College Psychology
Mrs. Lia
elia@nfschools.net

Remind : Text 81010, @ee3hb6b

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Article #1

Treatment of Bipolar Disorder in Children and Adolescents

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Treatment of Bipolar Disorder in Children and Adolescents

[Special Section: Bipolar Affective Disorder in Children and Adolescents]

Kafantaris, Vivian MD

PHARMACOLOGICAL TREATMENT OF MANIA

Lithium

Lithium remains the treatment of choice for acute mania and prophylaxis in adults. The efficacy of lithium in adult mania was established by four placebo-controlled crossover studies with treatment duration of 7 to 14 days (Goodwin et al., 1969; Maggs, 1963; Schou et al., 1954; Stokes et al., 1971) [46,65,92,97]. Response rates of approximately 75% to lithium and 40% to placebo were reported (Stokes et al., 1971) [97]. A recent large study, the first to use lithium in a parallel groups design, reported a response rate of 49% to lithium and 25% to placebo (Bowden et al., 1994) [10]. Spurred by a significant (and possibly increasing) rate of nonresponse to lithium among bipolar adults, placebo-controlled studies of alternative medications such as carbamazepine, valproate, clonazepam, and clonidine were undertaken. There also have been parallel group comparisons of lithium with neuroleptics (for review see Goodwin and Zis, 1979) [47], of carbamazepine with neuroleptics or lithium (for review see Small, 1990) [93], and of valproate and lithium (Bowden et al., 1994; Freeman et al., 1992) [10,34].

In contrast with the research on adults, there are no methodologically sound, controlled studies on which to base treatment decisions for bipolar children and adolescents. Efficacy in adults cannot be taken as evidence of efficacy in children and adolescents. Tricyclic antidepressants, for example, were not superior to placebo in the treatment of childhood or adolescent depression (reviewed by Ambrosini et al., 1993) [3].

The only two comparisons of lithium and placebo in bipolar children (DeLong and Nieman, 1983; McKnew et al., 1981) [26,68] were based on very small samples in crossover designs. McKnew and colleagues (1981) [68] studied lithium response in six children with heterogeneous diagnoses who had a lithium-responding parent in a double-blind multiple crossover study lasting 16 to 18 weeks. Lithium, at serum levels of 0.8 to 1.2 mEq/L, was superior to placebo only in the two children, aged 8 and 12 years, who met adult criteria for bipolar disorder, mixed phase, by modified Research Diagnostic Criteria (RDC). DeLong and Nieman (1983) [26] studied lithium response in 11 children, aged 6.3 to 13.5 years, "with symptoms suggesting manic-depressive illness" in a double-blind, placebo-controlled crossover study lasting 3 weeks. For inclusion in the study, the child had to be a known lithium responder with more than two previous episodes in 2 years. A family history of major affective disorder also was required. Doses of lithium ranged from 600 to 1,200 mg/day with blood levels from 0.3 to 1.3 mEq/L (mean, 0.6 mEq/L). Subjects tended to improve when they were taking lithium and deteriorate while they were taking placebo. Parental ratings were the sole outcome measure.

In adolescents, the only placebo-controlled trials of lithium are ongoing. Two involve outpatients, one inpatients. A preliminary report from one study, of lithium in substance-dependent bipolar adolescents, is encouraging (Geller et al., 1992) [39]. However, the main focus of this study, which is sponsored by the National Institute on Drug Abuse, is on whether lithium treatment will reduce substance use in this population, although effect on mood is measured also. Subjects may be bipolar (in a manic or depressed phase), or unipolar with "purported predictors" of bipolarity. The other outpatient study, funded by the National Institute of Mental Health (NIMH), is a multicenter, double-blind, placebo-controlled discontinuation study in bipolar adolescents on lithium maintenance (principal investigators: M. Keller, N. Ryan, and M. Strober). The NIMH-funded inpatient study addresses the treatment of acute mania (principal investigator: V. Kafantaris).

Two large open lithium treatment studies suggest that lithium is efficacious in bipolar children and adolescents. DeLong and Aldershof (1987) [25] reported on long-term treatment of bipolar outpatients, the majority of whom were under age 14 years. They found that 45 (73.7%) of the 59 bipolar children who continued to take lithium for more than 2 months were treated successfully, a rate similar to that reported in early studies of adults. Over the long run, 39 (66%) of 59 bipolar children benefited. The response rate did not differ for the 48 children under age 14 years (mean 9.4 years, range 3.1 to 13.9 years) from that for the 11 older adolescents (mean age, 16.4 years, range 14.3 to 20 years). The other large open treatment study involved 50 hospitalized, acutely manic adolescents, aged 13 to 17 years (Strober et al., 1988) [100]. Although its main focus was to examine the family history of adolescent bipolar probands, response to lithium treatment was reported. Dosage of lithium was titrated to achieve a serum lithium level in the range of 0.9 to 1.5 mEq/L. Psychoactive medications, including carbamazepine and neuroleptics, were administered concurrently with lithium in some patients. Overall, 34 (68%) of the 50 subjects showed a good response after 6 weeks of treatment. It is not known how many might have responded to lithium alone. Of interest is a decreased response rate in those with an Axis I diagnosis before the age of 12 years. Only 6 (40%) of 15 improved, in contrast with 28 (80%) of 35 in the group who first exhibited psychiatric symptoms in adolescence. The childhood diagnoses in 12 of the 15 subjects were attention deficit disorder with hyperactivity plus conduct disorder. The issue of whether these disorders are actually part of a bipolar prodrome remains unresolved (see Akiskal, 1995; Carlson, 1995) [1,17]. The group with the earlier psychiatric diagnoses also tended to have a greater familial loading for bipolar disorder, but did not differ from the others in lithium dosage or plasma concentration, baseline severity ratings, including psychotic symptoms, or use of supplementary neuroleptics.

The only effort on the efficacy of lithium prophylaxis was a naturalistic study of 37 bipolar adolescents who were stabilized while taking lithium and told to continue to take the medication throughout adolescence (Strober et al., 1990) [101]. During the 18-month follow-up period, 13 (35%) of the 37 adolescents were no longer compliant with lithium treatment, as determined by subtherapeutic serum lithium levels. Of those 13, 12 (92.3%) had a relapse compared to 9 (37.5%) of 24 who continued to take lithium (Strober et al., 1990) [101]. The relapse rate, despite good compliance, is similar to the 33% failure rate in adults (Prien and Potter, 1990) [81]. No systematic studies address the treatment of such breakthrough episodes.

The lithium resistance associated with mixed and rapid cycling mania in adults (reviewed by Prien and Potter, 1990) [81] also has been reported in children and adolescents, but all reports are based on uncontrolled studies. Himmelhoch and Garfinkel (1986) [48] found 23 of 46 lithium-resistant patients to be between the ages of 12 and 19 years. They noted an association between neuropsychiatric disorders, mixed mania, and lithium resistance in these bipolar adolescents; a majority required "complex pharmacologic treatment programs" consisting of adjunct treatment with carbamazepine and/or other medications. Hsu (1986) [50] reported that three of seven first-episode bipolar adolescents failed to respond to lithium after 28 days of treatment; their serum lithium levels were greater than 1.0 mEq/L. Carbamazepine proved useful in two of these patients. Clinical descriptions gave no indication of mixed mania. Rapid cycling (more than four mood episodes per year) was described

in four children, aged 11 to 12 years, all with a mild mental handicap (Full Scale IQs 68 to 80). Only two responded to treatment with lithium. The two nonresponders had more frequent mixed episodes (Jones and Berney, 1987) [53].

Comorbidity with personality disorder also has been associated with decreased responsiveness to lithium in adolescents and increased likelihood of postdischarge neuroleptic treatment (Kutcher et al., 1990) [60]. None of the 7 bipolar adolescents with a comorbid personality disorder, but 6 (46%) of 13 without a personality disorder, were lithium responders. The two groups did not differ in age at onset, presence of rapid cycling, substance abuse, alcohol abuse, or suicide attempts. However, other factors such as severity of illness, which could account for the differential response, were not assessed. Furthermore, the authors acknowledge some difficulty with distinguishing borderline personality disorder from incomplete recovery from a manic episode. There is no well-established correlation between the presence of a personality disorder and response to lithium in adult mania (Goodwin and Jamison, 1990) [45].

Substance dependence and conduct disorder are common comorbid conditions in bipolar children and adolescents. As noted above, the ongoing work of Geller et al. (1992) [39] on lithium treatment of bipolar adolescents with comorbid substance dependence is promising. Lithium also is an effective treatment for children with conduct disorder characterized by explosiveness and aggression (Campbell et al., 1984b, 1990, 1995) [15,16,12], so comorbidity with this particular profile of conduct disorder is unlikely to decrease responsiveness to lithium.

