OPTN/SRTR 2011 Annual Data Report:

intestine

ABSTRACT Since 2006, the number of new intestinal transplant candidates listed each year has declined, likely reflecting increased medical and surgical treatment for intestinal failure. Historically, intestinal transplant occurred primarily in the pediatric population; in 2011, 41% of prevalent candidates on the waiting list were aged 18 years or older. The most common etiology of intestinal failure remains short-gut syndrome, which encompasses several diagnoses. The proportion of candidates with high medical urgency status decreased and time on the waiting list increased in 2011. The overall rate of transplant decreased from a peak of 92.7 transplants per 100 wait-list years in 2005 to 49.2 in 2011. The number of intestines recovered and transplanted per donor has decreased since 2007, possibly due to fewer listed patients. Almost 50% of deceased donor intestines were transplanted with another organ in 2011. Historically, the most common organ transplanted with the intestine was the liver, but in 2011 it was the pancreas. Graft survival has continued to improve over the past decade, and the number of recipients alive with a functioning intestinal graft has steadily increased since 1998. Hospitalization is common, occurring in 84.8% of recipients by 6 months posttransplant and in almost all by 4 years.

KEY WORDS Intestinal failure, intestinal transplant, parenteral nutrition, transplant outcomes.

The donor who blessed our family is anonymous for now, but we will never stop thanking them and their family. In the midst of their mourning they cared enough to give us a precious gift. I hope they know because of their loving spirit a five-year-old is alive and well today.

recipient mother

Introduction

Treatment of intestinal failure has advanced in major ways in the past decade. Survival has improved, and morbidity associated with parenteral nutrition, including liver failure, has declined. Nevertheless, intestinal transplant still plays an important role in the treatment of intestinal failure. In the past 20 years, intestinal transplant has progressed from an experimental therapy to an accepted treatment for children and adults with intractable, life-threatening intestinal failure.

Intestinal transplants may be performed in isolation, with a liver transplant, or as part of a multi-visceral transplant including any combination of liver, stomach, pancreas, colon, spleen, and kidney. For patients receiving long-term parenteral nutrition therapy, awareness is growing that if consideration for intestinal transplant is delayed until development of end-stage liver disease, outcomes before and after transplant are worse than if referral occurs earlier when only intestinal transplant is needed.

Waiting List

Since 2006, the number of new candidates listed every year for intestinal transplant has decreased (Figure 1.1), likely reflecting increased medical and surgical treatments for patients with intestinal failure. Approximately one-third of prevalent candidates on the waiting list in 2011 were inactive. In 2011, 55.4% of candidates on the waiting list were diagnosed with congenital or other short-gut syndrome, 13.7% with necrotizing enterocolitis, 5.2% with pseudo-obstruction, 0.5% with enteropathies, and 25.3% with other or unknown diagnosis (Figure 1.2). Historically, intestinal transplant occurred primarily in the pediatric population, which is reflected in the age distribution of prevalent candidates on the waiting list. The most common age group was 0 to 5 years, constituting 41.2% of wait-listed candidates in 2011 (Figure 1.2). This is a decrease from a peak of 56.6% in 2000. The percentage of candidates aged 6 to 17 years increased from 13.3% in 2008 to 18.0% in 2011, possibly also reflecting improvements in intestinal failure management. Forty-one percent of prevalent candidates on the waiting list in 2011 were aged 18 years or older. However, the proportion of new additions to the waiting list aged 18 years or older increased dramatically, from 29.0% in 1998 to 58.9% in 2011 (Figure 1.3). Sex and ethnicity distributions of new listings for intestinal transplants have not changed, nor have cause of disease distributions. The most common etiology of intestinal failure remains short-gut syndrome, which encompasses a large group of diagnoses. Medical urgency (status 1) decreased from 84.1% of listings in 2002 to 69.1% in 2011 for new additions to the waiting list (Figure 1.3). For all candidates on the waiting list, time spent on the waiting list (Figure 1.2) increased. In 2011, 41.7% of candidates were wait-listed for less than 1 year, 25.1% for 1 to 2 years, and 33.2% for more than 2 years (Figure 1.2).

The overall rate of intestinal transplant declined from a peak of 92.7 transplants per 100 wait-list years in 2005 to 49.2 transplants per 100 wait-list years in 2011 (Figure 1.4).

In 2011, the most common reason for removal from the waiting list was deceased donor transplant (75.6%), followed by death (11.9%), improvement in condition (4.8%), and being too sick to undergo transplant (2.4%) (Figure 1.5). Pre-transplant mortality has decreased dramatically over time for all age groups, from 51.5 per 100 wait-list years in 1998-1999 to 6.7 per 100 wait-list years for candidates listed in 2010-2011 (Figure 1.9).

For candidates wait-listed in 2010, the median time to transplant was 14.9 months for those aged younger than 18 years and 2.8 months for those aged 18 years or older (Figure 1.7).

Donation

The highest rate of deceased donor intestine donations has been from donors aged younger than 15 years (Figure 2.1). The number of intestines recovered and transplanted per donor has decreased since 2007 (Figure 2.2), possibly due to a decrease in listed patients. Almost 50% of deceased donor intestines were transplanted with another organ

in 2011 (Figure 2.3). Historically, the most common organ transplanted with the intestine was the liver; this practice decreased substantially from a peak of 67.7% in 2007 to the current low of 39.1% in 2011. In 2011, pancreas was the most common organ transplanted with the intestine (Figure 2.3). The overall discard rate for donor intestines decreased from 12.8% in 1998 to 5.1% in 2011 (Figure 2.4).

Transplant

Numbers of both intestine-only and intestine-liver transplants have declined since 2009 (Figure 3.1). The rate of intestinal transplants peaked in 2005 at 92.6 transplants per 100 wait-list years and steadily declined to 49.2 transplants per 100 wait-list years in 2011 (Figure 3.4). By age, intestinal transplant recipients have changed substantially; adults now outnumber pediatric recipients (Figure 3.2). The decline in pediatric rates is likely attributable to improved medical and surgical care of intestinal failure patients. Approximately 25% of patients aged 6 to 17 years waiting for an intestinal transplant are waiting for a re-transplant (Figure 3.3). In 2011, 32.6% of intestinal transplant recipients had Medicaid as their primary insurance provider, and 44.2% had private insurance (Figure 3.5). Over the past decade, the primary cause of intestinal failure has changed little (Figure 3.6). The number of patients waiting longer than 1 year for an intestinal transplant has increased (6.2% in 2001 vs. 18.6% in 2011), reflecting the improved general health of this population and the decreased number who require liver transplant.

