Annual Report 2013

UZ Leuven Transplant Council

UZ LEUVEN | RAAD VOOR TRANSPLANTATIE

IN COLLABORATION WITH **LSGO**
(Leuven Organ Donation Partnership)

Annual Report 2013

UZ Leuven Transplant Council

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PREFACE

Dear Professor, Colleague, Sir, Madam,

We are proud to present the Transplant Council's 2013 annual report. This brochure provides a summary of donor activities and results of the various transplant care programmes undertaken during the past year, i.e. 2013, compared to previous years. I would like to thank all those involved for the preparation of this annual report.

In 2013 we saw a slight reduction (4%) in the number of registered actual donors (97) compared to 2012, (101) following both brain death (80% heart-beating or DBD) and cardiac arrest (20% non-heart-beating or DCD). An increasing number of donors originated from UZ Leuven (21%), for most (79%) we can still rely on our partner donor hospitals (LSGO – Leuven Organ Donation Partnership). Remarkably, 15 living kidney donors came forward in 2013 (as opposed to 11 in 2012). Nationally we recorded a slight drop from 320 to 306 effective donors in Belgium. The Leuven Organ Donation Partnership (LSGO) accounts for 31.7% of all deceased donors in Belgium. Activities involving tissue procurement increased considerably (compared to 2012) with 968 (782) femur head donations and 533 (474) umbilical cord blood samples. We would like to thank the transplant coordinators (Dirk Claes, Bruno Desschans, Nele Grossen, Glen Van Helleputte and Xavier Van Vlasselaer) and tissue coordinators (Dimitri Aertgeerts, Luc Ampe, Henk Desplentere and Bert Verduyckt) for their unstinting efforts.

In 2013 a total of 289 patients underwent transplantations at UZ Leuven involving an organ from a deceased donor (a drop of 20 compared to 2012) representing a 33.1% share of all transplantations in Belgium: 113 (26%) kidney, 86 (25%) liver, 59 (60%) lung, 29 (39%) heart (lung), 1 (17%) pancreas and 1 (100%) trachea transplants. No intestinal transplantations were conducted in 2013. Remarkably, there was a spectacular increase in the number of liver transplants (from 65 in 2012 to 86 in 2013), the highest number ever at UZ Leuven.

With guidance from Professor (emer) Dr. Patrick Ferdinande, Professor Dr. Diethard Monbaliu and Professor Dr. Nadine Ectors and professional support from Stijn Dirix services to the referring donor hospitals were developed in more detail. Additional training could be offered to local donor coordinators as part of the national GIFT project. This resulted in the fourth successful LSGO training day and official meeting of our internal transplant board on 5 February 2014, preceded by the annual donor and transplantation symposium. Our special thanks goes to Stijn Dirix and Margriet Goedhuys for organizing this annual meeting. The Royal Decrees published in 2012 pertaining to 1) organ removal and transplant (RD 3 July 2012) and 2) the acceptance standards for cooperation between donor hospitals and transplant centres (RD 10 November 2012) were scrutinized in conjunction with other Belgian transplant centres, the Belgian Transplant Association and the National Transplant Council. In a recent letter to the cabinet of the Minister for Public Health, Laurette Onkelinx, the risks and shortcomings associated with these new laws were listed and edited by Professor (emer) Dr. Patrick Ferdinande. It remains to be seen whether the new minister in the next federal government will undertake to amend these RDs in order not to lose potential donors and keep the already well organized procurement activities within a legal framework.

We would like to express our gratitude all those responsible in referring donor hospitals for the trust they place in UZ Leuven by entering into an agreement with our transplant centre as part of the 'Local Donor Coordination Function' contract. We would specifically like to thank the individual care providers in the emergency department, intensive care, the surgical wing and other departments for their tireless efforts and commitment, which made the donor procedures in their hospital possible in 2013.

If necessary, our board members are at your disposal to provide further information on the content of this annual report and our procedure regarding donor availability on location in your hospital. Speaking on behalf of all members of the Transplant Council I would like to express our hope that we can continue our successful cooperation in the coming year.