Lithium carbonate has been used to treat a variety of childhood disorders (for review see Alessi et al., 1994, and Campbell et al., 1984a) [2,13]. In large placebo-controlled studies of children with conduct disorder with a profile of aggressiveness and explosiveness, for example, lithium has been used safely with careful monitoring. No changes in renal, thyroid, or cardiac function or other side effects were observed in short-term or long-term (more than 6 months) lithium administration (Campbell et al., 1984b, 1990, 1991, 1995) [15,16,14,12]. One case of mild thyroid enlargement without hypothyroidism was reported after 4 years of treatment in an 11-year-old boy (DeLong and Aldershof, 1987) [25]. Weight gain, stomachache, vomiting, headache, and tremor were the most common untoward effects associated with short-term administration of lithium in children, as they are in adults (Campbell et al., 1984a,b, 1990, 1991; Reisberg and Gershon, 1979) [13,15,16,14,84]. All untoward effects disappeared with decrease of dosage or discontinuation of lithium. Within the age range of 6 to 12 years, however, the younger children tended to have more side effects than the older children (Campbell et al., 1991) [14].

There is little information about untoward effects of lithium in adolescents. From the larger studies of lithium (DeLong and Aldershof, 1987; Strober et al., 1988) [25,100] there are no reports of side effects. Long-term effects of lithium on kidney function are of concern (for review, see Reisberg and Gershon, 1979) [84]. However, renal function was reportedly unimpaired in four adolescents who received lithium for 3 to 5 years (Khandelwal et al., 1984) [58]. Also, a concern for females of childbearing age is the risk of cardiovascular and other anomalies in infants with lithium exposure in utero during the first trimester (Weinstein and Goldfield, 1975) [103]. A recent review found this risk to be much lower than previously reported, but still several times greater than in the general population (Cohen et al., 1994) [21].

Adverse effects of medication on cognitive functioning are of great concern in children and adolescents. Lithium has been reported to lower qualitative performance scores on the Porteus mazes in children with aggressive conduct disorder (Platt et al., 1984) [78]. However, this effect may have been due to lithium-induced tremor. Carlson and colleagues (1992) [18] studied lithium effects in a heterogeneous group of children, most of whom were comorbid for bipolar disorder and a disruptive behavior disorder. They found no evidence of impaired attention, cognitive functioning, or learning.

Neuroleptics

It has been suggested that adolescents with mania may have more psychotic and "schizophreniform" symptoms than adults (Ballenger et al., 1982; Joyce, 1984; Rosen et al., 1983) [5,54,90]. Coadministration of neuroleptic medication and lithium is safe (Baastrup et al., 1976; Goldney and Spence, 1986) [4,43] and common in clinical practice. Despite early case reports suggesting the presence of a toxic interaction between lithium and neuroleptics (Cohen and Cohen, 1974; Spring, 1979) [22,95], large, comparative (albeit retrospective) studies found no greater incidence of adverse effects from their concurrent administration than from either drug alone (Baastrup et al., 1976; Goldney and Spence, 1986) [4,43].

However, there is no definitive evidence that the addition of neuroleptics is necessary to treat psychotic symptoms associated with mania in children and adolescents. From small open trials there is preliminary evidence that lithium alone is effective in treating hallucinations and delusions. Full resolution of mood-congruent delusions and hallucinations within a mean of 11 days was reported from an open trial of lithium alone in 10 psychotic manic children, aged 6 to 12 years (Varanka et al., 1988) [102]. Horowitz (1977) [49] reported on lithium response in eight manic-depressive adolescents, aged 15 to 18 years. All eight had delusions and five had hallucinations. All symptoms responded to lithium alone within 5 to 14 days. There also is evidence that psychotic symptoms in adult mania, and schizoaffective-mania, respond to lithium alone (reviewed by Goodnick and Meltzer, 1984) [44], though, in some studies, achievement of "comparable remission" may take significantly longer for schizoaffective than manic patients (4 weeks or more, as compared to 2 weeks, respectively).

There is an increased risk of tardive dyskinesia in mood-disordered patients treated with neuroleptics (Kane, 1988, 1991; Mukherjee et al., 1986) [56,57,74]. Due to longer lifetime neuroleptic exposure, children with bipolar disorder may be especially vulnerable. In a prospective long-term study, autistic children, aged 3.4 to 6.7 years, were given individualized doses of haloperidol for 6 months and then switched to placebo for 1 month (Malone et al., 1991) [66]. Twenty-nine (27.9%) of 104 children experienced a dyskinesia, most upon drug withdrawal, but all dyskinesias were reversible (the longest in duration was 7.5 months.) There is no information on the long-term use of neuroleptics in older children with other diagnoses.

Anticonvulsants

The anticonvulsants carbamazepine and valproic acid are used frequently as alternatives or adjuncts to lithium treatment in clinical practice. It has been suggested that anticonvulsants may be more effective than lithium in mixed mania and rapid cycling (Himmelhoch and Garfinkel, 1986) [48], but no studies in adults have yet demonstrated their superiority (McElroy et al., 1992) [67]. Garfinkel and colleagues (1985) [37] reported on a series of 19 treatment-resistant bipolar adolescent patients (11 with acute mania and 8 with mixed disorder) with excellent response to the combination of lithium and carbamazepine. Valproic acid has been used in open studies of hospitalized manic adolescents in conjunction with other psychoactive medications (Papatheodorou and Kutcher, 1993; West et al., 1994) [77,106].

Carbamazepine has been used to treat behavioral disorders in a large number of children and adolescents (Remschmidt, 1976; for review, see Evans et al., 1987) [86,30], including conduct disorder with a profile of explosiveness and aggression (Kafantaris et al., 1992) [55]. Behavioral toxicity (Pleak et al., 1988) [79] and hematological adverse effects in children have been reported (Evans et al., 1989) [29]. Valproic acid is less well-studied for behavioral disorders in children, possibly because of its association with fatal hepatotoxicity (Dreifuss et al., 1987) [27]. As with lithium, an increased incidence of congenital anomalies has been reported in the offspring of women who took carbamazepine (Jones et al., 1989) [52] or valproate (Lindhout and Schmidt, 1986; Robert and Guibaud, 1982) [64,89] during pregnancy.

Benzodiazepines

The high-potency benzodiazepines have been studied in adults as alternatives to neuroleptics for the acute management of agitation and insomnia in mania (Lenox et al., 1986, 1992; Modell et al., 1985; Pope et al., 1991) [61,62,70,80] and psychotic agitation (Battaglia et al., 1992; Bodkin, 1990) [6,9]. Lorazepam has been the best-studied. Two recent controlled studies with large samples found no difference between lorazepam and haloperidol in magnitude of response or time to response when used as an adjunct to lithium treatment (Lenox et al., 1992) [62] or used to reduce psychotic agitation in the emergency room (Battaglia et al., 1992) [6]. Lorazepam administration is considered safe in children and adolescents (Relling et al., 1989) [85].

Electroconvulsive Therapy

Electroconvulsive therapy (ECT) is rarely used in children and adolescents. The recent literature on the use of ECT to treat mood disorders in children and adolescents consists of case reports (for review see Bertagnoli and Borchardt, 1990) [8]. ECT was reported to be successful for eight of nine patients, aged 5 to 15 years, treated for mania; for two rapid cycling adolescents, aged 15 and 18 years, and all 11 depressed adolescents, aged 12 to 18 years. The renewed interest in ECT to treat adult mania (Small et al., 1988) [94] may encourage systematic research on the safety and efficacy of ECT, particularly for the acute treatment of severe mania, in children and adolescents.

PSYCHOSOCIAL TREATMENT OF MANIA

Open and controlled studies of psychosocial treatments for depression in children and adolescents have begun to appear in the literature, but none for mania. Behavior in mania tends to be much more disruptive and judgment to be more severely impaired than in depression. Consequently, unless a child is hospitalized, psychosocial treatments of mania are used adjunctly in acute episodes and, after their resolution, as part of maintenance treatment. Interpersonal psychotherapy (Klerman et al., 1984) [59] has been adapted for use in adult bipolar patients (Frank et al., 1990) [33] and depressed adolescents (Moreau et al., 1991; Mufson et al., 1993, 1994) [71,72,73]. It will have to be modified further for use with bipolar adolescents.

