Suicide in Primary Affective Disorders Revisited: A Systematic Review by Treatment Era

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Background: We reviewed suicide rates in affective disorder and their variation with electroconvulsive therapy (ECT) and antidepressant availability.

Method: Suicide rates were calculated from 75 follow-up studies, identified by systematic literature searches and analyzed for differences over time eras characterized by the availability of specific treatments.

Data Sources and Study Selection: MEDLINE, EMBASE, BIOSIS Previews, and Psychological Abstracts literature searches were conducted for the years 1966 to 1995. References from review articles identified from these sources from 1985 onward and textbook references were also included. Publications prior to 1966 were obtained from article references identified for the period 1966 to 1976 and reviews. Inclusion criteria were (1) articles written in English, French, or German; (2) sample size > 30; (3) age at recruitment between 18 and 64 years for each subject; (4) sample had to contain subjects hospitalized at time of recruitment; and (5) naturalistic follow-up of at least 6 months.

Results: Suicide rates decreased with longer follow-up periods. For follow-up periods over 20 years, the mean rate was 3.76/1000 person-years (95% confidence interval [CI] = 2.35 to 5.17). Suicides accounted for 12.3% (95% CI = 8.52 to 16.04) of all deaths in samples in which 40% or more of patients had died. For studies with minimal overlap between eras, the mean suicide rate differed significantly between eras (pretreatment, before 1940: 6.3/1000; ECT treatment, 1940 to 1959: 5.7/1000; antidepressant treatment, 1960 onward: 3.3/1000; $F = 31.4$, $df = 2,42$; $p < .001$).

Conclusion: The risk of suicide in follow-up studies of affective disorder has decreased compared to that reported in previous reviews. The availability of ECT and antidepressants may have contributed to this decrease, but prescription of these treatments cannot be assumed for all patients.

(J Clin Psychiatry 2001;62:804–811)

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The authors thank Joan Kelsey, librarian at the Institute of Public Health, and Ian Preston, librarian at Fulbourn Hospital, for assistance with literature searches.

In the spirit of full disclosure and in compliance with all ACCME Essential Areas and Policies, the faculty for this CME activity were asked to complete a full disclosure statement. The information received is as follows: Drs. O'Leary, Paykel, Todd, and Vardulaki have no significant commercial relationships to disclose relative to the presentation.

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Suicide is a cardinal outcome in affective disorders. Reviews estimate that 15% of all deaths are by suicide.[1–4] Many samples include subjects treated prior to the availability of electroconvulsive therapy (ECT) and antidepressant drugs for management of depression. The large body of published follow-up studies currently available provides an opportunity to (1) reexamine the proportion of all deaths by suicide; (2) calculate actual suicide rates on follow-up; and (3) address the clinically important issue of whether the introduction of ECT in the late 1930s and antidepressants in the 1950s reduced the suicide rates in subjects with affective disorder. Any reduction would most likely be seen in subjects with diagnosed affective disorders presenting to psychiatric care.

METHOD

A MEDLINE[5] literature search was conducted for the years 1966 to 1995. Affective disorder nomenclature has changed over time, and in order to identify articles, the keywords *depression*, *bipolar*, *affective disorder*, *depressive neurosis*, *manic*, and *endogenous* were used and combined with the keywords *course*, *outcome*, *follow-up*, *prognosis*, *death*, *mortality*, *suicide*, and *unnatural*. All keywords were confined to title searches. Searches of EMBASE,[6] BIOSIS Previews,[7] and Psychological Abstracts[8] using the keywords *depression* and/or *bipolar* and *mortality* and/or *suicide* were also performed as title searches. References from review articles identified from these sources from 1985 onward were also obtained,[3,9–13] as were textbook references.[4] Publications prior to 1966

were obtained from the references from articles identified in the literature search of the period from 1966 to 1976 and from reviews.[1,2,4,14,15]

Inclusion criteria were (1) articles were written in English, French, or German; (2) sample size was greater than 30; (3) age at recruitment was between 18 and 64 years for each subject; (4) sample had to contain some subjects hospitalized at time of recruitment, in order to control for severity; (5) follow-up was naturalistic rather than entirely within a controlled treatment design; and (6) follow-up length was greater than 6 months. When multiple reports from a cohort were identified, the most recent follow-up data were used. In multicenter studies, the combined results from all centers were included.

