What is the relapse risk during treatment? Survivor analysis of single and multiple relapse events in inpatients with alcohol use disorder as part of an observational study

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Abstract

Introduction: During treatment for alcohol use disorder (AUD), about 40% of patients return to drinking. Whether the risk of relapse changes during treatment and how relapses may affect the risk of subsequent relapse are unclear, however. The current study, therefore, aims to identify when and with what probability relapses occur.

Methods: One hundred and three inpatients at an AUD treatment center participated in this observational study. The study documented relapse to drinking using breath analyzers, urine tests, and self-reported incidents for 42 days after the start of treatment. Time to the first relapse event and to any subsequent relapse event served as the outcome measures. The study determined the proportion of patients who had not experienced a relapse event at any given point by Kaplan-Meier estimates and Cox proportional hazards models. The study team computed the instantaneous probability of experiencing an event at any given point using generalized estimating equation (GEE) models of the binomial family with log-link and exchangeable correlation structure to estimate unadjusted and adjusted hazards.

Results: Whereas the hazards of experiencing a first relapse event declined steadily over the 42 days, the hazards of experiencing a subsequent relapse following an initial event remained stable. Both first-time and recurrent relapses were positively associated with the number of DSM-5 AUD criteria.

Conclusion: Whereas the risk of relapse declines with each day of abstinence during treatment, it remains high after an individual relapse for the first time. This finding implies that therapy should focus on strengthening self-efficacy for low-risk groups and on relapse-prevention strategies for high-risk groups.

Introduction

The harmful use of alcohol is a widespread phenomenon linked to high costs and detrimental effects on society, including more than 5% of the global burden of disease (WHO, 2018). Furthermore, harmful alcohol use is connected with an increased risk of committing or experiencing violence in partnerships (Lipsky et al., 2014). Alcohol use disorders (AUD), which number among the most prevalent mental disorders worldwide, are associated with high mortality and burden of disease, including liver disease, heart disease, and cancer (Carvalho et al., 2019).

The course of AUD treatment is often characterized by relapse to drinking, even when patients seek treatment voluntarily. However, “relapse” has been defined in a variety of ways in the literature (e.g., Brandon et al., 2007; Maisto, Witkiewitz, et al., 2016). The range of definitions extends from any return to drinking (e.g., drinking a single sip of alcohol) as a static, discrete event to a return to the original drinking pattern as a dynamic process (e.g., daily consumption of a large amount of alcohol). The various definitions mostly agree, though, that relapse represents a return to drinking after a period of abstinence. Maisto, Witkiewitz, et al. (2016) emphasized in their review, that more systematic research is needed to make the construct of “relapse” more scientifically and theoretically valuable.

Data from Switzerland show that 40% of inpatients in relapse-prevention treatment return to drinking during treatment (Klingemann et al., 2013), and at one-year follow-up, only about 40.5% of former inpatients report being abstinent (Moggi et al., 2007). Europe and the United States have similar relapse rates to that in Switzerland (e.g., Dandaba et al., 2020; Witkiewitz, 2011). Several studies have demonstrated that drinking during treatment is a predictor of long-term alcohol misuse (Gueorguieva et al., 2015; Ludwig et al., 2013; Maisto, Roos, et al., 2016).

Previous studies have investigated the predictors of relapse (Adamson et al., 2009; Senn et al., 2020; Sliedrecht et al., 2019), but research has explored much less the actual pattern of relapses. To the best of our knowledge, after searching the literature, only one attempt exists to identify patterns of relapses during treatment, undertaken by Charney et al. (2010). The authors established that relapsing at the beginning of treatment is associated with a worse prognosis. Witkiewitz and Masyn (2008), who investigated the pattern of relapses after treatment, discovered that after a relapse for the first time following treatment, the majority of the affected individuals find their way

back to infrequent, moderate drinking or abstinence. Despite these findings, which indicate the relevance of examining the temporal distribution and pattern of relapses, no other studies have sought to describe a specific pattern or a period of time in which the risk of relapse during treatment may increase. It is thus still unclear how the relapse risk is distributed over the course of treatment, whether it changes or remains stable, and how it can be affected by actual relapse events. Furthermore, to date and according to our knowledge, no studies have explored in depth multiple relapses during treatment; therefore, we do not know how the risk of multiple relapses might change after an initial relapse. The current study seeks to identify the risk of one relapse and of multiple relapses during the course of treatment to better understand when and why relapses occur, thereby facilitating the optimization of treatment procedures and the reduction of the relapse risk.

When examining relapse risk, it is important to take into account the risk factors that have already been identified by previous research, such as sociodemographic variables and substance-related variables. With regard to sociodemographic variables, age and gender have been the most studied, with partially inconsistent results summarized in two reviews (Adamson et al., 2009; Sliedrecht et al., 2019). Generally speaking, female gender and higher age are associated with a higher probability of remaining abstinent. For substance-related variables, the number of years since the onset of addiction and the severity of AUD have been consistently linked to relapses in the literature (Sliedrecht et al., 2019), in that younger age of onset of AUD and more severe forms of AUD are associated with a higher risk of relapse. We, therefore, include age and gender as well as number of years since onset of addiction and the severity of AUD as covariates in the analyses.