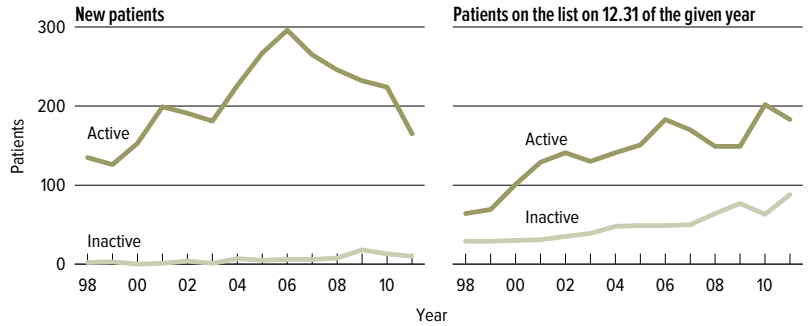
Outcomes

Graft survival has continued to improve over the past decade. Graft failure for deceased donor transplants in 2010-2011 was 16% at 6 months and 26% at 1 year; graft failure for transplants in 2008-2009 was 46% at 3 years, and for transplants in 2006-2007, 48% at 5 years (Figure 4.2). These numbers should be interpreted with caution, as they represent graft failure for two separate populations: recipients of liver-intestine transplants and of intestine-alone transplants. Outcomes are similar in adult and pediatric intestinal transplant recipients (Figure 4.3). The number of recipients alive with a functioning intestinal graft has steadily increased since 1998 (Figure 4.5). The incidence of first acute rejection increased over time post-transplant; 42.6% of all patients experienced rejection in the first 12 months (Figure 4.6). Hospitalization is very common among intestinal transplant recipients, occurring in 84.8% by 6 months post-transplant, and in almost all by 4 years post-transplant (Figure 4.7). For patients who underwent transplant in 2005-2009, the incidence of post-transplant lymphoproliferative disorder was 2.9% at 6 months, 5.3% at 1 year, 7.2% at 2 years, 8.2% at 3 years, and 10.2% at 5 years, with slightly higher rates in recipients negative for Epstein-Barr virus (Figure 4.8).

Immunosuppression

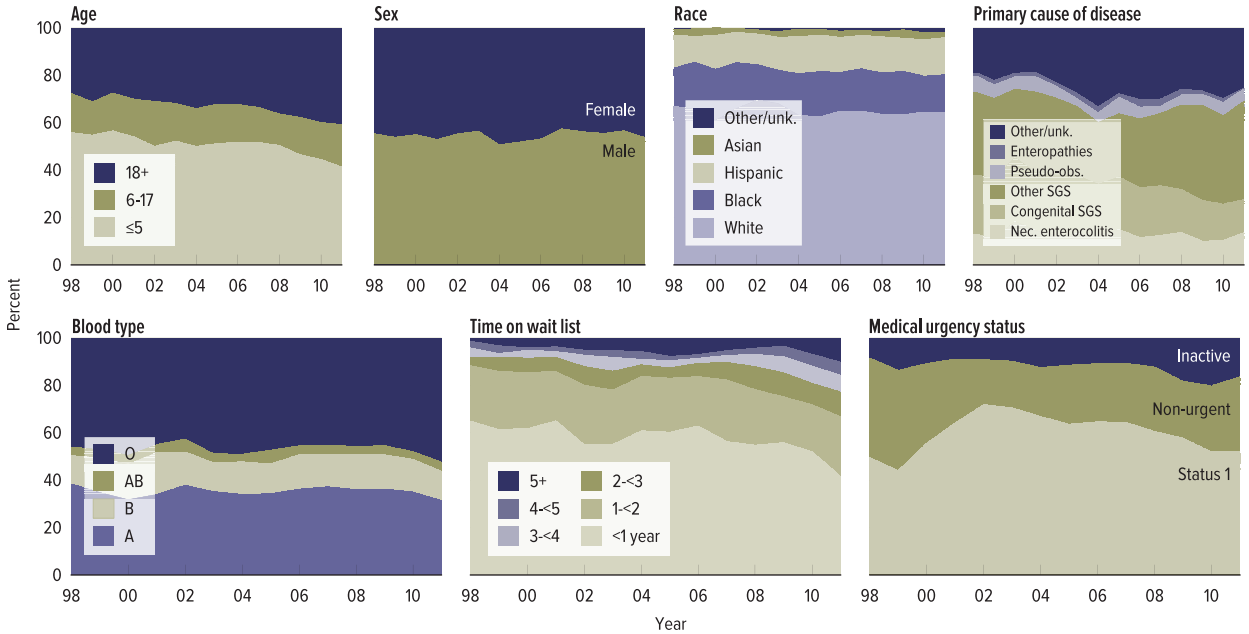
Among patients who underwent transplant in 2011, the most common initial immunosuppression regimen was tacrolimus and steroids (35.8%), followed by tacrolimus, mycophenolate (MMF/MPA), and steroids (18.7%); tacrolimus and MMF/MPA (15.4%); tacrolimus alone (13.8%); and tacrolimus, mammalian target of rapamycin (mTOR) inhibitor, and steroids (11.4%) (Figure 5.1). For induction therapy, 61.0% of patients received T-cell depleting agents, 12.2% received interleukin-2 receptor antagonists, and 22.0% received no induction (Figure 5.2). At 1 year post-transplant, the most common immunosuppression was tacrolimus alone (30.4%), followed by tacrolimus and steroids (28.6%); tacrolimus, MMF/MPA, and steroids (13.4%); and tacrolimus, mTOR inhibitor, and steroids (8.0%) (Figure 5.3). Over the past decade, tacrolimus has been the main calcineurin inhibitor, used in 96.7% of patients in 2011 (Figure 5.4). MMF/MPA use increased to 35.0% in 2011, while mTOR inhibitor use decreased from 37.7% in 2000 to 13.0% in 2011. Steroids were used in 66.7% of patients at the time of transplant and in 58.9% at 1 year post-transplant.

