

Suicide Prevention

A Pragmatic Review of Recent Studies

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Summary. Because of the almost complete absence of randomized controlled trials demonstrating the effectiveness of specific treatments, there is sometimes a degree of pessimism about our ability to prevent suicidal behaviors. However, the methodological challenges to produce such research are formidable and may never be overcome. Therefore, a pragmatic review of evidence-based methods of suicide prevention is required. This review of recent studies using a variety of research strategies, both nonpharmacological and pharmacological, particularly at the community level, provides persuasive data that suicide prevention is possible. This is achievable by the application of broad community and professional education programs, as well as by the optimum management of mental disorders.

Keywords: suicide prevention, research, depression

At the outset it is acknowledged that this is not a systematic review of specific management strategies for suicide prevention. Indeed, it has been prompted by the pessimism that has been engendered by some systematic reviews, whose exclusion criteria have at times resulted in analyses of subjects that bear little relationship to the suicidal people seen in general clinical practice. As noted previously (Goldney, 1998), there are limitations to the application of usual evidence-based research in demonstrating suicide prevention, and it is argued that a more pragmatic evidence-based approach is necessary.

The Challenge of Evidence-Based Practice

In 1993 the World Health Organization promulgated what it described as “Six basic steps for suicide prevention.” These were: The treatment of psychiatric patients, gun-possession control, detoxification of domestic gas, detoxification of car emissions, control of toxic substance availability, and “toning down” reports in the press. While these recommendations appeared to be logical and noncontroversial, being based on clinical wisdom of the time, within a year Wilkinson (1994) had stated that “the reality is that there is no convincing evidence that education, improved social conditions and support, or better training play a substantive part in preventing suicide,” and, in a similar pessimistic vein, Gunnel and Frankel (1994), in a paper entitled “The prevention of suicide: Aspirations and evidence,” concluded

that “no single intervention has been shown in a well-conducted, randomized controlled trial to reduce suicide.”

That such comments were technically correct was subsequently substantiated by systematic reviews of the treatment literature. Thus, Hawton et al. (1998), in a review of the efficacy of psychosocial and pharmacological treatments for the prevention of repetition of suicidal behavior, concluded that “currently there is insufficient evidence on which to make firm recommendations about the most effective forms of treatment for patients who have recently deliberately harmed themselves.” Similarly, in a review of the role of lithium maintenance treatment of mood disorders in preventing suicide, Burgess et al. (2001) concluded that “there is no definitive evidence from this review as to whether or not lithium has an anti-suicidal effect.”

These reviews and comments were prompted by the desirable focus on evidence-based practice in the latter part of the 20th century. However, such a focus needs to be considered in the perspective that suicide, for all its drama and the clarity that retrospective analyses provide, has a low base rate, with the attendant clinical and research limitations that this imposes, particularly in terms of demonstrating the effectiveness of treatments (Goldney, 2000; Cuijpers, 2003).

The challenge of detecting those who may suicide, which is a necessary requirement if one is to mount a research methodology to prevent such behavior, has been well recognized for 50 years. Rosen (1954) was probably the first to draw attention to the limitations of the prediction of infrequent events in suicidal subjects, with a co-

gent description of the interaction between the low incidence of suicide itself and the large number of false positives that are predicted on the basis of those subjects possessing the conventional risk factors associated with suicide. At the individual level this was later emphasized by Pokorny (1983), who stated that "We do not possess any item of information or any combination of items that permits us to identify to a useful degree the particular persons who will commit suicide."

Because of the lack of specificity of the risk factors for suicide, the numbers required for conclusive aggregate data analysis are particularly daunting. For example, Gunnell and Frankel (1994) calculated that to demonstrate a 15% reduction in suicide for those who have attempted suicide, where there is a 2.8% chance of suicide in the subsequent 8 years, it would require a sample size of almost 45,000 subjects. This was also illustrated well by Lewis et al. (1997), who provided a mathematical model for deriving the numbers needed to demonstrate the effectiveness of suicide prevention measures in high-risk populations, and noted that for an intervention that would reduce the suicide rate in doctors and farmers by 25%, 25,000 and 33,000 subjects, respectively, would be required. Not unexpectedly, they expressed reservations about the feasibility and affordability of studies to demonstrate such effectiveness.

It is acknowledged that the numbers required to demonstrate the effectiveness of the prevention of repetition of suicidal behavior are appreciably less than for suicide per se. However they are still daunting and Hawton et al. (1998), in their previously noted review on the prevention of repetition of suicidal behavior, reported that even when data from 20 randomized controlled trials were combined in a meta-analysis, numbers were too small to detect differences in outcome. Indeed, they advised that for future research in preventing repetition of suicidal behavior, "If the predicted rate were 10% in the experimental group vs 15% in the control, with α set at 0.05 and β set at 0.2, a total of 687 subjects would be required in each treatment group, while if the rates were 20% and 30%, 293 subjects would be required in each group."

