PAPERS AND ORIGINALS

Statistical Approach to Planning an Integrated Haemodialysis/Transplantation Programme

S. C. FARROW, D. J. H. FISHER, D. B. JOHNSON

British Medical Journal, 1971, 2, 671-676

Summary

A mathematical model has been constructed to assist in planning the future requirements of a combined haemodialysis and transplantation centre. It has been used to predict the number of patients in the dialysis unit, the general wards, and at home on dialysis, as well as providing further information on transplantation rates and overall costs. The model can be adapted for units with different facilities from our own.

It can be primed with data from an individual unit or with pooled data from the whole country. The purpose of this paper is to demonstrate the methodology of a particular statistical approach.

Introduction

Since chronic haemodialysis was first started in this country in the early 1960s there has been a rapid expansion in this field, and there are now 37 units in the British Isles. Less than half of these have access to transplantation.

Problems encountered in running these units include calculating the number of patients on dialysis at home and in the unit as well as the number of transplant operations, as these will influence the number of support beds and transplantation side rooms required. The increase in the number of patients on dialysis will determine the extra number of dialysis monitors

needed, with important bearing on the overall costs. The simultaneous rejection of several transplanted kidneys together with the unexpected return to the unit of patients on home dialysis may severely embarrass the bed state on the dialysis unit. With this in mind we have attempted to estimate an optimum input rate of new patients and to show how the national demand for treatment of chronic renal failure will be met by such an input rate.

Our Unit and Problems

The London Hospital unit opened in February 1968 and now combines unit and home dialysis with transplantation (Dathan *et al.*, 1970). The unit operates six days a week, has nine bed stations, and each patient is dialysed overnight for 14 hours twice a week. This gives a maximum capacity of 27 patients. The daytime is spent training staff and new patients as well as dealing with dialysis commitments arising outside the unit. These include patients who have been recently transplanted or referred with acute renal failure.

In addition to the beds on the dialysis unit, there are three sterile transplant side wards and free access to male and female beds in the general medical wards. Our current unit policy is to accept every patient for whom we have room, unless they are over 50, seem incapable of managing home dialysis, or have a positive Australia antigen reaction in their serum. Providing home dialysis facilities in the East End of London poses special difficulties as many of the patients have to be rehoused. This may take six months or more. This time is used to train the patient for home dialysis and prepare him for transplantation. After arriving home all patients who are agreeable enter the transplant pool. We try, however, to ensure at least two months of satisfactory home dialysis before offering a transplant, as we feel this period enables the patients, in the event of a subsequent rejection episode, to return home in the shortest space of time. A few patients, however, refuse transplantation or are found unsuitable on medical grounds. After transplantation if a patient requires dialysis to cover a period of acute tubular necrosis this is carried out in a transplant side room and not on the unit.

London Hospital, London E1 1BB

S. C. FARROW, M.B., B.CHIR., Registrar, Department of Nephrology
D. J. H. FISHER, M.B., M.R.C.P., Senior Registrar, Department of Nephrology
D. B. JOHNSON, M.Sc., Operational Research Unit

Method of Analysis

We started by constructing a flow chart of 26 states (Fig. 1), attempting to incorporate any situation or sequence of events which might befall a patient from the time of his first haemodialysis. The states were based on a time unit of one month. Such a progression from state to state at regular intervals can be analysed mathematically in several ways. We have adopted a method based on the Markov Chain principle (Kemeny and Snell, 1960; Lu, 1968), which in this context makes two basic assumptions. The first is that the probability of passing through more than one state in any one month is zero. Thus single transactions can occur only at monthly intervals. It is, however, possible for a patient to be transplanted, reject his kidney, and die all in the space of a few days, but this potential source of error is negligible in terms of five-year planning. The second assumption is that all probabilities are constant with time and are independent of the previous progress of the patient through the unit. We have tested the constant probability assumption by analysing dialysis and transplant survival figures and this appears to be valid. However, as yet we have insufficient data to test the validity in the latter part of the model where, for example, transplantation may have a deleterious effect on subsequent dialysis survival.

FIG. 1—Transplant and dialysis flow chart. Circular figures represent recurring monthly states. The square boxes represent single monthly states.

