EBM IN ACTION

Clinical practice guidelines for depression in young people: are the treatment recommendations outdated?

Raphael T W Chan, Joseph M Rey and Philip L Hazell

ABSTRACT

- The 1997 NHMRC clinical practice guidelines for depression in young people included recommendations for treatment that need to be modified in light of more recent research.
- Changes to the guidelines should include the findings that selective serotonin reuptake inhibitors and some forms of psychotherapy are effective in treating adolescent depression.
- It is increasingly recognised that depression in adolescents often recurs and that prevention of recurrences should be a priority for research and practice.

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AS PART OF A NATIONAL PLAN to improve outcomes in clinical practice, the National Health and Medical Research Council (NHMRC) embarked on a program to produce clinical practice guidelines based on the best evidence available. These were to assist clinicians in their practice and to provide consumers with information about treatment choices. One of the first guidelines published was concerned with depression in young people aged 13–20 years,[1] acknowledging the high prevalence of this condition and the impairment it causes.[2] More than five years have elapsed since publication of the guidelines, and it is time to examine whether there is sufficient new evidence to warrant updating them. This article will focus on treatments for which there has been some clear indication of effectiveness.

Antidepressants

Selective serotonin reuptake inhibitors (SSRIs) are commonly prescribed for the treatment of depressive disorders in adults. Based on the results of one randomised controlled trial (RCT) of fluoxetine (20–60 mg daily), which found no global benefit in a small sample of adolescents,[3] the 1997 guidelines did not recommend antidepressants as the first line of treatment in young people. The guidelines stated that medication should be used only if cognitive behaviour therapy (CBT) was unsuccessful, if the depression was so severe that it interfered with the young person's capacity to engage in counselling, or if it was life-threatening.[4] This may explain the low rates of antidepressant use among depressed adolescents in Australia.[2]

Since 1997, there have been three RCTs[5-7] and one systematic review[8] supporting the efficacy of SSRIs in depressed young people. The systematic review[8] evaluated SSRIs and other, newer antidepressant drugs. It identified two RCTs of SSRIs for children and adolescents, which included the fluoxetine study[3] mentioned in the guidelines.

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In the other RCT identified,[5] 96 depressed patients aged 7–17 years were randomly allocated to receive fluoxetine (20 mg daily) or placebo. Over an eight-week period, the response rate for fluoxetine (56%) was significantly higher than that for placebo (33%).

An RCT by Keller et al,[6] published since the systematic review, has shown paroxetine to be well tolerated and effective in depressed adolescents. This multicentre study involved 275 patients aged 12–18 years with major depression, who were randomly assigned to one of three treatments: paroxetine (20–40 mg daily), imipramine (50–300 mg daily) or placebo. After eight weeks, paroxetine led to significantly greater improvement in depressive symptoms than placebo, while patients taking imipramine did no better than the placebo group. A multicentre RCT of fluoxetine[7] involving 219 depressed children and adolescents also demonstrated significant benefit for fluoxetine-treated subjects. However, a full report of this study has not yet appeared in the peer-reviewed literature, and it is not possible at present to judge its quality. If results of the clinical global rating across the fluoxetine and paroxetine studies[5,6] are combined using a fixed-effects model, participants taking medication are more likely to show improvement (odds ratio, 2.05; 95% CI, 1.24–3.38).

The evidence available refers specifically to fluoxetine and paroxetine. Open-label studies of sertraline, citalopram and fluvoxamine for adolescents with major depression or dysthymic disorder have shown positive findings.[9-13] It is likely that these other SSRIs have a similar effect, but this has not yet been proven.

The results of the paroxetine/imipramine study[6] are consistent with systematic reviews[14,15] that have found little benefit of tricyclic antidepressants in children and adolescents, apart from a small experimental study of pulse

intravenous clomipramine[16] that showed some short-term benefit in depressed adolescents. There have been small RCTs of moclobemide[17] and venlafaxine[18] in adolescents, the former showing inconclusive results and the latter showing no benefit. Thus, tricyclic drugs and other antidepressants, with the exception of SSRIs, cannot be recommended as first-line treatment for depressed young people.

Little is known about the optimal duration of treatment and the effectiveness of maintenance pharmacotherapy in young people, and further research is necessary to examine these issues.

