FACTORS DETERMINING INTRERRATER AGREEMENT WITH RATING GLOBAL CHANGE IN DEMENTIA: THE CIBIC-PLUS

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SUMMARY

Global ratings of change were obtained from 17 clinicians on eight patients, as though participating in an antidementia drug trial. Simultaneous rating was made possible by the use of videotaped semi-standardized interviews, and clinical change was simulated by providing raters with adjusted initial assessment documentation representing the situation 6 months earlier. In a second study, seven more ratings were obtained on the two patients who had commanded best and worst agreement in order to clarify important variables for levels of agreement. The main finding was that levels of interrater agreement on a global rating of change (which included carer information) varied widely from patient to patient. An important contributor to this variation was carer information. The order in which information for rating had been presented was found to be of overriding importance; if carer information was presented before patient information, considerably higher levels of agreement were achieved on the global rating than if the reverse order was used.

KEY WORDS—dementia; global change; CIBIC; interrater agreement

A key element of psychiatric research in the latter half of this century has been the evolution of ever more elaborate methods of quantifying nebulous entities such as depression, psychosis and dementia. Questionnaires are 'standardized' and diagnoses are 'operationalized' with an overall intention to eliminate/minimize the maverick tendencies of individual doctors and the differing effects of culture and education worldwide. Such is the inherent distrust of individual clinical judgements in research that early epidemiological studies conducted before standardization are now quoted as historical reference. It comes as a surprise, therefore, to encounter a research instrument to be used to assess progress in a clinical trial which simply asks a clinician: 'Has this patient got better, worse or stayed the same?'. The clinician, it appears, has returned to the position of final referee as to whether change has taken place. This instrument, the 'clinical interview based impression of change' (CIBIC), was designed by researchers in consultation with the Federal Drugs Administration (FDA) in response to growing research activity concerning antidementia medication. It was necessary to decide what level and type of improvement justifies the considerable expenditure needed to develop medications that a patient may need to take continuously. The FDA's solution was a requirement that improvement be sufficiently dramatic to be apparent to an independent doctor after conducting a normal clinical interview with the patient. The improvement was then 'clinically significant' and a medication deserved consideration for a licence. The CIBIC has since been developed to take account of information provided by a carer (CIBIC-plus).

In multicentre drug trials, involving doctors/raters from several different countries, this method of assessment must raise anxiety. What level of
conformity exists in such clinical observation of change? Do large changes in the subject's condition command higher levels of agreement? If more information is available to the rater, is there a corresponding convergence of view with fellow raters? How important is the carer's view in influencing the rater's opinion, compared with his/her own assessment of the patient? What characteristics of the subject and/or rater determine high or low levels of interrater agreement?

An investigation of these questions, about which there has been little research, might promote an understanding of clinical decision-making and may lead to a more accurate outcome assessment in drug trials.

The emphasis in dementia assessment has shifted from a purely cognitive assessment of the patient to include 'carer-centred' measurements of function and behaviour. The core measures of cognitive change remain in the form of instruments such as the Mini Mental State Examination (Folstein et al., 1975), the cognitive section of the Cambridge Examination for the Mental Disorders of the Elderly (CAMDEX; Roth et al., 1988) and the Alzheimer Disease Assessment Schedule (ADAS: Mohse and Cohen, 1988), while behavioural change is monitored by the Blessed Dementia Scale (Blessed et al., 1968) and the Interview for Deterioration in Daily Living Activities in Dementia (IDDD; Teunisse et al., 1991). These instruments command a high level of interrater reliability but the cognitive measures have limited functional relevance and were not validated in the context of clinical change assessment. The behavioural measures, on the other hand, have doubtful objectivity due to suspicions that carers under stress may perceive behaviour disturbance which is not actually present (Homer and Gilleard, 1994).

