Psychological Medicine, 2006, **36**, 1551–1562. © 2006 Cambridge University Press
doi:10.1017/S0033291706008579 Printed in the United Kingdom

Remission and relapse in psychosis: operational definitions based on case-note data

PAUL E. BEBBINGTON[1]*, TOM CRAIG[2], PHILIPPA GARETY[2], DAVID FOWLER[3], GRAHAM DUNN[4], SUSANNAH COLBERT[1], MIRIAM FORNELLS-AMBROJO[2] AND ELIZABETH KUIPERS[2]

[1] *Royal Free & University College London Medical School, UCL – Department of Mental Health Sciences (Bloomsbury Campus), London, UK*; [2] *King's College, Institute of Psychiatry, London, UK*; [3] *School of Medicine, Health Policy and Practice, UEA, UK*; [4] *School of Epidemiology and Health Sciences, University of Manchester, UK*

ABSTRACT

Background. In psychosis, the prime indicator of outcome has been relapse, but hospital readmission can no longer be used for this purpose. Researchers now require methods for assessing relapse that are objective, blind, reliable and valid. We describe the reliability and validity of such a technique using case-notes.

Method. Information from routine clinical notes of participants in the Lambeth Early Onset (LEO) study (less all references that would unblind the assessor) were recorded on a form divided into 1-month sections. Operational definitions of remission and relapse enabled clinicians to identify remissions and relapses blindly from the summary information. We calculated reliability regarding both the fact and the timing of remission and relapse. PANSS ratings at 6 and 18 months provided a measure of validity.

Results. The kappa value for the identification of remission by individuals ranged from 0·64 to 0·82, while that for consensus between paired raters was 0·56. The corresponding values for relapse were 0·57–0·59 and 0·71. Intra-class correlations for time to remission and to relapse were very high. Raters guessed correctly whether the participants came from the intervention or control group on 60–75% of occasions. Independent PANSS ratings were strongly related to the remission/relapse status of participants.

Conclusions. The reliability of the technique described here was moderate to good, its validity was good, and it provides a useful and timely addition to methods of evaluating remission and relapse in psychosis. On the basis of our experience, we recommend consensus rather than individual ratings.

INTRODUCTION

The assessment of outcome is crucial to the evaluation of mental health interventions and services. In studies of psychosis, relapse has largely been used as the prime indicator, notwithstanding arguments that other aspects are as important (Trivedi & Wykes, 2002; Andreasen *et al.* 2005; Slade *et al.* 2005). The development of reasonably effective community-based services has reduced the value of admission to hospital as a proxy of relapse, as many people with appreciable psychotic symptoms are now managed at home. As a result, clinical trials and epidemiological studies are now in need of objective, reliable and valid ways of assessing relapses that may not necessarily lead to admission. Ideally, this should also be capable of being carried out blind to the nature of the treatment, particularly difficult in studies of psychological treatments or of whole services.

* Address for correspondence: Professor Paul Bebbington, Royal Free & University College London Medical School, UCL – Department of Mental Health Sciences (Bloomsbury Campus), Wolfson Building, 48 Riding House Street, London W1W 7EY, UK. (Email: P.Bebbington@ucl.ac.uk)

https://doi.org/10.1017/S0033291706008579 Published online by Cambridge University Press

Conceptualizing course in variable disorders

A number of related concepts connoting temporal variation in illness status have been imported into psychiatry from physical medicine (Gleeson, 2001). These include remission, recovery and relapse. In illnesses for which treatment is oriented towards cure, remission may be conceptualized as the complete absence of symptoms. However, many illnesses, physical as well as psychiatric, are characterized by a waxing and waning of symptoms and disabilities. One way of measuring the course of such illnesses is by sampling indicators of illness at different time-points. Clearly, the more frequently this is done, the more accurate will be the representation of the course of the disorder. Implicit in this approach is the use of continuous measures. Research can then be based on the mean score at a given time on these measures for the whole group. This has its attractions, and may be the method of choice where patients remain symptomatic over long periods. Thus, most studies of cognitive behaviour therapy in psychosis have been of treatment-resistant cases, where this approach is appropriate (Pilling *et al*. 2002). However, the method loses information in patient groups that are relatively or completely asymptomatic for appreciable periods, but at risk of acute exacerbation at any time. This is because the point of assessment is random in relation to the individual's course of illness. In particular, people whose downturn had already ameliorated at a predetermined assessment point would not be identified as having experienced an exacerbation at all.

In contrast, the concepts of remission, recovery and relapse require a review of the course in a way that is particular to the individual patient. Moreover, the concepts are categorical, not dimensional. In conditions where clinical state fluctuates, the use of these concepts therefore requires an arbitrary decision whereby categories are imposed upon continuously distributed disturbances. This is apparent in definitions of remission in psychiatric illnesses such as anxiety disorders and major depressive disorder (Frank *et al*. 1991). An early example of this approach in psychosis was proposed by Ventura and colleagues (1989), who used scores on the Brief Psychiatric Rating Scale (BPRS) to provide research definitions of remission, relapse, and 'significant psychotic exacerbation', whether following remission or persistent psychotic symptoms. A similar approach has been adopted by the recent American task force on remission in psychosis (Andreasen *et al*. 2005), and used successfully by Lasser *et al*. (2005). Remission was defined as a 'low-mild' level of symptoms, where such absent, borderline, or mild symptoms do not influence the individual's behaviour. Such approaches have gained considerable impetus from interest in first episodes of psychosis (Ram *et al*. 1992).

