I. STATISTICAL METHODS AND MODELS

This section provides a brief summary of the statistical methods used to determine survival rates for pancreas transplants, both nationally and at each transplant program. It is not necessary to read this section in order to utilize the rest of the report. For additional statistical details, please see the Technical Methods chapter in the Executive Summary.

Model Significance -- R^2

The conclusion that there is a "center effect" in pancreas transplantation often is based on the observation that actual survival rates vary considerably among pancreas transplant programs. However, in reality, only part of the variability can be attributed to the quality of the program (the so called "center effect"); the rest can be attributed to the differences in donor and recipient characteristics among transplant programs. The degree to which the variability in actual survival rates can be attributed to the specific donor and recipient characteristics in each analysis appears in Table V-10.In the table, the values in the column labeled R^2 estimate the percentage of variability in the actual survival rates that can be attributed to the covariates in each analysis. The higher the percentage, the better the analysis explained the individual program outcomes, based on the characteristics examined. Theoretically, if an analysis contained every covariate that affected survival outcomes, and there were no differences in quality among programs (i.e., no "center effect"), then R^2 would equal 100%. In practice, we can never capture every factor that affects outcomes, and it is likely that real differences among programs do exist. This means that any unexplained variation can probably be attributed to a combination of true center effect and covariates not considered in this study. (For details on the R^2 calculation, refer to the *Model Significance* section in the *Technical Methods* chapter of the *Executive Summary.*)

The value of R^2 estimated from analyses in the 1994 Report was compared to the value of the R^2 analyses in the 1997 Report. Note that these analyses are not *directly* comparable since each was used with a different cohort of transplants. Despite the refinements in the 1997 Report, as compared to the 1994 Report, much of the variation in actual survival rates among the 96 transplant programs in the study remains unexplained by the analyses. This suggests that much of the risk involved in transplantation is due to characteristics not described in this report.

Table V-10. Pancreas Model R^2: Comparison of the 1994 and 1997 Reports

Outcome	Time Point	Report Year	Number of Covariates	R^2
Graft Model R^2	3 Months	1997 1994	12 13	33.7 29.7
	1 Year	1997 1994	12 13	34.1 36.9
	Conditional 3 Years*	1997 1994	3 N.A.	31.0 N.A.
Patient Model R^2	3 Months	1997 1994	11 9	15.6 14.1
	1 Year	1997 1994	11 9	8.3 20.7
	Conditional 3 Years*	1997 1994	8 N.A.	32.6 N.A.

* Conditional 3 year analysis was not performed in the 1994 report.

Estimated Coefficients and Standard Errors from the Logistic Regression Models

Tables V-11 and V-12 list the coefficients and the standard errors of the coefficients at each time point for all of the donor and recipient characteristics used in the logistic regression models. Each coefficient is reported on the logistic scale and represents the $\log_e$ odds of graft failure or the $\log_e$ odds of patient mortality for the corresponding characteristic at the specified time after transplant. The adjusted odds ratio on the probability scale may be obtained by applying the exponential function to the coefficient. For further details, see the *Odds Ratios* section in the *Technical Methods* chapter of the *Executive Summary.*

Table V-11. Model Coefficients ana Standard Errors for Donor and Recipient Characteristics in Short Term Pancreas Transplant Survival

Short Term Characteristics	Graft Survival				Patient Survival			
	3 Months		1 Year		3 Months		1 Year	
	Model Coeff.	Std. Error	Model Coeff.	Std. Error	Model Coeff.	Std. Error	Model Coeff.	Std. Error
Intercept	-1.265	0.162	-1.038	0.151	-2.699	0.296	-1.992	0.219
Donor Age - Linear (per 10 years)[1,2]	0.214	0.038	0.196	0.034	0.221	0.098	0.110	0.064
-Quadratic (per 10 years)	---	---	---	---	-0.106	0.066	-0.028	0.041
Cold Ischemic Time (per hour)[1]	---	---	---	---	-0.031	0.017	-0.015	0.011
Previous Pancreas Transplant -- Yes vs No	0.112	0.243	0.616	0.215	---	---	---	---
Recipient Age -Linear (per 10 years)[1,2]	0.003	0.070	0.036	0.060	0.026	0.133	0.308	0.090
-Quadratic (per 10 years)	0.019	0.072	0.102	0.061	---	---	---	---
Recipient Black vs non-Black	---	---	---	---	0.529	0.361	-0.070	0.310
Pancreas After Kidney vs Simultaneous Kidney-Pancreas	0.749	0.191	0.884	0.172	---	---	---	---
Pancreas Alone vs Simultaneous Kidney-Pancreas	0.380	0.181	1.067	0.150	---	---	---	---
TX Year 1989 vs 1988	-0.462	0.206	-0.187	0.186	-0.184	0.365	-0.226	0.274
TX Year 1990 vs 1988	-0.279	0.192	0.139	0.175	-0.061	0.342	-0.032	0.254
TX Year 1991 vs 1988	-0.668	0.201	-0.388	0.180	-0.349	0.361	-0.548	0.274
TX Year 1992 vs 1988	-0.595	0.198	-0.426	0.180	-0.391	0.362	-0.315	0.262
TX Year 1993-1994 vs 1988	-0.608	0.180	-0.321	0.164	-1.059	0.361	-0.529	0.247

Notes:

1 In the analysis, the continuous covariates (donor age, cold ischemic time, and recipient age) were centered at their mean. The mean donor age was 28. The mean cold ischemic time was 14 hours. The mean recipient age was 36.

2 Modeling the continuous covariates with a linear and a quadratic term (the square of the linear term) is necessary due to the relationship between the covariate and the odds of graft failure or patient death.

Table V-12. Model Coefficients and Standard Errors for Donor and Recipient Characteristics in Long Term Pancreas Transplant Survival

Long Term Characteristics	Graft Survival		Patient Survival	
	Model Coefficient	Standard Error	Model Coefficient	Standard Error
Intercept	-2.704	0.122	-2.848	0.153
Donor Age - Linear (per 10 years)[1]	---	---	0.209	0.079
Donor Black vs Non-Black	---	---	0.573	0.318
Cold Ischemic Time - Linear (per hour)[1,2]	---	---	-0.016	0.015
-Quadratic (per hour)	---	---	0.004	0.002
Recipient Age - Linear (per 10 years)[1,2]	---	---	0.112	0.158
-Quadratic (per 10 years)	---	---	0.207	0.140
Years Between Diabetes Onset and Transplant - Linear (per year)[1]	---	---	0.026	0.017
Pancreas After Kidney vs Simultaneous Kidney-Pancreas	1.826	0.313	---	---
Pancreas Alone vs Simultaneous Kidney-Pancreas	1.988	0.287	---	---

Notes:

1 In the analysis, the continuous covariates (donor age, cold ischemic time, and recipient age) were centered at their mean. The mean donor age was 28. The mean cold ischemic time was 14 hours. The mean recipient age was 36. The mean years between diabetes onset and transplant was 23 years.

2 Modeling the continuous covariates with a linear and a quadratic term (the square of the linear term) is necessary due to the curvilinear relationship between the covariate and the odds of graft failure or patient death.

Expected Pancreas Transplant Survival Rates

Table V-13 shows the 1 year *expected graft* survival rates for pancreas transplants for a given set of donor and recipient characteristics; Table V-14 shows the 1 year *expected patient* survival rates. These rates were determined using the following characteristics: recipient age, donor age, and procedure type. For these analyses, all other characteristics were set to the values for the reference groups, with the exception of the year of transplant (1993 or 1994). The complete list of reference groups is shown on page 77.

For example, in Table V-13, the expected 1 year graft survival for a 35 year old recipient of a pancreas alone from a 20 year old donor was 61%. In contrast, a simultaneous kidney-pancreas transplant of a 20 year old donor into a 35 year old recipient was 82%. Please note that procedure type did not significantly impact 1 year patient survival, so there was no difference reported in expected 1 year patient survival across procedure types.

Table V-13. Expected U.S. 1 Year Graft Survival Rates--Pancreas Transplants Stratified by Recipient Age, Donor Age, and Procedure Type

Recipient Age	Donor Age	Procedure Type		
		Simultaneous Kidney-Pancreas	Pancreas After Kidney	Pancreas Alone
20	20	78.73	60.47	56.02
	30	75.27	55.71	51.16
	35	73.41	53.28	48.71
	40	71.45	50.84	46.27
	50	67.30	45.95	41.46
30	20	81.65	64.77	60.49
	30	78.54	60.19	55.73
	35	76.84	57.82	53.31
	40	75.05	55.42	50.87
	50	71.21	50.54	45.98
35	20	81.89	65.13	60.87
	30	78.80	60.56	56.12
	35	77.12	58.20	53.70
	40	75.35	55.80	51.26
	50	71.54	50.94	46.37
40	20	81.36	64.32	60.03
	30	78.21	59.72	55.25
	35	76.49	57.34	52.82
	40	74.69	54.93	50.38
	50	70.81	50.06	45.50
50	20	77.74	59.06	54.58
	30	74.17	54.26	49.70
	35	72.25	51.82	47.26
	40	70.25	49.38	44.83
	50	66.00	44.51	40.05

Table V-14. Expected U.S. 1 Year Patient Survival Rates--Pancreas Transplants Stratified by Recipient Age, Donor Age, and Procedure Type

Recipient Age	Donor Age	Procedure Type		
		Simultaneous Kidney-Pancreas	Pancreas After Kidney	Pancreas Alone
	20	95.71	95.71	95.71
	30	95.17	95.17	95.17
20	35	94.98	94.98	94.98
	40	94.85	94.85	94.85
	50	94.80	94.80	94.80
	20	94.25	94.25	94.25
	30	93.55	93.55	93.55
30	35	93.30	93.30	93.30
	40	93.13	93.13	93.13
	50	93.06	93.06	93.06
	20	93.36	93.36	93.36
	30	92.55	92.55	92.55
35	35	92.27	92.27	92.27
	40	92.08	92.08	92.08
	50	92.00	92.00	92.00
	20	92.34	92.34	92.34
	30	91.42	91.42	91.42
40	35	91.10	91.10	91.10
	40	90.88	90.88	90.88
	50	90.79	90.79	90.79
	20	89.86	89.86	89.86
	30	88.68	88.68	88.68
50	35	88.27	88.27	88.27
	40	87.99	87.99	87.99
	50	87.88	87.88	87.88

J. SUMMARY

Study Period

The 1997 Report was based on 3,222 pancreas transplants performed in 3,142 patients between January 1, 1988, and April 30, 1994, from 96 transplant programs in the United States. In order to assess changes within transplant programs over time, the data were divided into 2 eras. The first era included transplants performed from January 1, 1988, through April 30, 1992; and the second era covered the two year time period from May 1, 1992, through April 30, 1994.

Survival Rates

Survival rates were computed at 3 months, 1 year, and 3 years, both nationally and for each transplant program. Three year survival was determined in two ways: (1) conditional 3 year survival (i.e., survival at 3 years for those who survived at least 1 year post-transplant), and (2) unconditional 3 year survival. The emphasis on long term survival in this chapter is on the conditional 3-year survival rates because the conditional 3-year analysis provides an assessment of characteristics independent of those limited to the first year (e.g., surgical complications and early acute rejection events).

The national graft and patient survival rates and completeness of follow-up at 3 months, 1 year, and conditional 3 years are shown in Tables V-1 and V-2. The percent of programs with graft and patient follow-up data at 1 year was more than 96%; at conditional 3 years the percent of programs with follow-up data was 94%.

There was a marked increase in both the number of pancreas transplants and in the actual graft and patient survival rates from Era 1 to Era 2. As demonstrated in Table V-15, graft survival rates increased 2.8% at 3 months and 3.8% at 1 year in Era 2 from Era 1. Patient survival rates increased 2.6% at 3 months and 1.7% at 1 year during the study period.

For the majority of transplant programs, the difference between actual and expected survival rates was not statistically significant (See Figures V-1 and V-3). In general, large differences (either higher or lower) were nearly always found among programs that reported relatively few transplants (see Figure V-2). Therefore, when evaluating survival rates for a program, it is also important to consider the number of transplants performed there.

Table V-15. Comparison of 3 Month and 1 Year Actual Survival Rates Between Eras

	3 Months		1 Year	
	Era 1	**Era 2**	**Era 1**	**Era 2**
Graft Survival (%)	82.4%	85.2%	71.9%	75.7%
Average No. of Transplants/ Month	35.1	58.2	35.1	58.2
Patient Survival (%)	94.9%	97.5%	90.4%	92.1%
Average No. of Patients/Month	34.5	57.5	34.5	57.5

Differences Between Short Term and Long Term Characteristics

The 1997 Report includes an extensive list of characteristics that have a significant impact on both short and long term graft and patient survival.

Characteristics with the strongest impact on *short term graft survival* were:

- Procedure type
- Previous pancreas transplant
- Year of transplant

Characteristics with the strongest impact on *short term patient survival* were:

- Recipient race
- Recipient age
- Donor age
- Year of transplant

Characteristic with the strongest impact on *long term graft survival* was:

- Procedure type

Characteristics with the strongest impact on *long term patient survival* were:

- Donor race
- Donor age
- Recipient age

K. FINAL WORDS

The purpose of this report is to provide updated information on survival outcomes both nationally and at specific transplant programs, and to enhance the awareness of program performance in the U.S. However, the assessment of a transplant program should not be based solely on the survival rates provided in this report. Some of the other important factors to consider are the experience of the transplant team, support personnel, the cost of the procedure, and the quality and location of post-transplant services.

VI. HEART CHAPTER

VI. HEART TRANSPLANT SURVIVAL RATES

For the Summary of this chapter, see page 101. For definitions of any terms used here, please refer to the User's Guide in the Heart volume.

A. INTRODUCTION

This report of heart transplant survival rates is based upon verified Scientific Registry data for 12,627 transplants involving 12,428 patients from 161 heart transplant programs in the United States. Each program reporting at least one heart transplant between January 1, 1988, and April 30, 1994, was included. Multi-organ, heterotopic and living donor transplants were excluded.

Short term survival is defined as survival at 1 month and 1 year post-transplant. Short term survival rates are based on all transplants in the study for which there are follow-up data.

Long term survival is defined in two ways:

- unconditional survival at 3 years post-transplant, and
- survival at 3 years post-transplant for those who survived at least 1 year, referred to as **conditional 3 year survival.**

The long term survival rates are based on all transplants between January 1, 1988, and April 30, 1992, for which there are follow-up data. This cohort was chosen to ensure that the maximum number of transplants with follow-up data was used to determine long term survival rates. Please note that this report emphasizes *conditional* 3-year survival rates. This is because the conditional 3-year analysis assesses characteristics independent of those limited to the first year (e.g., surgical complications and early acute rejection events).

B. COMPLETENESS OF FOLLOW-UP DATA AND OVERALL GRAFT AND PATIENT SURVIVAL RATES

For graft survival, completeness of follow-up data and overall actual survival rates at each time point are shown in Table VI-1; patient survival data are shown in Table VI-2.

Patient (graft) follow-up data were considered complete when:

- the patient was alive (heart was functioning) and the duration of survival (function) was equal to or exceeded the specified time after transplant (i.e., 1 month, 1 or 3 years), or
- the patient died (heart failed) and a valid date of death (failure) was reported.

The percentages of complete follow-up data ranged from a low of 97.9% for the conditional 3 year time point to a high of 99.7% for the 1 month time point. Patient survival rates are similar to graft survival rates since patient death follows graft failure unless the patient is retransplanted.

Overall survival rates also are presented in the tables. If a graft had incomplete follow-up data, the observation was weighted to account for the time during which the graft was known to be functioning. Therefore, the actual graft survival rate reflects the weighted proportion of grafts functioning at the specified time interval. Patient survival rates were computed in a similar way (see the *Technical Methods* chapter of the *Executive Summary*).

In the cohort of transplants (1/1/88 - 4/30/92) used to compute conditional 3 year survival rates, patients (grafts) who did not survive to 1 year after transplant were excluded from the analyses. Therefore, the total number of patients (grafts) for the conditional 3 year analysis was less than that for the 1 month and 1 year analyses.

Please note that the conditional 3 year graft and patient survival rates in Tables VI-1 and VI-2 may be higher than the 1 year graft survival rates. This is possible because the conditional 3 year survival rate is the 3 year survival rate for patients (grafts) who (which) survived at least 1 year post-transplant.

For example: Program A performed a total of five transplants between 1/1/88 and 4/30/92. Two of the hearts failed prior to 1 year post-transplant and the remaining three hearts survived to 3 years after transplant. In this example, Program A has a 1 year graft survival rate of 60% (3 out of 5 hearts were functioning at 1 year post-transplant). However, the conditional 3 year survival rate for Program A is 100% because all three hearts that were functioning at 1 year after transplant also were functioning at 3 years post-transplant. The same calculations are used for patient survival. See the *Technical Methods* chapter of the *Executive Summary* for more specific definitions of follow-up data and the calculations for actual graft and patient survival.

Overall Graft and Patient Survival Rates by Era

In this report, short term survival also is reported by era. Separate eras were used to determine whether there were any improvements over time in the short term survival rates. Era 1 is defined as all transplants occurring between January 1, 1988, and April 30, 1992; Era 2 includes all transplants occurring between May 1, 1992, and April 30, 1994. The overall graft and patient survival rates by era are presented in the last two columns of Table VI-1 and Table VI-2, respectively. The results demonstrate consistent high graft and patient survival rates over time.

C. GRAFT SURVIVAL -- PERCENTAGES OF ACTUAL AND EXPECTED SURVIVAL RATES

For each transplant program, actual and expected survival rates were calculated at 1 month, 1 year, and 3 years conditional on survival at 1 year. Survival rates at each time point were determined using a specific cohort of transplants (shown in Tables VI-1 and VI-2). Expected survival rates were determined for each transplant program based on its specific patient and donor characteristics. These expected outcomes were statistically adjusted for many important prognostic variables, or covariates, that were used in the survival analysis. In other words, they take into account the many different characteristics that affect survival. For example: *if Program A transplanted many more "high risk" recipients than Program B, then Program A would*

Table VI-1. Completeness of Graft Follow-Up Data and Actual Survival Rates for Heart Transplants

Time	Cohort	Number of Transplants	Percent with Follow-Up Data	Graft Survival (%)		
				Overall	Era 1	Era 2
1 Month	1/1/88 - 4/30/94	12,627	99.7	91.6	91.6	91.5
1 Year	1/1/88 - 4/30/94	12,627	98.9	81.7	81.5	81.9
Cond. 3 Years	1/1/88 - 4/30/92	6640	98.0	90.2*	90.2*	N/A*

Table VI-2. Completeness of Patient Follow-Up Data and Actual Survival Rates for Heart Transplants

Time	Cohort	Number of Patients	Percent with Follow-Up Data	Patient Survival (%)		
				Overall	Era 1	Era 2
1 Month	1/1/88 - 4/30/94	12428	99.7	92.1	92.1	92.0
1 Year	1/1/88 - 4/30/94	12428	98.9	82.5	82.4	82.8
Cond. 3 Years	1/1/88 - 4/30/92	6620	97.9	90.7*	90.7*	N/A*

* The cohort used to determine the overall conditional 3 year survival rate is the same as the Era 1 cohort. Therefore, the overall conditional 3 year survival rates are identical to the conditional 3 year survival rates for Era 1. There is no conditional 3 year survival rate calculated for Era 2 due to insufficient follow-up data on patients who received transplants in Era 2.

have a lower expected survival rate than Program B.

If a program's *actual* survival rate was *greater* than its expected survival rate, this means that the program's actual results were higher than the national results for transplants *with the same donor and recipient characteristics*. If a program's *actual* survival rate was *less than* its expected survival rate, this means that the program's actual results were lower than the national results for transplants *with the same donor and recipient characteristics. The difference between actual and expected rate may have occurred by chance, and therefore, may not be statistically significant.* Furthermore, even a statistically significant difference, one that most likely did not occur by chance, may not be clinically significant (i.e. medically important). A formal description of the methods used to determine actual and expected rates appears in the *Technical Methods* chapter of the *Executive Summary*.

Table VI-3 shows the percentages of heart transplant programs by category of graft survival rates, both for actual and expected survival. The majority of the transplant programs had actual survival rates greater than 70% at all time points. The 1 year survival rates showed a greater variation among programs than the 1 month and conditional 3 year survival rates. At 1 month, 61% of programs had actual survival rates greater than 90%. At 1 year, this fell to 13%. However, this percentage increased to 57% for the conditional 3 year survival rates. The distribution of the expected survival rates shows a similar trend. The results indicate that there are more programs with high survival rates (>90%) at the conditional 3 year time point than there are at the 1 year time point. *This is because the most critical period of time for graft survival is the first year post-transplant.* Those who survive the first year are very likely to survive 3 years post-transplant.

The percentages of programs by short term graft survival rates and eras, both for actual and expected survival, are summarized in Table VI-4. The results demonstrate a slight improvement in graft survival over time because a greater percentage of programs had actual survival rates higher than 90% in Era 2.

Differences in Actual and Expected Survival Rates

For most programs, the difference between the actual survival rate and the expected survival rate was not statistically significant. Figure VI-1 shows the percentages of programs whose actual graft survival rates were either above, not significantly different, or below expected graft survival rates at three time points. Actual survival rates shown in the figure to be either greater than or less than expected survival rates were statistically significant. Overall, there were more programs that fell significantly below expected results than programs that where significantly above expected results. However, for

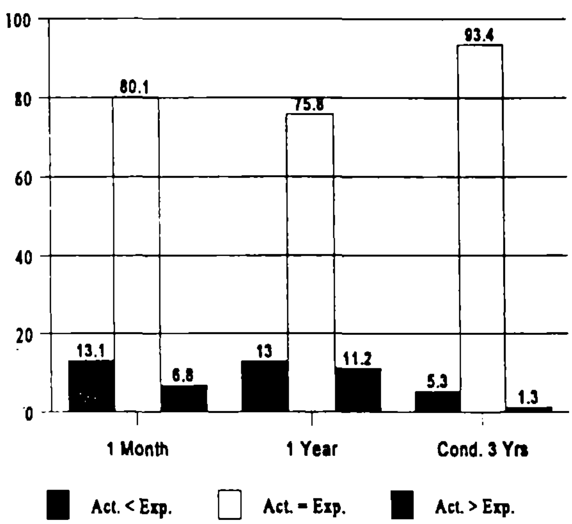
Table VI-3. Percentages of Heart Transplant Programs by Graft Survival Rates

Graft Survival Rates (%)	Actual			Expected		
	1 Month (n= 161)	1 Year (n=161)	Cond. 3 Yrs (n=150)	1 Month (n=161)	1 Year (n=161)	Cond. 3 Yrs (n=150)
0-60	3.7	10.6	2.7	0.0	0.0	0.0
>60-70	1.8	8.1	2.6	0.0	6.2	0.7
>70-80	5.6	32.3	7.3	0.6	16.1	0.0
>80-90	28.0	36.0	30.7	16.8	77.6	40.0
>90-100	60.9	13.0	56.7	82.6	0.0	59.3
TOTAL	100.0	100.0	100.0	100.0	100.0	100.0

Table VI-4. Percentages of Heart Transplant Programs by Graft Survival Rates and Era

Graft Survival Rates (%)	Actual				Expected			
	1 Month		1 Year		1 Month		1 Year	
	Era 1 (n=153)	Era 2 (n=150)	Era 1 (n=153)	Era 2 (n=150)	Era 1 (n=153)	Era 2 (n=150)	Era 1 (n=153)	Era 2 (n=150)
0-60	5.2	2.7	11.8	8.7	0.0	0.0	0.0	0.0
>60-70	1.3	3.3	9.8	10.0	0.0	0.0	7.2	4.0
>70-80	7.2	5.3	26.8	20.6	2.6	0.0	13.7	21.3
>80-90	26.1	24.7	34.6	36.0	17.0	18.7	79.1	74.7
>90-100	60.1	64.0	17.0	24.7	80.4	81.3	0.0	0.0
TOTAL	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0

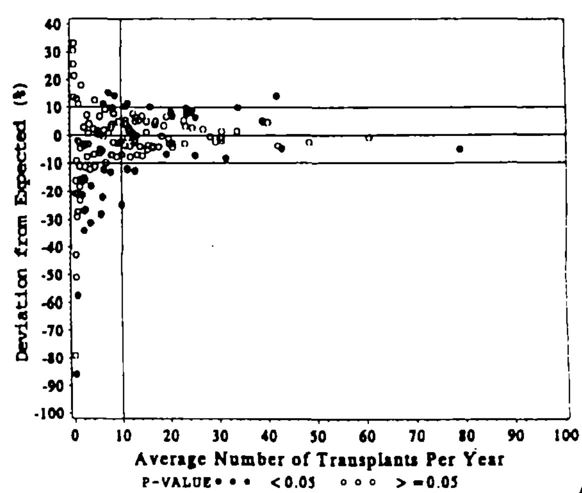
Figure VI-1. Percentages of Heart Transplant Programs with Actual Graft Survival Rates Above, Below, or Equal to Expected Survival Rates. *



*Actual survival rates above or below expected survival rates are statistically significant and varied little across time points.