Nevertheless, the CIBIC protocol has developed in step with this trend; having begun as an instrument which allowed the clinician access to the patient only, it then incorporated an interview with the carer and now includes two structured questionnaires, the Blessed Dementia Scale and the Interview for Deterioration in Daily Living Activities in Dementia (IDDD; Teunisse et al., 1991). These instruments command a high level of interrater reliability but the cognitive measures have limited functional relevance and were not validated in the context of clinical change assessment. The behavioural measures, on the other hand, have doubtful objectivity due to suspicions that carers under stress may perceive behaviour disturbance which is not actually present (Homer and Gilleard, 1994).

We set out in this study to obtain a measure of the reliability of the CIBIC-plus for a range of patients. Crucially, the same body of 17 or more raters was used throughout the core study so that differences in the levels of agreement from case to case could be directly attributed to variables in the patient and carer information and the factors contributing to this variation could then be studied.

A second study was designed using seven more clinicians to rate the two patient-carer pairs which had commanded the best and worst agreement for a more qualitative enquiry of the rater's attitudes to the information as to why such disparity existed. This second study provided an opportunity to compare two rater groups: clinicians drawn from all over the country (the core study) and those drawn from one centre (the second group).

**METHOD**

**Strategy**

This study set out to mimic the situation faced by a researcher in a clinical trial of a putative antidementia compound. In order to create simultaneously for all participants in this research a realistic situation for CIBIC use, all participants were exposed to videotaped interviews of a series of patients and carers that were said to have taken place after 24 weeks on a treatment trial. Participants were also provided with a patient and carer assessment in documentary form that represented assessment at entry into the treatment...
trial. For this experimental situation these data from the initial assessment were adjusted to create evidence of apparent improvement, no change or of deterioration in the patient over the 24 weeks of the trial. Agreement among raters in applying the CIBIC to these paired data derived from initial and week-24 assessment was the key variable for this research study.

**Raters**

Eighteen clinicians experienced in old age psychiatry (psychologists and psychiatrists) agreed to attend a 2-day meeting. All were likely to participate in a forthcoming clinical trial of antidementia medication.

**Subjects**

Eight subjects over 65 with a diagnosis of probable Alzheimer's disease, satisfying NINCDS/ADRDA criteria (McKhann et al., 1985) were videotaped. These subjects had agreed to enter the clinical trial mentioned above, a condition of which was that a carer was available. Written consent was obtained from both patient and carer for the videotape to be used in the rating study.

**Preparation of videotapes and documents for rating**

The patient and carer were interviewed on videotape using the CIBIC-plus protocol. This consists of a semi-structured interview of the patient which covers all areas of a conventional mental state examination but with emphasis on aspects of cognition, using items drawn from CAMCOG (Roth et al., 1988) and GMS (Cope-land et al., 1976) schedules. The interview with the carer covered the patient's mood and functional ability and then led on to the Blessed Dementia Scale (Blessed et al., 1968) and the IDDD (Teunisse et al., 1991). Once the videotape was made, the documentation to represent the initial assessment 6 months earlier was prepared using standard CIBIC-plus forms; thus the raters were provided with an initial assessment of mental and baseline responses for the Blessed Dementia Scale and the IDDD. These assessments were adjusted so that at the time of videotaping two patients appeared to show improvement by 24 weeks, two deterioration and four little or no change.

**Rating scales**

Raters entered their impression of clinical change on watching the videotape. This impression was entered as a CIBIC-plus score on a seven-point scale where 1 is marked improvement, 4 is no change and 7 is marked deterioration. Also on this CIBIC score sheet is an analogue scale, by which the rater indicates whether any impression of change was based on holistic impressions or cognitive mental state data. The Blessed Dementia Scale and the IDDD both measure functional ability from information supplied by a carer, the former on a three-point, the latter on a seven-point scale. Additional data to the CIBIC-plus score were also obtained, recording the confidence of the clinicians in their rating, the relative importance of the carer's view of the patient's data, the clinical significance of any change noted and a ranking in order of importance of the various subsections of the patient and carer interview.