It could be argued that multicentered collaborative trials could be utilized to fulfill the need for sufficient numbers to demonstrate the effectiveness of intervention programs in preventing repeated suicide attempts. However, the logistical demands, let alone the financial requirements, are daunting. For example, in the World Health Organization/European Union follow-up study of those who had attempted suicide, 2,159 subjects in eight centers with a special interest in suicide prevention research were asked to participate (Kerkhof et al., 1998). Of those, 1,098 (50%) completed a first interview within 1 week or as soon as possible after medical treatment for their suicide attempt, and 601 (only 28% of the original sam-

ple) were reexamined after 1 year. When one combines this retention rate after 1 year with the need for randomization of treatment and control subjects in future studies, the challenge in designing outcome research in this area is quite evident, even with highly motivated researchers in dedicated centers such as in this study.

The importance of this for future research has been further emphasized by Hawton (1998), who has gone so far as to state that unless sufficient numbers are utilized, it "is a waste of scientific time and funding, and could be deemed unethical in terms of patient participation."

Those charged with responsibility for suicide prevention could be forgiven for being pessimistic following the above reviews. However, the results of such reviews not only fail to support long-held clinical beliefs, but they also ignore research methodologies other than the randomized controlled trial, the so-called gold standard. Investors are aware of the fluctuations of the price of gold, and there are fluctuations in the value of randomized controlled trials, particularly when such trials are logistically impractical. When that is the case, obstacles to elucidating a valid result need to be circumvented by other research methodologies.

Therefore, a more pragmatic approach needs to be adopted in considering other research that could give clinicians confidence in their practice to reduce suicidal behavior.

Pragmatic Evidence-Based Practice

It is logical to consider that by alleviating risk factors there should be an impact on suicidal behavior. It should be noted at this point that the words "suicidal behavior" have been used, not just "suicide" or "attempted suicide." It is acknowledged that there are some differences between these groups, but there are also major similarities and their overlapping nature has been accepted (Lester et al., 1979; Beautrais, 2001), to the extent that Ottosson (1979) stated "that they are expressions of a common suicidal process." Also included in suicidal behavior is suicidal ideation, although sometimes its importance is minimized (Goldney et al., 2001). However, it is at the very least a necessary, though not sufficient requirement for suicide, and its association with suicide attempts (Sokero et al., 2003) and suicide (Joiner et al., 2003) indicates that it is appropriate to also consider studies that have used suicidal ideation as an outcome measure.

In the last few decades there have been a number of studies using different methodologies, which have more clearly delineated and quantified important risk factors. Psychological autopsy studies have consistently demonstrated, across countries with different cultures, that 80%

to 90% of suicides had mental disorders, particularly depression and substance abuse (Cheng, 1995). Twin studies have confirmed the importance of inherited as well as environmental factors (Statham et al., 1998). Case-control studies of serious suicide attempts have demonstrated the importance of mood disorders and substance abuse (Beautrais et al., 1996). Large retrospective cohort studies have demonstrated "a strong, graded relationship to attempted suicide" of adverse childhood experiences, including emotional, physical, and sexual abuse; household substance abuse, mental illness and incarceration; and parental domestic violence, separation, or divorce (Dube et al., 2001). Longitudinal cohort analyses have shown that "vulnerability/resiliency to suicidal responses among those depressed (and those not depressed) is influenced by an accumulation of factors including: family history of suicide, childhood sexual abuse, personality factors, peer affiliations and school success" (Fergusson et al., 2003). Large population-based nested case-control studies based on Danish register data have found the strongest risks for suicide to be mental illness necessitating hospitalization, unemployment, and low income (Mortensen et al., 2000; Qin et al., 2003).

It is evident that many of these risk factors, particularly those in childhood and adolescence, are not specific for suicidal behaviors, as they are related to adult mental disorders in general (Fergusson et al., 2003). Furthermore, one does not have to invoke the risk of future suicide as a reason for addressing them. Such issues, for example childhood sexual abuse, parental domestic violence, and unemployment, are important in their own right, and they demand the attention not only of health professionals, but of the community as a whole.

Clinicians cannot influence what has happened in the past, although they may wish to lobby for social change that might influence future generations. However, in regard to the contemporaneous practice of suicide prevention, it is important to ensure that a correct perspective be maintained on the relative importance of various risk factors. In this regard Danish register studies have been particularly valuable (Mortensen et al., 2000; Agerbo et al., 2002; Qin et al., 2003), as they have used the Population Attributable Risk (PAR) statistic. This is a singularly appropriate statistic for research assessing the differing impact of various contributing factors to suicidal behavior, as it has the potential to place risk factors in perspective at the population level.