It has been difficult to obtain accurate information in order to assess the probabilities of moving into and out of the various states, and also to estimate death rates. In applying the analysis to any particular centre it would be ideal to use a complete set of figures from that centre, but this is impossible when setting up a new unit or considering one so relatively new as our own. Further, few units can supply adequate data about the survival of second transplants. We have, therefore, incorporated reliable facts from our own unit to cover the first few sets of probabilities, and used data from similar but older units for calculations in the later parts of the scheme. With this information we constructed a matrix of estimated probabilities giving a patient's chance of remaining in, moving on from, or dying while in any of these monthly states (Fig. 2). We chose to examine a five-year period. By a process of matrix multiplication the probabilities can be calculated for any number of months in the future.

FIG. 2—The matrix. Reinforced squares represent the possible transitions from one state to another, and the figures are the probabilities of doing so. x represents the probability of remaining in state 7 and y the probability of moving to state 8 when the wait for a transplant is varied from one to six months.

By varying the intake on to the unit from one to five patients per month, we assessed the respective increase in numbers of patients expected in the various states over these next five years. A further extension of the matrix algebra provided estimates of the variance, and from these we calculated the 95% confidence limits relating to our results. The necessary allowances were also made to incorporate our present quota of patients into the scheme.

We found it was important to allow for variations in donor kidney availability and in this respect have been helped by advice from the Transplantation Immunology Department at the London Hospital (Festenstein *et al.*, 1969). Accordingly, we examined all our results, allowing for a wait of one to six months for a transplant after arriving home on dialysis. It did not seem that such a variation in the wait for a transplant significantly affected any of the principle results over a five-year period. In the case of our unit the average wait for a kidney is four months after they are on home dialysis, and it is this figure which we have used in presenting our results.

The algebraic matrix multiplication was performed on a 1900 Series I.C.L. machine using FORTRAN programming language.

The Model

States 1-6 represent the first six months on dialysis. During this period of training the patient is fully investigated with a view to future transplantation, rehoused if necessary, and his home equipped for dialysis. Training of his wife or nearest relative is also supervised during this period.

State 7 represents a variable number of months spent waiting for transplantation. Most patients will be on home dialysis and we have estimated this on our programme as being 80%. The other 20% is made up of patients whose homes are not ready for use at six months or those who, for a variety of medical or social reasons, have had to return to the unit.

State 8 represents the first month after transplantation and is spent in a sterile side room. States 9 and 10 represent the second and third months respectively after transplantation when it is hoped that the patient will be at home. State 11 is a recurring state representing the fourth and subsequent months after a successful transplantation.

State 12 represents the first month of rejection of a transplant and is spent in a sterile side ward. During the subsequent two months, states 13 and 14, the patient will be living at home. However, he will be receiving dialysis on the unit and the time is used to re-equip his home as well as retraining him and his spouse.

State 15 represents patients awaiting a second transplant, 95% of whom are on home dialysis. The other 5% are on the dialysis unit for reasons similar to those in state 7.

States 16-19 represent the first, second, third, and subsequent months of the second transplant and are comparable to states 8-11. Similarly, states 20-22 represent the second rejection episode and are comparable to states 12-14. In state 22 the patients are again undergoing necessary training before going home on dialysis for a third time. At this point one could expand the model to accommodate third and subsequent transplants. At present we have no precise information on this very small group of patients and we have ignored them in our five-year planning.

State 23 represents patients on home dialysis who are not being considered for future transplantation. They enter this state from states 6, 7, 14, 15, 22, and 24. The patients from states 6 and 7 are those who either refuse to consider transplantation at any time—namely, for religious reasons—or else are found unsuitable on medical grounds. Those coming from states 14 and 15 are patients who, following rejection of their first transplant, are not suitable for a second attempt, perhaps due to cytotoxic antibodies.

State 25 represents those patients who remain permanently in the unit and who prove impossible to discharge on home dialysis. State 24 has been incorporated to indicate that some patients on home dialysis will return to the unit from time to time. They will not, however, remain in the unit as in state 25.

State 0 represents death.

Dialysis Survival

Separate probabilities have been calculated for states 1 to 6, and for the seventh and subsequent months we have assumed that survival is constant, showing an exponential decay pattern. We have analysed our own results up to 31 October 1970 (see Table) and have incorporated our own figures into the matrix. The figure we have used for survival after the first six months was 0.98 and this has been used in states 7, 15, 23, and 25. This is somewhat lower than figures published from other units. We have selected a figure of 0.95 to show the decreased chance of survival in states 12, 13, 14, 20, 21, and 22—all periods following a rejection episode. It has also been used in state 24 where the patient has returned to the unit from home dialysis with some medical complication.

