Chapter seven

Transplantation

Life is a petty thing unless it is moved by the indomitable urge to extend its boundaries. Only in proportion as we are desirious of living more do we really live.

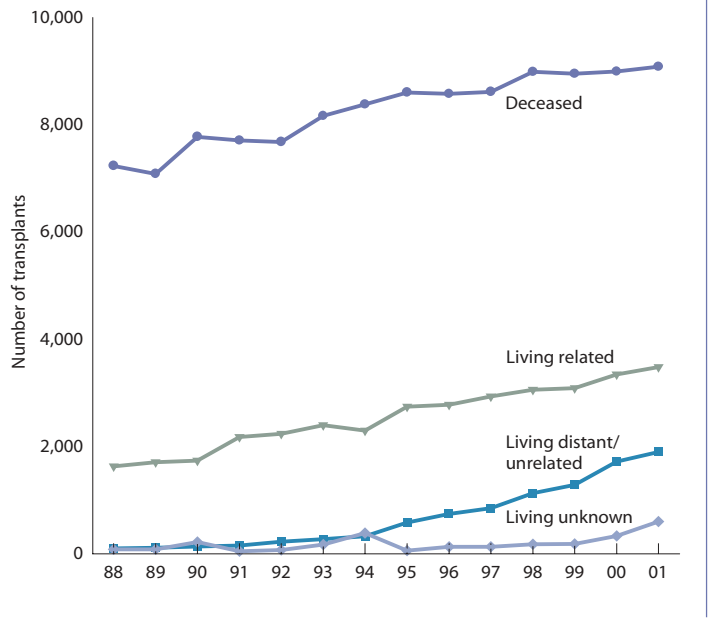
José Ortega Y Gasset, The Dehumanization of Art

The number of kidney transplants performed in the U.S. has risen steadily over the past decade. The number of transplants from deceased donors, however, has increased little in the past three to four years, and most of the growth in the total number of transplants has come from increased use of living donors, particularly living unrelated and distantly related donors. Unfortunately, the number of transplants performed has not kept pace with demand, and the transplant rate has steadily declined. ■ Deceased donors are more often older and male, while living donors are more often younger and female. Donation rates for blacks are only slightly lower than for whites, and lowest among Asians and Native Americans. Geographically, the highest and lowest rates of donation—whether from deceased or living donors—differ more than two-fold across the country, differences evident whether rates are expressed per million population or per million deaths. ■ There has been steady improvement in one-year graft survival, a result of declining one-year mortality and death-censored graft failure (defined by return to dialysis or re-transplantation). Unfortunately, there has been little overall alteration in the rate of late graft failure, reflected by the lack of substantial change in the half-lives of grafts that survive at least one year. After adjusting for multiple risk factors, there was a 16 percent reduction in the risk of graft failure in deceased donor transplants performed in 1999–2001, compared to those in 1995–1998. Similarly, there has been an 11 percent reduction in the risk of graft failure for living donor transplants. ■ This year's Annual Data Report includes data on the incidence and clinical correlates of several major post-transplant complications which increase the morbidity and cost of transplantation, and may lead to death. Data on complications are taken from a subset of USRDS transplant recipients identified as having Medicare as the primary insurance payor; a detailed description of the methods used to identify these patients is provided in Appendix A. ■ This subset of patients represents a large proportion of the USRDS transplant population, but differs from it as well. Because complications are identified here using specific billing codes, and some complications may occur without generating a code, their actual incidence may be higher or lower than that represented by the codes. It is likely that the specificity of billing codes to detect complications is relatively high, but the sensitivity of this method may be somewhat lower. ■ Fractures are common after transplantation, and are associated with an increased

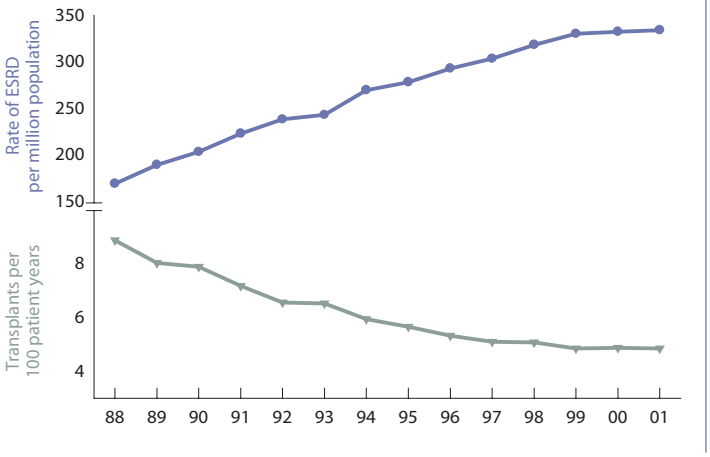
CHAPTER HIGHLIGHTS ■ **Figure 7.2** The number of transplants performed in the U.S. has not kept pace with the increasing incidence of end-stage renal disease. ■ **Figures 7.14–15** Although there has been steady improvement in one-year graft survival, there has been little change in the rate of late graft failure. ■ **Figures 7.16, 7.22, & 7.25** The rates of fractures, new-onset diabetes, infections, and malignancies are very high after kidney transplantation. ■ **Figure 7.23** Infections are associated with an increased risk of graft failure, and an almost five-fold increase in the risk of death with a functioning graft.

7.1 · Number of transplants, by donor type

transplant counts as known to the USRDS (reconciled from various sources).



7.2 · Incident & transplant rates



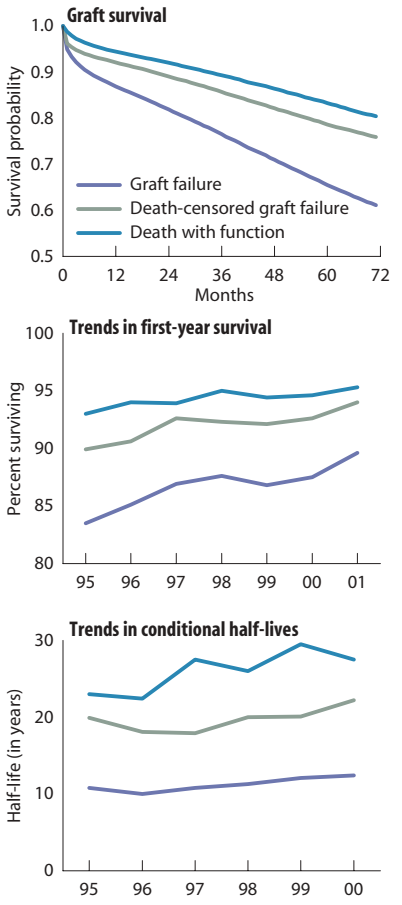
risk of death, but not of death-censored graft failure. There are a number of risk factors for fractures after kidney transplantation. ■ The incidence of new onset, post-transplant diabetes mellitus (PTDM) is very high, particularly in the first six months after transplantation. PTDM is associated with an increased risk of graft failure, and a number of risk factors for PTDM can be identified. ■ The incidence of major infections after transplantation is also very high, especially in the first six months after transplantation. Not surprisingly, infections are associated with a higher risk of graft failure, due primarily to the higher risk of death with function. Risk factors for infections include age (both young and old are at higher risk for infections), gender, donor age, and body mass index. ■ Finally, both skin and non-skin malignancies are common complications after kidney transplantation. Risk factors for malignancies include older age, male gender, and ethnicity.

Transplant survival

Since 1995 there has been steady improvement in one-year graft survival, but little change in the rate of late graft failure, reflected by the half-lives of grafts that survive at least one year (Figures 7.14–15). After adjustments for multiple risk factors, the risk of graft failure in deceased donor transplants fell 16 percent between 1995–1998 and 1999–2001, while that for living donor transplants decreased 11 percent (Tables 7.a–b).

