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ORIGINAL PAPER

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Intensive case management for severe psychotic illness: is there a general benefit for patients with complex needs?

A secondary analysis of the UK700 trial data

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Abstract The UK700 trial failed to demonstrate an overall benefit of intensive case management (ICM) in patients with severe psychotic illness. This does not discount a benefit for particular subgroups, and evidence of a benefit of ICM for patients of borderline intelligence has been presented. The aim of this study is to investigate whether this effect is part of a general benefit for patients with severe psychosis complicated by additional needs. In the UK700 trial patients with severe psychosis were randomly allocated to ICM or standard case management. For each patient group with complex needs the effect of ICM is compared with that in the rest of the study cohort. Outcome measures are days spent in psychiatric hospital and the admission and discharge rates. ICM may be of benefit to patients with severe psychosis complicated by borderline intelligence or depression, but may cause patients using illicit drugs to spend more time in hospital. There was no convincing evidence of an effect of ICM in a further seven patient groups. ICM is not of general benefit to patients with severe psychosis complicated by additional needs. The benefit of ICM for patients with borderline intelligence is an isolated effect which should be interpreted cautiously until further data are available.

Key words case management – co-morbidity – data interpretation – statistical – hospitalisation – psychotic disorders – randomised controlled trials

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Introduction

The UK700 study was a randomised trial comparing intensive case management (ICM; case-load of 10–15 patients per worker) with standard case management (SCM; case-load, 30–35) for patients with severe psychosis [1]. There was no evidence of a general effect of ICM for either the primary outcome of days spent in hospital for psychiatric disorder over a 2-year period or for a range of secondary outcome measures [2]. ICM may still be of benefit to particular patients, perhaps for those with complex needs not easily met by standard services [1, 3]. While provision was made in the primary statistical analysis plan to investigate two clinical subgroups, further subgroups were mentioned in a rationale paper [1]. One of the latter subgroups has been investigated: it has been reported that patients with borderline intelligence benefit from ICM [3, 4].

As for previous analyses of the UK700 data, the primary outcome measure for this study will be the number of days spent in psychiatric hospital during

the 2-year follow-up period [1]. In addition the effect of ICM on admission rates and discharge rates will be investigated. If ICM is found to be of general benefit to different groups of patients with complex needs, a common set of mechanisms, with similar involvement of admission and discharge processes, might be expected to underlie that general effect.

The aims of this study are, first, to investigate all subgroups mentioned in the rationale paper [1] to determine whether there is a general benefit of ICM for patients with complex needs and, second, to investigate the effect of ICM on admission and discharge rates, so revealing the mechanisms by which ICM impacts upon the primary outcome measure.

Subjects and methods

The UK700 study

In this four-centre trial, 708 patients with severe psychotic illness were recruited. Psychotic illness was diagnosed according to a structured examination, OPCRIT [5], and defined as severe if the illness was at least 2 years in duration and if the patient's history included two or more psychiatric hospital admissions, at least one of which had been during the previous 2 years. Patients were randomised to ICM, where case managers had a case-load of 10 to 15 cases, or SCM, with a case-load of 30 to 35 [1]. Patients were interviewed at baseline, 12 months, and 24 months. By 2 years there had been 15 deaths and 14 losses to follow-up. The primary outcome measure, chosen at the outset [1], was total days in hospital for psychiatric reasons for each patient over 2 years.

Patients in the UK700 trial were followed up for their hospital admissions and discharges through routine hospital records systems. Researchers at each centre used that information to calculate the total number of hospitalisations and the total number of days spent in hospital over the 24 months subsequent to randomisation. Only these derived outcome measures were then passed onto the study statisticians. For the present paper we also wished to examine the separate effects of ICM on the rates of admission and discharge, and for this the dates of admission and discharge were required. Research staff from the four centres were re-contacted and asked if they had kept the information on admission and discharge dates. These were available in three of the four UK700 centres (St George's Hospital, St Mary's Hospital, and Manchester), on which this paper is therefore based, accounting for 555 of the 708 study participants.