Transplant Survival

Graft survival seems to vary during the first three months, and separate probabilities have been calculated for states 8-10. For the fourth and subsequent months we have assumed that graft survival is constant, showing an exponential decay pattern. Our own transplantation programme was not far enough advanced to allow us to use our own figures. We therefore took the figures published by the Royal Infirmary, Edinburgh (Woodruff *et al.*, 1969), and arrived at probabilities of graft survival from month to month from this centre. A histogram shows these figures plotted as survival probabilities (Fig. 3). A computer analysis was then used to arrive at "best fit" estimates for the probabilities of the four transplant states, and the results are drawn in over the histogram as a curve. This appears to justify our policy of allowing four states for transplantation, but we obviously require more data. The inset in Fig. 3 shows the estimated probabilities as applied to the flow chart.

Results

DIALYSIS UNIT BEDS

The numbers of patients requiring dialysis in the unit has been calculated by adding the numbers in states 1, 2, 3, 4, 5, 6, 7,* 13, 15, 21, 22, 24, and 25.

In order to give a 95% chance of there being 27 patients or fewer on the unit in five years time, it will be seen from Fig. 4 that this limits the intake to 2.3 patients per month. This does, however, give only a mean number of 18 patients in the unit at one year and 20 at five years, allowing for the four-month wait for a transplant. If we were to take on three patients per month the mean number in one year's time would be 22 with a 95% confidence limit of 29, and in five years the figures would be 26 and 34 respectively. We include calculations based on such an intake of three patients per month, as this is the figure that all dialysis units must approach in this country if the national requirements for dialysis are to be met (see Discussion).

TRANSPLANT SIDE ROOMS

The number of transport side rooms required has been calculated by adding the numbers in states 8, 12, 16, and 20. With an input of three patients per month 3.8 side rooms will be required in one year's time and 5.1 in five years' time. The 95% confidence limits are 7.5 and 9.4 respectively (Fig. 5).

With the same input the transplantation rate is 2.6 per month at the end of one year and 3.1 per month at the end of five years. The proportion of first and second transplants is shown in Fig. 6.

*As explained earlier, only 20% of those in state 7 and 5% of those in state 15 would be on the unit.

London Hospital Dialysis Survival Figures (Until 31 October 1970). Monthly survival shows probability of moving from one month to next succeeding one. Matrix survival figures represent monthly dialysis survival as applied to states 1-6 and also to subsequent months when in state 7.

Months	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30					
No. of patients surviving	79	77	66	61	56	53	48	44	41	38	35	31	29	27	26	25	23	20	19	19	17	15	13	12	10	9	9	7	7	6					
	79	78	71	68	64	61	56	52	51	47	46	42	40	38	37	36	34	30	29	29	25	23	20	18	15	12	12	10	10	9					
Overall survival	1.00	.99	.93	.90	.88	.87	.86	.85	.80	.81	.76	.74	.73	.71	.70	.70	.68	.67	.66	.66	.68	.65	.65	.67	.67	.75	.75	.70	.70	.67					
Monthly survival	1.00	.99	.94	.96	.98	.99	.99	.99	.95	1.00	.94	.97	.98	.98	.99	.99	.97	.99	1.0	1.00	.96	1.00	1.00	1.00	1.00	1.00	1.00	.93	1.00	.95					
Matrix survival	1.00	.99	.94	.96	.98	.99	<-----98----->

FIG. 3—A histogram is shown of the Edinburgh transplant survival results (Woodruff *et al.*, 1969) with a fitted computer curve drawn in using these results. The inset shows how transplant survival probabilities calculated from these results have been incorporated into the model for states 8-11.

SUPPORT BEDS

During the year 22 September 1969 to 22 September 1970 there were 192 admissions to the general wards from an average complement of 50 patients. The number of patients who will be alive in five years' time has been calculated from the model by adding the numbers in states 1-25. This gives a figure of 142 patients with an input of three per month.

FIG. 4—Number of patients in dialysis unit. Lower line represents the mean number of patients in the unit over the next five years with a four-month wait for transplant, and the upper line the 95% confidence limits of these results.

FIG. 5—Transplantation side rooms. Mean numbers and 95% confidence limits are shown as for Fig. 4—again with a four-month wait for transplantation.

FIG. 6—Rates of transplantation. Four-month wait for transplant.

