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**Long-term Treatment and Suicidal Behaviour in Severe Depression.
ECT and Antidepressant Pharmacotherapy May Have Different Effects on
the Occurrence and Seriousness of Suicide Attempts**

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ABSTRACT

The objective of the present paper was to assess the relation between long-term treatments of depressive episodes and attempted or completed suicide in patients who had had a severe depression at index admission.

A blind record evaluation of 96 suicides with a primary severe depression and matched controls has been performed. Out of those 57 and 33, respectively, had made suicide attempts. Occurrence of attempt was less common after ECT. However, seriousness of suicide attempt appeared to be reduced in those with at least four weeks of antidepressant medication compared to no treatment and ECT. The theory of a suicidal syndrome independent of depression seems supported. Continuation treatment after ECT would be recommended.

INTRODUCTION

Mood disorder is the single diagnosis with the greatest impetus on suicide, and among completed suicides 29-88% (mean 52%) could be considered to have suffered from such a disorder (Lönnquist, 2000). Among depressed patients suicide attempt is known to be related to suicide (Sainsbury, 1986; Goldstein *et al*, 1991; Nordström *et al*, 1994; Brådvik and Berglund, 2002). Treatment of depression would be assumed to reduce the rates of attempted and completed suicide. However, in the prevention of suicide it has been difficult to evaluate the role of ECT and antidepressants, which are usually efficient in the acute phase of severe depression. The ideal randomised double blind placebo controlled study could never be performed on a suicidal population for ethical reasons. Thus those randomised studies have only been performed as secondary analyses of studies concerning the effect of pharmacotherapy on depressive symptoms. Suicidal patients have usually been excluded for ethical reasons. Individual studies, meta-analyses and reviews (Beasley *et al*, 1991; Khan *et al*, 2000, 2001, 2003; Leon *et al*, 1999; Mequies *et al*, 1998; Montgomery *et al*, 1995; Storosum *et al*, 2001; Tollefsen *et al*, 1993) have failed to show any significant difference for suicidal acts in favor of antidepressant medication. Still a non-significant reduction in suicide attempts has sometimes been shown (Beasley *et al*, 1991, Leon *et al*, 1999, Tollefsen *et al*, 1993) and also a non-significant tendency towards a reduced intention in suicide attempts during antidepressant pharmacotherapy (Leon *et al*, 1999). On the contrary, however, another study actually showed a higher rate of suicidal acts, attempts plus completed suicide, among patients treated with maprotiline (Rouillon *et al*, 1989). Moreover, an increased risk of suicidal behavior has recently been shown in the first month after starting antidepressant therapy with tricyclics or SSRI (Jick *et al*. 2004).

To our knowledge, no randomized studies on Electroconvulsive Therapy (ECT) and suicidal acts have been performed. Controlled studies have given contradictory results; a positive effect

for females was shown long ago in an early study (Flood and Seager, 1968). However, in a more recent investigation suicides and controls showed similar rates of treatment with ECT (Sharma, 1999). In a review it was concluded that ECT had an acute but not a long-term effect on suicidality (Sharma 2001).

A comparison between ECT and antidepressant pharmacotherapy showed a lower frequency of suicide attempts after ECT (Avery and Winokur, 1978). In a previous case-control study we found that antidepressant continuation treatment after ECT was more common in controls than in suicides (Brådvik and Berglund, 2000). Moreover, psychomotor retardation turned out to be a risk factor for suicide after ECT (Brådvik and Berglund, 2004) despite the good effect of ECT on this symptom reported in literature (Rasmussen 2003).

In one of the previous studies (Brådvik and Berglund 2000) we found that suicide victims and controls had received treatment with ECT or antidepressant medication about equally often at last contact and showed similar rates of treatment response. The aim of the present study was two-fold; first to investigate whether there were also similar rates of treatment and response in the long-term course for those who exhibited suicidal behavior and those who did not; second to compare the effect on occurrence and seriousness of suicide attempts for ECT and antidepressant pharmacotherapy.

The following questions were addressed: Does antidepressant treatment in the long-term course of depression differentiate between those who exhibit suicidal behavior (attempted or completed suicide) and those who do not? Did the response rate of adequately treated depressive periods differ between suicides and controls? Do future suicide victims more often make suicide attempts despite adequate treatment? Was suicide attempt less frequent after ECT than during antidepressant pharmacotherapy? Did adequate treatment of depression reduce the seriousness of attempt?

MATERIAL AND METHOD

Sample

In the fifties and sixties all in-patients at the Department of Psychiatry, University Hospital, Lund were rated on a multi-axial diagnostic schedule at discharge (Essen-Möller and Wohlfart, 1947). This database enabled the selection of patients with a severe depression/melancholia for an investigation into suicide.

The design of the sampling procedure is presented in a flow diagram (fig. 1).