In light of several decades of research on the predictors of relapse, we suggest a complementary approach that focuses on the temporal distribution and patterns of relapse during treatment to better understand relapse risk and improve treatment. The objective of this article is to explore the patterns of one relapse and multiple relapses during the course of treatment, while including potential covariates. We use Kaplan-Meier estimates and Cox proportional hazards models to estimate the unadjusted and adjusted survivor functions, respectively.

Method

Study site and treatment

The study recruited participants from an inpatient treatment center for alcohol use disorder treatment (Forel Clinic) in Switzerland. The preconditions for entering this inpatient treatment were (a) an age of ≥18 years, (b) a diagnosis of alcohol dependence according to ICD-10 (WHO, 1992), (c) abstinence since alcohol detoxification, and (d) agreement with the drinking-related treatment goal of abstinence and a commitment to abide by clinic rules. Psychiatric comorbidity, as determined by the presence of the criteria listed for each disorder in the ICD-10, was not a reason for treatment exclusion, with the exception of acute schizophrenia.

The treatment program in the Forel Clinic is characterized by voluntariness. It includes psychosocial relapse-prevention content provided in weekly individual psychotherapy sessions and group therapy sessions, as well as through exercise therapy, occupational therapy, and social counseling. The content of the therapy is basically the same for all patients. Patients transition from the detoxification unit to the inpatient treatment program when all withdrawal symptoms have fully resolved. Weekend leaves are permitted starting with the second weekend after transition. Patients are allowed to leave the clinic every weekend from that date on, to attempt abstinence in an every-day environment. If one is not feeling well (e.g., craving, illness), patients can decide autonomously to stay in the clinic or return to the clinic at any time during the weekend. Treatment duration is normally set between 8 and 12 weeks, depending on disease severity, psychiatric comorbidity, and a patient's private professional situation. Planned short-term therapy with a minimum duration of four weeks is also allowed. Due to the open structure of the clinic, premature termination of therapy by patients is possible but relatively rare.

Prior to entering treatment, patients agree to self-report any infringements of abstinence and to participate in alcohol and drug testing. The contact for the self-report of relapses is the nursing staff, who note the date and the amount of the relapse (e.g., the number of standard drinks) and send the information to the attending physician.

Breathalyzer tests are conducted with the AlcoTrueM model manufactured by Labtec. Its measuring principle consists of an electrochemical sensor with a precision sampling system, and it features a measuring range from 0.00 to 2.6 mg/l and 0.00 to 5.50‰. Breathalyzer tests are employed when (a) patients re-enter the clinic after a weekend

leave or (b) clinical staff suspect a patient has used alcohol. Additional breathalyzer tests as well as urine and blood tests are conducted in a random and unannounced manner. Drinking during treatment is not a reason for exclusion from therapy; on the contrary, in the Forel Clinic, drinking during treatment is considered a symptom of the disease, and the treatment concept encompasses drinking during treatment (i.e., relapse prevention). However, any manipulation of urine tests (e.g., diluting or substituting a urine sample), refusal of treatment, or violations of the clinic rules (e.g., alcohol or drug use on clinic property, violent behavior) will result in the termination of treatment.

Due to the open structure of the clinic and the voluntary nature of the treatment, relapses can happen at any time. During the week, the inpatients can leave the clinic if they do not have therapy sessions. Weekends present another possibility for leaves. Typical relapse situations are: anxiety, depressed mood, positive mood, conflicts with family or friends, waiting (e.g., transportation), cravings, etc. (see also: Rösner et al., 2016).

When a relapse is detected, the patient must stay in his or her room; in the event of a severe relapse, the patient is transferred to the detoxification unit. As soon as a breathalyzer test shows an alcohol level of 0‰, the patient is allowed to participate in the normal therapy program and to leave the clinic campus again.

Design and procedure

The study team conducted this observational study in accordance with the Declaration of Helsinki (World Medical Association, 2013) and the Ethics Committee of the Canton Zurich approved this study.

The inclusion criteria for participation in the study were similar to the criteria for entering treatment (see above). Exclusion criteria were insufficient language comprehension skills to follow staff instructions or to complete questionnaires, cognitive deficits that would limit the patient's ability to provide informed consent, and acute suicidality or schizophrenia (as assessed by the research assistant at the first appointment).

Patients fulfilling the inclusion criteria were recruited by the research assistant within the first week of admission to the clinic. After the research assistant explained the objectives and procedures of the study, they asked patients to grant their informed consent. The respondents then completed the questionnaires anonymously.