At all time points, the larger differences in actual and expected rates were nearly always seen in programs that reported relatively few transplants during the period. This occurs because programs that do not perform many transplants tend to have highly variable outcomes. To illustrate this, Figure VI-2 shows a scatter plot of the average number of transplants per year (transplant volume) versus the difference in 1 year actual and expected graft survival. Nearly all differences greater than 10% (either positive or negative) are found among the majority of the transplant programs, the difference in actual and expected graft survival was not statistically significant and varied little across time points.

Figure VI-2. Heart Transplant Volume vs Difference in Actual and Expected 1 Year Graft Survival Rates.



transplant programs performing fewer than 10 heart transplants per year.

Please note that actual survival rates which differ from expected survival rates are not always statistically significant and even statistically significant differences may not be clinically significant.

D. PATIENT SURVIVAL – PERCENTAGES OF ACTUAL AND EXPECTED SURVIVAL RATES

The percentages of programs by patient survival rates for both actual and expected survival are shown in Table VI-5; the percentages of programs by survival rates and eras are shown in Table VI-6. Note that both actual and expected patient survival rates were higher and less variable at each time point than were actual and expected graft survival rates. As with graft survival, the outcomes in Era 2 were better than in Era 1.

Differences in Actual and Expected Survival Rates

The percentage of programs with actual patient survival rates significantly above their expected rates was greatest at 1 year (see Figure VI-3). Overall, there were more programs that fell significantly

Table VI-5. Percentages of Heart Transplant Programs by Patient Survival Rates

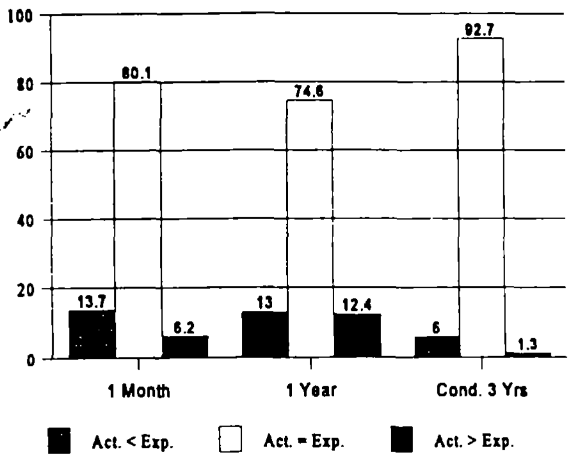
Patient Survival Rates (%)	Actual			Expected		
	1 Month (n= 161)	1 Year (n=161)	Cond. 3 Yrs (n=150)	1 Month (n=161)	1 Year (n=161)	Cond. 3 Yrs (n=150)
0-70	5.6	18.0	5.3	0.0	3.7	0.0
>70-80	5.6	26.7	7.3	0.0	14.3	0.7
>80-90	25.5	41.0	28.0	16.8	82.0	29.3
>90-95	32.9	7.5	34.7	81.4	0.0	70.0
>95-100	30.4	6.8	24.7	1.9	0.0	0.0
TOTAL	100.0	100.0	100.0	100.0	100.0	100.0

Table VI-6. Percentages of Heart Transplant Programs by Patient Survival Rates and Era

Patient Survival Rate (%)	Actual				Expected			
	1 Month		1 Year		1 Month		1 Year	
	Era 1 (n=153)	Era 2 (n=150)	Era 1 (n=153)	Era 2 (n=150)	Era 1 (n=153)	Era 2 (n=150)	Era 1 (n=153)	Era 2 (n=150)
0-70	6.5	5.3	19.0	16.7	0.0	0.0	5.2	2.0
>70-80	6.5	5.3	24.8	19.3	1.3	0.0	13.1	18.0
>80-90	24.2	22.7	37.3	38.0	15.0	18.0	81.7	80.0
>90-95	26.8	24.7	11.1	14.0	81.0	79.3	0.0	0.0
>95-100	35.9	42.0	7.8	12.0	2.6	2.7	0.0	0.0
TOTAL	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0

below expected results than above expected results. However, for the majority of transplant programs, the difference in actual and expected patient survival was not statistically significant and varied little across time points.

Figure VI-3. Percentages of Heart Transplant Programs with Actual Patient Survival Rates Above, Below or Equal to Expected Survival Rates. *



*Actual survival rates above or below expected survival rates are statistically significant and varied little across time points.

E. NATIONAL DISTRIBUTION OF DONOR AND RECIPIENT CHARACTERISTICS

The national distribution of donor and recipient characteristics for heart transplants, presented in percentages, is shown in Table VI-7. Each of these donor and recipient characteristics was included in the analyses for graft or patient survival, and used to determine an expected survival rate for each transplant. The majority of hearts transplanted were recovered from white male donors between the ages of 18 and 49. Forty-five percent of the donor hearts had cold ischemic times less than 2.5 hours. The majority of heart recipients were white males greater than 50 years of age. Most recipients were either not hospitalized (46%) or in the ICU (45%) prior to transplant. The main indication for transplant was evenly divided between coronary artery disease (41%) and cardiomyopathy (46%). Of the 12,627 heart transplants performed, less than 3% were due to repeat transplants.

Donor and Recipient Trends

National donor and recipient characteristics differed slightly between Era 1 and Era 2. There was an increase in the percentage of younger donors in Era 2, and the percent of donors older than 50 years almost doubled (3.6% to 6.5%). There was a 5% increase in the percentage of minority donors from Era 1 to Era 2. Transplant recipients were older in the second era; those over age 49 comprised 56% of recipients in Era 2 as compared to 53% in Era 1. More minorities were transplanted in Era 2 than in Era 1. Cardiomyopathy accounted for just under half of all diagnosis in Era 2 compared to only 44% in Era 1. More recipients were in the ICU at time of transplant in Era 2 than in Era 1. Also, mean cold ischemic time increased 4% from Era 1 to Era 2.

F. SHORT TERM SURVIVAL -- IMPACT OF DONOR AND RECIPIENT CHARACTERISTICS

To determine the expected survival for each transplant or patient, separate analyses were performed for graft and patient survival at three time points. (The analyses were performed using logistic regression, for a description see the *Technical Methods* chapter in the *Executive Summary.*) The analyses also identified donor and recipient characteristics that had a significant impact on survival outcomes. For each *characteristic* (e.g., race, gender) considered in the analyses, a *reference group* was chosen (e.g., White, male) with which the other groups were compared. As a general rule, the largest group or the mean of the characteristic (e.g., mean recipient age=45) is often used as the reference group.

The following served as the characteristics and reference groups for ***short term graft and patient*** survival:

- Mean Donor Age -- 26 years
- Donor Race -- White
- Donor Gender -- male
- Mean Cold Ischemic Time -- 163 minutes
- Previous Heart Transplant -- none
- Mean Recipient Age -- 45 years
- Recipient Race -- non-Black
- Recipient Gender -- male

(Cont.)

Table VI-7. National Donor and Recipient Characteristics in Heart Transplants: Percentages by Era and Overall.

		ERA 1	ERA 2	OVERALL
		1/88-4/92	5/92-4/94	1/88-4/94
Risk Factor by Category		N=8192	N=4435	N=12627
Donor Age (years)	0-5	6.2	6.7	6.3
	6-10	1.9	2.6	2.2
	11-17	15.1	17.9	16.1
	18-49	73.2	66.0	70.7
	50-64	3.6	6.5	4.7
	65+	0.0	0.2	0.1
Donor Gender	Female	29.0	30.5	29.5
	Male	71.0	69.5	70.5
Donor Race	White	81.1	76.5	79.5
	Black	9.1	11.7	10.0
	Hispanic	8.4	10.2	9.1
	Asian	0.7	0.8	0.7
	Other	0.7	0.7	0.7
	Not Reported	0.0	0.1	0.1
Recipient Age (years)	<1	4.4	4.3	4.3
	1-10	3.1	4.1	3.4
	11-17	2.8	2.9	2.8
	18-49	37.2	32.6	35.6
	50-64	49.8	51.8	50.5
	65+	2.8	4.3	3.3
Recipient Gender	Female	21.5	22.6	21.9
	Male	78.5	77.4	78.1
Recipient Race	White	84.3	81.1	83.2
	Black	8.9	10.7	9.6
	Hispanic	4.3	5.0	4.5
	Asian	0.7	1.4	1.0
	Other	1.7	1.7	1.7
	Not Reported	0.0	0.0	0.0
Previous Heart Transplant	No	97.2	96.2	96.9
	Yes	2.8	2.7	2.7
	Not Reported	0.0	1.1	0.4

		ERA 1	ERA 2	OVERALL
On Ventilator at Transplant	No	94.3	93.9	94.2
	Yes	5.3	5.2	5.3
	Not Reported	0.4	0.9	0.6
On VAD at Transplant	No	97.3	95.0	96.5
	Yes	2.2	4.1	2.9
	Not Reported	0.4	0.9	0.6
On IABP at Transplant	No	92.8	93.5	93.1
	Yes	6.8	5.6	6.3
	Not Reported	0.4	0.9	0.6
Diagnosis at Transplant	Coronary Artery Disease	43.3	37.7	41.4
	Cardiomyopathy	43.8	49.4	45.8
	Eisenmenger's Syndrome/Congenital	7.1	8.0	7.4
	Valvular Heart Disease	4.2	3.0	3.8
	Other Diagnosis	1.3	1.6	1.4
	Not Reported	0.3	0.2	0.3
Medical Condition at Transplant	In ICU	45.2	52.2	47.7
	Hospitalized	8.8	6.0	7.8
	Not Hospitalized	45.9	41.6	44.4
	Not Reported	0.1	0.2	0.1
Cold Ischemic Time	Up to 2 hrs	29.6	23.2	27.4
	> 2 - 2.5 hrs	18.3	17.4	18.0
	> 2.5 - 3 hrs	18.2	20.7	19.1
	> 3 - 3.5 hrs	14.8	16.5	15.4
	> 3.5 hrs	18.1	21.9	19.4
	Not Reported	0.9	0.2	0.7
Year of Transplant	1988	20.1	0.0	13.1
	1989	20.5	0.0	13.3
	1990	25.3	0.0	16.4
	1991	25.6	0.0	16.6
	1992	8.5	32.6	17.0
	1993	0.0	51.1	17.9
	1994	0.0	16.3	5.7

- Primary Heart Disease -- cardiomyopathy (see Table VI-8 for a complete list of disease diagnoses)
- Medical Status -- not in ICU prior to transplant
- On Ventilator at Transplant -- no
- On VAD at Transplant -- no
- On IABP at Transplant -- no
- Year of Transplant -- 1988-1992

The relative impact of each donor and recipient characteristic on short term graft and patient survival outcomes is listed in Table VI-9. For each characteristic, the ***odds ratio*** is the odds of patient death (graft failure) as compared to the reference group, after adjusting for the effects of all other donor and recipient characteristics. An *odds ratio of less than 1* indicates that the characteristic was associated with a *reduced odds* of patient death or graft failure relative to the reference group. An odds ratio of *greater than 1* indicates that the characteristic was associated with an *increased odds* of death relative to the reference group. The corresponding p-value measures how significant the odds ratio is. A p-value less than 0.05 indicates statistical significance and means that there is less than a 5% probability that such difference is due to chance alone. The smaller the p-value, the greater the statistical significance and the less likely the difference is due to chance alone.

Examples

In Table VI-9, the odds ratio of graft failure within 1 month, if the recipient was in the ICU at time of transplant, was 1.31. This means that, after adjusting for all of the other donor and recipient characteristics, the odds of graft failure within 1 month was 31% greater for recipients in the ICU than for those hospitalized or at home at time of transplant ((1.31-1)×100%=31%). As another example, the odds ratio of graft failure within 1 month post-transplant for a recipient who had a previous transplant versus a recipient who received a first transplant was 2.39. After adjusting for the effects of both donor and recipient characteristics, the odds of graft failure within 1 month for a patient who had a previous transplant was 139% higher ((2.39-1)×100%=139%) than that for a patient who received a first transplant.

The estimated odds ratios for continuous variables (i.e., variables with many possible values) such as cold ischemic time and donor and recipient ages, are less easily interpreted. For these variables, the estimated odds is determined for every 10 or 15 unit increase or decrease from the mean (reference group) of the variable. For example, in Table VI-9, the estimated odds of 1 month graft failure for 178 minutes of cold ischemic time compared to the mean of 163 minutes is 1.03. This means that, after adjusting for the effects of all other characteristics, the odds of graft failure was estimated to increase by 3% for the first 15 minute increase from the mean cold ischemic time.

An increase of 1 hour (60 minutes) from the mean cold time (i.e., the cold ischemic time is 163 min+60 min=223 min) would result in an 12% increase in the odds of graft failure at 1 month.

Mathematically, this 12% was calculated as follows:

$$\text{Odds ratio} = \exp^{\left(\frac{60}{15}\times 0.0296\right)} = 1.12$$

Table VII-8. Heart Primary Disease Diagnoses at Time of Transplant

Coronary Artery Disease
Valvular Heart Disease
Congenital Heart Disease
Cardiomyopathy
-Dilated
- Idiopathic, Adriamycin, Post Partum, Familial, Myocarditis, Alcoholic, Viral, Ischemic, Other
-Restrictive
- Idiopathic, Amyloidosis, Endocardial Fibrosis, Sarcoidosis
-Hypertrophic
Other
-Retransplant due to:
- Hyperacute Rejection, Acute Rejection, Coronary Artery Disease, non-Specific, Restrictive/Constrictive
-Eisenmenger's syndrome: Ventricular Septal Defect
-Primary Pulmonary Hypertension
-Cystic Fibrosis
-Other

Table VI-9. Impact of Donor and Recipient Characteristics on Short Term Graft and Patient Survival–Heart Transplants

Short Term Risk Characteristics	Graft Survival				Patient Survival			
	1 Month		1 Year		1 Month		1 Year	
	Odds Ratio	P-value	Odds Ratio	P-value	Odds Ratio	P-value	Odds Ratio	P-value
Donor Age 36 vs 26[1]	1.169	<0.001	1.140	<0.001	1.167	<0.001	1.142	<0.001
Donor Black vs White	0.882	0.276	1.149	0.074	0.885	0.306	1.154	0.073
Donor Hispanic vs White	1.141	0.234	1.276	0.002	1.169	0.170	1.272	0.003
Donor Asian, Other vs White	0.837	0.529	1.463	0.034	0.855	0.593	1.483	0.032
Donor Female vs Male	1.264	0.001	1.171	0.003	1.232	0.005	1.154	0.008
Cold Ischemic Time - 178 min vs 163 min[1]	1.030	<0.001	1.022	<0.001	1.029	<0.001	1.021	<0.001
Recipient Age 55 vs 45[1]	1.118	<0.001	1.151	<0.001	1.138	<0.001	1.171	<0.001
Recipient Age <=1	0.670	0.065	0.945	0.743	0.700	0.111	0.958	0.811
Recipient Female vs Male	1.283	0.002	1.099	0.108	1.289	0.002	1.095	0.135
Recipient in ICU vs at Home or Hospitalized	1.315	<0.001	1.130	0.017	1.313	<0.001	1.132	0.018
Recipient Black vs not Black	0.938	0.587	1.310	<0.001	0.998	0.987	1.336	<0.001
Previous Heart Transplant: Yes vs No	2.397	<0.001	3.312	<0.001	2.352	<0.001	3.368	<0.001
On Ventilator at Transplant: Yes vs No	2.402	<0.001	1.999	<0.001	2.404	<0.001	2.034	<0.001
On VAD at Transplant: Yes vs No	1.758	<0.001	1.328	0.031	1.612	0.006	1.300	0.059
On IABP at Transplant: Yes vs No	1.346	0.013	1.179	0.084	1.338	0.020	1.166	0.118
Coronary Heart Disease vs Cardiomyopathy	1.168	0.051	1.078	0.173	1.181	0.043	1.081	0.170
Congenital Diagnosis vs Cardiomyopathy	2.012	<0.001	1.339	0.019	1.928	<0.001	1.364	0.016
Valvular Heart Disease vs Cardiomyopathy	1.504	0.012	1.207	0.126	1.498	0.017	1.235	0.092
Other Heart Disease[2] vs Cardiomyopathy	1.714	0.021	1.154	0.449	1.490	0.121	1.098	0.639
Transplant year 1993-1994 vs 1988-1992	0.895	0.156	0.868	0.013	0.888	0.143	0.875	0.022

Notes:

1 Odds ratios for continuous covariates (donor age, recipient age and cold ischemic time) do not have a linear relationship. The odds ratios presented in this table are 10 years (donor and recipient age) or 15 minutes (cold ischemic time) unit increases from the mean of each covariate. The mean donor age was 26. The mean recipient age was 45. The mean cold ischemic times was 163 minutes.

2 See Table VI-8 for a listing of Other heart diagnoses.

where 60 is the amount of increase in minutes and 15 minutes is the per unit of increase; 0.0296 corresponds to the coefficient of cold ischemic time per 15 minute difference (see Table VI-12 for coefficients). Therefore, the increase in the odds of death or graft failure is $(1.12-1)\times100\%=12\%$. For some variables such as recipient age index, it is necessary to add a quadratic term. For more details on calculating odds ratios for continuous variables, refer to the section on *Odds Ratios* in the *Technical Methods* chapter of the *Executive Summary*.

Short Term Graft and Patient Survival

The characteristics with the strongest impact on short term graft and patient survival were, having a previous heart transplant, being on a ventilator or VAD at time of transplant, and having a congenital diagnosis. The odds of 1 year graft failure was 231% higher if the transplant was a repeat transplant. If a ventilator was used at time of transplant, then the odds of 1 year mortality was 103% higher than if a ventilator was not being used at time of transplant.

G. LONG TERM SURVIVAL – IMPACT OF DONOR AND RECIPIENT CHARACTERISTICS

In this report, *long term* survival analyses were developed separately from the short term survival analyses. Because this narrative focuses on conditional 3 year survival (survival at 3 years for grafts or patients surviving at least 1 year post-transplant), only conditional 3 year survival data are presented in this text. Both conditional and unconditional 3 year survival rates are provided in the tables for each transplant program presented in each organ specific volume.

The conditional 3 year survival analyses assesses donor and recipient characteristics that are independent of those limited to the first year (e.g., surgical complications). The impact of each donor and recipient characteristic on graft and patient long term survival is listed in Table VI-10.

Table VI-10. Impact of Donor and Recipient Characteristics on Long Term Graft and Patient Survival – Heart Transplants

Long Term Risk Characteristics	Graft		Patient	
	Odds Ratio	P-value	Odds Ratio	P-value
Donor Age 36 vs 26[1]	1.144	<0.001	1.126	0.003
Donor Hispanic vs White, Black	1.544	0.001	1.515	0.003
Donor Asian, Other vs White, Black	1.622	0.116	1.734	0.074
Recipient Age 55 vs 45[1]	1.021	0.640	1.041	0.387
Previous Heart Transplant: Yes vs No	1.956	0.005	2.113	0.007
Recipient Black vs White	1.691	<0.001	1.725	<0.001
Recipient Hispanic vs White	1.491	0.030	1.522	0.025
Recipient Asian, Other vs White	1.654	0.025	1.561	0.060

Notes:

[1] Odds ratios for continuous covariates (donor age, recipient age) do not have a linear relationship. The odds ratios presented in this table are 10 unit increases from the mean of each covariate. The mean donor age was 26 and mean recipient age was 45.

The following characteristics and reference groups were used for ***long term graft and patient*** survival:

- Mean Donor Age -- 26 years
- Donor Race -- White, Black
- Previous Heart Transplant -- no
- Mean Recipient Age -- 45 years
- Recipient Race -- White

Graft and Patient Survival

The characteristics with the strongest impact on long term graft and patient survival were, having a previous heart transplant, donor race and recipient race. The odds of conditional 3 year patient death was 111% higher if the transplant was a repeat transplant. Blacks, Hispanics and recipients of other Races had worse long term graft and patient survival than did White recipients. Recipients of hearts from Hispanic donors had at 54% higher odds of graft failure than did recipients of hearts from White or Black donors.

H. COMPARISON BETWEEN SHORT TERM AND LONG TERM CHARACTERISTICS

The majority of the donor and recipient characteristics that had a strong impact on short term graft survival did not appear to have a strong impact on long term graft survival. Some exceptions were donor and recipient race and age and if it was a first or repeat transplant.

Medical condition at transplant and diagnosis had a strong impact for short term survival, but were not significant predictors for long term survival.

I. STATISTICAL METHODS AND MODELS

This section provides a brief summary of the statistical methods used to determine survival rates for heart transplants, both nationally and at each transplant program. It is not necessary to read this section in order to utilize the rest of the report. For additional statistical details, please see the Technical Methods chapter in the Executive Summary.

Model Significance -- R^2

The conclusion that there is a "center effect" in heart transplantation often is based on the observation that actual survival rates vary considerably among heart transplant programs. However, in reality, only part of the variability can be attributed to the quality of the program (the so called "center effect"); the rest can be attributed to the differences in donor and recipient characteristics among transplant programs. The degree to which the variability in actual survival rates can be attributed to the specific donor and recipient characteristics in each analysis appears in Table VI-11.

In the table, the values in the column labeled R^2 estimate the percentage of variability in the actual survival rates that can be attributed to the covariates in each analysis. *The higher the percentage, the better the analysis explained the individual program outcomes, based on the characteristics examined.* Theoretically, if an analysis contained every covariate that affected survival outcomes, and there were no differences in quality among programs (i.e., no "center effect"), then R^2 would equal 100%. In practice, we can never capture every factor that affects outcomes, and it is likely that real differences among programs do exist. This means that any unexplained variation can probably be attributed to a combination of true center effect and covariates not considered in this study. (For details on the R^2 calculation, refer to the *Model Significance* section in the *Technical Methods* chapter of the *Executive Summary.*)

The value of R^2 estimated from analyses in the 1994 Report was compared to the value of the R^2 analyses in the 1997 Report. Note that these analyses are not *directly* comparable since each was used with a different cohort of transplants. Nevertheless, the extensive characteristics considered in the 1997 Report appear to explain more of the variability in the actual survival rates. Despite the refinements in the 1997 Report, as compared to the 1994 Report, much of the variation in actual survival rates among the 161 transplant programs in the study remains unexplained by the analyses. This suggests that much of the risk involved in transplantation is due to characteristics not described in this report.

Table VI-11. Heart Model R^2: Comparison of the 1994 and 1997 Reports

Outcome	Time Point	Report Year	Number of Covariates	R^2
Graft Model R^2	1 Month	1997 1994	22 15	26 19
	1 Year	1997 1994	22 15	36 29
	Cond. 3 Year*	1997 1994	8 NA	8 NA
Patient Model R^2	1 Month	1997 1994	22 15	25 18
	1 Year	1997 1994	22 15	36 33
	Cond. 3 Year*	1997 1994	8 NA	9 NA

* Conditional 3 year analysis was not performed in the 1994 report.

Estimated Coefficients and Standard Errors from the Logistic Regression Models

Tables VI-12 and VI-13 list the coefficients and the standard errors of the coefficients at each time point for all of the donor and recipient characteristics used in the logistic regression models. Each coefficient is reported on the logistic scale and represents the $\log_e$ odds of graft failure or the $\log_e$ odds of patient mortality for the corresponding characteristic at the specified time after transplant. The adjusted odds ratio on the probability scale may be obtained by applying the exponential function to the coefficient. For further details, see the *Odds Ratios* section in the *Technical Methods* chapter of the *Executive Summary*.

Expected Heart Transplant Survival Rates

Table VI-14 shows the 1 year *expected graft* survival rates for heart transplants for a given set of donor and recipient characteristics; Table VI-15 shows the 1 year *expected patient* survival rates. These rates were determined using the following characteristics: recipient age, diagnosis, gender and primary or repeat transplant. For these analyses, all other characteristics were set to the values for the reference groups, with the exception of the year of transplant. The complete list of reference groups is shown on page 94.

For example, in Table VI-14, the expected 1 year graft survival for a 40 year old male recipient of a first cadaveric heart transplant with coronary heart disease was 90%. In contrast, the expected 1 year graft survival for a female heart recipient of the same age and disease was 89%.

J. SUMMARY

Study Period

The 1997 Report was based on 12,627 heart transplants performed in 12,428 patients between January 1, 1988, and April 30, 1994, from 161 transplant programs in the United States. In order to assess changes within transplant programs over time, the data were divided into 2 eras. The first era included transplants performed from January 1, 1988, through April 30, 1992; the second era covered the two year time period from May 1, 1992, through April 30, 1994.