The high recurrence rate of mood disorder (37.5%), despite adherence to a regimen of lithium prophylaxis (Strober et al., 1990) [101], makes adjunctive psychosocial treatments, which may reduce the risk of recurrence, very attractive. Family factors in adult bipolar patients have been shown to influence rate of relapse (Miklowitz et al., 1988) [69] and level of social support to influence long-term outcome (O'Connell et al., 1985) [75]. Psycho-educational family intervention that focuses on stress reduction and provides follow-up care, developed for families of hospitalized adults with mood disorders (Clarkin et al., 1990) [20], could be modified for use with families of children and adolescents with mania.

Group therapy has been reported to decrease relapse and rehospitalization rates in adult mania (Prien and Potter, 1990) [81], but there are no controlled studies of its use in any age group. Given the importance of peer groups to young people, this approach deserves exploration. Adjunct psychosocial treatments that help these young patients and their families to cope with the disruptiveness of bipolar illness, improve social functioning after the episode remits, and maintain and prolong remissions warrant study.

PHARMACOLOGICAL TREATMENT OF BIPOLAR DEPRESSION

No data are available on the treatment of depression in children or adolescents who are bipolar or at high risk for bipolar disorder. A bipolar course ensues in 8.6% to 20% of depressed adolescents (Strober and Carlson, 1982; Strober et al., 1993) [98,99]. Predictors of bipolarity in adolescents include rapid onset of the episode, psychosis, psychomotor retardation, multigenerational family history of affective disorders, and hypomanic response to treatment with tricyclics (Strober and Carlson, 1982) [98]. In a 24-month follow-up of 58 adolescents (18 psychotic, 40 nonpsychotic) who were hospitalized because of

major depression, 5 (28%) of 18 psychotics, but none of the nonpsychotics, had switched into mania. In a nortriptyline study of prepubertal depression, 34% of the subjects had a family member with mania (Geller et al., 1989) [38]. During follow-up of the prepubertal sample, it was noted that the 8 (14.8%) of 54 children who developed mania did so during or after treatment with a tricyclic antidepressant (Geller et al., 1993) [42]. It is still not known whether tricyclic use increases the risk of switching into mania or developing rapid cycling. ECT is an effective, but little-used alternative treatment (Bertagnoli and Borchardt, 1990) [8], particularly for severe, delusional depressions. Geller and colleagues are currently conducting the first study that specifically evaluates the treatment of prepubertal bipolar depression, comparing lithium to placebo for the treatment of depression in outpatient children, aged 6 to 12 years, who are bipolar or have a multigenerational family history of bipolar disorder. However, preliminary results from the first 20 subjects (12 assigned to active treatment, 8 to placebo) showed no difference in improvement between the two treatment groups as measured by the Children's Global Assessment Scale (Geller et al., 1994) [40].

PSYCHOSOCIAL TREATMENT OF DEPRESSION

Brief, reproducible psychosocial treatment, including individual, group, and family treatment, deserves further study. The development of psychosocial therapy for depressed children and adolescents is very important, given the lack of proven efficacy for pharmacotherapy in this population and the tremendous impact of family and peers on children's functioning. Robbins and colleagues (1989) [88] reported that 47% of 38 hospitalized adolescents with major depression responded to 6 weeks of psychosocial treatment alone. Predictors of response to psychosocial treatment alone included nonmelancholic subtype and suppression on the dexamethasone suppression test.

Interpersonal psychotherapy (Klerman et al., 1984) [59] and cognitive therapy (Beck et al., 1979) [7], developed for the treatment of depression in adults, have been adapted for depressed adolescents (Moreau et al., 1991; Mufson et al., 1993, 1994; Wilkes and Rush, 1988) [71,72,73,107]. For bipolar depressed children and adolescents, who have a higher incidence of delusional thinking and psychomotor retardation than unipolar depressed children, this form of therapy may need additional modifications for use during acute episodes.

Controlled studies of psychosocial treatment of childhood and adolescent depression have shown significant improvement relative to the wait list controls, but little difference in efficacy between active treatments. For example, self-control and behavioral problem-solving therapy were equally efficacious in 29 moderately to severely depressed children, aged 9 to 12 years (Stark et al., 1987) [96]. Both cognitive-behavioral therapy and relaxation training were effective treatments for 30 adolescent outpatients with symptoms of moderate depression (Reynolds and Coats, 1986) [87]. A shortcoming of these early studies is that subjects were not given standardized diagnoses.

A recent open clinical trial of interpersonal psychotherapy for adolescents with 14 depressed adolescents (12 with major depression) used a structured interview for diagnosis and repeated assessments with other commonly used rating instruments for depression. The results were promising, and a randomized, controlled trial is planned (Mufson et al., 1994) [73].

Comparisons of two types of group therapy, social skills training and therapeutic support, in 66 adolescent outpatients (83% female) with major depression (88%) or dysthymia (12%) found an unexpected short-term advantage for therapeutic support, but no differences at 9-month follow-up (Fine et al., 1991) [31]. In a well-designed study of 59 depressed adolescent outpatients (49% with DSM-III major depression, 7% RDC minor depression, and 44% RDC intermittent depression), two versions of a cognitive-behavioral group intervention, the "Coping with Depression Course" (one version involved an additional group for parents of the depressed adolescent), were superior to the wait list controls, and improvement was maintained at 2-year follow-up (Lewisohn et al., 1990) [63]. However, at the end of the treatment protocol, a significant number of adolescents continued to

meet entry criteria for the study (52.4% with parent groups and 57.1% adolescent only). From the wait list condition, however, 94.7% remained ill. There was a trend for greater efficacy when a parent was involved in treatment, and further studies that include joint sessions for the depressed teenager and their parents are planned.

Systematic study of family therapy in childhood and adolescent depression is sorely lacking. A brief family treatment model for adolescent suicide attempters and their families called Successful Negotiation Acting Positively (SNAP) has been described and is being tested in a large open trial (Rotheram-Borus et al., 1994) [91].

To delineate the "active ingredient" in psychosocial therapy, studies should include a control condition with therapist contact, so that a "placebo" response can be ruled out. It may be that much larger sample sizes will be required to detect differences between active treatments.

DISCUSSION

In summary, there are no controlled studies with adequate sample size of pharmacological or psychosocial treatments of bipolar disorder in children and adolescents. Ongoing studies of pharmacological treatment of bipolar disorder include two placebo-controlled trials of lithium in adolescent outpatients and one study of lithium in prepubertal depressed children who are bipolar or have a strong family history of bipolar disorder. Response rates to lithium of manic children and adolescents in open studies overall appear similar to the 75% rate reported in the early adult studies of lithium. Factors reported to contribute to lithium resistance in this age group include the presence of an Axis I diagnosis before the age of 12 years (Strober et al., 1988) [100], mixed states (Himmelhoch and Garfinkel, 1986) [48], and the presence of a personality disorder when euthymic (Kutcher et al., 1990) [60]. Case reports suggest that ECT may be effective for treating mania and depression in children and adolescents.

Psychosocial treatments are necessary to address problems in functioning within the family, at school, and with peers (Puig-Antich et al., 1993) [82]. Individual and group therapies are being developed and tested for children and adolescents with depression, but not for mania. The development and study of family therapy in this population lags behind other psychosocial treatment modalities.

Clearly, there is a great need for the critical assessment of currently available treatments for bipolar disorder in children and adolescents. As a first step, the efficacy of lithium, widely used in clinical practice, needs to be assessed under double-blind and placebo-controlled conditions. Subsequently, alternatives and adjuncts to lithium need to be explored for the patients who do not respond to lithium alone. A placebo arm also remains important in this episodic disorder, because one must control for the possibility of spontaneous remission of symptoms, reported to range from 22% (Janicak et al., 1989) [51] to as high as 40% in adult mania (Stokes et al., 1971) [97]. No information is available about spontaneous or placebo-induced remission of mania in children or adolescents.

It is important to explore the possibility that lithium alone may be adequate to treat all symptoms, including delusions and hallucinations, associated with mania in children and adolescents. The report from the NIMH Workshop on Treatment of Bipolar Disorder that focused on adults stated that ". . . while it is clear that neuroleptics are helpful in managing acute mania, it would be helpful if there were research-generated guidelines for identifying patients who can be treated with lithium alone. Such guidelines would protect patients from unnecessary risks associated with neuroleptic treatment" (Prien and Potter, 1990, p. 410) [81].

There is an increased risk of tardive dyskinesia in mood-disordered patients treated with neuroleptics (Kane, 1988, 1991; Mukherjee et al., 1986) [56,57,74], and patients with childhood onset of bipolar disorder may be especially vulnerable because of longer lifetime neuroleptic exposure.