Qin et al. (2003) examined data for 21,169 suicides and 423,128 comparison subjects, and the PAR for having ever had a psychiatric admission was 40.3%, whereas those PARs for other statistically significant contributors, including unemployment, having a sickness-related absence from work, being in the lowest income quartile, and being on a disability or age pension were 2.8%,

6.4%, 8.8%, 3.2% and 10.2%, respectively. While these other issues cannot be ignored, clearly the focus of attention needs to be on those persons who have required psychiatric hospitalization. Indeed, using the same data base, Agerbo et al. (2002) emphasized that in 496 young people between 10 and 21 years of age, the strongest risk factor for suicide was mental illness, and that the effect of the parents' socioeconomic factors decreased after adjusting for family history of mental illness and suicide.

The PAR statistic has been used in other studies with broadly similar results. For example, Beautrais et al. (1996) stated that "population attributable risk estimates suggest that elimination of mood disorders would result in very substantial reductions, up to 80%, in risk of a serious suicide attempt." Beautrais (1999) also reanalyzed data from the American work on suicide of Shaffer et al., Gould et al., and Brent et al., and calculated a PAR of mood disorders for suicide of 46% for the first two studies and 37% for the third. There have also been other PAR studies, utilizing different measures of depression and suicidal ideation (Goldney et al., 2000, 2003; Pirkis et al., 2000), which have found PARs of 47%, 57%, and 39%, respectively, of depression for suicidal ideation, and 40% of depression for attempted suicide (Pirkis et al., 2000). This does not mean that other factors are not important; it simply means that other factors need to be placed in perspective when considering their contribution to suicidal behaviors in those particular populations.

It is important to acknowledge that these PAR studies have come from developed countries with similar rates of suicide, and it may well be that different results, perhaps with a greater contribution from psychosocial factors, could emerge from other countries. Indeed, it is imperative that such studies are undertaken elsewhere to allow health providers to make informed decisions when allocating resources.

Other research methodologies have also pointed to the importance of the recognition and adequate treatment of mental diseases in suicide prevention. Isaccson et al. (1999) and Marzuk et al. (1995) have emphasized the lack of congruence between the use of psychotropic medication at the time of suicide and the patterns of diagnoses made at psychological autopsy. Hulthen and Wasserman (1998) have commented on the lack of continuity of care. Waern et al. (1999) have reported on the absence of enquiry about suicidal thoughts in elderly suicides. In two large surveys of suicides in England (National Confidential Inquiry, 2001) and Australia (Burgess et al., 2000), no fewer than 21% and 20% in the respective studies were considered to have been preventable, but for poor assessment and treatment, poor staff-patient communication and relationships, inadequate supervision, and lack of continuity of care.

Such findings add weight to the view of Whitlock

(1977), who stated that “putting it bluntly, we can do a lot to prevent suicide if we make use of the medical facts associated with the behavior.” Indeed, it is sobering that such a comment is virtually identical to that of Burrows, made in 1828, that “the medical treatment of the propensity to suicide, whether prophylactic or therapeutic, differs not from that which is applicable in cases of ordinary insanity.” However, it is all too clear that this has not always occurred, and that a sense of pessimism has prevailed, in part engendered by the absence of randomized controlled trials proving the efficacy of our interventions. Nevertheless, there are intervention studies that give considerable confidence that suicidal behaviors can be prevented. The remainder of this review presents selected reports, which are by no means exhaustive, but which illustrate the diverse paths to suicide prevention.

Standard Management Practices

That standard management practices addressing the antecedents of suicidal behavior should prevent such behavior appears self-evident, but, for the reasons outlined before, the challenge is to substantiate this. Nevertheless, research has indicated that routine clinical care may be of value. For example, Hickey et al. (2001) reported that deliberate self-harm patients who left an accident and emergency department in Oxford without a psychiatric assessment not only had a greater past history of self-harm, but they were more likely to self-harm again in the subsequent year than a matched comparison group who had been assessed. Similarly, Kapur et al. (2002), in a study of six hospitals in Northwest England, noted that patients who had deliberately self-poisoned and who had not received psychosocial assessment were more likely to poison themselves again. Furthermore, they calculated that only 12 patients needed to receive a psychosocial assessment to prevent one repetition of self-poisoning, and they concluded that “if we assume that 50% of patients are assessed currently, we might prevent 7000 repeat episodes of self poisoning by complying with existing guidelines and ensuring that all patients are properly assessed.”