Yours faithfully,

Professor Dr. Dirk Van Raemdonck
Chairman of the Transplant Council
dirk.vanraemdonck@uzleuven.be

TRANSPLANT BOARD MEMBERS

• Luc Ampe	tissue bank activity centre, tissue coordinator representative
• Dr. Johan De Coster	anaesthesiology, donor work group representative
• Professor Dr. Pierre Delaere	ear, nose & throat department, head and neck surgery, trachea transplant representative
• Professor Dr. Paul De Leyn	thorax surgery, lung transplant representative
• Dr. Didier Desruelles	emergency medicine, donor work group representative
• Bruno Desschans	transplant coordination activity centre, lead transplant coordinator
• Professor Dr. Daan Dierickx	haematology
• Stijn Dirix [1]	donor work group representative
• Professor Dr. Nadine Ectors	bio banking activity centre, coordinator, donor work group representative
• Professor Dr. Marie-Paule Emonds	medical director HILA, tissue typing representative
• Professor Dr. Patrick Ferdinande	intensive medicine, chairman of the donor work group
• Professor Dr. Pieter Gillard	endocrinology, beta-cell and pancreas transplant representative
• Professor Dr. Ina Jochmans	abdominal transplant surgery and transplant coordination, kidney, pancreas, intestine and liver transplant representative
• Dr. Noël Knops	paediatrics, paediatric transplant representative
• Professor Dr. Dirk Kuypers	nephrology, kidney transplant representative
• Professor Dr. Johan Maertens	haematology, bone marrow transplant representative
• Professor Dr. Bart Meyns	cardiac surgery, heart transplant representative
• Professor Dr. Diethard Monbaliu	abdominal transplant surgery and transplant coordination, procurement representative, donor work group representative, kidney, pancreas, intestine and liver transplant representative
• Professor Dr. Frederik Nevens	hepatology, liver transplant representative
• Professor Dr. Arne Neyrinck	anaesthesiology, donor work group representative
• Professor Dr. Jacques Pirenne	abdominal transplant surgery and transplant coordination, medical supervisor transplant coordination, kidney, pancreas, intestine and liver transplant representative
• Professor Paul Schotsmans	centre for biomedical ethics and rights, medical ethics commission representative
• Professor Dr. Peter Sinnaeve	cardiology, donor work group representative
• Professor Dr. Sophie Van Cromphaut	intensive medicine, donor work group representative
• Professor Dr. Steven Vanderschueren	donor lawyer living donation transplants
• Professor Dr. Johan Vanhaecke [2]	cardiology, heart transplant representative
• Professor Dr. Johannes Van Loon	neurosurgery, donor work group representative
• Professor Dr. Wim Van Paesschen	neurology, donor work group representative
• Professor Dr. Dirk Van Raemdonck	thorax surgery, chairman of the transplant council
• Professor Dr. Geert Verleden	pneumology, lung transplant representative
• Professor Dr. Joost Wauters	general internal medicine, donor work group representative

[1] secretary

[2] vice chair

TRANSPLANT COORDINATION

Head of department

Professor Dr. Jacques Pirenne | abdominal transplant surgery and transplant coordination