Psychological treatments

Cognitive behaviour therapy

CBT is a short-term psychological intervention targeting thought processes and related behaviours of depressed patients. It can be delivered in the clinic or school setting to individuals, groups or families. Two meta-analyses of CBT have been published since 1997.[19,20] Their conclusions were consistent with the guidelines that CBT was a treatment of confirmed efficacy for depressed young people, although one of the meta-analyses[20] indicated that efficacy was only established for depression of mild to moderate severity. The effect sizes indicating improvement in the CBT group compared with controls were relatively large: 1.0 (95% CI, 0.8–1.2) at the end of treatment, and 0.6 (95% CI, 0.4–0.9) at one- to three-month follow-up.[19] (These effect sizes can be interpreted as the extent of difference between the average CBT-treated patient and the average control, expressed in standard deviation units. A value of 0.5 indicates a moderate effect, and 0.8 a large effect.) The odds ratio for remission in the CBT group relative to controls was 3.2 (95% CI, 1.9–5.2).[20]

Interpersonal psychotherapy

Interpersonal psychotherapy (IPT) is a short-term psychological intervention originally developed for treating adults with major depression.[21] It deals with the social and interpersonal difficulties associated with the onset of depressive symptoms, and focuses on specific problem areas such as grief, role disputes, role transition or interpersonal deficits. There is an adaptation of IPT for depressed adolescents.[22] Similar to IPT for adults in format, the adolescent version involves parents and school in the therapy. It also has the capacity to deal with issues relevant to adolescents, such as the impact of living in single-parent families.

There have been two RCTs of IPT for adolescents. In one, 48 young people with major depression were randomly allocated to either 12 weekly sessions of IPT or 12 shorter, less frequent supportive therapy sessions.[23] Treatment completion rate was higher in the IPT group (88%) than the comparison group (46%). Patients who received IPT had a greater reduction in depressive symptoms and a higher recovery rate (75% versus 46%). Another study[24] randomly allocated 71 adolescents with major depression to IPT, CBT or a waiting list to receive treatment at a later date. At the completion of treatment, those who received IPT or CBT were less depressed than the waiting-list group, with no difference between IPT and CBT.

There is also a need for studies that evaluate treatment in real-world clinical settings. They are different from efficacy studies such as those previously discussed, which employed experienced therapists and had strict criteria to exclude subjects with comorbid conditions such as conduct disorder. An open trial of IPT for adolescents with major depression[25] showed that it was feasible for novice therapists who did not have extensive training in IPT to administer the therapy under supervision.

Systemic behaviour family therapy

There has been one RCT evaluating the efficacy of family therapy for adolescents with major depression.[26] This study used systemic behaviour family therapy, which combines systemic understanding of the family with behavioural techniques to promote communication, problem-solving and resolution of conflict. One hundred and seven patients were randomly assigned to one of three treatments for 16 weeks: CBT, systemic behaviour family therapy or non-directive supportive therapy. The remission rate for the CBT group was significantly higher than that for the family therapy or supportive therapy groups. Although family therapy had greater impact on reducing family conflict and parent–adolescent relationship problems than CBT,[27] it was no better than supportive therapy in inducing remission from depression. Therefore, family therapy for depressed young people requires further empirical evaluation.

Other treatments

The guidelines considered that several other interventions could have a role in the treatment plan. These included relaxation therapy, therapeutic support groups, social skills training, exercise and electroconvulsive therapy. However, there is insufficient evidence to support their use as first-line treatments.

Many complementary treatments for depression have become popular. Their effectiveness in adults has recently been reviewed in the Journal.[28] Of these, St John's wort has been the most thoroughly researched. There is evidence to support its use in adults with mild to moderate depression.[28] However, more recent trials have cast doubt on its effectiveness for treating major depression in adults.[29,30] It is not known whether these treatments are effective for adolescents with major depression.

Prevention of recurrences

The guidelines dedicated one chapter to the prevention of depression, but there was little mention of prevention of recurrences. Remissions and recurrences are so common in people with depression that many experts suggest that depression should be treated as a chronic illness.[31] In a two-year follow-up study,[32] 83% of 104 depressed adolescents treated with one of three forms of psychotherapy had

Summary of the 1997 National Health and Medical Research Council recommendations for treating non-bipolar major depression in young people[1]

- Cognitive behaviour therapy (CBT) was the treatment of first choice (E1*).
- Other treatments considered to have a possible role in the treatment plan were relaxation therapy (E1), therapeutic support groups (E31), social skills training (E31), interpersonal psychotherapy (IPT) (E33), family therapy (E4), and exercise (E4).
- Pharmacological treatment was not recommended as a first-line therapy. However, it could be considered when first-line treatments had been unsuccessful. In such cases, selective serotonin reuptake inhibitors (SSRIs) might be the treatment of choice (E4).
- Electroconvulsive therapy (ECT) might be a useful treatment in young people with severe depression that did not respond to appropriate trials of other treatments (E4).

Proposed changes to the previous recommendations

- CBT is one of the treatments of first choice (E1). However, CBT may be more appropriate for mild to moderate cases of major depression. There is growing evidence that other psychotherapies, such as IPT, are also effective (E2).
- SSRIs, particularly fluoxetine and paroxetine, should also be considered as a first-line treatment (E1). These drugs may be particularly appropriate when the skills and resources required for CBT or other psychological interventions are unavailable, or when the depression is severe.
- There is inconclusive evidence to support the use of other types of drugs (including tricyclic antidepressants) and herbal treatments.
- The recommendation about ECT should remain.