The identification of remission, relapse, and recovery

In the field of mental health, remission, relapse, and recovery have largely been conceptualized in symptomatic terms. However, early research studies relied strongly on using discharge from and admission to hospital as a proxy for symptomatic remission and relapse. Thus, three major first-episode studies relied on readmission to hospital for their definition of relapse (Crow *et al*. 1986; Scottish Schizophrenia Research Group, 1992; Zhang *et al*. 1994). Changes in admission policies have attenuated the link between symptomatic relapse and admission. This has been underlined by Gitlin *et al*. (2001), who demonstrated a glaring discrepancy between readmission rates (13%) and symptomatic relapse rates (78%). The waning value of admission to hospital as a proxy has emphasized the importance of usable definitions of relapse.

The course of psychosis could be illustrated by change in a number of related states. These would include positive symptoms, but also negative symptoms and cognitive deficits. Moreover, the significance of affective symptoms in psychosis is such that remission and relapse could be conceptualized in terms of these symptoms too. Linzsen *et al*. (1994) used four separate sets of criteria to define relapse, and found that, although the overall rates of relapse were similar, the criteria varied considerably in the identification of individual cases. However, Andreasen and colleagues (2005) are of the opinion that our knowledge of social or cognitive dysfunction in schizophrenia is not yet sufficient for it to be incorporated into definitions of remission or

https://doi.org/10.1017/S0033291706008579 Published online by Cambridge University Press

recovery. It is unclear to what extent symptomatic remission must occur in order to achieve improved functioning and ultimately recovery and autonomy.

Duration criteria of remission, relapse, and recovery

As well as symptomatic criteria, Falloon (1983) emphasized the requirement for duration criteria in definitions of remission, recovery, and relapse. Thus, recovery is conceived as a more complete and prolonged phenomenon than remission, which can be seen as a necessary but not sufficient step towards it. In three relatively recent studies, duration criteria for remission have varied from 1 to 3 months (Linszen *et al*. 1996; Wiersma *et al*. 1998; Robinson *et al*. 1999*a*). In contrast, the Scottish Schizophrenia Research Group (1992) did not include duration criteria.

In the same way, symptomatic exacerbation must persist for an appreciable time in order for it to be usefully recognized as a relapse. Falloon noted this need for separating short- lived exacerbations from relapse. Linszen *et al*. (1994), Robinson *et al*. (1999*b*) and Tarrier *et al*. (2004) all used a 1-week duration criterion to distinguish a minor flurry of symptoms from a relapse. In our view this period is too short: it identifies variations in the symptom state that may arise by chance from small variations in the external environment and that cannot be controlled by a service or therapeutic intervention. Moreover, where the information used to define relapse is derived from entries in clinical records, these may be too infrequent to pick up short-lived variations consistently.

Maximizing the value of information: blindness and coverage

In the absence of reliable proxies, the assessment of outcome in psychosis requires further considered methodological decisions. Clearly the chosen mechanism for identifying relapse depends on the purpose of the researcher or the clinician. The constraints in treatment trials are greater than in purely epidemiological studies. This is because of the trade-off between competing requirements: for accurate and standardized information and for assessment blind to any hypotheses under test. In a treatment trial, it has been argued that the latter is particularly important (Tarrier & Wykes, 2004).

Whatever the purpose, the assessment of outcome requires a retrospective symptomatic evaluation at a follow-up point in order to establish the fact and timing of any relapse occurring within the preceding period. The assessment may be based on research interviews or derived from data routinely recorded in case-notes by the clinical workers providing treatment. The latter has the advantage of independence, and requires less investment by the research team. It also avoids the common problem of those patients who are reluctant to take part in detailed, frequently repeated, interviews, but do not forbid access to clinical notes.

This paper describes a case-note-based technique of assessing remission and relapse, together with its psychometric evaluation. A somewhat similar approach was used by Barrowclough *et al*. (1999) and by Tarrier *et al*. (2004), but has not been published in detail.

METHOD

Techniques for the reliable rating of complex events date back to the methods developed by Brown and colleagues (1973) to assess the threat of life events by consensus. Similar consensual procedures were used to assess clinical crises in the Islington Crisis Team studies (Johnson *et al*. 2005). The technique described in this paper builds on these examples, and relies on extraction of information from routine clinical notes, with the removal of all references that would unblind the assessor. Research workers sought access to all clinical notes relating to the specific period of assessment and scanned them for information that indicated changes in symptom state, and in social circumstance, together with identifiable service responses to these changes (e.g. hospital admission, changes in medication). The research worker then recorded the information on a form divided up into 1-month sections. An anonymized example of a completed form is provided in Appendix 1. When developing the technique, our procedure was to use the consensus judgements of two clinicians to rate the information on the form according to operational definitions of remission and relapse. The procedure was developed for the Lambeth Early Onset (LEO) project (Craig *et al*. 2004; Garety *et al*. 2006) and is being used in the Prevention of Relapse in Psychosis project

https://doi.org/10.1017/S0033291706008579 Published online by Cambridge University Press

(ISRCTN83557988). The operational criteria were deliberately made stringent in order to maximize reliability and minimize false positives, while acknowledging the consequent risk of sometimes missing a judgement because of insufficient information. Thus, indications both of remission and of relapse had to be corroborated by later information before they could be adjudged present.