Of the 555 participants, 11 in the SCM and 14 in the ICM groups had less than the full 2 years of follow-up, either due to death or loss to follow-up. In contrast to the main report [2] these patients are included in the analyses for this paper. Whereas in the main report it was possible to exclude extended periods of leave from the calculation of time spent in hospital, the data required to do this could not be retrieved from all centres for the present study. Hence, in the present study "days in hospital" is more correctly considered as days spent under the care of ward-based professionals.

Definitions of subgroups

Where a subgroup analysis for the UK700 trial has been previously published [2, 3], the definition of subgroups used before is adopted here. Hence, ethnic group distinguished those of African-Caribbean background from other groups; severe disability was defined as a score of one or more on the Disability Assessment Schedule [6]; and borderline intelligence was defined as 40 or more errors on the National Adult Reading Test [4]. Given the available data, the following operational definitions were used for the remaining factors (attention is focused on that subgroup with complex needs and likely to pose the greatest challenge to services):

- No family support with treatment—no family involvement with monitoring of medication, with treatment decisions, nor in providing extra support in order to avoid admission.
- Refusal of aftercare services—detained under the Mental Health Act at baseline.
- Frequent prior hospitalisation—two or more psychiatric hospital admissions during the 2 years prior to baseline.
- Poor premorbid adjustment—first psychiatric illness before the age of 21 years.
- Long prior duration of illness—ten years or more since a first recorded contact with psychiatric services, not necessarily for psychotic illness.
- Affective symptoms—a baseline Montgomery–Asberg Depression Rating Scale (MADRS) score of 11 or more [7].
- Use of illicit recreational drugs—the individual reported using illicit drugs in the previous year during the interview. The interview questions used have since been adapted for use in the COSMIC study of substance abuse and mental illness, where they were successfully validated against hair and urine testing [8]. Note that individuals with a primary diagnosis of substance abuse were excluded from the UK700 trial.

The only pre-specified factor [1] not included as a subgroup analysis is homelessness; this information was not collected at baseline for individuals recruited to the study whilst in hospital.

Analysis: total number of days in hospital

The statistical methods used in this paper have been compared to other possible approaches using the same UK700 trial data [9]. Writing $E(D_i)$ as the expected total days spent in hospital by patient i, we used regression models such as:

$$E(D_i) = \beta_{D0} + \beta_{D1}x_{1i} + \beta_{D2}x_{2i} + \beta_{D3}x_{3i}$$

Here and below, x_{1i} indicates SCM (x_{1i}=0) or ICM (x_{1i}=1); x_{2i} indicates the subgroup membership for patient i, with x_{2i}=1 if the patient is in that subgroup expected to be associated with greater care needs (x_{2i}= 0 otherwise); and x_{3i} is the product of x_{1i} and x_{2i}, indicating that patient i has been allocated to ICM and is in the high-needs group (x_{3i}=1, otherwise x_{3i}=0). Consequently β_{D0} is the expected outcome in patients without complex needs randomised to SCM, β_{D1} is the effect of ICM in those patients, and β_{D2} is the difference in outcome in the SCM arm between patients with and without complex needs. β_{D3} is the difference in the effect of ICM between patients with and without complex needs and thus assesses "effect modification" or "interaction". If there is evidence against the null hypothesis β_{D3}=0, then this indicates that the effect of ICM differs between the two subgroups.

In order to accommodate the skewed distribution of this outcome measure, confidence intervals (CIs) for the βs were calculated using the bias-corrected and accelerated (BCa) stratified percentile bootstrap method [10, 11], implemented in Stata 8 using 999 bootstrap samples [12]. "Robust" standard errors were used when calculating p values [13].

Analysis: admission and discharge rates

A treatment effect on the total number of days in hospital may arise through effects on the admission rate or on the discharge rate. Figure 1 is the basis of a multi-state model analysis, which allows the treatment effects on the admission and discharge rates to be investigated separately [14]. At each point in time each patient under observation is in one of two states: outpatient or inpatient. Interest is in the effect of ICM on rates of transition between the two states. ICM may reduce time in hospital by reducing the admission rate or by increasing the rate of discharge

once admitted. The effect of ICM on these two rates is estimated within each subgroup using Cox's proportional hazards regression [15]. How the effect of ICM varies between the subgroups is investigated by calculating the ratio of the two effects.