More specific standard treatments will now be considered under the broad headings of nonpharmacological and pharmacological approaches, following which reference will be made to several broad programs with demonstrated effectiveness.

Nonpharmacological Approaches

Methods to enhance affective contact with those who are suicidal have been practiced for the last century. Telephone

crisis services were established in the United States from as early as 1895 and 1906 (Retterstol, 1996), and from those beginnings suicide prevention centers emerged during the 1950s and 1960s in Europe, the United States, and in other parts of the world, sometimes under the auspices of volunteer organizations such as the Samaritans, Befrienders International, the International Federation of Telephonic Emergency Services (IFOTES), and Lifeline. Formidable methodological problems exist in demonstrating their efficacy, and inconsistent results have emerged (Bagley, 1968; Barraclough et al., 1977). However, a review of 14 studies by Lester (1997) demonstrated a preventive effect, “albeit small and inconsistently found.” Bearing that in mind, it is not unexpected that a recent assessment of a telephone counseling service for adolescents found significant decreases in measures of suicidality between the beginning and end of counseling sessions (King et al., 2003).

The effectiveness of the principles of befriending have been demonstrated in a remarkable project from Sri Lanka, initiated by Sumithrayo, a volunteer organization dedicated to suicide prevention (Marecek & Ratnayake, 2001). In response to suicidal behavior in rural areas, ongoing emotional support was offered to a village, with another village used as a comparison. The village with the intervention had had 13 suicides and 18 other episodes of self-harm in the 6 years before the program, but there were no examples of suicidal behavior in the subsequent 4½ years. That contrasted with the comparison village which had previously had 16 suicides and 25 other episodes of self-harm, and which had a further 3 suicides and 10 other episodes of self-harm in the next 2 years, following which the investigators extended the program to that village.

A deceptively simple form of contact has been reported by Motto and Bostrom (2001). Subjects who had attempted suicide were contacted 1 month after their suicide attempt and those who had not pursued further treatment were randomly assigned to contact and no-contact groups. The contact group received correspondence each month for 4 months, then every other month for 8 months, and then every 3 months for a further 4 years, a total of 5 years and 24 contacts per person. Over a 5-year period there was a significant decrease in death by suicide for those who had had contact when compared to the no-contact group.

Another example of enhancing ongoing contact is that of a service to prevent suicide in the elderly reported by De Leo et al. (2002). They used a Tele-Help and Tele-Check service for patients who had been discharged from the hospital. The Tele-Help component was a portable device that allowed patients to send an alarm signal if they needed help, and the Tele-check was a regular check of patients by telephone on an average of twice a week.

They reported that over 10 years there were only six suicides compared to an expected 20.86 for their population of 18,641 elderly persons, a highly significant result ($p < .001$).

More specific effective psychotherapeutic interventions date from the innovative work of Linehan, whose dialectical behavior therapy model, which involved cognitive, behavioral, and supportive psychotherapies, was demonstrated to reduce the number and severity of suicide attempts and decrease inpatient admissions for borderline patients (Linehan et al., 1991). There have also been other variations of the psychotherapeutic approach, which have been effective in carefully selected groups of borderline patients. Stevenson and Meares (1992) reported that a "coherent consistently applied" psychotherapy based on a "psychology of self" resulted in a significant reduction in self-harm in the year after therapy, compared to the year before. Bateman and Fonagy (1999, 2001) demonstrated the superiority of psychoanalytically oriented partial hospitalization over standard psychiatric treatment in reducing suicide attempts and acts of self-harm. Bohus et al. (2000), using Linehan's dialectical behavior therapy model, reported a "highly significant decrease in the number of parasuicidal acts"; and Verheul et al. (2003), also using Linehan's model in a randomized trial, found the treatment group had less self-mutilating and self-damaging behaviors than a treatment-as-usual group.

It is pertinent that these patient groups were chosen for their borderline diagnosis, rather than the suicidal behavior per se. That this may be important is illustrated by the fact that a recent multi-center randomized trial utilizing manual-assisted cognitive behavior therapy, which incorporated Linehan's (1992) concepts, found no difference in the repetition of deliberate self-harm between the experimental and treatment-as-usual groups (Tyrer et al., 2003). However, subjects were not chosen for their clinical diagnosis, but on the basis of having had a previous episode of self-harm; not requiring inpatient care; and not having psychotic or bipolar disorders or substance dependence.