Suicide Rates

Suicide was regarded as having occurred when defined as such by either a coroner and/or death certification, or when reported as such by the original authors when a certified cause of death was not clearly indicated. Deaths referred to as "unnatural," "open verdict," or "death by misadventure" were excluded.

The number of person-years of observation was determined in alternative ways, depending on the methodology of each article: (1) by using the actual number of person-years of observation reported in the studies; (2) by multiplying the reported mean or median period of observation/follow-up by the number of persons at risk, which in these circumstances was calculated as the number entering the study minus the number without follow-up information; and (3) by categorizing the studies for which the mean and/or median length of follow-up was not reported into 2 types—those following each subject for the same length of time after entry to the study and those for whom the length of follow-up differed among subjects. In the former instance, length of follow-up used was that described for the study; in the latter, the estimated length of follow-up used was half the means of the maximum and minimum follow-up periods. In both circumstances, a correction was made for deaths during follow-up by subtracting from the number at risk half the number of subjects who died. The number of suicides per 1000 person-years of follow-up for each study was calculated by multiplying the number of suicides by 1000 and dividing the product by the number of person-years of follow-up.

The term *pretreatment era* referred to cohorts recruited between January 1, 1900, and December 31, 1939, and for whom at most 10% of the person-years of follow-up were after January 1, 1940. The term *ECT treatment era* referred to cohorts recruited between January 1, 1940, and December 31, 1959, and with at most 10% of the person-years of follow-up after January 1, 1960. The term *antidepressant treatment era* referred to recruitment after January 1, 1960.

The period of follow-up bridged the 1940 or 1959 cutoff dates in some studies that were excluded from the within–treatment era analysis (Table 1). In other studies, suicide rates for subjects treated with ECT and/or antidepressant drugs were compared with those of other subjects who were admitted at the same time but not given these treatments. In analysis, both groups were combined so that they could not be differentiated by treatment, due to likely selection bias by patient characteristics in determining treatment choice (see Table 1).[50,56,58,70]

Analyses

Statistical analysis was carried out in Stata 5.0.[16] As recommended in combining rates, the mean suicide rate for each treatment era was calculated after first weighting the studies in each era by the inverse of their variance (1/[suicide rate/person-years] = person-years/suicide rate). The studies (N = 10) with a suicide rate of zero were excluded from the pooled analysis as their weight was not calculable (person-years/zero = infinity).

RESULTS

Suicide Rates and Length of Follow-Up

Seventy-five studies were included in the review (see Table 1). Figure 1 plots the number of suicides per 1000 person-years of follow-up for each study as a function of years of follow-up. Suicide rates decreased as the length of follow-up increased but were approximately stable and in a narrow range from 20 years onward. For the 10 studies with a follow-up period longer than 20 years, the rate was between 1.25 and 9.30 suicides per 1000 person-years of follow-up. The mean was 3.76 (95% confidence interval [CI] = 2.35 to 5.17) suicides per 1000 person-years of follow-up. For follow-up periods of longer than 30 years (N = 3), the suicide rate was between 1.25 and 2.52 suicides per 1000 person-years of follow-up.

Suicides as a Percentage of All Deaths

In keeping with earlier reviews, the percentage of all deaths in each sample due to suicide was examined (Figure 2). This percentage was as high as 100% for some studies in which the proportion of subjects dying was less than 10% and as low as 5% for the study in which over 90% of the sample had died. The percentage varied between 4.69% to 16.37% (mean = 12.28%, 95% CI = 8.52 to 16.04) for those 6 studies in which more than 40% of the sample had died.