At present transplant patients represent 12/50 of the complement. In five years' time it will be 77/142. The average stay of transplant patients when they required medical admission was 13.6 days compared with 12.6 days for the dialysis patients. However, transplant patients averaged only one admission per year compared with four per year for the dialysis patients. We have calculated the position in five years' time as follows:

WITH AN INTAKE OF THREE PATIENTS PER MONTH:

Dialysis patients: 65 will require 260 admissions
 Transplant patients: 77 will require 80 admissions
 Total bed stay: $260 \times 12.6 = 3,276$
 $80 \times 13.6 = 1,088$

Total 4,364

Average daily bed occupancy = $\frac{4,364}{365} = 11.95$

Programme Costing

From the above figures it is possible to assess the costs of running such a programme. This involves looking at the separate groups of dialysis and transplantation. Our present number of patients on home dialysis is 20, and the predicted

mean numbers over the next five years are shown in the Fig. 7.

With an intake of three patients per month there will be 39 on home dialysis in five years' time, an increase of 19 on our present numbers. It is this figure of 19 which represents the number of new machines needed over the next five years. It has been assumed that machines from patients who have been transplanted or who have died will be returned to the unit and used again. No allowance has been made for the replacement of old machines. The cost of repairs has been included in the maintenance costs.

FIG. 7—Numbers of patients expected on unit and home dialysis, as well as those with a functioning transplant, are shown for the next five years in dark shadowing. The numbers for the following 10 years indicate how the system eventually reaches a steady state.

Assessment have been made of future costs both on 1971 prices and also assuming a 5% increase per year. These latter figures are shown in parentheses. At present the hospital buys and installs equipment for the home, as well as bearing the cost of repairs, whereas home conversion is paid for by the local authority. Though statistics from the Department of Health and Social Security (*Nature*, 1970) suggest a figure of £1,500 a year for maintaining a patient on home dialysis, our own costs approximate to £1,000 per annum and we have used this figure.

With an intake of three per month the maintenance costs in the fifth year are £39,000 (£50,000). New machines will cost £11,000 (£14,000). The number of patients on home dialysis rises less quickly each year as it approaches the steady state and fewer new machines are required. In 1971 terms it would seem that the home dialysis costs tend to rise to a maximum of about £55,000 per year.

The cost of dialysing a patient in our hospital in 1970 was about £2,500. In five years' time with an intake of three per month the cost of running the unit will be £65,000 (£83,000). Thus the fifth-year total for unit and home dialysis would seem to be £115,000 (£147,000).

Discussion

A mathematical model of a combined haemodialysis and transplantation centre has been constructed in an attempt to forecast future monetary and bed requirements. Such a model can only approximate to overall results and in no way represents the progress of individual patients in the scheme. Individual units with different protocols from our own can readily adapt

the model for their own uses. Advances in the surgical or immunological fields which favourably influence the survival probabilities can also be incorporated into the scheme. In this method of analysis the results of dialysis and transplantation were reviewed and the relevant sets of probabilities obtained. These have then been incorporated into the matrix and used to project a picture for the next five years, varying the input on to the unit from between one and five patients per month. As stated earlier, results were examined varying the wait for a transplant from between one and six months and this seemed to have little appreciable effect over a five-year period. We did not allow for transplantation to occur during the initial training period, though in the presence of a rare tissue-type we accept that this may well be indicated.

In calculating an optimum input of new patients we felt initially inclined to accept the figure of 2.3 patients per month as this gave a 95% chance of there being 27 or fewer patients in the dialysis unit in five years' time. The mean bed occupancy figures, however, would be 18 after one year and 20 in five years' time, and this policy would result in turning down patients with several empty beds in the unit. With the more realistic input of three patients per month then in one year the mean occupancy of the unit would be 22 with a 95% confidence limit of 29, and at the end of the fifth year the figures would be 26 and 34 respectively. Thus on many occasions the unit would be overfull, requiring presumably two dialysis sessions per day. This form of prediction will both serve to warn when the overcrowding is likely to occur, and also help shape the policy best adopted to deal with it. This will include supplying the unit with machines capable of performing two dialysis cycles every 24 hours, perhaps along the lines of the Portsmouth coil system (Down *et al.*, 1970).

At present we have three sterile side rooms used for isolation of patients and this is shortly to be increased to five. Using our input of three patients per month, we will require a mean number of 3.8 rooms at one year and 5.1 in five years, with confidence limits of 7.5 and 9.4 respectively. Obviously a total of five sterile rooms will not cover our future requirements and we should now start planning further additions.

Data are also presented suggesting the probable monthly transplant operative rates which will be necessary over the next five years. With the increase in overall surgical work, including the reinvestigation of potential second transplants, the format of the surgical team will have to change, possibly with increasing numbers of junior staff.

