Personality disorder and the outcome of depression: meta-analysis of published studies

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Background There is conflicting evidence about the influence of personality disorder on outcome in depressive disorders.

Aims Meta-analysis of studies in which a categorical assessment of personality disorder or no personality disorder was made in people with depressive disorders, and categorical outcome (recovered/not recovered) also determined.

Method Systematic electronic search of the literature for relevant publications. Hand searches of *Journal of Affective Disorders* and recent reviews, with subsequent meta-analysis of selected studies.

Results Comorbid personality disorder with depression was associated with a doubling of the risk of a poor outcome for depression compared with no personality disorder (random effects model OR=2.18, 95% CI 1.70–2.80), a robust finding maintained with only Hamilton-type depression criteria at outcome (OR=2.20, 95% CI 1.61–3.01). All treatments apart from electroconvulsive therapy (ECT) showed this poor outcome, and the ECT group was small.

Conclusions Combined depression and personality disorder is associated with a poorer outcome than depression alone.

Declaration of interest P.T. and T.J. belong to a UK Medical Research Council Cooperative Group (Mencog) evaluating mental health interventions. P.T. is Editor of the *British Journal of Psychiatry* but had no part in the evaluation of this paper.

Reports in the psychiatric literature that comorbid personality disorder is associated with a poor outcome in depression have recently been challenged (Brieger *et al*, 2002; Mulder, 2002). This is an important clinical issue that needs to be resolved and we judged that there have now been sufficient high-quality studies to enable a definitive answer to be obtained from a systematic review. Before the introduction of DSM–III (American Psychiatric Association, 1980) there were few studies examining the influence of personality disorder on the outcome of depression, although clinical opinion suggested that people with personality disorder responded less well to treatment (Sargant, 1966) and follow-up studies supported this (Greer & Cawley, 1966). However, both before and since the introduction of DSM–III, personality problems have been studied in some depth using self-rating questionnaires in which personality abnormality is assessed dimensionally (Eysenck, 1959; Eysenck & Eysenck, 1964; Cloninger, 1987). Although there is good evidence that personality abnormality is best viewed as a dimensional construct (Livesley, 1991), in clinical practice decisions are dichotomous and are aided by a categorical diagnostic system; hence we used this in our systematic review.

METHOD

The aim of the meta-analysis was to examine all studies of outcome in depressive disorders in which: (a) personality disorder was assessed formally and (b) outcome was recorded either using standard rating scales, such as the Hamilton Rating Scale for Depression (HRSD; Hamilton, 1960) or another measure, such as clinical judgement.

Inclusion criteria

Inclusion criteria were broad to ensure maximum accrual of information for systematic review. Papers were selected if: (a) written in English; (b) participants were assessed for both depression and personality disorder using a scale published in a peer-reviewed journal; (c) the population studied was aged at least 18 years; (d) assessment of outcome of depression was at least 3 weeks after initial assessment, this being considered the minimum time necessary for treatment response. Both observational studies and randomised trials were included and there were no restrictions with regard to type of treatment or its duration.

Exclusion criteria

Studies that examined personality using a dimensional scale were excluded, as these could not be compared directly with those in which a categorical diagnosis of personality disorder was made.

Search method

Medline, Clinhal and Psychinfo were searched online from 1966, 1982 and 1882, respectively. The terms DEPRESSION, MENTAL ILLNESS and PERSONALITY DISORDER were entered and combined. All abstracts were reviewed and those with data suggesting satisfaction of the inclusion criteria read in full.

In addition, a hand search of the *Journal of Affective Disorders* was carried out by G.N.-H. This served as an audit of the online search and provided additional sources of information. All relevant review articles were also examined closely for eligible studies, especially those by McGlashan (1987), Reich & Green (1991), Reich & Vasile (1993), Shea *et al* (1992), Ilardi & Craighead (1995), Corruble *et al* (1996), Dreessen & Arntz (1998) and Mulder (2002). The 'grey' literature was not examined as it was considered unlikely to provide further data.

Data extraction and checking

Two-by-two tables of the numbers of patients with or without personality disorder cross-classified by response to treatment (and stratified by treatment modality when possible) were drawn up for each paper, either by direct extraction from published tables and text (including associated papers), derived from summary percentages, or reconstructed from summary statistics such as χ^2. The resultant 2×2 tables were cross-checked against all

information within each published paper (counts, percentages, summary statistics, test statistics) to check for and resolve (multiple) inconsistencies. For papers that did not report a dichotomous outcome but presented outcome as a mean and standard deviation (s.d.) on a rating scale such as the HRSD, the number of patients who responded was defined as the percentage with outcome score <6 and estimated using the methods of Whitehead *et al* (1999), assuming a normal distribution of scores at outcome and allowing different variances in those with and without personality disorders. In papers that reported means alone, standard deviations were estimated by interpolation, from a regression of ln(s.d.) on ln(mean) in the six studies that reported these for the HRSD. Only the earliest outcome was allowed for each study; continuous outcomes were used only when no dichotomous outcome was reported.

For some recent papers where the required data on personality status (or depression) seemed to be implied but could not be extracted or derived, authors were contacted with a request for relevant information in the form of a 2×2 table.

Every paper included in the meta-analysis was read and the data were extracted and cross-checked independently by two authors (G.N.-H. and T.J.); discrepancies were resolved by discussion.

Statistical analysis

Log (odds ratios, ORs) and their standard errors from each study were entered into the RevMan 4.2. meta-analysis program (Cochrane Collaboration, Oxford, UK; see http://www.cc-ims.net/RevMan/current.htm) using the generic inverse variance option. Results have been summarised using conventional Forest plots and ORs, stratified by features of the studies included. Summary ORs were estimated using a random effects model.

RESULTS

The search

Online search found 890 potentially relevant papers. Abstracts from all of these were reviewed for useful data and 759 were rejected as obviously unsuitable (e.g. rodent studies). The remaining 131 were read in full and 99 were rejected for a variety of reasons, including (a) no usable data; (b) no categorical diagnosis of personality disorder; and (c) no recognised instrument used for diagnosis. The remaining 32 studies were included in the review. Hand search of the *Journal of Affective Disorders* and cross-checking of papers cited by review articles revealed no extra papers, indicating that our search strategy was reasonably comprehensive. Review of the literature in August 2004 highlighted two papers published since the initial review in February 2002, which have been included (Kool *et al*, 2003; Casey *et al*, 2004).

