: Exposed non-ATS users (ENU)	Total	F (5, 272)	p	η_p^2

Positive life events (SD)	1.7 (2.0)	2.0 (2.2)	1.9 (1.9)	1.5 (1.6)	1.5 (2.5)	2.2 (2.8)	1.8 (2.2)	0.73	0.605	0.01
Neutral life events (SD)	3.8 (4.3)	2.5 (3.1)	2.2 (3.2)	2.5 (2.7)	1.8 (2.4)	3.5 (3.5)	2.7 (3.3)	2.98	0.012	0.05
Negative life events (SD)	3.3 (2.5)	2.6 (2.7)	0.9 (1.0)	1.4 (1.6)	0.9 (1.2)	1.1 (1.3)	1.7 (2.1)	13.16	0.000	0.20
All life events (SD)	8.8 (5.1)	7.1 (5.4)	5.0 (3.9)	5.4 (4.2)	4.2 (4.6)	6.8 (4.7)	6.2 (4.9)	5.75	0.000	0.10

368

369

370 Discussion

371 . Findings from our analysis of drug use and life event data from 279 ATS user and non-users across Europe
372 demonstrate clear differences amongst our six pre-defined user groups. Both in terms of both the types of
373 ATS used, and in relation to patterns of consumption (table 1). Intensive, daily ATS use was evident in groups
374 1 and 2 (dependent - CDU and FDU), and indicative of the overall severity of their drug “career”. In contrast,
375 this consumption pattern was considerably less common in groups 3 and 4 (frequent - CFU and FFU). The type
376 of ATS consumed was also associated with severe (or dependent) use trajectories. Specifically, we found that
377 methamphetamine use was markedly more prevalent amongst current or former dependent user (group 1
378 and 2 compared to groups 3, 4 and 5), involving periods of daily or at least weekly consumption. We found
379 similar patterns of intensive use amongst groups 1 and 2 (dependent -CDU and FDU) for other non-
380 amphetamine substances, which again contrasted with that reported by our other user groups.

381 Whilst few differences were seen in the total number of life events reported by different ATS user and non-
382 user groups, we found significant associations between the number and type of negative life events and ATS
383 consumption trajectories. Exposed non-users and non-dependent ATS users, regardless of the frequency of
384 use, reported lower rates of adverse life events than dependent users.

385 Dependent users, both current and former, reported higher rates of negative life events before their first use
386 of ATS, and fewer positive or neutral experiences. Although small, these differences were nevertheless
387 statistically significant, and may suggest that dependent users are more to have experienced difficulties during
388 childhood and adolescence.

389 Negative life events after the initiation of ATS use can be partially interpreted as consequences of the
390 substance use patterns and our results point out that these numerous consequences are exclusively limited
391 to the dependent or formerly dependent users of group 1 and group 2. We do not find any relevant differences
392 between the other four groups.

393 At the same time, the negative life events experienced by dependent ATS user groups appeared to derive from
394 a variety of life domains, making it challenging to identify clear and causal pathways. Whilst existing evidence
395 implies that experiencing negative life events results in sustained ATS consumption (6, 10, 20), our study
396 suggests holistic, tailored interventions and specialist treatment services are needed for this group, as a single,
397 simple intervention is unlikely to cover all the life domains affected. A standardized short screening tool for
398 life domains affected by negative life events for dependent ATS user in contact with drug services could serve
399 as a guiding action for further support.

400 For frequent and non-frequent ATS users negative life events from the period of ATS use do not become
401 obvious in our analysed data. Besides preventing a pathway into ATS dependency, the aim of an intervention
402 should be to reduce the harm from the illicit drug itself. Evidence suggests this can be achieved by offering
403 quality and quantity control through drug testing which is well accepted by the users and offers the
404 opportunity for interventions to prevent developing a substance use dependency (33).

405 Overall, our findings show that formerly or current ATS dependent users are more likely to have experienced
406 higher numbers of negative life events compared to other user groups. However, at present, there is no
407 standardized instrument available to support accurate measurement of negative life events. The development
408 and implementation of such an instrument would be helpful in counselling and treatment settings to provide
409 adequate responses to a client's need.

410

411 Strengths and limitations

412 The whole spectrum of ATS careers reaching from dependent use to non-dependent, from frequent to non-
413 frequent use as well as non-use, even though opportunities for ATS use were given; from ongoing use to

414 former use, and from experiences to no experiences with drug treatment are represented in the sample and
415 the six groups.

416 In order to reveal more accurately the context of “change” for ATS trajectories, we established the inclusion
417 criterion “ATS abstinence in the last 12 months” for group 2 (FDU -formerly ATS dependent users) and group
418 4 (FFU - formerly frequent, non-ATS dependent users).

419 The use of a calendar technique such as timelines (34) for the combination of life events and time-points is
420 novel and understudied in the field of substance use in general (26, 35, 36), has yet not been used for
421 examining stimulant use and might tackle partially the individual recall bias of life events.

422 ATS covers a variety of different substances and the often-observed use of more than one type of ATS in life
423 by the respondents has not been explored in detail in this study as well as the effect of a single ATS. We also
424 have significantly more methamphetamine users in the dependent user groups (CDU&FDU), therefore we
425 cannot rule out that some results are influenced by the specific experiences of this user group. The same can
426 be said in relation to other poly-substance use and non-amphetamine substances consumed by the
427 respondents. Although further results from the ATTUNE project should disclose such interactions.