Effect of Treatment Era

Table 2 shows the mean suicide rates by treatment eras for those studies in which no more than 10% of person-years of follow-up occurred after the end of the recruitment period. The studies were also subdivided by length of follow-up (using 10 years as a cutoff point), and the 2 groups were analyzed separately by treatment era. There were no studies over 10 years from the ECT treatment era

Table 1. Percentage of All Deaths Due to Suicide for the Total Study Sample

Name of Study (Year of Publication)	Recruitment Onset	Sample Size	Country	Years of Follow-Up	Suicide/ Death %	Suicide Rate (per 1000 Person-Years[a])
Recruitment era, 1/1/1900–12/31/1939 (pretreatment era)						
Schulz (1949)[40]	1904	2004	Germany	16	13.4	7.5
Langeluddecke (1941)[41]	1904	337	Germany	21.5	15.5	9.3
Slater (1951)[42]	1904	138	Germany	24	15.3	3.5
Lundquist (1945)[43]	1912	319	Sweden	20.5	14.3	3.2
Stephens and McHugh (1991)[44]	1913	1017	United States	5	?	21.3
Bond and Morris (1954)[45]	1925	464	United States	5	50	7.6
Bond (1954)[46]	1925	124	United States	5	20.6	13.1
Bond and Braceland (1937)[47]	1927	159	United States	5	50	16.3
Bond and Braceland (1937)[47]	1927	45	United States	5	15.4	10.4
Lewis (1936)[48]	1928	57	United Kingdom	7	30	8.2
10% of follow-up occurred after 1940						
Follow-up between 1/1/1940 and 12/31/1959						
Stenstedt (1952)[49]	1919	216	Sweden	15.5	14.3	3.0
Kinkelin (1954)[50]	1920	146	Switzerland	21.8	26	4.1
Huston and Locher (1948)[51]	1930	80	United States	6.8	60	11.0
Huston and Locher (1948)[52]	1930	93	United States	6.4	36.4	20.2
Ziskind et al (1945)[53]	1938	193	United States	3.3	50	15.7
Hastings (1958)[54]	1938	229	United States	9	23.1	4.8
Astrup et al (1959)[55]	1938	256	Norway	13	17.1	2.3
Follow-up ended after 1/1/1960						
Kay and Petterson (1977)[56]	1900	69	Sweden	65	4.7	1.3
Coryell (1981)[57]	1924	71	United States	43	13.5	1.6
Tsuang and Woolson (1978)[58]	1935	315	United States	34.5	8.3	2.5
Recruitment era, 1/1/1940–12/31/1959 (ECT treatment era)						
Karagulla (1950)[59]	1940	434	United Kingdom	4.9	18.9	7.2
Stenstedt (1959)[60]	1940	307	Sweden	6.5	6.3	3.4
Bond and Morris (1954)[45]	1940	105	United States	5	26.7	8.2
Bond (1954)[46]	1940	253	United States	5	42.9	12.7
Huston and Locher (1948)[51]	1941	74	United States	3	50	4.5
Huston and Locher (1948)[52]	1941	61	United States	3	100	5.5
Jarvie (1954)[61]	1947	97	United Kingdom	3	15.4	7.3
Clark and Mallett (1963)[62]	1949	74	United Kingdom	3	NA	0.0
Seager (1958)[63]	1954	206	United Kingdom	2	50	4.9
10% of follow-up occurred after 1959						
Opjordsmoen (1989)[64]	1946	50	Norway	22.3	17.7	2.7
Pokorney (1964)[65]	1949	316	United States	11	?	5.3
Shobe and Brion (1971)[66]	1949	111	United States	17.8	9.1	1.0
Perris and d'Elia (1966)[67]	1950	797	Sweden	8	22.6	3.6
McGlashan (1984)[68]	1950	63	United States	14.3	50	8.9
Bratfos and Haug (1968)[69]	1952	207	Norway	6	12.1	3.2
Fukuda et al (1983)[70]	1955	498	United Kingdom	12	12.6	1.8
Gittleson (1966)[71]	1956	371	United Kingdom	1.6	?	5.8
Berglund and Nilsson (1987)[72]	1956	1206	Sweden	20.5	21.6	5.2
Avery and Winokur (1976)[73]	1959	519	United States	3	25	5.3
Angst and Preisig (1995)[74]	1959	243	Switzerland	27	16.4	4.3
Recruitment era, 1/1/1960 and after (antidepressant era)						
Carlson et al (1974)[75]	1960	49	United States	3.2	100	12.8
d'Elia et al (1974)[76]	1960	78	Sweden	10	50	4.0
Dunner et al (1976)[77]	1960	163	United States	5	?	12.7
Venkoba and Nammalvar (1977)[78]	1961	109	India	8	14.3	1.2
Nystrom (1979)[79]	1961	94	Sweden	10	0	0
Murphy et al (1974)[80]	1962	37	United States	5	NA	0
Lee and Murray (1988)[81]	1965	89	United Kingdom	17.5	20	2.9
Paykel et al (1974)[82]	1967	211	United States	0.83	100	5.7
James and Chapman (1975)[83]	1967	46	United Kingdom	2	NA	0
Smith and North (1988)[84]	1968	68	United States	11	10	1.4
Black et al (1987)[85]	1970	1593	United States	7.5	26.1	3.6
Copeland (1983)[86]	1970	65	United Kingdom	5	22.2	6.6
Weeke and Vaeth (1986)[87]	1970	2168	Denmark	6	24.6	5.8
Sharma and Markar (1994)[88]	1970	472	United Kingdom	13.9	14	1.3
Jorgensen (1985)[89]	1970	114	Denmark	13	43.8	4.7
Akiskal et al (1978)[90]	c1970	100	United States	3.5	?	9.5
Robinson and Spiker (1985)[91]	1972	102	United States	1	100	9.9