* Levels of evidence graded according to the NHMRC classification.[1]

recovered after an average of eight months. However, 38% of these had a recurrence on average four months after recovery. Although CBT was associated with earlier improvement, it did not confer any long-term advantage over family or supportive therapy with regard to rates of remission, recovery, recurrence, or level of functioning. Preventing recurrence is therefore an area of major clinical concern, although the evidence about how to achieve this is lacking.

Implications for the guidelines

There have been substantial advances in the treatment of depression in young people in the past five years. These advances would warrant changes in the NHMRC guidelines that could have an impact on clinical care (see Box). The main change is that pharmacological treatment has become an evidence-based option for practitioners managing young people with depression. For example, a general practitioner may choose to prescribe an SSRI after careful clinical assessment and discussion with the patient and parents about its benefits and potential side effects. This may be the best course of action when the GP lacks the resources to provide structured psychological treatment and there is substantial delay or difficulty in referring the patient to an appropriate mental health professional.

Another change is that CBT, although the best researched, is not the only effective psychotherapy. GPs and other healthcare professionals with an interest in counselling or psychotherapy should consider acquiring skills in CBT or IPT. As the full form of CBT requires considerable training, a modified, briefer version of CBT is recommended by the NHMRC for GPs.[4] IPT is a relatively new intervention that is not yet widely practised in Australia.

A further issue is that preventing recurrences increasingly appears to be a critical aspect in the management of depression in young people.[33] Too little is known about the best way to achieve this, and prevention of recurrences will need to be the focus of research.

It is clear that treatment guidelines need to be updated regularly. The question is how frequently revisions should occur to obviate the risk of their becoming guidelines for suboptimal practice. In the case of depression in young people, a period of five years seems appropriate. Furthermore, authors of guidelines should consider presenting them in a more concise format and in electronic form.

Competing interests

JMR was a member of the group that prepared the guidelines. PLH has been paid a fee by Pfizer, the manufacturer of sertraline, for speaking to GPs about the evidence for the treatment of depression in young people.

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OBITUARY

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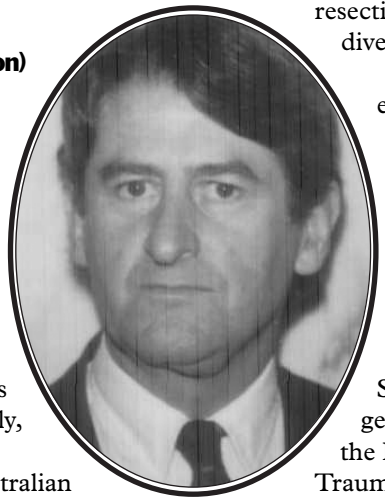

THERE WERE MANY FACETS to Peter Ryan's busy life. He was a family man, surgeon, scientist, teacher and serviceman. Born on 25 November 1925 in Dookie, Victoria, to farming parents, he was the eldest of four boys. He was dux of Assumption College, Kilmore, and studied medicine at Melbourne University. He graduated in 1948 and was a Resident Medical Officer at St Vincent's Hospital. In 1950, he married Margery Manly, an Arts graduate.

Peter served as a Major in the Royal Australian Army Medical Corps in Japan and Korea (1953–1954), then worked for a number of years in England. After obtaining his Fellowship of the Royal College of Surgeons, he spent three years at the Leicester General Hospital.

Upon his return to Australia in 1960 he joined the surgical staff at St Vincent's Hospital, Melbourne. In 1972, the Ryan Unit was established, with Peter as the Inpatient Surgeon. It later became the Department of Colon and Rectal Surgery, with Peter as its first Director. He retired from St Vincent's in 1990.

Peter had a keen intellect and an inquiring, even restless, mind. His laboratory work included studies of the effects of a proximal colostomy on bowel anastomoses. In 1986, his Hunterian address to the Royal College of Surgeons was on diverticular disease. He was the first to advocate immediate resection (with anastomosis) in selected cases of diverticular perforation.

Peter was keen to share Australian surgical expertise with medical colleagues in Asia. In 1965–1966, he led a St Vincent's surgical team to Long Xuyen, in Vietnam. He also established a program of visiting Fellows from Japan and Indonesia, and lectured in Kuala Lumpur and Jakarta. He was the first Honorary Fellow of the Indonesian Surgical Association.

Peter was President of the International Society of University Colon and Rectal Surgeons (1986–1988) and an original member of the Royal Australasian College of Surgeons' Road Trauma Committee, which was responsible for the introduction of compulsory car seatbelts.

His knowledge of anatomy and ability to sketch clearly made him a popular teacher. He was proud of his small red book entitled *A very short textbook of surgery*, which ran to several editions and was translated and widely used in China. He was an author of over 50 journal articles.

Peter and Margery raised 10 children and, despite his busy professional and academic schedule, he instilled in them his love of literature and music. Three of his children — Rowena, Jeremy and Roderick — followed him into medicine.

Peter was a pioneer in colorectal surgery and was awarded the Medal of the Order of Australia in 2002, shortly before his death on 3 June 2002.

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