Transplant coordinators

Dirk Claes

Bruno Desschans

Nele Grossen

Glen Van Helleputte

Xavier Van Vlasselaer

Stijn Dirix | Transplant Council

TISSUE COORDINATION

AC bio banking coordinator

Professor Dr. Nadine Ectors | tissue and cell banks

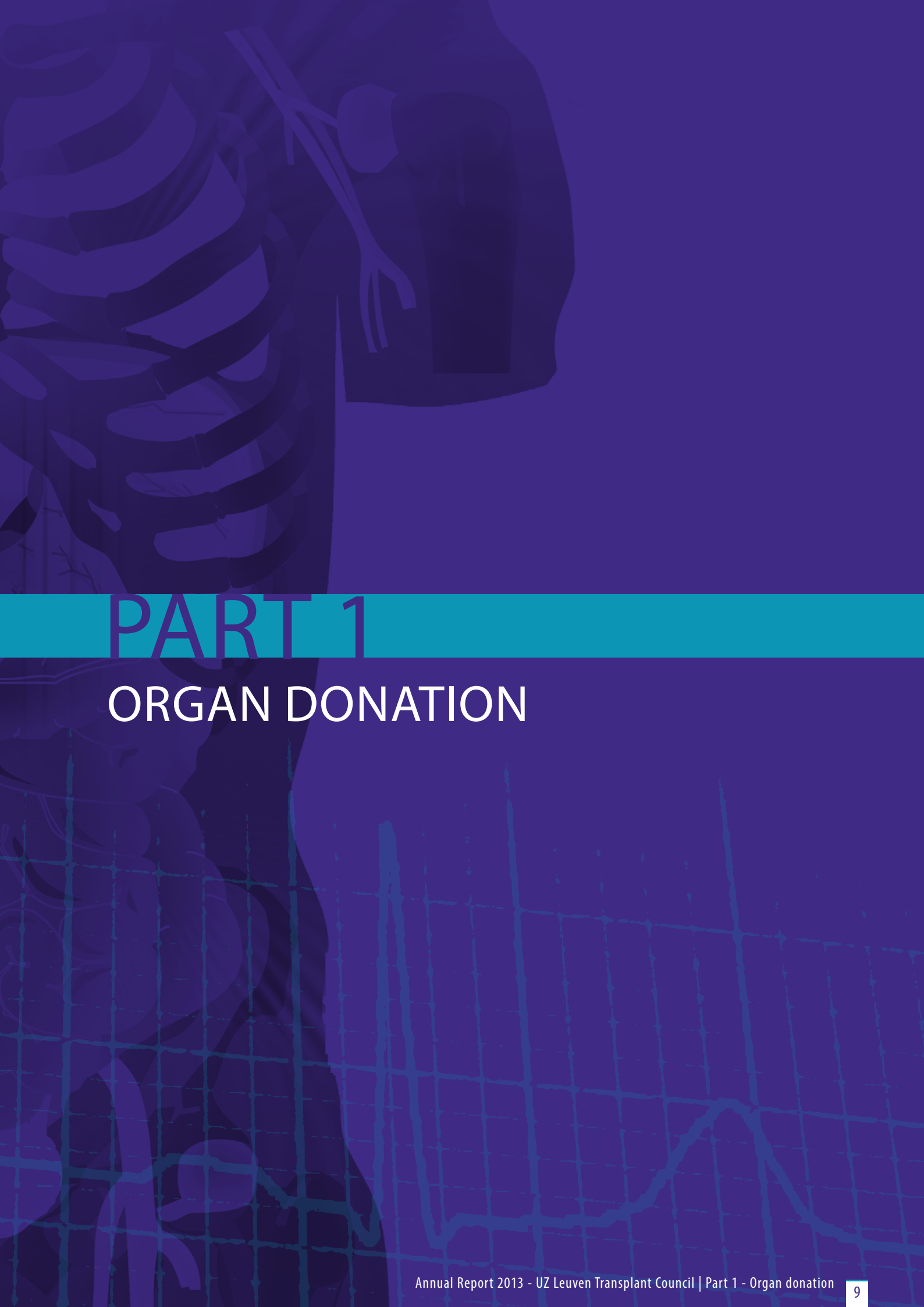
Tissue coordinators

Dimitri Aertgeerts

Luc Ampe

Henk Desplentere

Bert Verduyckt



PART 1
ORGAN DONATION

Potential and effective donor registrations: UZ Leuven and partner hospitals

Table 1.1 illustrates the annual evolution of donor potential in the group of partner donor hospitals and UZ Leuven.

TABEL 1.1 | evolution of number of potential donor registrations 1999-2013. DBD or heart-beating donors (DCD or non-heart-beating donors) (hospitals with at least one donor registration in the past fifteen years)