Data assessment took place between January 2016 and February 2017. During data collection, 163 patients entered into relapse-prevention treatment and fulfilled the inclusion criteria. Of these 163 screened patients, 103 decided to take part in the study. Of the 63 non-participants, 18 individuals did not show up for the first appointment and 45 individuals did not provide consent to participate in the study. We examined whether participants differed from patients who met the inclusion criteria but chose not to participate. Statistical testing showed that the two groups did not differ in terms of substance-related factors (years since onset of addiction, frequency of alcohol consumption prior to treatment, severity of addiction) or in sociodemographic characteristics (age, sex, civil status, nationality, employment status).

Outcomes and covariates

The outcome measures were time to the first relapse event (single-failure-per-subject) and time to the first or subsequent relapse event (multiple-failure-per-subject) within a 42-day period after the start of treatment. Analyses for both outcome variables were based on the same sample, consisting of 103 participants.

A patient was classified as consistently abstinent if neither the results of the breathalyzer tests nor the patient's self-reports indicated alcohol consumption during his or her stay. The study categorized this group of patients as “abstainers”. Accordingly, we defined “relapse” as any infringement of abstinence, in terms of any drinking during the inpatient treatment program. When at least one relapse occurred, the study classified the patient in the dataset as a “relapser”. The study recorded the exact dates of relapses and put in relation to the entry date to calculate the number of days until the relapse event. Premature termination of therapy by patients was not classified as a relapse.

The single-failure-per-subject sample comprised 103 patients, representing 796 observations and a total of 3206 days at risk. Patients remained in the sample until they experienced their first relapse event or were censored (i.e., the end of their recorded data was reached before a first relapse event occurred). The multiple-failure-per-subject sample comprised the same 103 patients, representing 969 observations and a total of 3837 days at risk. Patients remained in the sample until they were censored (i.e., the end of their recorded data was reached).

Our selection of covariates was guided by previous research and included age, gender, years since the onset of addiction, and the number of DSM-5 criteria (Adamson et al.,

2009; Sliedrecht et al., 2019). The research assistant assessed the covariates in the form of an interview conducted at the first appointment. The study defined “years since onset of addiction” as the number of years since the beginning of alcohol use disorder. Furthermore, adjusted multiple-failure-per-subjects models included a covariate reflecting the number of previous relapse events to capture the effects of previous relapse events on subsequent events. With the exception of gender, the study centered all covariates at their mean value.

Due to the standardized questionnaires and measurement instruments, the clear and unified procedures, the risk for measurement bias is minimized. In addition, the study invited all eligible patients to the first appointment, so a small probability exists for selection bias.

Statistical analysis

The study team used Kaplan-Meier estimates and Cox proportional hazards models to estimate the unadjusted and adjusted survivor functions, respectively; that is, the proportion of patients who had not experienced a relapse event at any given point. Relapse events are described as single or multiple-failure-per-subject. In the context of the survival analysis literature, failure is used in the sense of “event”, i.e., occurrence of a relapse. In statistics, this term is used in nonjudgmental way. The study used generalized estimating equation (GEE) models of the binomial family with log-link and exchangeable correlation structure to estimate unadjusted and adjusted hazards (i.e., the instantaneous probability of experiencing an event at any given point). Adjusted models included age, gender, years since the onset of addiction, the number of DSM-5 criteria, and the number of previous relapse events where appropriate. The study included these variables into the calculations of adjusted hazards, to adjust for confounding effects. Furthermore, all GEE models included a time covariate. We reported survivor functions (where appropriate), hazard ratios, and hazards with corresponding 95% confidence intervals (95% CI). Statistical significance was established at $p < .05$.

Results

Overall, 103 inpatients participated in this study. Table 2 lists the characteristics of the participants. The baseline sociodemographic characteristics are as follows: At admission, the mean age of the subjects was 45.6 years, and 22.4% were female. Of the participants, 25.5% were married, 43.7% were employed, and 80.6% were Swiss citizens. Patients met a median of 8 DSM-5 criteria with an interquartile range of 3 DSM-5 criteria. They reported an average of 7.7 years since the onset of addiction. The participants who drank on a daily basis in the last six months before admission amounted to 79.4%. Furthermore, 15 patients (14.6%) were in a planned short-term therapy program.

Table 2. Characteristics of patients.