The methodology for clinical trials of medications in bipolar children and adolescents has advanced in recent years. For subject selection, structured diagnostic interviews have identified previously undiagnosed bipolar disorder in 5 (29%) of 17 adolescent inpatients (Gammon et al., 1983) [36] and 3 of 10 consecutively hospitalized adolescents with psychotic features during the Diagnostic Interview Schedule for Children (DISC 2.1) field trial (Fisher et al., 1993; Kafantaris, unpublished data) [32]. Comorbidity with other Axis I diagnoses could also be identified with standardized diagnostic instruments such as the Schedule for Affective Disorders and Schizophrenia for Children-Present Episode (Chambers et al., 1985; Puig-Antich and Ryan, 1986) [19,83] and Epidemiologic Version (Orvaschel and Puig-Antich, 1987) [76]. The Mania Rating Scale (Young et al., 1978) [108] has been studied for its ability to differentiate prepubertal mania from attention-deficit hyperactivity disorder (Fristad et al., 1992) [35]. Dose prediction tools are available for the rapid and safe attainment of therapeutic lithium levels based on the child's weight (Weller et al., 1986) [104] or serum level 24 hours after a single 600-mg dose (Cooper et al., 1973; Cooper and Simpson, 1976; Geller and Fetner, 1989) [23,24,41]. Suggested predictors of a decreased probability of response to lithium also need to be examined. However, to ensure representative samples of prepubertal or adolescent mania, subjects with mixed mania and rapid cycling should be included in initial studies. Appropriate measures to capture any special features (e.g., depressive symptoms) during the episode should be included. If controlled data from these subgroups suggest decreased lithium responsiveness, subsequent studies would be warranted to evaluate this question further and to test adjunct and alternative treatments. Promising adjunct and alternative treatments from the adult literature include carbamazepine and valproic acid. The role of neuroleptics and high-potency benzodiazepines needs to be further defined.

The methodology for controlled study of psychosocial treatments in this population has been advanced by the development of treatment manuals, procedures to ensure the therapist's compliance with the treatment protocol, the use of standard diagnostic practices, and the use of contact-control conditions. Adjunct psychosocial treatments to help patients and their families cope with the disruptiveness of bipolar illness, improve functioning between episodes, and maintain and prolong remissions need to be studied. Finally, studies defining the efficacies of various psychosocial and pharmacological approaches, separately and in combination, are needed. In summary, much work remains to be done to address the treatment needs of children and adolescents with bipolar disorder.

ARTICLE #2

BIG BOYS DO CRY; Peer pressure, gaming addiction, social media, knife crime has there ever been a more challenging time to be a teenage boy - or the parent of one? Sally Williams reports main photographs: maud fernhout.

Date: Dec. 21, 2019

From: Daily Mail (London, England)

Teenage boys have always had to struggle with the discrepancy between how they are supposed to be - strong, stoic, only interested in one thing (sex) - and what they are actually like. But these are particularly tumultuous times: 25 per cent of 16- to 18-year-old boys are said to experience mental health problems at least once a week, while the number of teenage boys receiving treatment for eating disorders has doubled in recent years. New challenges - from sexting to gaming addiction, alongside the pressure to have a perfectly muscled body and be popular on social media - must now be navigated in order to cross the threshold into maturity. The recent story of 17-year-old Jarvis Kaye is an example of how conventional teenage lives have changed irrevocably as a result of the internet. Growing up in a middle-class family, Jarvis was, he says, a 'bit quiet and shy'. Then he got his first PlayStation. Soon he was playing Fortnite, the online game hugely popular with teenage boys and played by 250 million people worldwide. One hundred players are pitted against each other on a virtual island, fighting to the death until only one is left. It can be very addictive. (Some boys are gaming online for up to five hours a day, and while experts say it can 'improve practical skills', it can also 'alienate boys from real life'.) A legal firm in Canada recently launched a lawsuit against Fortnite's creators Epic Games, claiming the game operated in a similar way to slot machines. Jarvis was skilled at Fortnite and soon became an influential figure online, amassing 2.2 million followers on YouTube. Just as with traditional sports, boys today look up to star

videogamers. As a professional gamer, Jarvis earned hundreds of thousands of euro through winnings and advertising, and moved to a mansion with a swimming pool in Los Angeles. Then he was caught 'cheating'; he used something called 'aimbots', which make killing opponents easier. He was banned for life from Fortnite and publicly shamed. The digital world has evolved and is shaping teenage minds, with who knows what corrosive effect. Jarvis came of age in front of millions of people he had never met, in an environment where his identity was monetised (ads even appeared on the apology video he uploaded; it's estimated that saying sorry has earned him over [euro]20,000) and where there is fierce competition for our attention spans and a constant demand to perform. Whereas teenage girls are more likely to excel at school, teenage boys are more likely to be diagnosed with ADHD, get suspended or excluded, and end up in trouble with the police. And while girls have inspirational figures such as Beyonce to look up to, there is no influential voice gunning for adolescent boys. And what about parenting boys in this era of seismic shifts? How are we supposed to teach boys about what it means to be a man against a backdrop of the #MeToo movement and easily accessed online porn? Here, three mothers share their trials, experiences and realities of raising a son today. 'I FOUND HIM ON THE SOFA, SHAKING' Victoria Woodhall is mum to two children, including Marcus, 12 When I first found out that I was having a boy, I was slightly panicked. I knew nothing about boys: I'm one of two sisters, I was brought up by a single mother and my four-year-old daughter was as My Little Pony as it gets. But Marcus's gender never seemed to be a big part of who he was. While his friends were going gaga over football and dinosaurs, Marcus was into clothes and was a prolific reader and Lego builder. He was just Marcus. Now he's on the cusp of turning into a young man and the idea of what his future self might look like is at the forefront of his mind. Every day there's a new career possibility: 'I think I'd like to be a weather presenter, design a board game, write a book. Do you think I'd be good at that, Mum?' I'm blessed that this is his only concern, knowing what, according to news reports, might lie ahead for teenage boys: online grooming on video games, crime, the lure of gangs. But I'm not complacent. I know how quickly things can turn. Two years ago my husband and I found him on the sofa, white and shaking and asking to be taken to hospital. He was having a panic attack. We still don't know why. He had a swift referral to child mental health services and was assigned a counsellor. But this made him more anxious; he felt a failure because he couldn't tell the counsellor why he felt the way he did. 'It didn't help that it was in a hospital with noticeboards telling you about horrible diseases,' he says now. Every day he needed reassurance that he wasn't going to succumb to meningitis or diabetes. What he really needed was to feel safe; that we, his parents, were there to do the worrying for him, but the system told him he needed to talk. He did voluntarily quarantine his Nintendo DS, sensing that it wasn't making him feel good, even though he was playing nothing more combative than the Lego Harry Potter game. It took months for him to regain confidence and there is still an underlying fragility. He does have an awareness of how tech can affect mental health, though now he goes to secondary school and homework is filed online it's much harder to oversee his screen time. Communication is the one thing I can try to influence and that underpins everything. I find those nuggets tend to come out when you're not facing each other - in the car, cooking dinner or going for a walk. These are the golden times that, however busy we are as parents, we need to make space for as well as having fun together. 'I LOVE THEM FOR WHO THEY ARE' Lucy Cavendish is mum to four children, including Leonard, 16 When I tell people I have four children, three of whom are boys - they roll their eyes in horror. I think the assumption is that teenage boys are rude, aggressive and either constantly gaming, watching porn or getting up to no good with drugs/drink/girls. But raising boys right now is complicated; they are far more vulnerable than we think. I'm also a trained counsellor and every week teenage boys tell me of their deep fears, anxiety and feelings of depression. In the past year two boys from our local community have taken their own lives. Everyone is in shock. But teenage male suicide is on the rise and I feel very mindful of this. As a parent it's hard to spot when boys are going off track. Even though, as a generation, they have been far more encouraged to show their emotions, boys find it hard to tell people when they are suffering. They don't want to let their parents down or admit they are struggling with feelings of 'not belonging' or being a 'disappointment'. There is still you're a C-grade student. As a counsellor, the biggest issue I find with boys is feeling stereotyped. Their parents don't trust them or rate them or - in their eyes - try to understand them. Neither does society. This doesn't help when it comes to the increase in depression and anxiety. What's helped me live with my teenage boys is that I've decided to trust them. Are they drinking and taking drugs? I have no evidence 'BOYS FIND IT HARD TO TELL PEOPLE WHEN THEY ARE SUFFERING' an adage that 'boys don't cry'. Today, it's hard to find out who you are as a young man. Boys are in crisis: worrying about their feelings, pressure to succeed and what it is to be a man. For every 'climb every mountain' type, oozing 'masculine success', there's a man who can cry in public, care for his children and speak out about mental health issues. I've seen my boys trying on different personas to see if they fit. It's very hard to keep up a facade - having to be a 'sporty' boy or feeling pressure to do well academically when actually of this. Are they having sex? I don't need to know about that unless they want help or are getting in trouble. But I have discussed parameters with them; I ask them to be respectful of women - not to shame or humiliate them, not to share sex texts. Their female friends tell me how respectful my sons are. #MeToo has had an effect. The main thing is to accept them for who they are and love them for it. And tell them that. Regularly. When I see my boys having a laugh, it makes me happy. They are not just good kids, they are good people and that makes me very proud. 'i realised i hadn't lost him' Clover Stroud is mum to five children, including Jimmy, 19 On a train recently, I overheard a conversation between two mothers that was so familiar. Trading anecdotes about how difficult parenting had become since adolescence had arrived in their sons' lives, they talked about their boys bunking off school, smoking weed, flunking exams, staying out and rejecting everything about family life they had enjoyed before. These women expressed confusion about who seemed to have taken their sweet sons away. I wanted to reach over and say, 'Don't fret. This is normal. It will almost certainly pass.' My son Jimmy is now 19 and as he leaves his childhood behind, I can see the arc of motherhood falling, as if he and I have walked through all four seasons together. After the mostly sunny slopes of childhood, Jimmy's adolescence arrived like turbulence we all needed to buckle up for. His teenage life was complicated, too, by the fact I had three more children to care for from my second marriage, born when he hit 12, 14 and 16, as well as his sister Dolly, now 15. Guilt is a fundamental characteristic of maternal life, and when I look back at Jimmy's middle teenage years, I feel guilty that I was often preoccupied by the demands of three babies. My distraction allowed Jimmy to slip away from me. He was naughty, in the way that almost all teenage boys are. He didn't want to be at home