A number of donor and recipient transplant characteristics are independently associated with graft failure. For deceased donor transplants the highest relative risks of graft failure are associated with recipient and donor ages 65 and older, while in living donor transplants the highest risks are found with recipient age 65 and older.

7.14 Survival: deceased donor transplants



7.a · Risk factors for graft & patient survival: deceased donor transplants (n=47,998)

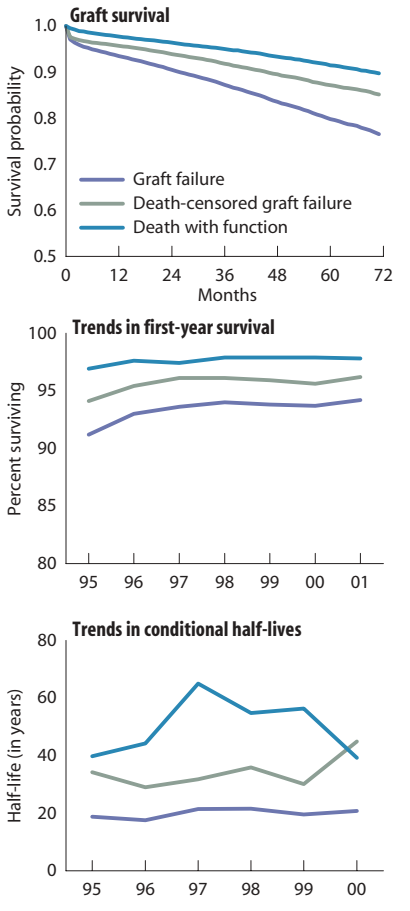
	% of pts	All-cause graft failure Haz. ratio	95% CI	P-value	Death-censored graft failure Haz. ratio	95% CI	P-value	Death with functioning graft Haz. ratio	95% CI	P-value
Transplant era (reference: 1995–1998, 56.2% of patients)										
1999–2001	43.8	0.84	(0.80–0.88)	<.0001	0.79	(0.75–0.84)	<.0001	0.91	(0.85–0.97)	0.0043
Recipient age (years) (reference: 18–34, 15.7% of patients)										
0–17	3.7	1.28	(1.15–1.42)	<.0001	1.33	(1.18–1.50)	<.0001	1.07	(0.81–1.42)	0.6287
35–49	33.7	0.87	(0.83–0.92)	<.0001	0.70	(0.66–0.74)	<.0001	2.00	(1.76–2.27)	<.0001
50–64	37.1	1.01	(0.96–1.07)	0.6695	0.55	(0.51–0.59)	<.0001	3.86	(3.41–4.36)	<.0001
65+	9.8	1.42	(1.33–1.52)	<.0001	0.56	(0.51–0.62)	<.0001	6.70	(5.86–7.65)	<.0001
Recipient gender (reference: female, 39.4% of patients)										
Male	60.7	1.01	(0.97–1.04)	0.7116	0.97	(0.92–1.01)	0.1565	1.06	(1.01–1.12)	0.0299
Recipient race (reference: white, 62.2% of patients)										
Black	29.8	1.12	(1.08–1.17)	<.0001	1.32	(1.26–1.40)	<.0001	0.86	(0.80–0.91)	<.0001
Asian	5.3	0.72	(0.66–0.79)	<.0001	0.79	(0.70–0.89)	<.0001	0.62	(0.54–0.72)	<.0001
Other	2.8	0.88	(0.79–0.99)	0.0323	0.86	(0.74–1.01)	0.0602	0.89	(0.75–1.05)	0.1673
Recipient ethnicity (reference: non-Hispanic, 87.5% of patients)										
Hispanic	12.5	0.74	(0.70–0.79)	<.0001	0.83	(0.77–0.89)	<.0001	0.63	(0.57–0.69)	<.0001
Primary cause of ESRD (reference: glomerulonephritis, 23.3% of patients)										
Diabetes	22.1	1.26	(1.20–1.33)	<.0001	0.90	(0.84–0.96)	0.0023	2.02	(1.86–2.19)	<.0001
Hypertension	19.6	1.13	(1.07–1.19)	<.0001	1.05	(0.99–1.12)	0.1191	1.35	(1.23–1.47)	<.0001
Cystic kidney disease	9.2	0.78	(0.72–0.84)	<.0001	0.80	(0.73–0.89)	<.0001	0.82	(0.73–0.93)	0.0016
Other	25.8	1.01	(0.96–1.06)	0.7812	0.87	(0.81–0.92)	<.0001	1.36	(1.25–1.49)	<.0001
Pre–transplant serology										
Hepatitis B Positive	7.8	0.99	(0.93–1.06)	0.7964	0.96	(0.88–1.04)	0.3012	1.05	(0.95–1.16)	0.3361
Hepatitis C Positive	5.7	1.34	(1.26–1.44)	<.0001	1.35	(1.24–1.47)	<.0001	1.34	(1.21–1.49)	<.0001
Education level (reference: <college, 56.4% of patients)										
College+	12.2	0.91	(0.86–0.97)	0.0031	0.86	(0.79–0.93)	0.0003	0.97	(0.89–1.06)	0.5157
Unknown	31.4	1.07	(1.03–1.11)	0.0004	1.08	(1.03–1.14)	0.0016	1.05	(0.99–1.11)	0.1055
Employment status (reference: unable to work, 34.1% of patients)										
Able to work	50.0	0.87	(0.84–0.91)	<.0001	0.93	(0.88–0.98)	0.0033	0.80	(0.75–0.85)	<.0001
Unknown	15.9	1.02	(0.96–1.07)	0.5496	0.99	(0.92–1.06)	0.7601	1.05	(0.97–1.14)	0.2610
Primary payor (reference: Medicare, 59.3% of patients)										
Private	25.7	0.84	(0.80–0.88)	<.0001	0.82	(0.77–0.87)	<.0001	0.87	(0.82–0.93)	<.0001
Other	13.5	0.91	(0.86–0.97)	0.0023	0.85	(0.79–0.92)	<.0001	1.01	(0.92–1.11)	0.8076
Unknown	1.6	1.00	(0.87–1.15)	0.9854	1.01	(0.85–1.22)	0.8740	0.97	(0.79–1.19)	0.7671
Prior dialysis time (years) (reference: <1, 14.2% of patients)										
None (preemptive)	5.4	0.93	(0.85–1.03)	0.1487	0.89	(0.78–1.01)	0.0669	1.00	(0.87–1.16)	0.9617
1–<2	22.4	1.11	(1.05–1.18)	0.0005	1.10	(1.02–1.18)	0.0153	1.13	(1.03–1.23)	0.0112
2–<3	18.9	1.13	(1.06–1.20)	<.0001	1.09	(1.00–1.18)	0.0400	1.21	(1.10–1.33)	<.0001
3+	35.3	1.17	(1.10–1.24)	<.0001	1.05	(0.97–1.13)	0.2420	1.38	(1.26–1.51)	<.0001
Unknown	3.8	0.97	(0.87–1.09)	0.6201	0.85	(0.73–0.98)	0.0268	1.19	(1.01–1.40)	0.0425
Donor age (years) (reference: 18–34, 24.7% of patients)										