Table VI-12. Model Coefficients and Standard Errors for Donor and Recipient Characteristics in Short Term Heart Transplant Survival

Short Term Risk Characteristics	Graft				Patient			
	1 Month		1 Year		1 Month		1 Year	
	Model Coeff.	Std. Error	Model Coeff.	Std. Error	Model Coeff.	Std. Error	Model Coeff.	Std. Error
Intercept	-3.2272	0.087	-2.0973	0.060	-3.2949	0.091	-2.1587	0.061
Donor Age - Linear (per 10 years)[1,2]	0.0868	0.038	0.0848	0.027	0.0894	0.040	0.0830	0.028
Donor Age - Quadratic (per 10 years)[1,2]	0.0693	0.020	0.0478	0.015	0.0653	0.020	0.0494	0.015
Donor Black vs White	-0.1258	0.115	0.1393	0.078	-0.1220	0.119	0.1432	0.080
Donor Hispanic vs White	0.1320	0.111	0.2436	0.079	0.1562	0.114	0.2404	0.081
Donor Asian, Other vs White	-0.1775	0.282	0.3808	0.179	-0.1569	0.294	0.3942	0.184
Donor Female vs Male	0.2346	0.071	0.1581	0.052	0.2084	0.074	0.1432	0.054
Cold Ischemic Time (per 15 min)[1,2]	0.0296	0.007	0.0217	0.006	0.0288	0.008	0.0204	0.006
Recipient Age - Linear (per 10 years)[1,2]	0.1116	0.032	0.1404	0.023	0.1296	0.033	0.1577	0.023
Recipient Age-Quadratic(per 10 years)[1,2]	0.0453	0.014	0.0530	0.010	0.0538	0.015	0.0557	0.011
Recipient Age <=1	-0.4000	0.217	-0.0567	0.173	-0.3563	0.224	-0.0426	0.178
Recipient Female vs Male	0.2493	0.079	0.0948	0.059	0.2539	0.082	0.0906	0.061
Recipient in ICU vs at Home or Hospitalized	0.2740	0.073	0.1219	0.051	0.2724	0.075	0.1240	0.052
Recipient Black vs Not Black	-0.0644	0.118	0.2703	0.079	-0.0098	0.121	0.2897	0.081
Previous Heart Transplant: Yes vs No	0.8741	0.147	1.1976	0.117	0.8553	0.183	1.2143	0.140
On Ventilator at Transplant: Yes vs No	0.8762	0.116	0.6924	0.098	0.8770	0.121	0.7099	0.102
On VAD at Transplant: Yes vs No	0.5641	0.158	0.2838	0.132	0.4773	0.172	0.2621	0.139
On IABP at Transplant: Yes vs No	0.2970	0.120	0.1644	0.095	0.2909	0.125	0.1534	0.098
Coronary Heart Disease vs Cardiomyopathy	0.1552	0.079	0.0755	0.055	0.1661	0.082	0.0778	0.057
Congenital Heart Disease vs Cardiomyopathy	0.6991	0.159	0.2919	0.124	0.6566	0.166	0.3104	0.129
Valvular Heart Disease vs Cardiomyopathy	0.4078	0.163	0.1878	0.123	0.4038	0.169	0.2111	0.125
Other Heart Disease vs Cardiomyopathy	0.5388	0.234	0.1430	0.189	0.3991	0.257	0.0931	0.199
Transplant year 1993-1994 vs 1988-1992	-0.1113	0.078	-0.1411	0.057	-0.1188	0.081	-0.1335	0.058

Notes:

[1] In the analysis, the continuous covariates (donor and recipient age, cold ischemic time) were centered at their mean. The mean donor age was 26. The mean cold ischemic time was 163 minutes. The mean donor age was 45.

[2] Modeling the continuous covariates with a liner and quadratic term (the square of the linear term) is necessary due to the relationship between the covariate and the odds of graft failure or death.

Table VI-13. Model Coefficients and Standard Errors for Donor and Recipient Characteristics in Long Term Heart Transplant Survival

Long Term Characteristics	Graft		Patient	
	Model Coeff.	Std. Error	Model Coeff.	Std. Error
Intercept	-2.4229	0.063	-2.4838	0.065
Donor Age (per 10 years) [1,2]	0.1348	0.038	0.1185	0.034
Donor Hispanic vs White, Black	0.4341	0.134	0.4155	0.138
Donor Asian, Other vs White, Black	0.4839	0.308	0.5505	0.308
Recipient Age - Linear (per 10 years)[1,2]	-0.0018	0.038	0.0143	0.039
Recipient Age - Quadratic (per 10 years)[1,2]	0.0229	0.014	0.0256	0.014
Previous Heart Transplant: Yes vs No	0.6711	0.241	0.7483	0.277
Recipient Black vs White	0.5251	0.130	0.5455	0.132
Recipient Hispanic vs White	0.3997	0.184	0.4200	0.188
Recipient Asian, Other vs White	0.5031	0.224	0.4453	0.236

Notes:

[1] In the analysis, the continuous covariates (donor and recipient age, cold ischemic time) were centered at their mean. The mean donor age was 26. The mean cold ischemic time was 163 minutes. The mean donor age was 45.

[2] Modeling the continuous covariates with a liner and quadratic term (the square of the linear term) is necessary due to the relationship between the covariate and the odds of graft failure or death.

<u>Survival Rates</u>

Survival rates were computed at 1 month, 1 year, and 3 years, both nationally and for each transplant program. Three year survival was determined in two ways: (1) conditional 3 year survival (i.e., survival at 3 years for those who survived at least 1 year post-transplant), and (2) unconditional 3 year survival. The emphasis on long term survival in this chapter is on the conditional 3-year survival rates because the conditional 3-year analysis provides an assessment of characteristics independent of those limited to the first year (e.g., surgical complications and early acute rejection events).

The national graft and patient survival rates and completeness of follow-up at 1 month, 1 year, and conditional 3 years are shown in Tables VI-1 and VI-2 The percent of programs with graft and patient follow-up data at 1 year was more than 98%; at conditional 3 years the percent of programs with follow-up data was also 98%.

There was a marked increase in the number of heart transplants from Era 1 to Era 2. As demonstrated in Table VI-16, the number of heart transplants increased by 17% from an average of 157 transplants per month in Era 1 to 185 transplants per month in Era 2.

For the majority of transplant programs, the difference between actual and expected survival rates was not statistically significant (See Figures VI-1 and VI-3). In general, large differences (either higher or lower) were nearly always found among programs that reported relatively few transplants (see Figure VI-2). Therefore, when evaluating survival rates for a program, it is also important to consider the number of transplants performed there.

Table VI-14. Expected U.S. 1 Year Graft Survival Rates -- Heart Transplants Stratified by Recipient Age, Diagnosis, Gender, and Primary or Repeat Transplant

Age	Diagnosis	Male		Female	
		Primary	Repeat	Primary	Repeat
5	Cardiomyopathy	87.6	68.0	86.5	65.9
	Coronary Heart Disease	86.7	66.3	85.6	64.2
	Congenital Disease	84.0	61.3	82.7	59.1
	Valvular Disease	85.4	63.8	84.1	61.6
	Other Disease	85.9	64.8	84.7	62.6
25	Cardiomyopathy	90.9	75.2	90.1	73.4
	Coronary Heart Disease	90.3	73.8	89.4	71.9
	Congenital Disease	88.2	69.4	87.2	67.3
	Valvular Disease	89.3	71.5	88.3	69.6
	Other Disease	89.7	72.4	88.8	70.5
40	Cardiomyopathy	90.8	75.0	90.0	73.2
	Coronary Heart Disease	90.2	73.5	89.3	71.7
	Congenital Disease	88.1	69.1	87.1	67.1
	Valvular Disease	89.2	71.3	88.2	69.3
	Other Disease	89.6	72.2	88.7	70.3
50	Cardiomyopathy	89.6	72.3	88.7	70.3
	Coronary Heart Disease	88.9	70.7	87.9	68.7
	Congenital Disease	86.6	66.0	85.4	63.9
	Valvular Disease	87.7	68.3	86.7	66.3
	Other Disease	88.2	69.3	87.2	67.3
60	Cardiomyopathy	87.1	67.1	86.0	64.9
	Coronary Heart Disease	86.2	65.4	85.0	63.2
	Congenital Disease	83.4	60.3	82.1	58.0
	Valvular Disease	84.8	62.8	83.6	60.5
	Other Disease	85.4	63.8	84.2	61.6

Table V-15. Expected U.S. 1 Year Patient Survival Rates -- Heart Transplants Stratified by Recipient Age, Diagnosis, Gender, and Primary or Repeat Transplant

Age	Diagnosis	Male		Female	
		Primary	Repeat	Primary	Repeat
5	Cardiomyopathy	88.4	69.4	87.5	67.4
	Coronary Heart Disease	87.6	67.7	86.6	65.7
	Congenital Disease	84.8	62.4	83.6	60.3
	Valvular Disease	86.1	64.7	84.9	62.6
	Other Disease	87.4	67.4	86.4	65.3
25	Cardiomyopathy	91.6	76.3	90.8	74.6
	Coronary Heart Disease	90.9	74.9	90.2	73.1
	Congenital Disease	88.8	70.3	87.9	68.3
	Valvular Disease	89.8	72.3	88.9	70.5
	Other Disease	90.8	74.6	90.0	72.8
40	Cardiomyopathy	91.3	75.8	90.6	74.1
	Coronary Heart Disease	90.7	74.4	89.9	72.6
	Congenital Disease	88.6	69.7	87.6	67.7
	Valvular Disease	89.5	71.7	88.6	69.9
	Other Disease	90.6	74.1	89.8	72.3
50	Cardiomyopathy	90.0	72.8	89.2	71.0
	Coronary Heart Disease	89.3	71.2	88.4	69.4
	Congenital Disease	86.9	66.3	85.8	64.2
	Valvular Disease	88.0	68.4	87.0	66.4
	Other Disease	89.2	70.9	88.2	69.0
60	Cardiomyopathy	87.3	67.2	86.3	65.1
	Coronary Heart Disease	86.4	65.4	85.3	63.4
	Congenital Disease	83.5	60.0	82.2	57.8
	Valvular Disease	84.8	62.4	83.6	60.2
	Other Disease	86.3	65.1	85.2	63.0

Table VI-16. Comparison of 1 Month and 1 Year Actual Survival Rates Between Eras

	1 Month		1 Year	
	Era 1	Era 2	Era 1	Era 2
Graft Survival (%)	91.6%	91.5%	81.5%	81.9%
Average No. of Transplants/Month	157	185	158	185
Patient Survival (%)	92.1%	92.0%	82.4%	82.8%
Average No. of Patients/Month	155	183	155	184

Differences Between Short Term and Long Term Characteristics

The 1997 Report includes an extensive list of characteristics that have a significant impact on both short and long term graft and patient survival.

Characteristics with the strongest impact on *short term survival* were:

- Recipient received a previous heart transplant
- Recipient on ventilator at transplant
- Recipient had a congenital heart diagnosis
- Year of transplant was 1993 or 1994

Characteristics with the strongest impact on *long term survival* were:

- Recipient received a previous heart transplant
- Donor was Hispanic
- Recipient was Black or Hispanic

K. FINAL WORDS

The purpose of this report is to provide updated information on survival outcomes both nationally and at specific transplant programs, and to enhance the awareness of program performance in the U.S. However, the assessment of a transplant program should not be based solely on the survival rates provided in this report. Some of the other important factors to consider are the experience of the transplant team, support personnel, the cost of the procedure, and the quality and location of post-transplant services.

VII. LUNG CHAPTER

VII. LUNG TRANSPLANT SURVIVAL RATES

For the Summary of this chapter, see page 119. For definitions of any terms used here, please refer to the User's Guide in the Lung volume.

A. INTRODUCTION

This report of lung transplant survival rates is based upon verified Scientific Registry data for 2,135 transplants involving 2,079 patients from 75 lung transplant programs in the United States. Each program reporting at least one lung transplant between January 1, 1988, and April 30, 1994, was included. Multi-organ and living donor transplants were excluded.

Short term survival is defined as survival at 1 month and 1 year post-transplant. Short term survival rates are based on all transplants in the study for which there are follow-up data.

Long term survival is defined in two ways:

- unconditional survival at 3 years post-transplant, and
- survival at 3 years post-transplant for those who survived at least 1 year, referred to as **conditional 3 year survival.**

The long term survival rates are based on all transplants between January 1, 1988, and April 30, 1992, for which there are follow-up data. This cohort was chosen to ensure that the maximum number of transplants with follow-up data was used to determine long term survival rates. Please note this report emphasizes *conditional* 3-year survival rates. This is because the conditional 3-year analysis assesses characteristics independent of those limited to the first year (e.g., surgical complications and early acute rejection events).

B. COMPLETENESS OF FOLLOW-UP DATA AND OVERALL GRAFT AND PATIENT SURVIVAL RATES

For graft survival, completeness of follow-up data and overall actual survival rates at each time point are shown in Table VII-1; patient survival data are shown in Table VII-2.

Patient (graft) follow-up data were considered complete when:

- the patient was alive (lung was functioning) and the duration of survival (function) was equal to or exceeded the specified time after transplant (i.e., 1 month, 1 or 3 years), or
- the patient died (lung failed) and a valid date of death (failure) was reported.

The percentages of complete follow-up data ranged from a low of 95.2% for the conditional 3 year time point to a high of 99.5% for the 1 month time point. Patient survival rates are similar to graft survival rates since patient death follows graft failure unless the patient is retransplanted.

Overall survival rates also are presented in the tables. Patient survival rates are comparable to graft survival rates because patient death usually follows graft failure. If a graft had incomplete follow-up data, the observation was weighted to account for the time during which the graft was known to be functioning. Therefore, the actual graft survival rate reflects the weighted proportion of grafts functioning at the specified time interval. Patient survival rates were computed in a similar way (see the *Technical Methods* chapter of the *Executive Summary*).

In the cohort of transplants (1/1/88 - 4/30/92) used to compute conditional 3 year survival rates, patients (grafts) who did not survive to 1 year after transplant were excluded from the analyses. Therefore, the total number of patients (grafts) for the conditional 3 year analysis was less than that for the 1 month and 1 year analyses.

Please note that the conditional 3 year graft and patient survival rates in Tables VII-1 and VII-2 may be higher than the 1 year graft survival rates. This is possible because the conditional 3 year survival rate is the 3 year survival rate for patients (grafts) who (which) survived at least 1 year post-transplant.

For example: Program A performed a total of five transplants between 1/1/88 and 4/30/92. Two of the lungs failed prior to 1 year post-transplant and the remaining three lungs survived to 3 years after transplant. In this example, Program A has a 1 year graft survival rate of 60% (3 out of 5 lungs were functioning at 1 year post-transplant). However, the conditional 3 year survival rate for Program A is 100% because all three lungs that were functioning at 1 year after transplant also were functioning at 3 years post-transplant. The same calculations are used for patient survival. See the *Technical Methods* chapter of the *Executive Summary* for more specific definitions of follow-up data and the calculations for actual graft and patient survival.

Overall Graft and Patient Survival Rates by Era

In this report, short term survival also is reported by era. Separate eras were used to determine whether there were any improvements over time in the short term survival rates. Era 1 is defined as all transplants occurring between January 1, 1988, and April 30, 1992; Era 2 includes all transplants occurring between May 1, 1992, and April 30, 1994. The overall graft and patient survival rates by era are presented in the last two columns of Table VII-1 and Table VII-2, respectively. The results demonstrate substantial improvement for both graft and patient survival rates over time.

C. GRAFT SURVIVAL -- PERCENTAGES OF ACTUAL AND EXPECTED SURVIVAL RATES

For each transplant program, actual and expected survival rates were calculated at 1 month, 1 year, and 3 years conditional on survival at 1 year. Survival rates at each time point were determined using a specific cohort of transplants (shown in Tables VII-1 and VII-2). Expected survival rates were determined for each transplant program based on its specific patient and donor characteristics. These expected outcomes were statistically adjusted for many important prognostic variables, or covariates, that were used in the survival analysis. In other words, they take into account many different characteristics that affect survival. For example: if Program A transplanted many more "high risk" recipients than Program B, then Program A would have a lower *expected* survival rate than Program B.

Table VII-1. Completeness of Graft Follow-Up Data and Actual Survival Rates for Lung Transplants

Time	Cohort	Number of Transplants	Percent with Follow-Up Data	Graft Survival (%)		
				Overall	Era 1	Era 2
1 Month	1/1/88 - 4/30/94	2,135	99.5	86.8	83.5	89.3
1 Year	1/1/88 - 4/30/94	2,135	98.7	70.4	66.6	73.4
Cond. 3 Years	1/1/88 - 4/30/92	608	95.4	74.7*	74.7*	N.A.*

Table VII-2. Completeness of Patient Follow-Up Data and Actual Survival Rates for Lung Transplants

Time	Cohort	Number of Patients	Percent with Follow-Up Data	Patient Survival (%)		
				Overall	Era 1	Era 2
1 Month	1/1/88 - 4/30/94	2,079	99.5	87.7	84.5	90.0
1 Year	1/1/88 - 4/30/94	2,079	98.6	71.9	68.4	74.5
Cond. 3 Years	1/1/88 - 4/30/92	606	95.2	75.9*	75.9*	N.A.*

* The cohort used to determine the overall conditional 3 year survival rate is the same as the Era 1 cohort. Therefore, the overall conditional 3 year survival rates are identical to the conditional 3 year survival rates for Era 1. There is no conditional 3 year survival rate calculated for Era 2 due to insufficient follow-up data on patients who received transplants in Era 2.

If a program's *actual* survival rate was *greater* than its expected survival rate, this means that the program's actual results were higher than the national results for transplants *with the same donor and recipient characteristics*. If a program's *actual* survival rate was *less than* its expected survival rate, this means that the program's actual results were lower than the national results for transplants *with the same donor and recipient characteristics*. The difference between the actual and expected rate may have occurred by chance and, therefore, may not be statistically significant. Furthermore, even a statistically significant difference, one that most likely did not occur by chance, may not be clinically significant (i.e., medically important). A formal description of the methods used to determine actual and expected survival rates appears in the *Technical Methods* chapter of the *Executive Summary*.

Table VII-3 shows the percentages of lung transplant programs by category of graft survival rates, both for actual and expected survival. The majority of the transplant programs had actual survival rates greater than 70% at all time points. At 1 month, 43% of programs had actual survival rates greater than 90%. At 1 year, this fell to 11%. However, this percentage increased to 33% for the conditional 3 year survival rates. The distribution of the expected survival rates shows a similar trend. The results indicate that there are more programs with high survival rates at the conditional 3 year time point than there are at the 1 year time point. *This is because the most critical period of time for graft survival is the first year post-transplant.* Those who survive the first year are more likely to survive 3 years post-transplant.

The percentages of programs by short term graft survival rates and eras, both for actual and expected survival, are summarized in Table VII-4. The results demonstrate a substantial improvement in graft survival over time because a greater percentage of programs had actual survival rates higher than 80% in Era 2.

<u>Differences in Actual and Expected Survival Rates</u>

For most programs, the difference between the actual survival rate and the expected survival rate was not statistically significant. Figure VII-1 shows the percentages of programs whose actual graft survival rates were either above, not significantly different from, or below expected graft survival rates at three time points. Actual survival rates shown in the figure to be either greater than or less than expected survival rates were statistically significant. Overall, there were more programs that fell significantly below expected results than programs that were significantly above expected results. However, for the majority of the transplant programs, the difference in actual and expected graft survival was not statistically significant and varied little across time points.

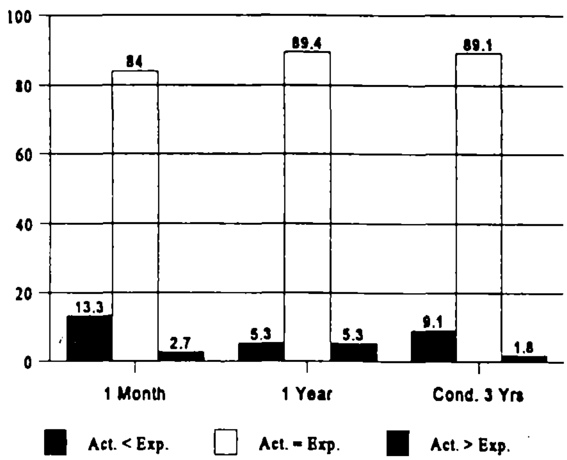
Table VII-3. Percentages of Lung Transplant Programs by Graft Survival Rates

Graft Survival Rates (%)	Actual			Expected		
	1 Month (n=75)	1 Year (n=75)	Cond. 3 Yrs (n=55)	1 Month (n=75)	1 Year (n=75)	Cond. 3 Yrs (n=55)
0-60	9.3	28.0	21.8	0.0	8.0	1.8
>60-70	8.0	20.0	18.2	2.7	29.3	18.2
>70-80	10.7	25.3	12.7	5.3	62.7	70.9
>80-90	29.3	16.0	14.6	68.0	0.0	9.1
>90-100	42.7	10.7	32.7	24.0	0.0	0.0
TOTAL	100.0	100.0	100.0	100.0	100.0	100.0

Table VII-4. Percentages of Lung Transplant Programs by Graft Survival Rates and Era

Graft Survival Rates (%)	Actual				Expected			
	1 Month		1 Year		1 Month		1 Year	
	Era 1 (n=65)	Era 2 (n=67)	Era 1 (n=65)	Era 2 (n=67)	Era 1 (n=65)	Era 2 (n=67)	Era 1 (n=65)	Era 2 (n=67)
0-60	21.5	4.5	46.2	22.4	0.0	0.0	16.9	3.0
>60-70	3.1	3.0	13.8	17.9	6.2	0.0	58.5	16.4
>70-80	20.0	13.4	16.9	29.9	18.5	0.0	24.6	79.1
>80-90	12.3	17.9	4.6	10.4	64.6	47.8	0.0	1.5
>90-100	43.1	61.2	18.5	19.4	10.8	52.2	0.0	0.0
TOTAL	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0

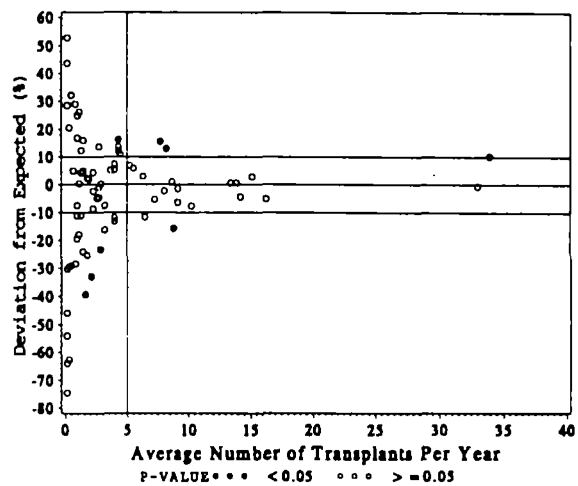
Figure VII-1. Percentages of Lung Transplant Programs with Actual Graft Survival Rates Above, Below, or Equal to Expected Survival Rates. *



* Actual survival rates above or below expected survival rates are statistically significant and varied little across time points.

At all time points, the larger differences in actual and expected rates were nearly always seen in programs that reported relatively few transplants during the period. This occurs because programs that do not perform many transplants tend to have highly variable outcomes. To illustrate this, Figure VII-2 shows a scatter plot of the average number of transplants per year (transplant volume) versus the difference in 1 year actual and expected graft survival. Nearly all differences greater than 10% (either positive or negative) are found among transplant programs which perform very few transplants per year.

Figure VII-2. Lung Transplant Volume vs Difference in Actual and Expected 1 Year Graft Survival Rates.



Please note that actual survival rates which differ from expected survival rates are not always statistically significant and even statistically significant differences may not be clinically significant.

D. PATIENT SURVIVAL -- PERCENTAGES OF ACTUAL AND EXPECTED SURVIVAL RATES

The percentages of programs by patient survival rates for both actual and expected survival are shown in Table VII-5; the percentages of programs by survival rates and eras are shown in Table VII-6. As with graft survival, the outcomes in Era 2 were better than in Era 1.

Differences in Actual and Expected Survival Rates

Overall, there were more programs that fell significantly below expected results than above expected results (see Figure VII-3). However, for the majority of transplant programs, the difference in actual and expected patient survival was not statistically significant and varied little across time points.