Variations in the rates of transitions over time are accommodated by Cox's proportional hazards regression, and it was not assumed that the rates of first, second, third, etc., transitions varied in the same way over time (i.e. baseline hazards were stratified by the order of event k), giving models of the following form:

$$\lambda_{i1k}(t) = \lambda_{01k}(t) \exp\{\beta_{11}x_{1i} + \beta_{12}x_{2i} + \beta_{13}x_{3i}\} \text{ for admission}$$

and

$$\lambda_{i2k}(t) = \lambda_{02k}(t) \exp\{\beta_{21}x_{1i} + \beta_{22}x_{2i} + \beta_{23}x_{3i}\} \text{ for discharge,}$$

where t is the time since randomisation, $\lambda_{ijk}(t)$ is the expected rate of the kth transition of type j for patient i at time t, and where j=1 indicates admission and j=2 indicates discharge. $\lambda_{0jk}(t)$ is the expected rate of transitions of type j in patients without complex needs randomised to SCM; β_{j1} is the effect of ICM on the rate of transitions of type j in patients without complex needs; β_{j2} is the effect of complex needs on patients under SCM; and β_{j3} is the difference in the effect of ICM between patients with and without complex needs.

The stratification of baseline hazards accommodates within-individual associations between inter-event times where that association arises through early events, leaving the individual susceptible to a higher rate of further events [16]. Patients were censored either after 24 months of follow-up or at the point where they were lost to follow-up. Estimates of model parameters were obtained by maximising the partial likelihood [17].

Results

For the three centres included in our analysis, the mean total days in hospital was 77 in the ICM group and 78 in the standard-care group (first line of Table 1). These means are slightly higher than those reported for the UK700 trial as a whole (ICM 73.5 days vs SCM 73.1 days [2]), probably due to the inclusion of extended leave days in the present data. However, as for the trial as a whole, there is no evidence for an overall effect of ICM.

Table 1 also presents the estimated mean difference between ICM and SCM in days spent in hospital, separately for the two subgroups defined by each factor in turn. "Effect modification" is the difference between those two estimated mean differences, a measure of how the effects of ICM differ between the two subgroups. Subgroup membership is nearly completely observed except for borderline intelligence (16% missing). It is of interest to note that, in the SCM arm, only five of the ten factors clearly lead to patients spending more time in hospital: borderline intelligence, a first psychiatric diagnosis before the age of 21, having been admitted to psychiatric hospital twice or more in the previous 2 years, detention under the Mental Health Act at randomisation, and severe disability.

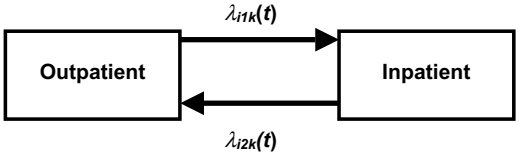

Fig. 1 Two-state model for the analysis of the UK700 data

Table 1 shows that there is evidence of a benefit of ICM in reducing time spent in hospital by patients with borderline intelligence and weak evidence of a trend for ICM to cause patients of above borderline intelligence to spend more time in hospital. There is strong evidence that the effect of ICM differs between these two subgroups (t=2.82, p=0.005); the largest difference in effect in Table 1 is between these two subgroups.

A strong challenge to the idea that ICM may be of general benefit to patients with complex needs comes from the factor with the second-largest difference in effects between its subgroups. The analysis in Table 1 indicates that ICM caused those patients who admitted illicit drug use to spend more time in hospital, whilst in contrast, ICM may reduce the time spent in hospital by those patients who did not admit to illicit drug use. The estimate of effect modification provides strong evidence that the effect of ICM differs between the two subgroups (t=3.03, p=0.003).