wait list



IN 1.1 Patients waiting for an intestinal transplant

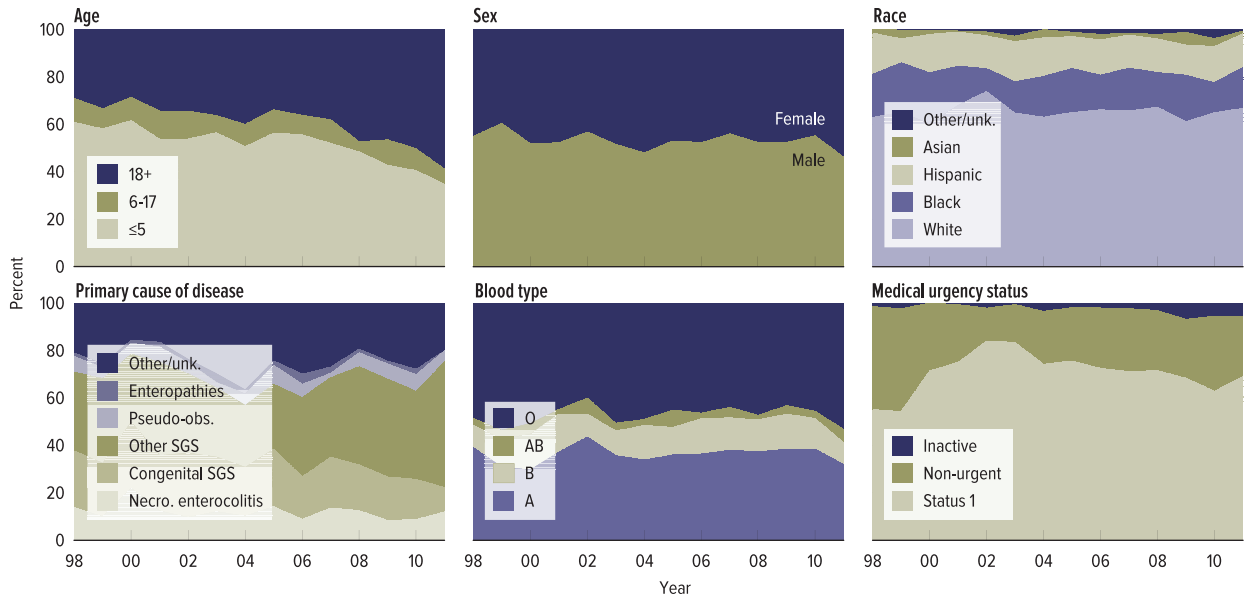
Patients waiting for a transplant. A "new patient" is one who first joins the list during the given year, without having listed in a previous year. However, if a patient has previously been on the list, has been removed for a transplant, and has relisted since that transplant, the patient is considered a "new patient." Patients concurrently listed at multiple centers are counted only once. Those with concurrent listings and active at any program are considered active; those inactive at all programs at which they are listed are considered inactive.



IN 1.2 Distribution of patients waiting for an intestinal transplant

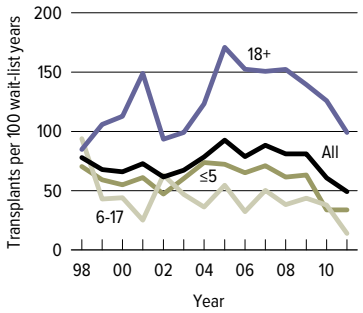
Patients waiting for a transplant any time in the given year. Age determined on the earliest of listing date or December 31 of the given year. Concurrently listed patients are counted once.

wait list



IN 1.3 Distribution of patients newly listed for an intestinal transplant

A newly listed patient is one who first joins the list during the given year, without having listed in a previous year. However, if a patient has previously been on the list, has been removed for a transplant, and has relisted since that transplant, the patient is considered a newly listed patient. Patients concurrently listed at multiple centers are counted only once.



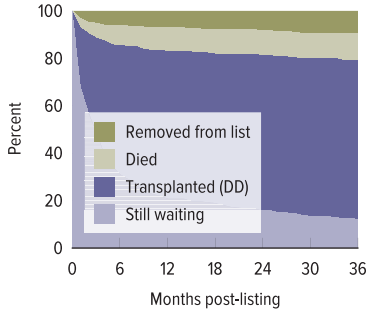
IN 1.4 Intestinal transplant rates among waiting list candidates, by age

Patients waiting for a transplant; age as of January 1 of the given year. Yearly period-prevalent rates computed as the number of deceased donor transplants per 100 patient years of waiting time in the given year. All waiting time per patient per listing is counted, and all listings that end in a transplant for the patient are considered transplant events.

	2009	2010	2011
Patients at start of year	213	226	264
Patients added during year	250	237	175
Pts removed during year	237	198	168
Patients at end of year	226	265	271
Removal reason			
Deceased donor transplant	178	149	127
Living donor transplant	1	1	-
Patient died	29	18	20
Patient refused transplant	1	0	2
Improved, tx not needed	17	21	8
Too sick to transplant	5	4	4
Other	6	5	7

IN 1.5 Intestinal transplant waiting list activity

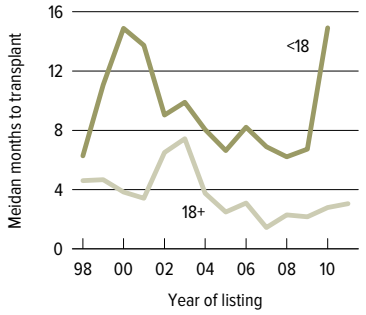
Patients with concurrent listings at more than one center are counted once, from the time of earliest listing to the time of latest removal. Patients listed, transplanted, and re-listed are counted more than once. Patients are not considered "on the list" on the day they are removed. Thus, patient counts on January 1 may be different from patient counts on December 31 of the prior year.



IN 1.6 Outcomes for patients waiting for an intestinal transplant among new listings in 2008

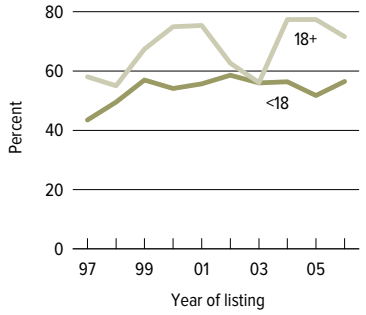
Patients waiting for a transplant and first listed in 2008. Patients with concurrent listings at more than one center are counted once, from the time of the earliest listing to the time of latest removal.

wait list



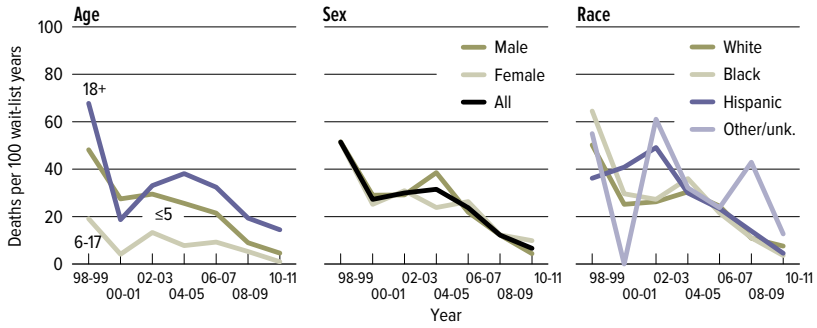
IN 1.7 Median months to intestinal transplant for wait-listed patients, by age

Patients waiting for a transplant, with observations censored at December 31, 2011; Kaplan-Meier method used to estimate time to transplant. If an estimate is not plotted for a certain year, 50% of the cohort listed in that year had not been transplanted at the censoring date. Only the first transplant is counted.



