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## Psychopharmacological treatment is not associated with reduced suicide ideation and reattempts in an observational follow-up study of suicide attempters

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#### ARTICLE INFO

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#### ABSTRACT

*Background:* Disorders of mental health are major risk factors for suicidal behavior and require adequate treatment. However, the effect of psychotropic medication on suicidal behavior is unclear.

Methods: The 120 participants in a randomized clinical trial of a brief therapy for suicide attempters (Attempted Suicide Short Intervention Program, ASSIP) reported on repeated suicide attempts, suicidal ideation, depression, and medication in the treatment as usual (TAU), at baseline, 6, 12, 18, and 24 months follow-up. The RCT had no influence on medication prescribed. Drugs prescribed were categorized as any psychotropic, antidepressants plus lithium, and antipsychotics. To assess the effect of long-term medication we identified participants with periods of continuous use of psychotropics and antidepressants plus lithium over twelve months or more, and medication-free participants for the same drug categories during the same time period.

Results: Reattempts and suicide ideation decreased in all drug categories. When comparing participants on medication fulfilling the definition of long-term use with participants without medication, reattempts and suicidal ideation were higher in the psychotropics and the antidepressants/lithium groups. These drug categories were associated with higher depression scores in comparison to no-medication. The survival analysis revealed a higher risk of reattempts in the long-term antidepressants/lithium group in comparison to no-medication. Treatment with the brief psychological therapy ASSIP, added to medication, was associated with a lower risk of reattempts.

*Limitations*: The study relied on the patients' reports on treatment as usual in a randomized controlled clinical trial. Blood levels of the psychotropic compounds were not assessed.

Conclusions: In this observational study of the TAU condition in a clinical trial of a brief psychological therapy for patients who had recently attempted suicide, psychotropic drug use over twelve months or more was not associated with reduced suicide ideation and reattempts. Depression scores suggest that patients on psychotropic medication had more psychiatric pathology. This may be a confounding factor for the effect of medication on suicidal behavior.

### 1. Introduction

Approximately 800,000 people die by suicide each year, and the number of suicide attempts may be more than twenty times higher (World Health Organization, 2012; Naghavi, 2019). There is an interrelation between suicide ideation and suicidal behavior (Kessler et al., 2005). Bertolote, Fleischmann (Bertolote et al., 2005) reported a 13.5% prevalence of suicide ideation and a 4.6% lifetime prevalence of

attempted suicide in the general population.

Patients who attempt suicide usually enter the medical system through admission to general and psychiatric institutions, where therapeutic interventions can be implemented, and, if indicated, psychopharmacological treatment installed. The effect of treatment on suicidal behavior is of special interest in these patients, considering that attempted suicide is the main risk factor for suicide (Suokas et al., 2001; Ribeiro et al., 2016; Bostwick and Pankratz, 2000), especially when

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characterized by hopelessness and high intent (Suominen et al., 2004). Gibb and Beautrais (2004) reported that within 10 years 28.1% of patients admitted after a suicide attempt made reattempts, and 4.6% died by suicide. Importantly, the risk of death by suicide in the first year after attempted suicide is much higher in patients with mood disorders (Bostwick and Pankratz, 2000; Nordstrom et al., 1995).