0–17	16.4	1.03	(0.97–1.09)	0.3285	1.08	(1.00–1.16)	0.0453	0.95	(0.87–1.05)	0.3296
35–49	24.0	1.12	(1.06–1.18)	<.0001	1.10	(1.03–1.18)	0.0065	1.13	(1.04–1.22)	0.0027
50–64	17.7	1.32	(1.25–1.40)	<.0001	1.28	(1.18–1.38)	<.0001	1.37	(1.26–1.50)	<.0001
65+	3.4	1.69	(1.55–1.84)	<.0001	1.90	(1.70–2.13)	<.0001	1.51	(1.32–1.71)	<.0001
Unknown	13.8	0.74	(0.65–0.83)	<.0001	0.56	(0.48–0.66)	<.0001	1.19	(0.96–1.47)	0.1123
Donor gender (reference: female, 38.7% of patients)										
Male	56.9	1.04	(1.00–1.08)	0.0306	1.10	(1.05–1.15)	0.0001	0.97	(0.91–1.02)	0.2360
Unknown	4.5	1.19	(0.94–1.51)	0.1444	1.55	(1.13–2.12)	0.0060	0.83	(0.58–1.19)	0.3193
Donor race (reference: white, 81.7% of patients)										
Black	10.7	1.24	(1.18–1.30)	<.0001	1.32	(1.24–1.40)	<.0001	1.11	(1.01–1.21)	0.0227
Asian	1.9	0.99	(0.87–1.12)	0.8270	0.99	(0.84–1.17)	0.9412	0.98	(0.80–1.20)	0.8311
Other	0.7	1.26	(1.04–1.51)	0.0165	1.27	(1.00–1.62)	0.0489	1.22	(0.91–1.64)	0.1871
Unknown	5.0	1.20	(0.96–1.50)	0.1111	1.36	(1.01–1.83)	0.0410	1.01	(0.73–1.42)	0.9381
Donor cause of death (reference: non–trauma, 48.7% of patients)										
Trauma	51.3	0.87	(0.84–0.91)	<.0001	0.82	(0.77–0.86)	<.0001	0.96	(0.90–1.02)	0.1724
HLA mismatches (reference: 3, 19.7% of patients)										
0	12.3	0.85	(0.80–0.91)	<.0001	0.75	(0.69–0.83)	<.0001	0.96	(0.87–1.06)	0.4288
1	3.8	0.95	(0.86–1.04)	0.2651	0.97	(0.86–1.11)	0.6806	0.91	(0.78–1.05)	0.2051
2	9.7	1.00	(0.94–1.07)	0.9720	1.00	(0.92–1.09)	0.9421	1.00	(0.90–1.10)	0.9585
4	22.2	1.08	(1.03–1.14)	0.0020	1.13	(1.06–1.20)	0.0004	1.02	(0.94–1.11)	0.6269
5	17.4	1.14	(1.08–1.20)	<.0001	1.18	(1.10–1.27)	<.0001	1.07	(0.98–1.17)	0.1099
6	8.6	1.21	(1.13–1.30)	<.0001	1.31	(1.20–1.42)	<.0001	1.08	(0.97–1.21)	0.1514
Unknown	6.3	1.19	(1.10–1.30)	<.0001	0.96	(0.85–1.08)	0.4992	1.50	(1.33–1.69)	<.0001
Cold ischemia time (hours) (reference: 0–12, 16.9% of patients)										
13–24	48.7	1.07	(1.02–1.12)	0.0094	1.07	(1.01–1.14)	0.0313	1.06	(0.98–1.14)	0.1546
25–36	21.3	1.12	(1.06–1.18)	<.0001	1.14	(1.06–1.23)	0.0003	1.09	(1.00–1.18)	0.0606
37+	3.3	1.29	(1.18–1.41)	<.0001	1.42	(1.27–1.60)	<.0001	1.10	(0.95–1.28)	0.2093
Unknown	9.9	1.10	(1.01–1.18)	0.0206	1.09	(0.98–1.21)	0.1089	1.11	(0.99–1.25)	0.0805
Donor documented history of:										
Diabetes	3.0	1.09	(1.00–1.20)	0.0533	1.15	(1.02–1.29)	0.0189	1.04	(0.90–1.20)	0.5873
Hypertension	17.7	1.23	(1.17–1.29)	<.0001	1.39	(1.31–1.47)	<.0001	1.04	(0.97–1.12)	0.2526
Body surface area matching (reference: R≤D, 69.6% of patients)										
R 1.6–2.2 m^2, D<1.6 m^2	10.1	1.13	(1.07–1.20)	<.0001	1.18	(1.10–1.28)	<.0001	1.06	(0.96–1.16)	0.2455
R>2.2 m^2, D<1.6 m^2	1.3	1.28	(1.11–1.46)	0.0005	1.19	(0.98–1.43)	0.0723	1.36	(1.11–1.67)	0.0027
Unknown	19.0	1.37	(1.24–1.52)	<.0001	1.66	(1.47–1.87)	<.0001	0.93	(0.77–1.12)	0.4449
Recipient body mass index (BMI) (reference: 18.5–24.9 kg/m^2, 39% of patients)										
<18.5 kg/m^2	4.7	1.01	(0.93–1.11)	0.7672	0.96	(0.86–1.07)	0.4536	1.17	(1.01–1.36)	0.0410
25.0–29.9 kg/m^2	31.5	1.02	(0.98–1.07)	0.2848	1.03	(0.98–1.09)	0.2157	0.99	(0.93–1.06)	0.8339
30.0–34.9 kg/m^2	15.2	1.11	(1.06–1.17)	<.0001	1.16	(1.09–1.24)	<.0001	1.03	(0.95–1.11)	0.4598
≥35.0 kg/m^2	6.3	1.23	(1.15–1.32)	<.0001	1.28	(1.17–1.40)	<.0001	1.13	(1.01–1.26)	0.0299
Unknown	3.4	0.79	(0.70–0.90)	0.0005	0.69	(0.59–0.81)	<.0001	1.07	(0.86–1.34)	0.5308
PRA (reference: ≤50, 96.8% of patients)										
>50%	3.2	1.37	(1.25–1.49)	<.0001	1.46	(1.30–1.63)	<.0001	1.25	(1.08–1.44)	0.0024
CMV serology (reference: Donor–/Recipient–, 12.6% of patients)										
Donor–/Recipient+	20.8	1.12	(1.05–1.19)	0.0005	1.11	(1.02–1.20)	0.0157	1.12	(1.01–1.24)	0.0244
Donor+/Recipient+	35.4	1.15	(1.09–1.23)	<.0001	1.16	(1.08–1.25)	0.0001	1.13	(1.03–1.25)	0.0083
Donor+/Recipient–	17.5	1.21	(1.13–1.29)	<.0001	1.20	(1.10–1.30)	<.0001	1.21	(1.10–1.35)	0.0002
Unknown	13.6	1.09	(1.00–1.18)	0.0377	0.99	(0.89–1.10)	0.7974	1.23	(1.09–1.39)	0.0009