Included studies

Characteristics of the 34 studies available for meta-analysis are summarised in Table 1 in chronological order of publication. There were 17 (50%) studies from North America, 15 (44%) from Europe and 2 (6%) from the Far East. Four studies were located in Iowa, USA (Pfohl *et al*, 1984, 1987; Zimmermann *et al*, 1986; Black *et al*, 1988), and have been selectively included in the meta-analysis since the first three clearly report different aspects of the same study. Four studies located in Pittsburgh, USA (Pilkonis & Frank, 1988; Shea *et al*, 1990; Stuart *et al*, 1992; Hirschfeld *et al*, 1998) have all been included since they report independent data-sets (P. Pilkonis, personal communication, 2004). For the Nottingham study of neurotic disorders (Tyrer *et al*, 1990), only data for patients with dysthymia have been abstracted, and from the study of Leibbrand *et al* (1999), only data for patients with comorbid major depressive disorder.

Out of the 34 studies, 17 (50%) were prospective case series (cohort studies), 14 (41%) were randomised controlled trials (RCTs) and 3 (9%) were case series reviews; the majority (22 out of 34, 65%) focused on out-patients. The interval from the start of treatment to assessment of outcome varied from 3 weeks to just over a year (median=16 weeks, interquartile range 8–24); this parameter was not given in 3 studies. Response was based on rating scales for depression in 24 (71%), objective criteria for relapse in 1 (3%) and less objective criteria in 9 (26%). Out of the 24 studies using common depression scales as outcomes (HRSD, Beck Depression Inventory or Montgomery–Åsberg Depression Rating Scale), 5 (21%) reported only means (with or without s.d.), 3 (13%) reported percentages achieving at least 50% reduction from baseline, 12 (50%) reported percentages below a declared cut-off point and 4 (17%) used a complex combination. Table 1 also shows the numbers of patients with and without personality disorder with good or poor outcome, except for 6 studies that did not report a dichotomised response; overall 45% (746 out of 1663) of those with personality disorder had a 'good' outcome compared with 57% (1054 out of 1860) of those without.

Table 2 summarises the results from studies reporting mean outcome scores on the HRSD, BDI and MADRS, together with estimates of ORs obtained from means (and s.d.) using the methods of Whitehead *et al* (1999). Also shown for comparison are ORs obtained from dichotomised outcomes reported by individual studies. Given the width of the 95% CI around the ORs, it is difficult to detect divergence between the two sets. However, it should be noted that the point estimates of the ORs estimated from means (and s.d.) are reasonably close to those reported for dichotomised outcomes, with the exception of Zimmerman *et al* (1986) (which occurs only when treatment is stratified by modality), Casey *et al* (1996) and Viinamaki *et al* (2002). On this basis we consider that the methods of Whitehead *et al* are sufficiently robust to allow inclusion of the six studies in Table 2 that do not report a dichotomised outcome. For the other ten studies in Table 2, the dichotomised outcome is used in the meta-analysis.

Figure 1 shows a funnel plot of ORs (under a fixed-effects model) from the 34 studies in Table 1. In the absence of publication bias the points should be symmetrical about the vertical line at the pooled ORs. Although reasonably symmetrical, it does suggest the possible absence of small studies (large standard errors) with negative associations (ORs around 1 or less), which may be a natural consequence of the general tendency to publish 'positive' studies.

Figure 2 is a forest plot of ORs from the 34 studies, stratified by type of outcome measure and ordered by date of publication. Within the two largest groups, Hamilton-type criteria and miscellaneous criteria, there is heterogeneity and in view of this, the meta-analysis employs a random-effects model. Despite this heterogeneity, the ORs from the studies that employed Hamilton-type criteria show a degree of consistency that is perhaps remarkable given the diverse methodologies of the studies included. All except two of the point estimates of the ORs lie to the

Table 1 Characteristics of studies reporting association between personality disorder and outcome in depression