The first stage is the operationalization of a definition of remission. This may be full, partial or absent. Clearly, if no remission has occurred, the concept of relapse is irrelevant. Our criteria for remission and relapse were couched in terms of positive psychotic symptoms. Logically, full relapse can only follow a full remission, i.e. a progression from a state asymptomatic in terms of positive psychotic symptoms to one characterized by a re-emergence of such symptoms. Partial relapse implies significant exacerbation of an incompletely remitted state (and is consequently more difficult to rate). Partial relapse could equally be termed exacerbation: it should be noted that the use of the qualifier 'partial' does not connote anything about the severity of the change in state in comparison with a full relapse. Partial relapses may still be clinically catastrophic. Judgements of relapse are thus nested within judgements of remission, and this has an effect on procedures for assessing the reliability of the former. In our rating procedure, remission and relapse both require an initial statement drawn from the notes indicating they may be occurring, followed up by a second statement that corroborates the first in a subsequent entry at a defined interval. The information used for these judgements concerns positive symptom status. The ancillary information about social circumstances and service response was used sparingly to corroborate judgements where they were not completely clear-cut (we should note there were instances when hospital admissions did not correspond to relapse judgements). The full criteria are set out in Appendix 2. There is now a manual describing the procedure, available from the authors.

The data used here to establish reliability were originally extracted in the course of the LEO project by S.C. and M.F-A., and entered on the standard form (Appendix 2). Entry in the study led to a 6- and 18-month follow-up, so 18 months' worth of data were entered. P.G. and T.C. made the original ratings on 35 cases, and then developed a consensus relating to the fact and timing of remission and relapse for use in the LEO project. D.F. and P.B. then repeated this procedure on 28 of the 35 cases. As a result, we are able to present reliability for the two pairs of raters, and also, on the 28 shared cases, for the paired consensus ratings. Our use of consensus was designed to increase validity in the face of necessarily complex judgements. We also hoped that it might lead to better reliability.

The raters also all made guesses about which group (intervention or control) the individual patients belonged to, as a way of evaluating the possibility of breaking blindness to allocation. They recorded the confidence with which they made this guess. In the reliability exercise for relapse, T.G. and P.G. rated 26 cases, and P.B. and D.F. rated 21.

The data were initially analysed with weighted kappa (Cohen, 1968), using the remission categories 'no', 'partial', 'full', and the relapse categories 'relapsed' or 'not'. We did not analyse *relapse type* as this judgement followed automatically from remission type. We then examined reliability over the *timing* of remission and relapse, potentially a more stringent test of reliability than mere presence or absence.

Validity was assessed by relating participants, remission/relapse status at 6 and 18 months to Positive and Negative Syndrome Scale (PANSS) total scores and subscores and to the Global Assessment of Function (GAF) score established by research workers at interview around the same times. We predicted that people categorized as in full remission at the end of the reference period would have the lowest PANSS scores and subscores and the highest GAF scores. Next would be participants in partial remission, followed by the relapsed group, and finally the never-remitted. Data at 6 and 18 months relating to individual participants are clearly not independent. For this reason, analyses were carried out using the xtreg command in STATA (Version 8.0, StataCorp, 2003).

RESULTS

Reliability

Kappa values for agreement over remission and over relapse are shown in Tables 1 and 2. They can be compared with the conventional

https://doi.org/10.1017/S0033291706008579 Published online by Cambridge University Press

Table 1. *Agreement on identification of remission*

	None	Partial	Full
P.B.'s rating		D.F.'s rating	
None	3	1	1
Partial	1	7	0
Full	0	0	15
		$\kappa = 0{\cdot}82$ (S.E. $= 0{\cdot}1$)	
T.C.'s rating		P.G.'s rating	
None	8	1	0
Partial	0	5	2
Full	0	5	14
		$\kappa = 0{\cdot}64$ (S.E. $= 0{\cdot}11$)	
Consensus P.B./D.F.		Consensus T.C./P.G.	
None	2	2	0
Partial	0	6	2
Full	0	3	13
		$\kappa = 0{\cdot}56$ (S.E. $= 0{\cdot}14$)	

Table 2. *Agreement on identification of relapse*

	No relapse	Relapse
P.B.'s rating	D.F.'s rating	
No relapse	12	4
Relapse	0	5
	$\kappa = 0{\cdot}59$ (S.E. $= 0{\cdot}17$)	
T.C.'s rating	P.G.'s rating	
No relapse	15	1
Relapse	4	6
	$\kappa = 0{\cdot}57$ (S.E. $= 0{\cdot}17$)	
Consensus P.B./D.F.	Consensus T.C./P.G.	
No relapse	15	1
Relapse	2	6
	$\kappa = 0{\cdot}71$ (S.E. $= 0{\cdot}16$)	

evaluation of kappa values: moderate (0·4–0·6); good (0·6–0·8); very good (>0·8) (Silman, 1995).