7.b · Risk factors for graft & patient survival: living donor transplants (n=28,469)

	% of pts	All-cause graft failure Haz. ratio	95% CI	P-value	Death-censored graft failure Haz. ratio	95% CI	P-value	Death with functioning graft Haz. ratio	95% CI	P-value
Transplant era (reference: 1995–1998, 49.2% of patients)										
1999–2001	50.8	0.89	(0.80–0.99)	0.0301	0.82	(0.72–0.94)	0.0045	1.03	(0.87–1.22)	0.7607
Donor relationship (reference: identical twin/2 haplotype sibling, 11.0% of patients)										
Parent	16.9	1.52	(1.15–2.00)	0.0032	1.27	(0.85–1.90)	0.2508	1.52	(1.01–2.29)	0.0456
Child	16.2	1.02	(0.77–1.34)	0.9028	0.54	(0.36–0.82)	0.0040	2.20	(1.50–3.22)	<.0001
Sibling (other)	24.9	1.11	(0.84–1.45)	0.4602	0.76	(0.51–1.13)	0.1719	1.64	(1.12–2.40)	0.0102
Distant/unrelated	26.1	1.08	(0.82–1.43)	0.5726	0.73	(0.49–1.10)	0.1350	1.71	(1.17–2.52)	0.0061
Unknown	5.0	0.46	(0.30–0.70)	0.0004	0.18	(0.10–0.33)	<.0001	1.89	(1.08–3.34)	0.0271
Recipient age (years) (reference: 18–34, 26.1% of patients)										
0–17	8.8	0.99	(0.87–1.13)	0.8975	0.92	(0.79–1.06)	0.2523	1.06	(0.78–1.44)	0.7097
35–49	33.4	0.91	(0.83–1.00)	0.0384	0.79	(0.72–0.88)	<.0001	1.63	(1.36–1.95)	<.0001
50–64	26.6	1.17	(1.05–1.30)	0.0038	0.75	(0.65–0.86)	<.0001	2.82	(2.31–3.43)	<.0001
65+	5.1	1.68	(1.44–1.96)	<.0001	0.76	(0.59–0.98)	0.0320	4.57	(3.57–5.85)	<.0001
Recipient gender (reference: female, 41.8% of patients)										
Male	58.2	0.90	(0.85–0.95)	0.0005	0.78	(0.72–0.84)	<.0001	1.15	(1.04–1.27)	0.0076
Recipient race (reference: white, 76.9% of patients)										
Black	16.1	0.90	(0.78–1.05)	0.1916	0.95	(0.79–1.14)	0.5934	0.86	(0.66–1.12)	0.2668
Asian	3.6	0.64	(0.48–0.84)	0.0014	0.59	(0.42–0.84)	0.0030	0.69	(0.44–1.10)	0.1198
Other	3.4	1.15	(0.95–1.40)	0.1529	1.31	(1.04–1.64)	0.0218	0.80	(0.55–1.17)	0.2477
Recipient ethnicity (reference: non-Hispanic, 87.0% of patients)										
Hispanic	13.0	0.78	(0.70–0.85)	<.0001	0.84	(0.74–0.94)	0.0029	0.65	(0.55–0.77)	<.0001
Primary cause of ESRD (reference: glomerulonephritis, 26.0% of patients)										
Diabetes	20.2	1.15	(1.06–1.26)	0.0009	0.73	(0.65–0.82)	<.0001	2.37	(2.05–2.74)	<.0001
Hypertension	12.3	1.08	(0.98–1.19)	0.1076	0.99	(0.88–1.11)	0.8417	1.49	(1.26–1.78)	<.0001
Cystic kidney disease	7.5	0.74	(0.64–0.86)	<.0001	0.61	(0.51–0.74)	<.0001	1.16	(0.93–1.46)	0.1969
Other	34.1	0.88	(0.82–0.96)	0.0026	0.74	(0.67–0.82)	<.0001	1.40	(1.19–1.63)	<.0001
Pre-transplant serology										
Hepatitis B Positive	6.0	0.97	(0.86–1.11)	0.6879	1.03	(0.88–1.20)	0.7485	0.92	(0.74–1.13)	0.4155
Hepatitis C Positive	2.8	1.38	(1.20–1.60)	<.0001	1.46	(1.21–1.76)	<.0001	1.35	(1.06–1.71)	0.0137
Education level (reference: <college, 57.9% of patients)										
College+	17.0	0.82	(0.75–0.90)	<.0001	0.82	(0.73–0.92)	0.0009	0.83	(0.72–0.95)	0.0091
Unknown	25.1	0.95	(0.89–1.02)	0.1634	0.96	(0.87–1.05)	0.3206	0.97	(0.87–1.09)	0.5895
Employment status (reference: unable to work, 25.2% of patients)										
Able to work	58.5	0.82	(0.77–0.88)	<.0001	0.84	(0.77–0.91)	<.0001	0.77	(0.69–0.86)	<.0001
Unknown	16.2	0.96	(0.88–1.05)	0.4224	0.92	(0.82–1.03)	0.1457	1.01	(0.88–1.17)	0.8774
Primary payor (reference: Medicare, 16.2% of patients)										
Private	15.5	0.91	(0.79–1.05)	0.1796	0.82	(0.68–0.99)	0.0353	1.04	(0.83–1.30)	0.7209
Other	15.0	1.01	(0.88–1.15)	0.9259	0.86	(0.72–1.02)	0.0868	1.28	(1.03–1.60)	0.0237
Unknown	53.4	1.22	(1.01–1.46)	0.0343	1.16	(0.92–1.47)	0.2050	1.21	(0.91–1.62)	0.1910
Prior dialysis time (years) (reference: <1, 37.3% of patients)										
None (preemptive)	21.5	0.78	(0.71–0.85)	<.0001	0.87	(0.78–0.97)	0.0113	0.66	(0.56–0.77)	<.0001
1–<2	20.0	1.15	(1.07–1.25)	0.0002	1.08	(0.98–1.20)	0.1083	1.28	(1.13–1.44)	0.0001
2–<3	7.8	1.22	(1.10–1.36)	0.0002	1.09	(0.95–1.25)	0.2420	1.44	(1.22–1.70)	<.0001
3+	8.3	1.35	(1.22–1.50)	<.0001	1.16	(1.01–1.33)	0.0329	1.73	(1.47–2.03)	<.0001
Unknown	5.2	0.98	(0.84–1.15)	0.8426	0.91	(0.75–1.11)	0.3615	1.15	(0.90–1.48)	0.2617
Donor age (years) (reference: <35, 34.0% of patients)										
35–49	44.5	0.92	(0.85–0.99)	0.0189	0.78	(0.71–0.85)	<.0001	1.21	(1.07–1.36)	0.0027
50–64	16.2	0.93	(0.84–1.03)	0.1615	0.68	(0.59–0.78)	<.0001	1.51	(1.28–1.79)	<.0001
65+	1.0	1.17	(0.90–1.53)	0.2300	0.95	(0.66–1.37)	0.7892	1.77	(1.21–2.59)	0.0036
Unknown	4.4	1.71	(1.21–2.40)	0.0021	2.00	(1.39–2.88)	0.0002	1.13	(0.61–2.07)	0.6982
Donor gender (reference: female, 56.0% of patients)										
Male	42.1	1.13	(1.06–1.20)	<.0001	1.27	(1.18–1.37)	<.0001	0.95	(0.86–1.04)	0.2706
Unknown	1.9	2.84	(2.00–4.02)	<.0001	3.53	(2.31–5.39)	<.0001	1.40	(0.73–2.67)	0.3092
Donor race (reference: white, 78.7% of patients)										
Black	13.4	1.50	(1.28–1.76)	<.0001	1.78	(1.47–2.15)	<.0001	0.99	(0.75–1.32)	0.9691
Asian	2.6	1.13	(0.84–1.54)	0.4161	1.18	(0.81–1.73)	0.3916	1.11	(0.67–1.84)	0.6914
Other	1.9	1.00	(0.77–1.29)	0.9847	0.94	(0.68–1.31)	0.7261	1.14	(0.74–1.76)	0.5462
Unknown	3.3	1.23	(0.86–1.78)	0.2614	1.82	(1.16–2.87)	0.0098	0.76	(0.41–1.41)	0.3862
HLA mismatches (reference: 3, 29.9% of patients)										
0	12.7	0.73	(0.57–0.94)	0.0145	0.47	(0.32–0.69)	<.0001	1.23	(0.88–1.72)	0.2227
1	7.2	0.84	(0.75–0.95)	0.0060	0.80	(0.68–0.93)	0.0035	0.93	(0.77–1.13)	0.4777
2	20.4	0.97	(0.90–1.05)	0.4339	0.96	(0.87–1.05)	0.3631	1.01	(0.89–1.15)	0.8696
4	10.1	1.07	(0.96–1.21)	0.2300	1.14	(0.99–1.32)	0.0720	0.93	(0.77–1.13)	0.4828
5	10.4	1.12	(1.00–1.26)	0.0484	1.10	(0.95–1.28)	0.2082	1.12	(0.93–1.34)	0.2393
6	5.2	1.22	(1.05–1.41)	0.0073	1.28	(1.06–1.53)	0.0085	1.12	(0.88–1.42)	0.3504
Unknown	4.3	0.82	(0.69–0.97)	0.0244	0.81	(0.65–1.00)	0.0515	0.87	(0.66–1.15)	0.3299
Body surface area matching (reference: R≤D, 31.8% of patients)										
R 1.6–2.2 m^2, D<1.6 m^2	2.4	0.98	(0.74–1.30)	0.8880	1.10	(0.76–1.59)	0.6053	0.81	(0.51–1.28)	0.3677
R>2.2 m^2, D<1.6 m^2	0.2	1.80	(0.93–3.47)	0.0818	2.70	(1.27–5.72)	0.0096	0.81	(0.20–3.26)	0.7658
Unknown	65.6	0.95	(0.83–1.10)	0.5059	0.96	(0.80–1.15)	0.6780	1.00	(0.80–1.24)	0.9838
Recipient body mass index (BMI) (reference: 18.5–24.9 kg/m^2, 41.6% of patients)										
<18.5 kg/m^2	7.1	0.92	(0.80–1.04)	0.1787	0.83	(0.71–0.96)	0.0134	1.20	(0.94–1.53)	0.1391
25.0–29.9 kg/m^2	27.6	1.02	(0.95–1.10)	0.6138	1.06	(0.96–1.16)	0.2562	0.96	(0.85–1.08)	0.5018
30.0–30.4 kg/m^2	12.6	1.10	(1.00–1.20)	0.0566	1.05	(0.93–1.19)	0.4178	1.12	(0.97–1.30)	0.1242
≥35.0 kg/m^2	5.5	1.36	(1.21–1.54)	<.0001	1.36	(1.17–1.58)	<.0001	1.31	(1.08–1.59)	0.0061
Unknown	5.6	1.16	(1.01–1.32)	0.0306	1.14	(0.96–1.35)	0.1318	1.14	(0.92–1.42)	0.2301
PRA (reference: ≤50, 98.3% of patients)										
>50%	1.7	1.19	(0.97–1.46)	0.0991	1.27	(0.99–1.62)	0.0603	1.05	(0.73–1.52)	0.7933
CMV serology (reference: donor–/recipient–, 9.5% of patients)										
Donor–/Recipient+	7.3	1.05	(0.86–1.27)	0.6453	1.03	(0.80–1.33)	0.8183	1.07	(0.79–1.46)	0.6642
Donor+/Recipient+	13.7	0.95	(0.80–1.13)	0.5596	0.95	(0.76–1.19)	0.6575	0.94	(0.71–1.26)	0.6998
Donor+/Recipient–	6.9	1.13	(0.92–1.37)	0.2454	1.00	(0.77–1.29)	0.9850	1.35	(0.97–1.86)	0.0711
Unknown	62.6	0.99	(0.82–1.21)	0.9582	0.90	(0.71–1.16)	0.4183	1.18	(0.87–1.60)	0.2872