but out, as late as possible, with his friends. I took it personally. I brought him and Dolly up as a single mother for a decade before I remarried. As a trio, we were an exceptionally tight unit. Jimmy did all the stuff that those mums on the train were despairing over: skiving, drinking, smoking. He shouted a lot; so did I, sometimes so hard I'd make myself hoarse. He seemed as disobedient as any of my toddlers, only he was huge and could walk away from me. I felt hurt and didn't understand how he could do this. For two or three years, I really felt I'd lost him. Now I know it was the natural and inevitable wrenching apart that has to happen. I realise that we hadn't lost one another but needed to reimagine our relationship as two adults. He is a grown-up now - he headed off to art school this September - and doesn't belong to me any more. This is heartbreaking - and also wonderful. Now we are very close; we share jokes and enjoy one another's company. Watching him grow into an adult, and grow into himself, is one of the greatest privileges of motherhood.

Article #3

'THE DIGITAL WORLD IS SHAPING TEEN MINDS, WITH WHO KNOWS WHAT CORROSIVE EFFECT'

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In the Netherlands, about 40% of all people who die by suicide are in specialist mental health care [1]. The implementation of suicide prevention guideline recommendations into routine care appears to be an effective strategy to prevent suicides in MHIs. A large-scale study in the United Kingdom showed a significant reduction in suicide rates after implementation of 16 service improvements (including training of clinical staff, policy on the follow-up of discharged patients and ward safety) in MHIs [2]. In the Netherlands, the multidisciplinary guideline for the diagnosis and treatment of suicidal behavior was published in 2012 [3]. This guideline was developed to optimize the care for patients with suicidality in mental healthcare. However, its uptake by the field is varying, resulting in different suicide prevention policies and practices within and between MHIs in the Netherlands [4, 5]. To optimize guideline implementation and reduce the suicide rate in Dutch MHIs, 113 Suicide Prevention (the Dutch expertise center on suicide prevention and lifeline) formed a Suicide Prevention Action Network (SUPRANET) in mental healthcare (www.supranetggz.nl). SUPRANET is a confidential learning network of at present 16 specialist MHIs in the Netherlands.

SUPRANET aims at optimizing the quality and safety of care to enhance suicide prevention. This network collects data on suicide and suicide attempts, provides biannual benchmark feedback reports to participant organizations and organizes meetings for the exchange of best-practices [6]. To improve the quality of care and prevent suicides as well as eliminate discrepancies in specialist mental healthcare, it is of great importance to prioritize the guideline recommendations and to define measurable elements designed to evaluate aspects of the quality of care [7-10]. These QIs should be relevant, actionable, reliable, show room for improvement and data collection of the indicator should be feasible [11]. Using QIs to monitor changes in adherence to the suicide prevention guideline in specialist mental healthcare is an essential step towards the delivery of evidence-based care [12]. Because all patients with an increased risk for suicidality should receive evidence-based care within MHIs, the literature should try to underpin the effectiveness of every QI and its relation to reduced suicide (attempt) rates. Up until now, the literature examined the effectiveness of several guideline recommendations [3]. A variety of pharmacological and psychotherapeutic interventions have repeatedly been found effective in the treatment of suicidality [13-17]. For example, a study of Linehan et al. [18] found evidence for the effectiveness of dialectical behavior therapy (DBT) in decreasing the number of suicide attempts as well as reducing the number of hospitalization visits for suicide ideation in women with a borderline personality disorder [19]. To our knowledge, however, not all recommendations from the suicide prevention guideline have been extensively researched in the literature [3]. For example, safety planning is often informed by research and clinical practice as an important guideline recommendation but does not yet have a body of research to support it. Fortunately, the evidence is building. A randomized controlled trial (RCT) by Bryan et al. [20] found a positive association between crisis response planning (an intervention related to safety planning) and reduced suicide attempt rates compared to the use of contracts for safety (e.g., which states that the patient with suicidality should not engage in suicidal behavior during a crisis) in US soldiers. Although several studies have been published on the effectiveness and use of safety planning [21], more research is still needed. A recent publication by Brent, Oquendo, and Reynolds [22] emphasized that formulating a safety plan is one of the seven key elements to treat patients with suicidality effectively. As suggested by the review of Zalsman et al. [13], no single suicide prevention strategy is way more effective compared to the others. Multiple relevant and action-oriented key recommendations should therefore be implemented at the same time. Also, While etal. [23] showed that mental healthcare services who implement multiple strategies (seven to nine recommendations) at the same time

show the most significant reduction in the number of suicides compared to those implementing fewer recommendations. This study aimed to prioritize the suicide prevention guideline recommendations and to develop a set of relevant and actionable Qis for suicide prevention in specialist mental healthcare. The Delphi technique was used to create common definitions and terminology, and to achieve convergence of opinion among the participants. Participants of this study were suicide experts, health care professionals, and experts with experiences in suicidal behavior and members of patients' advisory boards. Criteria for selection were

1) relevance (it affects the number of suicides in the institution) and 2) action orientation (the institutions or professionals themselves can influence it). In the last step, data analysts scored the QIs on 3) feasibility to monitor and extract them from existing systems. The Delphi technique is a reliable method in selecting QIs and uses a structured, iterative process of collecting knowledge from a group of experts with the primary goal of reaching consensus [24-26].

Methods

As part of the SUPRANET study [6], a Delphi study was done to prioritize the guideline recommendations and to select and standardize the terminology of QIs. This study has been approved by the Central Committee on Research Involving Human Subjects in the Netherlands (CCMO) and does not fall under the scope of the Medical Research Involving Human Subjects Act (WMO). The CCMO states that: "In general, research with human subjects only falls under the Medical Research (Human Subjects) Act (WMO) if there is an infringement of the physical and/or psychological integrity of the subject" (https://english.ccmo.nl/investigators/legalframework- for-medical-scientific-research/your-research-is-it-subject-to-the-wmo-or-not). For this study, the SQUIRE 2.0 checklist (Standards for Quality Improvement Reporting Excellence) was used as a reporting guideline [27]. The procedure for the development of the QIs is shown in Fig. 1 and described in the procedure section below.

Fig. 1: Flowchart of Delphi study with procedure for QI development

Procedure

The procedure was conducted in two phases:

* Phase one: Development and selection of guideline recommendations and Qis From the 49 key recommendations described in the suicide prevention guideline, an inventory of potential recommendations was

selected (Fig. 1). These key recommendations were selected based on the possibility to operationalize them on a patient level. Furthermore, it was preferred that there was an evidence-based association between the key recommendations and reduced suicide (attempt) rates. This procedure resulted in a selection of 12 key recommendations from the guideline. The selected key recommendations were modified into 12 process QIs (on a patient level) by describing them into detail, including definitions, numerators, and denominators and target values (see Additional files). Next, two small multidisciplinary workgroups of healthcare professionals (workgroup one; n = 16; workgroup two; n = 15) discussed the list of 12 QIs. During three sessions of one hour each, participants in both workgroups were instructed to discuss the 12 proposed QIs, based on their knowledge and expertise in the field. Furthermore, the participants appraised each QI individually with an overall score, reflecting whether the study should reject the QIs or rephrase them.