The kappa value for agreement over the identification of remission was 0·82 for D.F. and P.B., and 0·64 for P.G. and T.C. The kappa value for agreement between the two consensus ratings was 0·56. This rose to 0·63 if a binary outcome (remitted or not) was used.

Table 2 shows the rating data relating to relapse in those people who had remitted. The kappa value for agreement was 0·59 for D.F. and P.B., and 0·57 for P.G. and T.C. The kappa value for agreement between the consensus ratings was 0·71.

We then examined agreement as to the individual month in which remission and relapse occurred. This is important if these events are to be related to other types of event (life events, or changes in treatment or medication for example) in the course of the disorder. In those cases where the raters agreed that remission had occurred, the intra-class correlation for time to remission for P.G. and T.C. was 0·85 (95% CI 0·78–0·89), while that for time to relapse was 0·88 (95% CI 0·76–0·94). The corresponding figures for D.F. and P.B. were 0·97 (95% CI 0·95–0·98) and 0·87 (95% CI 0·32–0·98).

Finally, raters attempted to guess which group the subjects came from, as a way of testing the effectiveness of blinding. In this exercise, P.G. guessed correctly on 72% of occasions, T.C. was right on 60·1%, D.F. on 75%, and PB on 63·3%. It should be noted that the misclassification rate was considerably *greater* than expected from the raters' ratings of the confidence they placed in their individual judgements.

Validity

Table 3 shows the means of PANSS total scores and subscores and of the GAF score, collected by independent raters, together with coefficients derived from regressions in which the reference category was full remission. As predicted, in each analysis, the mean scores increased considerably through the categories (full remission, partial remission, relapse, no remission) to a highly significant degree. The only exception was that the GAF score for the 'relapsed' category was to a marginal degree clinically more adverse that that for the 'no remission' group.

DISCUSSION

The value and place of the method described here

In this paper we have demonstrated that it is feasible to use routine data to quantify the course of disorder, and we have shown that the reliability of the technique is moderate or good. Moreover, once a judgement had been made that remission or relapse had occurred, the dating was very reliable. This is of importance if different sorts of events need to be related in time, and it may also add to the power of comparison, using survival analysis.

The data were collected as part of the LEO project, in which outcomes from a specialist early intervention team were compared with

https://doi.org/10.1017/S0033291706008579 Published online by Cambridge University Press

Table 3. *Relation between remission/relapse status and clinical measures*

	n	Mean	Coefficient	S.E.	*p*	95% CI
PANSS positive						
Full remission	86	9·7	—	—	—	—
Partial remission	36	13·7	3·66	0·86	<0·0001	1·97 to 5·36
Relapse remission	14	17·3	6·78	1·22	<0·0001	4·39 to 9·16
No remission	35	18·1	8·08	0·88	<0·0001	6·35 to 9·81
PANSS negative						
Full remission		11·2	—	—	—	—
Partial remission		14·9	2·58	0·97	0·008	0·68 to 4·48
Relapse remission		16·1	3·22	1·27	0·011	0·73 to 5·71
No remission		19·0	5·77	1·03	<0·0001	3·76 to 7·79
PANSS general						
Full remission		25·1	—	—	—	—
Partial remission		31·7	6·07	1·34	<0·0001	3·44 to 8·70
Relapse remission		32·4	6·48	1·89	<0·0001	2·77 to 10·19
No remission		37·9	12·14	1·37	<0·0001	9·46 to 14·83
PANSS total						
Full remission		46·0	—	—	—	—
Partial remission		60·4	12·69	2·52	<0·0001	7·75 to 17·63
Relapse remission		65·7	16·89	3·50	<0·0001	10·03 to 23·76
No remission		75·1	26·82	2·58	<0·0001	21·76 to 31·88
GAF						
Full remission		68·6	—	—	—	—
Partial remission		55·3	−13·13	2·22	<0·0001	−17·48 to −8·78
Relapse remission		46·9	−20·76	3·04	<0·0001	−26·72 to −14·80
No remission		44·0	−23·13	2·24	<0·0001	−27·53 to −18·74

CI, Confidence interval; PANSS, Positive and Negative Syndrome Scale; GAF, Global Assessment of Function.

those from routine care (Craig *et al*. 2004; Garety *et al*. 2006). In this project, it was possible for the raters to guess at a level better than chance which group the individual subjects came from. This was because the quality of the clinical information recorded by the LEO team was noticeably better than that in the comparison services, and thereby informed the guess. The raters found that it was more difficult to rate remission and relapse when the case-note entries were vague or imprecise (e.g. 'doing well'; 'does not complain of any symptoms'): this particularly affected the entries from comparison services. Thus, the performance and reliability of the technique should be better in situations where the quality of recording is more equivalent (for example, where two novel services, each with a dedication to comprehensive record keeping, were being compared). For this reason, researchers adopting our method would be well advised to conduct their own studies of reliability. Raters require training in identifying relevant information in case-notes. This can be done by assessment and feedback from a few trial extractions, with constant referral to the operational criteria. During the conduct of the study, the assessment procedure itself provides routine quality control.