	Mean	***SD****	***Median***	***25th percentile***	***75th percentile***
Men (n, %)	80 (77.6)				
Women (n, %)	23 (22.4)				
Age	45.6	9.6	46	39	53
Civil status					
Single (n, %)	36 (38.3)				
Married (n, %)	24 (25.5)				
Separated (n, %)	2 (2.1)				
Divorced (n, %)	29 (30.9)				
Widowed (n, %)	1 (1.1)				
Registered partnership (n, %)	2 (2.1)				
Nationality: Swiss (n, %)	83 (80.6)				
Employment status: employed (n, %)	45 (43.7)				
Years since onset of addiction	7.7	7.4	5	2	11
Frequency of alcohol consumption in the last six months before admission					
Daily (n, %)	77 (79.4)				
4-6 days per week (n, %)	8 (8.2)				
2-3 days per week (n, %)	8 (8.2)				
1 day per week or less (n, %)	4 (4.2)				

Number of DSM-5 criteria	7.8	2.0	8	6	9
Planned short-term therapy (n, %)	15 (14.6)				

*SD = Standard deviation

No significant differences existed in the sociodemographic variables between abstinent and relapsing patients.

In total, 594 announced and 357 unannounced alcohol tests were conducted in the overall sample, indicating a median per patient of 6 (IQR 5–7) announced tests and 3 (IQR 2–5) unannounced tests. Thirteen participants terminated the therapy prematurely at their own request.

We examined the distribution of alcohol tests and test results by weekdays (see Table 3). The empirical average probability of a positive test result over all weekdays was p = .047. The probability of a positive test was highest on Fridays (p = .133) and Saturdays (p = .203). The lowest probability (p = .015) of a positive test was on Sundays—the day on which most of the tests were performed.

Table 3. Overview of the number of alcohol tests per day of the week and their result (positive/negative).

Test result	***Day of the week***							
	Sunday	Mon-day	Tues-day	Wed-nesday	Thurs-day	Friday	Satur-day	Total
Negative (n, %)	590 (98.50)	72 (93.51)	55 (93.22)	63 (95.45)	57 (90.48)	39 (86.67)	47 (79.66)	923 (95.35)
Positive (n, %)	9 (1.50)	5 (6.49)	4 (6.78)	3 (4.55)	6 (9.52)	6 (13.33)	12 (20.34)	45 (4.65)
Total (n, %)	599 (100.0)	77 (100.0)	59 (100.0)	66 (100.0)	63 (100.0)	45 (100.0)	59 (100.0)	968 (100.0)

First relapse event

Of the 103 patients, 33 (32.0%) experienced a first relapse during the observation period. The incidence rate was 0.0102932 first-time relapse events per treatment day, which amounts to approximately 10 first-time relapse events per 1000 treatment days.

The estimated unadjusted proportion of patients who had not experienced a first relapse declined steadily (Figure 1, panel A). After 7 days of treatment, 92.2% (95% CI 82.6–94.6) had not had a relapse. After 14, 21, and 28 days, the respective estimated percentages of relapse-free patients were 84.4% (95% CI 75.7–90.1), 79.3% (95% CI 70.1–86.0), and 71.7% (95% CI 61.6–79.5). At the end of the observation period, 65.3% (95% CI 54.5–74.0) of the patients had been continuously abstinent. Similarly, the adjusted proportion of patients, centered at the mean covariate values, declined steadily, reaching 73.3% at the end of the observation period (Figure 1, panel C). Moreover, both unadjusted and adjusted hazards of experiencing a relapse event declined over time (Figure 1, panels B and D) and were of similar magnitude across the two models. At day 7, the adjusted hazard was 0.0107 (95% CI: 0.0059–0.0155), whereas the unadjusted hazard was 0.0110 (95% CI: 0.0060–0.0162). The respective adjusted and unadjusted hazards for days 14, 21, 28, and 42 were 0.0095 (95% CI 0.0060–0.0130) vs. 0.0097 (95% CI 0.0062–0.0132), 0.0084 (95% CI 0.0050–0.0118) vs. 0.0085 (95% CI 0.0051–0.0119), 0.0075 (95% CI 0.0035–0.0116) vs. 0.0075 (95% CI 0.0034–0.0115), and 0.0056 (95% CI 0.0003–0.0108) vs. 0.0057 (95% CI 0.0004–0.0110).

With regard to the association between covariates and first-time relapses (Table 4, single-failure-per-subject), only the number of DSM-5 criteria was positively associated with relapse and was statistically significant. More specifically, the hazard of experiencing a first-time relapse was 44% higher for an increase of one DSM-5 criteria (HR = 1.44, 95% CI 1.17–1.79).