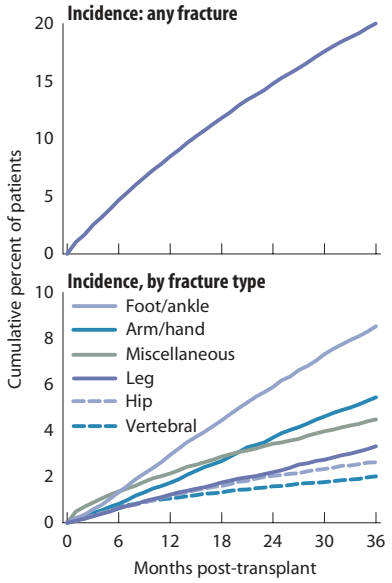
■ ***Tables 7.a–b*** *Cox proportional hazards models modeling all-cause graft failure, death-censored graft failure (return to dialysis), & death with a functioning graft, 1995–2001 combined. Patients with multiple organ transplants are excluded. In the first column are the patient or transplant characteristics (covariates) that most closely correlate with graft failure, & the proportion of the population with each characteristic. The hazard ratios in columns 3, 6, & 9 indicate the relative risk associated with each characteristic for graft failure, death-censored graft failure, & death with a functioning graft, respectively. Also shown are the 95 percent confidence intervals & P-values for each hazard ratio. Hazard ratios should be compared to the reference risk of 1.00, arbitrarily assigned to one category for each characteristic. Abbreviations: HLA, human leukocyte antigen; R, recipient; D, donor; PRA, panel reactive antibody; CMV, cytomegalovirus. Recipients of transplants from deceased donors are modeled separately from recipients of living donor transplants due to characteristics unique to each type of transplant.* ■ ***Figure 7.14*** *estimates obtained from a Cox proportional hazards model adjusted for all covariates shown in Table 7.a. Half-life estimates are conditional on first-year graft survival, & indicate the time that one-half of the patients will still have a functioning graft.* ■ ***Figure 7.15*** *estimates obtained from a Cox proportional hazards model adjusted for all covariates shown in Table 7.b. Half-life estimates are conditional on first-year graft survival.*