In our study, the rate of unblinding varied, such that 10–22% of cases were correctly guessed *over and above* what would occur by chance. It is hard to say whether this level of unblinding leads to significant bias – the procedure is obviously an improvement on unconcealed allocation. (The issue here is not whether the rate of unblinding is significantly different from chance but whether the raw difference from chance expectation would affect the results of the trial). The problem of unblinding has been recognized albeit relatively infrequently even in pharmacological trials: thus Kane *et al*. (1988) used benztropine in their RCT of clozapine in an attempt to disguise allocation. However, it should be noted that there is as yet no tradition of reporting rates of unblinding in controlled trials described as blind, whether of pharmaceutical or psychological interventions (e.g. Tran *et al*. 1998; Csernansky *et al*. 2002; Wykes *et al*. 2002). Tarrier and colleagues (2004) describe one of the few studies to include this information, although only by indicating that the unblinding was no better than chance.

https://doi.org/10.1017/S0033291706008579 Published online by Cambridge University Press

The construct validity of the judgements about remission and relapse was evaluated by relating these categories at the end of 6 and 18 months to PANSS and GAF scores obtained by research interviewers around the same time. The scores were sizably and significantly different between the ascribed groups in the predicted manner. There was sometimes a discrepancy between the date of the reference period for remission/relapse ratings and that of the PANSS and GAF measures, but at most this was only a month. In any case this discrepancy would have attenuated the relationship. The data on which the blind judgements of remission and relapse were based were extracted from the clinical notes by the same team of research workers as were responsible for establishing the PANSS and GAF scores. However, although the data related to the same periods, they were established at different times, and not necessarily by the same research worker.

We originally used consensus ratings in an attempt to improve reliability. Our results were equivocal – the comparison of consensus ratings did not always yield better kappa values than the comparison of individual ratings. However, we did feel that the establishment of a consensus through a process of detailed discussion about the recorded information led to ratings that were more defensible, and therefore probably more valid. This may be of particular importance in those areas where one rater did not record any remission or any relapse and the other did. On the basis of our experience, we are inclined to recommend the use of consensus rather than individual ratings.

Using routinely collected data in this manner thus has attractions. It can be extracted at a time chosen for the convenience of the research project, and thus may use less resource. If information about group allocation is omitted at the point of extraction, the data can be evaluated blind to allocation. Consent to use routinely collected data is usually easier to obtain than cooperation with an interview, and information will thus be more complete, and results more generalizable. The required sample size may in consequence be smaller. Routinely collected data also have the considerable advantage of being recorded by individuals completely independent of a trial: decisions are likely to be made solely on the basis of the clinical context at the time.

Retrospective epidemiological studies using case-note data can also employ this technique. However, our method does rely on the quality of routinely recorded clinical information, which may be sparse, ambiguous or non-existent. Steps can be taken to encourage improved recording, although these may not always be successful. Nevertheless, in situations where researchers are interested in changes in levels of positive symptoms of psychosis, we think the technique described here provides a useful addition to methods of evaluating remission and relapse.

DECLARATION OF INTEREST

None.

REFERENCES

Andreasen, N. C., Carpenter Jr., W. T., Kane, J. M., Lasser, R. A., Marder, S. T. & Weinberger, D. R. (2005). Remission in schizophrenia: proposed criteria and rationale for consensus. *American Journal of Psychiatry* **162**, 441–449.

Barrowclough, C., Tarrier, N., Lewis, S., Sellwood, W., Mainwaring, J., Quinn, J. & Hamlin, C. (1999). Randomised controlled effectiveness trial of a needs-based psychosocial intervention service for carers of people with schizophrenia. *British Journal of Psychiatry* **174**, 505–511.

Brown, G. W., Sklair F., Harris T. O. & Birley, J. L. T. (1973). Life events and psychiatric disorder: some methodological issues. *Psychological Medicine* **3**, 74–87.

Cohen, J. (1968). Weighted kappa: nominal scale agreement with provision for scales disagreement of partial credit. *Psychological Bulletin* **70**, 213–220.

Craig, T. J. C., Garety, P., Power, P., Rahaman, N., Colbert, S., Fornells-Ambrojo, M. & Dunn, G. (2004). The Lambeth Early Onset (LEO) Team: a randomised controlled trial of assertive outreach for early psychosis *British Medical Journal* **329**, 1067–1070.

Crow, T. J., MacMillan, J. F., Johnson, A. L. & Johnstone, E. C. (1986). The Northwick Park study of first episodes of schizophrenia. II. A randomized controlled trial of prophylactic neuroleptic treatment. *British Journal of Psychiatry* **148**, 120–127.

Csernansky, J. G., Mahmoud, R. & Brenner, R. (2002). A comparison of risperidone and haloperidol for the prevention of relapse in patients with schizophrenia. *New England Journal of Medicine* **346**, 16–22.

Falloon, I. R. H. (1983). Relapse in schizophrenia: a review of the concept and its definitions. *Psychological Medicine* **13**, 469–477.

Frank, E., Prien, R. F., Jarrett, R. B., Keller, M. B., Kupfer, D. J., Lavori, P. W., Rush, A. J. & Weissman, M. M. (1991). Conceptualization and rationale for consensus definitions of terms in major depressive disorder: remission, recovery, relapse, and recurrence. *Archives of General Psychiatry* **48**, 851–885.