A major problem in all units is to give the administration some idea of how many support beds will be required in the future by such a programme. Our statistics regarding beds include patients only from the time of their first cannulation. Patients referred to the renal unit for assessment of chronic renal failure remain under the care of the referring consultant until they are accepted for chronic haemodialysis. Our estimates show that in five years' time an input of three patients per month increases the support bed requirements from the present average of 7 to 12. Daily bed returns obviously fluctuate widely and we present average figures. Many of the extra bed demands arise through cannula problems and, hopefully, these will decrease as internal fistulae become more standardized and refined.

In costing our unit we have used our own figures and those provided by the Department of Health and Social Security. It has been shown that home dialysis costs rise more slowly year by year. Obviously this has a great bearing on the overall costs borne by the hospital. We also believe that providing a figure of £95,000 as an average yearly outlay over the next five years for running unit and home dialysis will be of help to our own hospital planning and financial committees. This figure has been obtained by calculating the yearly costs of unit and home dialysis over the next five-year period.

So far we have been concerned mainly with estimating bed and monetary requirements. However, once the number of patients in each category in five years' time becomes known

then it is easy to estimate expected utilization of other resources. One important aspect concerns the increased work load placed on the haematological, biochemical, and bacteriological departments associated with such units. Another might be in assessing the nursing and medical requirements for the future. With our particular unit and policy this system of integrating unit and home dialysis with transplantation eventually appears to reach a "steady state" in 13 to 15 years' time. At this point the numbers of patients in the various states remain constant.

IMPROVEMENTS IN PREDICTING DIALYSIS UNIT REQUIREMENTS

The sources of our figures have been indicated and some are based on quite small numbers of cases. With the publication of the completed returns from the Combined Colleges Committee Circular on Haemodialysis and Transplantation more accurate probability assessments will be possible, with valuable application in setting up new units. We also suggest that units could make six-monthly or yearly appraisals of their own results and thus keep their future requirements in perspective. Furthermore, if units had to complete only one questionnaire each year along the lines of the above circular, then interested parties such as the European Dialysis and Transplant Association and the Department of Health could extract all the relevant information from this single source.

Dialysis centres in the British Isles fall into three groups. Those units like our own, those who transplant solely from the dialysis unit and have no home dialysis commitments, and those with unit and home dialysis but without access to transplantation. The figures obtained from the College Circular should give reliable average probabilities for the units using these three systems. The Markov Chain can be suitably modified and the results obtained can give average predicted requirements for the future. A comparison can then be made between the three systems with respect to mean patient survival, total numbers treated, and the respective costs. This involves further extension of the matrix algebra and will give an estimate of the mean time before reaching the absorbing state (state 0) in the three systems. This will be the subject of a further communication.

NATIONAL PICTURE

It is difficult to predict accurately the requirements for the whole country in five years' time as precise demands for chronic renal dialysis treatment each year are unknown. Estimates vary between 18 and 75 per million (Alwall, 1966; de Wardener, 1966; Lipworth, 1968; Branch *et al.*, 1970). On reviewing these surveys it would seem that about 1,500 new patients per

year are potentially suitable for haemodialysis therapy—using the current criteria for selection. If all the present units in the country accepted three new patients per month this would mean about 1,350 new patients treated yearly. If all offered unit and home dialysis combined with transplantation the situation in the fifth year would be as follows: there would be about 1,000 patients on unit dialysis, 1,500 on home dialysis, and 2,850 in the transplant group. About 1,400 transplant operations would have been carried out during this fifth year.

If we accept these estimates it will cost £2,500,000 during the fifth year to support patients in the dialysis units and £2,250,000 for those on home dialysis. In this context we have used the Department of Health figures of £1,500 per patient per year for home dialysis. This gives an overall cost of £4,750,000 for dialysis throughout the country in five years' time, which rises to £6,000,000 with the 5% annual increase. This sum does not include the cost of transplantation or of replacement of dialysis monitors. No allowance has been made for new units which may be set up. The sum covers only the cost of maintaining patients at home and in existing units together with the cost of additional machines. It is difficult to assess the cost of a transplant operation, but certainly the capital outlay involved is far less than that needed to support a dialysis patient.

We hope that these concepts will help to solve some of the problems surrounding dialysis planning.

We would like to express our appreciation to Professor J. M. Ledingham, Professor C. Wilson, Professor J. P. Blandy, and Dr. B. Barber for their helpful advice during preparation of the manuscript. Our thanks are also due to the staff of the dialysis unit, the secretaries of the medical unit, and to Mrs. P. Hannaford, the medical artist.

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