like one of the cases in the case-control study,[1] not associated with appreciable paternal radiation before conception.[18] The hypothesis therefore originated largely in a subgroup of the cases that aroused the concern which led to the study. It is well known that hypotheses based on subgroups are often unreliable.

The findings provide little support for a relation between paternal preconceptional radiation and subsequent leukaemia and non-Hodgkin's lymphoma in the offspring. Indeed, if considered with the findings of studies of radiation workers in Canada[7] and of atomic bomb survivors[9] they weigh against such a relation.

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Effects of computer generated reminder charts on patients' compliance with drug regimens

D K Raynor, T G Booth, A Blenkinsopp

Department of Pharmacy, Seacroft and Killingbeck Hospitals, Leeds LS14 6UH
D K Raynor, *director of pharmacy and sterile services*

Pharmacy Practice Research Unit, University of Bradford, Bradford BD7 1DP
T G Booth, *professor of pharmacy practice*

Centre for Pharmacy Postgraduate Education, University of Manchester, Manchester M60 7LP
A Blenkinsopp, *director*

Correspondence to:
Dr Raynor.

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Abstract

***Objective*—To investigate whether a reminder chart improved patients' compliance with their drug regimen after discharge from hospital.**

***Design*—Patients were randomly allocated to one of four groups. Two groups received the reminder chart: one also received routine counselling from a nurse and the other received structured counselling from a pharmacist, which included an explanation of the reminder chart. The other two groups received only counselling, either from a nurse or from a pharmacist. Patients were visited about 10 days later: they were questioned about their drug regimen, and their compliance was measured by tablet counting.**

***Setting*—The pharmacy in a district general hospital and patients' homes.**

***Patients*—197 patients being discharged from hospital who were regularly taking two or more drugs.**

***Intervention*—An individualised reminder chart, which listed each person's medicines and when they were to be taken and was automatically generated by a medicine labelling computer.**

***Main outcome measures*—Patient's compliance with and knowledge of their drug regimen.**

***Main results*—Of the patients who received the reminder chart, 83% (95% confidence interval 74% to 90%) correctly described their dose regimen compared with 47% (37% to 58%) of those without the chart ($p<0.001$). The mean compliance score was 86% (81% to 91%) in both groups not given the reminder chart; 91% (87% to 94%) in the group given the chart without an explanation; and 95% (93% to 98%) in the group given the chart and an explanation. A mean compliance score of >85% was achieved by 63% (53% to 73%) of patients without a reminder chart and by 86% (78% to 93%) of those receiving the chart ($p<0.001$).**

***Conclusions*—An automatically generated reminder chart is a practical and cost effective aid to compliance.**

Introduction

Patients often have poor knowledge of their prescribed drug regimen and so do not comply fully with it.[1,2] Well designed reminder charts can help with

Information about your medicine

Name:

Date:

How to use this chart

- This chart shows you when to take each of your medicines
- At each meal time, look down the column to see which medicines you need to take **with or just after** the meal. Do the same about half an hour before bedtime.
- A **spoon** means a 5ml plastic medicine spoon
- Medicines which you take only when you need them are **not** included in the chart.

Medicine	Breakfast	Lunch-time	Evening-meal	Bedtime
ATENOLOL Tablets 100mg	1 Tablet			
NAPROXEN Suspension 125mg/5ml	2 Spoons		2 Spoons	
AMOXYCILLIN Capsules 250mg	1 Capsule		1 Capsule	1 Capsule
BECLOMETHASONE Inhaler 50µg	2 Puffs	2 Puffs	2 Puffs	2 Puffs

Reminder chart of computer generated information sheet

factors associated with poor compliance with drug regimens[3]: they combat forgetfulness by linking times for medicines to be taken with daily events to which most patients can relate; they overcome ignorance arising from vague instructions on the timing of doses, such as "three times a day," by giving specific times for medicines to be taken; and they prevent the confusion that arises when many different medicines have to be taken by indicating those medicines which can be taken at the same time. Reminder charts have had to be completed by hand, however, and have not come into routine use.