Of special interest is the question if pharmacotherapy for patients who attempt suicide can reduce the frequency of suicide reattempts and suicide. Between 56 and 87% of suicide victims suffer from major depressive disorders (Bostwick and Pankratz, 2000; Coryell and Young, 2005), however, the evidence for the effect of antidepressant treatment on suicide is controversial (Van Praag, 2003; Simon et al., 2006). For instance, Leon, Keller (Leon et al., 1999) reported that treatment with Fluoxetine was associated with a decrease of suicidal behavior. Others found that the use of antidepressants was associated with a lower risk of completed suicide, while the risk of attempted suicide increased (Tiihonen et al., 2006). Stone, Laughren (Stone et al., 2009) in a meta-analysis of randomized controlled trials found an age-dependent effect of antidepressants on suicidal behavior, with an increased risk in participants aged below 25 and a protective effect for adults above 65. Olfson, Marcus (Olfson et al., 2006) similarly reported an association between antidepressant drug treatment in adolescents but not in adults. A meta-analysis of 29 placebo-controlled studies concluded that the incidence rates of suicide and suicide attempts were higher among patients treated with antidepressants compared to placebo (Braun et al., 2016). In the active drug arms suicides occurred 5 times more often and the risk of suicide attempts was 9-fold. Yerevanian, Koek (Yerevanian et al., 2004) compared the rates of suicidal behavior in 521 unipolar depressed patients during, and after discontinuation of long-term antidepressant (SSRIs and TCAs) pharmacotherapy. Suicidal behavior increased substantially after medication discontinuation. There is good evidence for the antisuicidal properties of lithium in long-term treatment. A meta-analysis of RCTs in unipolar and bipolar disorders showed that lithium significantly reduces suicide compared with placebo (Cipriani et al., 2013). Furthermore, long-term treatment with the antipsychotic drug clozapine, compared with other antipsychotics, has been associated with a reduced incidence of suicidal behavior (Hennen and Baldessarini, 2005).

In view of the long-term elevation of suicide risk in people with a history of attempted suicide, the effect of long-term pharmacotherapy is a particular focus of interest. Angst, Stassen (Angst et al., 2002) followed 406 formerly hospitalized patients with unipolar and bipolar depression over 22 years or more. Patients on psychotropic medication (antidepressants, antipsychotics, and/or lithium) had a significantly lower suicide mortality compared to untreated patients. The minimal duration of pharmacotherapy was 6 months, but the precise length of treatment was not determined. Leon, Fiedorowicz (Leon et al., 2014) in a 27-year observational follow-up study involving 706 patients found a significant effect of antidepressant medication on suicidal behavior, with a risk reduction of 54% for bipolar I disorder and 35% for bipolar II disorder, but no effect for unipolar depression. Length of antidepressant exposure was defined as the number of consecutive weeks of antidepressant medication until suicidal behavior. Intervals of exposure were compared with intervals of nonexposure.

With detailed 24-months follow-up information on treatment as usual, including psychotropic drug treatment, the participants of the ASSIP RCT (Gysin-Maillart et al., 2016) represented an ideal population to investigate the relationship between psychotropic drug treatment and suicide reattempts and suicidal ideation in a naturalistic clinical setting. We hypothesized that long-term psychopharmacological treatment, here defined as the use of psychotropic drugs over more than 12 months, would be associated with reduced suicidal behavior.

## 2. Materials and methods

The study is part of the ASSIP effectiveness trial published elsewhere

(Gysin-Maillart et al., 2016). ASSIP is an add-on therapy, administered in addition to the usual clinical treatment (TAU), which included inpatient or outpatient care, any form of psychotherapy, and pharmacotherapy. In this study a total of 120 patients who had recently attempted suicide were randomly assigned to ASSIP therapy (60) or the control group (60). Exclusion criteria were habitual self-injury, severe cognitive impairment and psychotic disorders. Current suicide risk was not an exclusion criterion, that is, the trial included patients with high suicide risk. Psychiatric diagnoses at baseline were based on the hospital records. Sixty-three percent of participants were diagnosed with affective disorders. The ASSIP treatment group received three one-to-one manual-based therapy sessions followed by regular outreach contact through semi-standardized letters over 24 months in addition to treatment as usual (TAU). The control group received a single suicide assessment interview, in addition to TAU.

The present study is a secondary analysis of data on medication as part of TAU. The clinical trial of ASSIP had no influence on medication prescribed in TAU. Information on drug use was collected through questionnaires sent to study participants every 6 months during the 24 months follow-up. Patients were asked to report trade names of all prescribed drugs and the exact dosages. For analysis, drugs were classified as (1) any psychotropic drug, with the subgroups of (2) antidepressants, (3) lithium, and (4) antipsychotics (Zohar et al., 2015). These are the drug categories with some evidence of effectiveness in preventing suicidal behavior (Hennen and Baldessarini, 2005; Leon et al., 2014). Because of the small number of patients on lithium (n = 5), antidepressants and lithium were combined as one group (AD/Li). Similar to the Angst et al. (2002) study, pharmacotherapy was classified as long-term, when the same class of drug was taken over a time period of 12 months or more. We therefore identified participants with continuous use of the same drug category over three or more timepoints within the 24-months follow-up. Similarly, we identified participants who over three consecutive timepoints reported that they were not using any of these drugs. As the three-timepoint periods could be anywhere between t1 and t5, the definition included participants without medication at baseline but starting on drugs later during follow-up.