A total of 1206 patients received this diagnosis. Their mortality was followed up in two sessions to January 1st 1984 (Berglund and Nilsson, 1987) and to January 1st 1998 (Brådvik and Berglund, 2001). There were 114 suicide victims up to 1998. For these patients we thus had prospective data from the multi-axial schedule including diagnosis.

The case-records were performed for a thorough blind evaluation of the suicides and matched controls from the total sample (Brådvik and Berglund, 1993) and in a similar procedure at second follow up for the present study. Secondary depressions were excluded according to Research Diagnostic Criteria (Spitzer *et al*, 1978). Thus we obtained 98 suicides, 44 men and 54 women, and with a primary severe depression. One case record in the second follow up could not be found and one control from the first evaluation had later committed suicide and was excluded for that reason, leaving 96 suicide victims (43 men and 53 women). Matched controls were selected in two sessions (up to 1984 and 1998) by the criteria diagnosis, sex, age, and index admission year. Further, the controls were selected to be alive long enough to be followed to the time of death of the suicide victim they matched. The entire course of the disease documented in the records was studied.

Evaluation of the course of depression and treatment at last contact has been presented in a previous paper in the 1984 year follow up (Brådvik and Berglund, 2000). In the present study the

additional patients followed up to 1998 were also included. A retrospective diagnostics according to DSM IV (APA, 1994) has been performed. It turned out that 91% of the patients met the criteria for major depressive disorder with melancholia or psychosis. Though the case-records were carefully written and very informative, individual symptoms might have been underreported. Thus the actual number was probably higher. In the suicide group 19 patients at some time had at least one episode of elevated mood, indicating bipolarity, versus 21 in the control group.

Record evaluation

A blind record evaluation was performed on a series of variables, among others suicide attempt and treatment of individual episodes.

There were 57 suicides and 33 controls that had made suicide attempts. In this sub sample there was a similar distribution of year of birth and index admission year. There was a slight but non-significant overrepresentation of women in the suicide group (58% vs. 48%).

Severity of attempt was divided into non-serious (gestures/ambivalent) and serious (definite/severe) according to a previous study on these severely depressed patients (Brådvik and Berglund, 2002). The evaluation was based on the following definitions:

1. Suicidal gestures. An act of self-harm with little or no physical injury where the intent to die is not clearly stated.
2. Ambivalent suicide attempt. A patient initiates a suicidal act, which is potentially fatal, but interrupts this action and thus does not cause much self-damage.
3. Definite suicide attempt. Life-threatening behaviour with a moderately high risk of death and low chance of rescue.

4. Severe suicide attempt. Highly lethal suicide attempts, i.e. requiring intensive care.

Precautions against discovery and strong regret at failure to die are considered psychologically severe.

“Ambivalent” attempts have been described as “aborted attempts” by other investigators (Marzuk *et al*, 1997). They have been shown to correlate with more serious suicide attempts (Barber *et al*, 1998).

Treatment was evaluated as follows:

1. Adequate doses were scored as follows: A full dose of at least 150 mg of tricyclic or tetracyclic antidepressants should be continued for at least 2 months. (A few patients who had received MAO-inhibitors were included.)
2. ECT (adequate treatment): A series of at least 6 treatments (given three times a week) was considered adequate. (According to the tradition of the clinic treatment was sometimes discontinued after 4 seizures. These cases were included if there was a persistent effect on depression.)
3. ECT and continuation treatment with antidepressants: Continuation treatment should be initiated within 2 weeks after the last ECT. No sign of relapse of depression should be reported.

Adequate doses do not always mean successful treatment. Therefore response to treatment in the suicide and control group was also noted, according to the judgment in the case records (improved or recovered).

Further, the occurrence of suicide attempts during different phases of treatment was taken into consideration. A suicide attempt could occur before the patient applied for help, during the first four weeks of antidepressant medication or during the course of ECT, during initial 6 months of pharmacotherapy or after ECT, or later during maintenance treatment. Sometimes treatment was

insufficient with too small a dose of antidepressants or too few seizures of ECT. Finally, some suicide attempts occurred during contact with the clinic but the patient did not receive any treatment.

Suicide attempts during treatment with ECT and antidepressant pharmacotherapy for depressive episodes were compared. The analyses were made in two steps. First individuals were compared. Second all suicidal events were presented.

Lithium treatment was rare, as it was mainly used in bipolar I cases at the time. (4 suicides and 6 controls had received Lithium in the long term course). Therefore this treatment was only noted but excluded from the analysis despite a probable positive preventive effect on suicidal behaviour (Baldessarini *et al*, 2003).

The study was approved of by the ethics committee.

Statistics

MacNemar's test was used for comparison between matched groups and chi-square tests for comparisons between non-matched groups (and Fisher's exact test when applicable). Wilcoxon's test was used for a comparison of ranks. A likelihood-ratio test was performed for a comparison of the occurrence of suicide attempts during different months.