Other nonpharmacological approaches include reducing media publicity and restricting access to the means of suicide. With regard to the media, Sonneck et al. (1994) reported that a sustained decrease of 75% in the number of subway suicides in Vienna occurred for 5 years following initiatives to abstain from reporting on such suicides. There have also been a number of studies that have indicated that restricting access to the means of suicide is an effective intervention. In 1972 Oliver and Hetzel in Australia noted that a decrease in suicide in women was related to the restriction on prescribing barbiturates. Kreitman (1976) reported that there was a sustained reduction in suicide rates in England and Wales

when coal gas was replaced by nontoxic North Sea gas; and in 1983 Harvey and Solomons reported that in the then 52 years that the Sydney Harbour Bridge had been in operation, 60 of the 92 suicide attempts (78 of which had been fatal) occurred in the first 4 years before a safety barrier was erected.

Legislation restricting access to firearms has also been reported to have had an impact on suicide rates in Canada (Leenaars et al., 2003), and a recent study from the USA by Grossmann et al. (2005) found that the "practices of keeping a gun locked, unloaded, storing ammunition locked, and in a separate location are each associated with a protective effect" against youth suicide.

It is also important that in the U.K. Hawton et al. (2001), using a rigorous research design, demonstrated that legislation restricting paracetamol pack sizes had "substantial beneficial effects on mortality and morbidity associated with self-poisoning using these drugs." This has clear implications for other countries where there is ready access to substances such as pesticides. Indeed, in some communities restriction of access to pesticides could well be the most important step in reducing suicide, although the challenges of introducing prevention programs in such settings has been described well by Gunnell and Eddleston (2003).

It is evident that there are a number of nonpharmacological approaches that have predominantly used before-and-after methodologies to demonstrate their effectiveness. It is probable that a common thread to these interventions is that they provide a sense of caring for those who are suicidal, even if it is in an anonymous restriction of means to suicide, which buys time for the suicidal crisis to dissipate. At the very least such approaches are consistent with what has been described in the psychotherapy literature as enhancing a sense of "connectedness to others" (Frank, 1971). It is also evident that the interpersonal interaction with those who are suicidal is likely to fulfill the therapeutic ingredients of psychotherapy of accurate empathy, nonpossessive, warmth and genuineness (Truax et al., 1971).

Pharmacological Approaches

There are a number of ways in which the effect of psychotropic medication can be examined in regard to suicidal behavior. As long ago as 1972, Barraclough in England emphasized the importance of Lithium for recurrent affective disorders when he noted that as many as a fifth of 100 suicides he examined may have been prevented by its use. Since then Modestin and Schwarzenbach (1992) in Switzerland demonstrated that a significantly higher proportion of a control group, compared to 64

former psychiatric patients who had suicided, had been receiving psychotropic drugs, and a significantly higher proportion had been on Lithium. Similarly, Marzuk et al. (1995) in the United States reported that only 16.4% of 1635 subjects who had suicided were on psychotropic medication and they commented: "Given the high prevalence of serious mental disorders among individuals who commit suicide, only a small proportion had used any of the more standard prescription psychotropic drugs at the time of death." Such findings are congruent with other research from Finland (Suominen et al., 1998) and Sweden (Isacsson et al., 1999, 2005).

These general studies have been supplemented by more specific studies involving antidepressant, mood stabilizer, and antipsychotic medications.

Antidepressants

Randomized controlled trials of antidepressants vs. placebo have demonstrated statistically significant reductions in the suicidal-ideation items of depression scales (Montgomery et al., 1995; Letizia et al., 1996) and more recently Szanto et al. (2003) have demonstrated a reduction of suicidal ideation during the course of antidepressant treatment of late-life depression. There has also been a 34 to 38-year follow up by Angst et al. (2002) of affective disordered patients, which demonstrated that "long term medication treatment with anti-depressants alone or with a neuroleptic, or with Lithium in combination with anti-depressants and/or neuroleptics significantly lowered suicide rates even though the treated were more severely ill."

Probably the most persuasive data have come from large population studies. One of the earliest was that reported by Rutz et al. (1992) of a program to enhance the recognition and treatment of depression by general practitioners on the Swedish island of Gotland. This was followed by a decrease in suicide, although there has been debate about the statistical significance of that (McDonald, 1993, 1995; Williams & Goldney, 1994). Further population data have emerged from Isacsson (2000) in Sweden, who had predicted that a five-fold increase in antidepressant use might reduce the Swedish suicide rate by 25%. A naturalistic experiment was made possible by the fact that antidepressant prescribing, particularly of serotonin specific reuptake inhibitors (SSRIs), did increase more than three fold, and the reduction in suicide correlated significantly with that. He also presented similar data from Finland, Norway, and Denmark, and concluded that the increased use of antidepressants was "one of the contributing factors to the decrease in the suicide rate." Similar findings have been reported from Australia by Hall et al. (2003), who noted that "the higher the ex-

posure to anti-depressants the larger the decline in rate of suicide," and that "their effect is most apparent in older age groups, in which rates of suicide decreased substantially in association with exposure to anti-depressants." They acknowledged that it may not have simply been the antidepressants per se, and that increased prescribing may have been "a proxy marker for improved overall management of depression." Similar findings have recently been reported from the United States (Gibbons et al., 2005).