**Study procedure**

The 18 participating clinicians were divided into two groups to participate in four rating sessions so that a crossover design was established (see Fig. 1). The videos were arranged so that they were rated carer first, patient second by nine clinicians, patient first, carer second by the other nine. Four videos were rated in one session by the first group and the same videos were presented in reverse order to the parallel group in the second session. The raters were asked to rate their impression of change on the CIBIC score sheet after seeing the patient video and after seeing the carer video, having already been shown most of the week 0 data. They then entered an overall rating after being shown the 'week 0' Blessed and IDDD score sheets, which amounted to a CIBIC-plus score (see Appendix).

**Statistical analysis**

*Variability of ratings of individual videos.* The interest here is in the range of responses among the different raters. In order to display this variability we chose to plot the standard deviations (SD) around the mean score given to each video.

*Measurement of agreement between raters across all patients.* The intra-class correlation coefficient (ICC) is the appropriate method of assessing the level of agreement among raters across two or
more patients. It is appropriate where ratings made on a continuous scale of two or more stimuli by two or more judges. Since the CIBIC data had an approximately normal distribution over a seven-point range, the ICC was considered a suitable summary statistic for this study. The analysis of variance (ANOVA), which provides the basis for the analysis, offers advantages over other methods such as the product-moment correlation and the rank-order correlation, which fail to adjust for differences in the average level of raters.

Each ICC summarizes the ratings by all the clinicians across all the patient assessments, all the carer assessments and all the CIBIC-plus assessments. Thus, when summarizing the entire study population, there were 145 ratings for each of the three ICCs (17 raters × 8 videos = 136 ratings, plus nine extra ratings by raters who did not attend for the whole series of videos).

Second study

Having analysed the data from the study described above, the two video pairs which commanded the highest and lowest levels of agreement were further investigated. Ratings were obtained from seven new clinicians on these two patients, as was qualitative information on what aspects of the videos most influenced individual raters.

RESULTS

Variations between ratings of eight videotapes

Table 1 shows the mean and standard deviation for the eight ratings.

It can be seen that the lowest mean scores, suggesting improvement, refer to patient 1 and the highest, suggesting deterioration, refer to patient 2. The standard deviations ranged from 0.48 to 0.87 for the CIBIC-plus, 0.56 to 0.93 for the post carer ratings and 0.35 to 0.86 for the post patient ratings. Lower figures indicate better agreement between the raters. There was no association between the size of standard deviation and the mean change score, the level of agreement thus not being affected by ratings of improvements or deteriorations. The intraclass correlation coefficient calculated for all the eight videotapes was 0.725 for the patient information, 0.649 for the carer information and 0.702 for the CIBIC-plus (higher intraclass correlation means better agreement).

The effect on agreement of the order of receiving information

Table 2 shows the effect that order of presentation of information had on levels of agreement. It can be seen that agreement on the CIBIC-plus
Table 1. Mean CIBIC scores for each set of 17 ratings on all eight patients made post patient information, post carer information and post CIBIC-plus (global) information. Standard deviations (SD) in brackets

<table>
<thead>
<tr>
<th>Means of 17 ratings</th>
<th>Patient/carer videos</th>
<th>Overall mean (ICC)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 (2)</td>
<td>2 (4)</td>
</tr>
<tr>
<td>Patient information</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.0 (0.35)</td>
<td>5.2 (0.75)</td>
<td>4.9 (0.57)</td>
</tr>
<tr>
<td>Carer information</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.8 (0.56)</td>
<td>6.2 (0.64)</td>
<td>5.4 (0.88)</td>
</tr>
<tr>
<td>CIBIC-plus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.4 (0.62)</td>
<td>6.0 (0.79)</td>
<td>5.4 (0.73)</td>
</tr>
</tbody>
</table>

**Notes**
1. Overall significantly higher mean score on the CIBIC-plus ratings than on patient information ratings (the higher the score, the more deterioration detected).
2. Intraclass correlation coefficients (ICC) across all patients for CIBIC-plus ratings, post patient video ratings and post carer video ratings.
3. ICCs over 145 ratings
   - Patient information: 0.725
   - Carer information: 0.649
   - CIBIC-plus information: 0.702

Table 2. Differences on CIBIC-plus (global) levels of agreement when patient information is shown first or when carer information is shown first. Levels of agreement are expressed as intraclass correlation coefficients (ICCs) (note: ICCs close to 1.0 denote high agreement.); 145 ratings overall