Garety, P. A., Craig, T., Dunn, G., Fornells-Ambrojo, M., Colbert, S., Rahaman, N., Read, J. & Power, P. (2006). Specialised care for early psychosis: symptoms, social functioning and patient satisfaction. Randomised controlled trial. *British Journal of Psychiatry* **188**, 37–45.

https://doi.org/10.1017/S0033291706008579 Published online by Cambridge University Press

Gitlin, M., Nuechterlein, K., Subotnik, K. L., Ventura, J., Mintz, J., Fogelson, D. L., Bartzokis, G. & Aravagiri, M. (2001). Clinical outcome following neuroleptic discontinuation in patients with remitted recent-onset schizophrenia. *American Journal of Psychiatry* **158**, 1835–1842.

Gleeson, J. F. (2001). Early signs and risk factors for relapse in early psychosis. Ph.D. thesis, Department of Psychology, The University of Melbourne.

Johnson, S., Nolan, F., Hoult, J., White, I. R., Bebbington, P. E., Sandor, A., McKenzie, N., Patel, S. & Pilling, S. (2005). The outcomes of crises before and after introduction of a crisis resolution team: Islington Crisis Studies 1. *British Journal of Psychiatry* **187**, 68–75.

Kane, J., Honigfeld, G., Singer, J., Meltzer, H., for the Clozaril Collaborative Study Group (1988). Clozapine for the treatment-resistant schizophrenic: a double-blind comparison with chlorpromazine. *Archives of General Psychiatry* **45**, 789–796.

Lasser, R. A, Bossie, C. A., Gharabaw, G. M. & Kane, J. M. (2005). Remission in schizophrenia: Results from a 1-year study of long-acting risperidone injection. *Schizophrenia Research* **77**, 215–227.

Linszen, D., Dingemans, P., Van der Does, J. W., Nugter, A., Scholte, P., Lenior, R. & Goldstein, M. J. (1996). Treatment, expressed emotion and relapse in recent onset schizophrenic disorders. *Psychological Medicine* **26**, 333–342.

Linszen, D. H., Dingemans, P. M., Lenior, M. E., Nugter, M. A., Scholte, W. F. & Van der Does, A. J. W. (1994). Relapse criteria in schizophrenic disorders: different perspectives *Psychiatry Research* **54**, 273–281.

Pilling, S., Bebbington, P., Kuipers, E., Garety, P., Geddes, J., Martindale, B., Orbach, G. & Morgan, C. (2002). Psychological treatments in schizophrenia. I: Meta-analysis of family intervention and cognitive behaviour therapy. *Psychological Medicine* **32**, 763–782.

Ram, R., Bromet, E. J., Eaton, W. W., Pato, C. & Schwartz, J. E. (1992). The natural course of schizophrenia: a review of first-admission studies. *Schizophrenia Bulletin* **18**, 185–207.

Robinson, D. G., Woerner, M. G., Alvir, J. M. J., Bilder, R., Goldman, R., Geisler, S., Koreen, A., Sheitman, B., Chakos, M., Mayerhoff, D. & Lieberman, J. A. (1999*b*). Predictors of relapse following response from a first episode of schizophrenia or schizoaffective disorder. *Archives of General Psychiatry* **56**, 241–247.

Robinson, D. G., Woerner, M. G., Alvir, J. M. J., Geisler, S., Koreen, A., Sheitman, B., Chakos, M., Mayerhoff, D., Bilder, R., Goldman, R. & Lieberman, J. A. (1999*a*). Predictors of treatment response from a first episode of schizophrenia or schizoaffective disorder. *American Journal of Psychiatry* **156**, 544–549.

Scottish Schizophrenia Research Group (1992). The Scottish first episode schizophrenia study VIII. Five-year follow-up: clinical and psychosocial findings. *British Journal of Psychiatry* **161**, 496–500.

Silman, A. J. (1995). *Epidemiological Studies: A Practical Guide*, p. 78. Cambridge University Press: Cambridge.

Slade, M., Leese, M., Cahill, S., Thornicroft, G. & Kuipers, E. (2005). Meeting mental health needs causes quality of life to improve. *British Journal of Psychiatry* **187**, 256–261.

Tarrier, N., Lewis, S., Haddock, G., Bentall, R., Drake, R., Kinderman, P., Kingdon, D, Siddle, R, Everitt, J., Leadley, K., Benn, A., Grazebrook, K., Haley, C., Akhtar, S., Davis, L., Palmer, S. & Dunn, G. (2004). Cognitive-behavioural therapy in first-episode and early schizophrenia. 18-month follow-of a randomised controlled trial. *British Journal of Psychiatry* **184**, 231–239.

Tarrier, N. & Wykes, T. (2004). Is there evidence that CBT is an effective treatment for schizophrenia? A cautious or cautionary tale. *Behaviour Research and Therapy* **42**, 1371–1401.

Tran, P. V., Dellva, M. A., Tollefson, G. D., Wentley, A. L. & Beasley Jr., C. M. (1998). Oral olanzapine versus oral haloperidol in the maintenance treatment of schizophrenia and related psychoses. *British Journal of Psychiatry* **172**, 499–505.

Trivedi, P. & Wykes, T. (2002). From passive subjects to equal partners: qualitative review of user involvement in research. *British Journal of Psychiatry* **181**, 468–472.

Ventura, J., Nuechterlein, K. H., Lukoff, D. & Hardesty, J. P. (1989). A prospective study of stressful life events and schizophrenic relapse. *Journal of Abnormal Psychology* **98**, 407–411.