That this decrease in suicide with increased use of antidepressants is not confined to older age groups has recently been demonstrated by Olfson et al. (2003), who found a significant negative relationship between antidepressant treatment and suicide in different regions of the United States. They noted that a 1% increase in adolescent use of antidepressants was associated with a decrease of 0.23 suicides per 100,000 adolescents each year, and concluded that their results raised "the possibility of a role for using anti-depressant treatment in youth suicide prevention efforts."

Such findings for the effectiveness of measures to treat depression having an impact on suicide are not unexpected in view of the earlier clinical risk findings, particularly those delineated by PAR analyses. Indeed, it has only been by large population studies, rather than randomized controlled trials, that the impact of treatment for depression on suicide has been demonstrated.

Notwithstanding the persuasive nature of these findings, there has been concern that the newer SSRI antidepressants could be associated with an increased risk of suicidal behavior (Healy, 2003). However, a recent report from Jick et al. (2004) has addressed this and shown in a rigorously designed study of about 160,000 patients in a General Practice Research Database that there was no difference between two older tricyclic antidepressants and two newer SSRI antidepressants in the emergence of suicidal behaviors, and that suicidal behaviors were reduced after time on the medications. In a commentary on those results, Wessely and Kerwin (2004) stated that "the results confirm that anti-depressant prescription is indeed associated with suicidal behavior, and strongly so. This simply means that anti-depressants are being prescribed for the right indication, and that they do not immediately eliminate suicide risk. That we knew." However, they added perceptively that "it is unlikely that this study alone will restore confidence," and that is particularly in relation to the use of antidepressants in young persons. In that regard Jick et al. (2004) found no person aged 10–19 years who had been on one of the antidepressant study drugs had died by suicide, although there were 15 in that age group who suicided and who had not received any antidepressant. This finding is similar to the recent report from Isacsson et al. (2005), who noted that

no SSRIs were detected in the 52 suicides under the age of 15 years in Sweden between 1992 and 2000.

It is accepted that none of these antidepressant studies can prove that they prevent suicide, but it is reassuring that the best available evidence is emerging as favoring their use.

Mood Stabilizers

Following the previously noted early work of Barraclough (1972), Coppen et al. (1990) in the U.K. reported that consistent use of Lithium in patients with affective disorders resulted in their having a cumulative mortality risk similar to the normal population, rather than having the increased mortality traditionally associated with such illnesses. Subsequently, Ahrens et al. (1993) studied 512 patients in centers in Germany and Canada and found a "meaningful reduction in mortality" occurred if patients were treated with Lithium for longer than 2 years, at which time their risk of suicide was reduced to that of the general population.

Coppen (1994) extended his earlier work and noted that a number of studies without Lithium had found that there are between 5.1 and 11.6 suicides per 1,000 patient-years in untreated unipolar and bipolar illness, whereas Nilsson (1992), Muller-Oerlinghausen et al. (1992), and Coppen (1994) demonstrated that with long term Lithium treatment there were only 1.5, 1.3, and 0.7 suicides per 1,000 patient-years, respectively.

More recent reviews have confirmed these earlier reports. Baldessarini et al. (2003) collated a number of studies with an aggregate of 16,221 patients with exposure to Lithium of 64,233 person-years and reported that the risk per 100 person-years for attempted suicide was 4.65 without Lithium vs. 0.312 with Lithium, a 93% difference, and for suicide the risk was 0.942 without Lithium vs. 0.174 with Lithium, an 82% difference. They concluded that use of Lithium in bipolar and unipolar affective disorders reduced suicidal risk "to overall levels close to general population rates." Others, including Schou (2000) and Tondo et al. (2003) have come to similar conclusions, and Muller-Oerlinghausen et al. (2003) have also noted that although Lithium probably prevents about 250 suicides per year in Germany, "rational treatment strategies most likely would demand that prescription rates be about 10 times higher."

The question of whether or not anticonvulsant mood stabilizers have suicide protective qualities has been addressed by Goodwin et al. (2003) in a retrospective cohort study of 20,638 health plan members with bipolar disorder, and both suicide and suicide attempts were significantly fewer in those treated with Lithium, compared to Divalproex (sodium valproate), an anticonvulsant and

the most commonly prescribed mood stabilizer in the United States.

None of these studies involved randomized controlled trials, but the results are compelling.