IN 1.8 Wait-listed patients who received a deceased donor intestinal transplant within five years, by age

Patients with concurrent listings at more than one center are counted once, from the time of earliest listing to the time of latest removal. Patients listed, transplanted, and re-listed are counted more than once.



IN 1.9 Pre-transplant mortality rates among patients wait-listed for an intestinal transplant

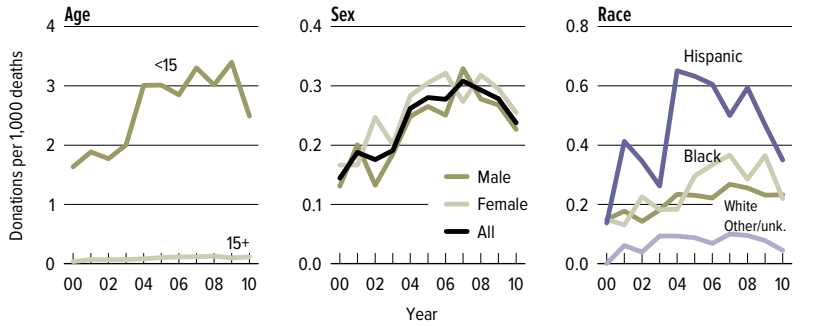
Patients waiting for a transplant. Mortality rates are computed as the number of deaths per 100 patient-years of waiting time in the given 2-year interval. For rates shown by different characteristics, waiting time is calculated as the total waiting time in the interval for patients in that group. Only deaths that occur prior to removal from the waiting list are counted. Age is calculated on the latest of listing date or January 1 of the given interval. Other patient characteristics come from the OPTN Transplant Candidate Registration form.

		2001		2011	
	Level	N	%	N	%
Age	0-5	84	52.5	126	46.5
	6-17	40	25.0	66	24.4
	18-34	12	7.5	20	7.4
	35-49	15	9.4	30	11.1
	50-64	9	5.6	26	9.6
	65+	0	0.0	3	1.1
Sex	Female	85	53.1	156	57.6
	Male	75	46.9	115	42.4
Race	White	102	63.8	161	59.4
	Black	34	21.3	48	17.7
	Hispanic	20	12.5	50	18.5
	Asian	3	1.9	7	2.6
	Other/unk.	1	0.6	5	1.9
Primary cause of disease	Necrotizing enterocolitis	25	15.6	40	14.8
	Congenital SGS	38	23.8	45	16.6
	Other SGS	50	31.3	91	33.6
	Pseudo-obstruction	9	5.6	16	5.9
	Entero-pathies	2	1.3	1	0.4
	Other/unk.	36	22.5	78	28.8
Transplant history	Listed for for first tx	147	91.9	242	89.3
	Listed for subseq tx	13	8.1	29	10.7
Blood type	A	50	31.3	83	30.6
	B	31	19.4	42	15.5
	AB	6	3.8	10	3.7
	O	73	45.6	136	50.2
Time on wait list	<1 yr	85	53.1	86	31.7
	1-<2	27	16.9	60	22.1
	2-<3	18	11.3	35	12.9
	3-<4	9	5.6	27	10.0
	4-<5	6	3.8	20	7.4
	5+	15	9.4	43	15.9
Medical urgency status	Status 1	91	56.9	98	36.2
	Non-urgent	39	24.4	86	31.7
	Inactive	30	18.8	87	32.1
Total		160	100.0	271	100.0

IN 1.10 Characteristics of patients on the intestinal transplant waiting list on December 31, 2001 & December 31, 2011

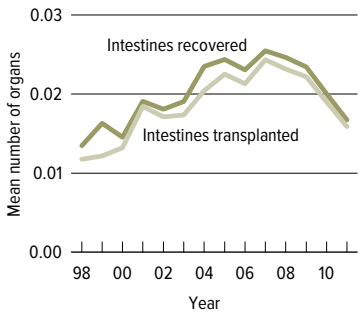
Patients waiting for a transplant on December 31, 2001 and December 31, 2011, regardless of first listing date; active/inactive status is on this date, and multiple listings are not counted.

deceased donation



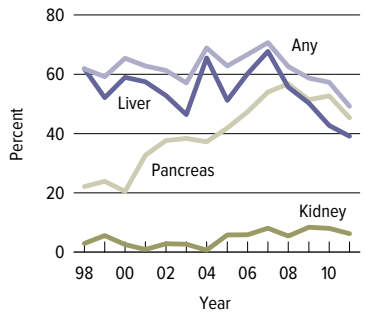
IN 2.1 Deceased donor intestinal donation rates

Numerator: Deceased donors age less than 65 whose intestine was recovered for transplant. Denominator: US deaths per year, age less than 65. (Death data available at http://www.cdc.gov/nchs/products/nvsr.htm.)



IN 2.2 Intestines recovered per donor & intestines transplanted per donor

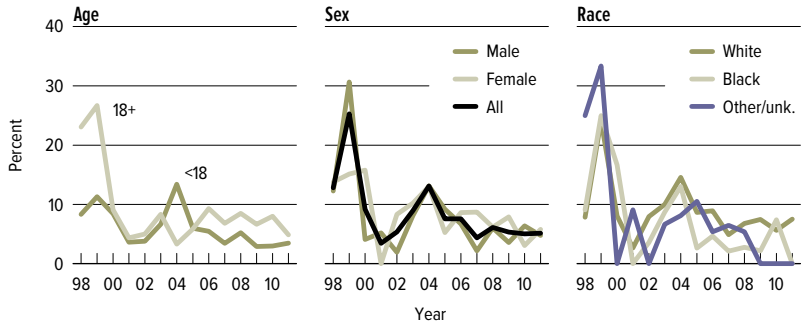
Denominator: all deceased donors with at least one organ of any type recovered for transplant. Numerator for recovery rate: number of intestines recovered for transplant in the given year; intestines recovered for other purposes are not included. Numerator for transplant rate: all deceased donor intestines transplanted in given year.



IN 2.3 Deceased donor intestines transplanted with another organ

All patients receiving a deceased donor intestine transplant. A transplant is considered multi-organ if any organ of a different type is transplanted at the same time. A multi-organ transplant may include more than two different organs in total; if so, each non-intestine organ will be considered separately.