RESULTS

Long-term treatment and response to treatment

The frequencies of adequate treatment in the long-term course

A comparison of treatment of all individual depressive episodes in suicides and controls was made. There were a similar number of episodes in suicides and controls (mean 4).

The relative frequencies of adequate treatment of the total number of episodes in suicides and controls and attempters and non-attempters within the groups are presented in table 1. In the present study there was no significant difference between suicides and controls in the frequencies of adequately or inadequately treated episodes. Further, within the suicide group as well as within the control group suicide attempters showed about equal rates of adequate treatment as did non-attempters.

There was a similar rate of response to treatment in both groups during antidepressant medication 82% in the suicide group versus 86% in the control group (non-significant). A similar high rate of response to ECT was found; 93 vs. 95%.

Thus, neither lack of treatment nor response to treatment could be shown to discriminate between suicides and controls.

The occurrence of suicide attempt despite adequate treatment

The number of individuals who had made suicide attempts, when treated or not treated, among suicides and controls are presented in table 2. The ratios of attempters making their suicide attempts despite adequate treatment were 19/57 (33%) among suicides versus 15/33 (45%) among controls. If the total amount of attempts that occurred despite adequate treatment were compared, there were 28/125 (22%) in the suicide group versus 28/75 (37%) in the control group. As controls were slightly more often adequately treated (ratio 1.12:1) a higher frequency of attempts during adequate treatment may be expected, but it was even higher than expected

(1.68:1). Thus we could not conclude that future suicide victims attempted suicide despite adequate treatment more often than did controls.

To sum up; there was no difference in treatment or response to treatment between suicide victims and controls in the long-term course to be detected.

Occurrence and seriousness of attempt related to treatment

The analysis was performed on the total sample, as there was no difference in the treatment between suicides and controls and a similar pattern of occurrence and seriousness during full time antidepressant medication was found in both groups.

Occurrence of suicide attempt and type of treatment

In comparing the frequencies of suicide attempts during different kinds of adequate treatment we found that 23/113 (20%) of those who sometimes received antidepressant pharmacotherapy made a suicide attempt at some time versus 11/133 (8%) of those treated with ECT and 1/62 (2%) of those who received ECT plus continuation pharmacotherapy. (ECT versus antidepressants; chi-square = 7.49, $p < .01$). The total number of suicide attempts related to treatment is presented in figure 2.

Phases of treatment and suicide attempt

The occurrence of suicide attempt related to phases of treatment is presented in a flow diagram (fig. 3). Most suicide attempts occurred before the patient applied for help. These constituted 51% of the attempts in the suicide group versus 43% in the control group (table 2). Thus suicides could not be shown to seek help before their suicide attempts less often than did controls.

Suicide attempts during antidepressant pharmacotherapy occurred much more often during the first month, as compared to the following five months of acute depression (13, 5, 3, 4, 2, and 1 patients had attempted suicide at least once during month 1, 2, 3, 4, 5, and 6; chi-square= 19.0, $p < 0.000013$).

Two suicide attempts occurred during the course of ECT.

Seriousness of suicide attempt and treatment

Though the likelihood of making a suicide attempt despite adequate treatment appeared similar for suicides and controls, treatment with antidepressant medication might affect the seriousness of the attempt. Figure 4 shows the seriousness of the total number of suicide attempts related to treatment.

Serious attempts were more common when patients were untreated as compared to after at least four weeks of antidepressant medication, when non-serious attempts predominated. When individuals were compared, sometimes serious attempt was significantly related to lack of treatment at suicide attempt as compared to during antidepressant therapy after 4 weeks (42/56 versus 3/12, chi-square= 11.04, $p < .001$). (The case of maintenance treatment with antidepressants and Lithium was not included.)

The majority of attempts that occurred despite adequate treatment with antidepressants after 4 weeks were “ambivalent” attempts (7/9). These attempts per se were significantly related to treatment (7/12 versus 13/56, chi-square = 5.87, $p < .02$). Further, if suicidal gestures (the lowest degree of severity) were excluded the significance remains (7/10 versus 13/50, chi-square = 7.26, $p < .01$). However, there was no indication of a general later occurrence of less serious attempts for the total sample, which might have been a confounding factor.

Finally, low seriousness of attempts during antidepressant therapy was also found in comparison to suicide attempts after ECT. In the ECT group 8/10 had made serious attempts versus 3/12 in the antidepressant group (chi-square = 6.60, $p < 0.02$). There were somewhat more ambivalent attempts in the pharmacotherapy group (7/12 versus 4/10) but numbers are too small to be conclusive. Those who had received ECT were somewhat older compared to those who received antidepressants (44 years versus 36 years on the average), but ECT was the most

common treatment in the long term course in this severely depressed sample and most commonly given already for the first episode.