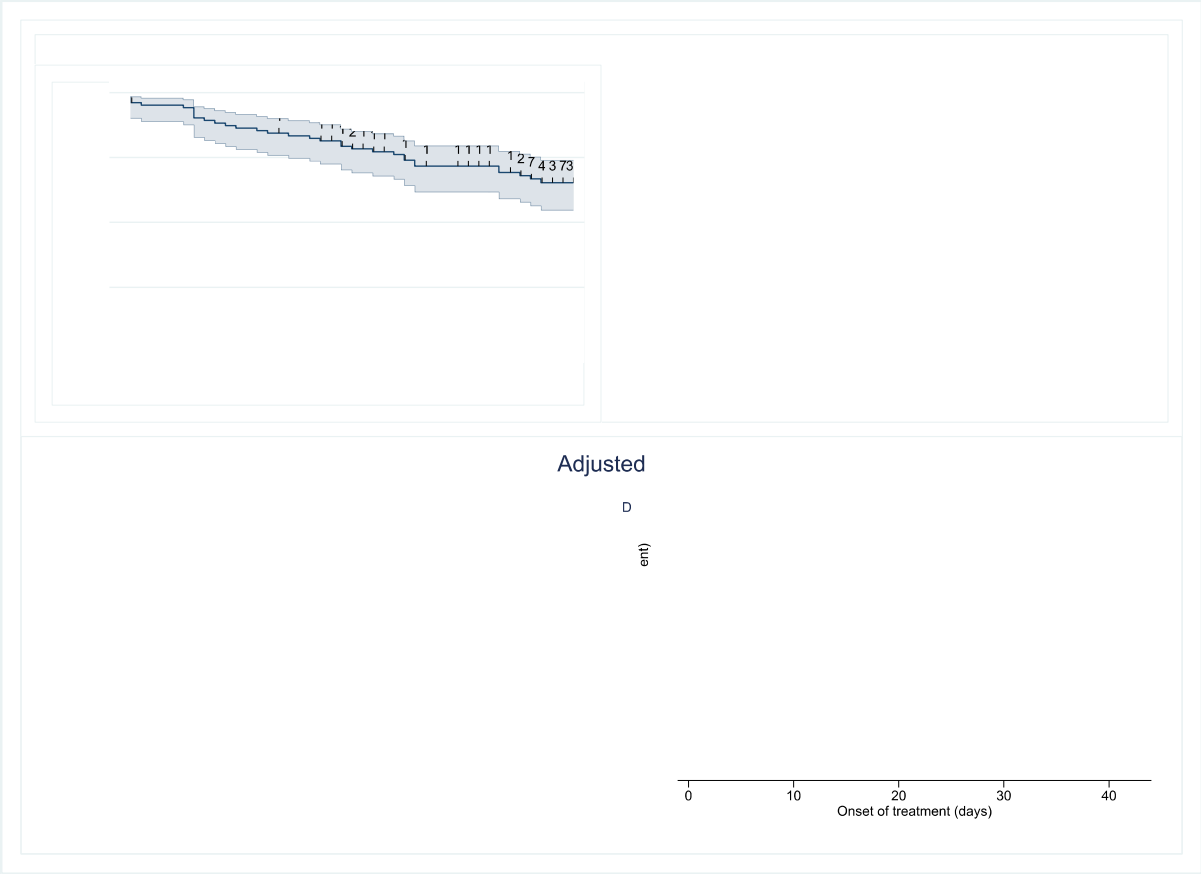

Figure 1. Single-failure-per-subject survivor function and hazard estimates for relapse during treatment.

Panel A: Kaplan-Meier survivor estimates. Panel B: generalized estimating equation (GEE)-based unadjusted hazard estimates. Panel C: Cox regression-based estimates adjusted for covariates centered at their mean. Panel D: GEE-based adjusted hazard estimates. Adjustment for age, gender, years since onset of addiction, and the number of DSM-5 criteria.

Table 4: Adjusted Cox regression results for relapse events during treatment.

Variable	***HR***	***SE***	***P***	***95% CI***
Single-failure-per-subject[A)]				
Women	1.00	Reference		
Men	1.18	0.5111	0.7030	0.50 - 2.76
Age	0.99	0.0198	0.6440	0.95 - 1.03
Onset of addiction (years)	0.96	0.0297	0.2240	0.91 - 1.02
Number of DSM-5 criteria	1.44	0.1580	0.0010	1.17 - 1.79
Multiple-failure-per-subject[B)]				
Women	1.00	Reference		
Men	1.00	0.3620	0.9900	0.49 - 2.03
Age	0.98	0.0159	0.3350	0.95 - 1.02

Onset of addiction (years)	0.98	0.0262	0.4160	0.93 - 1.03
Number of DSM-5 criteria	1.34	0.1242	0.0020	1.12 - 1.60
Number of previous events	1.28	0.3658	0.3850	0.73 - 2.24

HR = hazard ratio; SE = standard error; P = probability; 95% CI = 95% confidence interval

[A)] Number of subjects: 103, number of failures: 33, number of observations: 796. χ (4) = 15.4, $p < 0.01$

[B)] Number of subjects: 103, number of failures: 45, number of observations: 996. χ (5) = 18.6, $p < 0.01$

First and recurrent relapse events

The study recorded a total of 45 first or recurrent relapse events. The incidence rate for the multiple-failure-per-subject sample was slightly higher than for single events, amounting to approximately 12 relapse events per 1000 treatment days. Of the 33 patients who experienced at least one relapse event, 23 (22.3%) did not have any further relapse events during the observation period. Nine patients (8.7%) had a second relapse, and only one patient had a total of four relapse events.