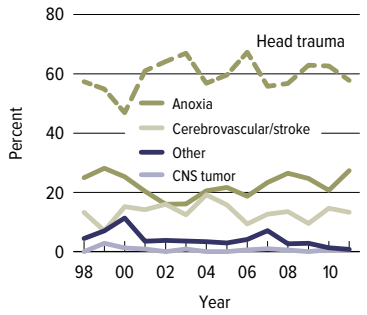
deceased donation



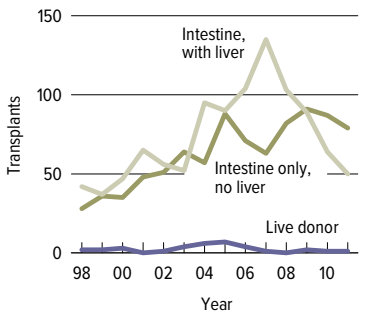
IN 2.4 Discard rates for intestines recovered for transplant
Percent of intestines discarded out of all intestines recovered for transplant.

Reasons for discard	Percent	N
Anatomical abnormalities	28.6	2
Diseased organ	28.6	2
Missing	14.3	1
Other, specify	14.3	1
Recipient determined to be unsuitable	14.3	1

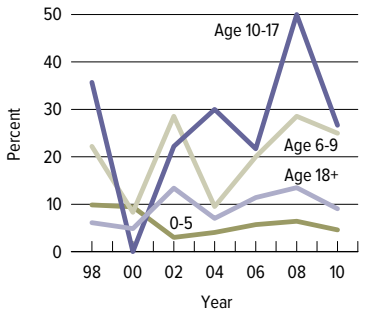
IN 2.5 Reasons for discards, 2011
Reasons for discard among intestines recovered for transplant but not transplanted in 2011.



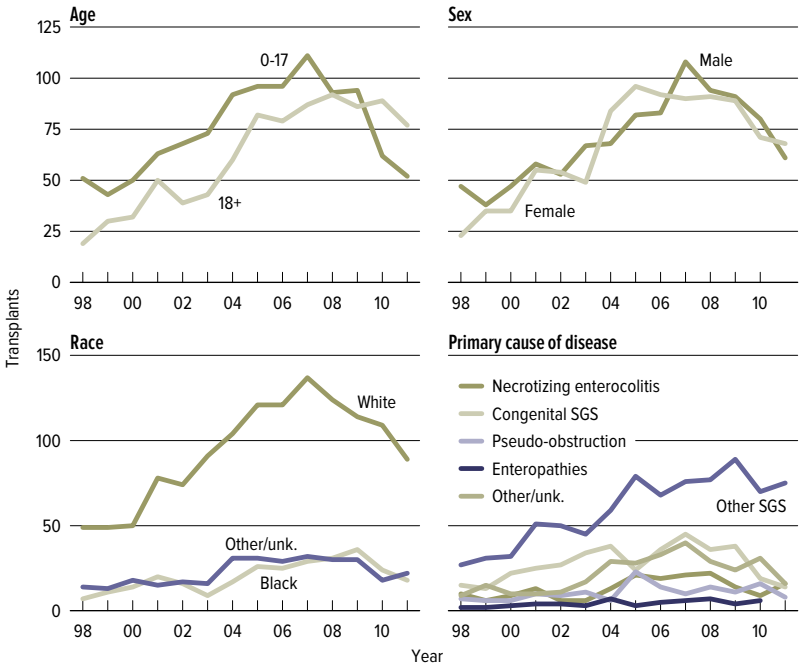
IN 2.6 Cause of death among deceased intestinal donors
Deceased donors whose intestine was transplanted. CNS = central nervous system.



IN 3.1 Total intestinal transplants
Patients receiving a transplant. Retransplants are counted.

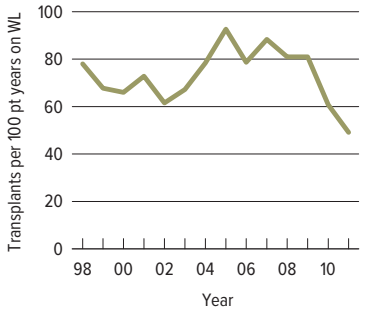


IN 3.3 Prior transplants in patients waiting for an intestinal transplant
Prior transplant of any organ is obtained from the OPTN Transplant Candidate Registration form.



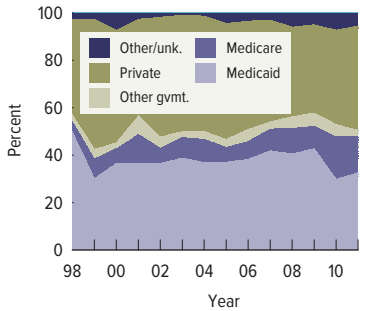
IN 3.2 Intestinal transplants
Patients receiving a transplant. Retransplants are counted.

transplant



IN 3.4 Intestinal transplant rates in waiting list candidates

Patients waiting for a transplant. Transplant rates are computed as the number of transplants per 100 patient-years of waiting time in the given year. All waiting time per patient per listing is counted, and all listings that end in a transplant for the patient are considered transplant events.



IN 3.5 Insurance coverage among intestinal transplant recipients at time of transplant

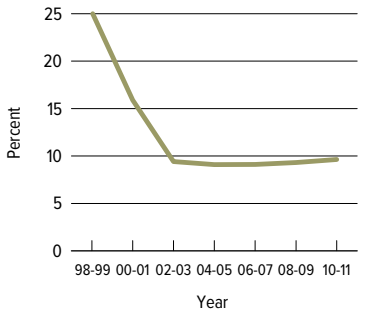
Patients receiving a transplant. Retransplants are counted.