7.15 Survival: living donor transplants

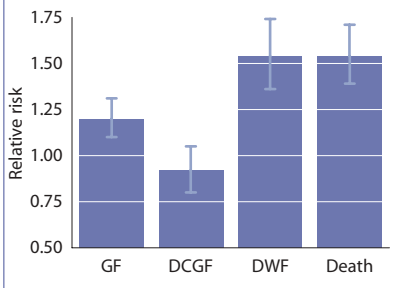


Post-transplant fractures

7.16 · Cumulative incidence of fractures



7.17 · RR of graft failure/mortality: fractures

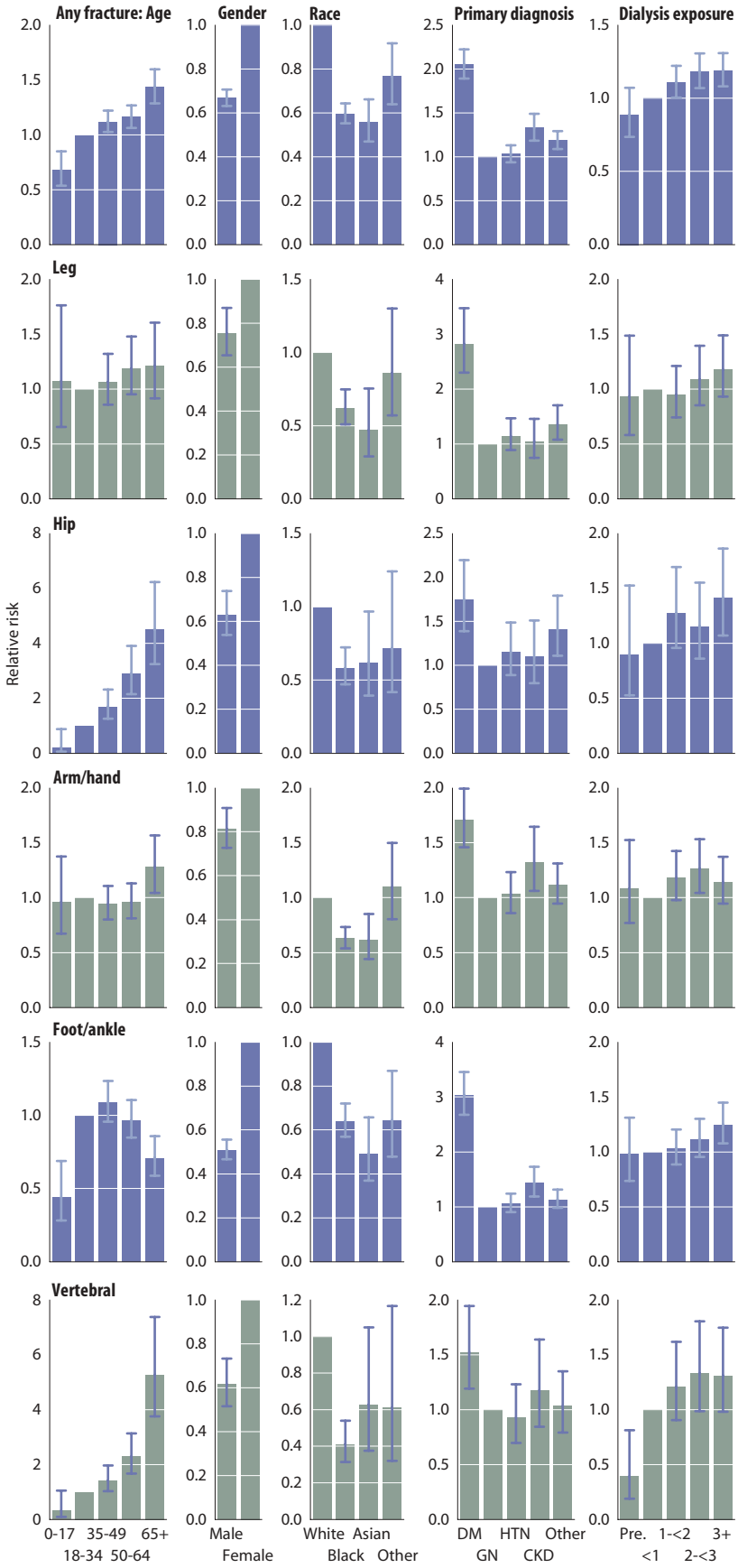


Abbreviations
GF · Graft failure
DCGF · Death-censored graft failure
DWF · Death with function

Fractures, a common occurrence after kidney transplantation (Figure 7.16), are not only an important cause of morbidity, but may also contribute to mortality after transplantation. Indeed, fractures are associated with an increased risk of death, though not of death-censored graft failure (Figure 7.17).

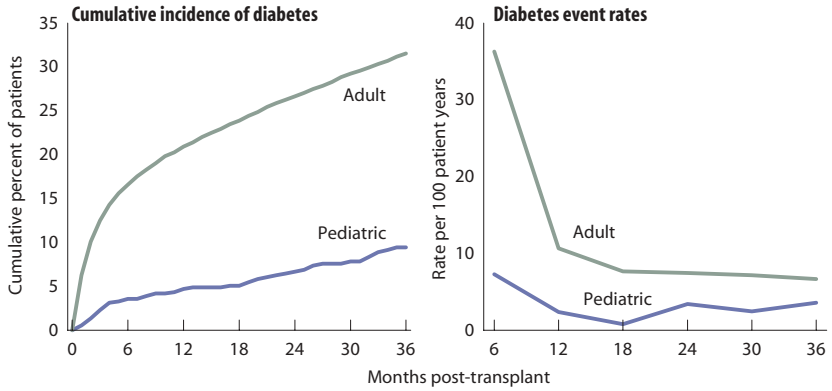
There are a number of risk factors for fractures. Older patients are more likely to have them, as are women compared to

7.18 · Relative risk of fractures, by age, gender, race, primary diagnosis, & prior dialysis exposure

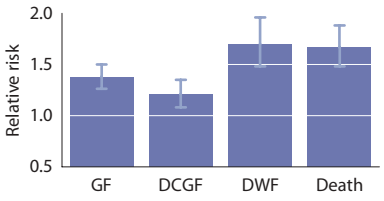


Post-transplant diabetes

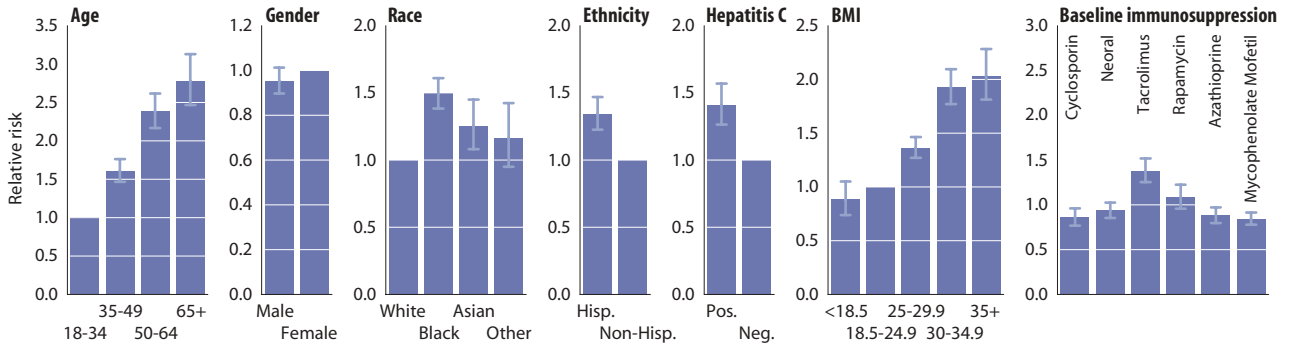
7.19 · Cumulative incidence of diabetes & associated rates of development



7.20 · RR of graft failure/mortality: diabetes



7.21 · Relative risk of post-transplant diabetes, by age, gender, race, ethnicity, hepatitis C serology, BMI, & baseline immunosuppression



men, and whites compared to racial minorities (Figure 7.18). Diabetes is an important risk factor for fractures at all sites, as is the duration of dialysis prior to transplantation.

The incidence of new onset, post-transplant diabetes mellitus (PTDM) is very high, particularly in the first six months after transplantation (Figure 7.19). Even pediatric transplant recipients are not immune to developing PTDM, albeit at a much lower rate than in adults. Age is the strongest risk factor for PTDM (Figure 7.21), with the risk of PTDM in patients age 65 and older more than two and a half times higher than that in individuals 18–34 years old. African Americans and Hispanics are more likely to develop PTDM than whites, while obesity and positive hepatitis C serology prior to transplant are also strong risk factors.

PTDM is associated with a higher risk for graft failure, death-censored graft failure, and death (Figure 7.20). These associations do not prove cause and effect. While it is plausible that PTDM contributes to worse outcomes, it may also be that other factors—such as acute rejection and its treatment with corticosteroids—cause both PTDM and graft failure, and explain the association between them.

When analyzed with an intent-to-treat model, the type of immunosuppression used at the time of transplantation is associated with a risk of PTDM (Figure 7.21). In particular, the use of tacrolimus is associated with an increased risk, while the use of mycophenolate mofetil and azathioprine are associated with a lower risk.