Centre		'99	'00	'01	'02	'03	'04	'05	'06	'07	'08	'09	'10	'11	'12	2013 DBD/(DCD)
Aalst	OLV ZH – campus Aalst	9	11	11	5	4	3	4	5 (1)	6	3	-	2	3 (1)	3	**6**
Antwerpen	ZNA Stuivenberg	-	-	-	-	-	-	-	-	-	-	-	-	1	1	**-**
Assebroek	AZ St-Lucas	1	5	1	4	1	1	1	2 (1)	2	2	-	2	3	3	**2**
Bonheiden	Imelda ZH	2	4	1	-	4	3	1	2 (2)	7	4	3	4	4	5	**9**
Brugge	AZ St-Jan	2	4	2	2	3	4	2	4	5	3	11	3	9	3	**2 (3)**
Brussel	Kliniek St-Jan	-	-	-	-	-	-	-	-	1	-	-	-	-	-	**-**
Deinze	St-Vincentius ZH	-	1	1	-	-	-	(1)	1	-	-	-	1	-	-	**-**
Dendermonde	AZ St-Blasius	1	-	-	-	-	-	-	-	-	-	-	-	-	2	**-**
Genk	ZOL – campus St-Jan	13	15	12	10 (1)	10	6	13(1)	15 (2)	15 (1)	9	9	12 (1)	11 (2)	12 (1)	**13**
Gent	AZ Maria Middelares	-	-	-	-	-	-	-	-	(1)	-	-	-	-	-	**-**
Gent	AZ St-Lucas	2	6	8	3	3 (1)	7 (1)	4 (2)	4	-	-	-	-	-	-	**-**
Hasselt	Jessa ZH – campus Virga Jesse	4	4	12	1	5	5	5	2	7	2 (3)	10 (3)	10	8 (3)	9 (6)	**12 (5)**
Hasselt	Jessa ZH – campus Salvator	4	3	3	2	3	-	2	4	2(1)	5	1	-	3 (1)	-	**-**
Herentals	AZ St-Elisabeth	-	-	-	-	-	-	-	-	1	-	-	-	-	1	**2**
Heusden	St-Franciskus ZH	-	1	1	-	2	6	3	7 (1)	3	5	2	3	9 (1)	7 (1)	**6**
Ieper	Jan Yperman ZH	-	-	1	-	-	-	1	1	1	-	1	6	2 (1)	3 (1)	**1**
Izegem	St-Jozefskliniek	-	-	-	-	-	-	-	-	-	-	(1)	-	(1)	-	**-**
Knokke - Blankenberge	AZ Zeno	-	1	-	-	-	-	-	1	-	-	-	2	1 (1)	-	**1 (1)**
Kortrijk	AZ Groeninge	4	1	3	2	4	2	11	7	10	6	7 (1)	2	14	11	**5 (1)**
Lier	H. Hart ZH	2	5	3	2	5	2	3	7 (1)	7	6	4 (1)	3 (1)	8	4 (2)	**6 (1)**
Malle-Zoersel	AZ St-Jozef	-	1	-	2	-	1	2	1	-	1	(1)	1	1 (1)	-	**-**
Mechelen – Duffel	AZ St-Maarten	-	-	-	-	-	-	-	-	-	1	-	2	1	-	**3**
Menen	AZ Delta – campus Rijselstraat	2	2	3	1 (1)	1	-	1	2	-	-	-	1	-	-	**1 (1)**
Mol	H. Hart ZH	-	-	-	-	-	-	1 (1)	1	(1)	1	1	-	2	-	**2 (1)**
Oostende	AZ Damiaan	2	2	3	5	4	6	1	7	4 (1)	6 (2)	2 (1)	1	1	3 (1)	**2 (2)**
Overpelt	Maria ZH	-	-	-	-	-	-	-	-	(1)	1	1 (1)	-	(1)	(1)	**-**
Roeselare	AZ Delta – campus Wilgenstraat	15	11	14	16	12	19	13 (1)	14 (4)	13 (1)	10 (6)	12 (4)	15 (3)	9 (8)	15 (13)	**18 (17)**
St-Niklaas	AZ Nikolaas	-	3	5	5	3	4 (1)	-	-	3	3	1	2 (1)	3	1	**2**
St-Truiden	Regionaal ZH St-Trudo	-	5	2	-	1	3	-	1	1	1	6	4	1	2	**3**
Tielt	St-Andries ZH	-	2	3	-	-	2	-	1	3	1	-	1	2	1	**1**
Tienen	Regionaal ZH H. Hart	-	-	-	-	-	-	1	-	-	-	-	-	-	-	**-**
Tongeren	AZ Vesalius	-	1	-	-	-	-	-	2	-	1	1	-	-	2	**-**
Torhout	St-Rembert ZH	2	1	-	-	-	-	-	2	-	1	-	2	1 (1)	1	**-**
Turnhout	AZ – campus St-Jozef	-	-	-	-	-	-	-	-	1 (2)	-	-	-	-	-	**-**
Turnhout	AZ – campus St-Elisabeth	2	2	2	2	4	4	6	3	2 (1)	4	4	7	12	8	**5 (1)**
Veurne	AZ St-Augustinus	4	-	-	2	1	2	3	1	3 (3)	8 (5)	7 (8)	13 (15)	8 (10)	8 (6)	**10 (10)**
Vilvoorde	AZ Jan Portaels	-	-	-	-	-	-	1	-	-	-	1	1	1	1 (2)	**1**
Waregem	OLV van Lourdes ZH	1	-	-	1	-	-	1	-	(1)	1	1 (1)	1	-	1	**-**
Zottegem	St-Elisabeth ZH	2	-	-	3	1	-	1	1	1	-	-	-	-	-	**-**
Leuven	UZ Leuven	16	22	18	19	25 (1)	19 (2)	34(4)	21	31 (4)	17 (11)	28 (5)	31 (11)	35 (15)	30 (12)	**36 (19)**
SUBTOTAL	DBD - heart-beating	**90**	**113**	**109**	**87**	**96**	**99**	**115**	**119**	**129**	**102**	**113**	**132**	**153**	**137**	**149**
SUBTOTAL	DCD non-heart-beating	**-**	**-**	**-**	**2**	**2**	**4**	**10**	**12**	**18**	**27**	**27**	**32**	**47**	**46**	**62**
TOTAL		**90**	**113**	**109**	**89**	**98**	**103**	**125**	**131**	**147**	**129**	**140**	**164**	**200**	**183**	**211**