Table 1 also shows weak evidence that ICM was of benefit to those patients with symptoms of depression at baseline, as measured by the MADRS schedule. There was no apparent benefit in those patients without symptoms of depression, but evidence that the effect of ICM differed between the two subgroups (t=2.22, p=0.027). A baseline assessment may miss those patients for whom depression has been a problem but who have responded to medication. As an alternative measure of affective symptoms, we also compared patients' prescribed anti-depressants in the previous 2 years to the rest of the cohort. Despite the differences between these two measures, very similar results are obtained. Firstly, there is evidence of reduced days spent in hospital with ICM in individuals prescribed antidepressants (−32.7 days; 95% CI −67.2 to −6.7) but not in the rest of the cohort (+8.6 days; 95% CI −15.2 to 33.5). Secondly, there is evidence that the effect of ICM differs between the two subgroups (effect modification of −41.3 days; 95% CI −81.1 to −6.7; t=2.06, p=0.040).

There was very weak evidence to suggest that ICM was less effective in those with a psychiatric illness before the age of 21 years than in others (difference between subgroups t=1.58, p=0.12), but more effective in those with illness duration of ten years or more than in others (difference between subgroups t=1.59, p=0.11). There was no evidence of differential effects of ICM for the other subgroups investigated (Table 1).

Table 2 presents estimates of the effects of ICM on admission and discharge rates separately. Overall, ICM reduced the rate of admission but also delayed discharge once admitted (first line of Table 2). The consequence is that ICM had no effect on the overall duration of hospitalisation (first line of Table 1).

Table 1 Mean (standard deviation) days in hospital for subgroups defined by treatment allocation and each factor in turn

		Intensive case management			Standard case management			Mean difference	95% CI
		Mean	(SD)	*n*	Mean	(SD)	*n*		
Whole sample (three centres)		77	(130)	276	78	(116)	279	−1.0	−16.4, 20.2
Borderline intelligence	Yes	33	(80)	36	106	(164)	35	−73.3	−143.0, −23.7
	No	90	(137)	193	70	(106)	203	19.6	−2.8, 44.8
Effect modification								−92.92	−171.6, −44.1
Any illicit drug use in past year	Yes	119	(162)	57	57	(86)	66	61.9	21.6, 113.5
	No	66	(118)	219	84	(123)	213	−18.4	−42.0, 2.3
Effect modification								80.3	34.6, 128.9
Symptoms of depression	Yes	66	(120)	106	97	(134)	110	−30.3	−64.5, 3.9
	No	83	(135)	170	65	(100)	169	17.7	−7.7, 43.2
Effect modification								−48.0	−90.5, −5.5
First psychiatric illness before age 21	Yes	113	(158)	93	88	(135)	92	24.3	−18.0, 67.4
	No	58	(109)	183	72	(104)	187	−14.1	−35.2, 8.1
Effect modification								38.4	−11.4, 83.2
Illness duration of 10 years or more	Yes	63	(107)	154	79	(122)	129	−16.4	−43.1, 10.8
	No	94	(153)	122	76	(111)	150	17.8	−14.6, 53.6
Effect modification								−34.2	−76.6, 0.5
2+ admissions in past 2 years	Yes	94	(133)	149	88	(116)	153	6.7	−24.9, 33.9
	No	56	(123)	127	65	(114)	126	−9.7	−37.2, 22.2
Effect modification								16.4	−26.1, 54.4
Mental Health Act detention at baseline	Yes	120	(148)	50	112	(138)	43	8.0	−47.6, 64.7
	No	67	(124)	225	71	(110)	236	−4.2	−25.8, 19.4
Effect modification								12.3	−45.1, 75.4
Severe disability	Yes	84	(128)	135	91	(117)	125	−7.3	−36.9, 23.1
	No	69	(132)	141	66	(113)	154	2.9	−23.1, 31.9
Effect modification								−10.2	−50.2, 31.9
No family support with treatment	Yes	71	(115)	171	75	(114)	189	−4.0	−30.4, 20.1
	No	86	(151)	105	84	(119)	90	2.4	−33.1, 41.8
Effect modification								−6.4	−46.2, 38.5
African-Caribbean	Yes	75	(121)	65	78	(121)	58	−3.4	−41.3, 38.0
	No	77	(133)	211	77	(114)	221	−0.3	−23.6, 22.9
Effect modification								−3.1	−48.2, 37.1

Effects of intensive case management are given within the two levels of each factor, and the difference between the two effects calculated ("effect modification")