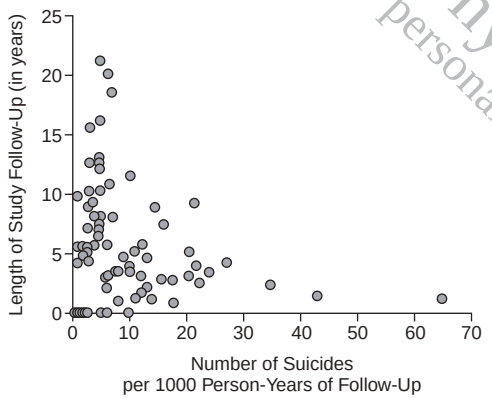
cont.

Table 1 (cont.). Percentage of All Deaths Due to Suicide for the Total Study Sample[a]

Name of Study (Year of Publication)	Recruitment Onset	Sample Size	Country	Years of Follow-Up	Suicide/ Death %	Suicide Rate (per 1000 Person-Years[a])
Thornicroft and Sartorious (1993)[92]	1972	300	Multiple	10	?	11.6
Evans and Whitlock (1983)[93]	1973	112	United Kingdom	5	22.2	12.2
Bronisch et al (1985)[94]	1973	49	Germany	7	100	18.6
Algulander (1994)[95]	1973	38,529	Sweden	12	15.6	3.2
Merikangas et al (1983)[96]	1976	59	United States	2	NA	0
Surtees and Barkley (1994)[97]	1976	80	United Kingdom	12	31.3	5.8
Fawcett (1993)[98]	1978	954	United States	10	?	3.6
Rothschild et al (1993)[99]	c1980	42	United States	1	NA	0
Harrow et al (1990)[100]	c1980	139	United States	1.7	NA	0
Lonnqvist and Koskenvuo (1988)[101]	c1980	783	Finland	3	30.3	10.3
Kettering et al (1987)[102]	c1980	59	United States	1.2	NA	0
Frommberger et al (1988)[103]	c1980	112	Germany	3	75	9.1
Vestergaard and Aagaard (1991)[104]	1981	133	Denmark	4	22.7	8.2
Lykouras et al (1994)[105]	1982	73	Greece	6	33.3	2.3
Brodaty et al (1993)[106]	1985	139	Australia	3.8	37.5	5.7
Delaunay (1992)[107]	1986	39	France	10	0	0
Muller-Oerlinghausen et al (1992)[108]	1990	471	Multiple	1	33.3	4.3
Verdoux et al (1994)[109]	1992	33	France	6	0	0