First author (year)	Study			Criteria		Response	Treatment	Time (weeks)[7]	Personality disorder		No personality disorder	
	Location	Type[1]	IP/OP	Depression	Personality disorder				Good[8]	Poor[9]	Good[8]	Poor[9]
Charney (1981)	USA	CNR	IP	DSM–III	DSM–III	Good or complete	Drugs, PSY	12	20	20	22	2
Tyrer (1983)	England	RCT	Both	HRSD	PAS	⩾50% ↓HRSD, HRSA	Drugs	4	3	29	13	15
Pfohl (1984, 1987)	USA	PCS	IP	DSM–III	DSM–III	⩾50% ↓HRSD	ECT, drugs, neither	4 (mean)	10	31	22	15
Davidson (1985)	USA	RCT	IP	RDC	DSM–III	HRSD[2]	Drugs	4	–	–	–	–
Shawcross (1985)	England	PCS	OP	ICD–9	PAS	Clinical judgement	Drugs	60 (mean)	5	12	28	5
Sauer (1986)	Germany	PCS	IP	DSM–III	DSM–III	⩾50% ↓HRSD	Drugs	3	–	–	–	–
Black (1988)	USA	CNR	IP	DSM–III	DSM–III	Recovered – case notes	Drugs, ECT, other	NK	32	44	91	61
Goethe (1988)	USA	CNR	IP	DSM–III	DSM–III (?)	Clinical judgement	Drugs, ECT	20 (mean)	40	84	40	37
Pilkonis (1988)	USA	PCS	OP	RDC	DSM–III	Complex[3]	Drugs, PSY	16+	17	32	34	19
Thompson (1988)	USA	RCT	OP	RDC	DSM–III	No MDD	PSY	24	13	12	40	10
Andreoli (1989)	Switzerland	PCS	IP	DSM–III–R	DSM–III–R	Symptomatic recovery	Drugs+IP	NK	11	16	6	14
Joffe (1989)	Canada	PCS	OP	DSM–III, RDC	DSM–III	HRSD < 5	Drugs	5	16	17	7	2
Keitner (1989)	USA	PCS	IP	DSM–III	DSM–III (?)	HRSD < 7 for 3 months	Drugs, PSY	26	2	6	27	43
Reich (1990)	USA	PCS	OP	RDC	PDQ, GAS	Not taking drugs	Drugs	26	14	11	6	4
Shea (1990)	USA	RCT	OP	RDC	DSM–III	HRSD ⩽ 6	Drugs, PSY	16	54	124	30	31
Tyrer (1990)	England	RCT	OP	DSM–III	PAS	MADRS < 6	Drugs, PSY	10	5	26	10	20
Ansseau (1991)	Belgium	PCS	OP	DSM–III	DSM–III	Completing study	Drugs	8	19	3	17	7
Stuart (1992)	USA	PCS	OP	DSM–III–R	DSM–III–R	HRSD < 7 for ⩾4 weeks	PSY	16	7	7	23	16
Diguer (1993)	USA	PCS	OP	DSM–III–R, RDC	DSM–III–R	BDI[2]	PSY	~16	–	–	–	–
Sato (1993)	Japan	PCS	OP	DSM–III–R	DSM–III–R	Complex[4]	Drugs	17	27	25	32	12
Fava (1994)	USA	RCT	OP	DSM–III–R	DSM–III–R	HRSD[2]	Drugs	8	–	–	–	–
Sullivan (1994)	New Zealand	RCT	OP	DSM–III–R	DSM–III–R	HRSD < 8	Drugs	6	28	25	22	24
Hardy (1995)	England	RCT	OP	DSM–III	DSM–III–R	BDI < 7 (?)	PSY	NK	13	14	53	32
Patience (1995)	Scotland	RCT	OP	DSM–III	PAS	HRSD ⩽ 6	Drugs, PSY	16	18	20	42	21
Casey (1996)	Ireland	PCS	IP	DSM–III–R	PAS	Readmission	ECT	52	10	8	13	9
Ilardi (1997)	USA	PCS	IP	DSM–III–R	DSM–III–R	Depressive relapse	Drugs, ECT	26	5	17	24	4
Ekselius (1998)	Sweden	RCT	OP	DSM–III–R	SCID	Complex[5]	Drugs	24	171	18	110	9
Hirschfeld (1998)	USA	RCT	OP	DSM–III–R	DSM–III–R	Complex[6]	Drugs	12	153	153	171	146
Ezquiaga (1998)	Spain	PCS	OP	DSM–III–R	DSM–III–R	HRSD < 8	Drugs, PSY	26	4	21	37	25
Leibbrand (1999)	Germany	PCS	IP	DSM–IV	DSM–IV	BDI[2]	PSY	10 (mean)	–	–	–	–
Fava (2002)	USA	RCT	OP	DSM–III–R	SCID–P	HRSD[2]	Drugs	8	–	–	–	–
Viinamaki (2002)	Finland	PCS	OP	DSM–III–R	SCID–II–P	BDI < 10	Drugs, PSY	26	8	44	35	30
Kool (2003)[10]	Netherlands	RCT	OP	DSM–III–R	DSM–III–R	HRSD < 8	Drugs, PSY	24	30	55	14	29
Casey (2004)[10]	Europe	RCT	OP	ICD–10, DSM–IV	PAS	BDI < 7	PSY	26	11	43	85	164

↓, reduction; BDI, Beck Depression Inventory; CNR, case note review; ECT, electroconvulsive therapy; GAS, Global Assessment Scale; HRSA, Hamilton Rating Scale for Anxiety; HRSD, Hamilton Rating Scale for Depression; IP, in-patient; MADRS, Montgomery–Åsberg Depression Rating Scale; MDD, major depressive disorder; NK, not known; OP, out-patient; PAS, Personality Assessment Schedule; PCS, prospective case series; PDQ, Personality Diagnostic Questionnaire; PSY, psychological therapy; RCT, randomised controlled trial; RDC, Research Diagnostic Criteria; SCID, Structured Clinical Interview for DSM–IV Disorders.

1. Prospective case series include non-randomised trials.
2. Continuous outcome only reported (no dichotomy).
3. Using own algorithm.
4. 17-item HRSD < 6 and full recovery of social functioning 16 weeks after starting treatment and no sign of recurrence of depression during 4 weeks after first two criteria met.
5. ⩾ 50% reduction in MADRS score at 24 weeks, Clinical Global Impression (CGI) scale score 1–3 and CGI Improvement (CGI–I) scale rated at least 'much improved'.
6. CGI–I score of 1 or 2 and HRSD > 9, or ⩾ 50% reduction in HRSD score with HRSD < 15 and CGI severity 3.
7. Time interval from start to outcome evaluation.
8. Meets response criteria.
9. Does not meet response criteria.
10. Study added to the original data-set after a further literature review in August 2004.

Table 2 Odds ratios estimated from continuous scales and reported from dichotomous outcomes[1]

First author (year)	Scale	Score: mean (s.d., *n*)				Odds ratio (95% CI)	
		Personality disorder		No personality disorder		Normal	Dichotomy
		Baseline	End	Baseline	End		
Zimmerman (1986)	HRSD	24.2 (4.9, 10)	10.2 (6.9, 10)	21.0 (5.6, 15)	8.5 (7.7, 15)	1.7 (0.4–7.3)	4.6 (0.7–29)
Shea (1990)	HRSD	20.6 (4.5, 187)	11.3 (7.5, 178)	20.4 (4.8, 62)	9.6 (7.5, 61)	1.5 (0.8–2.5)	2.2 (1.2–4.0)
Tyrer (1990)	MADRS	22.4 (7.9, 31)	14.6 (8.0, 31)	21.8 (7.0, 30)	13.4 (10.5, 30)	2.0 (0.7–5.7)	2.1 (1.0–4.1)
Sullivan (1994)	HRSD	21.9 (4.5, 46)	8.3 (6.0, 46)	21.7 (4.7, 39)	8.4 (6.4, 39)	1.0 (0.5–2.1)	0.8 (0.3–1.8)
Patience (1995)	HRSD	19.6 (6.3, 38)	9.2 (–, 38)	16.7 (5.5, 63)	5.6 (–, 63)	2.5 (1.2–4.9)	2.2 (0.9–5.1)
Hardy (1995)	BDI	25.0 (7.5, 27)	13.5 (8.6, 27)	20.3 (6.3, 87)	8.2 (7.0, 85)	2.6 (1.1–6.0)	1.8 (0.7–4.3)
Casey (1996)	HRSD	31.1 (–, 18)	16.7 (–, 18)	28.4 (–, 22)	9.0 (–, 22)	5.7 (1.2–26)	1.2 (0.3–41)
Ekselius (1998)	MADRS	29.0 (5.2, 189)	5.2 (5.8, 189)	27.2 (4.7, 119)	4.8 (6.8, 119)	1.1 (0.7–1.6)	1.2 (0.7–1.9)
Viinamaki (2002)	HRSD	20.0 (6.7, 52)	13.9 (6.4, 52)	18.0 (6.3, 65)	10.0 (6.8, 65)	3.2 (1.4–7.2)	6.4 (2.6–16)
Kool (2003)	HRSD	20.4 (4.7, 85)	12.7 (7.9, 85)	20.4 (5.2, 43)	11.6 (7.8, 43)	1.3 (0.6–2.6)	1.1 (–)
Davidson (1985)	HRSD	–	12.4 (6.1, 15)	–	12.7 (9.1, 20)	1.7 (0.4–7.3)	–
Sauer (1986)	HRSD	–	23.8 (–, 13)	–	16.8 (–, 37)	5.3 (0.3–81)	–
Diguer (1993)	BDI	29.1 (7.2, 12)	19.2 (9.9, 12)	26.8 (6.8, 13)	8.8 (6.2, 13)	4.7 (0.7–28)	–
Fava (1994)	HRSD	–	8.2 (–, 62)	–	5.7 (–, 21)	1.9 (0.8–4.2)	–
Leibbrand (1999)	BDI	25.1 (10.8, 39)	13.3 (11.6, 39)	22.5 (10.8, 18)	12.7 (9.1, 18)	0.8 (0.3–2.4)	–
Fava (2002)	HRSD	–	10.8 (–, 243)	–	9.9 (–, 135)	–	–