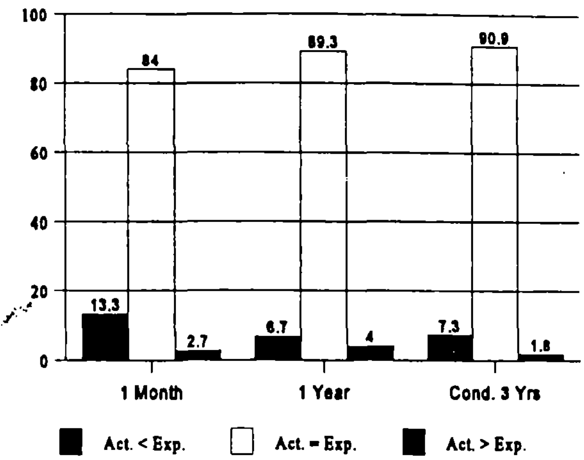
Table VII-5. Percentages of Lung Transplant Programs by Patient Survival Rates

Patient Survival Rates (%)	Actual			Expected		
	1 Month (n=75)	1 Year (n=75)	Cond. 3 Yrs (n=55)	1 Month (n=75)	1 Year (n=75)	Cond. 3 Yrs (n=55)
0-70	16.0	46.7	40.0	2.7	29.3	16.4
>70-80	12.0	25.3	10.9	5.3	68.0	74.5
>80-90	24.0	17.3	14.6	60.0	2.7	9.1
>90-95	18.7	0.0	1.8	32.0	0.0	0.0
>95-100	29.3	10.7	32.7	0.0	0.0	0.0
TOTAL	100.0	100.0	100.0	100.0	100.0	100.0

Table VII-6. Percentages of Lung Transplant Programs by Patient Survival Rates and Era

Patient Survival Rates (%)	Actual				Expected			
	1 Month		1 Year		1 Month		1 Year	
	Era 1 (n=65)	Era 2 (n=67)	Era 1 (n=65)	Era 2 (n=67)	Era 1 (n=65)	Era 2 (n=67)	Era 1 (n=65)	Era 2 (n=67)
0-70	23.1	6.0	58.4	38.8	6.2	0.0	66.2	14.9
>70-80	16.9	14.9	18.5	28.4	13.8	0.0	33.8	80.6
>80-90	12.3	17.9	3.1	11.9	66.2	32.8	0.0	4.5
>90-95	10.8	17.9	0.0	6.0	13.8	67.2	0.0	0.0
>95-100	36.9	43.3	20.0	14.9	0.0	0.0	0.0	0.0
TOTAL	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0

Figure VII-3. Percentages of Lung Transplant Programs with Actual Patient Survival Rates Above, Below, or Equal to Expected Survival Rates. *



* Actual survival rates above or below expected survival rates are statistically significant and varied little across time points

E. NATIONAL DISTRIBUTION OF DONOR AND RECIPIENT CHARACTERISTICS

The national distribution of donor and recipient characteristics for lung transplants, presented in percentages, is shown in Table VII-7. Each of these donor and recipient characteristics was included in the analyses for graft or patient survival, and used to determine an expected survival rate for each transplant. The transplant types were evenly divided among single left lung transplants (34%), single right lung transplants (33%) and double lung transplants (33%). The majority of lungs transplanted were recovered from white male donors between the ages of 18 and 35 (52%). Most of the lung recipients were white males greater than 50 years of age (41%), and were neither hospitalized (85%) nor on ventilator (94%) prior to transplant. Of the 2,135 lung transplants performed, only 3% were due to repeat transplants. The most common disease diagnoses were Chronic Obstructive Pulmonary Disease (COPD) and Emphysema (33%), followed by Cystic and Idiopathic Fibrosis (27%). In general, cold ischemic time for single lung transplants was shorter than double lung transplants.

<u>Donor and Recipient Trends</u>

There were 1,216 lung transplants performed in the last two years of the study period (Era 2); this represents a 30% increase from the 919 transplants performed in the previous four years (Era 1).

National donor and recipient characteristics changed slightly between Era 1 and Era 2. There was a slight increase in young donors in Era 2, and the percent of donors age 50 and older almost doubled (2.6% to 5.0%). There was also a 3% increase in minority donors. Transplant recipients were older in the second era; those over age 49 comprised 46% of recipients in Era 2 as compared to 34% in Era 1. There were fewer recipients in the ICU at the time of transplant in Era 2 than in Era 1. COPD and Emphysema accounted for 26% of the diseases in Era 1 and increased to 39% in Era 2. Alpha-1-Antitrypsin Deficiency and Primary Pulmonary Hypertension decreased from 17% to 12% and from 13% to 10%, respectively. Also, cold ischemic time increased from Era 1 to Era 2.

Despite more older donors and older recipients in Era 2, the national survival rates at 1 year post transplant improved from Era 1 to Era 2 (See Tables VII-1 and VII-2 on page 108).

F. SHORT TERM SURVIVAL -- IMPACT OF DONOR AND RECIPIENT CHARACTERISTICS

To determine the expected survival for each transplant or patient, separate analyses were performed for graft and patient survival at three time points. (The analyses were performed using logistic regression, see the *Technical Methods* chapter in the *Executive Summary*.) The analyses also identified donor and recipient characteristics that had a significant impact on survival outcomes. For each *characteristic* (e.g., race, gender) considered in the analyses, a *reference group* was chosen (e.g., White, male) with which the other groups were compared. As a general rule, the largest group or the mean of the characteristic (e.g., mean age for patients who received a single lung transplant was 48 and mean age for patients who received a double lung transplant was 33) is often used as the reference group.

Table VII-7. National Donor and Recipient Characteristics in Lung Transplants: Percentages by Era and Overall.

Characteristics by Category		ERA 1 1/88-4/92 N=919	ERA 2 5/92-4/94 N=1216	OVERALL 1/88-4/94 N=2135
Type of Transplant	Single Left Lung Transplant	36.0	32.3	33.9
	Single Right Lung Transplant	35.1	32.2	33.4
	Double Lung Transplant	28.8	35.5	32.6
Donor Age	0-5	1.6	1.5	1.5
	6-10	2.4	2.6	2.5
	11-17	20.2	21.6	21.0
	18-35	55.2	49.1	51.7
	36-49	18.0	20.1	19.2
	50+	2.6	5.0	4.0
Donor Gender	Female	28.7	30.3	29.6
	Male	71.3	69.7	70.4
Donor Race	White	79.1	75.8	77.2
	Black	11.3	15.7	13.8
	Hispanic	8.6	7.2	7.8
	Asian	0.4	0.8	0.7
	Other	0.4	0.3	0.4
	Not Reported	0.1	0.2	0.1
Recipient Age	0-5	1.2	1.2	1.2
	6-10	1.0	1.3	1.2
	11-17	3.6	3.5	3.6
	18-35	22.1	19.5	20.6
	36-49	38.1	28.4	32.6
	50+	34.1	46.1	40.9
Recipient Gender	Female	52.8	53.0	52.9
	Male	47.2	47.0	47.1
Recipient Race	White	90.2	92.0	91.2
	Black	4.1	3.9	4.0
	Hispanic	4.0	1.7	2.7
	Asian	0.5	1.0	0.8
	Other	0.8	1.4	1.1
	Not Reported	0.3	0.0	0.1

		ERA 1	ERA 2	OVERALL
Previous Lung Transplant	No	96.0	97.0	96.6
	Yes	4.0	2.2	3.0
	Not Reported	0.0	0.7	0.4
On Ventilator at Transplant	No	95.5	92.6	93.9
	Yes	3.9	3.6	3.7
	Not Reported	0.5	3.8	2.4
Medical Condition at Transplant	In ICU	7.7	5.8	6.6
	Hospitalized	9.5	7.6	8.4
	Not Hospitalized	82.4	86.2	84.5
	Not Reported	0.4	0.4	0.4
Primary Lung Disease at Transplant	COPD/Emphysema	26.0	38.7	33.3
	Fibrosis (Cystic/Idiopathic)	28.2	25.6	26.7
	Alpha-1-Antitrypsin Deficiency	17.2	12.1	14.3
	Primary Pulmonary Hypertension	12.5	9.5	10.8
	Eisenmenger's Syndrome/Congenital	4.5	4.5	4.5
	Retransplant	0.9	0.5	0.7
	Other	10.4	8.9	9.6
	Not Reported	0.3	0.2	0.2
Year of Transplant	1988	3.6	0.0	1.5
	1989	10.0	0.0	4.3
	1990	22.0	0.0	9.5
	1991	43.6	0.0	18.8
	1992	20.8	28.3	25.1
	1993	0.0	54.3	30.9
	1994	0.0	17.4	9.9
Cold Ischemia Time:				
Single Lung, Left	Up to 2.5 hrs	14.5	18.3	16.6
	> 2.5 to 3 hrs	16.3	13.2	14.6
	> 3 - 3.5 hrs	18.1	11.2	14.4
	> 3.5 - 4.5 hrs	25.7	32.1	29.1
	> 4.5 hrs	23.0	22.9	22.9
	Not Reported	2.4	2.3	2.3

		ERA 1	ERA 2	OVERALL
Single Lung, Right	Up to 2.5 hrs	14.2	14.6	14.4
	> 2.5 to 3 hrs	16.1	11.0	13.3
	> 3 to 3.5 hrs	18.3	14.1	16.0
	> 3.5 to 4.5 hrs	30.0	30.9	30.5
	> 4.5 hrs	18.6	26.9	23.1
	Not Reported	2.8	2.6	2.7
Double Lung, Left	Up to 3.5 hrs	18.1	17.8	17.9
	> 3.5 to 4.5 hrs	20.4	21.1	20.8
	> 4.5 to 5.5 hrs	19.6	23.8	22.2
	> 5.5 to 6.5 hrs	18.1	18.1	18.1
	> 6.5 hrs	19.2	15.5	16.9
	Not Reported	4.5	3.7	4.0
Double Lung, Right	Up to 3.5 hrs	20.8	24.5	23.1
	> 3.5 to 4.5 hrs	24.5	23.1	23.7
	> 4.5 to 5.5 hrs	19.6	20.4	20.1
	> 5.5 to 6.5 hrs	11.7	12.7	12.3
	> 6.5 hrs	13.6	14.6	14.2
	Not Reported	9.8	4.6	6.6

The following served as the characteristics and reference groups for ***short term graft and patient*** survival:

- Donor Race -- White, Hispanic, or Asian
- Donor Gender -- male
- Previous Lung Transplant -- none
- Transplant Type -- single lung transplant
- Mean Recipient Age -- 48 years for single lung transplants and 33 years for double lung transplants.
- Recipient Race -- White or Black
- Recipient Gender -- male
- Lung Disease -- COPD/Emphysema (see Table VII-8 for a complete list of disease diagnoses)
- Medical Status -- not hospitalized or in ICU prior to transplant
- Recipient on Ventilator -- no
- Year of Transplant -- 1988 or 1989

The relative impact of each donor and recipient characteristic on short term graft and patient survival outcomes is listed in Table VII-9. For each characteristic, the ***odds ratio*** is the odds of patient death (graft failure) as compared to the reference group, after adjusting for the effects of all other donor and recipient characteristics. An *odds ratio of less than 1* indicates that the characteristic was associated with a *reduced odds* of patient death or graft failure relative to the reference group. An odds ratio of *greater than 1* indicates that the characteristic was associated with an *increased odds* of death relative to the reference group. The corresponding p-value measures how significant the odds ratio is. A p-value less than 0.05 indicates statistical significance and means that there is less than a 5% probability that such difference is due to chance alone. The smaller the p-value, the greater the statistical significance and the less likely the difference is due to chance alone.

Examples

In Table VII-9, the odds ratio of graft failure at 1 month post-transplant for a recipient on a ventilator

Table VII-8. Lung Primary Disease Diagnoses at Time of Transplant

COPD [1] /Emphysema
Primary Pulmonary Hypertension
Cystic/Idiopathic Fibrosis
Alpha-1-Antitrypsin Deficiency (A1A)
Congenital
- Eisenmenger's syndrome
- Other congenital defects
Other
- Inhalation burns/trauma
- Sarcoidosis
- Bronchiectasis
- Rheumatoid disease
- Occupational lung disease
- Lymphangioleiomyomatosis
- Obliterative bronchiolitis
- Pulmonary vascular disease
- Other lung disease

[1] Chronic Obstructive Pulmonary Disease

at the time of transplant was 4.12. This means that, after adjusting for all of the other donor and recipient characteristics, the odds of graft failure within 1 month was 312% greater for recipients on a ventilator than for those not on a ventilator at the time of transplant ((4.12-1)×100%=312%). As another example, the odds ratio of graft failure within 1 month post-transplant for a recipient who had a repeat transplant versus a recipient who received a first transplant was 2.71. After adjusting for the effects of both donor and recipient characteristics, the odds of graft failure within 1 month for a patient who had a repeat transplant was 171% higher ((2.71-1)×100%=171%) than that for a patient who received a first transplant.

The estimated odds ratios for continuous variables (i.e., variables with many possible values) such as cold ischemic time and donor and recipient ages, are less easily interpreted. For these variables, the estimated odds is determined for a set unit increase or decrease from the mean (reference group) of the variable. For example, in Table VII-9, the estimated odds of 1 year graft failure for single lung recipients age 58 compared to the recipient mean age of 48 is 1.28. This means that, after adjusting for the effects of all other characteristics, the odds of graft failure increased by 28% for the first 10 year increase from the mean age.

Mathematically, this 28% was calculated as follows:

$$\text{Odds ratio} = \exp^{\left[\left(\frac{58-48}{10}\right)\times 0.18+\left(\frac{58-48}{10}\right)^2\times 0.063\right]} = 1.28$$

where (58-48) is the amount of increase in years and 10 years is the unit of increase; 0.18 and 0.063 correspond to the coefficients of age per 10 year difference (See Table VII-12 for coefficients). Therefore, the increase in the odds of death or graft failure is (1.28-1)×100%=28%.

Short Term Graft and Patient Survival

The characteristics with the strongest impact on short term graft and patient survival were having a previous lung transplant, being on a ventilator at the time of transplant, and having a congenital or pulmonary hypertension diagnosis. The odds of 1 year graft failure was 174% higher if the transplant was a repeat transplant. Double lung transplants had reduced odds of failure or death by 28% at 1 year. If a ventilator was being used at the time of transplant, then the odds of 1 year graft failure was 324% higher than if a ventilator was not being used at the time of transplant. Nearly 99% of the patients that were on a ventilator were also in the intensive care unit (ICU); and 60% of the patients that were in the ICU were on a ventilator. This might explain why being in the ICU did not turn out to be a significant characteristic in the analysis, because most of its impact had already been explained by the use of a ventilator just prior to transplant. Transplants performed after 1989 have a significantly reduced odds of graft failure and patient death. In particular, transplants performed in 1993 and 1994 had a 59% reduced odds of patient death at 1 year post transplant.

G. LONG TERM SURVIVAL -- IMPACT OF DONOR AND RECIPIENT CHARACTERISTICS

In this report, *long term* survival analyses were developed separately from the short term survival analyses. Because this narrative focuses on conditional 3 year survival (survival at 3 years for grafts or patients surviving at least 1 year post-transplant), only conditional 3 year survival data are presented in this text. Both conditional and unconditional 3 year survival rates are provided in the tables for each transplant program presented in each organ specific volume. The conditional 3 year survival analyses provide an assessment of the donor and recipient characteristics that are independent of those limited to the first year (e.g., surgical complications). Due to the small number of transplants used in the long term analysis (n=608), only a few donor and recipient characteristics were identified (Table VII-10).

The following characteristics and reference groups were used for ***long term graft and patient*** survival:

- Lung Disease -- non-other group (see Table VII-8 for a complete list of disease diagnoses)
- Mean Cold Ischemic Time -- 224 minutes for single lung transplants and 341 minutes for double lung transplants.
- Mean Recipient Age -- 48 years for single lung recipients and 33 years for double lung recipients.
- Recipient Race -- White, Hispanic, or Asian

Graft and Patient Survival

Recipient age, race, and disease diagnoses remain important predictors of survival outcomes. Black had 132% increased odds of patient death and Other (i.e., non-White, non-Hispanic and non-Asian) races had 83% increased odds of patient odds. Medical condition at transplant, donor characteristics, transplant type (single or double lung), whether recipient had a previous transplant, and recipient gender were no longer significant. It is unclear why older recipients and longer cold ischemic times had lower odds ratios. This could be due to the limited number of transplants in the long term analysis. Or perhaps, these factors were associated with a particular characteristic that had a positive impact on long survival but was not taken into account in the analysis.

H. STATISTICAL METHODS AND MODELS

This section provides a brief summary of the statistical methods used to determine survival rates for lung transplants, both nationally and at each transplant program. It is not necessary to read this section in order to utilize the rest of the report. For additional statistical details, please see the Technical Methods chapter in the Executive Summary.

Model Significance -- R^2

The conclusion that there is a "center effect" in lung transplantation often is based on the observation that actual survival rates vary considerably among lung transplant programs. However, in reality, only part of the variability can be attributed to the quality of the program (the so called "center effect"); the rest can be attributed to the differences in donor and recipient characteristics among transplant programs. The degree to which the variability in actual survival rates can be attributed to the specific donor and recipient characteristics in each analysis appears in Table VII-11.

In the table, the values in the column labeled R^2 estimate the percentage of variability in the actual survival rates that can be attributed to the covariates in each analysis. *The higher the percentage, the better the analysis explained the individual program outcomes, based on the characteristics examined.* Theoretically, if an analysis contained every covariate that affected survival outcomes, and there were no differences in quality among programs (i.e., no "center effect"), then R^2 would equal 100%. In practice, we can never capture every factor that affects outcomes, and it is likely that real differences among programs do exist. This means that any unexplained variation can probably be attributed to a combination of true center effect and covariates not considered in this study. (For details on the R^2 calculation, refer to the *Model Significance* section in the *Technical Methods* chapter of the *Executive Summary*.)

The value of R^2 estimated from analyses in the 1994 Report was compared to the value of the R^2 analyses in the 1997 Report. Note that these analyses are not *directly* comparable since each was used with a different cohort of transplants. The R^2 calculations for the 1994 and 1997 reports are similar at the 1 month time point; at 1 year the R^2 calculation in the 1997 report is improved by 5%-6% from the 1994 report. Despite the refinements in the 1997 Report, much of the variation in actual survival rates among the 75 transplant programs in the study remains unexplained by the analyses. This suggests that much of the risk involved in transplantation is due to characteristics not described in this report.

Table VII-9. Impact of Donor and Recipient Characteristics on Short Term Graft and Patient Survival–Lung Transplants

Short Term Characteristics	Graft Survival				Patient Survival			
	1 Month		1 Year		1 Month		1 Year	
	Odds Ratio	P-value	Odds Ratio	P-value	Odds Ratio	P-value	Odds Ratio	P-value
Donor Black vs White	1.303	0.168	1.329	0.046	1.256	0.259	1.356	0.037
Donor Hispanic, Asian, Other vs White	1.435	0.103	1.426	0.037	1.386	0.158	1.458	0.030
Donor Female vs Male	1.345	0.051	1.268	0.037	1.270	0.134	1.187	0.144
Previous Lung Transplant: Yes vs No	2.711	0.001	2.742	<0.001	3.307	0.002	3.001	0.005
Type of TX: Double vs Single Lung	0.866	0.342	0.718	0.004	0.819	0.210	0.697	0.003
Recipient Age 58 vs 48 for Single Lung, 43 vs 33 for Double Lung [1]	1.103	0.214	1.275	<0.001	1.127	0.147	1.309	<0.001
Recipient Hispanic, Asian, Other vs White, Black	1.329	0.307	1.266	0.294	1.367	0.277	1.355	0.183
Recipient Male vs Female	1.474	0.008	1.304	0.013	1.447	0.015	1.247	0.044
Pulmonary vs COPD/Emphysema	4.272	<0.001	2.039	<0.001	4.712	<0.001	2.192	<0.001
Congenital vs COPD/Emphysema	5.295	<0.001	2.889	<0.001	5.820	<0.001	2.940	<0.001
Fibrosis vs COPD/Emphysema	1.879	0.003	1.942	<0.001	1.908	0.004	1.963	<0.001
A1A vs COPD/Emphysema	1.790	0.013	1.564	0.006	1.903	0.008	1.582	0.006
Other Diagnosis [3] vs COPD/Emphysema	2.269	0.001	1.789	0.002	2.273	0.002	1.753	0.004
In Hospital vs Home or in ICU	1.137	0.584	1.503	0.018	1.161	0.541	1.426	0.046
On Ventilator at Transplant: Yes vs No	4.118	<0.001	4.243	<0.001	4.226	<0.001	4.898	<0.001
Transplant Year 1990 vs 1988-1989	0.422	0.003	0.491	0.004	0.432	0.005	0.463	0.003
Transplant Year 1991 vs 1988-1989	0.422	<0.001	0.595	0.017	0.397	<0.001	0.571	0.012
Transplant Year 1992 vs 1988-1989	0.288	<0.001	0.560	0.006	0.290	<0.001	0.564	0.008
Transplant Year 1993-1994 vs 1988-1989	0.266	<0.001	0.422	<0.001	0.257	<0.001	0.408	<0.001

Notes:

[1] The odds ratio for recipient age does not have a linear relationship. The odds ratio presented in this table is a 10 year increment from the mean age. The mean single and double lung recipient ages were 48 and 33, respectively.

[2] See Table VII-8 for a listing of lung diagnoses.

Table VII-10. Impact of Donor and Recipient Characteristics on Long-Term Graft and Patient Survival -- Lung Transplants

Long Term Characteristics	Graft Survival		Patient Survival	
	Odds Ratio	P-value	Odds Ratio	P-value
Cold Ischemic Time (min) --284 vs 224 for Single Lung and 401 vs 341 for Double Lung [1]	0.965	0.043	0.961	0.029
Recipient Age - 58 vs 48[1]	0.834	0.026	0.871	0.098
Recipient Black vs White	2.777	0.028	2.317	0.075
Recipient Hispanic, Asian, Other vs White	1.914	0.096	1.833	0.129
Other Diagnosis vs Baseline[2]	0.527	0.057	0.593	0.119

Notes:

[1] The odds ratios for recipient age and cold ischemic time do not have a linear relationship. The odds ratios presented in this table are 10 (age) or 15 (cold ischemic time) unit increases from the mean of each characteristic. The mean single lung recipient age was 48; the mean double lung recipient age was 33. The mean single lung cold ischemic time was 224 minutes; the mean double lung cold ischemic time was 341 minutes.

[2] Baseline includes all the disease groups except "Other" listed in Table VII-8.

Estimated Coefficients and Standard Errors from the Logistic Regression Models

Tables VII-12 and VII-13 list the coefficients and the standard errors of the coefficients at each time point for all of the donor and recipient characteristics used in the logistic regression models. Each coefficient is reported on the logistic scale and represents the $\log_e$ odds of graft failure or the $\log_e$ odds of patient mortality for the corresponding characteristic at the specified time after transplant. The adjusted odds ratio on the probability scale may be obtained by applying the exponential function to the coefficient. For further details, see the *Odds Ratios* section in the *Technical Methods* chapter of the *Executive Summary.*

Expected Lung Transplant Survival Rates

Table VII-14 shows the 1 year *expected graft* survival rates for lung transplants for a given set of donor and recipient characteristics; Table VII-15 shows the 1 year *expected patient* survival rates. These rates were determined using the following characteristics: recipient age, diagnosis, transplant type, and whether or not the recipient was using a ventilator at the time of transplant. For these analyses, all other characteristics were set to the values for the reference groups, with the exception of the year of transplant (1993-1994). The complete list of reference groups is shown on page 115.

For example, in Table VII-14, the expected 1 year graft survival for a 50 year old male recipient of a first single lung transplant with pulmonary hypertension was 76% if the patient did not require ventilator prior to transplant. In contrast, the expected 1 year graft survival for the same patient was 43% if he was using a ventilator prior to transplant.

I. SUMMARY

Study Period

The 1997 Report was based on 2,135 lung transplants performed in 2,079 patients between January 1, 1988, and April 30, 1994, from 75 transplant programs in the United States. In order to assess changes within transplant programs over time, the data were divided into 2 eras. The first era included transplants performed from January 1, 1988, through April 30, 1992; the second era covered the two year time period from May 1, 1992, through April 30, 1994.

Table VII-11. Lung Model R^2: Comparison of the 1994 and 1997 Reports

	Time Point	Report Year	Number of Covariates	R^2
Graft Model R^2	1 Month	1997 1994	20 11	30 30
	1 Year	1997 1994	20 11	36 30
	Cond. 3 Year*	1997 1994	5 NA	16 NA
Patient Model R^2	1 Month	1997 1994	20 11	32 34
	1 Year	1997 1994	20 11	37 32
	Cond. 3 Year*	1997 1994	5 NA	18 NA

* Conditional 3 year analysis was not performed in the 1994 Report.