<table>
<thead>
<tr>
<th>Day 1</th>
<th>Patients 1–4</th>
<th>ICC</th>
<th>Patients 5–8</th>
<th>ICC</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Raters group A</td>
<td></td>
<td>Raters group B</td>
<td></td>
</tr>
<tr>
<td>Patient information</td>
<td>1st</td>
<td>0.813</td>
<td>1st</td>
<td>0.716</td>
</tr>
<tr>
<td>Carer information</td>
<td>2nd</td>
<td>0.764</td>
<td>2nd</td>
<td>0.640</td>
</tr>
<tr>
<td>CIBIC-plus</td>
<td></td>
<td>0.688</td>
<td></td>
<td>0.662</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Day 2</th>
<th>Patients 1–4</th>
<th>ICC</th>
<th>Patients 5–8</th>
<th>ICC</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Raters group B</td>
<td></td>
<td>Raters Group A</td>
<td></td>
</tr>
<tr>
<td>Carer information</td>
<td>1st</td>
<td>0.777</td>
<td>1st</td>
<td>0.449</td>
</tr>
<tr>
<td>Patient information</td>
<td>2nd</td>
<td>0.788</td>
<td>2nd</td>
<td>0.611</td>
</tr>
<tr>
<td>CIBIC-plus</td>
<td></td>
<td>0.815</td>
<td></td>
<td>0.758</td>
</tr>
</tbody>
</table>

The second study

The tapes for patients 4 and 6, which displayed the lowest and the highest standard deviations on the CIBIC-plus, were rated again by seven new raters.

Table 3 shows mean and standard deviations based on 24 ratings representing a good statistical sample, the seven new ratings being pooled with the 17 from the core study. The difference in agreement on ratings for these two patients is compared in this large dataset.

Raters’ attitudes to patient and carer information

Table 4 summarizes raters’ attitudes to the information they were presented with.

In answer to the first question, whether subject or carer information was more important in helping to reach a decision about change, for the majority of tapes the mean score was on or above 5, indicating a bias towards carer information. Only in tapes 1 and 8 was patient information considered more important. In answer to the second question,
how much importance the raters attached to the carer's perception of change, it can be seen that for the majority of tapes apart from 1 and 8 the bias of the group was to consider the carer's information more important. Finally, the group was asked whether the level of change reported in any of the eight tapes was regarded as clinically significant. The majority reported that the changes they detected were clinically significant.

The relative importance of mental state versus 'activities of daily living' information

Table 5 shows that ADL information was ranked first in importance by 50% of the raters and cognitive mental state information first by 35%.

DISCUSSION

The main findings of this study were that levels of agreement among raters on CIBIC-plus varied widely from patient to patient, and the greater contribution to this variation came from the carer information rather than patient data. When comparison was made between the relative levels of agreement among raters on carer information, patient information and global assessment, the intraclass correlation coefficient was found to be highest on the patient information and lowest on the carer information, with CIBIC-plus (global) falling in the middle. This generated a working hypothesis that carer information distorts the rater's assessment of the patient and thus lowers agreement on the CIBIC-plus (global) rating. An order effect emerged, indicated by higher levels of agreement when carer information was shown before patient information. Agreement was then appreciably better on all ratings, the global rating commanding a slightly higher level of agreement than the post patient rating on its own.

Methodological limitations

Consensus among a group of clinicians was the key issue addressed by this study and for practical reasons measurement could only be made by the use of artifice. Such standardization of information could never occur in a real-life situation—if 20-odd raters assessed a particular patient on 20 separate occasions, a wide range could be expected

Table 3. Mean scores on 24 CIBIC ratings of patients 4 and 6 (the ratings on days 1 and 2 were combined with the additional seven collected on day 3) with standard deviations (SD) in brackets

<table>
<thead>
<tr>
<th></th>
<th>Patients 4</th>
<th>Patients 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post patient information</td>
<td>4.72 (0.614)</td>
<td>3.88 (0.797)</td>
</tr>
<tr>
<td>Post carer information</td>
<td>4.72 (0.792)</td>
<td>3.67 (0.761)</td>
</tr>
<tr>
<td>Post CIBIC-plus information</td>
<td>5.04 (0.455)</td>
<td>3.58 (0.776)</td>
</tr>
</tbody>
</table>

Note: Confidence of seven clinicians in their ratings expressed as a comparison between patients 4 and 6.