In line with the single-failure-per-subject analyses, the estimated unadjusted proportion of patients who had not experienced any relapse declined over time (Figure 2, panel A). However, because patients were not censored after their first event, the proportion of relapse-free patients was approximately 2.5% lower on average. After 7 days of treatment, 89.7% (95% CI 82.1–94.1) of participants had not had any relapse. After 14, 21, and 28 days, the respective estimated percentage of relapse-free patients was 82.8% (95% CI 74.4–88.7), 77.0% (95% CI 68.1–83.7), and 69.4% (95% CI 60.1–76.9). At the end of the observation period, 61.0% (95% CI 51.3–69.3) of the patients at risk were relapse free. Similarly, the adjusted proportion of relapse-free patients, centered at the mean covariate values, declined steadily, reaching 68.2% at the end of the observation period (Figure 2, panel C). Unlike the single-failure-per-subject analyses, unadjusted and adjusted hazards of experiencing any relapse event did not markedly decline over time (Figure 2, panels B and D); these hazards were of similar magnitude in the two models. At day 7, the estimated adjusted hazard was 0.0125 (95% CI: 0.0071–0.0179), whereas the unadjusted hazard was 0.0126 (95% CI: 0.0065–0.0187). At days 21 and 42, the respective adjusted and unadjusted hazards were 0.0118 (95% CI: 0.0081–0.0156) vs. 0.0110 (95% CI: 0.0079–0.0161) and 0.0102 (95% CI: 0.0026–0.0178) vs. 0.0111 (95% CI: 0.0034–0.0190).

With regard to the association between covariates and recurrent relapse (Table 4, multiple-failure-per-subject), the number of DSM-5 criteria was again positively

associated with relapse: the hazard of experiencing any relapse was 34% higher for an increase in one DSM-5 criteria (HR = 1.34, 95% CI 1.12–1.60). As with the single-failure-per-subject, the remaining covariates were not statistically significant.

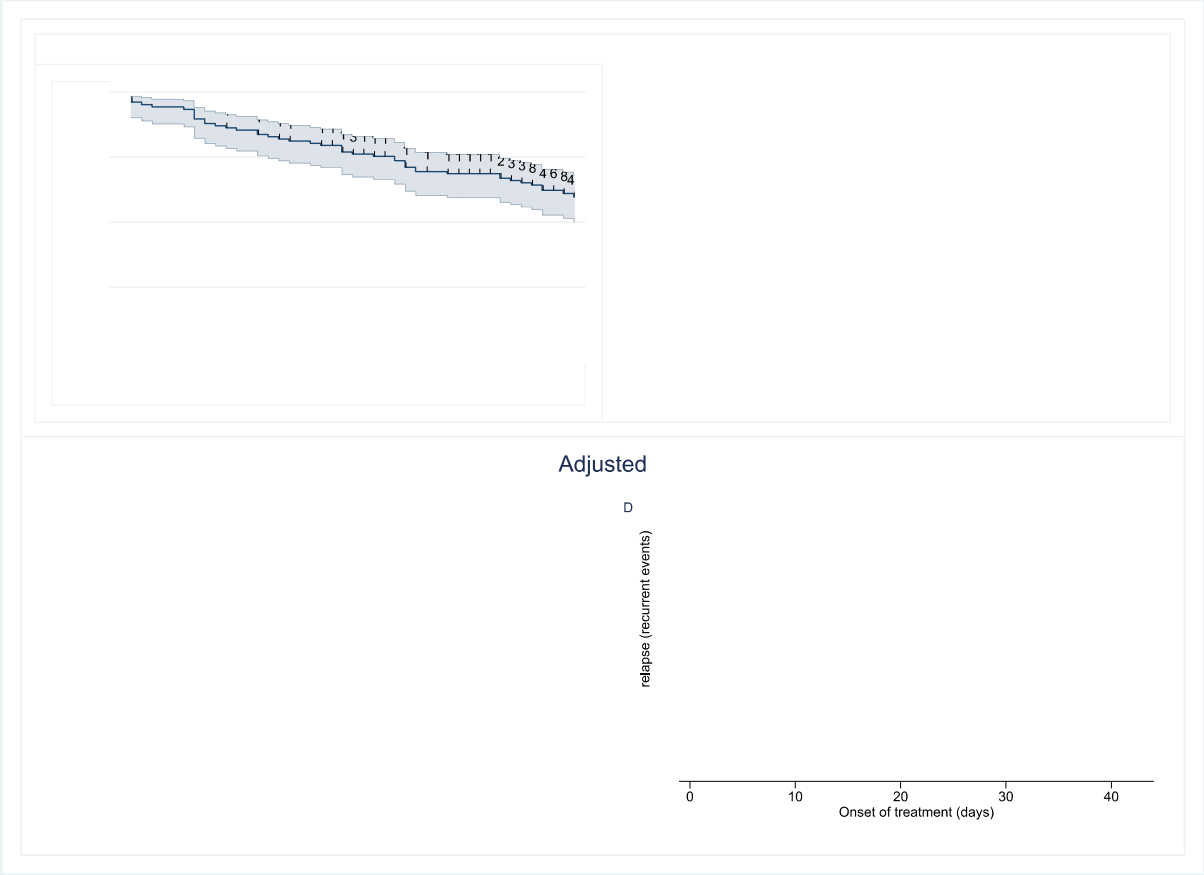

Figure 2: Multiple-failure-per-subject survivor function and hazard estimates for relapse during treatment