BDI, Beck Depression Inventory; HRSD, Hamilton Rating Scale for Depression; MADRS, Montgomery–Åsberg Depression Rating Scale.
1. Odds ratios (and 95% CI) were estimated from continuous data using the methods of Whitehead *et al* (1999), assuming a normal distribution of scores at outcome (with different variances in the with and without personality disorder groups) and a cut-off point of 6.0. Also shown are odds ratios estimated from dichotomous data as reported in the same papers though not necessarily with the same definition of response. For five studies (Sauer *et al*, 1986; Fava *et al*, 1994; Patience *et al*, 1995; Casey *et al*, 1996; Fava *et al*, 2002) that report only means at outcome (or percentage change from baseline), the standard deviations (s.d.) have been estimated by interpolation from a linear regression of ln(s.d.) on ln(mean) for the remaining six studies (12 points) that used the HRSD.

right of the (null effect) vertical line, 10 out of the 18 fail to demonstrate statistical significance at $P=0.05$, and the remaining 8 achieve significance with ORs in excess of 1. Overall the odds of response to treatment for depression are roughly doubled in the absence of a personality disorder. This estimate is also consistent with the overview from all 34 studies.

Figure 2 also shows, as expected, that the results from the studies that used miscellaneous criteria for response are more diverse than those that used Hamilton-type criteria, but none the less provide a consistent overview. There are fewer studies, six in total, that report continuous outcomes only, and only one of these excludes association with ORs greater than 2. There

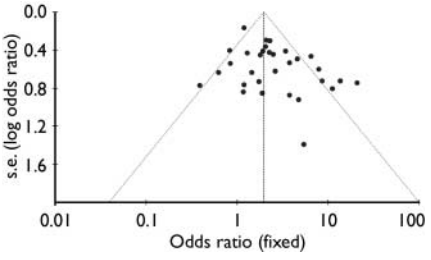

Fig. 1 Funnel plot of studies included in the meta-analysis.

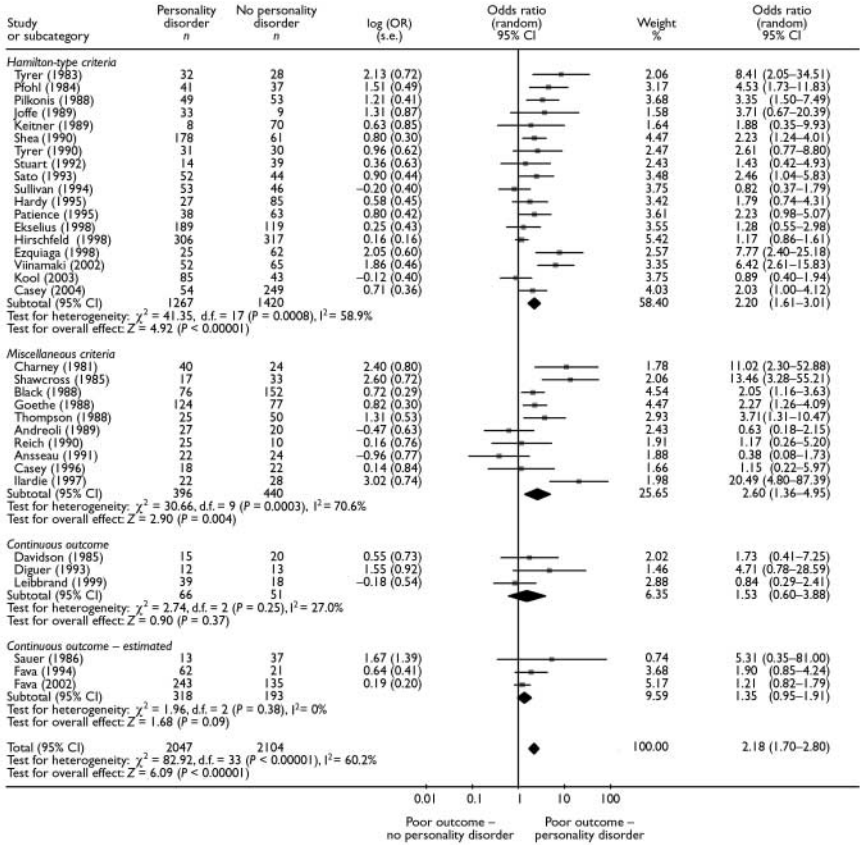

Fig. 2 Random-effects meta-analysis stratified by outcome type and ordered by year of publication (only first authors are shown).

is no evidence of a trend with year of publication within any of the strata.