Table VII-12. Model Coefficients and Standard Errors for Donor and Recipient Characteristics in Short Term Lung Transplant Survival

Short Term Characteristics	Graft Survival				Patient Survival			
	1 Month		1 Year		1 Month		1 Year	
	Model Coeff.	Std. Error	Model Coeff.	Std. Error	Model Coeff.	Std. Error	Model Coeff.	Std. Error
Intercept	-1.9361	0.276	-1.0654	0.224	-1.9652	0.288	-1.0617	0.230
Donor Black vs White	0.2644	0.192	0.2845	0.143	0.2276	0.201	0.3048	0.146
Donor Hispanic, Asian, Other vs White	0.3615	0.222	0.3552	0.171	0.3261	0.231	0.3772	0.174
Donor Female vs Male	0.2963	0.152	0.2371	0.113	0.2391	0.159	0.1710	0.117
Previous Lung Transplant: Yes vs No	0.9975	0.310	1.0086	0.296	1.1961	0.394	1.0990	0.389
Type of TX: Double vs Single Lung	-0.1442	0.152	-0.3317	0.116	-0.1993	0.159	-0.3605	0.120
Recipient Age-Linear (per 10 years) [1]	0.1059	0.067	0.1801	0.050	0.1207	0.070	0.2065	0.051
Recipient Age-Quadratic (per 10 years)[1,2]	-0.0076	0.029	0.0626	0.023	-0.0015	0.031	0.0632	0.023
Recipient Hispanic, Asian and Other vs White, Black	0.2841	0.278	0.2356	0.225	0.3129	0.288	0.3039	0.228
Recipient Male vs Female	0.3880	0.146	0.2654	0.107	0.3692	0.152	0.2209	0.110

Short Term Characteristics	Graft Survival				Patient Survival			
	1 Month		1 Year		1 Month		1 Year	
	Model Coeff.	Std. Error	Model Coeff.	Std. Error	Model Coeff.	Std. Error	Model Coeff.	Std. Error
Pulmonary vs COPD/Emphysema	1.4520	0.241	0.7126	0.189	1.5502	0.250	0.7850	0.193
Congenital vs COPD/Emphysema	1.6668	0.302	1.0609	0.251	1.7614	0.310	1.0786	0.256
Fibrosis vs COPD/Emphysema	0.6305	0.216	0.6637	0.152	0.6459	0.227	0.6743	0.156
A1A vs COPD/Emphysema	0.5821	0.233	0.4472	0.164	0.6434	0.243	0.4558	0.168
Other Diagnoses [3] vs COPD/Emphysema	0.8193	0.258	0.5814	0.187	0.8213	0.272	0.5612	0.193
In Hospital vs Home or in ICU	0.1286	0.235	0.4072	0.172	0.1497	0.245	0.3550	0.178
On Ventilator at Transplant: Yes vs No	1.4154	0.280	1.4452	0.269	1.4412	0.301	1.5888	0.290
Transplant Year 1990 vs 1988-1989	-0.8620	0.287	-0.7108	0.247	-0.8395	0.297	-0.7703	0.256
Transplant Year 1991 vs 1988-1989	-0.8638	0.251	-0.5190	0.217	-0.9248	0.262	-0.5605	0.224
Transplant Year 1992 vs 1988-1989	-1.2433	0.251	-0.5805	0.211	-1.2383	0.259	-0.5720	0.216
Transplant Year 1993-1994 vs 1988-1989	-1.3235	0.239	-0.8630	0.205	-1.3577	0.248	-0.8960	0.210

Notes:

[1] In the analysis, the continuous covariates recipient age, was centered about its mean. The mean single and double lung recipient ages were 48 and 33, respectively.

[2] Modeling the continuous covariate, recipient age, with a linear and quadratic term (the square of the linear term) is necessary due to the relationship between the covariate and the odds of graft failure or patient death.

[3] See Table VII-8 for a listing of Other lung diagnosis.

Table VII-13. Model Coefficients and Standard Errors for Donor and Recipient Characteristics in Long Term Lung Transplant Survival

Long Term Characteristics	Graft Survival		Patient Survival	
	Model Coeff.	Std. Error	Model Coeff.	Std. Error
Intercept	-1.1550	0.170	-1.2077	0.109
Cold Ischemia Time (per 15 minutes) [1]	-0.0359	0.018	-0.0395	0.018
Recipient Age (per 10 years) [1]	-0.1814	0.081	-0.1381	0.083
Recipient Black vs White, Hispanic, Asian	1.0215	0.466	0.8403	0.471
Recipient Other vs White, Hispanic, Asian	0.6493	0.390	0.6061	0.399
Other Diagnosis vs Baseline [2]	-0.6399	0.336	-0.5223	0.335

Notes:

[1] In the analysis, the continuous covariates, recipient age and cold ischemic time, were centered about their mean. The mean single and double lung recipient ages were 48 and 33, respectively. The mean single lung cold ischemic time was 224 minutes; the mean double lung cold ischemic time was 341 minutes.

[2] Baseline includes all the disease groups except "Other" in Table VII-8.

Table VII-14. Expected U.S. 1 Year Graft Survival Rates -- Lung Transplants Stratified by Recipient Age, Diagnosis, Transplant Type and Ventilator Status

Age	Diagnosis	Single Lung Transplant		Double Lung Transplant	
		No Ventilator	Ventilator	No Ventilator	Ventilator
5	COPD/Emphysema*	NA	NA	NA	NA
	Fibrosis (Cystic/Idiopathic)	70.7	36.3	83.3	54.1
	Alpha-1-Antitrypsin*	NA	NA	NA	NA
	Pulmonary Hypertension	69.7	35.2	82.6	52.9
	Congenital	61.9	27.7	77.1	44.2
	Other	72.4	38.2	84.5	56.1
20	COPD/Emphysema	87.5	62.2	91.6	72.0
	Fibrosis (Cystic/Idiopathic)	78.2	45.8	84.9	56.9
	Alpha-1-Antitrypsin	81.7	51.2	87.4	62.2
	Pulmonary Hypertension	77.4	44.6	84.2	55.7
	Congenital	70.7	36.3	79.0	47.1
	Other	79.6	47.9	85.9	58.9
35	COPD/Emphysema	88.7	64.8	90.2	68.5
	Fibrosis (Cystic/Idiopathic)	80.1	48.7	82.6	52.8
	Alpha-1-Antitrypsin	83.3	54.1	85.5	58.2
	Pulmonary Hypertension	79.3	47.5	81.9	51.6
	Congenital	73.0	39.0	76.1	42.9
	Other	81.4	50.8	83.8	54.9
50	COPD/Emphysema	86.9	60.9	85.5	58.1
	Fibrosis (Cystic/Idiopathic)	77.3	44.5	75.2	41.7
	Alpha-1-Antitrypsin	80.9	49.9	79.0	47.0
	Pulmonary Hypertension	76.4	43.3	74.3	40.5
	Congenital*	NA	NA	NA	NA
	Other	78.7	46.6	76.7	43.7
65	COPD/Emphysema	80.9	49.9	73.9	40.1
	Fibrosis (Cystic/Idiopathic)	68.5	33.9	59.4	25.6
	Alpha-1-Antitrypsin	73.0	38.9	64.5	30.0
	Pulmonary Hypertension	67.5	32.8	58.2	24.7
	Congenital*	NA	NA	NA	NA
	Other	70.3	35.8	61.3	27.2

* - Disease not applicable to age group.

Table VII-15. Expected U.S. 1 Year Patient Survival Rates -- Lung Transplants Stratified by Recipient Age, Diagnosis, Transplant Type and Ventilator Status

Age	Diagnosis	Single Lung Transplant		Double Lung Transplant	
		No Ventilator	Ventilator	No Ventilator	Ventilator
5	COPD/Emphysema*	NA	NA	NA	NA
	Fibrosis (Cystic/Idiopathic)	70.7	36.3	83.3	54.1
	Alpha-1-Antitrypsin*	NA	NA	NA	NA
	Pulmonary Hypertension	69.7	35.2	82.6	52.9
	Congenital	61.9	27.7	77.1	44.2
	Other	72.4	38.2	84.5	56.1
20	COPD/Emphysema	87.5	62.2	91.6	72.0
	Fibrosis (Cystic/Idiopathic)	78.2	45.8	84.9	56.9
	Alpha-1-Antitrypsin	81.7	51.2	87.4	62.2
	Pulmonary Hypertension	77.4	44.6	84.2	55.7
	Congenital	70.7	36.3	79.0	47.1
	Other	79.6	47.9	85.9	58.9
35	COPD/Emphysema	88.7	64.8	90.2	68.5
	Fibrosis (Cystic/Idiopathic)	80.1	48.7	82.6	52.8
	Alpha-1-Antitrypsin	83.3	54.7	85.5	58.2
	Pulmonary Hypertension	79.3	47.5	81.9	51.6
	Congenital	73.0	39.0	76.1	42.9
	Other	81.4	50.8	83.8	54.9
50	COPD/Emphysema	86.9	60.9	85.5	58.1
	Fibrosis (Cystic/Idiopathic)	77.3	44.5	75.2	41.7
	Alpha-1-Antitrypsin	80.9	49.9	79.0	47.0
	Pulmonary Hypertension	76.4	43.3	74.3	40.5
	Congenital*	NA	NA	NA	NA
	Other	78.7	46.6	76.7	43.7
65	COPD/Emphysema	80.9	49.9	73.9	40.1
	Fibrosis (Cystic/Idiopathic)	68.5	33.9	59.4	25.6
	Alpha-1-Antitrypsin	73.0	38.9	64.5	30.0
	Pulmonary Hypertension	67.5	32.8	58.2	24.7
	Congenital*	NA	NA	NA	NA
	Other	70.3	35.8	61.3	27.2

* - Disease not applicable to age group.

Table VI-16. Comparison of 1 Month and 1 Year Actual Survival Rates Between Eras

	1 Month		1 Year	
	Era 1	Era 2	Era 1	Era 2
Graft Survival (%)	83.5%	89.3%	66.6%	73.4%
Average No. of Transplants/Month	18	51	18	51
Patient Survival (%)	84.5%	90.0%	68.4%	74.5%
Average No. of Patients/Month	17	50	17	50

Survival Rates

Survival rates were computed at 1 month, 1 year, and 3 years, both nationally and for each transplant program. Three year survival was determined in two ways: (1) conditional 3 year survival (i.e., survival at 3 years for those who survived at least 1 year post-transplant), and (2) unconditional 3 year survival. The emphasis on long term survival in this chapter is on the conditional 3-year survival rates because the conditional 3-year analysis provides an assessment of characteristics independent of those limited to the first year (e.g., surgical complications and early acute rejection events).

The national graft and patient survival rates and completeness of follow-up at 1 month, 1 year, and conditional 3 years are shown in Tables VII-1 and VII-2. The percent of programs with graft and patient follow-up data at 1 year was more than 98%; at conditional 3 years the percent of programs with follow-up data was 95%.

There was a marked increase in the number of lung transplants from Era 1 to Era 2. As demonstrated in Table VII-16, the number of lung transplants nearly tripled, from an average of 18 transplants per month in Era 1 to an average of 51 per month in Era 2.

For the majority of transplant programs, the difference between actual and expected survival rates was not statistically significant (See Figures VII-1 and VII-3). In general, large differences (either higher or lower) were nearly always found among programs that reported relatively few transplants (see Figure VII-2). Therefore, when evaluating survival rates for a program, it is also important to consider the number of transplants performed there.

Differences Between Short Term and Long Term Characteristics

The 1997 Report includes an extensive list of characteristics that have a significant impact on both short and long term graft and patient survival.

Characteristics with the strongest impact on *short term survival* were:

- Recipient received a previous lung transplant
- Transplant type was double or single lung transplant
- Disease diagnosis
- Recipient on a ventilator at transplant
- Transplant year

Characteristics with the strongest impact on *long term survival* was:

- Recipient race
- Recipient age
- Disease diagnosis

J. FINAL WORDS

The purpose of this report is to provide updated information on survival outcomes both nationally and at specific transplant programs, and to enhance the awareness of program performance in the U.S. However, the assessment of a transplant program should not be based solely on the survival rates provided in this report. Some of the other important factors to consider are the experience of the transplant team, support personnel, the cost of the procedure, and the quality and location of post-transplant services.

VIII. HEART-LUNG CHAPTER

VIII. HEART-LUNG TRANSPLANT SURVIVAL RATES

For a Summary of this chapter, see page 139. For definitions of any terms used here, please refer to the User's Guide in the Heart-Lung volume.

A. INTRODUCTION

This report of heart-lung transplant survival rates is based upon verified Scientific Registry data for 373 transplants involving 370 patients from 58 heart-lung transplant programs in the United States. Each program reporting at least one heart-lung transplant between January 1, 1988, and April 30, 1994, was included. Multi-organ transplants were excluded.

Short term survival is defined as survival at 1 month and 1 year post-transplant. Short term survival rates are based on all transplants in the study for which there are follow-up data.

Long term survival is defined in two ways:

- unconditional survival at 3 years post-transplant, and
- survival at 3 years post-transplant for those who survived at least 1 year, referred to as **conditional 3 year survival.**

The long term survival rates are based on all transplants between January 1, 1988, and April 30, 1992, for which there are follow-up data. This cohort was chosen to ensure that the maximum number of transplants with follow-up data was used to determine long term survival rates. Please note that this report emphasizes *conditional* 3-year survival rates. This is because the conditional 3-year analysis assesses factors independent of those limited to the first year (e.g., surgical complications and early acute rejection events).

B. COMPLETENESS OF FOLLOW-UP DATA AND OVERALL GRAFT AND PATIENT SURVIVAL RATES

For graft survival, completeness of follow-up data and overall actual survival rates at each time point are shown in Table VIII-1; patient survival data are shown in Table VIII-2.

Patient (graft) follow-up data were considered complete when:

- the patient was alive (heart and lung were functioning) and the duration of survival (function) was equal to or exceeded the specified time after transplant (i.e., 1 month, 1 or 3 years), or
- the patient died (both heart and lung failed) and a valid date of death (failure) was reported.

The percentages of complete follow-up data ranged from a low of 96.7% for the conditional 3 year time point to a high of 99.6% for the 1 month time point. Patient survival rates are similar to graft survival rates since patient death follows graft failure unless the patient is retransplanted.

Overall survival rates also are presented in the tables. If a graft had incomplete follow-up data, the observation was weighted to account for the time during which the graft was known to be functioning. Therefore, the actual graft survival rate reflects the weighted proportion of grafts functioning at the specified time interval. Patient survival rates were computed in a similar way (see the *Technical Methods* chapter of the *Executive Summary*).

In the cohort of transplants (1/1/88 - 4/30/92) used to compute conditional 3 year survival rates, patients (grafts) who did not survive to 1 year after transplant were excluded from the analyses. Therefore, the total number of patients (grafts) for the conditional 3 year analysis was less than that for the 1 month and 1 year analyses.

Please note that the conditional 3 year graft and patient survival rates in Tables VIII-1 and VIII-2 may be higher than the 1 year graft survival rates. This is possible because the conditional 3 year survival rate is the 3 year survival rate for patients (grafts) who (which) survived at least 1 year post-transplant.

For example: Program A performed a total of five transplants between 1/1/88 and 4/30/92. Two of the heart-lungs failed prior to 1 year post-transplant and the remaining three heart-lungs survived to 3 years after transplant. In this example, Program A has a 1 year graft survival rate of 60% (3 out of 5 heart-lungs were functioning at 1 year post-transplant). However, the conditional 3 year survival rate for Program A is 100% because all three heart-lungs that were functioning at 1 year after transplant also were functioning at 3 years post-transplant. The same calculations are used for patient survival. See the *Technical Methods* chapter of the *Executive Summary* for more specific definitions of follow-up data and the calculations for actual graft and patient survival.

Overall Graft and Patient Survival Rates by Era

In this report, short term survival also is reported by era. Separate eras were used to determine whether there were any improvements over time in the short term survival rates. Era 1 is defined as all transplants occurring between January 1, 1988, and April 30, 1992; Era 2 includes all transplants occurring between May 1, 1992, and April 30, 1994.

The overall graft and patient survival rates by era are presented in the last two columns of Table VIII-1 and Table VIII-2, respectively. The results demonstrate an increase in 1 year graft and patient survival rates over time.

C. GRAFT SURVIVAL -- PERCENTAGES OF ACTUAL AND EXPECTED SURVIVAL RATES

For each transplant program, actual and expected survival rates were calculated at 1 month, 1 year, and 3 years conditional on survival at 1 year. Survival rates at each time point were determined using a specific cohort of transplants (shown in Tables VIII-1 and VIII-2). Expected survival rates were determined for each transplant program based on its specific patient and donor characteristics. These expected outcomes were statistically adjusted for many important prognostic variables, or covariates, that were used in the survival analysis. In other words, they take into account many different characteristics that affect survival. For example: if Program A transplanted many more "high risk" recipients than Program B, then Program A would have a lower *expected* survival rate than Program B.

Table VIII-1. Completeness of Graft Follow-Up Data and Actual Survival Rates for Heart-Lung Transplants

Time	Cohort	Number of Transplants	Percent with Follow-Up Data	Graft Survival (%)		
				Overall	Era 1	Era 2
1 Month	1/1/88 - 4/30/94	373	99.5	81.9	82.2	81.3
1 Year	1/1/88 - 4/30/94	373	98.1	61.9	58.5	70.5
Cond. 3 Years	1/1/88 - 4/30/92	153	96.7	80.1*	80.1*	N/A*

Table VIII-2. Completeness of Patient Follow-Up Data and Actual Survival Rates for Heart-Lung Transplants

Time	Cohort	Number of Patients	Percent with Follow-Up Data	Patient Survival (%)		
				Overall	Era 1	Era 2
1 Month	1/1/88 - 4/30/94	370	99.2	82.2	82.5	81.3
1 Year	1/1/88 - 4/30/94	370	98.1	61.9	58.7	69.7
Cond. 3 Years	1/1/88 - 4/30/92	151	96.7	81.2*	81.2*	N/A*

* The cohort used to determine the overall conditional 3 year survival rate is the same as the Era 1 cohort. Therefore, the overall conditional 3 year survival rates are identical to the conditional 3 year survival rates for Era 1. There is no conditional 3 year survival rate calculated for Era 2 due to insufficient follow-up data on patients who received transplants in Era 2.

If a program's *actual* survival rate was *greater* than its expected survival rate, this means that the program's actual results were higher than the national results for transplants *with the same donor and recipient characteristics*. If a program's *actual* survival rate was *less than* its expected survival rate, this means that the program's actual results were lower than the national results for transplants *with the same donor and recipient characteristics*. The difference between the actual and expected rate may have occurred by chance and, therefore, may not be statistically significant. Furthermore, even a statistically significant difference, one that most likely did not occur by chance, may not be clinically significant (i.e., medically important). A formal description of the methods used to determine actual and expected survival rates appears in the *Technical Methods* chapter of the *Executive Summary*.

Table VIII-3 shows the percentages of heart-lung transplant programs by category of graft survival rates, both for actual and expected survival. The 1 year survival rates showed a greater variation among programs than the 1 month and conditional 3 year survival rates. At 1 month, 47% of programs had actual survival rates greater than 90%. At 1 year, this fell to 26%. However, this percentage increased to 48% for the conditional 3 year survival rates. The distribution of the expected survival rates shows a similar trend. The results indicate that there are more programs with high survival rates (>90%) at the conditional 3 year time point than there are at the 1 year time point. *This is because the most critical period of time for graft survival is the first year post-transplant.* Those who survive the first year are very likely to survive 3 years post-transplant.

The percentages of programs by short term graft survival rates and eras, both for actual and expected survival, are summarized in Table VIII-4. The results demonstrate a substantial improvement in graft survival over time because a greater percentage of programs had actual survival rates higher than 90% in Era 2.

Differences in Actual and Expected Survival Rates

For most programs, the difference between the actual survival rate and the expected survival rate was not statistically significant. Figure VIII-1 shows the percentages of programs whose actual graft survival rates were either above, not significantly different from, or below expected graft survival rates at three time points. Actual survival rates shown in the figure to be either greater than or less than expected survival rates were statistically significant. Overall, there were more programs that fell significantly below expected results than programs that were significantly above expected results. However, for the majority of the transplant programs, the difference in actual and expected graft survival was not statistically significant and varied little across time points.

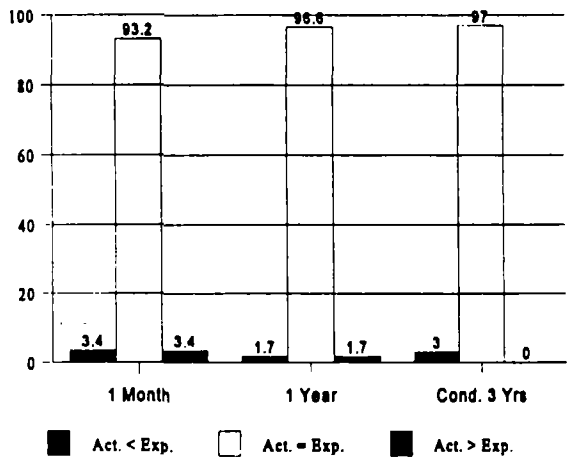
Table VIII-3. Percentages of Heart-Lung Transplant Programs by Graft Survival Rates

Graft Survival Rates (%)	Actual			Expected		
	1 Month (n= 58)	1 Year (n=58)	Cond. 3 Yrs (n=33)	1 Month (n=58)	1 Year (n=58)	Cond. 3 Yrs (n=33)
0-60	22.4	50.0	18.2	5.2	32.8	9.1
>60-70	13.8	10.3	18.2	5.2	48.3	9.1
>70-80	13.8	10.3	9.1	12.1	19.0	27.3
>80-90	3.4	3.4	6.1	72.4	0.0	39.4
>90-100	46.6	25.9	48.5	5.2	0.0	15.2
TOTAL	100.0	100.0	100.0	100.0	100.0	100.0

Table VIII-4. Percentages of Heart-Lung Transplant Programs by Graft Survival Rates and Era

Graft Survival Rates (%)	Actual				Expected			
	1 Month		1 Year		1 Month		1 Year	
	Era 1 (n=46)	Era 2 (n=33)	Era 1 (n=46)	Era 2 (n=33)	Era 1 (n=46)	Era 2 (n=33)	Era 1 (n=46)	Era 2 (n=150)
0-60	30.4	15.2	63.0	36.4	8.7	0.0	43.5	15.2
>60-70	6.5	12.1	4.3	3.0	4.3	6.1	43.5	45.5
>70-80	15.2	3.0	10.9	3.0	10.9	9.1	10.9	39.4
>80-90	4.3	3.0	4.3	6.1	76.1	72.7	2.2	0.0
>90-100	43.5	66.7	17.4	51.5	0.0	12.1	0.0	0.0
TOTAL	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0

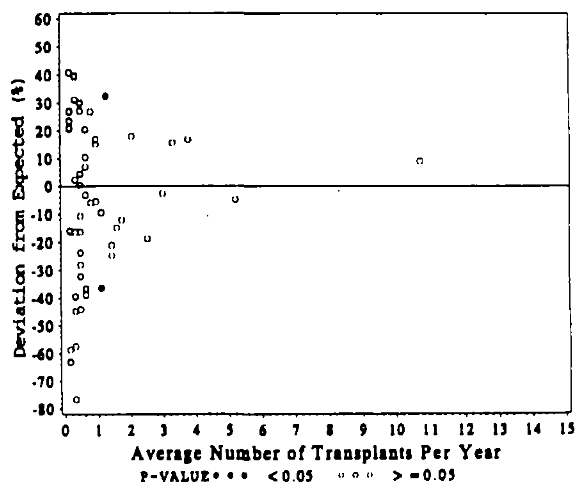
Figure VIII-1. Percentages of Heart-Lung Transplant Programs with Actual Graft Survival Rates Above, Below, or Equal to Expected Survival Rates. *



*Actual survival rates above or below expected survival rates are statistically significant and varied little across time points.

At all time points, the larger differences in actual and expected rates were nearly always seen in programs that reported relatively few transplants during the period. This occurs because programs that do not perform many transplants tend to have highly variable outcomes. To illustrate this, Figure VIII-2 shows a scatter plot of the average number of transplants per year (transplant volume) versus the difference in 1 year actual and expected graft survival. Nearly all differences greater than 10% (either positive or negative) are found among transplant programs that perform very few transplants per year.

Figure VIII-2. Heart-Lung Transplant Volume vs Difference in Actual and Expected 1 Year Graft Survival Rates.



Please note that actual survival rates which differ from expected survival rates are not always statistically significant and even statistically significant differences may not be clinically significant.