As illustrated in Fig. 1, participants rejected two QIs the Collaborative Assessment & Management of Suicidality (CAMS) and the Chronological Assessment of Suicide Events (CASE approach) due to low feasibility. Also, the participants in the workgroups argued that both indicators are not yet sufficiently implemented into routine care. The QI social connectedness was rejected by the participants due to a lack of scientific evidence. Also, the participants stated that social connectedness showed much overlap with other QIs and categorized this as a structural QI instead of an indicator that should be measured on a patient level. The numerator of the QI involvement of family or significant others was split into two components: A) there is contact with family or significant others and B) contact person is registered in patients' electronic medical record (Additional files). Next, one QI was split into two Qis because the participants stated that the QI EHealth actually contains two important measurable components: 1) active usage and 2) availability of EHealth (Additional files). Finally, the participants also split the QI continuity of care: members of both workgroups agreed to divide this indicator into two QIs continuity of care and follow-up after discharge. Between each workgroup session, Qis were further clarified by the first author (KS) in terms of their clarity and definition. This resulted in a final set of 11 defined and operationalized QIs (Additional files). After final approval from the participants in both workgroups, the Delphi study was performed (phase two).

* Phase two: Rating of guideline recommendations and QIs (Delphi study)

The Delphi study consisted of two rounds:

Round one: Rating QIs on relevance and action orientation

To achieve convergence of opinion, we developed an anonymous electronic survey with the 11 selected key recommendations and their QIs (Additional file 1). All MHIs participating in the SUPRANET network were involved in this study. Participants working in the field of suicide prevention were recruited from each MHI. Participants were approached in the first round via e-mail to complete the survey (Additional file 1) by following a web link. Written consent of participants was given by filling in the survey. A total of 90 participants recruited from each MHI (23 suicide experts, 23 members of patients' advisory boards or experts with experiences in suicidal behavior and 44 health care professionals), filled in the survey. They rated the QIs independently on two aspects: relevance (it affects the number of suicides in the institution) and action orientation (institutions or professionals themselves can influence it). All participants rated the QIs on both aspects using a 5-point Likert-scale (1 = strongly disagree, 2 = disagree, 3 =neither disagree or agree, 4 = agree and 5 = strongly agree).

Round two: Rating QIs on feasibility

In the second round, members with specific expertise on data such as data analysts working in MHIs (n = 6), independently rated the QIs on feasibility (is it feasible to monitor and extract from existing systems) using an online survey (Additional file 2). The QIs were scored on

a 5-point Likert scale (1 = not feasible at all, 2 = not feasible, 3 = neither not feasible or feasible, 4 = feasible and 5 = completely feasible). After both Delphi rounds, outcomes were analyzed, resulting in a specific set of relevant, action-oriented and feasible QIs.

Data analyses

Analysis of both rounds of the Delphi study yielded consensus results by computing medians, and percentage of consensus for each item to determine which QIs achieved positive consensus. Data of respondents were anonymized prior to analysis. Agreement percentages were calculated for each item by assessing if at least 70% of the participant response rates were within the range of the median scores of four and five. The level of consensus achieved concerning the 11 QIs included in the first round was assessed using the following cut-off score [24, 28]:

1. Consensus = median score of four or higher on both selection criteria (relevance and action orientation) with > 70% consensus.

2. No consensus = median score of four or higher with < 70% consensus for one of the selection criteria (relevance or action orientation).

3. Not suitable = median score of three or lower for one of the selection criteria (relevance or action orientation). Median scores and percentage of consensus was analyzed between the three groups of participants: 1) suicide experts (n = 23), 2) members of patients' advisory boards and experts with experiences in suicidal behavior (n = 44) and 3) health care professionals (n =23). Analyses were performed with SPSS version 24.0.

Results

Participants

The Delphi survey was sent to 154 experts by e-mail, and a total of 90 experts filled in the online questionnaire (response percentage of 58%). Of the 90 participants, 23 people (25.6%) were suicide experts, 23 (25.6%) were members of patients' advisory boards or experts with experiences in suicidal behavior, and 44 (48.9%) were healthcare professionals. Almost all participants were from the Netherlands (n = 88), two participants lived in Belgium. From the participants that filled in the Delphi survey (N = 90), the mean age of the participants was 48.6 (SD = 11.39) years, of which 58.9% (n = 53) was female. The mean years of experience of healthcare professionals in Dutch mental healthcare was 18.10 years (SD = 9.73).

Round one: Rating QIs on relevance and action orientation In the first round of the Delphi study, participants reached a consensus regarding the relevance for eight of the 11 QIs, and five of the 11 QIs were rated as action-oriented (Table 1). The participants scored the following five QIs that belonged to the guideline as both relevant and action-oriented: 1) screening suicidal thoughts and behavior, 2) safety plan, 3) early follow-up on discharge, 4) continuity of care, and 5) involving family or significant others. As Table 1 shows, between-group differences for relevance and action orientation were found for several prioritized QIs (screening, continuity of care, early follow-up on discharge, and involving family or significant others). Participants reached consensus on relevance, and action orientation for QIs highlighted in bold. Percentage of consensus for both relevance and action orientation (round one) No consensus was reached on relevance and action orientation for three QIs: 1) availability of EHealth, 2) active usage of EHealth, and 3) evidence-based medication. Further, 1) structural diagnosis, 2) waiting list duration, and 3) evidence-based psychotherapy achieved consensus for relevance but were not rated as action-oriented by the participants.

Round two: Rating QIs on feasibility

During the second round of the Delphi study, data analysts (n = 6) rated the QIs on feasibility (Table 2). The percentage of consensus and median scores for the rated QIs on feasibility are shown in Table 2. When looking at the consensus cut-off score, participants rated only one of the 11 QIs as feasible. Early follow-up after discharge was prioritized as the only relevant, action-oriented, and feasible QI. For the QI waiting list duration, participants reached borderland consensus. As for the other nine QIs, no consensus on feasibility was reached. Both rounds of the Delphi study resulted in a final list of relevant, actionable and feasible QIs derived from the guideline. These results are presented in Table 3. Percentage of consensus and median scores for feasibility (round two). Percentage in bold achieved consensus Final list of relevant, actionable and feasible quality indicators derived from the guideline Discussion This study aimed to generate a set of relevant, action-oriented, and feasible QIs derived from the guideline by using a Delphi method. Only one QI was rated by six Dutch data analysts as feasible to monitor and register in MHIs in the Netherlands and reached consensus on all three criteria (relevancy, action orientation, feasibility). This QI was early follow-up on discharge. According to the literature, the risk of suicide is three times higher in the first week after discharge from a psychiatric facility [29] and remains significantly higher during the next few months [30, 31] or even years [32]. While the study of Zalsman et al. [13] reported that there is insufficient evidence for the efficacy of supportive contacts after discharge from the emergency department (ED), a large UK-study of Kapur et al. [2] found an association between rapid follow-up contact after inpatient discharge and lower suicide rates in mental healthcare services. Also, Luxton et al. [33] argued that brief supportive contacts by phone, text, postcards, or letters could be effective in reducing suicide (attempts) during high-risk periods (i.e., hospitalization or ED visits). Even though more high-quality RCTs are still needed to examine its impact further, numerous studies [14, 22, 34, 35], quality standards and suicide prevention guidelines [3, 36] repeatedly recommend improving early follow-up contact after discharge. However, whether a QI is rated as feasible will differ between institutions and countries. Following the total group of experts, consensus on relevance (it affects the number of suicides in the institution), and action orientation (the institutions or professionals themselves can influence it) was reached on the following four QIs:

1. Screening of suicidal thoughts and behavior

Based on our results, the QI screening of suicidal thoughts and behavior was rated as a high priority. While some clinicians hold a belief that asking about suicide could trigger a patient into a suicidal act [37], a recent review found no iatrogenic effects [38]. An extensive systematic review of Zalsman et al. [13] reported inconclusive results on the costs and effects of routine screening and its association with reduced suicide (attempt) rates. Results from other studies also found that screening instruments are not very accurate in identifying the risk of suicide attempts or suicide death in individuals [39, 40]. A study by Coffey [41], however, showed that routine screening could be a useful and feasible method if screening results are regularly fed back to care teams and if it is included in the registration systems of MHIs. Although more empirical research on the effects of routine screening is needed, it is perceived by the literature as a very helpful strategy [22, 34, 35, 42]. To effectively treat individuals whose risk of suicide is high, it is very important to identify those individuals. Although evidence shows that predicting suicide with certainty is rather complex, it is not necessary to perfectly predict suicide in order to intervene effectively. For example, the National Action Alliance for Suicide Prevention [42] argues that by identifying individuals with an elevated risk, it allows mental healthcare professionals to detect those high-risk individuals who could then be treated with adequate and effective interventions.