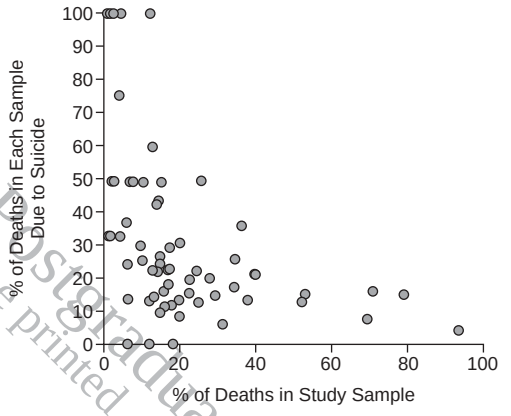
[a]Abbreviations: ECT = electroconvulsive therapy, NA = not applicable. Symbol: ? = unknown (data not available).

Figure 1. Suicide Rate for Each Study (number of suicides × 1000/person-years of follow-up) as a Function of Length of Study Follow-Up (years)[a]



[a]Suicide rate = number of suicides × 1000/person-years of follow-up.

Figure 2. The Percentage of All Deaths Due to Suicide as a Function of the Percentage of Deaths in the Sample



satisfying the criteria for inclusion. There were significant differences in suicide rates among the eras for all 3 analyses. As shown in Table 2, there was a decrease in suicide rate from the pretreatment to ECT treatment era, most marked in studies selected to ensure they had up to 10 years of follow-up, and there was a further smaller decrease in suicide rate in the antidepressant treatment era. Inspection of the confidence intervals revealed that (1) the antidepressant treatment era differed from the pretreatment era in all 3 of the analyses; (2) the antidepressant treatment era differed from the ECT treatment era in the analysis including all studies; and (3) the ECT treatment era differed from the pretreatment era but not from the antidepressant treatment era in the analysis of studies with up to 10 years of follow-up.

DISCUSSION

In this report, we have updated the risk of suicide in follow-up studies of subjects with affective disorder. The majority of studies in previous reviews[1–4] were early ones that were conducted prior to the antidepressant treatment era. The present review differs from previous reviews by the addition of many recent studies. We also excluded data from population or family studies to focus on treated disorder. Even with such inclusion and exclusion criteria, more than twice as many studies (N = 75) were available as in earlier reviews.[1–4] The present review also differs from earlier reviews by including estimates of suicide rates per 1000 person-years of follow-up, rather than solely the percentage of deaths due to suicide. Our re-

Table 2. Suicide Rates (per 1000 person-years) for Each Treatment Era and Effect of Length of Follow-Up[a]

Treatment Era	No. of Studies	Mean Suicide Rate	95% CI	F Value	df	p Value
All follow-up periods						
Pretreatment	10	6.3	(5.4 to 7.2)	31.4	2,42	p < .001
ECT	8	5.7	(3.8 to 7.5)			
Antidepressant	26	3.3	(3.1 to 3.4)			
Up to 10 years of follow-up						
Pretreatment	6	13.3	(10.9 to 15.7)	43.6	2,35	p < .001
ECT	8	5.7	(3.8 to 7.5)			
Antidepressant	20	4.5	(4.0 to 5.4)			
More than 10 years of follow-up						
Pretreatment	4	5.2	(4.2 to 6.3)	4.92	1,9	p < .001
ECT	0					
Antidepressant	6	3.2	(3.0 to 3.3)			

[a]Abbreviation: CI = confidence interval, ECT = electroconvulsive therapy.

view does not calculate standardized mortality ratios, however.[17,18]