Wiersma, D., Nienhuis, F. J., Slooff, C. J. & Giel, R. (1998). Natural course of schizophrenic disorders: a 15-year followup of a Dutch incidence cohort. *Schizophrenia Bulletin* **24**, 75–85.

Zhang, M., Wang, M., Li, J. & Phillips, M. R. (1994). Randomised-control trial of family intervention for 78 first-episode male schizophrenic patients: an 18-month study in Suzhou, Jiangsu. *British Journal of Psychiatry* **164** (Suppl. 24), 96–102.

https://doi.org/10.1017/S0033291706008579 Published online by Cambridge University Press

APPENDIX 1

Extraction template for clinical information and remission/relapse rating sheet

Participant ID: _____
Period from: _____

At time of induction: _____
Episode number: _____
Social circumstances: _____
_____
_____
Presentation: _____
_____
_____

Outcome of the episode at time of randomization and relapse factors (e.g. mental state, social circumstances, medication, finances on discharge if admitted):

Please try to include the following information in the main part of the baseline report:

- Age
- Gender
- Ethnicity
- Living status, their accommodation at the time of entry into the trial.
- Relationship status
- Vocational status
- Financial situation, i.e. income from benefits or job, or family support
- Substance misuse
- Symptom presentation
- Previous psychiatric history
- Outcome of the episode at time of induction. This relates to what was happening to the person as a consequence of the episode at the time of entry into the study, e.g. whether they were admitted to hospital or being treated in the community, whether they were seeing a crisis resolution team, whether they were admitted involuntrarily. Include what medication they were on and if this had been recently changed due to the current episode.
- If possible try to include: Relapse factors (early warning signs). These are included to give the raters as much information as possible to enable them to make a judgement as to whether a relapse has occurred or not. There is often a section on CPA forms that covers this.

[*continues overleaf*

https://doi.org/10.1017/S0033291706008579 Published online by Cambridge University Press

Example of a remission/relapse rating sheet
Rater: _____

Month and date	Social circumstances	Information on symptoms	Type of response	Judgement
Month 1 29.3.02–28.4.02	In contact with friends, trying to reduce his alcohol intake	10.4.02 – Key-worker: avoiding large crowds, otherwise no other concerns 15.4.02 – Key-worker: no paranoid ideation since discharge	2.4.04 – discharged	Partial recovery from in-patient state
Month 2 From 29.4.02	No change	6.5.02 – Doctor: feels slightly elated, buzzing feeling, when he wakes up in the night. Tendency to paranoid self-reference remains.	Medication review, olanzapine to be phased out	
Month 3 From 29.5.02	Wants to distance himself from his friends and he feels they use him for money, wants to stop work at the homelessness centre as the new manager is autocratic. 26.7.02 – Key-worker: not answered door all week due to his resentment of friends	8.6.02 – Key-worker: experiencing 'ghost' injections at night 19.6.02 – Key-worker: continues to experience feelings that people living locally know about him and consider him a 'thief'. Feeling fed up and unmotivated	Clopixol reduced to 200 mg fortnightly. Offered respite care	
Month 4 From 29.6.02	Resumed work at homelessness centre	2.7.02 – Doctor admitted he had felt slightly agitated recently, had not heard anyone calling him names, but maintained this could happen at any time. Better than on previous appointments	No change	
Month 5	Recommenced going to local pub.	No evidence of paranoid ideation.	Home visits.	
From 29.7.02	Has not left the flat for a few days, as he is afraid he might get beaten up	27.8.02 – Key-worker: woke up about midnight to find a 'bright white light' reflecting on his bedroom wall, heard 2 boys saying 'do it when he stands up'. Light lasted for a few minutes. Believes it was a gun and the boys intended to shoot him as punishment as they believe he is a thief.	Referred to crisis team	
Month 6 From 29.8.02	Going out of the flat again	Doctor: paranoid about a bright light which he felt had been a gun. Now less certain it was a gun, willing to consider it might be kids playing with a torch.	Offered increase in medication which he refused	
Month 7 From 29.9.02	Recommenced going to local pub	Key-worker: generally settled since discharge, intermittent recurrent nightmares about the devil, no longer feels he is being watched or talked about in the streets. Turned up drunk to CPA meeting	No change	
Month 8 From 29·10·02	No change	6·11·02 – Key-worker: has disturbed sleep pattern and is using alcohol to help him sleep	26·11·02 – olanzapine 10 mg nocte, clopixol 200 mg fortnightly	
Month 9 From 29·11·02	No change	No information	No change	
Month 10 From 29·12·02	Sees friends regularly, visits local pub ×2 a week	8.1.03 – Doctor: no clear recurrence of psychotic symptoms, fleeting paranoid ideation under the influence of cannabis. 14.1.03 – Key-worker: no evidence of any paranoid ideation or perceptual anomalies.	No change	Full recovery, confirmed at month 12
Month 11 From 28.1.03	No change	No information	No change	
Month 12 From 29.2.03	No change	22.2.03 – Key-worker: mental state seems stable at present	No change	
Month 13 From 29.3.03	No change	No information	No change	
Month 14 From 29.4.03	No change	18.4.03 – Key-worker: denies any paranoid ideation and no apparent signs of persecutory delusions	No change	
Month 15 From 29.5.03	No change	26.6.03 – Key-worker: denied any paranoid/persecutory ideation.	No change	
Month 16 From 29.6.03	No change	10.7.03 – Key-worker: no apparent signs of abnormal thoughts or perceptions.	No change	
Month 17 From 29.7.03	Got into fight in pub with man who he thought said something derogatory	7.8.03 – Key-worker: believes people are accusing him of being a paedophile, follow him about, keep him under surveillance in cars. 7.8.03 – Doctor: clear return of paranoid symptoms	Referred to crisis team. Olanzapine increased 15 mg.	Type I relapse
Month 18 From 29.8.03	Staying at home	4.9.03 – Key-worker: less upset, but still feels people are looking at him.	Crisis team still involved, visiting every 2 days.	