1. Safety plan

Safety plan was rated as an essential QI for mental healthcare. The Dutch multidisciplinary suicide prevention guideline and care quality standards recommend regular and collaborative safety planning for all patients at risk of suicide [3, 43]. Also, safety plans are embedded in cognitive behavioral therapy (CBT) for suicide prevention [44]. Literature shows that there is some empirical evidence on the effectiveness of safety plans in reducing suicide (attempt) rates. For example, an RCT study of Bryan et al. [20] examined the impact of crisis response safety planning on suicide (attempts) among US soldiers at high-risk of suicide. The authors found a significant reduction of suicide ideation, fewer hospitalization days, and a 76% reduction in suicide attempts. These results are in line with a cohort comparison study of Stanley et al. [21], where a significant association between a Safety Planning Intervention (SPI) and reduced suicidal behavior was found in veteran hospitals. It should be noted, however, that this study design is limited since both intervention and control emergency department sites were matched instead of being randomized. Furthermore, both studies were performed in a veteran population. The results from both studies on the impact of safety plans are promising, but more RCT studies on its impact, also in other study populations, are highly needed.

1. Continuity of care Consensus was achieved for continuity of care as a relevant andaction-oriented QI. In daily practice, it often happens that more than one clinician treats a patient at risk of suicide in a short period of time [3]. Transfer between clinicians, settings, or organizations could affect the continuity of care and is a well-known risk factor for patients at risk of suicide [45]. It is, therefore, important that clinicians collaborate and inform each other to ensure these patients receive the care they need. A few years ago, a report was published containing information about how continuity of care should be organized in Dutch mental healthcare [46]. This report aimed to stimulate and improve continuity of care by formulating recommendations (i.e., following suicide prevention training) to healthcare professionals (including general practitioners, medical specialists, emergency doctors). The literature highly recommends minimizing discontinuities in care for patients at risk of suicide during critical phases (i.e., transfers, post-discharge) [3, 34, 35]. However, more empirical research on its impact is needed. Fortunately, the scientific evidence is building. For example, the study of Kapur et al. [2] found a significant association between the implementation of policies aiming at optimizing continuity of care for patients at risk of suicide in mental healthcare services and a reduction in the number of suicides . The importance of close communication between clinicians and across mental healthcare settings is also emphasized by other literature [22, 47]. Other studies should try to replicate the results of Kapur et al. [2] to further determine the impact of continuity of care on reduced suicide rates in mental healthcare.

1. Involving family or significant others

Although the impact of involving family, carers or friends on suicide rates is rather understudied in the literature, this strategy on itself is highly recommended by the Dutch multidisciplinary suicide prevention guideline and various quality standards [3, 48]. Relatives can play an essential role in the prevention of suicide, but only if they are capable of supporting the mental healthcare services in the early detection and management of family members at risk [49]. They can provide valuable information to clinicians that could be helpful for the patients' treatment. The importance of actively involving and informing family members is also highlighted in other studies [50, 51]. However, it is important to take into account that patients should always be allowed to say whether they would like their family or friends to be involved in their treatment or not [48]. A clinician should bear in mind the patients' expressed wishes and views in relation to sharing information with their family, carers, or friends. On the contrary, relatives of a patient should be supported and provided with information as well. Based on a report of the department of Health and Social Care in England, relatives and carers have repeatedly raised their concerns about mental healthcare services who seem reluctant to take information from families or give them information about a patients' suicide risk (https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/271792/Consensus_statement_on_information_sharing.pdf). It is of great importance to address these concerns, given the fact that the collaboration between a therapist and patients' relatives is one of the components which can lead to better quality and safety improvement in specialist mental healthcare [34]. Not prioritized guideline recommendations Some guideline recommendations and their QIs were not endorsed as priorities, including evidence-based medication and psychotherapy for patients in specialist mental healthcare. This is surprising given the fact that both medication (lithium, clozapine, ketamine) and psychotherapy have shown promising results in reducing suicidality among patients in mental healthcare [13, 15-17]. It is possible that because medication and psychotherapy are already embedded in routine care, both recommendations were considered to be of less priority. Furthermore, participants in this study reported that medication and psychotherapy could not be influenced directly or changed by the MHIs or the healthcare professionals themselves, leading to a lower score on action orientation. Between-group differences were found for several guideline recommendations. For example, the expert group with members of patients' advisory boards or experts with experiences in suicidal behavior rated screening as highly relevant and action-oriented, whereas the other two groups reached borderland consensus for this guideline recommendation. Also, the suicide expert group did not reach an agreement on action orientation for several recommendations and their QIs: 1) early follow-up on discharge, 2) continuity

of care, and 3) involving family or significant others. This is in contrast with the outcomes of the other two participating expert groups, who did succeed in achieving consensus on action orientation for the same recommendations.

Guideline implementation is intended to result in a higher quality of mental healthcare, eventually leading to lower suicide rates. To achieve this goal, scientific evidence suggests that an optimal approach is required for implementing a combination of multiple relevant and action-oriented guideline recommendations at the same time. For example, a large UK-study examined the association between the implementation of key mental health service recommendations and suicide rates [23]. They found that services that had implemented seven to nine recommendations had a significantly lower suicide rate than those implementing fewer recommendations

[23]. These findings suggest that the effort of implementing recommendations in mental healthcare services can affect suicide rates.

Strengths and limitations

A key strength of this study is that experts from MHIs were continuously involved in both the development and selection of guideline recommendations and their QIs. Another strength was the breadth of expertise of the participants who participated in the Delphi study. Also, this survey sample (N = 90) was notably larger compared to other Delphi studies in the field of mental health [28]. The size of a Delphi panel is generally under 50, although more have been employed [25]. As for both rounds, the survey response rate was good overall. Nevertheless, there are some limitations. First, the participants in this study mainly came from the Netherlands. The established set of QIs might not match MHIs in other countries, and this applies in particular to the feasibility of the QIs. Second, the survey did not offer an opportunity for the 90 experts to suggest QIs that were not derived from the suicide prevention guideline.

Conclusions

This study stands to contribute to the scientific literature on prioritizing relevant and action-oriented suicide prevention guideline recommendations to improve the quality of care in specialist mental healthcare. The results of this study are an important step towards the use of a new set of relevant and actionable QIs that are clearly defined, operationalized, and contain target values, making them appropriate for benchmarking and monitoring guideline implementation in specialist mental healthcare. If needed, other countries can tailor the selected QIs to one's own (specialist) mental healthcare setting.

The prioritized QIs will be used to monitor the degree of guideline implementation within the specialist MHIs [6]. The five guideline recommendations selected as relevant and action-oriented might be of most importance for suicide prevention when implemented altogether. The SUPRANET study [6] will evaluate the implementation process of the prioritized recommendations in HIs in the Netherlands. When proven to be effective, MHIs should include the prioritized recommendations into their policy for suicide prevention. Abbreviations: CAMS: Collaborative Assessment & Management of Suicidality intervention; CASE: Chronological Assessment of Suicide Events; MHI: Mental healthcare institution; PHQ: Patient Health Questionnaire-9; QI: Quality indicator; QUIRE: Standards for Quality Improvement Reporting Excellence; SUPRANET: Suicide PRevention Action NETwork Acknowledgments: The authors would like to thank all suicide experts, members of the patients' advisory board, experts with experiences in suicidal behavior and healthcare professionals for their involvement and participation in this study. Thanks to the 16 specialist MHIs for their efforts and participation in the SUPRANET network.

Correspondence: Kim Setkowski:

Author details: 1113 Suicide Prevention, , Amsterdam, The Netherlands. 2grid.420193.d, 0000 0004 0546 0540, Department of

Psychiatry, Amsterdam UMC, location VUmc, Amsterdam Public Health research institute and GGZ inGeest, , Amsterdam, The

Netherlands. 3Department of Intensive Care Medicine, Amsterdam UMC, location AMC, , Amsterdam, The Netherlands. 4National

Intensive Care Evaluation (NICE) foundation, , Amsterdam, The Netherlands.