Suicide Rates and Percentage of All Deaths

Previous reviews have focused on suicide as a percentage of all deaths. However, this measure is problematic since deaths due to other causes will rise as the sample grows older and reaches a maximum in old age. In addition, suicide rates are highest in the early years of follow-up. True estimates of percentage of deaths due to suicide require lifetime follow-up that is rarely possible. Guze and Robins[1] noted that suicides were most common early in the follow-up period, and there was a tendency for the ratio of suicides to all deaths to approach an estimated value of 15% as the deaths approached 100%. This led them to conclude that the ultimate risk of suicide in affective disorders was about 15%. Later reviews did not differ greatly from these conclusions.[2–4] In addition, Goodwin and Jamison[3] noted that a weighted mean of 19% of manic-depressive deaths were secondary to suicide. Guze and Robins[1] also reported that in no study was suicide the cause of less than 12% of all deaths, and the upper end of the range was 60%. Identical findings were reported by Achte.[4] Miles[2] reported a range of 7% to 100% and Goodwin and Jamison,[3] a range of 9% to 60%. Where more than 40% of the sample had died, the respective range of the ratio of suicide to all deaths and the mean were the following: 15%–15% and 15% for 2 studies identified by Guze and Robins[1]; 10%–15% and 13.33% for 3 studies identified by Miles[2]; 15%–15% and 15% for 2 studies identified by Achte[4]; and 10%–18.6% and 14.65% for 4 studies identified by Goodwin and Jamison.[3]

In the present study, the values for suicides as a percentage of all deaths ranged from 4.7% to 100%. The ratio of suicides to all deaths decreased, as the percentage of deaths increased, to as low as 5% in the study in which more than 90% of the sample had died (see Table 1).[53] In addition, we found that in studies in which more than 40% of the sample had died, the mean ratio was about 12%.

In the present study, we have found it more useful to calculate actual suicide rates, which, although they drop with time, are not also subject to the increasing rates for other deaths with age. They also allow comparison with annual suicide rates in the general population. Although suicide rates fluctuate from country to country and from time to time, they are generally in the range of 10 to 30 per 100,000. Our annual suicide rate of 3.76 per 1000 person-years for long follow-up studies indicates a rate 10 to 30 times the general population rate.

Changes in Suicide Rates by Treatment Era

We have also analyzed suicide rates by treatment era. Mean suicide rates decreased successively throughout the 3 temporal eras, with the extent of this decrease in suicide rates varying depending on selection by length of follow-up, probably reflecting considerable variation in suicide rates among studies from any era and the effects of study selection. The paucity of studies with very long follow-up periods confined to a single treatment era and the absence of studies with follow-up longer than 10 years in the ECT treatment era also limited our capacity to categorize our results by length of follow-up.

While the decrease in suicide rates in more recent studies appears clear, its interpretation is more subject to debate. We have grouped studies by availability of predominant treatments in an attempt to explore an issue that so far has not been resolved—the possible impact of the modern (pharmacologic) treatments on suicide rates. Population suicide rates have fluctuated considerably over the years but did not drop markedly with the introduction of modern treatments. However, many people who commit suicide do not reach treatment by psychiatrists. It may be more reasonable to seek an impact in reducing suicide in psychiatrically treated subjects.

Prospective, long-term, controlled trials of antidepressants and other treatments in suicide prevention in psychiatry are difficult, due, at least, in part to ethical and sampling issues—large sample sizes and long treatment/no treatment arms would be required. Arguably, indirect evidence from systematic review is as much as can be achieved currently. However, interpretation of changes over time is difficult. It must be stressed that the findings demonstrate changes but not the causes of these changes. The approach is limited by the multiple potential confounders that are present, including patient selection; secular changes in service patterns, diagnostic practice, nomenclature, suicide attribution, and legal definition; suicide method; and publication bias and international differences in population suicide rates. Some of these confounding effects could work in either direction. We

did not include a multivariate analysis for the following reasons. This article is based on previous research and does not comprise any primary data. Multivariate analysis would require that we have considerable confidence in the data points (variables) reported by other authors and that such data were collected/reported in a consistent way across the various reports from which the data were drawn. While we were confident that the number of subjects, the number of deaths, the number of person-years of follow-up, and the allocated treatment era (generated from data about when the studies were conducted) in the various studies were recorded consistently, we were not confident that other variables that might meaningfully be entered into a multivariate analysis (e.g., age, social class, length of hospital stay) were consistently reported across studies.