One of us (DKR) has developed a computer generated information sheet to improve patients' understanding of their drug regimen.[4] The sheet is headed by the patients's name and the date and consists of a reminder chart listing the patient's prescribed medicines and when they should be taken (figure) and additional information about each medicine. We report the effectiveness of this reminder chart.

Methods

DESIGN OF REMINDER CHART

There are few comparative data on the effectiveness of reminder charts, but simplicity of design seems to be a key factor.[5] The language and layout service of the Plain English Campaign advised on the design of the chart used in this study and the wording of the information it contained. The four daily events listed on the horizontal axis are spread through the day, and the first three are meals (most restrictions on the timing of doses relate to meals). We decided against using subcolumns for before and after each meal as this produced an intimidating grid of 48 sections. Instead, drugs which should be taken before meals were marked with an asterisk, which referred to a footnote telling patients to take the medicine half or one hour before eating. The footnote appeared only when it applied to one or more of the patient's drugs. The names of the three mealtimes were chosen after careful consideration, and terms such as dinner, tea, and supper were avoided because these meals are taken at widely varying times.

The dispensary's computer was programmed to generate the information sheet automatically (the software used was Dispenser (Cortex Computer Systems)). When the computer produced the labels for a discharged patient's medicines, it stored the information for each label in a temporary file. The contents of this file were used to print the chart, and no additional input of data was needed. The printed sheet was folded and put into a clear plastic sleeve and would fit inside a medicine bag, handbag, or coat pocket. The computer translated instructions on the timing of doses (such as twice a day) into the daily events printed on the chart. A survey of 100 consecutive outpatients' mealtimes showed that medicines taken twice daily should be taken at breakfast and evening meal to give the best spacing during the day. Medicines taken three times a day should be taken at breakfast, evening meal, and bedtime for the best spacing.

STUDY POPULATION

For six months we recruited patients to our study from those being discharged from three general medical wards who were taking between two and six medicines on a regular basis. We excluded patients who were being discharged to a nursing home or other institution, were dependent on another person for taking their medicines, or were unable to give informed consent. We also excluded those who were illiterate, had severe reading difficulty, or were visually handicapped.

On each day of the six months we recruited the first three eligible patients whose prescriptions came to the pharmacy for dispensing. We randomised the patients to one of four groups. Patients in group A received brief counselling from a nurse (a standard procedure for patients being discharged), which varied in content and length. Patients in group B received the counselling from a nurse and a reminder chart, about which the nurse said, "This is a chart about your medicines, telling you when to take them during the day. Read it carefully when you get home." Patients in group C received structured counselling from a pharmacist, who described the name, purpose, and timing of doses of each medicine and asked the patients if they had any questions. Patients in group D received structured counselling from a pharmacist and a reminder chart, which the pharmacist described in detail, explaining how it should be used at home and showing when each medicine should be taken and which medicines should be taken at each time shown on the chart. The counselling given by a pharmacist lasted 5-10 minutes, depending on the patient's drug regimen.

ASSESSMENT OF PATIENTS' COMPLIANCE

The investigator visited the patients at home about 10 days after they had been discharged to conduct a structured interview and to collect their tablets. At the start of the interview the investigator asked the patients for all of their medicines and replaced them with a duplicate supply. He took the initial supply away for tablet counting. We calculated a compliance score for each medicine (the number of tablets taken divided by the correct number and expressed as a percentage) and a mean compliance score for each patient. Despite some shortcomings, tablet counting remains the only practical, quantitative method of measuring the compliance of patients taking several drugs. To maximise the count's validity we gave patients no overt clues that their tablets would be counted and, instead, told them to take their medicines only from the bottles given to them because we were interested in how helpful they found the bottles and labels. Their old medicines (brought into hospital on admission) were not returned to them. To reduce the possibility of their obtaining a further supply from their general practitioner we also told them that the investigator would bring a further supply when he visited them. Finally, we gave patients an excess quantity of tablets to minimise the chances of a patient adjusting the number remaining just before the interview. By visiting patients at home we minimised the problem of bottles being lost or forgotten.

