

strategies. This happens despite growing evidence substantiating a much reduced life-span risk for suicide in depression than that reported in earlier investigations (Bostwick & Pankratz, 2000). Given the complexity of its pathways, the prevention of suicide, like the prevention of many types of death, requires a combination of approaches, such as public and medical education, promoting community connectedness, controlling access to means, early identification and intervention, etc.

It is certainly true that risk factors for suicide are unstable and may change over time (De Leo, 2002), but probably more important is the (mostly unexplored) interaction between risk and protective factors. This is the really crucial issue in suicide prevention (by the way, protective conditions of course counteract also the risk of ischaemic heart disease: the Mediterranean diet and omega-3-fatty acids have already convincingly underlined the role of local differences in mortality rates). And this recalls another important point raised by Dr Ravi Shankar, which refers to the local (cultural/traditional) specificity of suicidal behaviour. In countries such as China, risk factors for suicide are not dissimilar from those of Western countries – what varies is their ranking in terms of importance and expressivity (Phillips *et al*, 2002). Furthermore, it is well-known that within the same country there may be contiguous areas with largely differing suicide rates and that the same risk factors may operate differently in different social contexts.

To identify the exact components of a multifaceted prevention programme, tailored to local characteristics, greater knowledge of risk and protective factors is needed for both the psychiatric and general populations. Prevention of suicide is currently based on scant evidence. Therefore, I fully agree with Dr Ravi Shankar's view that more sound research is required. Prevention must be grounded in evidence if it is likely to have an effect on suicide mortality.

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I would like to comment on the editorial by De Leo (2002) which came to the conclusion that little is new in suicide prevention. Since nothing was mentioned about pharmacotherapeutic advances in suicide, I would like to take the opportunity to discuss recent information concerning the role of novel antipsychotics in the reduction of suicidality.

Suicide rates in schizophrenia are about 13 times greater than in the general population, and make a substantial contribution to the overall suicide statistics in the UK. Suicide rates in schizophrenia were unaffected by the advent of conventional neuroleptics. This was not because these drugs are ineffective, rather that they also come with adverse events that put patients at risk for suicide – most particularly akathisia and depression. However, there is now evidence that atypical antipsychotics – most particularly clozapine – may have antisuicidal potential. This was first hinted at by a mirror-image study by Meltzer & Okayli (1995), which suggested an 86% reduction in suicidality. Subsequently, a large epidemiological study (Walker *et al*, 1997) including data on completed suicides showed that deaths from suicide in clozapine users occurred at a rate of 39 per 100 000 patient-years compared with 222 per 100 000 patient-years in former users of clozapine. Our own UK clozapine study (Munro *et al*, 1999) confirmed this result. There are also suggestions from pivotal studies of olanzapine that suicidality is also reduced in users of this drug (Tran *et al*, 1997).

All these observations have their limitations, which led Novartis, in collaboration with the US Food and Drug Administration (FDA), to embark on a randomised controlled trial of clozapine *v.* olanzapine in the reduction of suicidality in schizophrenia (the InterSePT study), the results of which have recently been reported (Meltzer *et al*, 2003). Overall there was a 25% reduction in all key measures for suicidality in favour of clozapine. This has recently led the Psychopharmacology Advisory Committee to the FDA to recommend that this body approves suicidality in schizophrenia (not restricted to treatment resistance) as a new indication for clozapine. It is disappointing that the National Suicide Prevention Strategy for England and Wales has little to say about the role of new treatments in suicide prevention. However, in a recent modelling study of ours (Warner *et al*, 2003), which also took into account drop-out rates

and treatment failure rates, we calculated that one-quarter of the target for suicide reduction in all patients in contact with mental health services could be achieved by the broader use of clozapine in treatment resistance. If clozapine were to be approved for suicidality, 50% of all patients with schizophrenia would be technically eligible. Again, calculating in drop-outs and failures an even more substantial proportion of the national target could be met. Much is made of the rates of thromboembolism and agranulocytosis with this drug. However, in comparison with overall reduction in all-cause mortality as well as the reduction in suicidality with treatment with clozapine, such caution is not supported by the epidemiological evidence for the overall advantage of this drug (Walker *et al*, 1997).

Declaration of interest

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Fluoxetine in relapse prevention of PTSD

Martenyi *et al* (2002) suggest that fluoxetine is effective and well-tolerated in the