A secondary analysis was carried out by subdividing studies into four predominant treatment modalities: electroconvulsive therapy (ECT), drug treatment alone, any form of psychotherapy alone, and both drugs and psychotherapy available, although not necessarily used in combination. The purpose of this was to explore whether any particular modality was suggestive of better outcome, irrespective of the outcome measure employed. Figure 3 shows that all treatment modalities except ECT had a poorer outcome for the treatment of depression if personality disorder was present. The greatest divergence between the groups was among those treated with a combination of psychotherapy and drugs, those without a personality disorder being more likely to respond (OR=2.66, 95% CI 1.31–5.42) than those with a personality disorder. We caution against overinterpretation of this against a background of varying treatments, treatment intensities and durations.

In Fig. 4 the studies are stratified by their design and ordered within design type by interval from baseline to outcome assessment. The RCTs are less heterogeneous than the cohort studies and also suggest a smaller effect of personality disorder (OR=1.60 *v.* 2.73). Interval from baseline to outcome assessment does not appear to be related to the outcome of treatment. Table 2 shows that those with personality disorder had slightly higher mean Hamilton scores at baseline than those without (21.1 *v.* 19.9), and this could be associated with poorer response. However, they also had a smaller mean change (9.5 *v.* 11.0) and the duration of five of the seven studies exceeded 15 weeks.

DISCUSSION

In the spirit of evidence synthesis, we have described fully our search strategy, study selection, data summary and analysis to allow replication or sensitivity analysis of any aspect of our approach. We have included every study that to our knowledge satisfies our inclusion criteria and employed techniques of estimation that allow integration of diverse outcome measures. The results are clear: the co-occurrence of a personality disorder in a person with depression is about twice as likely to be associated with a poor response as in an individual without a personality disorder. This is a robust finding which is not altered significantly by the nature of the instrument used to measure depression outcome. Furthermore, no treatment modality stands out as being more effective than any other in the treatment of a person with depression and personality disorder. The trend was for psychotherapy to be associated with poorer outcome in those with personality disorder.

Overall, about 55% of patients with personality disorder had a poor outcome compared with about 45% of those without, demonstrating that many of those with depression and personality disorder remain unwell, a feature that is particularly noticeable in the long term (Kennedy *et al*, 2004; Tyrer *et al*, 2004). The total number of patients necessary to detect this difference (or larger) with 90% power, using a (two-sided) statistical test of the difference between two proportions at the 5% level of significance, exceeds 1000. None of the individual studies approached this target. The largest, by Hirschfield *et al* (1998), which included over 600 patients, achieved only 70% power to detect this effect. This partly explains the confusion in the literature and reinforces the need to combine evidence from separate studies to reach a sound conclusion.

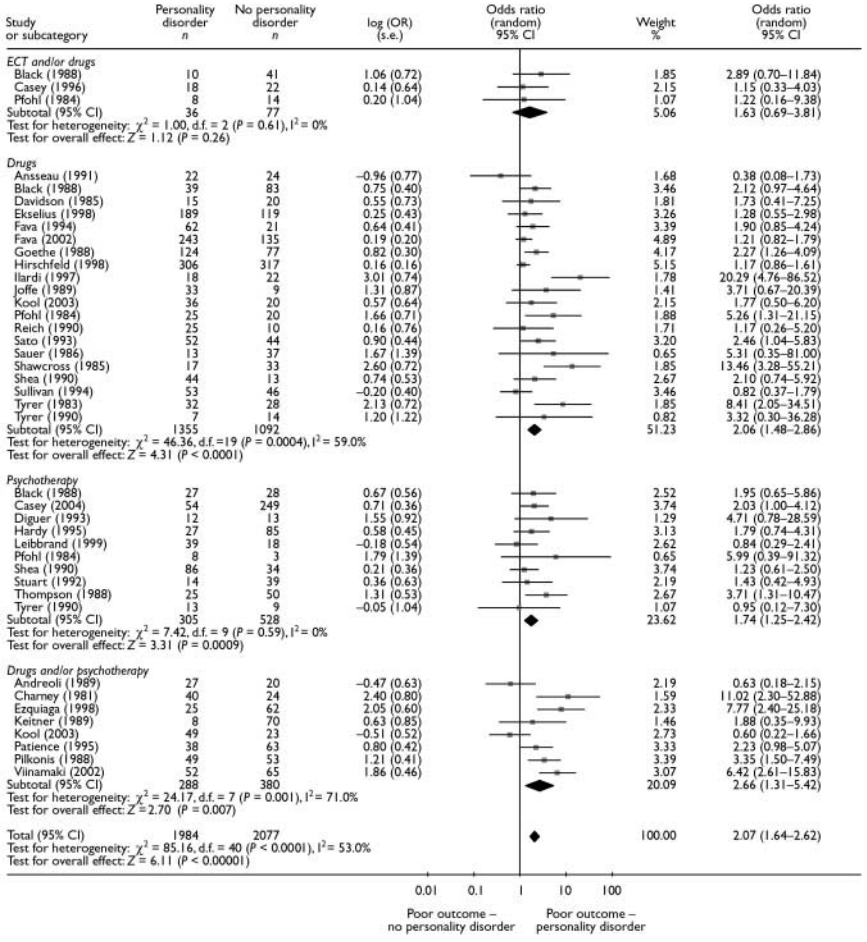

Fig. 3 Random-effects meta-analysis stratified by treatment modality. ECT, electroconvulsive therapy. For each study, only the first author is shown.

Methodological strengths and weaknesses

Our research strategy was comprehensive and studies excluded because they did not satisfy our inclusion criteria did not show important differences from the included papers. Resources to include searches for papers not written in English were unavailable.

A surprising finding was the relative dearth of studies exploring this issue either as a primary or secondary research aim. Depression is extremely common, the bread and butter of day-to-day psychiatry, and this is reflected in the research. Comorbidity with personality disorder is also common, but this is not as well reflected. Only a quarter of the studies identified as potentially useful provided the necessary data and only 14 were RCTs.