The only suicidal act that occurred during continuation treatment after ECT was a suicidal gesture.

To sum up; ECT seemed to reduce the frequency of suicide attempts better than antidepressant pharmacotherapy. However, suicide attempts appeared to be less serious on pharmacotherapy.

DISCUSSION

The sample

The present study deals with a sample of severely depressed suicides and their controls. The multiaxial ratings enabled the selection of well-matched controls based on prospective ratings of diagnosis. The agreement with DSM IV appears to be high in retrospect with a minimum of 91% of the patients fulfilling the criteria for a major depressive disorder with melancholia or psychosis. The exclusion of secondary depressions enhanced the homogeneity of the sample. The frequencies of bipolar, psychotic patients etc were similar in suicides and controls.

As the sample constitutes severely depressed patients, the applicability of the results on major depression in general remains to be shown.

The antidepressants prescribed were generally tricyclics, which are no longer a first-choice. However, a similar effect of these drugs as compared to selective serotonin reuptake inhibitors and serotonin norepinephrine reuptake inhibitors (SSRI and SNRI) on suicidal behaviour has recently been proposed (Jick *et al*, 2004, Yerevanian *et al*. 2004). Thus the effect of tricyclics appears interesting, though replication of the results in a study on newer antidepressants would be recommended.

Non-serious suicide attempts were included as attempt had been shown to be related to completed suicide independent of seriousness in this group of patients (Brådvik and Berglund, 2002). In comparing suicides and controls one assumes that they are equally prone to report suicide attempts. This could be assumed but not be proven. Possible underreport is probably less common during treatment.

Non-compliance and non-response to treatment limit the effect of antidepressant therapy once it has been prescribed. It is known that only about 70-80% of all depressed patients respond to antidepressant pharmacotherapy (Potter *et al*, 1991). The present sample shows a similar rate of

response for suicides and controls. Non-compliance also limits the effect of antidepressant therapy (Demyttenaere, 2003). In the present study we could only note the prescriptions of and response to antidepressants. We have no analysis of blood fluids, which is a limitation.

However, similar rates of suicide attempts during adequate treatment indicate similar frequencies of compliance in suicides and controls. Moreover, the reduction of seriousness of attempt is a positive effect that indicates response! But the lower rates of attempts after ECT could be due to the fact that ECT is received with certainty when administered. All we could conclude is that suicide attempts seem to be less common after ECT than after prescription of antidepressants.

Main findings

The main findings were that on the one hand occurrence of suicide attempts appeared less common during/after ECT as compared to during antidepressant pharmacotherapy, while on the other hand suicide attempts seemed to be less serious during pharmacotherapy.

First there was a lower frequency of attempts after ECT as compared to during antidepressant pharmacotherapy. It has been suggested that ECT has a better effect on suicide attempt as compared to antidepressants (Avery and Winokur, 1978). These findings are compatible with the present study. However, seriousness of attempt was not considered in Avery's study. It appeared that suicide attempts were more serious after ECT as compared to during antidepressant pharmacotherapy. This may be due to the fact that there is a relapse of a depressive episode, rather than "incomplete" recovery after ECT. A frequent recurrence of depression after ECT has been shown in approximately 50% of the cases or even higher rates in for instance delusional depression (Bourgon and Kellner, 2000). Further, in a review it was found that ECT had an acute but not a long-term beneficial effect on suicidality (Sharma 2001). However, to our knowledge the nature of recurrence has been little explored. In a previous study we found evidence that

patients with psychomotor retardation were at higher risk of committing suicide after ECT as were others (Brådvik and Berglund 2004) despite the good effect of ECT on this symptom (Rasmussen 2003). Finally, the better effect of ECT is partly due to the fact that the effect of ECT occurs earlier than that of antidepressant pharmacotherapy. There was a peak of suicide attempts during the first month of pharmacotherapy, which is in agreement with the study by Jick *et al.* (2004). This peak may contribute to the difference in favour of ECT.

The second positive finding in the present study was that suicide attempts during full time antidepressant medication (after at least 4 weeks) appeared to be less serious as compared to other attempts. Other investigators have also found a non-significant reduction of intention and lethality of attempts during antidepressant medication (Leon *et al.*, 1999). Those studies are compatible with the present significant finding.

A lower degree of depression may simply result in a reduction of suicidal intent. However, the attempts during full time pharmacotherapy were more often “ambivalent” rather than non-serious. They were characterized by a seemingly serious initial intent of the suicidal act, but the patient then changed his/her mind and interrupted his/her attempt without intervention by somebody else. We cannot explain why this type of attempt, described as aborted attempts in literature (Marzuk 1997), were more common once antidepressants could be supposed to exert an effect on depression. May be suicidal intent is not only “proportional” to depression. It is possible that relief of depressive feelings makes the patient hesitate to complete the suicidal act rather than extinguishing suicidal behaviour.