Table 2 also gives the effects of ICM on the admission and discharge rates for each factor in turn. A lower rate of admission appears to be responsible for the reduction in days spent in hospital by patients with borderline intelligence randomised to ICM. Patients of above borderline intelligence in the ICM arm do not experience such a reduction. An increase in the rate of admission and a decrease in the rate of discharge once admitted both contribute to the greater number of days spent in hospital by patients admitting to illicit drug use and randomised to the ICM arm. Finally, the greater benefit of ICM for patients with symptoms of depression may be due to a reduction in the rate of admission amongst those with such symptoms, coupled with ICM perhaps reducing the rate of discharge amongst the rest of the cohort. However, when considered individually, the evidence for these two effects is very weak.

Discussion

Intensive case management and borderline intelligence

The UK700 trial rationale proposed a number of patient subgroups who may derive particular benefit from ICM [1]. Patients in those subgroups may have additional needs of a case management team beyond those usually arising from severe psychotic illness, needs that are consequently not easily met by SCM. With data from three of the four participating centres in the UK700 trial, this study again found an apparent benefit of ICM to patients with psychosis and borderline intelligence compared to patients with psychosis and more than borderline intelligence [3, 4]. Analysis within a multi-state model framework suggested this arose from a particularly large reduction in the admis-

Table 2 Hazard ratios for the effect of intensive case management on the rates of admission and of discharge, estimated for the two levels of each factor in turn

		Admission		Discharge	
		Hazard ratio	95% CI	Hazard ratio	95% CI
Whole sample (three centres)		0.93	0.79, 1.09	0.91	0.78,1.05
Borderline intelligence	Yes	0.35	0.19, 0.63	0.96	0.58, 1.57
	No	1.13	0.93, 1.36	0.91	0.76, 1.09
Effect modification		0.31	0.17, 0.58	1.05	0.62, 1.78
Any illicit drug use in past year	Yes	1.50	1.07, 2.11	0.74	0.54, 1.01
	No	0.81	0.67, 0.97	0.98	0.82, 1.16
Effect modification		1.87	1.27, 2.75	0.76	0.53, 1.08
Symptoms of depression	Yes	0.83	0.65, 1.08	1.00	0.79, 1.27
	No	1.00	0.81, 1.24	0.85	0.70, 1.03
Effect modification		0.83	0.60, 1.16	1.18	0.87, 1.61
First psychiatric illness before age 21	Yes	1.13	0.88, 1.46	0.92	0.73, 1.17
	No	0.79	0.64, 0.98	0.90	0.74, 1.09
Effect modification		1.43	1.03, 2.00	1.02	0.75, 1.39
Illness duration of 10 years or more	Yes	0.96	0.76, 1.21	1.11	0.89, 1.37
	No	0.91	0.72, 1.15	0.75	0.61, 0.93
Effect modification		1.05	0.76, 1.46	1.48	1.09, 2.00
2+ admissions in past 2 years	Yes	1.01	0.83, 1.22	0.87	0.73, 1.04
	No	0.75	0.55, 1.01	0.94	0.71, 1.24
Effect modification		1.35	0.94, 1.93	0.93	0.67, 1.29
Mental Health Act detention at baseline	Yes	0.97	0.66, 1.44	0.95	0.70, 1.30
	No	0.92	0.77, 1.10	0.91	0.77, 1.08
Effect modification		1.06	0.69, 1.63	1.05	0.74, 1.49
Severe disability	Yes	0.79	0.62, 0.99	0.92	0.74, 1.13
	No	1.09	0.87, 1.36	0.90	0.72, 1.11
Effect modification		0.72	0.52, 1.00	1.02	0.76, 1.38
No family support with treatment	Yes	0.88	0.72, 1.07	0.85	0.71, 1.03
	No	1.03	0.78, 1.37	1.04	0.80, 1.34
Effect modification		0.85	0.60, 1.20	0.82	0.60, 1.13
African-Caribbean	Yes	0.93	0.64, 1.35	1.03	0.74, 1.43
	No	0.93	0.78, 1.12	0.88	0.74, 1.04
Effect modification		1.00	0.66, 1.50	1.17	0.80, 1.69

The two estimated effects are compared for each factor by calculating their ratio ("effect modification")

sion rate for patients with borderline intelligence; once admitted, the discharge rates were very similar in the two subgroups.