Antipsychotic (Neuroleptic) Medication

It is fair to state that there had been a sense of pessimism about suicide and schizophrenia until the observations of Meltzer and Okayli (1995) that 88 neuroleptic-resistant patients treated with Clozapine for between 6 months and 6 years (mean 3.5 years) had "markedly less suicidality" than non-Clozapine treated patients. This was noted on the basis of lower scores on the Hamilton Rating Scale for depression, attempted suicide decreased from 25% to 3.5%, the lethality of the suicide attempts that did occur was reduced, the suicidal intent was reduced, and there was a significant decrease in hopelessness. Subsequently Meltzer (1996) reported that of 102,000 patients treated for schizophrenia with Clozapine there were 39 suicides, with a rate adjusted for duration of treatment of 0.1% to 0.2% per year, which he noted was "one fourth of the rate that would have been expected based on the published annual incidence of completed suicide in schizophrenia."

Reid et al. (1998) reported similar findings from a study of 30,000 patients with schizophrenia and schizoaffective disorder, with Clozapine-treated patients having a suicide rate of 12.7 per 100,000 per year compared to the 63.1 per 100,000 per year for all patients with the disorders in the United States.

These findings led to the establishment of an ambitious randomized multi-center trial in 67 centers in 11 countries (Meltzer et al., 2003) comparing Clozapine with Olanzapine. In this study 980 patients were randomized to the treatments and nonpharmacological input was identical. Clozapine was significantly superior in reducing suicide attempts, hospitalization, and the need for emergency intervention, but the suicides were too few for statistical analysis. In a further analysis of these data, Potkin et al. (2003) demonstrated that Clozapine was more effective than Olanzapine regardless of any individual risk factor, such as substance abuse or number of previous suicide attempts. Meltzer et al. (2003) concluded that "use of Clozapine in this population should lead to a significant reduction in suicidal behaviour."

When it is appreciated that Clozapine is usually reserved for those with resistance to conventional antipsychotic medication, these results are particularly persuasive.

It should be emphasized that the pharmacological treatments described are not necessarily specific for the

prevention of suicide. Rather, they are part of the standard care that should be provided by a modern health service. Indeed, that was the conclusion of Nordentoft et al. (2004), who reported that a reduction of the suicide rate among patients with schizophrenia and related disorders in Denmark “may be due to better psychiatric treatment, reduced access to means of suicide, or improvements in treatment after suicide attempts.”

Large Population Studies

A number of governments have instituted National suicide prevention programs, but only two, one from a Western country and another from a developing country will be considered.

In 1985 Finnish health authorities inaugurated a program to lower the suicide rate by 20% over the next 10 years (Kerkhof, 1999). In fact, suicide increased initially, but then reduced to a figure about 9% below the initial level. This was the first research-based comprehensive national program in the world and involved community education about risk factors, with guidebooks for health promotion provided for schools, the armed services, and clergy, as well as the Social Services sector. It was acknowledged that there were gaps “between medical paradigms and socio-cultural paradigms in understanding and preventing suicidal behaviour” and that more attention could have been paid to reducing access to means of suicide and suicide prevention in the elderly. However, it was considered that “the project may have contributed to the reversal in the increasing suicide rate,” and that “the achievements of the project greatly outweigh its shortcomings” (Kerkhof, 1999).

A more recent national program from a developing country, Sri Lanka (previous Ceylon), has been associated with a reduction in reported suicides (De Silva & Jayasinghe, 2003). Between 1950 and 1985 the suicide rate in Sri Lanka increased six fold, and by 1995 the total number of suicides was 8,514. In 1997 a Presidential Committee was established to address the high rate of suicide, with a focus on the reduction of ready access to pesticides and the introduction of less toxic alternatives; the enhancement of medical services, including those for the management of serious mental illnesses; the discouragement of sensational media reporting; and the decriminalization of suicide. Although causality can not be claimed for any specific measure, it is reassuring that the number of suicides had reduced to 5,412 in 2000.

While such large population interventions can be criticized for their general nature and the lack of specific theoretical framework, there have been three recently published studies that have been more rigorous in their

research design, and which have produced very encouraging results.

In a cohort of over five million United States Air Force personnel, Knox et al. (2003) reported a reduction of 33% in suicide between 1990–1996 and 1997–2002 following the introduction of an 11-point community-based program to the Air Force population as a whole. This focused on removing the stigma of seeking help for psychosocial problems, enhancing mental health literacy, and changing administrative policies to facilitate access to intervention services. It is also pertinent that they reported “significant risk reductions” for accidental death, homicide, and family violence.

Positive results have also been reported by Hegerl et al. (2003), from the Nuremberg Alliance against Depression study, where a 2-year intervention campaign in Nuremberg, a city of about half a million, to inform the community about depression; train family doctors; encourage cooperation with community facilitators such as teachers, priests, and the media; and also support self-help groups; resulted in a statistically significant reduction in suicidal acts compared to Wuerzburg, which was used as a control region.