		2001		2011	
	Level	N	%	N	%
Age	0-17	63	55.8	52	40.3
	18-34	14	12.4	23	17.8
	35-49	22	19.5	19	14.7
	50-64	13	11.5	33	25.6
	65+	1	0.9	2	1.6
Sex	Female	55	48.7	68	52.7
	Male	58	51.3	61	47.3
Race	White	78	69.0	89	69.0
	Black	20	17.7	18	14.0
	Hispanic	13	11.5	17	13.2
	Asian	2	1.8	4	3.1
	Other/unknown	0	0.0	1	0.8
Primary cause of disease	Necrotizing enterocolitis	13	11.5	16	12.4
	Congenital SGS	25	22.1	14	10.9
	Other SGS	51	45.1	75	58.1
	Pseudo-obstruction	10	8.8	8	6.2
	Enteropathies	4	3.5	0	0.0
	Other/unk	10	8.8	16	12.4
Blood type	A	41	36.3	41	31.8
	B	20	17.7	10	7.8
	AB	5	4.4	7	5.4
	O	47	41.6	71	55.0
Time on waiting list	<30 days	28	24.8	41	31.8
	31-60 days	15	13.3	15	11.6
	61-90 days	12	10.6	15	11.6
	3-<6 months	34	30.1	19	14.7
	6-<12 months	17	15.0	15	11.6
	1-<2 years	5	4.4	18	14.0
	2-<3 years	1	0.9	3	2.3
	3+ years	1	0.9	3	2.3
Medical condition	Hospitalized: ICU	14	12.4	10	7.8
	Hospitalized: not ICU	18	15.9	26	20.2
	Not hospitalized	81	71.7	92	71.3
	Unknown	0	0.0	1	0.8
Primary payer	Private	46	40.7	57	44.2
	Medicaid	41	36.3	42	32.6
	Other	26	23.0	30	23.3
Donor type	Deceased	113	100.0	128	99.2
	Living	0	0.0	1	0.8
Intestine transplant history	First transplant	106	93.8	118	91.5
	Retransplant	7	6.2	11	8.5
Patient on life support	Yes	5	4.4	12	9.3
Total		113	100.0	129	100.0

IN 3.6 Characteristics of intestinal transplant recipients, 2001 & 2011

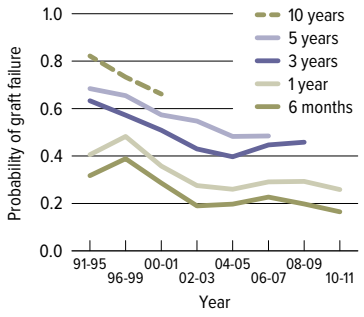
Patients receiving a transplant. Retransplants are counted.

outcomes



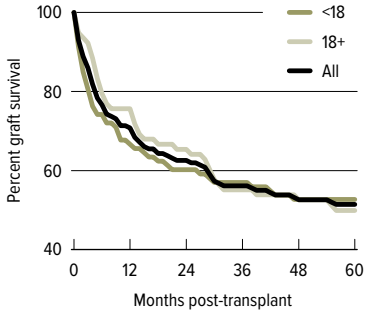
IN 4.1 Graft failure within the first 6 weeks among intestinal transplant recipients

All-cause graft failure is identified from multiple data sources, including the OPTN Transplant Recipient Registration, OPTN Transplant Recipient Follow-up, as well as death dates from the Social Security Administration.



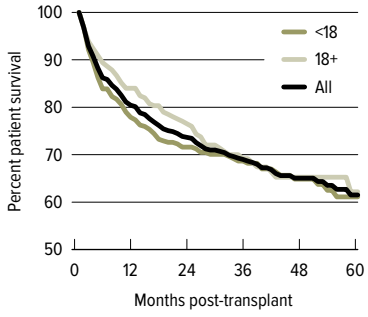
IN 4.2 Graft failure among intestinal transplant recipients: deceased donor

Cox proportional hazards models reporting probability, adjusting for age, sex, and race.



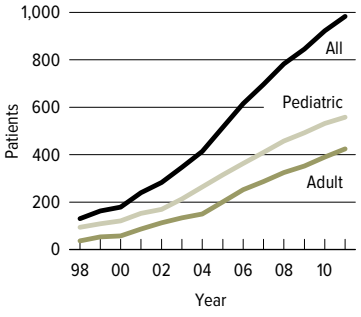
IN 4.3 Graft survival among intestinal transplant recipients transplanted in 2006, by age: deceased donors

Graft survival estimated using unadjusted Kaplan-Meier methods.



IN 4.4 Patient survival among intestinal transplant recipients, 2002–2006, by age: deceased donors

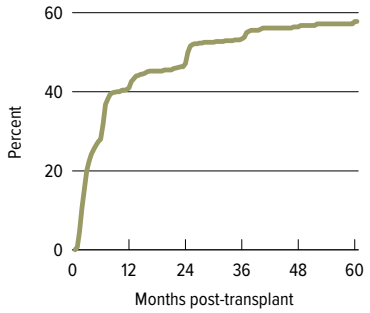
Percent patient survival using unadjusted Kaplan-Meier methods. For patients with more than one transplant during the period, only their first transplant is considered.



IN 4.5 Recipients alive & with a functioning intestinal transplant on June 30 of the year

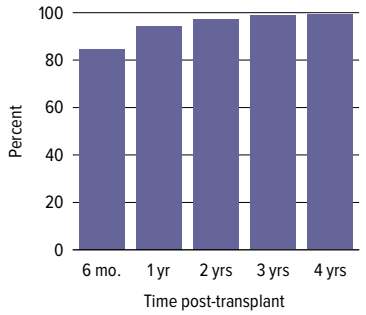
Transplants before June 30 of the year that are still functioning. Patients are assumed alive with function unless a death or graft failure is recorded. A recipient can experience a graft failure and drop from the cohort, then be retransplanted and re-enter the cohort.

outcomes



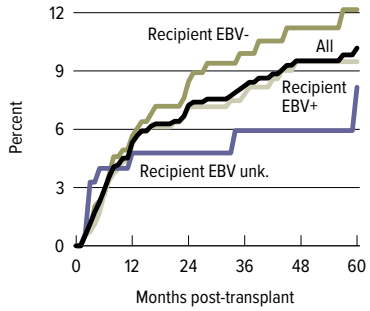
IN 4.6 Incidence of first acute rejection among patients receiving an intestinal transplant in 2005–2009

Acute rejection defined as a record of acute or hyperacute rejection, or a record of an anti-rejection drug being administered on either the Transplant Recipient Registration form or the Transplant Recipient Follow-up Form. Only the first rejection event is counted, and patients are followed for acute rejection only until graft failure, death, or loss to follow-up. Cumulative incidence, defined as the probability of acute rejection at any time prior to the given time, is estimated using Kaplan-Meier methods.



IN 4.7 Reported cumulative incidence of rehospitalizations among patients receiving an intestinal transplant in 2006–2011

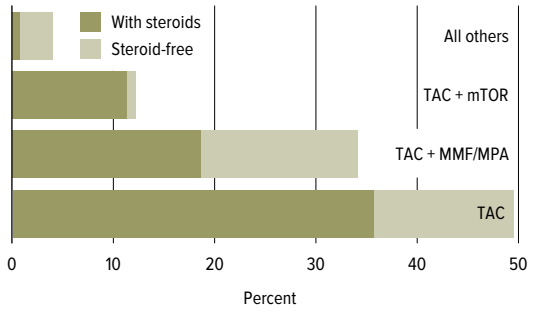
Cumulative incidence of rehosptalization post-transplant; hospitalization identified from the OPTN Transplant Recipient Follow-up form. Patients required to be alive with graft function at each time period, so denominators reduce over time.