[continue, to cover required period]

https://doi.org/10.1017/S0033291706008579 Published online by Cambridge University Press

APPENDIX 2. Operational procedure and criteria for rating remission and relapse

Rating remission

Ratings are made blind to the treatment group status of subjects, on the basis of case-note evaluation carried out by research assistants.

Instructions to research assistants. Please make clear whether relevant information is clearly entered in notes, whether there is an entry that does not refer to the domain in question, and whether there is no entry at all.

Full remission

A definition of full remission requires evidence from two separate months.

The first of these months must provide *positive evidence* of a mental state characterized by *no psychotic symptoms*.

The second month must be contiguous with the first, unless there is an intervening month in which no contact occurred. The second month must at the very least include clinical entries that do not specifically refer to a re-emergence of psychotic symptoms. If there is no second entry at all, rate 'not known'. If the second entry occurs after a gap of 2 months or more, only rate remission as present if all supporting evidence is consistent with sustained remission from the first entry.

Note that a minimum of two entries is required to define remission. The minimum separation of these entries is 4 weeks.

If these criteria are met, rate full remission present, dated from the first entry.

Partial remission

The criteria for full remission are not met, but there is evidence of *improvement* based on records from two separate months.

The first of the months must provide positive descriptions of clinically significant improvement in specified symptoms (e.g. 'No longer believes that …' or 'Auditory hallucinations now infrequent') that allows the inference of an overall improvement in mental state.

The second month must be contiguous with the first, unless no contact occurred during it. The second month must at the very least include clinical entries that do not specifically refer to a worsening of psychotic symptoms.

Note that a minimum of two entries is required to define remission. The minimum separation of these entries is 4 weeks.

Note also that the degree of improvement on which partial remission is based can be inferred from a broader range of information than full remission. This relatively non-specific description such as 'is much improved', 'functioning much better' etc., can be used.

If these criteria are met, rate partial remission present, dated from the first entry.

Non-remission

The criteria for full or partial remission are not met, and there is evidence of clinical entries referring to sustained psychotic symptoms that are at least of moderate severity

AND

There is no explicit reference to significant amelioration in clinical entries.

Non-remission may cover cases where there are some fluctuations in mental state, provided they do not meet the criteria for partial remission.

If these criteria are met, rate non-remission present.

Inadequate evidence

This situation arises where –

1. there is evidence of psychotic symptoms of at least moderate severity in clinical entries at the point of follow up
   and
2. there are no preceding entries in the notes that can be taken to indicate full or partial remission, or non-remission.

https://doi.org/10.1017/S0033291706008579 Published online by Cambridge University Press

OR

there is no relevant information at all.

In these circumstances, it is not possible to rate either remission or non-remission.

Rating relapse

This can only be rated if remission as defined above has been rated. The type of remission determines the type of relapse.

Type 1 relapse (true relapse)

This is based primarily on the re-emergence of positive psychotic symptoms of at least moderate degree following a period identified as full remission. It requires positive evidence of such symptoms in two clinical entries, dated at least two weeks apart. The level of symptoms can be *corroborated* by a consideration of the administrative response, for example, admission to hospital, referral to a crisis house, referral to a home treatment team or crisis resolution team, a significant change in management (increased visiting or medication levels), or a clear indication of increased social dysfunction. However, changes in management of themselves cannot be taken as an indication of relapse.

Type 2 relapse (exacerbation)

This is based on positive evidence in a clinical entry of positive psychotic symptoms of at least moderate degree where this appears to be a significant deterioration from a state of partial remission. The level of symptoms can be *corroborated* by a consideration of the administrative response, for example, admission to hospital, referral to a crisis house, referral to a home treatment team or crisis resolution team, a significant change in management (increased visiting or medication levels), or a clear indication of increased social dysfunction. However, changes in management of themselves cannot be taken on their own as an indication of relapse.

Non-relapse

The criteria for type (i) and type (ii) relapse are not met, and:

There is positive reference in clinical notes to indicate continued symptomatic wellbeing, e.g. 'remains symptom free', or 'functioning well', or 'no worsening of symptoms.

Non-relapse may cover cases where there are some fluctuations in mental state ('blips'), provided they do not meet the criteria for a type of relapse in terms of clinical significance and duration.

Inadequate evidence

There are no clinical records that relate to symptoms in a way that could be used to indicate either relapse or continued wellbeing.

https://doi.org/10.1017/S0033291706008579 Published online by Cambridge University Press