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Article #4

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Nursing can be a stressful profession; caring for children can cause secondary traumatic stress in the pediatric nurse (Kellogg et al., 2018). Secondary traumatic stress has been defined as "intrusion, avoidance and arousal symptoms resulting from indirect exposure to traumatic events using a professional helping relationship with a person or persons having directly experienced the events" (Bride et al., 2004, p. 28). Several publications can be found in health care literature exploring work-related stress and trauma. Terms used to describe the occurrence vary and include secondary traumatic stress, compassion fatigue, burnout, and vicarious traumatization. Studies of work-related stress in nursing explore many specialties, including labor and delivery (Beck & Gable, 2012), emergency care (Dominguez-Gomez, & Rutledge, 2009; Flarity et al., 2013; Jeon & Ha, 2012; van der Wath et al., 2013), oncology (Günüşen et al., 2019), trauma and critical care (Hinderer et al., 2014; Mason et al., 2014; Sacco et al., 2015; Salimi et al., 2019; Von Rueden et al., 2010; Young et al., 2011), hospice and palliative care (Melvin, 2015; Sullivan et al., 2019), and nursing coordination roles (Kim, 2013). Significant variance is

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Recalling Stress and Trauma in the Workplace: A Qualitative Study of Pediatric Nurses

Anna E. Kleis and Marni B. Kellogg

Anna E. Kleis, BSN, RN, is a Graduate, the University of Massachusetts Lowell, Lowell, MA; and Staff Nurse, Mount Auburn Hospital, Cambridge, MA.

Marni B. Kellogg, PhD, RN, CPN, CNE, is an Assistant Professor, the University of Massachusetts Dartmouth, Dartmouth, MA.noted in the prevalence of secondary traumatic stress or compassion fatigue, with mean scores ranging from low levels in nursing coordination (Kim, 2013), average levels in critical care nurses (Sacco et al., 2015), and moderate or high levels in pediatric nurses (Kellogg et al., 2018). These results indicate the occurrence of work-related stress or trauma is highly variable and should be further investigated so appropriate interventions can be implemented. Currently, little is reported in the literature about experiences in pediatric nursing that are most challenging emotionally and may cause secondary traumatic stress in pediatric nurses.

Qualitative studies in the literature related to stress in pediatric nursing are limited. McGibbon and colleagues (2010) published an ethnography on pediatric nursing stress studying nurses working in a pediatric intensive care unit of a pediatric hospital in Canada. Results focused on causes of nursing stress and revealed six themes: 1) emotional distress, 2) constant presence, 3) the burden due to responsibility, 4) hierarchical power, 5) bodily care, and 6) being mothers, daughters, aunts, and sisters.

Kleis, A.E., & Kellogg, M.B. (2020). Recalling stress and trauma in the workplace: A qualitative study of pediatric nurses. Pediatric Nursing, 46(1), 5-10.

Problem: Secondary traumatic stress has been identified as a problem in the nursing workforce, leading to adverse effects on mental health and job dissatisfaction.

Purpose: The purpose of this study was to begin to discover more about the events and stressors pediatric nurses experience that may lead to the development of secondary traumatic stress.

Results: Content analysis was performed with the open-ended responses from a cross-sectional survey asking, "Is there anything else you would like to share?" Seventy-two responses were analyzed and six prevalent themes were identified: pressure to perform despite emotion, feeling unsupported, inability to separate traumatic experiences from personal life, consumption by traumatic experiences, using positivity to cope, and the need for further research.

Conclusion: Pediatric nursing is stressful, yet many nurses also find it rewarding. Measures to improve the nurse's awareness of work-related stress, including education and breaks during the workday, should be encouraged. Further research is needed to determine which experiences are most traumatic for pediatric nurses, negative effects of secondary traumatic stress for patients, and interventions that best reduce secondary traumatic stress in nursing.

Article #5

Anxiety in teens

Authors: Susan D. Swick and Michael S. Jellinek

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It seems that every week there is a new headline about the rising rates of anxiety in today's adolescents. Schools often are asked to address high levels of stress and anxiety in their students, and the pediatrician's office is often the first place worried parents will call. We will try to help you differentiate between what is normal--even healthy--adolescent stress, and what might represent treatable psychiatric problems. And we will review how to approach stress management with your patients and their parents. For all adolescents, even those with psychiatric diagnoses, learning to manage stress and anxiety is critical to their healthiest development into capable, confident, resilient adults. Stress is the mental or emotional strain resulting from demanding or adverse circumstances. Anxiety is a feeling of unease about an imminent event with an uncertain outcome. An anxiety disorder is a psychiatric illness characterized by a state of excessive unease

leading to functional impairment. These distinctions are critical, as both stress and anxiety are normal-but-uncomfortable parts of the adolescent experience. When all of a teenager's stress and anxiety is medicalized, it promotes avoidance, which in turn may worsen your patient's functional impairment rather than improving it. This is not to suggest that there are not real (and common) psychiatric illnesses that can affect the levels of anxiety in your patients. Anxiety disorders start the earliest, with separation anxiety disorder, specific phobia, and social phobia all having a mean onset before puberty. Anxiety disorders are the most prevalent psychiatric disorders in youth (30% of youth psychiatric illness), and anxiety also may be related to substance use disorders (25%), disruptive behavior disorders (20%), and mood disorders (17%). There is no evidence of a statistically significant increase in the incidence of anxiety or mood disorders in young people over the past decade. The challenges facing teens are considerable. Of course, adolescence is a time of major change starting with puberty, in which young people actively develop independence, identity, and a rich array of deep relationships beyond their families. Typically, this is a 5- to 10-year process of risk-taking, new experiences, setbacks, delight, heartbreak, and triumphs all alongside growing autonomy. While development alone could be a full-time job for teens, they are also in a competition for admission to colleges, increasingly intense as more students from around the world apply for the same number of spots. The amount of debt a student must take on to attend college has increased dramatically, while the job market they face seems uncertain.

There is one dramatically different feature of adolescent life today: the constant presence of smartphones. While these devices can improve connectedness to school, family, and friends, use of smartphones also means that today's teenagers often have little downtime cognitively or socially. Use of smartphones can facilitate both supportive affirmation from friends and relentless social pressures, and the feeling of being excluded or bullied. Smartphone use can interfere with restful sleep, and some virtual activities may compete with the genuine experimentation and exploration where teenagers discover their interests and abilities and develop meaningful confidence and independence. Several factors might impair an adolescent's ability to cope with challenge and stress. Those teenagers who have not had the opportunity to face and manage modest setbacks, difficulties, and discomforts during their elementary and middle school years may be overwhelmed by starting with the higher-stakes strains of adolescence. This can happen when young children have not explored many new activities, have been shielded from the consequences of failures, or have tried only activities that came easily to them. Certainly, teenagers who are managing a depressive or anxiety disorder as well as those with learning disabilities may have limited ability to cope with routine stress, although those who have a well-treated disorder often have robust coping skills. Perhaps obvious, but still very important, chronic sleep deprivation can leave adolescents irritable, impatient, and distractible, all of which make coping with a challenge very difficult. Likewise, substance use can directly impair coping skills, and can create the habit of trying to escape stress rather than manage it. So what does this mean for you? When your patient complains of stress, worry, or anxiety, start with screening for an underlying psychiatric illness. If your patient has an anxiety, depressive, or substance use disorder, refer for appropriate therapy. For both those who screen in and those who do not, your next task is to help them improve their coping skills. What specifically has them so stressed? Are there family stressors or unrealistic expectations that can be addressed? Can they see their situation as a challenge and focus on what is within their control to do in response? Remind your patients that challenges are uncomfortable. Mastery comes with practice and, inevitably, some setbacks and failures. Have they identified personal goals or a transcendent purpose? This can improve motivation and keep a challenge in perspective. They might focus on learning about their coping style: Do they do better with a slow, steady, methodical approach or intense bursts of effort? Talk with them about self-care. Adequate sleep, regular exercise, putting effort into relaxation as well as work, and spending time with their actual (not just virtual) friends all are essential to keeping their batteries charged while doing the intense work of normal adolescence. For those patients who do not meet criteria for depression or anxiety disorders, there are circumstances in which a referral for therapy can be helpful. If they are noticeably disconnected from their parents or their parents seem to be more reactive to the stress and pressures than they are, an outside therapist can be a meaningful support as they build skills. Those patients who are socially isolated and stressed, are using substances regularly, are withdrawing from other interests to manage their source of stress, or are having difficulty telling facts from feelings are at risk for failing to adequately manage their stress and for the development of Psychiatric problems.

BY SUSAN D. SWICK, MD, AND MICHAEL S. JELLINEK, MD

Caption: Dr. Swick is an attending psychiatrist in the division of child psychiatry at Massachusetts General Hospital, Boston, and

director of the Parenting at a Challenging Time (PACT) Program at the Vernon Cancer Center at Newton Wellesley Hospital, also in Boston. Dr. Jellinek is professor emeritus of psychiatry and pediatrics, Harvard Medical School, Boston. Email them at fpnews@frontlinemedcom.com.

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