D. PATIENT SURVIVAL -- PERCENTAGES OF ACTUAL AND EXPECTED SURVIVAL RATES

The percentages of programs by patient survival rates for both actual and expected survival are shown in Table VIII-5; the percentages of programs by survival rates and eras are shown in Table VIII-6. Note that both actual and expected patient survival rates were higher and less variable at each time point than were actual and expected graft survival rates. As with graft survival, the outcomes in Era 2 were better than in Era 1.

Table VIII-5. Percentages of Heart-Lung Transplant Programs by Patient Survival Rates

Patient Survival Rates (%)	Actual			Expected		
	1 Month (n=58)	1 Year (n=58)	Cond. 3 Yrs (n=33)	1 Month (n=58)	1 Year (n=58)	Cond. 3 Yrs. (n=33)
0-70	36.2	60.3	36.4	10.3	79.3	21.2
>70-80	13.8	10.3	6.1	12.1	20.7	21.2
>80-90	3.4	3.4	9.1	72.4	0.0	42.4
>90-95	1.7	0.0	3.0	5.2	0.0	6.1
>95-100	44.8	25.9	45.5	0.0	0.0	9.1
TOTAL	100.0	100.0	100.0	100.0	100.0	100.0

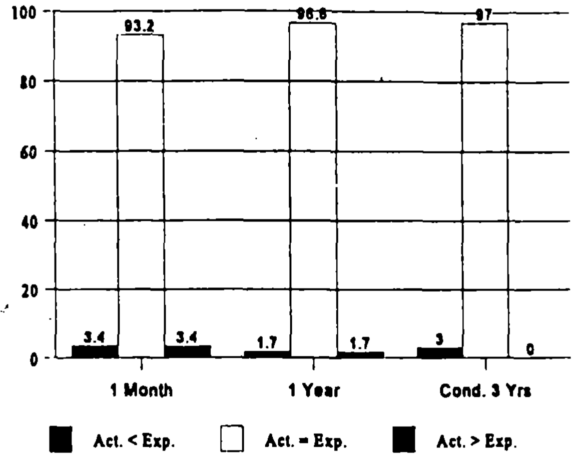
Table VIII-6. Percentages of Heart-Lung Transplant Programs by Patient Survival Rates and Era

Patient Survival Rates (%)	Actual				Expected			
	1 Month		1 Year		1 Month		1 Year	
	Era 1 (n=46)	Era 2 (n=33)	Era 1 (n=46)	Era 2 (n=33)	Era 1 (n=46)	Era 2 (n=33)	Era 1 (n=46)	Era 2 (n=33)
0-70	37.0	27.3	67.4	39.4	13.0	3.0	84.8	60.6
>70-80	15.2	3.0	10.9	3.0	10.9	12.1	15.2	39.4
>80-90	4.3	3.0	4.3	6.1	76.1	72.7	0.0	0.0
>90-95	2.2	3.0	0.0	0.0	0.0	12.1	0.0	0.0
>95-100	41.3	63.6	17.4	51.5	0.0	0.0	0.0	0.0
TOTAL	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0

Differences in Actual and Expected Survival Rates

The percentage of programs with actual patient survival rates significantly above their expected rates was greater at 1 month and conditional 3 years than at 1 year (see Figure VIII-3). Overall, there were more programs that fell significantly below expected results than above expected results. However, for the majority of transplant programs, the difference in actual and expected patient survival was not statistically significant and varied little across time points.

Figure VIII-3. Percentages of Heart-Lung Transplant Programs with Actual Patient Survival Rates Above, Below, or Equal to Expected Survival Rates. *



*Actual survival rates above or below expected survival rates are statistically significant and varied little across time points.

E. NATIONAL DISTRIBUTION OF DONOR AND RECIPIENT CHARACTERISTICS

The national distribution of donor and recipient characteristics for heart-lung transplants, presented in percentages, is shown in Table VIII-7. Each of these donor and recipient characteristics was included in the analyses for graft or patient survival, and used to determine an expected survival rate for each transplant. The majority of heart-lungs transplanted were recovered from white male donors between the ages of 18 and 35. Sixty percent of the donor heart-lungs had cold ischemic times less than 3.5 hours. The majority of heart-lung recipients were white females between the ages of 18-35. Most recipients (74%) were not hospitalized prior to transplant. The main indication for transplant was a congenital diagnosis or Eisenmenger's syndrome (32%). Of the 373 heart-lung transplants performed, only 2% were due to repeat transplants.

Donor and Recipient Trends

National donor and recipient characteristics differed between Era 1 and Era 2. The percentage of donors less 18 years increased to 50% in Era 2 compared to 37% in Era 1. Minority donation increased in Era 2 compared to Era 1. In Era 2 the percentage of recipients less than 18 years increased to 26% compared to only 14% in Era 1. The percentage of minority recipients also increased during the second era. A congenital diagnosis, including Eisenmenger's syndrome, was the main indication (51%) for transplant in Era 2. Mean cold ischemic time increased during the second era also.

F. SHORT TERM SURVIVAL -- IMPACT OF DONOR AND RECIPIENT CHARACTERISTICS

To determine the expected survival for each transplant or patient, separate analyses were performed for graft and patient survival at three time points. (The analyses were performed using logistic regression, for a description, see the *Technical Methods* chapter in the *Executive Summary.*) The analyses also identified donor and recipient characteristics that had a significant impact on survival outcomes. For each *characteristic* (e.g., race, gender) considered in the analyses, a *reference group* was chosen (e.g., White, male) with which the other groups were compared. As a general rule, the largest group or the mean of the characteristic (e.g., mean recipient age=45) is often used as the reference group.

The following served as the characteristics and reference groups for ***short term graft and patient*** survival:

- Mean Donor Age -- 22 years
- Mean Cold Ischemic Time -- 163 minutes
- Previous Heart-Lung Transplant -- none
- Mean Recipient Age -- 45 years
- Recipient Gender -- female
- Indication for Transplant -- congenital, including Eisenmenger's syndrome (see Table VIII-8 for a complete list of diagnoses)
- On Ventilator at Transplant -- no
- Year of Transplant -- 1988-1992

The relative impact of each donor and recipient characteristic on short term graft and patient survival outcomes is listed in Table VIII-9. For each characteristic, the ***odds ratio*** is the odds of patient death (graft failure) as compared to the reference group, after adjusting for the effects of all other donor and recipient characteristics. An *odds ratio of*

Table VIII-7. National Donor and Recipient Characteristics in Heart-Lung Transplants: Percentages by Era and Overall

Characteristics		ERA 1 1/88-4/92 N=265	ERA 2 5/92-4/94 N=108	OVERALL 1/88-4/94 N=373
Donor Age (years)	0-5	6.0	13.9	8.3
	6-10	3.8	6.5	4.6
	11-17	26.8	29.6	27.6
	18-35	45.3	27.8	40.2
	36-49	17.0	18.5	17.4
	50+	1.1	3.7	1.9
Donor Gender	Female	42.3	41.7	42.1
	Male	57.7	58.3	57.9
Donor Race	White	81.1	74.1	79.1
	Black	9.1	11.1	9.7
	Hispanic	7.5	13.9	9.4
	Asian	1.9	0.9	1.6
	Other	0.4	0.0	0.3
Recipient Age (years)	0-5	4.2	12.0	6.4
	6-10	3.4	1.9	2.9
	11-17	6.8	12.0	8.3
	18-35	46.0	41.7	44.8
	36-49	32.5	22.2	29.5
	50+	7.2	10.2	8.0
Recipient Gender	Female	55.1	56.5	55.5
	Male	44.9	43.5	44.5
Recipient Race	White	92.1	84.3	89.8
	Black	2.6	6.5	3.8
	Hispanic	3.0	4.6	3.5
	Asian	0.4	1.9	0.8
	Other	1.9	1.9	1.9
	Not Reported	0.0	0.9	0.3
Previous Heart-lung Transplant	No	97.7	93.5	96.5
	Yes	2.3	1.9	2.1
	Not Reported	0.0	4.6	1.3

		ERA 1	ERA 2	OVERALL
On Ventilator at Transplant	No	94.0	83.3	90.9
	Yes	4.2	8.3	5.4
	Not Reported	1.9	8.3	3.8
Medical Condition at Transplant	In ICU	14.0	17.6	15.0
	Hospitalized	11.3	6.5	9.9
	Not Hospitalized	74.7	73.1	74.3
	Not Reported	0.0	2.8	0.8
Diagnosis at Transplant	Congenital/Eisenmenger	32.1	51.9	37.8
	Primary Pulmonary Hypertension	34.0	24.1	31.1
	Cystic Fibrosis	13.2	1.9	9.9
	Alpha-1-Antitrypsin Deficiency	6.4	1.9	5.1
	COPD/Emphysema	2.6	3.7	2.9
	Retransplant	2.3	1.9	2.1
	Other	9.4	8.3	9.1
	Not Reported	0.0	6.5	1.9
Cold Ischemia Time	Up to 1.5 hrs	12.1	0.9	8.8
	> 1.5 - 2.5 hrs	23.8	15.7	21.4
	> 2.5 - 3.5 hrs	32.1	25.9	30.3
	> 3.5 - 4.5 hrs	22.3	30.6	24.7
	> 4.5 hrs	8.7	24.1	13.1
	Not Reported	1.1	2.8	1.6
Year of Transplant	1988	27.9	0.0	19.8
	1989	25.3	0.0	18.0
	1990	19.6	0.0	13.9
	1991	19.2	0.0	13.7
	1992	7.9	25.0	12.9
	1993	0.0	55.6	16.1
	1994	0.0	19.4	5.6

Table VIII-8. Heart-Lung Primary Disease Diagnoses at Time of Transplant

COPD/Emphysema
Primary Pulmonary Hypertension
Cystic and Idiopathic Fibrosis
Alpha-1-Antitrypsin Deficiency
Congenital, including Eisenmenger's Syndrome
- Congenital Heart Disease
- Ventricular and Atrial Septal Defect
- Patent Ductus Arteriosus
- Multiple Congenital Anomalies
- Other Congenital Defects
Other Diagnosis
- Idiopathic Dilated Cardiomyopathy
- Valvular Heart Disease
- Inhalation burns/Trauma
- Sarcoidosis
- Bronchiectasis
- Pulmonary Vascular Disease
- Other Lung Disease
- Retransplant/Graft Failure
- Non-Specific
- Obliterative Bronchiolitis
- Other

less than 1 indicates that the characteristic was associated with a *reduced odds* of patient death or graft failure relative to the reference group. An odds ratio of *greater than 1* indicates that the characteristic was associated with an *increased odds* of death relative to the reference group. The corresponding p-value measures how significant the odds ratio is. A p-value less than 0.05 indicates statistical significance and means that there is less than a 5% probability that such difference is due to chance alone. The smaller the p-value, the greater the statistical significance and the less likely the difference is due to chance alone.

Examples

In Table VIII-9, the odds ratio of graft failure within 1 year, if the recipient was male, was 1.81. This means that, after adjusting for all of the other donor and recipient characteristics, the odds of graft failure within 1 year was 81% greater for male recipients than for female recipients((1.81-1)×100%=81%). As another example, the odds ratio of graft failure within 1 year post-transplant for a recipient who had a repeat transplant versus a recipient who received a first transplant was 3.91. After adjusting for the effects of both donor and recipient characteristics, the odds of graft failure within 1 year for a patient who had a repeat transplant was 291% higher ((3.91-1)×100%= 291%) than that for a patient who received a first transplant.

The estimated odds ratios for continuous variables (i.e., variables with many possible values) such as cold ischemic time and donor and recipient ages, are less easily interpreted. For these variables, the estimated odds is determined for a set unit increase or decrease from the mean (reference group) of the variable. For example, in Table VIII-9, the estimated odds of 1 month graft failure for 206 minutes of cold ischemic time compared to the mean of 191 minutes is 1.03. This means that, after adjusting for the effects of all other characteristics, the odds of graft failure was estimated to increase by 3% for the first 15 minute increase from the mean cold ischemic time.

An increase of 1 hour (60 minutes) from the mean cold time (i.e., the cold ischemic time is 191 min+60 min=251 min) would result in an 11% increase in the odds of death or graft failure. Mathematically, this 11% was calculated as follows:

$$\text{Odds ratio} = \exp^{(\frac{60}{15}\times 0.0260)} = 1.11$$

where is 60 the amount of increase in minutes and 15 minutes is the per unit of increase; 0.0260 corresponds to the coefficient of cold ischemic time per 15 minute difference (see Table VIII-12 for coefficients). Therefore, the increase in the odds of death or graft failure is (1.11-1)×100%=11%. For some variables such as recipient age, it is necessary to add a quadratic term. For more details on calculating odds ratios for continuous variables, refer to the section on *Odds Ratios* in the *Technical Methods* chapter of the *Executive Summary*.

Short Term Graft and Patient Survival

The characteristics with the strongest impact on short term graft and patient survival were having a previous heart-lung transplant and being on a ventilator at time of transplant. The odds of 1 year graft failure was 291% higher if the transplant was a repeat transplant, but was not statistically significant. If a ventilator was used at time of transplant, then the odds of 1 year graft failure was 353% higher than if a ventilator was not being used at time of transplant

Table VIII-9. Impact of Donor and Recipient Characteristics on Short Term Graft and Patient Survival--Heart-Lung Transplants

Short Term Characteristics	Graft Survival				Patient Survival			
	1 Month		1 Year		1 Month		1 Year	
	Odds Ratio	P-value	Odds Ratio	P-value	Odds Ratio	P-value	Odds Ratio	P-value
Donor Age - 32 vs 22[1]	1.148	0.628	1.168	0.783	1.137	0.589	1.158	0.783
Recipient Age - 40 vs 30[1]	1.139	0.310	1.255	0.039	1.151	0.275	1.246	0.047
Previous Heart-Lung Transplant: Yes vs No	3.357	0.122	3.907	0.132	3.836	0.118	6.996	0.092
On Ventilator at Transplant: Yes vs No	6.428	<0.001	4.531	0.009	6.296	<0.001	4.349	0.011
Recipient Male vs Female	1.001	0.996	1.806	0.011	0.945	0.843	1.700	0.022
COPD/Emphysema vs All Others Diagnoses[2]	n.a.[3]	n.a.[3]	0.125	0.056	n.a.[3]	n.a.[3]	0.128	0.059
Cold Ischemic Time - 206 min vs 191 min[1]	1.026	0.415	1.043	0.112	1.027	0.413	1.044	0.103
Transplant Year 1990-1994 vs 1988-1989	0.716	0.276	0.401	<0.001	0.697	0.244	0.400	<0.001

Notes:

1 Odds ratios for some continuous covariates (donor age, recipient age and cold ischemic time) do not have a linear relationship. The odds ratios presented in this table are 10 or 15 unit increases from the mean of each covariate. The mean donor age was 22. The mean recipient age was 30. The mean cold ischemic times was 191 minutes.

2 See Table VIII-8 for a listing of heart-lung diagnoses.

2 Not able to calculate since all recipients with COPD/Emphysema were still alive 1 month after transplant.

G. LONG TERM SURVIVAL -- IMPACT OF DONOR AND RECIPIENT CHARACTERISTICS

In this report, *long term* survival analyses were developed separately from the short term survival analyses. Because this narrative focuses on conditional 3 year survival (survival at 3 years for grafts or patients surviving at least 1 year post-transplant), only conditional 3 year survival data are presented in this text. Both conditional and unconditional 3 year survival rates are provided in the tables for each transplant program presented in each organ specific volume. The conditional 3 year survival analyses provide an assessment of the donor and recipient characteristics that are independent of those limited to the first year (e.g., surgical complications). The impact of each donor and recipient characteristic on graft and patient long term survival is listed in Table VIII-10.The following characteristics and reference groups were used for ***long term graft and patient*** survival:

- Medical Condition at Transplant -- not hospitalized
- Mean Cold Ischemic Time -- 191 minutes
- Primary Pulmonary Hypertension -- all other diagnoses
- Year of Transplant -- 1988-1990

Graft and Patient Survival

The characteristics with the strongest impact on long term graft and patient survival were medical condition at transplant, cold ischemic time and diagnosis at time of transplant. The odds of conditional 3 year graft failure was 169% higher if the patient was in the ICU at time of transplant compared to being not hospitalized at transplant. Having a diagnosis of primary pulmonary

Table VIII-10. Impact of Donor and Recipient Characteristics on Long-Term Graft and Patient Survival – Heart-Lung Transplants

Long Term Characteristics	Graft		Patient	
	Odds Ratio	P-value	Odds Ratio	P-value
Hospitalized vs Not Hospitalized	3.085	0.077	2.737	0.139
In ICU vs Not Hospitalized	2.697	0.076	2.956	0.054
Cold Ischemic Time - 206 min vs 191 min [1]	0.869	0.015	0.861	0.012
Primary Pulmonary Hypertension vs All Other Diagnoses [2]	2.158	0.091	1.765	0.227
Transplant Year 1991-1992 vs All Other Years	2.208	0.126	2.518	0.081

Notes:

1 Odds ratios for continuous covariates (cold ischemic time) do not have a linear relationship. The odds ratios presented in this table is a 15 unit increase from the mean cold ischemic time. The mean cold ischemic time was 191 minutes.

2 See Table VIII-8 for listing of heart-lung diagnoses

hypertension increased the conditional 3 year odds of graft failure 116% compared to any other diagnosis.

H. COMPARISON BETWEEN SHORT TERM AND LONG TERM CHARACTERISTICS

Except for cold ischemic time and diagnosis, the donor and recipient characteristics that had an impact on short term survival did not appear to have an impact on long term survival.

I. STATISTICAL METHODS AND MODELS

This section provides a brief summary of the statistical methods used to determine survival rates for heart-lung transplants, both nationally and at each transplant program. It is <u>not</u> necessary to read this section in order to utilize the rest of the report. For additional statistical details, please see the Technical Methods chapter in the Executive Summary.

<u>Model Significance – R^2</u>

The conclusion that there is a "center effect" in heart-lung transplantation often is based on the observation that actual survival rates vary considerably among heart-lung transplant programs. However, in reality, only part of the variability can be attributed to the quality of the program (the so called "center effect"); the rest can be attributed to the differences in donor and recipient characteristics among transplant programs. The degree to which the variability in actual survival rates can be attributed to the specific donor and recipient characteristics in each analysis appears in Table VIII-11.

In the table, the values in the column labeled R^2 estimate the percentage of variability in the actual survival rates that can be attributed to the covariates in each analysis. *The higher the percentage, the better the analysis explained the individual program outcomes, based on the characteristics examined.* Theoretically, if an analysis contained every covariate that affected survival outcomes, and there were no differences in quality among programs (i.e., no "center effect"), then R^2 would equal 100%. In practice, we can never capture every factor that affects outcomes, and it is likely that real differences among programs do exist. This means that any unexplained variation can probably be attributed to a combination of true center effect and covariates not considered in this study. (For details on the R^2 calculation, refer to the *Model Significance* section in the *Technical Methods* chapter of the *Executive Summary.*)

The value of R^2 estimated from analyses in the 1994 Report was compared to the value of the R^2 analyses in the 1997 Report. Note that these analyses are not

Table VIII-11. Heart-Lung Model R^2: Comparison of the 1994 and 1997 Reports

	Time Point	Report Year	Number of Covariates	R^2
Graft Model R^2	1 Month	1997 1994	9 7	14 42
	1 Year	1997 1994	9 7	18 28
	Cond. 3 Year*	1997 1994	5 NA	49 NA
Patient Model R^2	1 Month	1997 1994	9 7	15 42
	1 Year	1997 1994	9 7	19 28
	Cond. 3 Year*	1997 1994	5 NA	51 NA

* Conditional 3 year analysis was not performed in the 1994 report

directly comparable since each was used with a different cohort of transplants. Despite the refinements in the 1997 Report, as compared to the 1994 Report, much of the variation in actual survival rates among the 58 transplant programs in the study remains unexplained by the analyses. This suggests that much of the risk involved in transplantation is due to characteristics not described in this report.

Estimated Coefficients and Standard Errors from the Logistic Regression Models

Tables VIII-12 and VIII-13 list the coefficients and the standard errors of the coefficients at each time point for all of the donor and recipient characteristics used in the logistic regression models. Each coefficient is reported on the logistic scale and represents the $\log_e$ odds of graft failure or the $\log_e$ odds of patient mortality for the corresponding characteristic at the specified time after transplant. The adjusted odds ratio on the probability scale may be obtained by applying the exponential function to the coefficient. For further details, see the *Odds Ratios* section in the *Technical Methods* chapter of the *Executive Summary*.

Expected Heart-Lung Transplant Survival Rates

Table VIII-14 shows the 1 year *expected graft* survival rates for heart-lung transplants for a given set of donor and recipient characteristics; Table VIII-15 shows the 1 year *expected patient* survival rates. These rates were determined using the following characteristics: recipient age, diagnosis, gender and ventilator status at transplant. For these analyses, all other characteristics were set to the values for the reference groups, with the exception of the year of transplant (1993). The complete list of reference groups is shown on page 130.

For example, in Table VIII-14, the expected 1 year graft survival for a 40 year old male recipient with a diagnosis of COPD and not on a ventilator was 97%. In contrast, the expected 1 year graft survival for a male heart-lung recipient of the same age, with COPD and on a ventilator was 88%.

J. SUMMARY

Study Period

The 1997 Report was based on 373 heart-lung transplants performed in 370 patients between January 1, 1988, and April 30, 1994, from 58 transplant programs in the United States. In order to assess changes within transplant programs over time, the data were divided into 2 eras. The first era included transplants performed from January 1,

Table VIII-12. Model Coefficients and Standard Errors for Donor and Recipient Risk Characteristics in Short Term Heart-Lung Transplant Survival

Short Term Characteristics	Graft Survival				Patient Survival[1]			
	1 Month		1 Year		1 Month		1 Year	
	Model Coeff.	Std. Error	Model Coeff.	Std. Error	Model Coeff.	Std. Error	Model Coeff.	Std. Error
Intercept	-1.488	0.285	-0.522	0.230	-1.474	0.286	-0.503	0.231
Donor Age - Linear (per 10 years)[1,2]	0.154	0.154	-0.004	0.124	0.134	0.156	-0.023	0.124
Donor Age - Quadratic (per 10 years)[1,2]	-0.016	0.096	0.159	0.077	-0.005	0.097	0.170	0.078
Recipient Age - Linear (per 10 years)[1]	0.130	0.128	0.227	0.110	1.141	0.129	0.220	0.111
Previous Heart-Lung TX: Yes vs No	1.211	0.784	1.363	0.905	1.345	0.859	1.945	1.154
On Ventilator at Transplant: Yes vs No	1.861	0.530	1.511	0.576	1.840	0.534	1.470	0.577
Recipient Male vs Female	0.001	0.285	0.591	0.231	-0.057	0.288	0.530	0.232
COPD/Emphysema vs All Other Diagnoses[3]	n.a.[4]	n.a.[4]	-2.077	1.089	n.a.[4]	n.a.[4]	-2.054	1.088
Cold Ischemic Time (per 15 minutes)[1]	0.026	0.032	0.042	0.026	0.026	0.032	0.043	0.026
TX Year 1990-1994 vs 1988-1989	-0.335	0.307	-0.914	0.254	-0.362	0.310	-0.915	0.255

Notes:

1 In the analysis, the continuous covariates (donor age, recipient age, cold ischemic time) were centered at their mean. The mean donor age was 22, the mean recipient age was 45 and the mean cold ischemic time was 163 minutes.

2 Modeling the continuous covariates with a linear and quadratic term (the square of the linear term) is necessary due to the relationship between the covariate and the odds of graft failure or patient death.

3 See Table VIII-8 for a listing of heart-lung diagnoses.

4 Not able to calculate since all recipients with COPD/Emphysema were still alive 1 month after transplant.

Table VIII-13. Model Coefficients and Standard Errors for Donor and Recipient Characteristics in Long Term Heart-Lung Transplant Survival

Long Term Characteristics	Graft		Patient	
	Model Coeff.	Std. Error	Model Coeff.	Std. Error
Intercept	-2.361	0.404	-2.407	0.416
Hospitalized vs Not Hospitalized	1.127	0.638	1.007	0.680
In ICU vs Not Hospitalized	0.992	0.560	1.084	0.563
Cold Ischemic Time (per 15 minutes)[1]	-0.140	0.058	-0.150	0.060
Primary Pulmonary Hypertension vs All Other Diagnoses[2]	0.769	0.455	0.568	0.470
Transplant Year 1991-1992 vs All Other Years	0.792	0.518	0.924	0.530

Notes:

1 In the analysis, the continuous covariate cold ischemic time, was centered about its mean. The mean cold ischemic time was 163 minutes.