IN 4.8 Incidence of PTLD among patients receiving an intestinal transplant in 2005–2009, by recipient Epstein-Barr virus (EBV) status at transplant

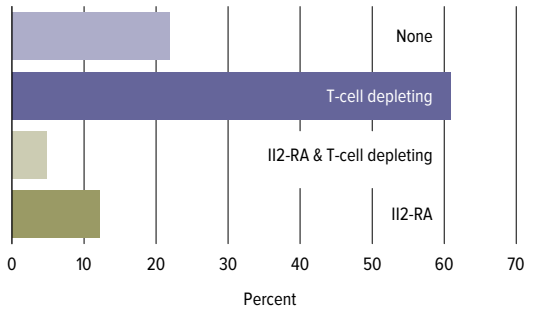
The cumulative incidence, defined as the probability of post-transplant lymphoproliferative disorder (PTLD) being diagnosed between the time of transplant and the given time, is estimated using Kaplan-Meier methods. PTLD is identified as either a reported complication or cause of death on the Transplant Recipient Follow-up forms or on the Post-transplant Malignancy form as polymorphic PTLD, monomorphic PTLD, or Hodgkin's Disease. Only the earliest date of PTLD diagnosis is considered, and patients are followed for PTLD until graft failure, death, or loss to follow-up. Patients are censored at graft failure because malignancies are not reliably reported after graft failure.

immunosuppression



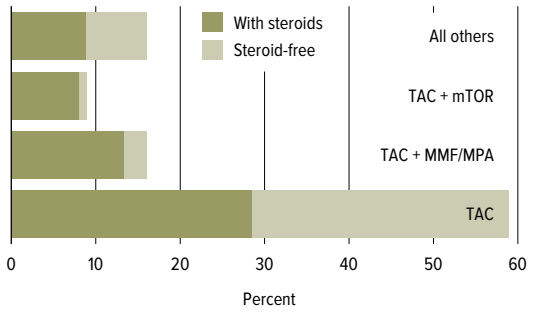
IN 5.1 Initial immunosuppression regimen in intestinal transplant recipients, 2011

Patients transplanted in 2011 and discharged with a functioning graft. Top three baseline immunosuppression regimens are given, plus the "all others" group. Regimens are defined by use of calcineurin inhibitors (TAC=Tacrolimus, Cyclo=Cyclosporine), anti-metabolites (AZA=Azathioprine, MMF/MPA=Mycophenolate), and mTOR inhibitors (mTOR). Data within each regimen are reported separately by steroid use.



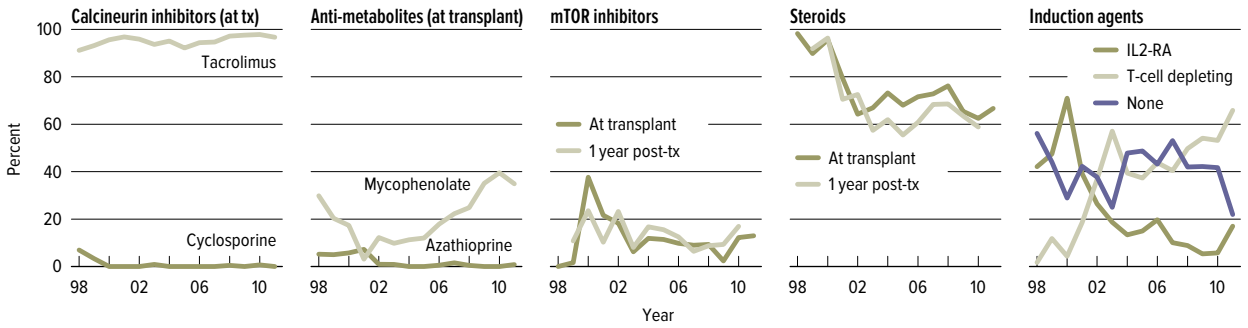
IN 5.2 Induction agents used at time of intestinal transplant, 2011

Patients transplanted in 2011 and discharged with a functioning graft.



IN 5.3 Immunosuppression regimen at one year in intestinal transplant recipients, 2010

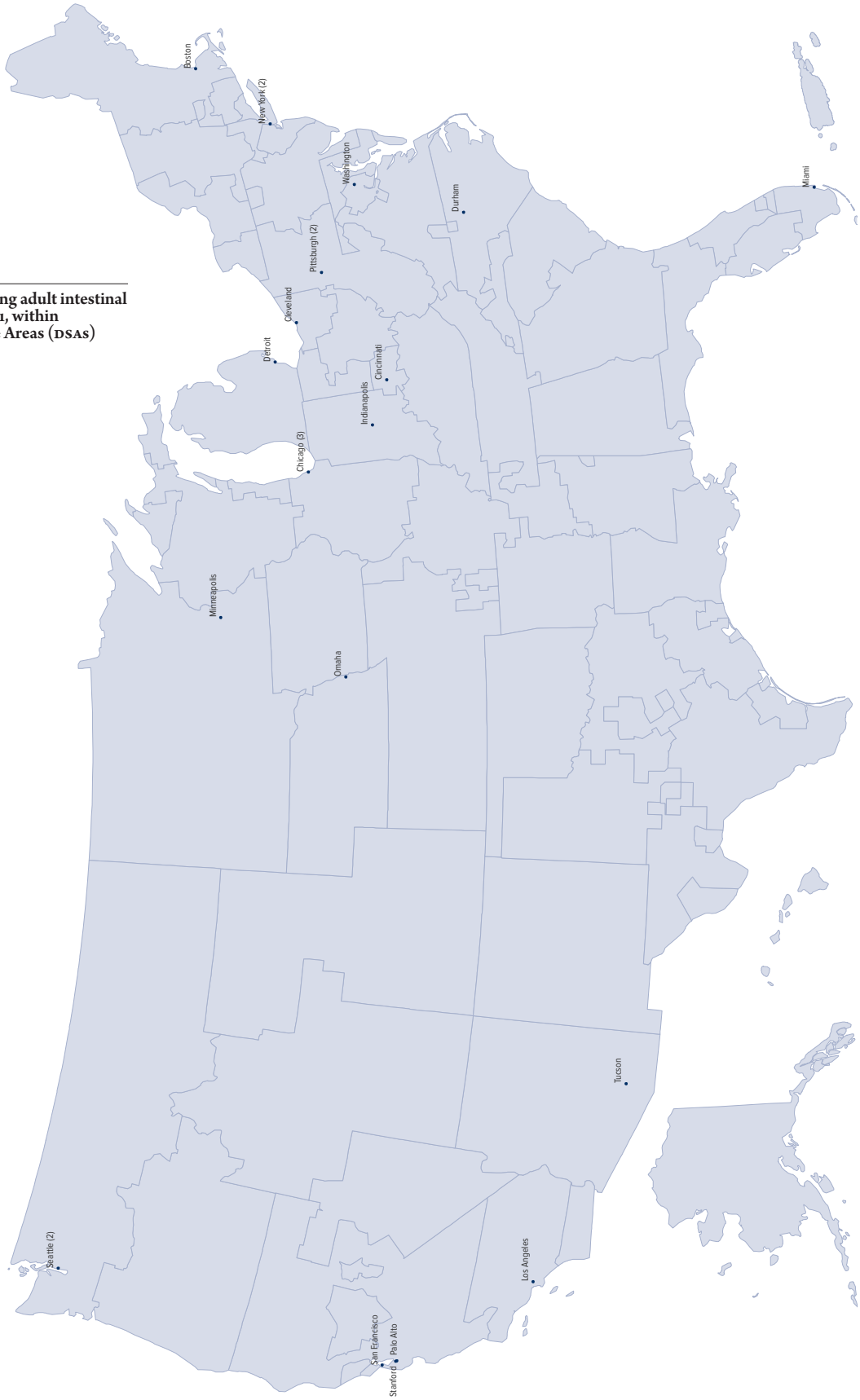
Patients transplanted in 2010 and remaining alive with graft function one year post-transplant. Top three one-year immunosuppression regimens are given, plus the "all others" group. Regimens are defined by use of calcineurin inhibitors (TAC=Tacrolimus, Cyclo=Cyclosporine), anti-metabolites (AZA=Azathioprine, MMF/MPA=Mycophenolate), and mTOR inhibitors (mTOR). Data within each regimen are reported separately by steroid use.