428 The age periods in the life course charts utilized were relatively large. We also only recorded one life event
429 per domain therefore multiple occurrences of life events could have occurred and could have gone
430 unrecorded. This could have resulted in both the underreporting of the sum of life events per domain but also
431 in total. Further, our focus on negative life events might have concealed consideration of positive life events
432 that serve as protective factors.

433 Whilst our sample was relatively substantial (n=279), we cannot fully adjust for differences such as country,
434 ATS consumed or other, may be important, participant characteristics due to small numbers per specific
435 group/variable.

436 The life chart data analysed was collected during semi-structured qualitative interviews and quasi-isolated
437 from the rich in-depth interview data. The sample size, the systematic and the number of recorded life events
438 in the life charts gave us the opportunity to employ standardized methods to test for statistical inferences,
439 although such a method is rather untypical for in-depth qualitative interview data.

440 **Conclusions**

441 By purposeful sampling of five ATS user groups and one ATS exposed non-user group we were able to study
442 the association between ATS pathways and life events in the entire life course. The data was systematically
443 collected using life course charts to capture key life events and substance use histories during in-depth
444 qualitative interviews. The applied method is novel for the examination of ATS trajectories.

445 Dependent ATS users experienced more negative life events for the entire life course after age adjustment.
446 Whilst, some of the group differences found could be attributed to the life course prior to ATS use, most
447 negative life events resulted from periods of ATS usage. A detailed analysis of the specific life domains reveal
448 that the social environment was mostly likely to be that affected by the negative life events. No difference
449 between the groups of non-dependent, frequent and non-frequent ATS users and exposed non-ATS users were
450 found.

451 For non- dependent, frequent and non-frequent ATS users negative life events from the period of ATS use do
452 not become obvious in our analysed data. Besides preventing a pathway into ATS dependency, the aim of an
453 intervention should be to reduce the harm by for example drug testing which offers also the opportunity for
454 interventions to prevent developing a substance use dependency.

455 For the group of dependent ATS user our study suggests holistic, tailored interventions and specialist
456 treatment services are needed, as a single, simple intervention is unlikely to cover all the life domains affected.

457

458

459 **List of abbreviations**

460 ANCOVA Analysis of covariance

461 ANOVA Analysis of variance

462 ATS Amphetamine Type Stimulant

463 ATTUNE “Understanding Pathways to Stimulant Use: a mixed methods examination of the individual,
464 social and cultural factors shaping illicit stimulant use across Europe”

465 CDU Currently ATS dependent (Group 1)

466	CFU	Currently frequent, non-dependent ATS users (Group 3)
467	EMCDDA	EU drugs agency: European Monitoring Centre for Drugs and Drug Addiction
468	ENU	Exposed non-ATS users (Group 6)
469	FDU	Formerly ATS dependent users (Group 2)
470	FFU	Formerly frequent, non-ATS dependent users (Group 4)
471	MDMA	3,4-methylenedioxy-methylamphetamin (also ecstasy)
472	NFU	Non-frequent ATS users, currently and formerly (Group 5)
473	SCORE	Sewage Analysis CORE group Europe
474	SDS	Severity of Dependence Scale
475	UK	United Kingdom of Great Britain and Northern Ireland
476	UNODC	United Nations Office on Drugs and Crime
477		

478 **Declarations**

479 All interviewees provided their informed consent to take part in the study and were made aware of the data
480 protection rules. The interviewees' anonymity is guaranteed.

481 In GER, UK, PL, CZ, the study has been reviewed and approved by the respective responsible ethics committee,
482 in NL no ethical approval was required. The respective reference numbers are as follows: GER: WF-03/17; UK:
483 17/NE/0283; PL: 160_2017/2018; CZ: 180326_EK-NMS.

484 **Consent for publication:** not applicable

485 **Availability of data and material:**

486 The dataset generated and analysed during the current study is in the ownership of the ATTUNE research
487 group and is available from the corresponding author on reasonable request.

488 **Competing interests:**

489 This paper reports on independent research and expresses the views of the authors. The authors declare that
490 they have no competing interests.

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496 **Authors' contributions:**

497 MM developed and analysed the dataset of the life course charts. HZ, MR, AM, LS, WM and RG were major
498 contributors in writing the manuscript. AD, RG, MA contributed to the background and discussion of the paper.
499 All authors read and approved the final manuscript.

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509

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590

ID of respondent

Insert the Frequency: 0=no use; 1=less than monthly; 2= monthly; 3= weekly; 4= daily / nearly daily

– if one of the substances was never used, insert a cross (X) in column B (never used)

Type of substance	Never used	until age of 13	14-16	17-19	20-25	26-30	31-39	40-49	50+
Amphetamines									
Methamphetamine									
NPS									
MDMA / Ecstasy									
Alcohol									
Cocaine									
Cannabis									
Opiates									
Nicotine									
Hallucinogenes/LSD									
Other									

Indicate important positive or negative life events – by short explanation (max. 100 charcters)

Life events	until age of 13	14-16	17-19	20-25	26-30	31-39	40-49	50+
Parents / Family								
School								
Education/Work								
Friends								
Living								
Romantic partner								
Illness								
Prison/criminal justice								
Treatment								
Religion / Spirituality								
Leisure								