The 21-item Beck Depression Inventory (BDI) was used to measure the severity of depression (Beck and Steer, 1987; Hautzinger et al., 1994). The Beck Scale for Suicide Ideation (BSS) was used to measure the intensity of the patients' suicidal ideation (Beck and Steer, 1991). The BSS consists of 21 items and is a self-report instrument to assess the intensity of the patient's attitudes, behaviors, and plans related to suicidal behavior during the past week, including the current day, with item scores ranging from 0 to 2. Three additional questions referred to suicidal behavior and differentiated between non-suicidal self-harm and suicide attempts. The German definition of attempted suicide is similar to the use in the US and the Silverman criteria (Silverman et al., 2007), which require the presence of intent to die. The total number of reattempts in the clinical trial was 46 (ASSIP group: n=5, control group n=41).

## 2.1. Statistics

Descriptive statistics were used for baseline measures at t1 (time of first interview with study participants after the suicide attempt). For the calculation of suicide reattempts and of suicidal ideation for all drug groups (antidepressants/lithium, antipsychotic, and psychotropic) across all timepoints (baseline, 6 months, 12 months, 18 months, and 24 months) linear mixed effect models were used by means of the *lmer* function from the lme4 package (Bates et al., 2015). The numbers of suicide attempts at t1 were reduced by 1, because t1 included the index attempt leading to referral. We then analyzed reattempts and suicidal ideation in relation to the medication taken over three or more consecutive timepoints vs no-medication for the same time period. BDI was added to the models as a covariate for suicide ideation. The survival probability and hazard ratio were calculated for each group of medication vs. no-medication, using the

Kaplan-Meier estimate and the coxph function respectively, by means of the survival package in R (Therneau, 2020). Furthermore, we included the two arms (ASSIP, Control) of the original clinical trial in the survival analysis, which resulted in a total of four groups (medication/intervention, medication/control, no-medication/intervention, and no-medication/control).

#### 3. Results

Baseline data at t1 (Table 1) were collected from the first interview with participants of the ASSIP clinical trial (N=120). Seventy-seven participants were on psychotropic drugs, 20 of those were taking antipsychotics, and 74 were taking antidepressants or lithium, 43 had no medication at baseline. Participants on medication had more diagnoses of mood disorders, more previous suicide attempts, and more suicidal ideation at baseline.

Focusing on participants who fulfilled the definition of long-term medication at any time period within the 24-months follow-up period reduced the number of participants to 56 for the psychotropic group, to 14 for the antipsychotic, and to 28 for the antidepressant/lithium group (AD/Li). The main substances prescribed long-term according to this definition are listed in Table 2. With the small number of participants on antipsychotics we decided to continue the further analysis without this group. Antidepressants were frequently combined (12/28), and all participants on lithium were co-medicated with antidepressants. With very few exceptions, the daily doses were considered to be adequate (e. g. amitriptyline 200 mg, paroxetine 40 mg, fluvoxamine 200 mg, duloxetine 120 mg).

Table 3 shows the clinical measures across time-points for participants using any psychotropic, and the AD/Li category as long-term medication, and for those with no long-term medication of the same category. These findings are presented graphically in Figs. 1 and 2.

We then compared the long-term use of any psychotropic (n = 56) with no psychotropic medication over the same time period (n = 27). Suicide reattempts decreased in both groups ( $F_{4,\ 248}=3.1;\ p=0.01;$   $Fig.\ 1a$ ), with no significant group difference ( $F_{1,\ 85}=0.9;\ p=0.34$ ). No significant interaction between group x timepoint was observed ( $F_{4,\ 248}=1.0;\ p=0.41$ ). Suicidal ideation (BSS) decreased in both groups, with higher scores in the psychotropic group ( $Fig.\ 1b$ ). No significant differences in timepoint, group, or group x timepoint interaction were found (all  $F<1.9;\ p>0.16$ ). BDI scores decreased in both groups over time ( $F_{4,\ 228}=20.1;\ p<0.0001$ ), but they were higher in the psychotropics group ( $F_{1,\ 74}=4.2;\ p=0.04$ ). BDI correlated with the BSS (rho>0.43; p<0.05) and had a significant effect on suicide ideation ( $F_{1,\ 291}=142.3;\ p=0.05$ )

Table 2
Most frequent substances prescribed long-term (>12 months).