2 See Table VIII-8 for a listing of heart-lung diagnoses.

Table VIII-14. Expected U.S. 1 Year Graft Survival Rates -- Heart-Lung Transplants Stratified by Recipient Age, Diagnosis, Gender and Ventilator Status

Age	Diagnosis	Male		Female	
		No Ventilator	Ventilator	No Ventilator	Ventilator
5	COPD/Emphysema*	NA	NA	NA	NA
	Other Diseases	88.1	62.1	80.4	47.5
25	COPD/Emphysema	97.4	89.2	95.4	82.1
	Other Diseases	82.5	50.9	72.3	36.5
40	COPD/Emphysema	97.1	88.1	94.9	80.4
	Other Diseases	80.8	48.1	69.9	33.9
50	COPD/Emphysema	96.4	85.5	93.7	76.5
	Other Diseases	77.0	42.5	64.9	29.0
60	COPD/Emphysema	95.5	82.4	92.2	72.2
	Other Diseases	72.7	37.0	59.6	24.6

* - Disease category not applicable to this age group.

VIII-15. Expected U.S. 1 Year Patient Survival Rates -- Heart-Lung Transplants Stratified by Recipient Age, Diagnosis, Gender and Ventilator Status

Age	Diagnosis	Male		Female	
		No Ventilator	Ventilator	No Ventilator	Ventilator
5	COPD/Emphysema*	NA	NA	NA	NA
	Other Diseases	87.7	62.2	80.8	49.2
25	COPD/Emphysema	97.3	89.2	95.5	82.9
	Other Diseases	82.2	51.5	73.1	38.4
40	COPD/Emphysema	97.0	88.1	95.0	81.3
	Other Diseases	80.5	48.7	70.8	35.8
50	COPD/Emphysema	96.3	85.6	93.8	77.8
	Other Diseases	76.8	43.3	66.1	31.0
60	COPD/Emphysema	95.4	82.7	92.4	73.7
	Other Diseases	72.7	38.0	61.0	26.5

* - Disease category not applicable to this age group.

Table VIII-16. Comparison of 1 Month and 1 Year Actual Survival Rates Between Eras

	1 Month		1 Year	
	Era 1	Era 2	Era 1	Era 2
Graft Survival (%)	82.2%	81.3%	61.9%	58.5%
Average No. of Transplants/Month	5	5	5	5
Patient Survival (%)	82.5%	81.3%	61.9%	58.7%
Average No. of Patients/Montn	5	5	5	5

1988, through April 30, 1992; the second era covered the two year time period from May 1, 1992, through April 30, 1994.

__Survival Rates__

Survival rates were computed at 1 month, 1 year, and 3 years, both nationally and for each transplant program. Three year survival was determined in two ways: (1) conditional 3 year survival (i.e., survival at 3 years for those who survived at least 1 year post-transplant), and (2) unconditional 3 year survival. The emphasis is on the conditional 3-year survival rates because the conditional 3-year analysis assesses characteristics independent of those limited to the first year (e.g., surgical complications and early acute rejection events).

The national graft and patient survival rates and completeness of follow-up at 1 month, 1 year, and conditional 3 years are shown in Tables VIII-1 and VIII-2. The percent of programs with graft and patient follow-up data at 1 year was 98%; at conditional 3 years the percent of programs with follow-up data was almost 97%.

The number of heart-lung transplants remained stable from Era 1 to Era 2. As demonstrated in Table VIII-16, there was an average 5 heart-lung transplants per month in each era. For the majority of transplant programs, the difference between actual and expected survival rates was not statistically significant (See Figures VIII-1 and VIII-3). In general, large differences (either higher or lower) were nearly always found among programs that reported relatively few transplants (see Figure VIII-2). Therefore, when evaluating survival rates for a program, it is also important to consider the number of transplants performed.

__Differences Between Short Term and Long Term Characteristics__

The 1997 Report includes an extensive list of characteristics that have a significant impact on both short and long term graft and patient survival.

Characteristics with the strongest impact on *short term survival* were:

- Recipient age
- Recipient gender
- Recipient on ventilator at transplant
- Year of transplant

Characteristics with the strongest impact on *long term survival* were:

- Recipient in ICU at transplant
- Cold ischemic time
- Year of transplant

K. FINAL WORDS

The purpose of this report is to provide updated information on survival outcomes both nationally and at specific transplant programs, and to enhance the awareness of program performance in the U.S. However, the assessment of a transplant program should not be based solely on the survival rates provided in this report. Some of the other important factors to consider are the experience of the transplant team, support personnel, the cost of the procedure, and the quality and location of post-transplant services.

IX. TECHNICAL METHODS

Cohort
Definitions of Survival Time and Complete Follow-Up
Actual Survival Rates
Expected Survival Rates
Testing for Significance of Program Effects
Calculation of R^2
Odds Ratio
Calculation of Individual Expected Survival Rates
Technical Oversight Committee

IX. TECHNICAL METHODS

This chapter provides details of the technical methods used in preparing this report. Sections A through F, written on a slightly more rigorous level than the preceding chapters, are intended for readers with a basic/some knowledge of epidemiology and statistics. Sections G and H illustrate how to calculate odds ratios and the expected survival rate for an individual. Section I lists the members of the Technical Oversight Committee for this study.

A. COHORT

A total of 97,587 transplants performed at 742 U.S. transplant programs between January 1, 1988 and April 30, 1994 were included in the study to calculate national and center specific graft and patient survival rates.

The entire cohort was analyzed to determine short term survival rates at 1 month (or 3 months for abdominal organs) and 1 year. A subset of the cohort, i.e., all transplants performed between January 1, 1988 and April 30, 1992, was used to determine long term survival rates at 3 years, which was defined in two ways:

- survival at 3 years post-transplant, and
- survival at 3 years post-transplant for those who survived at least 1 year, referred to as **conditional 3 year survival.**

Exclusions

All multiorgan (except kidney-pancreas and heart-lung) transplants, heterotopic heart transplants, and living donor (except kidney) transplants were excluded.

B. DEFINITIONS OF SURVIVAL TIME AND COMPLETE FOLLOW-UP

Survival Time

Transplants for which the reported graft status was "Failed" were counted as graft failures on the date of failure, and those with "Functioning" status were counted as functioning on the date of follow-up.

For kidney transplants, if the graft status was "Impaired," it was counted as "Functioning," but for pancreas transplants, if the status was "Partial Functioning," it was counted as "Failed."

In addition, in the short term (i.e. 3 month and 1 year) analyses, kidney or pancreas transplants for recipients who were reported to have "Died with a functioning graft" were treated as graft failures at the time of death. ***In the conditional 3 year analysis, death with a functioning kidney or pancreas*** was treated as censored or "Functioning" at the time of death because it is more likely that, in the long term, death might not be related to the transplant procedure.

Graft survival time was calculated as the number of days from the transplant date to:
1) the date of graft failure, or
2) if graft failure was not reported, the date of death, or,
3) if death was not reported, the date of follow-up.

Similarly, patient survival time was calculated as the number of days from the transplant date to:
1) the date of death, or
2) if death was not reported, the date of follow-up.

Complete Follow - up

For survival analysis, follow-up indicators were created for each transplant and time interval considered below. The criteria for complete graft (patient) follow-up are described as follows:

Interval	Complete Follow-up Definition
0-1 month:	A graft failure (patient death) between 0 and 30 days from the transplant date, or a functioning graft (patient alive) at 30 days or more.
0-3 months:	A graft failure (patient death) between 0 and 90 days from the transplant date, or a functioning graft (patient alive) at 90 days or more.
0-1 year [1]:	A graft failure (patient death) between 0 and 365 days from the transplant date,

or a functioning graft (patient alive) at 330 days or more.

conditional 3 years [1, 2]: A graft failure (patient death) between 366 and 1095 days from the transplant date, or a functioning graft (patient alive) at 1060 days or more for the cohort of transplants between January 1, 1988 and April 30, 1992.

C. ACTUAL SURVIVAL RATES

The binomial method was used to compute the transplant program actual graft and patient survival rates at each time point. The actual survival rate (%) at time t, t=1 month or 3 months, 1 year, or 3 years, for a transplant program is computed as:

$$\frac{N_{\text{survived},t} + A_t}{N_{\text{failed},t} + N_{\text{survived},t} + A_t} \times 100$$

where the terms $N_{\text{failed},t}$ is the number of grafts that failed (patients died) within and up to the end of the interval, t and $N_{\text{survived},t}$ is the number of grafts (patients) that survived beyond time, t. The term A_t, both in the denominator and numerator, is incorporated to adjust for the fact that some of the transplants (patients) were lost to follow-up before time t (referred to as incomplete follow-up). Specifically, A_t is the *weighted* number of grafts (patients) with *incomplete* follow-up, where the weight equal to the proportion of time in the interval the graft (patient) was still functioning (alive). This weight is fractional for those grafts (patients) with *incomplete* follow-up data. In contrast, the weight for those grafts (patients) that had complete follow-up data would always equal 1.

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1 Graft failure (patient death) takes precedence when determining survival outcomes. For example, if a graft failed at day 345, even though the graft was functioning at some point during the window for follow-up, it is considered a failure rather than being functioning at 1 year.

2 The time interval for the conditional 3 year analysis was from 1 year to 3 years post transplant.

Example

In the one year graft survival analysis, if a graft was last reported as functioning at 9 months after transplant, the weight would be 9/12=.75 for that graft. *The earlier a graft was lost to follow-up, the smaller the weight would be.*

More on Patient Survival Rates

Patient survival rates were calculated in a similar manner as graft survival rates. However, if a patient received more than one transplant of the same organ type, in estimating *center specific patient* survival rates, it is more appropriate to account for all the transplants the patient had than to consider only his or her first transplant. This is because the patient might have been transplanted at more than one center, and in this case, the patient's survival outcome should be attributed to more than one center.

For patients who had n transplants during the period of analysis (i.e., 1/1/88-4/30/94), the survival time for each transplant would be the time between the corresponding transplant date and the most recent follow-up date or the death date. To avoid over-weighting such a patient in the analysis of patient survival, each transplant was weighted by a factor equal to $1/n$. If transplant follow-up was not complete through the end of the time interval, the transplant was weighted by $1/n$ multiplied by the proportion of time for which there was follow-up data.

Example

Suppose Patient A had his first transplant on 1/1/91 and his second transplant on 7/1/91, and was still alive on 1/1/92. The follow-up time for the first transplant would receive a weight of (½)×(1)=½. However, the second transplant would receive a weight of (½)×(6/12)=1/4. Because the patient received two transplants, each transplant received a weighted factor of $1/n$ or ½, where n equals the number of transplants. The first transplant had complete follow-up data available for the 1 year survival analysis, therefore, the second term (1) indicates that complete follow-up data were available. For the second transplant, there were only 6 months of available follow-up time so the second term (6/12) indicates that 6 out of 12 months of follow-up data were available. Note that the total weight for a patient does not necessarily equal 1.

More on 3 Year Survival Rates

In each center specific survival table, the unconditional 3 year survival rate was also reported for the period of January 1, 1988 and April 30, 1992. Following the Bayes rule (a well known statistical formula), the unconditional 3 year survival rate was simply computed as the product of the conditional survival at 3 years and the net survival at 1 year. For instance, if the 1 year and the conditional 3 year survival rate are 80% and 70%, respectively, the unconditional 3 year survival rate would be 56%.

Caveat

The 1 year *expected* survival rate was based on the data from the entire cohort, i.e., January 1, 1988 through April 30, 1994. The conditional 3 year *expected* survival rate was based on the data from January 1, 1988 through April 30, 1992 only.

More on Death With Functioning Graft

In the one year analysis, death with a functioning *kidney* or *pancreas* was considered as graft failure. However, in the conditional 3 year analysis, they were considered as censored observations. The unconditional 3 year survival rate could be lower if death with a functioning *kidney* or *pancreas* was treated the same as graft failure in both the 1 year and conditional 3 year analyses, or higher if death with a functioning *kidney* or *pancreas* was treated the same as censored observation in both the 1 year and conditional 3 year analyses. Nevertheless, the center effect, i.e., the difference between actual and expected survival rates should be similar because the same convention is used for death with a functioning graft in the calculation of both actual and expected survival rates.

Comparison with Kaplan-Meier Survival Rates

Typically, survival data are analyzed using the Kaplan-Meier (K-M) method. The binomial method is a simple alternative to the K-M method, particularly when there is a high degree of completeness of follow-up data. It was chosen for computing actual survival rates in this report because it is a natural counterpart to logistic regression, which was used to determined the expected survival rates.

Using the weights described earlier in this section, the binomial survival rates were nearly identical to Kaplan Meier survival rates (see Table IX-1).

Table IX-1. Overall Graft and Patient Survival Rates Using Binomial Method (Kaplan Meier Survival Rates are in Parentheses).

Organ	Graft Survival %			Percent Patient Survival %		
	1 or 3 Months	1 Year	Cond. 3 Years	1 or 3 Months	1 Year	Cond. 3 Years
Kidney	88.8 (88.8)	83.4 (83.5)	90.8 (90.8)	97.2 (97.2)	94.3 (94.2)	94.5 (94.1)
Liver	77.7 (77.7)	69.9 (69.9)	89.0 (89.0)	85.3 (85.7)	79.0 (79.9)	90.4 (91.8)
Pancreas	83.6 (83.6)	73.5 (73.6)	91.3 (91.2)	96.1 (96.1)	91.1 (91.2)	92.3 (92.2)
Heart	91.6 (91.4)	81.7 (81.7)	90.2 (90.2)	92.1 (91.7)	82.5 (82.2)	90.7 (90.9)
Lung	86.8 (86.6)	70.4 (70.5)	74.7 (74.7)	87.7 (87.1)	71.9 (71.3)	75.9 (77.5)
Heart-Lung	81.9 (82.0)	61.9 (62.1)	80.1 (80.1)	82.2 (82.2)	61.9 (62.1)	81.2 (81.3)

D. EXPECTED SURVIVAL RATES

Model-Fitting

Separate graft and patient survival models were fit to the national data for each organ and time point using logistic regression with selection of covariates through backward elimination.[3] For the kidney and liver analyses, the significance level for a covariate to remain in the model was 0.05; due to small sample size, 0.15 was used as the significance level for the pancreas analyses and for the heart-lung conditional 3 year analysis. A significance level of 0.10 was used for the remaining analyses.

In general, continuous covariates were centered about their means and initially were modeled with both a linear and a quadratic term. If the quadratic term of a continuous covariate remained in the model, the linear term was forced to remain in the model as well (regardless of the p-value of the linear term). For categorical covariates with k levels, k-1 levels were modeled as indicator variables, with the remaining level serving as the baseline. The baseline category was often chosen to be the largest category.

Using the conventions established for the 1994 Center Specific Report, the final *graft* and *patient* survival models for liver, heart, heart-lung, and lung transplants at each time point contained the same covariates. Any covariate that appeared in the final models for *either* graft or patient survival was included in *both* the graft and patient survival models for these organs. Because graft and patient survival are markedly different for kidney and pancreas transplants, the above convention was not adopted in determining the final graft and patient survival models for these two organs. For all organs, any covariate that appeared in the final models for *either* 3 month or 1 year survival was included in *both* the 3 month and 1 year survival models; however, the models for conditional 3 year survival could contain different covariates.

Missing Observations and Data Imputation

Missing values for any covariate were set to the baseline value for that covariate, with a few exceptions. In the kidney data, depending on the type of donor, a missing cold ischemic time was set to the corresponding mean value for either living donor transplants or cadaveric donor transplants. If level of mismatch could not be determined at either the A, B or the DR locus, then the overall mismatch level for that observation was be considered to be missing. In the analysis, the total mismatch level for these observations would be incremented by one for each locus at which the mismatch level could not be determined. If the level of PRA was missing, it was reset to the median value.

Recipient body mass index was computed as W/H^2, where W=recipient weight in kilograms and H=recipient height in meters. If height was missing, it would be imputed according to a regression equation that was estimated using nonmissing gender and age:

Male:

$$H = 1.754 - 0.983 \times e^{-(0.009 \times age + 0.0066 \times age^2)},$$

Female:

$$H = 1.616 - 0.923 \times e^{-(0.038 \times age + 0.0066 \times age^2)}.$$

Alternatively, if weight was missing, it would be imputed using height, gender and age:

Male:

$$W = 31.688 + 1.151 \times age - 0.013 \times age^2 + 0.00003 \times age^3 - 58.208 \times H + 39.013 \times H^2$$

Female:

$$W = 17.667 + 0.771 \times age - 0.003 \times age^2 - 0.00005 \times age^3 - 33.967 \times H + 30.315 \times H^2$$

Outliers in the Covariates

Adjustments were made to ensure that aberrant observations did not unduly influence the fitted estimates for parameters corresponding to continuous covariates.

[3] PROC LOGISTIC of SAS, version 6.12 (SAS Institute, Cary, NC)

In determining the kidney models, reported values of cold ischemic time greater than 72 hours for cadaveric donor transplants were reset to 72 hours. Reported values of cold ischemic time greater than 8 hours for living donor transplants were reset to 8 hours. Any body mass index that exceeded the range of 10 to 55 were reset to 10 or 55, as appropriate.

In determining the liver and pancreas models, reported values of cold ischemic time greater than 33 hours and 38 hours, respectively, were reset to 33 hours and 38 hours. In determining the heart models, reported values of cold ischemic time less than 30 minutes were reset to 30 minutes.

Model Interactions

Due to the lack of substantial evidence in the transplant literature to warrant their investigation, specific interactions among main effects were not considered.

Transplant Program Expected Survival Rates

As with the actual survival rate, the expected graft (patient) survival rate at the end of the time interval, t, for a particular transplant program, would be the weighted average of the expected survival probabilities for each transplant (patient) at the end of the interval, t, where the expected survival probabilities were obtained from the logistic models and weights were as defined in Section C of this chapter.

E. TESTING FOR SIGNIFICANCE OF PROGRAM EFFECTS

A score statistic[4] was used to test for the significance of transplant program effects. Let γ be the vector of model parameters, and let $D(\gamma)$ be the vector of partial derivatives of the log likelihood with respect to the parameter vector γ.

$$\gamma=(\alpha,\beta_1,\ldots,\beta_k,\beta_{k+1}),$$

where α is the intercept term, $\beta_1,\ldots,\beta_k$ are the donor and recipient risk factor covariates and β_{k+1} is the indicator covariate for a particular transplant program.

Let $\hat{\alpha},\hat{\beta}_1,\ldots,\hat{\beta}_k$ denote the maximum likelihood estimates of the model intercept α and the covariates $\beta_1,\ldots,\beta_k$. Under the null hypothesis of no transplant program effect,

$$\gamma_0=(\hat{\alpha},\hat{\beta}_1,\ldots,\hat{\beta}_k,0),$$

so that the quantity

$$\chi_s^2=D(\gamma_0)I^{-1}(\gamma_0)D'(\gamma_0)$$

where $I^{-1}(\gamma_0)$ is the matrix of the negative second partial derivatives of the log likelihood with respect to γ_0, has an asymptotic chi-square distribution with one degree of freedom. The two-sided p-value for the transplant program effect is then

$$P(\chi_1^2>\chi_s^2).$$

For example, if the chi-square statistic for a particular transplant program was 2.36, then the corresponding p-value would be $P(\chi_1^2>2.36)=0.12$.

A chi-square statistic of 3.86 corresponds to a p-value of 0.05. Thus a chi-square statistic greater than 3.86 which has a p-value less than 0.05 is often referred to as statistically significant.

When the number of transplants performed at a transplant program is too small, the proposed chi-square test is not appropriate because the asymptotic theory does not necessarily hold with small sample size. In cases where the number of transplants for a transplant program is less than six, the p-value for that transplant program effect was obtained from a binomial distribution. This p-value is based on n_j (the number of transplants (patients) at time t_j) and p_j (the expected graft (patient) survival rate), for $j=1$ or 3 months, 1 year and 3 years. By assuming that $X_j \sim B(n_j, p_j)$ where x_j is the number of failures (deaths) in the jth time interval, $x_j = 0, 1, 2, 3, 4, 5$, the p-value for the transplant program effect can be computed as defined below.

If $x_j \geq n_j / 2$,

$$\text{p-value} = \min\{(P(X_j \geq x_j) + P(X_j \leq n_j - x_j)),\ 1\}.$$

4 Agresti, A. 1990. *Categorical Data Analysis*. New York: Wiley.

If $x_j < n_j / 2$,

p-value = min { $(P(X_j \le x_j) + P(X_j \ge n_j - x_j)), 1$ }.

The method of determining the p-value for the transplant program effect for patient survival is analogous.

F. CALCULATION OF R^2

This quantity is a measure (percentage) of how much of the program-to-program variation in actual survival rates is explained by each logistic regression model and applies to transplants and programs for each organ type.

Let A_i denote the actual survival rate and let E_i denote the expected survival rate for the ith transplant program. Let $\bar{A}$ be the average of the actual survival rates over all k transplant programs, computed as

$$\bar{A} = \frac{1}{k}\sum_{i=1}^{k} A_i$$

Let V_i denote the approximate variance of the difference between the actual and expected survival rates for the ith transplant program. We used $V_i = \frac{(A_i - E_i)^2}{\chi_i^2}$. Note that V_i^{-1} is used as a weight for each term of the summation in the equation below. This prevents the results for smaller volume programs from unduly influencing the calculation. Then for a given model, the percent reduction in variance was defined as

$$R^2 = 1 - \frac{\sum_{i=1}^{k} V_i^{-1}(A_i - E_i)^2}{\sum_{i=1}^{k} V_i^{-1}(A_i - \bar{A})^2}.$$

In this report, R^2 is expressed as a percentage and the values of the R^2 are presented in Table 11 of each organ specific summary chapter (Table 10 for pancreas).

C Statistic

As mentioned, R^2 is a measurement of how the program-to-program variation in actual survival rates is explained by each logistic regression model. It is, however, not a good indication of the predictive ability of a logistic regression model in general. A better way of assessing how well the model predicts an individual's expected probability is to use the C statistic[5], also known as the area under the receiver-operating-characteristic (ROC) curve. In theory, values for C range from 0.5 to 1, with 1 corresponding to a model that has perfect prediction.

The C statistics for the models considered in this report are presented in Table IX-2. Their values range from 0.585 for the 1 year patient survival model for pancreas to 0.719 for the conditional 3 year patient survival model for heart-lung. Because these values are not very close to 1, this suggests that there are factors not included in the models that might improve the prediction. Most important of which may be transplant programs related factors (i.e. center effects), such as transplant volume.

G. ODDS RATIO

In this report, the term "odds ratio" is used to compare the impact of two risk factors on graft and patient survival. Its concept is similar to "relative risk" which is the risk of one event relative to another and is also commonly used in statistical analyses.

For two events, let θ_1 denote the probability of event one and let θ_2 denote the probability of event two. The odds is defined as $\theta_l/(1-\theta_l)$, l=1,2, meaning the chance of one event occurring relative to the chance of the same event not occurring. The odds-ratio of event one relative to event two is defined as:

$$\frac{\theta_1/(1-\theta_1)}{\theta_2/(1-\theta_2)}.$$

5 Cox D.R. and Wermuth N. 1992. A comment on the coefficient of determination for binary responses. *Am Stat* 46:1-4.

Table IX-2. *C* Statistics.

Organ	Graft Survival (%)			Patient Survival (%)		
	1 or 3 Months	1 Year	Cond. 3 Years	1 or 3 Months	1 Year	Cond. 3 Years
Kidney	0.664	0.663	0.689*	0.707	0.700	0.704*
Liver	0.686	0.675	0.668	0.712	0.700	0.682
Pancreas	0.608	0.638	0.639	0.637	0.585	0.621
Heart	0.678	0.631	0.585	0.678	0.632	0.583
Lung	0.717	0.661	0.621	0.718	0.660	0.604
Heart-Lung	0.630	0.692	0.711	0.632	0.690	0.719

* The *C* statistics are based on Model I of Table III-12 and Table III-13. When including the two post-transplant covariates (Model II), the *C* statistics would be 0.697 for graft survival and 0.710 for patient survival.

The odds ratio for dichotomous variables is relatively easy to interpret. For example, "the odds ratio of graft failure at 1 year for repeat kidney transplants was 1.3." means that the odds of graft failure for repeat transplants was 30% higher than the odds of graft failure for primary transplants at 1 year. The reference category (baseline) was primary kidney transplants.

Note that *odds* is not the same as *probability*. The following example will illustrate this concept.