Table 4. Summary of 'additional ratings' requested from clinicians. Means of 17 ratings are entered

<table>
<thead>
<tr>
<th>Question: Was subject or carer information more important in helping you reach a final decision about change?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean of analogue Score 1-10*</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Question: Rate the importance you attributed to the carer's perception of change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean of analogue Score of 1-10†</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Question: Was the change you detected (if any) clinically significant?</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
</tr>
<tr>
<td>Yes</td>
</tr>
</tbody>
</table>

*0 = patient's information; 10 = carer information.  †0 = not at all important; 10 = highly important.
Table 5. Showing percentages of 17 raters ranking aspects of mental state and behaviour according to their importance in achieving an overall rating

<table>
<thead>
<tr>
<th>Ranking</th>
<th>Cognitive mental state (%)</th>
<th>Non-cognitive mental state (%)</th>
<th>Activities of daily living (%)</th>
<th>Difficult behaviours (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>35.1</td>
<td>10.8</td>
<td>50.7</td>
<td>3.3</td>
</tr>
<tr>
<td>2</td>
<td>39.6</td>
<td>17.7</td>
<td>35.1</td>
<td>8.2</td>
</tr>
<tr>
<td>3</td>
<td>17.2</td>
<td>53.1</td>
<td>13.4</td>
<td>18.0</td>
</tr>
<tr>
<td>4</td>
<td>8.2</td>
<td>17.7</td>
<td>0.7</td>
<td>67.2</td>
</tr>
</tbody>
</table>

both in style of assessment and overall impression, not to mention day-to-day changes in the patient's mental state.

One can therefore hypothesize (although this hypothesis remains untestable) that the levels of agreement we found were higher than those which would be found in a real-life situation. Inevitably, some discussion would have taken place among raters during the 2-day meeting which may have further enhanced levels of agreement. Another criticism which can readily be levelled at our method is that raters in the study are not comparing 'like with like'. They are comparing documentary information with a video interview. The CIBIC-plus rater in a real clinical trial, it could be claimed, is comparing a vivid recollection of the patient 3 or 6 months previously with the current situation. Anecdotal experience, however, is that little personal recollection survives (particularly of a routine drug trial assessment) after such an interval, and that the situation which in practice presents to a CIBIC-plus rater is one where the written assessment is compared with the current situation, thus resembling our design. If a genuine 'like with like' comparison is to be made, then before and after videos may, in trials, provide a more effective way of conveying comparative information about mental state.

A criticism of the experimental design itself is that the eight video pairs were viewed in the same sequence on both days. However, any effects of practice or fatigue were not apparent in the pattern of mean scores or SDs over the sessions. That each set of ratings might have been subtly affected by the previous video remains a possibility, and one that cannot be resolved by this dataset. In the field of clinical drug studies the impressive ability of global ratings (the CGI) to distinguish drug from placebo in 14 out of 17 antidementia drug trials has been attributed by some to halo effects due separately or in combination to optimistic raters 'reading' the drug's side-effect profile and raters having access to psychometric data (Lehmann, 1984). Clearly these are influences which this design sidesteps.

Agreement about carer accounts

Our results indicate a wide range of levels of agreement among raters from video to video with standard deviations on the CIBIC-plus ratings varying from 0.48 to 0.87. Such variation may have been due to properties intrinsic to the carer or patient information or a combination of the two, and in order to test this hypothesis the two video pairs commanding the best and worst agreement among raters were selected and extra information was obtained from the seven new raters. This identified confidence in carer information as the distinguishing variable—all seven raters were less confident about rating patient no 6's carer's video than patient no 4's. It is also important to observe that the two patients and their carers were all of similar educational background. It seemed that the main difference between the two couples was that patient no 4 (good agreement) lived with her husband (carer and informant) and patient no 6 (poor agreement) was visited twice weekly by her niece (carer and informant).