Patients treated by psychiatrists prior to 1940 are likely to have been severely ill, diagnosed using older classification systems, and resident within large institutions. However, the association between illness severity and higher suicide risk remains uncertain.[17–19] While the introduction of community-oriented psychiatric services from 1959 onward may have increased service contacts without increasing inpatient suicide rates,[20,21] recent reductions in the number of hospital beds may have increased the risk of suicide and increased the severity of inpatient samples.[22] Bipolar affective disorder and unipolar affective disorder do not have clearly different suicide risks.[12,23] Among the studies in the current review, 6 included comparisons of suicide rates between unipolar and bipolar subsets of the sample, and each concluded that polarity did not predict increased suicide risk (see Table 1).[64,71,82,84,95,101] However, these are findings from 6 (and less recent) studies only, clearly preempting any definitive statements on this issue.

With regard to other potential biases, psychiatrists are more likely than coroners to judge an unnatural death as suicide,[24] but exclusion of psychiatrist-based judgments would have reduced the number of studies from the pretreatment and ECT treatment eras too greatly for analysis. We have relied on coroner verdicts of suicide where possible, but the use of suicide as a verdict in coroners' courts has changed over time and differs among countries. This is due to opposing factors such as the introduction of more rigorous criteria for a coroner verdict of suicide (as in the United Kingdom) or less stigmatization (as in Ireland). Different international population suicide rates, the occurrence of sizable changes in rates within countries (attributable to changes in lethality of and/or methods), and the effects of war and social change (employment levels/social exclusion) are all confounding factors for our analysis.

Our 3 treatment eras were chosen because of availability of new treatments, although not all subjects may have received them or, if they did, at adequate dosages. Intriguingly, others have reported that the risk of suicide for cohorts of subjects with DSM-III-R major depression treated before 1970 was increased by 17 times and, after 1970, by 36 times, an increase attributed, possibly, to secular changes in care arrangements.[17] The use of electrical induction of convulsive therapy[25,26] as a treatment for depression spread slowly. The use of the antidepressants, imipramine and iproniazid, introduced in the late 1950s, spread rapidly. Longer-term use of antidepressants has developed more slowly since the 1970s. Other treatments such as lithium and mood stabilizers were also introduced.

Previous reports suggesting that actual receipt of ECT-reduced suicide rates have been based mainly on small numbers of studies and were subject to treatment selection bias.[27,28] It has also been argued that antidepressants may prevent suicidal behavior.[29–32] There are few controlled trials comparing suicide risk while subjects are on antidepressant treatment versus receiving placebo. The short-term evidence suggests that suicidal attempts are more frequent on antidepressant treatment but that the risk of actual suicide is not.[33] Possible complexities include increase in suicide risk due to increased psychomotor activation, the time lag in amelioration of suicidal ideas,[33] the relative toxicity of antidepressants taken in overdose, and a possible paradoxical increase in suicidal ideation in a small minority of patients.[34,35] In addition, the search period ended in 1995, curbing the availability within the antidepressant era of the newer antidepressants, which are less toxic in overdose.

A number of reports have suggested that patients on lithium have fewer suicidal deaths.[36–38] As with other treatments, interpretation of results is confounded by treatment bias and dropout effects and other difficulties in making comparisons. Only 2 lithium studies met the entry criteria for the review (see Table 1; Vestergaard and Aagaard[104] and Muller-Oerlinghausen et al.[108]). More recently, Brodersen and coworkers[39] were the first group to extend the period of naturalistic follow-up from 5 to 16 years and have reported that suicide rates were about 4 times higher in lithium-noncompliant subjects.

CONCLUSION

Our analyses address continuing suicide mortality for years after acute treatment, which appears to have decreased in more recent studies. The findings for follow-up periods of up to 10 years suggest that a major impact on suicide mortality may have followed the introduction of ECT. Since antidepressants have increasingly been substituted for ECT since the 1960s, the continuation of lower rates in the antidepressant treatment era and their further lowering also suggests that they may reduce suicide rates in affective disorders. These conclusions regarding treatment must be tentative.

Disclosure of off-label usage: The authors have determined that, to the best of their knowledge, no investigational information about pharmaceutical agents has been presented in this article that is outside U.S. Food and Drug Administration–approved labeling.

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