■ ***All figures*** *first-time, kidney-only transplant recipients, 1995–2001 combined.* ■ ***Figure 7.16*** *estimated from Cox proportional hazards models; adjusted for multiple covariates.* ■ ***Figure 7.17*** *relative risk of graft failure (including death), death-censored graft failure, death with functioning graft, & mortality (not censored at graft failure) estimated by time-dependent Cox proportional hazards models considering the first post-transplant fracture; adjusted for multiple covariates.* ■ ***Figure 7.18*** *obtained from a Cox proportional hazards model considering time to first fracture; adjusted for multiple covariates.* ■ ***Figure 7.19*** *pediatric patients (age <18) & adults, incidence estimated from Cox proportional hazards models; adjusted for multiple covariates.* ■ ***Figure 7.20*** *adult patients; relative risk of graft failure (including death), death-censored graft failure, death with functioning graft, & mortality (not censored at graft failure) estimated by time-dependent Cox proportional hazards models; adjusted for multiple covariates.* ■ ***Figure 7.21*** *adult patients, relative risks obtained from a Cox proportional hazards model; adjusted for multiple covariates.*

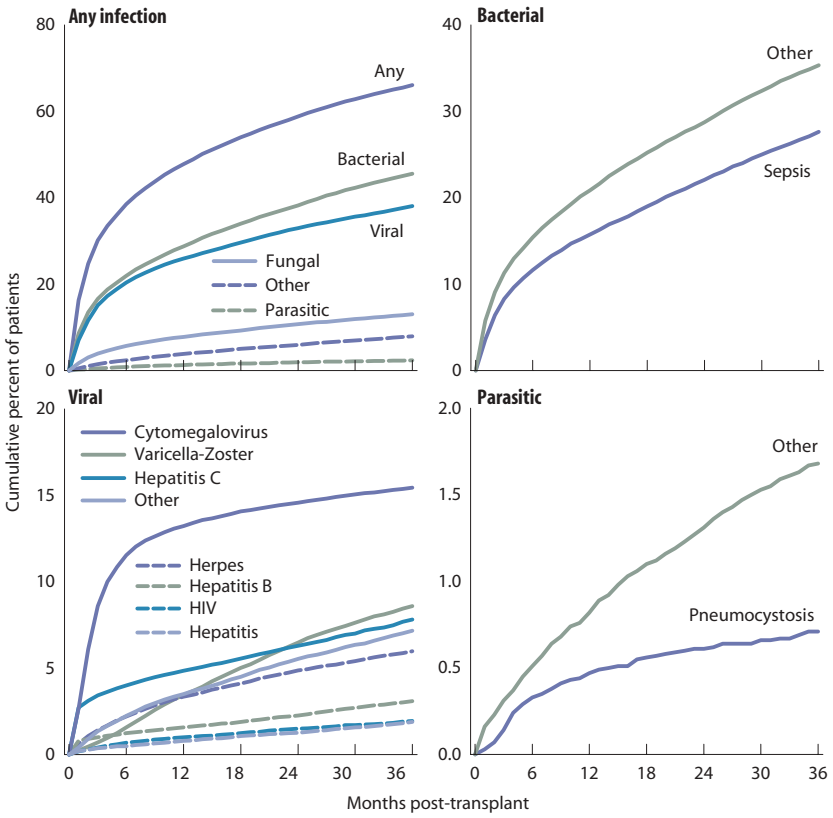
Post-transplant infections

The incidence of major infections after transplantation is very high, particularly in the first six months, although they continue to occur after this period (Figure 7.22). Bacterial and viral infections are especially frequent. Sepsis is common among bacterial infections, while cytomegalovirus infection is the most common viral type, and occurs primarily in the first six months.

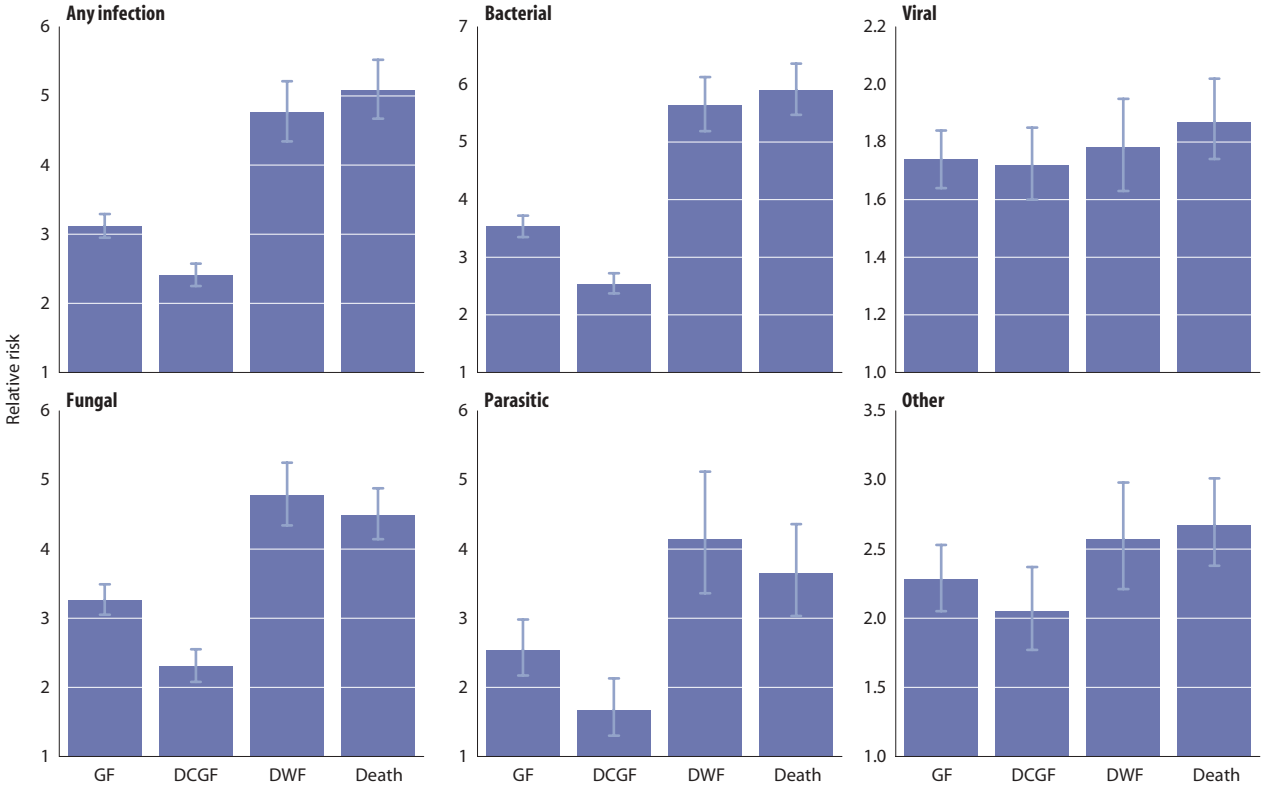
In many cases, hepatitis C and B may be present at the time of transplant, contributing to their high incidence immediately after the procedure. And despite the availability of good prophylactic agents for *pneumocystis Carinii*, infections from this parasitic organism continue to occur in a small number of transplant recipients.

Abbreviations
GF · Graft failure
DCGF · Death-censored graft failure
DWF · Death with function