Panel A: Kaplan-Meier survivor estimates. Panel B: generalized estimating equation (GEE)-based unadjusted hazard estimates. Panel C: Cox regression-based estimates adjusted for covariates centered at their mean. Panel D: GEE-based adjusted hazard estimates. Adjustment for age, gender, years since onset of addiction, number of DSM-5 criteria, and number of previous relapse events.

Discussion

In this article, we investigated whether and how the risk of relapse changed during treatment. To this end, we analyzed the unadjusted and adjusted survivor functions of one relapse and multiple relapses during the course of treatment, including potential covariates.

Results for the first and multiple relapse events show that both the adjusted and unadjusted proportions of patients who had not experienced a relapse declined steadily until the end of the observation period. These findings suggest that at no particular point in time does the relapse risk significantly spike or drop during treatment.

In the analyses of single relapse events, the unadjusted and adjusted hazards of experiencing a relapse event also declined over time. The unadjusted hazards ranged between 0.0057 and 0.0110; the adjusted hazards between 0.0056 and 0.0107 for single relapse events. A value of for example 0.0057 in the current context means that 57 cases with relapses can be expected on a specific day when examining a patient population of 10,000 individuals.

In contrast, the unadjusted and adjusted hazards of experiencing any relapse event did not markedly decline over time with multiple relapse events. These findings imply different trajectories, such that the risk of relapse declines for abstinent patients during the course of treatment, whereas the risk of relapse after relapsing for the first time remains stable.

These results have important implications for clinical practice. First, the risk of experiencing one relapse declines over the course of therapy. This finding means that the risk of relapse decreases day by day until the end of treatment. This knowledge could be actively used in therapy to strengthen a patient's therapy motivation and persistence: By communicating this study result, the patient can set the goal of abstinence one day at a time. Repeating this goal every day and achieving it, if possible, promotes the patient's own motivation, since the goal is achievable and clearly defined. In comparison, a period of six weeks (duration of treatment) may seem uncertain and difficult for the patient to achieve.

According to Bandura's social cognitive theory (1989), self-efficacy is defined as the confidence to carry out the courses of action necessary to accomplish desired goals. By achieving goals, self-efficacy is strengthened and further goals are more likely to be achieved. In the current context, this means that experiencing the ability to remain abstinent fosters the development of self-efficacy and in turn influences therapy

outcomes (Ludwig et al., 2013; Sliedrecht et al., 2019). Avoiding relapses during treatment also leads to better long-term prognoses (Gueorguieva et al., 2015; Ludwig et al., 2013; Maisto, Roos, et al., 2016).

Significantly, however, our results indicate that after experiencing one relapse, the risk of experiencing further relapses does not decline. This finding implies that after an inpatient has relapsed, the therapist must become even more vigilant to prevent further relapses. Interventions suggested by the widely applied relapse-prevention model proposed by Marlatt and Gordon (1985), such as coping skills training, cognitive restructuring, or decision matrices, may be useful in these situations and help to lead the patient back to abstinence. Although the Forel Clinic already offers such relapse-prevention training, the clinic should possibly intensify this training for relapsed patients.

Of all the covariates, only the number of DMS-5 criteria was positively and statistically associated with first and multiple relapse events. An increase of one DSM-5 criterion escalated the hazard of experiencing a first-time relapse by 44%, and that of experiencing any relapse by 34%. These results indicate that patients who suffer from a severe addiction have a higher risk of relapse during treatment. Thus, research and practitioners might find it useful to focus more on relapse-prevention strategies within this risk group.

Previously established associations among sociodemographic factors (i.e., age and gender), substance-related factors (i.e., younger age of onset of AUD) and relapses have not been confirmed in the current study. Studies have reported inconsistent results concerning sociodemographic variables; however, the age of onset of AUD has been a fairly reliable predictor of relapse (Adamson et al., 2009; Sliedrecht et al., 2019). The observation period of 42 days in this study may have been too short to make such effects visible. Alternatively, the age of onset in this sample may be irrelevant, as the severity of AUD already explains a great deal of the variance in the outcome variables.