The third report was of a randomized controlled trial of enhanced management of treating depression in the elderly in primary care by Bruce et al. (2004). This study was conducted in 20 primary care practices in the Northeastern United States and was of a carefully selected group of 598 depressed persons from an initial sample of 16,708. They were allocated to a treatment-as-usual group (278) or a group (320) that received treatment from primary care practitioners using a clinical algorithm for geriatric depression, and their treatment was overseen by depression care managers, including nurses, social workers, and psychologists, with psychiatric back up. They reported that suicidal ideation resolved more quickly in those receiving the enhanced care compared to those receiving treatment as usual.

Conclusions

The majority of these studies do not fulfill the required criteria for a randomized controlled trial, which is the usual gold standard of evidence-based research. However, it bears reiteration that the very fact that suicidal behaviors have such a low base rate makes it virtually impossible, at the very least with conventionally available resources, to mount the huge studies that would be necessary to have sufficient statistical power to demonstrate differences in outcome of different treatments, even if it was ethically possible to do so.

Indeed, it is pertinent to reflect on the previously noted

study of Tyrer et al. (2003), which involved 480 patients at a number of hospitals associated with five main centers. Subjects were confined to those who had had a previous episode of self-harm, did not require inpatient care, and did not have a psychotic or bipolar disorder, or a primary diagnosis of substance dependence. It is also pertinent that 40% of the experimental group did not return for treatment! Bearing these factors in mind, even if there had been a difference between the manual-assisted cognitive behavior therapy and treatment-as-usual groups, it is doubtful whether that information would have been of much value to individual clinicians. Indeed, this is a good example of the fact that "randomized controlled trials do not necessarily reflect real-world practice or experience" (Celermajer, 2001). Furthermore, when one considers the apparent initial methodological soundness of that randomized controlled research design, with a large number of subjects in many different dedicated centers, it would appear to be difficult to justify similar such studies in the future when interventions could be implemented on the basis of other research findings.

It is now no longer acceptable to state blandly that there is no convincing evidence for the effectiveness of suicide prevention measures, or that we do not know the relative importance of certain risk factors. Considerable knowledge is available, and the enigmatic comment of T.S. Eliot, who stated "Where is the wisdom we have lost in knowledge?" is worthy of contemplation.

Consider the fact that carefully controlled, longitudinal case-control studies have identified and teased out the interrelationship between risk factors (Fergusson et al., 2003); that twin studies have confirmed the importance of both inherited and environmental factors (Statham et al., 1998; Glowinski et al., 2001; Fu et al., 2002); that PAR research has placed various risk factors in perspective; and that innovative research methodologies have demonstrated the effectiveness of a number of interventions.

It is also sobering to reflect on the observation that over 20% of suicides in association with hospitalization could have been preventable (Burgess et al., 2000; National Confidential Inquiry, 2001), and this suggests that to be seen as focusing on issues such as unemployment, with a PAR of 2.8% (Qin et al., 2003), or the impact of the media, which may be responsible for a maximum of 1 to 5% of suicides, with no recognition of the potential benefits of media campaigns (Goldney, 2001), could be interpreted by a critical observer as an attempt to deflect attention from our own responsibility in suicide prevention.

The way ahead is clear. Broad social services efforts to counteract childhood antecedents of suicidal behavior are important in their own right and may pay dividends in terms of a reduction in suicide in the future. However, for more immediate results, community approaches such as those outlined in the United States Air Force project

(Knox et al., 2003) and the Nuremberg Alliance against Depression study (Hegerl et al., 2003), and the clinical intervention offered to the elderly in the report of Bruce et al. (2004), are models that could be emulated elsewhere, and, at the individual level, standard assessment and management health care practices should be implemented for all who are suicidal.

Finally, it is acknowledged that this is a selective review. The focus has been on research from developed countries, and one can not necessarily assume that the approaches described will be universally applicable. Furthermore, the question posed by Balon (2003), after noting that the arguments in relation to SSRI's and suicidality of Healy (2003) contained "mechanisms of good propaganda," of: "Is the Evidence, as with Beauty, in the Eye of the Beholder?" could well apply to the present reviewer. Nevertheless, it is suggested that far from being pessimistic about suicide prevention, by utilizing standard management practices, as well as the knowledge gained from innovative research projects, and by putting it into practice in a manner similar to the effective interventions described, there is every reason to believe that the optimism expressed in a previous review (Goldney, 1998) has been vindicated by more recent studies, and that the unacceptable rate of suicide worldwide can be reduced.

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