After the publication of Rouillon’s investigation on maprotiline (Rouillon *et al.*, 1989), it has been speculated that antidepressants may exert a different effect on depression and suicidal acts. Further, biological findings such as low 5-HIAA in cerebrospinal fluid (CSF) correlated with suicidal behavior independent of type of psychiatric disorder, has lead to a hypothesis of a suicidal syndrome (Åsberg 1986). Other authors tried to delineate this syndrome on a

phenomenological level describing core symptoms, such as hopelessness, etc. appearing independent of illness (Ahrens and Linden, 1996). Moreover, a stress-diathesis model has been proposed in which the risk for suicidal acts is determined not merely by a psychiatric illness (the stressor) but also by a diathesis, such as a tendency to experience more suicidal ideation and to be more likely to act on suicidal feeling (Mann *et al*, 1999). The present finding is compatible with such a theory of suicidality independent of depression. There is an interesting possibility that aborted attempts may be seen as another phenomenological level of the suicidal syndrome. The initial urge (impulse) to perform suicidal behaviour (diathesis) may, perhaps, persist after the reduction of the depressive feelings (the stressor). When the stressor is no longer there the patient does not complete the act! This needs further exploration.

Clinical implications

The impact on prevention of completed suicide could not easily be concluded from the present study. Reduced seriousness during pharmacotherapy may indicate a reduced risk but also a persistence of suicidal feelings after relief of depressive symptoms. There is a possibility that reduction of depressive feelings is sufficient to prevent suicide, as the patients interrupt their suicidal acts. On the other hand the persistent urge to perform suicidal acts, apart from non-compliance and non-response, could be an additional explanation for the fact that suicide sometimes occurs despite adequate antidepressant therapy. This remains to be shown.

The present study shows that suicide attempts were less frequent but still serious after ECT as compared to during antidepressant pharmacotherapy. Continuation treatment with antidepressants would be recommended in severely depressed patients exhibiting suicidal behaviour. This treatment appeared to have a preventive effect on completed suicide in a previous study (Brådvik and Berglund, 2000). Moreover, suicide attempt was very rare (and non-serious) during continuation treatment in the present study, which gives further support for a preventive effect.

CONCLUSION

ECT appears to have a better effect on the occurrence of suicide attempt on the one hand but a worse effect on seriousness on the other hand. Antidepressant pharmacotherapy may reduce the severity of suicide attempts. If this fact indicates a preventive effect or may be an additional explanation for some sparse suicide cases despite adequate treatment remains to be shown.

Continuation treatment with pharmacotherapy after ECT is recommended.

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LEGENDS

Figure 1

Flow-diagram for the sample of patients with severe depression admitted to the Department of Psychiatry, Lund University Hospital

Figure 2

Suicide attempts by type of treatment. All suicidal events related to the total number of treatments (percent).

Figure 3

Occurrence of suicide attempts related to course of treatment.

Every depressive episode was analyzed separately and divided into the phases: before treatment contact, initial treatment and ongoing treatment first six months.

Five suicide attempts were excluded from the figure: one patient, who had been on maintenance treatment with antidepressants and Lithium for more than a year. Three cases of inadequate treatment excluded as well. Finally, one case of continuation treatment with antidepressants after ECT.

Figure 4

Total number of serious suicide attempt versus non-serious by type of treatment

- 1. no treatment: before the patient applied for help or during contact without treatment.**
- 2. pharmacotherapy within four weeks.**

- 3. pharmacotherapy after four weeks. (One case of maintenance therapy in combination with Lithium included.)**
- 4. during course of ECT.**
- 5. After ECT without continuation therapy.**
- 6. ECT with continuation therapy.**

Three cases of inadequate treatment were excluded.