Limitations of the study

With 37% of the invited patients not providing consent to participate in the study, only two thirds of patients participated. Most of the nonparticipants indicated that they were not interested in participating in the study. The study did not assess the exact reasons for the lack of interest. Possible reasons could be: no interest in research, the time

required for the study, no financial compensation for study participation, or concerns that information about drinking events could be provided to therapeutic staff. However, our analyses showed that the participants did not differ from the nonparticipants in substance-related factors or sociodemographic characteristics.

The sample of this study consisted of 103 participants, yielding 796 and 969 observations, respectively. However, the comparably small number of participant clusters might have had an influence on the detection of statistically significant time-invariant covariates. Thus, future research should replicate the results with a larger sample and a new dataset.

Weekend leaves are allowed by the participating clinic after detoxification but are considered a risk factor. Our analyses showed that the days with the most positive alcohol tests are Fridays and Saturdays. Sundays, when patients come back from their weekend leaves, had the fewest positive tests. We conclude that the weekend leaves represent a definite risk factor for the patients; however, they are necessary to test abstinence in everyday life. Treatment providers should discuss relapse events therapeutically and develop new coping strategies with patients.

Fifteen patients in our sample decided to do a short-term therapy program of a minimum of four weeks. One might argue that these individuals do not fit into the study design. However, we assume that relapses are similarly distributed in both types of therapy (short-term and long-term), because, for example, patients did not differ in background variables, they receive the same therapy, and they are also exposed to the same risk situations; that is, fewer or more relapses should not occur in short-term therapy before the termination of treatment, and the relapses should not occur earlier or later than in long-term therapy. The short-term therapy patients would thus strengthen our results and, therefore, we included them in the analyses.

Another limitation of the study is that not all predictors of relapses found by Adamson et al. (2009) or Sliedrecht et al. (2019) could be included in the analyses (e.g., supportive social network, psychiatric comorbidity). On one hand, no indication existed of how the data should be assessed in an objective, reliable, and valid manner (e.g., definition and differentiation of the term “social network”). On the other hand, many variables had already been recorded so we had to have a restriction so as not to place an additional burden on the participants.

The combination of subjective and objective indicators assessing the participants' states of abstinence was one strength of the study. Within the spectrum of objective

testing methods, we mainly relied on breathalyzer tests due to reasons of practicability, cost, and acceptance. Breathalyzer tests only provide a narrow detection window, which means that some drinking events might have remained undetected. Nevertheless, our analyses have shown a comparatively strong correspondence between subjective and objective data, which could be seen as a validation of the nonjudgmental attitude and atmosphere in the clinic. Although the Forel Clinic is abstinence-oriented, drinking during treatment is recognized as part of the disease.

Due to the clinic's guidelines on the concept of relapse, we had to choose the “any use” criterion of relapse. We are aware that ambiguity and disagreement exist around the term (Maisto, Witkiewitz, et al., 2016). However, the advantage of accurately categorizing relapse as yes or no was that we could clearly define outcome measures and we could distinctly interpret them.

Furthermore, we studied only the risk of relapse during treatment. We do not know how this hazard evolves after treatment. Whether the different risk patterns for abstinent and relapsing patients continue as they had during treatment, or whether new patterns develop after treatment would be interesting for future research to determine. The study by Witkiewitz and Masyn (2008) could possibly provide an important hint. In their study, the authors examined patients in an outpatient setting. They also showed that the risk of relapse decreased over time. Further, they found three subgroups within patients who relapsed (infrequent moderate drinking, heavier drinking with decreased frequency, and frequent heavy drinking). The group of infrequent moderate drinkers represented the largest group. Combining the results of our study with the findings of Witkiewitz and Masyn (2008) and implementing them within a new study could be interesting.

Last, our results may not be generalizable to other study samples, treatment environments, and so on. Our results may not be replicated in similar institutions with similar treatment programs. The current study comprised a broad spectrum of patients in terms of age, gender, employment backgrounds, and history of addiction, which should allow us to generalize the results to others of similar age, gender, and so on; however, conducting a multi-center study would be helpful to attain clarity about our findings' generalizability to varying contexts.

Conclusion

The risk of relapse declines steadily for abstinent patients during the course of treatment, whereas the risk for patients who experience one or more relapses remains stable during treatment. For patients who stay abstinent over the course of a treatment program, this finding implies that the number of breathalyzer tests could be reduced as treatment progresses, that weekend leaves could be scheduled later in the program, and that treatment periods might be extended to improve self-efficacy beliefs and thereby the likelihood of remaining abstinent after treatment. For patients suffering from a more severe addiction and for those who relapse at least once during treatment, the findings suggest a stronger focus on relapse-prevention strategies. For instance, treatment providers should analyze the conditions and triggers of relapse and apply adapted, personalized therapeutic strategies to reduce relapse risks and prevent or manage critical situations. Overall, the different trajectories that the current study has demonstrated for patients who remain abstinent over the course of treatment, relative to those who relapse at least once, provide specific starting points for improving treatment and reducing relapse risk.

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