Tablet counting measures only the amount of a drug

TABLE I—*Details of patients in four study groups*

	Group A (n=49)	Group B (n=50)	Group C (n=50)	Group D (n=48)
No of men	29	29	28	24
Mean age (range) (years)	70 (38-89)	68 (36-87)	70 (39-89)	68 (38-91)
No of drugs prescribed:				
Two	12	16	12	7
Three	13	10	9	15
Four	12	13	13	15
Five	6	6	11	6
Six	6	5	5	5
Mean	3·6	3·5	3·8	3·7

taken, not whether it was taken at the right time. The investigator therefore asked the patients how many times a day they took their medicines, how many doses they took each time, and the actual times when they took the medicines. The investigator also asked patients who had received the reminder chart whether the times stated coincided with breakfast, lunch, evening meal, and bedtime. This indicated how far the daily pattern suggested by the reminder chart had been adopted. Patients who wanted to look at the labels on their medicine bottles or their reminder chart were asked to try to answer the questions without them. Patients who could not do so were given access to their bottles or the chart, and this was recorded on the questionnaire. The second part of the interview included questions on how the patients used the chart and their opinions of it.

The groups were compared for patients correctly answering the questions on their drug regimen with the χ^2 test. The groups were compared for patients' mean compliance scores by means of analysis of variance. A comparison of the numbers of patients with a mean compliance score of $>85\%$ compared with $\leq 85\%$ compliance was made with the χ^2 test. Confidence intervals were calculated with the confidence interval analysis program.[6]

Results

Of the 210 patients recruited, 197 completed the study. The 13 patients who were withdrawn included six readmitted to hospital before the investigator's visit and two who refused to complete the study. The mean time between discharge and the visit was 10 days in each group (range 8-12 days). All groups were similar with respect to age, sex, and number of drugs prescribed (table I).

Table II shows the numbers of patients in each group who correctly answered all three questions on their drug regimen without looking at their medicine bottles or the reminder chart. The two groups of patients who had received reminder charts (B and D) showed no significant difference in the proportions of correct answers given, and neither did the two groups of patients who had not received charts (A and C). We therefore compared the pooled results for groups B and D against those for groups A and C (table II). Altogether 83% (95% confidence intervals 74% to 90%) of patients in groups B and D answered correctly compared with 47% (37% to 58%) of those in groups A and C ($p<0·001$).

Patients' mean compliance scores (derived from counting patients' tablets) were averaged for each group. Groups A and C (patients not given a reminder chart) both had an average mean compliance score of 86% (81% to 91%), group B (patients given a reminder chart and counselled by a nurse) had a score of 91% (87% to 94%), and group D (patients given a reminder chart and counselled by a pharmacist) had a score of 95% (93% to 98%). Factorial analysis showed that the reminder chart had a significant effect on compliance ($p<0·001$).

Table III shows the number of patients in each group whose mean compliance score was more than 85%, which has been proposed as acceptable compliance with a multiple drug regimen for general medical patients.[17] The proportions in groups A and C were not significantly different (59% and 67%, respectively), nor were they in groups B and D (80% and 93%, respectively). Thus 86% (78% to 93%) of patients in groups B and D combined showed acceptable compliance compared with only 63% (53% to 73%) in groups A and C ($p<0·001$).