Figure 1

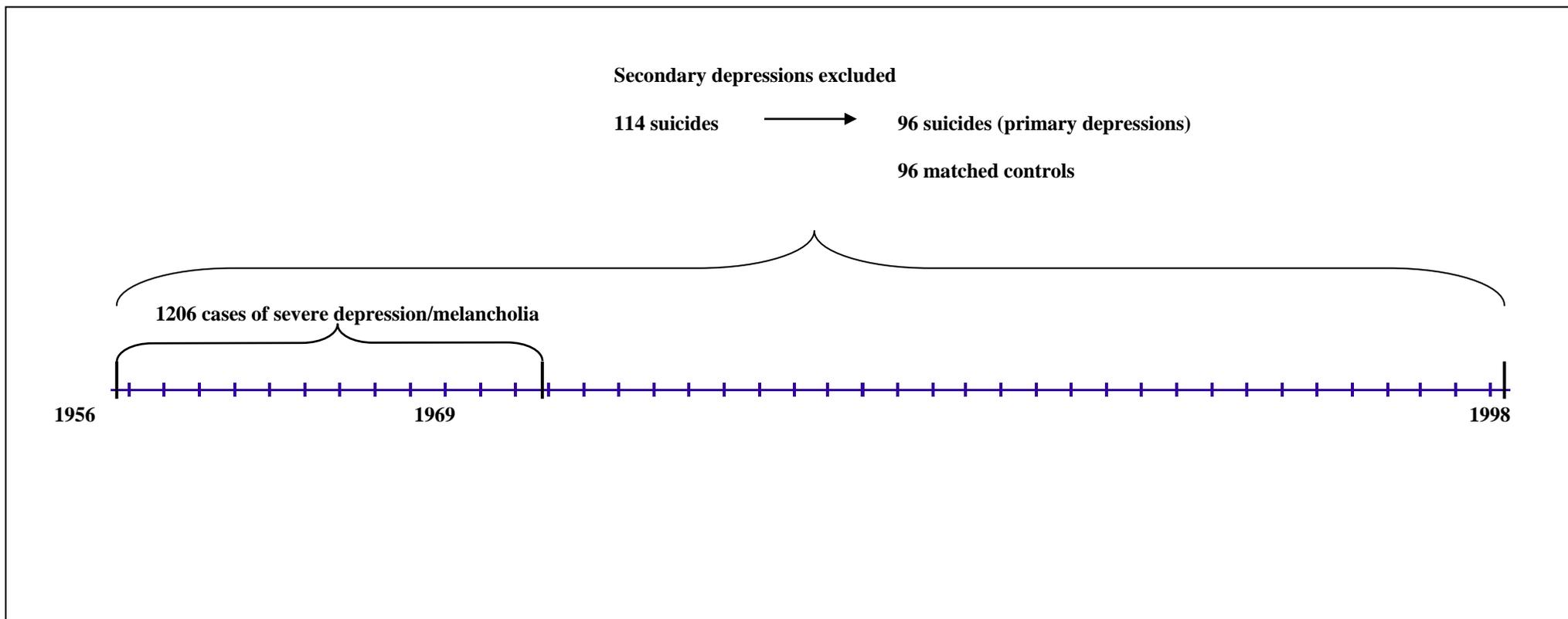


Figure 2

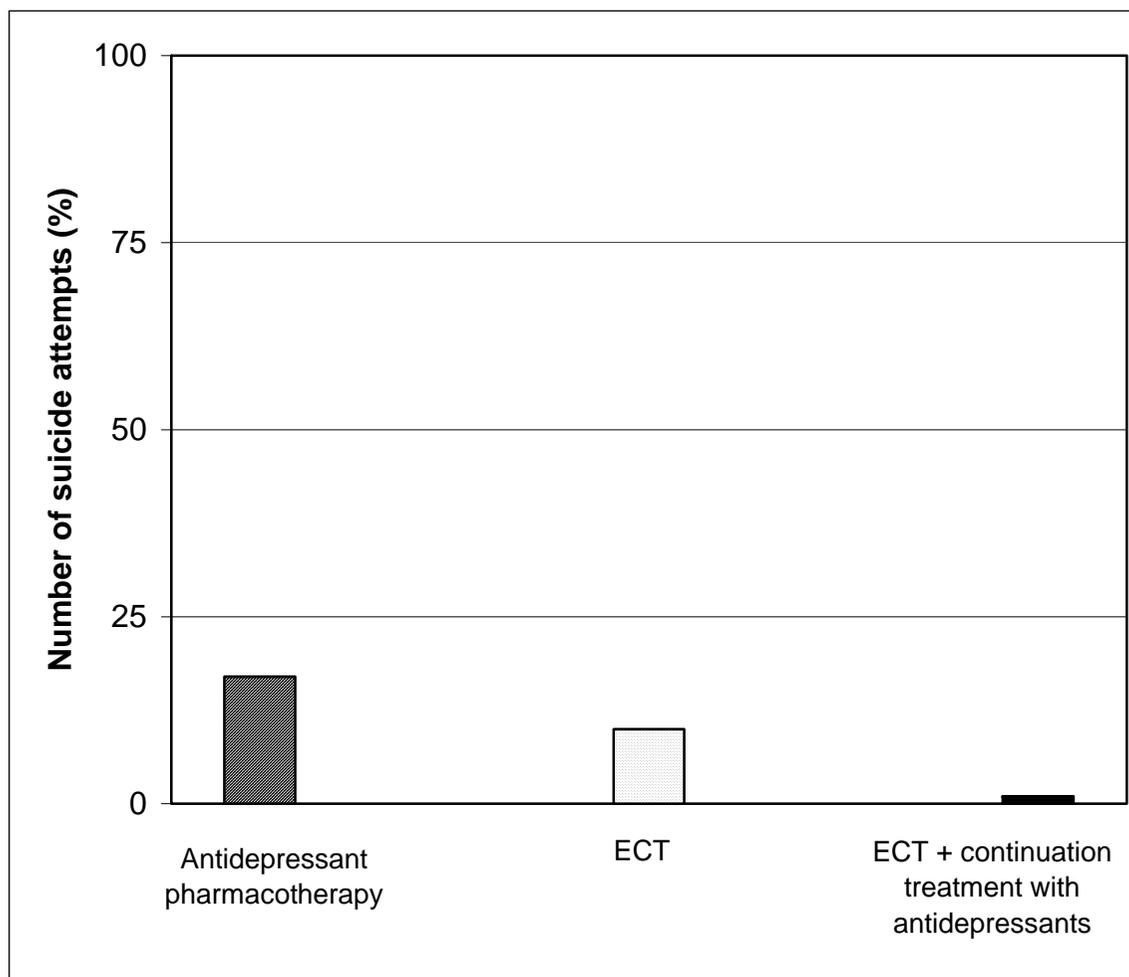


Figure 3

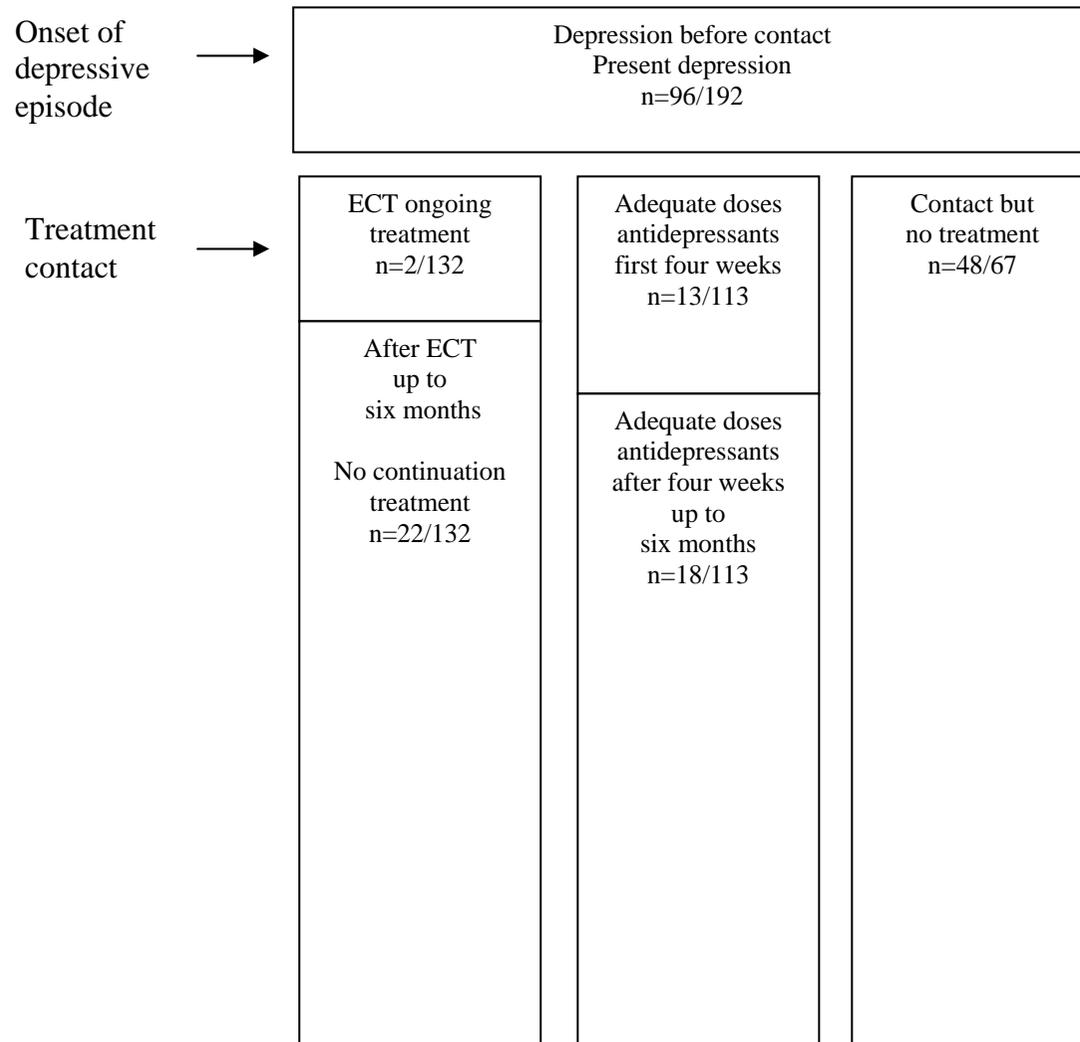


Figure 4

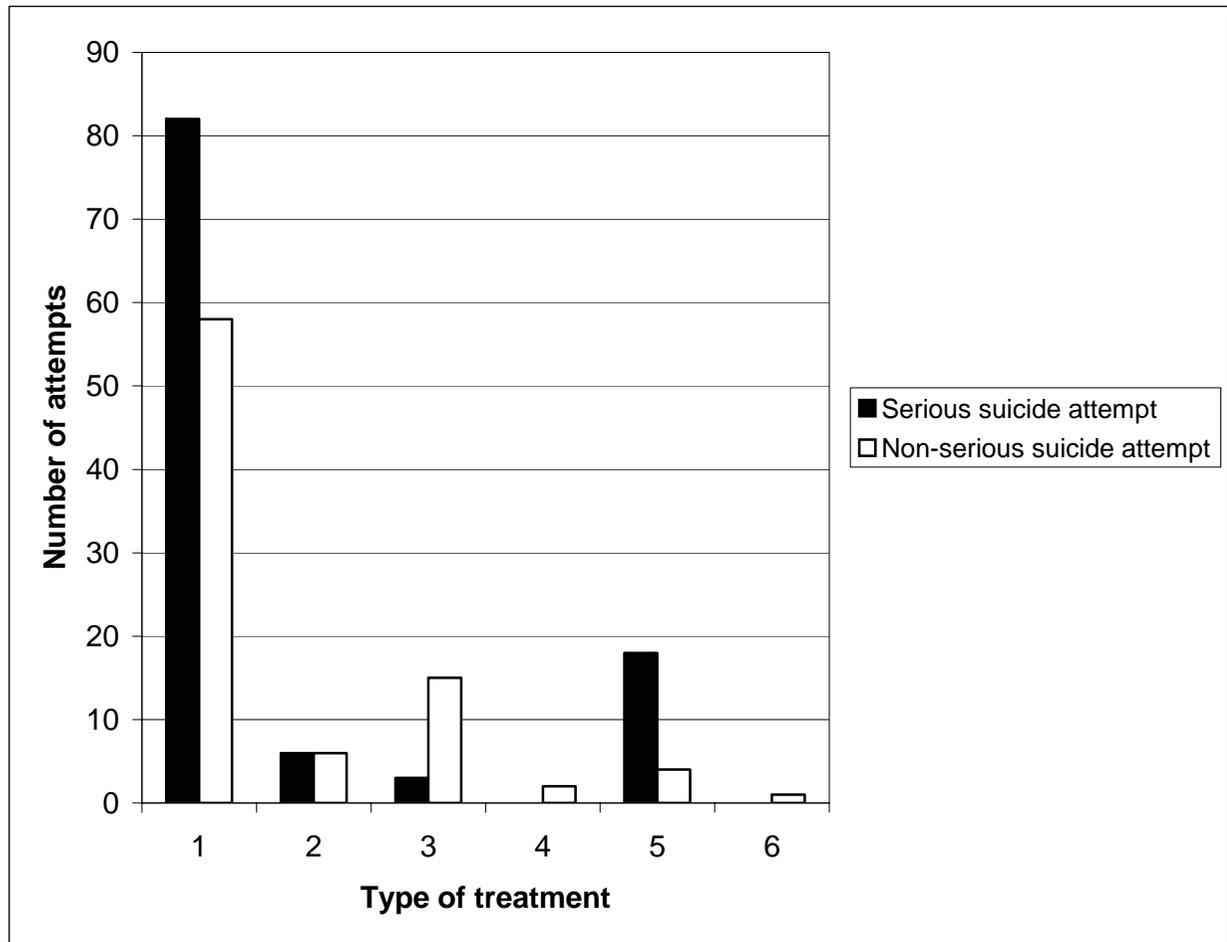


Table 1. Total number of adequately treated episodes in suicides and controls and attempters and non-attempters after inclusion in the study (percent.)

	Frequency of adequately treated episodes
Suicides	266/402 (66)
Attempters	158/ 253 (62)
Non-attempters	108/149 (72)
Controls	240/326 (74)
Attempters	89/127 (70)
Non-attempters	151/199 (76)

Table 2. Number of individuals who had made suicide attempts at some time by type of treatment and total number of suicidal events by type of treatment.

	Suicides	Controls
Individuals with suicide attempt	57	33
Total number of suicidal events	125	75
Before contact	44 (77) 64 (51)	20 (61) 32 (43)
Contact but no treatment	12 (21) 30 (24)	3 (9) 15 (20)
Inadequate treatment	3 (5) 3 (2)	0 (0) 0 (0)
ECT	6 (11) 9 (7)	5 (15) 15 (20)
Antidepressants	13 (23)* 18 (14)*	10 (30) 13 (17)
ECT + Continuation treatment with antidepressants	1 (2) 1 (2)	0 (0) 0 (0)

* in one case there was additional Lithium treatment