Drug group	# of cases	Dosage range (mg)
Antidepressants/lithium	28	
Amitriptyline	5	125-200
Clomipramine	2	37.5-300
Trimipramine	3	10-25
Venlafaxine	5	75–300
Mirtazapine	3	30-45
Duloxetine	3	60–120
Trazodone	3	50-300
Paroxetine	2	40
Escitalopram	3	10-30
Lithium	5	225-1325
Antipsychotics	14	
Quetiapine*	11	100-1000
Olanzapine	2	5
Clotiapine	1	20

 $<sup>^{*}</sup>$  In 9/11 participants quetiapine was prescribed as co-medication with anti-depressants, and one participant was taking quetiapine 1000 mg + valproate.

> 0.0001).

A similar picture emerged in the comparison of long-term AD/Li use  $(n=28)\,$  with no AD/Li medication (n=35). Suicide reattempts decreased in both groups, with no significant difference  $(F_{1,\,61}=2.5;\,p=0.11;\,Fig.\,2a),$  and no significant interaction between group x timepoint  $(F_{4,\,241}=1.1;\,p=0.33).$  BSS scores decreased in both groups  $(F_{4,\,187}=2.8;\,p=0.02;\,Fig.\,2b),$  but were higher in the medication group  $(F_{1,\,61}=5.1;\,p=0.02).$  BDI scores decreased in both groups  $(F_{4,\,189}=22.1;\,p<0.0001),$  but were higher in the medication group  $(F_{1,\,58}=7.1;\,p=0.01).$  BDI scores correlated with the BSS (rho  $>\!0.35;\,p<0.05),$  and had a significant effect on suicide ideation  $(F_{1,\,235}=43.5;\,p>0.0001).$ 

The reattempt-free survival probability for long-term use of psychotropics vs no psychotropics showed a significant difference, with more reattempts in the medication group (HR = 0.198, p = 0.03, Kaplan–Meier survival curves, Fig. 3). For AD/Li vs no AD/Li a decrease of reattempts in both groups was found, with a trend to lower survival probability (i.e. more suicide attempts) in the medication group (HR = 0.373, p = 0.07).

Finally, we related the medication use to the ASSIP/Control conditions from the original clinical trial. Fig. 4 shows the Kaplan–Meier survival curves for suicide reattempts related to long-term medication. Use of any psychotropic drug plus ASSIP treatment was associated with a significantly better outcome (HR = 3.853, p = 0.004). A similar pattern was found for antidepressants/lithium at trend level (HR = 2.053, p =

**Table 1**Demographic and clinical characteristics at baseline.

	Any Psychotropic ( $n = 77$ )	Antipsychotics (n $=$ 20)	Antidepressants/lithium  (n=74)	No Medication ( $n = 43$ )	One-way Anova (F; p-value)
Demographic					
Age (mean $\pm$ SD years)	$39.3\pm12.8$	$37.2\pm11.2$	$38.7\pm12.2$	$34.1\pm16.0$	$F_{3, 198} = 1.53; 0.30$
Gender (females %)	55.8%	73.7%	51.6%	51.0%	$F_{3, 198} = 0.97; 0.40$
Diagnosis (ICD-10%)					
F1	19.4	15	12.2	35.7	
F3	75.3	55	72.9	33.3	
F4	29.8	50	22.9	69.0	
F6	18.1	20	17.5	11.9	
Other	7.7	5	8.1	4.7	
Previous suicide attempt	s (%)				
0	39.0	47.4	36	69.0	
1	28.6	21.0	31.2	14.3	
2 or more	32.4	31.6	32.8	16.7	
Assessments (mean ± SD)					
BSS	$0.49 \pm 0.47$	$0.51 \pm 0.51$	$0.56 \pm 0.52$	$0.30 \pm 0.40$	F <sub>3, 196</sub> =2.63; 0.05
BDI	$19.8 \pm 9.6$	$19.6 \pm 12.6$	$20.0 \pm 13.2$	$15.3 \pm 9.6$	F <sub>3, 195</sub> =1.55; 0.20