The 50 patients in group B and 48 patients in group D answered questions on their use of the reminder charts: 42 in group B and 44 in group D said they had looked at the chart; 22 in group B and 19 in group D had looked at it between one and three times; 11 in group B and 17 in group D had looked at it once a day or every time they had taken a medicine; eight in group B and eight in group D had looked at it frequently at first and then less often; 28 in group B and 30 in group D had kept it with their medicines; 35 in group B and 34 in group D had taken their medicines in accordance with the four events on the chart; and 29 in group B and 37 in group D thought the chart useful in helping them to take their medicines at the right time. Only two patients in group B, who were given little explanation of the reminder chart, said that they would have liked more explanation before they left hospital.

TABLE II—*Number of patients in each group who correctly answered all questions on dose, frequency, and timing of all their medicines*

Group	No
A (n=49)	23
B (n=50)	40
C (n=50)	24
D (n=48)	41
A+C (n=99)	47
B+D (n=98)	81***

Groups given reminder charts were B and D.
***$p<0·001$, χ^2 test of A+C *v* B+D.

TABLE III—*Number of patients in each group whose mean compliance score was >85%*

Group	No
A (n=49)	29
B (n=50)	40
C (n=46)†	31
D (n=46)†	43
A+C (n=96)	60
B+D (n=95)	83***

Groups given reminder charts were B and D.
***$p<0·001$, χ^2 test of A+C *v* B+D.
†Tablet count not done for four patients in group C and two patients in group D.

Discussion

Effective ways of improving patients' compliance with their prescribed drug regimen are desirable. But for these to be adopted generally they must fit into normal professional practice, be inexpensive, and not require much staff time. Our results show that an individualised reminder chart significantly increased the proportion of patients who correctly answered questions about their drug regimen and the proportion whose compliance with their regimen was acceptable. The chart was effective whether or not a detailed explanation of it was given, though results were slightly improved when the chart was explained. This, together with its automatic production, means that use of the chart requires almost no extra labour, and the cost per chart is low.

Sandler *et al* reported that 95% of patients correctly answered questions about their drug regimen after they had been given a modified discharge prescription that incorporated a reminder chart (completed by hand by a junior doctor).[8,9] When the patients who used the reminder chart to give their answers were excluded, however, the proportion became 68%. These results show that the patients knew how to use the reminder chart but not whether they became familiar with or followed their drug regimen. Another form of individualised information given to patients on discharge (also completed by hand by a junior doctor) resulted in 61% of patients correctly remembering their dose regimen.[10] The main advantage of our computer generated reminder chart is that it does not contain handwritten information, which may be difficult to read[9] and is time consuming to complete.[11]

Mazzuca claimed that solely increasing patients' knowledge about their medicines is rarely successful in improving compliance, and a means of relating their drug regimen to their daily life is usually also needed.[12] Our reminder chart does this by incorporating patients' doses into a daily routine and giving cues for the dose taking. The reminder chart succeeded in getting patients to take their medicines at the four daily events selected, with 70-71% in complete accord with the chart.

The Department of Health has stated that patients and relatives need to be fully informed before being discharged from hospital and that important points

should be confirmed in writing, particularly details of medicines.[13] The reminder chart could help to satisfy these requirements. The labelling programmes used in general practice could easily be adapted to produce the reminder chart. Thus patients in hospital and general practice could be given this aid to compliance, which is effective, cheap, and not labour intensive.

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Abnormalities of sleep in patients with the chronic fatigue syndrome

Richard Morriss, Michael Sharpe, Ann L Sharpley, Philip J Cowen, Keith Hawton, Julie Morris

Abstract

***Objective*—To determine whether patients with the chronic fatigue syndrome have abnormalities of sleep which may contribute to daytime fatigue.**

***Design*—A case-control study of the sleep of patients with the chronic fatigue syndrome and that of healthy volunteers.**

***Setting*—An infectious disease outpatient clinic and subjects' homes.**

***Subjects*—12 patients who met research criteria for the chronic fatigue syndrome but not for major depressive disorder and 12 healthy controls matched for age, sex, and weight.**

***Main outcome measures*—Subjective reports of sleep from patients' diaries and measurement of sleep patterns by polysomnography. Subjects' anxiety, depression, and functional impairment were assessed by interview.**