Clinical practice, it should be remembered, is a continual process of global change assessments. Interpreting a carer's account, for example a nursing report at a ward round, is a process the complexity of which is familiar. In contrast to direct personal observation of the patient, information is weighed in the light of several factors which hinge on the clinician's attitude to the informant. The information is either taken at face value or judged critically. Doubts in the rater's mind might be the accuracy of the information (does the carer cohabit or only visit occasionally?) and his suspicion of a 'hidden agenda' (does the carer want the patient admitted to hospital or a home?). Patient no 4, for example, a woman living with her husband, commanded the second worst level of agreement among raters, a fact which may be explained by the husband's (carer) openly stated desire to win her acceptance of residential care. Finally, we should again mention the caution voiced in the introduction, namely that the carer's mental state itself can influence his perception of patient behaviour. With all these caveats in the raters' minds, it is perhaps
natural to anticipate a wider spread of opinion when carer information is interpreted.

Agreement among raters was highest for post patient ratings and lowest for post carer ratings, with the CIBIC-plus ICC falling in between but closer to the post patient ICC. When the data were reappraised after division of the ratings according to the order videos were presented to the raters, differences in levels of agreement were apparent (see Table 2). Watching the carer information first resulted in an agreement equal to that achieved after seeing the patient video only.

Why should the order in which the information is presented be important? One explanation is that patient assessment is the basis of clinical psychiatry, where training has drilled conformity, and that global ratings completed immediately after viewing patient information benefit from temporal proximity. Our findings, however, might suggest a resonance between carer and patient assessment, which produces a cumulative improvement and a final global ICC higher than or equal to the patient assessment alone. The situation where carer information is presented first corresponds with clinical practice, where a referral cues the main problems and directs the patient assessment into relevant domains. The reverse might result in a reappraisal when an informant reveals information inconsistent with the clinical picture so far obtained from the patient, producing confusion in the rater. This is particularly a risk in patients suffering from dementia, who are often without insight and therefore unaware of their shortcomings.

What information mattered to raters?

The additional data demanded in this study gave some insight into what the raters thought important. The carer information was thought more important than the patient data, particularly for those in whom a clinical improvement was detected. ADL information was ranked highest in importance followed by non-cognitive mental state data and finally difficult behaviours. This emphasis on carer information and ADL contrasts with the evidence of lower levels of agreement among raters when interpreting it.

CONCLUSION

Even in controlled circumstances there can be disappointing levels of agreement among raters assessing change in dementia using the CIBIC-plus procedures. Carer information is valued by the raters but by itself commands the lowest levels of agreement and if presented after the patient information results in a lowering of agreement on the CIBIC-plus rating. Agreement on the CIBIC-plus can be improved by (a) presenting carer data first and (b) making sure that the carer is ‘believable’.

It is tempting to conclude that carer information selected and presented properly contributes to a more valid and acceptable clinical decision.

REFERENCES

Extra questions

1. Rate the subject as you find her now according to the severity of her dementia:
   - Mild 1
   - Moderate 3
   - Severe 5

2. Rate the subject according to severity of her functional disability:
   - Mild 1
   - Moderate 3
   - Severe 5

3. Was the subject or carer information more important in reaching your final rating?
   - Subject
   - Carer

4. Rank the items of video material according to their importance in achieving an overall rating:
   - Cognitive mental state
   - Non-cognitive mental state
   - ADL abilities
   - 'Difficult' behaviours (eg repetitive questions, wandering at night)
   - Other, specify

5. If you detected either improvement or deterioration in the subject, record whether you consider this to be clinically significant. Yes/No.

6. Please record the raw pieces of data (ie ‘knew day of the week’) which particularly influenced your final rating.

<table>
<thead>
<tr>
<th>Subject Interview</th>
<th>Carer interview</th>
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</table>

7. Was the carer’s perception of change important in reaching your final decision?
   - Very
   - Moderately
   - Not at all