BSS: Beck Scale for Suicide Ideation; BDI: Beck Depression Inventory; ICD-10: International Classification of Diseases; F1: Substance abuse disorder; F3: Mood disorder; F4: Neurotic, stress-related and somatoform disorders; F6: Disorders of adult personality and behavior. The "Any Psychotropic" category includes patients on any psychopharmacological substance. Thus, subjects in the antipsychotic or antidepressant/lithium group are included in the psychotropic group but may overlap.

Table 3 Clinical measures (mean  $\pm$  *SD for each group*) across time-points for participants on long-term medication/no-medication (= more than three timepoints on the same drug category within the 24-months follow-up).

	Any psychotropic ( $n = 56$ )	No psychotropic ( $n = 27$ )	$Antidepressants/lithium\ (n=28)$	No Antidepressant/Lithium (n $= 35$ )
Suicide Attempt	is .			
Baseline	$0.38 \pm 0.82$	$0.37\pm1.01$	$0.44 \pm 0.93$	$0.36\pm0.96$
6 months	$0.27\pm0.90$	$0.00\pm0.00$	$0.42\pm1.02$	$0.00\pm0.00$
12 months	$0.02\pm0.16$	$0.13\pm0.51$	$0.10\pm0.44$	$0.09\pm0.44$
18 months	$0.14\pm0.55$	$0.00\pm0.00$	$0.21\pm0.71$	$0.08 \pm 0.29$
24 months	$0.21\pm0.68$	$0.00\pm0.00$	$0.21\pm0.78$	$0.00\pm0.00$
BSS scores				
Baseline	$0.50\pm0.52$	$0.29\pm0.42$	$0.58\pm0.57$	$0.29\pm0.41$
6 months	$0.36\pm0.50$	$0.23\pm0.33$	$0.46\pm0.57$	$0.22\pm0.31$
12 months	$0.33\pm0.44$	$0.09 \pm 0.30$	$0.34 \pm 0.48$	$0.06\pm0.25$
18 months	$0.32\pm0.46$	$0.10\pm0.18$	$0.36 \pm 0.52$	$0.12\pm0.20$
24 months	$0.21\pm0.38$	$0.04\pm0.12$	$0.24\pm0.40$	$0.03\pm0.11$
BDI scores				
Baseline	$19.7 \pm 11.4$	$15.4 \pm 9.60$	$21.3 \pm 10.7$	$14.7 \pm 9.73$
6months	$14.8 \pm 11.7$	$11.9 \pm 9.40$	$16.1 \pm 11.7$	$10.5 \pm 9.20$
12 months	$13.3 \pm 10.4$	$7.20 \pm 7.34$	$14.8 \pm 11.1$	$5.95 \pm 6.70$
18 months	$13.4 \pm 13.0$	$9.62 \pm 11.1$	$13.3 \pm 12.7$	$10.3 \pm 10.7$
24 months	$9.50 \pm 10.1$	$4.23 \pm 5.35$	$9.25 \pm 8.56$	$4.60 \pm 5.27$

BSS: Beck Scale for Suicide Ideation; BDI: Beck Depression Inventory. For suicide attempts and BSS scores see Fig. 1 (a and b), and Fig. 2 (a and b).

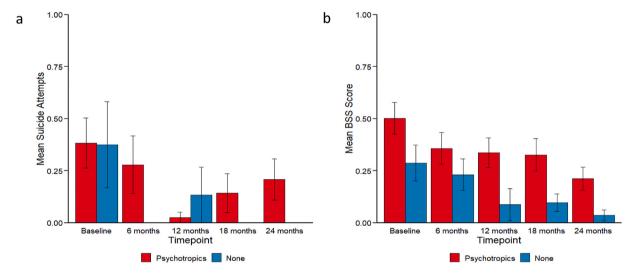


Fig. 1. a) Mean numbers of suicide attempts across timepoints for the long-term use of the any psychotropic group (n = 56, red) and the respective no-medication group (n = 27, blue). b) Mean BSS scores for the long-term use of the any psychotropic group (red) and the respective no-medication group (blue). Definition of long-term use: medication or no-medication over at least three timepoints. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

0.240).