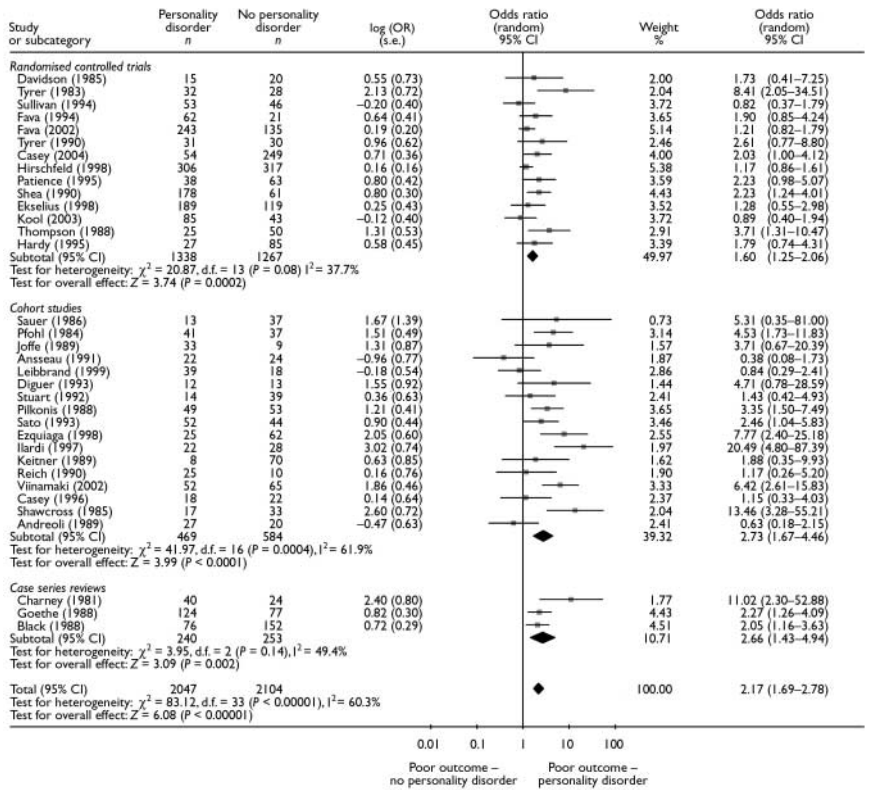

Fig. 4 Random-effects meta-analysis stratified by type of study and ordered by interval to assessment (shorter time periods shown first). For each study, only the first author is shown.

Our findings do not indicate whether the influence of personality disorder is independent of intervention. They suggest, however, that the treatment of depression with psychotherapy may be less effective in those with personality disorder. A recent study using interpersonal psychotherapy as maintenance treatment for women with depression found higher rates of recurrence and more rapid relapse in a subgroup with personality disorder (Cyranowski *et al*, 2004). It also found an increased need for pharmacotherapy, broadly supporting this conclusion. This somewhat counterintuitive finding needs cautious interpretation as the total numbers are not large and no effort has been made to substratify psychological treatment modalities. A specific type of psychological approach might have merit in this group, as has been shown for the specific treatment of borderline personality disorder (Linehan *et al*, 1991; Bateman & Fonagy, 1999; Verheul *et al*, 2003). The better result with drug treatment may also be a direct effect of treatment on personality pathology, as has been suggested in recent studies (Ekselius & von Knorring, 1998; Fava *et al*, 2002). There also might be important variation between the effects of different antidepressants in the presence of personality disorder (Mulder *et al*, 2003). The merits of combined drug and psychological treatment are also not yet known in the presence of personality disorder (Kool *et al*, 2003; de Jonghe *et al*, 2004).

Similarly the absence of a clear association with response to ECT requires cautious interpretation because of the comparatively small total numbers involved. Nevertheless there is some indication that ECT may be of benefit in those with severe depression and personality disorder. In many studies, initial depression scores were higher in the groups with personality disorder, potentially leading to a spurious conclusion of poor outcome when taking a fixed-scale score for recovery status. However, the difference was not large (an HRSD score difference of less than 1.5 between groups). The group with personality disorder also showed a smaller mean change with treatment regardless of the baseline measure, and there was no apparent relationship between the OR and the duration of study.

Finally by only analysing studies in which a categorical diagnosis was used, we excluded papers that provided dimensional ratings of personality only. This, however, allows for reproducible collation of the data in a fashion that is not only amenable to analysis but useful in day-to-day practice.

Implications for clinical practice

We conclude that if comorbid personality disorder is not treated patients will respond less well to treatment for depression than do those with no personality disorder; the same may apply even if no treatment is given. There is no particular treatment that defies this association, although there is some suggestion that the negative effect of personality disorder might be attenuated by drug treatment. The results emphasise the importance of studying the simultaneous treatment of depression and comorbid personality disorder, since there is now better evidence that both drug and psychological treatments, when specifically targeted at personality pathology, might be of value (Leichsenring & Leibing, 2003; Newton-Howes & Tyrer, 2003; Tyrer *et al*, 2003). Some of the contrary findings in the literature (Mulder, 2002) might reflect the extent to which personality disorder has been treated, either explicitly or covertly. Whatever the interpretation, a diagnosis of personality disorder is not necessarily a poor prognostic indicator. These patients simply require treatment of both the personality disorder and the depression. This offers a challenge to clinicians. Despite our best endeavours patients with personality disorder remain one of the most difficult groups in psychiatric practice.

STUDIES INCLUDED IN THE META-ANALYSIS

Andreoli, A., Gressot, G., Aapro, N., *et al* (1989) Personality disorders as a predictor of outcome. *Journal of Personality Disorders*, **3**, 307–320.

Ansseau, M., Troisfontaines, B., Papart, P., *et al* (1991) Compulsive personality as predictor of response to serotoninergic antidepressants. *BMJ*, **303**, 760–761.

Black, D. W., Bell, S., Hulbert, J., *et al* (1988) The importance of axis II in patients with major depression: a controlled study. *Journal of Affective Disorders*, **14**, 115–122.

Casey, P. & Butler, E. (1995) The effects of personality on response to ECT in major depression. *Journal of Personality Disorders*, **9**, 134–142.

Casey, P., Meagher, D. & Butler, E. (1996) Personality, functioning, and recovery from major depression. *Journal of Nervous and Mental Disease*, **184**, 240–245.

Casey, P., Birbeck, G., McDonagh, C., *et al* (2004) Personality disorder, depression and functioning: results from the ODIN study. *Journal of Affective Disorders*, **82**, 277–283.

Charney, D. S., Nelson, J. C. & Quinlan, D. M. (1981) Personality traits and disorder in depression. *American Journal of Psychiatry*, **138**, 1601–1604.

Davidson, J., Miller, R. & Strickland, R. (1985) Neuroticism and personality disorder in depression. *Journal of Affective Disorders*, **8**, 177–182.