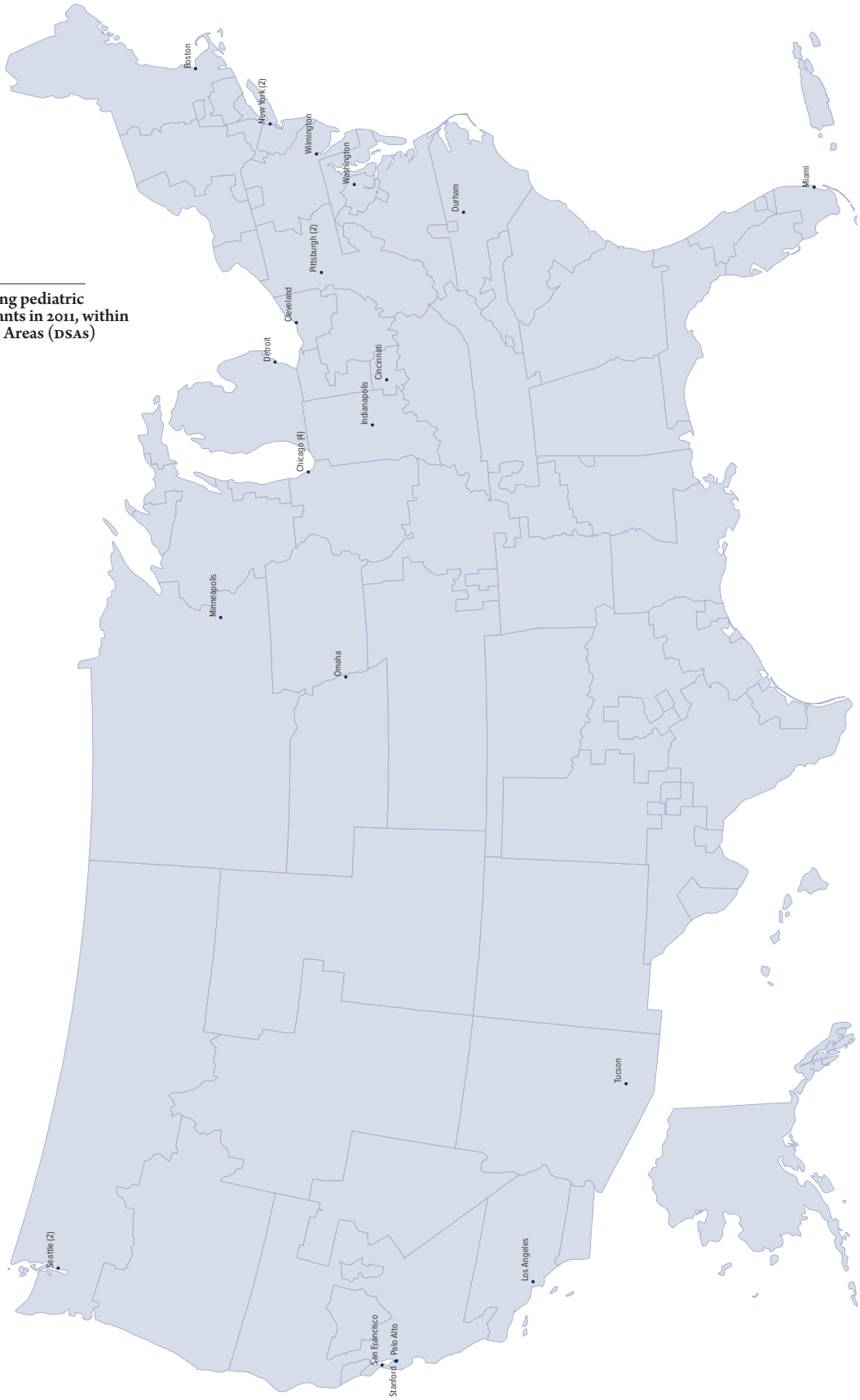


IN 5.4 Immunosuppression use in intestinal transplant recipients

One-year post-transplant data for mTOR inhibitors and steroids limited to patients alive with graft function one year post-transplant. One-year post-transplant data are not reported for 1998 transplant recipients, as follow-up data were very sparse.

IN 6.1 Centers performing adult intestinal transplants in 2011, within Donation Service Areas (DSAs)





IN 6.2 Centers performing pediatric intestinal transplants in 2011, within Donation Service Areas (DSAs)

IN 6.3 Centers performing adult intestinal transplants in 2011, within OPTN regions