## 4. Discussion

The results of this observational study (Grimes and Schulz, 2002) are based on the 24 months follow-up data collected from the participants of a previously published clinical trial with 120 individuals who had attempted suicide. The randomized controlled clinical trial investigated the effectiveness of ASSIP, a brief, structured therapy on reducing suicidal behavior, designed as add-on therapy to treatment as usual. The trial had no influence on treatment as usual. During follow-up over two years, patients filled in questionnaires in six-monthly intervals, which included questions about suicide reattempts and suicidal ideation, depression (BDI), suicidal ideation (BSS). Questions on treatment as usual included outpatient or inpatient treatment, and medication, with daily doses.

In the 24 months follow-up of TAU, suicide reattempts and suicidal ideation (measured by the BSS) decreased for the any psychotropic group as well as for the antidepressant plus lithium group. In the samples

of participants on medication over at least 12 months and the respective no-medication samples, suicide reattempts and suicidal ideation decreased in the medication groups and in the no-medication groups. However, medication was associated with more suicidal ideation, with the difference reaching statistical significance in the antidepressant/ lithium group. The medication groups recorded more suicide reattempts over 24 months. In the survival analysis we found a lower survival probability for reattempts in the antidepressants/lithium group compared to the corresponding no-medication group (HR = 0.373). Depression scores were higher in the long-term medication groups, although they decreased over time in both groups. The depression scores suggest that participants in the medication group had more psychopathology and were therefore more likely to use medication over 12 months or more. Furthermore, in our analysis, BDI was a strong predictor for suicide ideation (but not for attempts). This is not surprising, considering the positive correlation between the BDI and the Beck scale for suicide ideation (Beck et al., 1979).

Finally, when investigating the effect of the brief psychological therapy ASSIP on participants taking long-term medication, we found

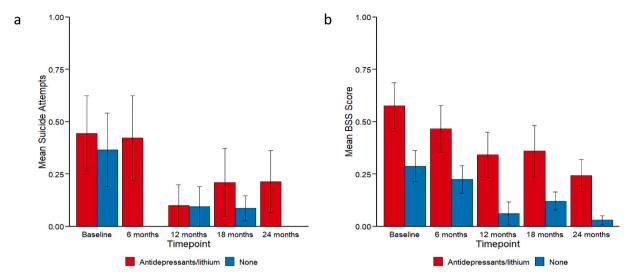


Fig. 2. a) Mean numbers of suicide attempts across timepoints for the long-term use of antidepressants/lithium group (n = 28, red) and its respective no-medication group (n = 35, blue). Error bars represent standard error of mean. b) Mean BSS scores for the long-term use of the antidepressants/lithium group (red) and the respective no-medication group (blue). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

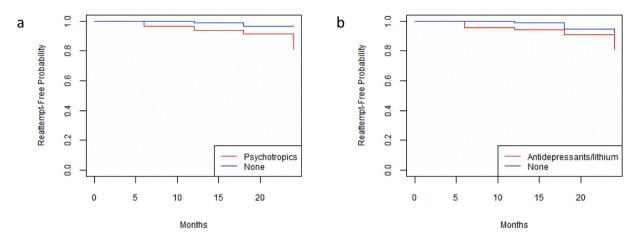


Fig. 3. a) Kaplan–Meier survival curves for reattempt-free probability by long-term psychotropics (n = 56) vs no medication (n = 27). b) Kaplan–Meier survival curves for reattempt-free probability by long-term antidepressants/lithium (n = 28) vs no medication (n = 35). Definition of long-term: medication or no-medication over at least three timepoints.