Example
Suppose the estimated probability of death at 12 months for repeat kidney transplants was 0.25 and that for primary transplants was 0.20, then the odds ratio is:

$$\frac{(0.25)/(0.75)}{(0.20)/(0.80)} = 1.3$$

When a particular variable is on a continuous scale (referred to as continuous variable), the odds ratio is less easy to interpret. In this report, the odds ratios for continuous variables such as recipient age refers to an unit increase or decrease from the mean of the variable. For example, the odds of graft failure at 1 month for a heart transplant in which the donor heart had a cold ischemic time of 5 hours (300 minutes), relative to that for a transplant in which the donor heart had a cold ischemic time of 163 minutes (the baseline) is calculated as:

$$e^{(\frac{300-163}{15} \times 0.0296)} = 1.31.$$

In the above calculation, the mean cold ischemic time for heart transplants (163 minutes) serves as the baseline, and 15 minutes is the incremental unit for cold ischemic time. The *logarithm* of the odds of graft failure increases 0.0296 (Table VI-12) for each unit increase beyond the mean. Therefore, the odds of mortality for an increase of (300-163)=137 minutes is 1.31.

Note that, as can be seen in the above equation, odds ratios have an exponential relationship. That is, the increase of the odds ratio is non-linear for any linear increase of the variable. Therefore, caution should be exercised when computing the odds ratios at different values for any continuous variables.

For some continuous variables, such as recipient and donor age, body mass index and peak PRA, a quadratic term was included in the models in additional to the linear term in order to provide a better fit. Similar to the previous example, the odds ratio of 1 year graft failure, for example, between a heart recipient of age 55 and a heart recipient of age 45 is:

$$e^{[(\frac{55-45}{10})\times 0.1404+(\frac{55-45}{10})^2\times 0.0530]}=1.15,$$

where the incremental unit for age is 10 years, and 0.1404 and 0.0530, respectively, correspond to the model coefficients of the linear and quadratic terms of the recipient age (Table VI-12).

H. CALCULATION OF INDIVIDUAL EXPECTED SURVIVAL RATES

Using Tables 12 and 13 in each organ specific chapter (Tables 11 and 12 for pancreas), one can calculate an individual's expected graft and patient survival rates at 1 month or 3 months, 1 year and conditional 3 years for the time period of 1988 to April of 1994. The steps are:

Step 1: Calculate X,

$$X= \beta_0+ \beta_1\times Z_1 + \beta_2\times Z_2 +...+ \beta_i\times Z_i +...$$

where β_0 is the coefficient that corresponds to the intercept in each graft (patient) survival model (Tables 12 and 13 or 11 and 12 for pancreas). β_i and Z_i are the coefficient and the value that correspond to the ith variable, respectively. *If a variable does not apply to the graft (patient) survival model, Z_i simply takes a value of zero.* Furthermore, continuous variables must be centered at their population mean and scaled by the appropriate unit.

Step 2: Using X, calculate P:

$$P=\frac{1}{1+e^{X}}$$

P is the individual's expected probability of graft (patient) survival at the time point of interest.

Example
Consider the 1 year patient survival rate for a patient who had a heart transplant (Table VI-13). X can be obtained from the following equation:

X= - 2.1587
+ .0830 × [(donor age-26)/10]
+ .0494 × [(donor age-26)/10]^2
+ .1432 × (if donor is Black)
+ .2404 × (if donor is Hispanic)
+ .3942 × (if donor is other)
+ .1432 × (if donor is female)
+ .0204 × [(cold time in minutes - 163)/15]
+ .1577 × [(recipient age-45)/10]
+ .0557 × [(recipient age-45)/10]^2
- .0426 × (if recipient age=0 or 1)
+ .0906 × (if recipient is female)
+ .1240 × (if recipient in ICU at transplant)
+ .2897 × (if recipient is black)
+ 1.2143 × (if previous heart transplant=Yes)
+ .7099 × (if on ventilator at transplant)
+ .2621 × (if on VAD at transplant)
+ .1534 × (if on IABP at transplant)
+ .0778 × (if recipient had coronary disease)
+ .3104 × (if recipient had congenital disease)
+ .2111 × (if recipient had valvular disease)
+ .0931 × (if recipient had other heart disease, not including cardiomyopathy)
- .1335 × (if transplant year=1993 or 1994)

For instance, for a 50 year old White man who received a primary heart transplant from a 35 year old Black female donor after being in ICU:

X= - 2.1587
+ .0830 × [(35-26)/10]
+ .0494 × [(35-26)/10]^2
+ .1432 × 1
+ .2404 × 0
+ .3942 × 0
+ .1432 × 1
+ ...
+ .1577 × [(50-45)/10]
+ .0557 × [(50-45)/10]^2
- .0426 × 0
+ .0906 × 0
+ .1240 × 1
+ .2897 × 0
+ 1.2143 × 0
+ ...

Suppose X= - 1.72, then P would be

$$P=\frac{1}{1+e^{-1.72}}=0.85$$

Therefore, expected probability of 1 year patient survival for this heart recipient would be 85%.

I. TECHNICAL OVERSIGHT COMMITTEE OF THE UNOS SCIENTIFIC ADVISORY COMMITTEE

Lawrence G. Hunsicker, M.D., Chairman
University of Iowa
University of Iowa Hospitals and Clinics
Dept. of Internal Medicine
200 Hawkins Drive, Room T304-6H
Iowa City, IA 52242
(319) 356-4763 or 356-4768
FAX (319) 356-7893

Charles F. Shield, III, M.D.
Chairman, Scientific Advisory Committee
Director, Organ Transplant Program
Wichita Surgical Specialists
818 N. Emporia, Suite 200
Wichita, KA 67214
Phone (316) 263-0296 or 268-7000
FAX (316) 291-7727

Steven Belle, Ph.D.
Liver Registry Representative
Assistant Professor of Epidemiology
130 DeSoto Street, 127 Parran Hall
Pittsburgh, PA 15216
Phone (412) 624-5447
FAX (412) 624-3775

Judith B. Braslow, Director
Division of Transplantation
Health Resources and Services Administration
Parklawn Building, Room 7-29
5600 Fishers Lane
Rockville, MD 20857
Phone (301) 443-7577
FAX (301) 594-6095

Dennis E. Daniels, Dr. P.H.
Epidemiologist
Indiana University
Popars Room 626
400 East 7th Street
Bloomington, IN 47405
Phone (812) 855-9295
FAX (812) 855-7092

David Gjertson, Ph.D.
Kidney Registry Representative
University of California Los Angeles
Tissue Typing Laboratory
950 Veteran Avenue
Los Angeles, CA 90024
Phone (310) 206-3056
FAX (310) 206-3216

Jeffrey D. Hosenpud, M.D.
Medical College of Wisconsin
Division of Cardiology, L 462
8700 West Wisconsin Avenue
Milwaukee, WI 53226
Phone (414) 257-5090
FAX (414) 257-6103

Gwen Mayes
Chief, Operations and Analysis Branch
Division of Transplantation
Health Resources and Services Administration
Parklawn Building, Room 7-29
5600 Fishers Lane
Rockville, MD 20857
Phone (301) 443-8654
FAX (301) 594-6095

David E.R. Sutherland, M.D,, PH.D.
Director, Pancreas Transplant Program
University of Minnesota Hospital
Department of Surgery, Box 280 Mayo
420 Delaware Street, W.E.
Minneapolis, MN 55455
Phone (612) 625-7600
FAX (612) 625-8496

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UNOS

United Network for Organ Sharing

ATTACHMENT F

Attachment F

Glen O. Robinson
University of Virginia – School of Law
Charlottesville, VA 22901

October 4, 1989

Mr. Gene A. Pierce
Executive Director
UNOS
1100 Boulders Parkway Suite 500
Post Office Box 13770
Richmond, Virginia 23225

Dear Mr. Pierce:

You have asked my opinion on several legal issues concerning the Organ Procurement and Transplantation Network (OPTN), created by the National Organ Transplant Act, as amended in 1988, 42 U.S.C., § 274, and operated by the United Network for Organ Sharing (UNOS) under contract with the Department of Health and Human Services (HHS). Specifically you have asked my opinion concerning the following: (1) the constitutionality of delegating legislative powers to OPTN; (2) the constitutionality of empowering OPTN to perform executive functions; (3) the antitrust implications of OPTN operating as an exclusive organ procurement and transplant network; (4) "due process" requirements for promulgating rules governing membership criteria and medical criteria for allocating organs through the OPTN. Issues (1), (3) and (4) are addressed in a letter from UNOS to Attorney General Richard L. Thornburgh, dated July 25, 1989 (UNOS Letter); issue (2) is not specifically addressed by the UNOS Letter but involves a constitutional concern that is related to issue (1).

Delegation of Legislative Power

The delegation doctrine -- or as it is also styled the nondelegation doctrine -- is derived from Article I § 1 of the Constitution, providing that "[a]ll legislative Powers herein granted shall be vested in a Congress of the United States." Despite early judicial rhetoric to the effect that the doctrine prohibited the delegation of legislative power, this strict interpretation has never been followed. Rather the doctrine has been interpreted to permit Congress to delegate power so long as it exercises its essential legislative prerogative by enacting standards to guide the exercise of delegated power. See, *e.g.*, *Mistretta v. United States*, 109 S.Ct. 647 (1989)(upholding delegation of power to Sentencing Commission to promulgate guidelines for criminal sentencing).

As is indicated in the UNOS Letter there has been no federal court decision invalidating a law for delegation of legislative authority for more than 50 years despite numerous invitations to do so. The Supreme Court itself has never formally overruled the doctrine, but conventional wisdom for a long time has been that it is lifeless, even if it has not been interred. Although some academic commentators (myself included) have argued that the Court should revive the notion that standardless delegations of legislative powers by Congress are unconstitutional, there are no significant signs of its being disposed to do so. To be sure there have been from time to time statements by members of the Court that suggested the possibility that in an extreme case a standardless delegation might be invalidated. The statements appear mostly by way of dicta or dissenting opinions and provide no real basis for predicting action by the Court. I think I can fairly represent it to be the virtual consensus of constitutional law scholars that the odds of a revival of the *Schechter* case are roughly the same as the odds of a revival of the infamous *Lochner v. New York.* The Supreme Court's most recent encounters with the delegation doctrine, in *Mistretta* and in *Skinner v. Mid-America Pipeline Co.*, 109 S.Ct. 1726 (1989)(upholding delegation of power to the Secretary of Transportation to impose user fees on pipelines), confirm this view.

It makes no difference whether the legislative delegation is to a federal agency or to private groups. Although the Court in the *Carter Coal* case did suggest that delegations to private entities were specially "obnoxious," it has never articulated a separate standard for such delegations. As mentioned in the UNOS Letter the Court, shortly after *Carter Coal*, sustained delegations of legislative power to private groups in *Currin v. Wallace*, in *United States v. Rock Royal Co-op*, and in *Sunshine Anthracite Coal v. Adkins*. Since that time it has not chosen to revisit the issue. However, the lower courts have done so. The *Corum* case, discussed in the UNOS Letter, is quite close on point to the present situation.

There are, of course, factual differences in the way in which delegated power was exercised in the foregoing cases and the way it is exercised by OPTN. In the former the private entity was given power to approve or disapprove policy initiatives taken by executive agencies whereas OPTN has been given power to initiate, and to implement, policies. This factual distinction has no significance under the delegation doctrine, however. Whether Congress has improperly delegated its powers -- whether it has abdicated its responsibility to make legislative judgments -- sensibly cannot turn on whether the power in question takes the form of initiation or approval of executive initiatives. The pertinent issue in either event is whether Congress has clothed its delegation with standards sufficient to discharge its legislative responsibility.

This last point bears emphasis. Although the conventional wisdom holds that the delegation doctrine is moribund, even if it were not, even if it were to be revitalized, it would not follow that the delegation of power under the National Organ Transplant Act would run afoul of it. The delegation doctrine does not forbid all congressional delegations of power but only those unaccompanied by standards sufficiently specific to permit it to be ascertained whether the delegate has conformed to the legislative will. See, *e.g.*, *Yakus v. United States*, 321 U.S. 414 (1944). The degree of specificity required depends upon the subject matter. In the nature of things less specificity should be required in cases where, as here, the "legislative judgment" depends on criteria that are constantly changing. Organ transplantation, involving as it does medical standards that are rapidly evolving with scientific advances and experience, presents a model case for accepting the necessity for broad delegation. At most one would expect Congress to set forth broad policy guidelines as to the nature of the network and its purposes and perhaps to provide some kind of review of the network and its operations. I believe the National Organ Transplant Act does this sufficiently to pass muster even under a revitalized delegation doctrine. Certainly it does so under currently applicable case law.

One final point on this issue deserves mention. If there is no constitutional basis for distinguishing the delegation to private groups from a delegation to HHS itself, any constitutional infirmity in the delegation would throw the question of standards not back to HHS but to the Congress. Obviously this would not only affect this legislation but would have potentially far-reaching implications for other legislation in health care areas where Congress has delegated broad powers to HHS, which HHS in turn has conferred on subordinate agencies. Without undertaking to examine other legislation to see how it might be affected if the National Organ Transplant Act were found defective, I feel comfortable in predicting that there would be many other pieces of important legislation that would be vulnerable to similar attack. It is precisely because of such general implications that almost no one thinks there is any serious prospect of the courts engaging in a strict scrutiny of federal delegations. I conclude, therefore, that the delegation here is not vulnerable to successful constitutional challenge under the delegation doctrine.

Executive Prerogative

Congressional grants of powers to a public or private entity may implicate both delegation doctrine and executive prerogative concerns. The two concerns are similar in that both involve the proper allocation of government powers and both are commonly associated with general separation of powers principles. However, they involve different constitutional questions: the delegation doctrine asks whether Congress has abdicated its lawmaking responsibility; the executive prerogative issue asks whether Congress has impermissibly interfered with powers and functions constitutionally assigned to the Executive Branch. The latter question can be subdivided into two questions: one, does Congress' action interfere with specific constitutional powers of the President; two, does it interfere with Executive Branch functions generally? See *Morrison v. Olson*, 108 S.Ct. 2597 (1988); *Bowsher v. Synar*, 478 U.S. 714 (1986).

In the present context two specific presidential powers are involved, the power to appoint and the power to remove government officials. The first power is expressly assigned by Article II, § 2 of the Constitution which provides that the President "shall nominate, and by and with the Advice and Consent of the Senate, shall appoint...all...Officers of The United States...." Though the Constitution does not define who is an "Officer of the United States," the Supreme Court has held that the term includes any appointee exercising "significant authority pursuant to the laws of the United States." *Buckley v. Valeo*, 424 U.S. 1 (1976)(members of the Federal Election Campaign Commission are officers of the United States). Article II, § 2 provides separately for appointment of "inferior officers." In the case of such officers Congress may vest the appointments power "in the President alone, in the Courts of Law, or the Heads of Departments." Again, there is no constitutional definition of such officers. The Court in *Morrison v. Olson* looked to such criteria as whether the officer is subject to removal by a higher executive official and the scope of the officer's authority and duties in holding that the independent counsel provided for by the Ethics in Government Act was an inferior officer. Under *Morrison* I think the officers of the OPTN would be properly classified as inferior officers. However, *in terms of presidential power*, the classification is unimportant for the National Organ Transplant Act does not in any way interfere with the President's appointment power. The Act gives the Secretary of HHS -- acting presumably under the control and direction of the President -- the power to contract for the establishment and operation of the OPTN. This contracting power is the functional equivalent of an appointment by the President.

The second specific power of the President is the removal power. Unlike the appointments power the Constitution makes no provision for removal of officials. However, since *Myers v. United States*, 272 U.S. 52 (1926), the power to remove executive officials has been deemed to be an inherent presidential prerogative. Nevertheless, this removal power need not in all cases be unqualified; in *Morrison* the Court held that the imposition of a "good cause" standard for removal was permissible. Again, it is very clear that the National Organ Transplant Act fully recognizes the President's removal power by virtue of the contracting authority of HHS. The present contract demonstrates the point: it is for a limited period (three years) and is subject to earlier termination in the event the Department makes certain findings enumerated in the contract. This is the functional equivalent of a power to "remove" OPTN officials for good cause.

There remains one final aspect of the executive prerogative issue, the question whether Congress has impermissibly undermined the functions of the Executive Branch generally -- the general separation-of-powers question. Apart from interference with discrete presidential prerogatives, principally those discussed above, we have no clear guidelines as to the required degree of separation of powers. The Court's approach to this issue in *Morrison* (and other recent cases not directly pertinent here) has been to apply a pragmatic and functional test to the separation-of-powers question in recognition of the fact that governmental powers cannot be hermetically sealed in separate branches but must of necessity be shared in part. In *Morrison* the Court gave particular weight to the fact that Congress had not attempted to aggrandize its own power at the expense of the Executive Branch. Compare *Bowsher v. Synar* (invalidating delegation of executive power to a congressional officer not removable by the President); *INS v. Chadha*, 462 U.S. 919 (1983)(invalidating legislative veto). It is quite plain that in creating the OPTN Congress has in no way aggrandized its power at the expense of the Executive Branch. Congress' prerogatives and power are in no way enhanced by its having done so. Another important consideration in *Morrison* was the fact that the functions involved were limited and were in any event subject to executive influence and control. Here too the OPTN's powers are limited and are subject to HHS contracting authority. Applying the *Morrison* criteria the essential executive prerogatives seem to me fully preserved.

Antitrust Implications

It may be helpful to give context to the antitrust question by assuming preliminarily no statutory immunity. As an organization engaged in setting *professional* standards UNOS would presumably enjoy a degree of discretion under the antitrust laws that would be denied ordinary commercial enterprises. The Court has acknowledged this in applying a rule of reason analysis to professional standard setting even in contexts that would normally be dealt with under a rule of per se illegality. See *National Society of Professional Engineers v. United States*, 435 U.S. 679 (1978). Nevertheless, the Court has held that professional standard setting by private groups is subject to the norms of competitive policy; the rule of reason does not permit a general defense that professional competition is not desirable. *Id.* Absent immunity the setting of mandatory standards for all persons engaged in organ procurement and transplantation would present a serious antitrust concern insofar as it would suppress competitive practices. However, imagining a case of competitive private standard setting does not address the scheme envisioned by Congress. First, OPTN is not merely a private standards-setting entity; it is a delegate of Congress and as such functions in a quasi-official capacity. Second, it is clear that Congress did not intend the OPTN to set standards in competition with any other private entity. OPTN was intended to be the exclusive network for organ procurement and transplantation as is evident from the fact that Congress specifically mandated that any health care facility receiving Medicare/Medicaid funds which is engaged in organ transplantation must be a member of the OPTN and subject to its rules. It is hard to imagine a clearer indication that Congress wished the OPTN to function as a self-regulating national private entity. By that fact alone it would have to be inferred that UNOS has implied immunity from the antitrust laws.

The facts bring this case squarely within the principle of the *Gordon* and *National Association of Securities* cases, noted in the UNOS Letter: where a regulatory scheme authorized by Congress and overseen by Congress and the executive (in the above cases the SEC) is inherently at odds with competition, which the antitrust laws enforce, immunity is implied. The Supreme Court has insisted that private organizations exercising such regulatory policies must accord basic due process to members subject to them, as the UNOS Letter states. Although it has never defined exactly what such due process encompasses, I think it clear that the current procedures governing UNOS membership policies are fully adequate to meet any antitrust concerns. It is important in this regard to note that the central problem that "antitrust due process" seeks to address is the conflict of interest problem raised when private entities are empowered to regulate competitors. That problem is minimized here given that Congress in the 1986 Budget Reconciliation Act has made a clear judgment that there are not to be competing organ procurement and transplant networks; health care facilities receiving Medicare or Medicaid payments must follow OPTN rules if they engage in organ procurement or transplantation. Thus this situation is different from the case where one private group is delegated power to regulate competing private groups; here by congressional judgment competition is not desired.

Nonantitrust precedents are pertinent here. Perhaps closest on point is *Association of American Physicians & Surgeons v. Weinberger*, 395 F. Supp. 125 (1975), *aff'd without opinion*, 423 U.S. 975 (1975). Plaintiff association challenged the constitutionality of the Professional Standards Review Law establishing a peer review program for health care facilities providing services covered by Medicare or Medicaid. Among the claims was that the statute improperly delegated adjudicatory authority to peer review groups (PSROs) that were inherently biased against plaintiffs by virtue of their contract with HHS (then HEW) and their economic self interest. The court dismissed the claim. First, it noted the nonprofit character of the PSROs and the fact their remuneration was not related to their performance. (See also *Schweiker v. McClure*, 456 U.S. 188 (1982)). Second, it observed that

> "it has been held permissible for agencies of the federal government to contract with private organizations in order to have such organizations perform governmental functions as long as the particular administrative scheme provides for a hearing on the determinations made by those private organizations."

395 F. Supp. at 140.

In evaluating this immunity it should be kept in mind that it does not imply that the constituent members of UNOS, who compete for patients on the basis of quality of service, price and convenience of access, have antitrust immunity for *all* organ procurement and transplantation activities. The immunity attaches to UNOS as an organization and to UNOS' members to the extent of their required conformance with UNOS' standards and operating rules. In short the immunity relates to the *development by the organ transplant community of uniform standards and rules* deemed necessary to equitable and efficient organ allocation. Within the framework of uniform allocation rules, however, competition among members remains the norm.

Rulemaking "Due Process"

Whether the procedures followed by UNOS meet the requirements of other applicable laws is a separate question, of course. We can quickly set to one side questions of constitutional due process. It is doubtful the Constitution requires any formal process for the promulgation of general rules; in any case UNOS' rulemaking procedures satisfy any constitutional formalities one could plausibly suppose being demanded by the due process clause. See *Bi-Metallic Investment Co. v. State Board of Equalization*, 239 U.S. 441 (1915). The only other law relevant to rulemaking procedures here would be the Administrative Procedure Act (APA). The APA is applicable to any "authority of the Government of the United States." This definition has been held not to embrace private entities that perform professional standards review functions -- functions similar to those of UNOS. See *Public Citizen Health Department v. Department of HEW*, 668 F.2d 537 (D.C. Cir. 1981)(PSROs not agencies subject to freedom of information provisions of APA). Cf. *Irwin Memorial Blood Bank v. American Red Cross*, 640 F.2d 1051 (9th Cir. 1981)(Red Cross not an agency subject to APA). An argument could be made that UNOS exercises a degree of quasi-official power in exercising rules affecting allocation of Medicare and Medicaid funds that distinguishes it from professional peer review organizations and makes it, to the extent of that power, an "authority of the government." Such an argument would not be frivolous, but it does not seem congruent with the reasoning in *Public Citizen Health Department*.

Even assuming, contrary to the *Public Citizen* case, that UNOS is an authority of the government for purposes of the APA it would not be subject to the APA's rulemaking procedures; under the act all matters relating to "public property, loans, grants, benefits and contracts" are exempt from the procedures prescribed for rulemaking generally. The exemption clearly applies to rules pertaining to eligibility for Medicare and Medicaid payments. See *Holy Cross Hospital-Mission Hills v. Heckler*, 749 F.2d 1340 (9th Cir. 1984)(exemption covers rules pertaining to Medicare coverage); *Humana of South Carolina v. Califano*, 590 F.2d 1070 (D.C. Cir. 1978); *Opelika Nursing Home, Inc. v. Richardson*, 356 F. Supp. 1338 (M.D. Ala. 1973), *aff'd*, 490 F.2d 841 (5th Cir. 1974)(exemption covers rules governing Medicaid payments). HHS has chosen to waive the exemption and to subject its own rules to APA rulemaking requirements. 36 Fed. Reg. 2532 (1971). However, nothing in that waiver purports to apply to rules established by HHS contractors. Nor is there any reason to strain to imply such a coverage of the HHS regulations since UNOS' own rules provide for full notice and opportunity for comment to members and to the public in a manner that conforms to the rulemaking procedures of the APA in spirit if not in precise form.

UNOS' rulemaking procedures appear, movcover, to meet fully Congress' own expectations in enacting the National Organ Transplant Act. The Act specifies that the OPTN shall establish membership and organ allocation criteria after allowing "members of the public an opportunity to comment with respect to such criteria." Although issues of due process were raised in connection with the 1988 amendments, Congress made no further provision for subjecting OPTN rules to the formal requirements of the APA. Indeed, it appears from Senate Committee Report No. 100-310 that the authors of that legislation contemplated that the design of rules governing membership and medical criteria would be left to the OPTN, subject to the general admonition that the processes should replicate "as closely as possible" the processes of "such agencies as the Health Care Financing Administration (HCFA) in promulgating regulations." The admonition suggests to me an assumption that OPTN would not be subject to the generic requirements of the APA even though HHS has embraced those requirements for itself and its agencies such as HCFA.

If UNOS' rulemaking procedures are fair and effective in evaluating and keeping pace with scientific, medical and technological advances, then I would conclude that the purposes of due process have been served.

* * *

I hope the foregoing is responsive to your request. I will be pleased to discuss these matters further with you or anyone in the government or in Congress, as you wish.

Sincerely,

Glen O. Robinson
John C. Stennis Professor
of Law