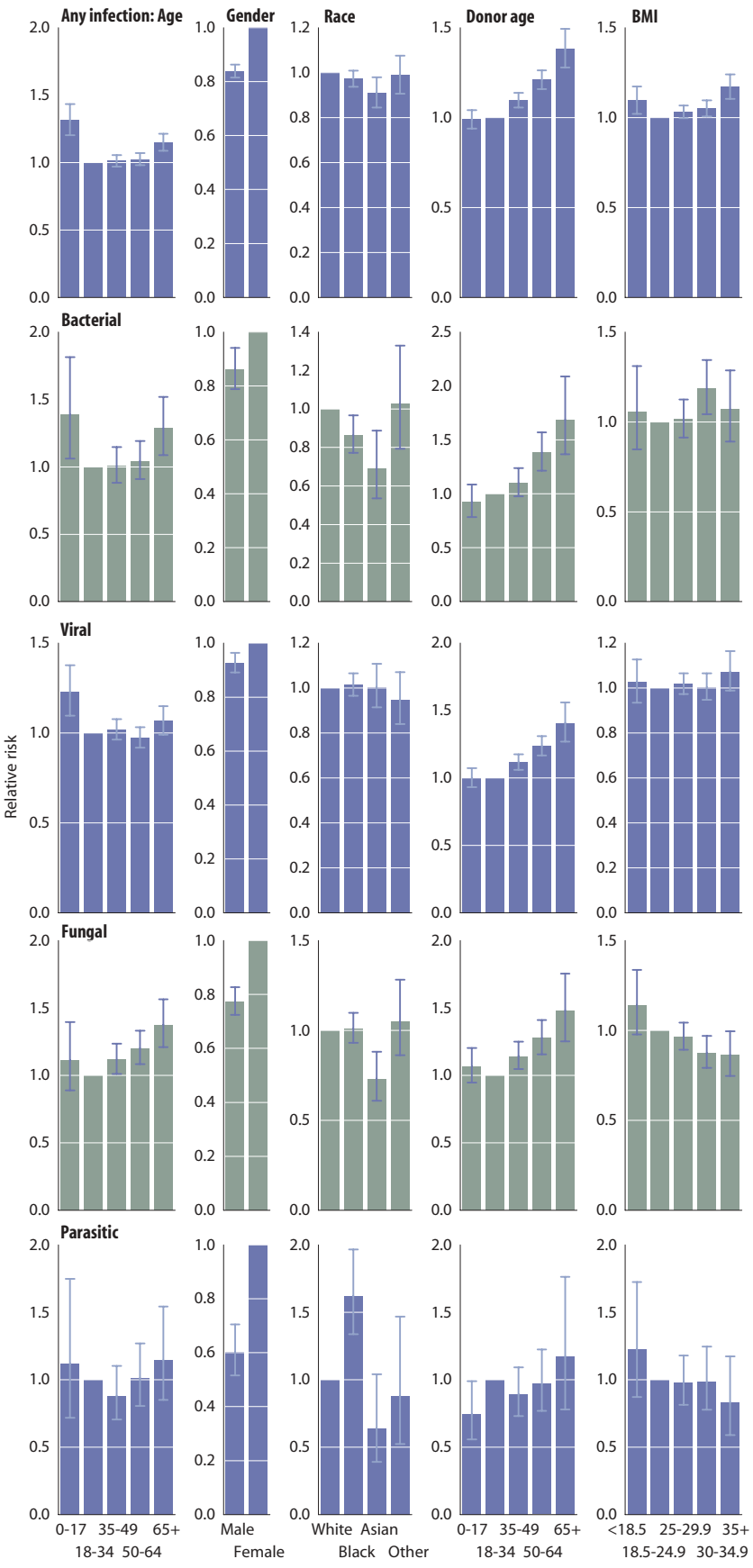
7.22 · Cumulative incidence of infection



7.23 · Relative risk of graft failure & mortality associated with infection



7.24 · Relative risk of infection, by age, gender, race, donor age, & BMI

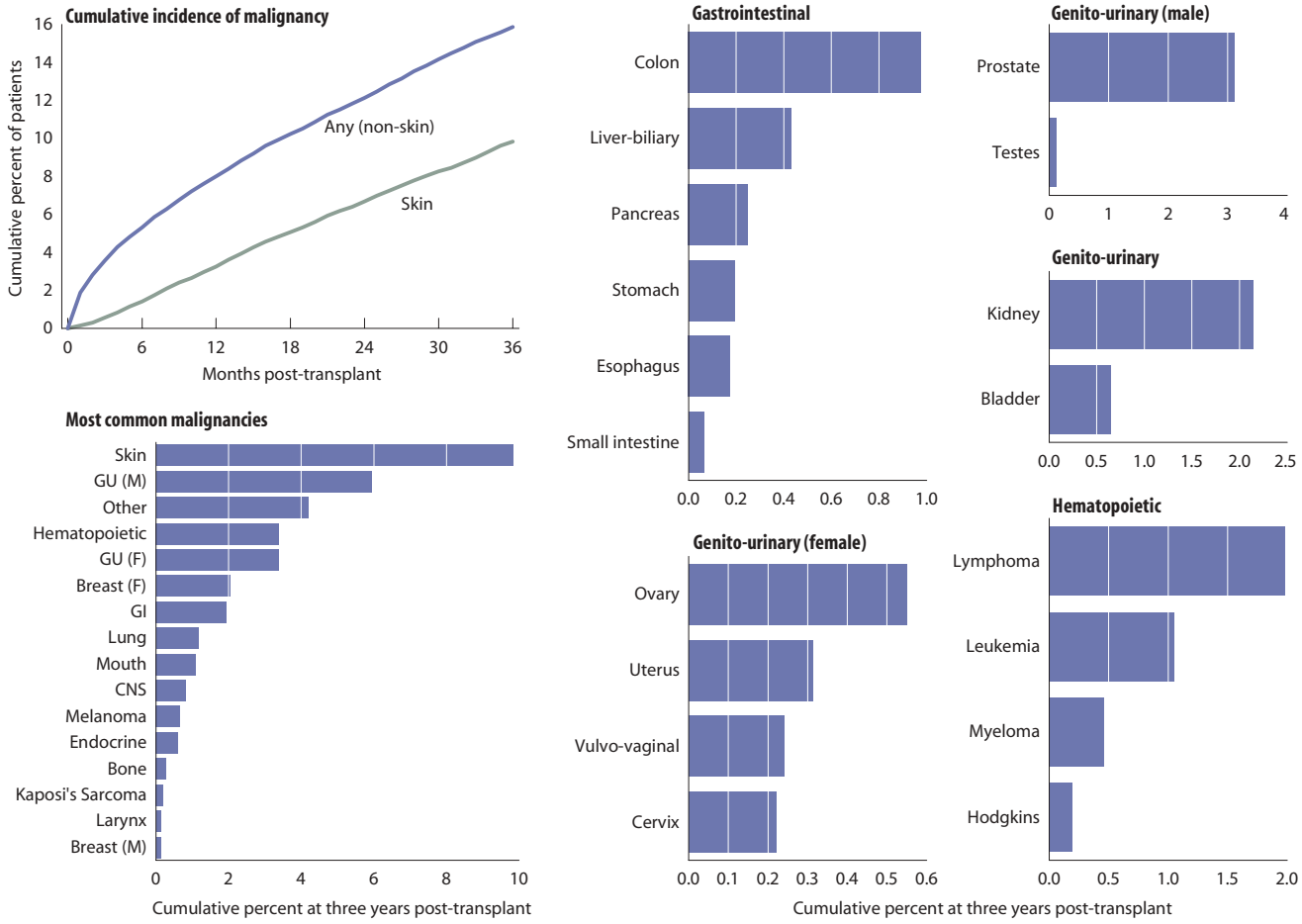


Not surprisingly, infections are associated with a higher risk of graft failure (Figure 7.23). Although much of this risk is from the almost five-fold increased risk of death, death-censored graft failure is also more than twice as likely in patients with major infections compared to those without. It is plausible that this association results from acute rejection and/or graft dysfunction causing both infections and death-censored graft failure.

Risk factors for infections include age (both young and old are at higher risk for infections), gender, donor age, and body mass index (Figure 7.24). These risk factors are similar for the different types of infection, supporting the notion that immunosuppression increases the risk of virtually all infection types.

■ ***All figures*** *first-time, kidney-only transplant recipients, 1995–2001 combined.* ■ ***Figure 7.22*** *estimated from Cox proportional hazards models; adjusted for multiple covariates.* ■ ***Figure 7.23*** *relative risk of graft failure (including death), death-censored graft failure, death with functioning graft, & mortality (not censored at graft failure) as estimated by time-dependent Cox proportional hazards models considering the time to first infection; adjusted for multiple covariates.* ■ ***Figure 7.24*** *obtained from Cox proportional hazards models; adjusted for multiple covariates.*

7.25 · Cumulative incidence of malignancy



7.26 · Relative risk of graft failure & mortality associated with malignancy