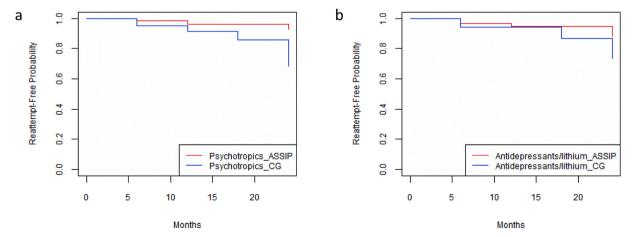


Fig. 4. a) Kaplan–Meier survival curves for reattempt-free probability by long-term psychotropics and ASSIP (n = 30) vs Control Group (n = 26). b) Kaplan–Meier survival curves for reattempt-free probability by long-term antidepressants/lithium and ASSIP (n = 15) vs Control Group (n = 13).

that, in comparison to the Control, ASSIP was associated with a significantly lower number of reattempts, and a similar trend in the antidepressant/lithium group.

We found only one study with a comparable naturalistic follow-up design of patients who attempted suicide, that is, a population with a high risk of repeated suicidal behavior. Irigoyen et al. (2019) followed 371 patients who had attempted suicide up over two years. All participants who reattempted suicide were taking antidepressants, therefore, the authors were unable to analyze the association between antidepressant medication and suicidal behavior, yet antipsychotics were related to more reattempts. Other studies have been based on randomized controlled drug trials with patients treated for affective disorders, using data on suicidal behavior as adverse events (Braun et al., 2016; Cipriani et al., 2013; Carpenter et al., 2011; Gunnell et al., 2005). Typically, these studies excluded participants with a suicide risk.

Our results are in line with reports that found no clear effect of antidepressant treatment on suicidal behavior (Simon et al., 2006; Leon et al., 1999; Braun et al., 2016). Similar to our study, Carpenter, Fong (Carpenter et al., 2011) found that major depression was associated with more suicidal behavior, and with more antidepressant treatment. With comparable findings in our observational study, we conclude that patients on psychotropic medication tend to have more psychiatric pathology and a higher suicide risk, and that this must be taken account of in the interpretation of the results.

#### 4.1. Limitations

The study has limitations and strengths. The study is a secondary analysis, which was not designed to show a difference between psychotropic treatment groups. No blood levels of the prescribed medications were taken to determine patient compliance. However, a strength of the study is that medication was not reported by the prescriber, which would leave open the question of patient compliance. Patients reported their medication to an independent third party, and in addition, they were asked to accurately indicate the daily dosages for each drug. The reported dosages were clinically realistic and consistent throughout the timepoints. We interpret this as a sign of a satisfactory patient compliance with the prescribed medication. Furthermore, in the vast majority, the daily dosages were in the clinically recommended ranges, with a tendency to polypharmacy. Because in t1 patients were not specifically asked about the date when medication was started, we could not determine if medication had been prescribed before, or following the index suicide attempt. We therefore excluded t1 from the medication/no medication comparison. TAU conditions have been criticized for being generally unclear [37]. It is important to note that in the original trial, both conditions (ASSIP/Control) were added to treatment as usual, that is, TAU was not the control condition. The trial had no influence on TAU, which included in- and outpatient treatment settings, and any medication if indicated. Regarding the survival probabilities related to the ASSIP trial conditions it is of interest that the ASSIP treatment group had 63% fewer days of hospitalization during follow-up. There was no difference in the numbers of outpatient sessions between ASSIP and control.

### 5. Conclusions

In this observational study of medication prescribed in the TAU condition to participants in a randomized clinical trial of a brief psychological treatment, the use of psychotropic medication was not associated with a decrease of suicidal ideation and suicide reattempts. Study participants who were using psychotropic drugs, including antidepressants and lithium, continuously over 12 months or more, reported more suicide ideation and more attempts compared to participants on no medication. However, as medicated patients had higher depression scores, severity of psychiatric pathology may be a confounding factor for the effect of medication on suicidal behavior. Interestingly, in an

additional analysis, a brief psychological therapy (ASSIP), added to medication, was associated with a lower number of suicide reattempts.

#### Contributors

Konrad Michel and Anja Gysin-Maillart conceived and designed the study. Anja Gysin-Maillart and Sigrid Breit prepared the data for analysis. Anastasia Pavlidou and Konrad Michel were responsible for the statistical analyses and the interpretation of the results. Konrad Michel wrote the article, which was reviewed by Sebastian Walther.

All authors have approved the final article.

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## Declaration of competing interest

None.

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