***Results*—Patients with the chronic fatigue syndrome spent more time in bed than controls (544 min *v* 465 min, $p<0.001$) but slept less efficiently (90% *v* 96%, $p<0.05$) and spent more time awake after initially going to sleep (31·9 min *v* 16·6 min, $p<0.05$). Seven patients with the chronic fatigue syndrome had a sleep disorder (four had difficulty maintaining sleep, one had difficulty getting to sleep, one had difficulty in both initiating and maintaining sleep, and one had hypersomnia) compared with none of the controls ($p=0.003$). Those with sleep disorders showed greater functional impairment than the remaining five patients (score on general health survey 50·4% *v* 70·4%, $p<0.05$), but their psychiatric scores were not significantly different.**

***Conclusions*—Most patients with the chronic fatigue syndrome had sleep disorders, which are likely to contribute to daytime fatigue. Sleep disorders may be important in the aetiology of the syndrome.**

MRC Clinical Pharmacology Unit, Littlemore Hospital, Oxford OX4 4XN
Richard Morriss, *senior registrar in psychiatry*
Ann L Sharpley, *Janssen research fellow*
Philip J Cowen, *clinical scientist*

University Department of Psychiatry, Warneford Hospital, Oxford OX3 7JX
Michael Sharpe, *clinical tutor in psychiatry*
Keith Hawton, *consultant psychiatrist*

Department of Medical Statistics, University Hospital of South Manchester, Manchester M20 8LR
Julie Morris, *medical statistician*

Correspondence to:
Dr R Morriss, Mental Illness Research Unit, Withington Hospital, Manchester M20 8LR.

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Introduction

The chronic fatigue syndrome has been defined as fatigue that is medically unexplained, has lasted at least six months, and is associated with impaired physical and mental functioning.[1] One of the commonest symptoms of the syndrome is subjective impairment of sleep.[2] That this might be important in the syndrome's aetiology is suggested by the finding that experimental manipulation of sleep leads to increased fatigue.[3] There have not, however, been any controlled studies of sleep patterns in patients with the chronic fatigue syndrome.

Many patients with the chronic fatigue syndrome also meet the criteria for major depressive disorder.[4] About 60-70% of outpatients with major depressive disorder have a specific sleep abnormality of a shortened interval from the start of sleep to rapid eye movement sleep.[5] It is therefore important to study the sleep of patients with the chronic fatigue syndrome who do not also have major depressive disorder. We have conducted a case-control study of such patients, using both subjective and objective measures of sleep.

Subjects and methods

We recruited the first 12 patients from the infectious disease outpatient clinic of a teaching hospital who met the following criteria: the patient's principal complaint was of subjective fatigue; the fatigue had been present at least half of the time for at least six months; fatigue was not a lifelong complaint; physical and mental functioning were both affected, with at least two types of activity (out of housework, recreation, social activity, occupation or studies, and independent living) being substantially impaired; the examining physician could find no evidence of physical disease; and, on a standardised psychiatric examination,[6] the patient did not meet criteria for major depressive disorder.[7] Thus the patients were not selected because of reported problems with sleeping. The patients were individually matched for age (within five years), sex, and weight (within 10 kg) with healthy controls recruited from hospital staff.

Exclusion criteria for both patients and controls were the use of psychotropic drugs in the preceding three months, intake of more than six units of alcohol four times a week in the preceding three months, and a body mass index (weight (kg)/(height (m))^2) of <18 or >25. All subjects gave their informed consent to participate in the study, which was approved by the local psychiatric ethics committee.

Subjective assessment of sleep—The subjects kept a 24 hour diary of their sleep covering nine nights, including the two nights that polysomnograms were recorded. They recorded when they switched off their lights to go to sleep; the estimated time when they fell asleep; how often they woke in the night; the time of final awakening; the total time spent in bed; the quality of sleep (rated on a 10 cm visual analogue scale from