Diguer, L., Barber, J. P. & Luborsky, L. (1993) Three concomitants: personality disorders, psychiatric severity, and outcome of dynamic psychotherapy of major depression. *American Journal of Psychiatry*, **150**, 1246–1248.

Ekselius, L. & von Knorring, L. (1998) Personality disorder comorbidity with major depression and response to treatment with sertraline or citalopram. *International Clinical Psychopharmacology*, **13**, 205–211.

Ezquiaga, E., Garcia, A., Bravo, F., *et al* (1998) Factors associated with outcome in major depression: a 6-month prospective study. *Social Psychiatry and Psychiatric Epidemiology*, **33**, 552–557.

Fava, M., Bouffides, E., Pava, J. A., *et al* (1994) Personality disorder comorbidity with major depression and response to fluoxetine treatment. *Psychotherapy and Psychosomatics*, **62**, 160–167.

Fava, M., Farabaugh, A. H., Sickinger, A. H., *et al* (2002) Personality disorders and depression. *Psychological Medicine*, **32**, 1049–1057.

Goethe, J. W., Szarek, B. L. & Cook, W. L. (1988) A comparison of adequately *vs.* inadequately treated depressed patients. *Journal of Nervous and Mental Disease*, **176**, 465–470.

Hardy, G. E., Barkham, M., Shapiro, D. A., *et al* (1995) Impact of cluster C personality disorders on outcomes of contrasting brief psychotherapies for depression. *Journal of Consulting and Clinical Psychology*, **63**, 997–1004.

Hirschfeld, R. M., Russell, J. M., Delgado, P. L., *et al* (1998) Predictors of response to acute treatment of chronic and double depression with sertraline or imipramine. *Journal of Clinical Psychiatry*, **59**, 669–675.

Ilardi, S. S., Craighead, W. E. & Evans, D. (1997) Modelling relapse in unipolar depression: the effects of dysfunctional cognitions and personality disorders. *Journal of Consulting and Clinical Psychology*, **65**, 381–391.

Joffe, R. T. & Regan, J. J. (1989) Personality and response to tricyclic antidepressants in depressed patients. *Journal of Nervous and Mental Disease*, **177**, 745–749.

Keitner, G. I., Miller, I. W., Ryan, C. E., *et al* (1989) Compounded depression and family functioning during the acute episode and at 6-month follow up. *Comprehensive Psychiatry*, **30**, 512–521.

Kool, S., Dekker, J., Duijsens, I. J., *et al* (2003) Efficacy of combined therapy and pharmacotherapy for depressed patients with or without personality disorders. *Harvard Review of Psychiatry*, **11**, 133–141.

Leibbrand, R., Hiller, W. & Fichter, M. (1999) Effect of comorbid anxiety, depressive, and personality disorders on treatment outcome of somatoform disorders. *Comprehensive Psychiatry*, **40**, 203–209.

Patience, D. A., McGuire, R. J., Scott, A. I., *et al* (1995) The Edinburgh Primary Care Depression Study: personality disorder and outcome. *British Journal of Psychiatry*, **167**, 324–330.

Pfohl, B., Stangl, D. & Zimmerman, M. (1984) The implications of DSM–III personality disorders for patients with major depression. *Journal of Affective Disorders*, **7**, 309–318.

Pfohl, B., Coryell, W., Zimmerman, B., *et al* (1987) Prognostic validity of self report and interview measures of personality disorder in depressed inpatients. *Journal of Clinical Psychiatry*, **48**, 468–472.

Pilkonis, P. A. & Frank, E. (1988) Personality pathology in recurrent depression: nature, prevalence, and relationship to treatment response. *American Journal of Psychiatry*, **145**, 435–441.

Reich, J. H. (1990) Effect of DSM–III personality disorders on outcome of tricyclic antidepressant-treated nonpsychotic outpatients with major or minor depressive disorder. *Psychiatry Research*, **32**, 175–181.

Sato, T., Sakado, K. & Sato, S. (1993) Is there any specific personality disorder or personality cluster that worsens the short-term treatment outcome of major depression? *Acta Psychiatrica Scandinavica*, **88**, 342–349.

Sauer, H., Kick, H., Minne, H. W., *et al* (1986) Prediction of the amitryptiline response: psychopathology versus neuroendocrinology. *International Clinical Psychopharmacology*, **1**, 284–295.

Shawcross, C. R. & Tyrer, P. (1985) Influence of personality on response to monoamine oxidase inhibitors and antidepressants. *Journal of Psychiatric Research*, **19**, 557–562.

Shea, M. T., Pilkonis, P. A., Beckham, E., *et al* (1990) Personality disorders and treatment outcome in the NIMH treatment of depression collaborative research program. *American Journal of Psychiatry*, **147**, 711–718.

Stuart, S., Simons, A. D., Thase, M. E., *et al* (1992) Are personality assessments valid in acute major depression? *Journal of Affective Disorders*, **24**, 281–290.

Sullivan, P F., Joyce, P. R. & Mulder, R. T. (1994) Borderline personality disorder in major depression. *Journal of Nervous and Mental Disease*, **182**, 508–516.

Thompson, L. W., Gallagher, D. & Czirr, R. (1988) Personality disorder and outcome in the treatment of late-life depression. *Journal of Geriatric Psychiatry*, **21**, 133–153.

Tyrer, P., Casey, P. & Gall, J. (1983) Relationship between neurosis and personality disorder. *British Journal of Psychiatry*, **142**, 404–408.

Tyrer, P., Seivewright, N., Ferguson, B., *et al* (1990) The Nottingham study of neurotic disorder: relationship between personality status and symptoms. *Psychological Medicine*, **20**, 423–431.

Viinamaki, H., Hintikka, J., Honkalampi, K., *et al* (2002) Cluster C personality disorder impedes alleviation of symptoms in major depression. *Journal of Affective Disorders*, **71**, 35–41.

Zimmerman, M., Coryell, W., Pfohl, B., *et al* (1986) ECT response in depressed patients with and without a DSM–III personality disorder. *American Journal of Psychiatry*, **143**, 1030–1032.

CLINICAL IMPLICATIONS

- As co-occurrence of personality disorder with depression increases the likelihood of a poor outcome, attention should be paid to concurrent treatment of comorbid personality disorder in patients with depression.
- The treatment of comorbid personality disorder by psychological means is not supported by the meta-analysis.
- Assessment of personality status early in the treatment of depression may help to predict outcome.