Intensive case management and other measures of complex need

On the basis of the results for patients with severe psychosis and borderline intelligence, it has been suggested that ICM may be of particular benefit to subgroups of patients with severe psychotic illness, rather than the patient group as a whole [3]. However, the result for patients with borderline intelligence cannot be understood as part of a general benefit of ICM for all patients with complex needs, as demonstrated by our investigation of all proposed subgroups. There is evidence in the current data that ICM may increase time spent in hospital by those patients who admit to having used illicit drugs in the previous year compared to the rest of the sample. This appeared to result from ICM both increasing the admission rate and, once admitted, decreasing the discharge rate among those patients admitting to illicit drug use.

Other than those patients with borderline intelligence, the only nominally significant benefit of ICM for patients with complex needs was seen for those patients with symptoms of depression. Analyses within the multi-state model framework suggested that as for patients with borderline intelligence, this reduction in time spent in hospital was due to a lower admission rate, rather than a higher discharge rate once admitted.

There was no convincing evidence when considering the primary outcome measure, that patients who had been diagnosed with a psychiatric illness before the age of 21, with an illness duration of 10 years or more, who had been admitted twice or more to a psychiatric hospital during the previous 2 years, who were being detained under the Mental Health Act at baseline, who had severe disability, who had no family support with treatment, and who were of African-Caribbean ethnic origin derived any benefit from ICM.

Admission and discharge

The general pattern is that ICM results in a decrease in the admission rate and a decrease in the discharge rate once admitted. A decrease in the admission rate results in fewer admissions per patient and will tend to result in fewer days in hospital as a consequence. In contrast, a decrease in the discharge rate for those patients in hospital will result in patients spending more time in hospital prior to each discharge, and consequently more days in hospital. It seems that smaller case-loads are allowing admissions to be avoided, but are not having a positive effect on the discharge process.

Investigating this issue further, a detailed examination of case management practice in a subsample of 39 cases (19 ICM, 20 SCM) revealed only one case, in the ICM arm, where there was strong evidence that the actions of a case manager had ensured an early discharge [18]. In both arms of the trial, discharge was sometimes delayed by difficulties in finding hostel accommodation and because it was felt that the admission itself had been delayed for too long. While the availability of hostel places is likely to be outside the control of individual case managers, it may be that smaller case-loads allowed some case managers to maintain patients in the community when a prompt admission would have led to a quicker resolution of the crisis.

Limitations

Admission and discharge dates were only available for three of the four UK700 study centres. Consequently the estimates of effect modification made in this secondary analysis have wide CIs, and important effects of ICM may not be apparent. That said, the finding that patients admitting to illicit drug use spend more time in hospital if allocated to ICM is strong evidence against the current hypothesis that ICM is of general benefit to patients with complex needs.

While the present study has indicated that the benefit of ICM for patients with borderline intelligence may be due to a reduced rate of admission, this elaborated finding remains difficult to attribute to greater contact between patients and case managers. Previously reported evidence suggests that ICM leads to a greater number of patients with borderline intelligence losing contact with their case manager (2% under SCM and 20% under ICM), which is not the case for patients with above borderline intelligence (9 and 11%, respectively, [4]).

Conclusions

There was no evidence in this study to suggest that the observed benefit of ICM for patients with severe psychosis and borderline intelligence in the UK700 study can be understood as part of a general benefit for all subgroups of patients with complex needs. The strongest challenge to this hypothesis was the finding that ICM may increase the time spent in psychiatric hospital by patients with severe psychosis who were also illicit drug users.

Focusing on patients with borderline intelligence, this study suggests they spend less time in psychiatric hospital with ICM due to a mechanism that reduces their rate of admission. Furthermore, that the benefit of ICM does not, in general, extend to other patients with complex needs points to mechanisms that are specific to the small group of patients with borderline intelligence. This in itself would appear to rule out mechanisms of a general nature such as ICM simply allowing more time to meet complex needs. Without an obvious mechanism, one should be cautious in drawing conclusions about the case management of patients with severe psychosis and borderline intelligence until further data are available.

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