LIMITATIONS

- Only papers using a categorical approach to personality disorder were included in the meta-analysis.
- People with a personality disorder generally had higher scores on depression rating scales at the beginning of treatment.
- It was not possible to conclude that personality disorder in itself caused the poorer outcome in depression.

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REFERENCES

American Psychiatric Association (1980) *Diagnostic and Statistical Manual of Mental Disorders* (3rd edn) (DSM–III). Washington, DC: APA.

Bateman, A. & Fonagy, P. (1999) Effectiveness of partial hospitalisation in the treatment of borderline personality disorder: a randomised controlled trial. *American Journal of Psychiatry*, **156**, 1563–1569.

Beck, A. T., Ward, C. H. & Mendelson, M., *et al* (1961) An inventory for measuring depression. *Archives of General Psychiatry*, **4**, 561–571.

Brieger, P., Ehrt, U., Bloeink, R., *et al* (2002) Consequences of comorbid personality disorders in major depression. *Journal of Nervous and Mental Disease*, **190**, 304–309.

Cloninger, C. R. (1987) A systematic method for clinical description and classification of personality variants. *Archives of General Psychiatry*, **44**, 573–588.

Corruble, E., Ginester, D. & Guelfi, J. D. (1996) Comorbidity of personality disorders and unipolar major depression: a review. *Journal of Affective Disorders*, **37**, 157–170.

Cyranowski, J. M., Frank, E. & Winter, E., *et al* (2004) Personality pathology and outcome in recurrently depressed women over 2 years of maintenance interpersonal psychotherapy. *Psychological Medicine*, **34**, 659–669.

De Jonghe, F., Hendriksen, M., van Alst, G., *et al* (2004) Psychotherapy alone and combined with pharmacotherapy in the treatment of depression. *British Journal of Psyciatry*, **185**, 35–45.

Dreessen, L. & Arntz, A. (1998) The impact of personality disorders on treatment outcome of anxiety disorders: best-evidence synthesis. *Behaviour Research and Therapy*, **36**, 483–504.

Eysenck, H. J. (1959) *The Maudsley Personality Inventory.* London: University of London Press.

Eysenck, H. J. & Eysenck, S. B. G. (1964) *Manual of the Eysenck Personality Inventory.* London: University of London Press.

Greer, H. S. & Cawley, R. H. (1966) Some observations on the natural history of neurotic illness. In *Australian Medical Association, Mervyn Archdall Medical Monograph No. 3.* Glebe, Australia: Australasian Medical Publishing Company.

Hamilton, M. (1960) A rating scale for depression. *Journal of Neurology, Neurosurgery and Psychiatry*, **23**, 56–62.

Ilardi, S. S. & Craighead, W. E. (1995) Personality pathology and response to somatic treatments for major depression: a critical review. *Depression*, **2**, 200–217.

Kennedy, N., Abbott, R. & Paykel, E. S. (2004) Longitudinal syndromal and sub-syndromal symptoms after severe depression: 10-year follow-up study. *British Journal of Psychiatry*, **184**, 330–336.

Leichsenring, F. & Leibing, E. (2003) The effectiveness of psychodynamic therapy and cognitive behavior therapy in the treatment of personality disorders: a meta-analysis. *American Journal of Psychiatry*, **160**, 1223–1232.

Linehan, M. M., Armstrong, H. E., Suarez, A., *et al* (1991) Cognitive–behavioural treatment of chronically parasuicidal borderline patients. *Archives of General Psychiatry*, **48**, 1060–1064.

Livesley, W. J. (1991) Classifying personality disorders: ideal types, prototypes, or dimensions? *Journal of Personality Disorders*, **5**, 52–59.

McGlashan, T. H. (1987) Borderline personality disorder and unipolar affective disorder: long-term effects and comorbidity. *Journal of Nervous and Mental Disease*, **175**, 467–473.

Montgomery, S. A. & Åsberg, M. (1979) A new depression scale designed to be sensitive to change. *British Journal of Psychiatry*, **134**, 382–389.

Mulder, R. (2002) Personality pathology and treatment outcome in major depression: a review. *American Journal of Psychiatry*, **159**, 359–371.

Mulder, R. T., Joyce, P. R. & Luty, S. E. (2003) The relationship of personality disorders to treatment outcome in depressed outpatients. *Journal of Clinical Psychiatry*, **64**, 259–264.

Newton-Howes, G. & Tyrer, P. (2003) Pharmacotherapy for personality disorders. *Expert Opinion on Pharmacotherapy*, **4**, 1643–1649.

Reich, J. H. & Green, A. I. (1991) Effect of personality disorders on outcome of treatment. *Journal of Nervous and Mental Disease*, **179**, 74–82.

Reich, J. H. & Vasile, R. G. (1993) Effect of personality disorders on the treatment outcome of axis I conditions: an update. *Journal of Nervous and Mental Disease*, **181**, 475–484.

Sargant, W. (1966) Psychiatric treatment in general teaching hospitals: a plea for a mechanistic approach. *BMJ*, **2**, 257–262.

Shea, M. T., Widiger, T. A. & Klein, M. H. (1992) Comorbidity of personality disorders and depression: implications for treatment. *Journal of Consulting and Clinical Psychology*, **60**, 857–868.

Tyrer, P., Sensky, T. & Mitchard, S. (2003) The principles of nidotherapy in the treatment of persistent mental and personality disorders. *Psychotherapy and Psychosomatics*, **72**, 350–356.

Tyrer, P., Seivewright, H. & Johnson, T. (2004) The Nottingham Study of Neurotic Disorder: predictors of 12-year outcome of dysthymic, panic and generalized anxiety disorder. *Psychological Medicine*, **34**, 1385–1394.

Verheul, R., van den Bosch, L. M. C., Koeter, M. J. W., *et al* (2003) Dialectical behaviour therapy for women with borderline personality disorder: 12-month, randomised clinical trial in The Netherlands. *British Journal of Psychiatry*, **182**, 135–140.

Whitehead, A., Bailey, A. J. & Elbourne, D. (1999) Combining summaries of binary outcomes with those of continuous outcomes in a meta-analysis. *Journal of Biopharmaceutical Statistics*, **9**, 1–16.