TABEL 1.2 | evolution of the number of effective and refused potential donors (+ reason for refusal)

	2010	2011	2012	2013
Effective donors	90 (54,9%)	108 (54%)	101 (55,2%)	97 (46%)
Potential donors refused of which:	74 (45,1%)	92 (46%)	82 (44,8%)	114 (54%)
Medical contra-indication, Of which in situ refusal	40 (54%), 5 (6,8%)	56 (60,9%), 9 (9,8%)	44 (53,7%), 1 (1,2%)	65 (57%), 5 (4,4%)
'Not brain dead'+ age (average) and no potential DCD cat. III because of various factors (no DCD cat. III protocol in donor ZH – patient too old – precarious condition ...)	25 (33,8%) 77 year (27-91)	10 (10,9%) 80 year (54-87)	19 (23,2%) 71 year (39-87)	15 (13,2%)
Donor refusal (National Register)	-	2 (2,2%)	1 (1,2%)	3 (2,6%)
Family refusal	8 (10,8%)	22 (23,9%)	16 (19,5%)	28 (24,6%)
Refused by Public Prosecutor's office	1 (1,4%)	2 (2,2%)	2 (2,4%)	-
Legal contra-indication	-	-	-	3 (2,6%)

TABEL 1.3 | evolution of the number of effective donors 1999-2013. DBD or heart-beating donors (DCD or non-heart-beating donors) (hospitals with at least one effective donor registration)

Centre		'99	'00	'01	'02	'03	'04	'05	'06	'07	'08	'09	'10	'11	'12	2013 DBD/(DCD)
Aalst	OLV ZH – campus Aalst	8	10	10	3	4	2	2	4	4	3	-	2	2 (1)	1	5
Antwerpen	ZNA Stuivenberg	-	-	-	-	-	-	-	-	-	-	-	-	1	-	-
Assebroek	AZ St-Lucas	1	5	-	3	1	-	-	-	2	1	-	2	3	3	-
Bonheiden	Imelda ZH	2	3	-	-	4	1	-	2	5	2	1	2	1	3	4
Brugge	AZ St-Jan	1	3	2	-	2	3	1	3	4	3	9	3	6	3	(3)
Deinze	St-Vincentius ZH	-	1	-	-	-	-	-	1	-	-	-	1	-	-	-
Dendermonde	AZ St-Blasius	1	-	-	-	-	-	-	-	-	-	-	-	-	1	-
Genk	ZOL – campus St-Jan	7	11	9	9	9	5	11	12 (1)	12 (1)	5	7 (1)	9 (1)	9 (1)	6 (1)	7
Gent	AZ Maria Middelares	-	-	-	-	-	-	-	-	(1)	-	-	-	-	-	-
Gent	AZ St-Lucas	2	5	6	1	2 (1)	5 (1)	2	4	-	-	-	-	-	-	-
Hasselt	Jessa ZH – campus Virga Jesse	3	1	10	-	3	4	3	1	3	(1)	4 (1)	9	5 (1)	5 (2)	6 (3)
Hasselt	Jessa ZH – campus Salvator	2	3	2	2	2	-	-	2	1	5	1	-	2 (1)	-	-
Heusden	St-Franciskus ZH	-	-	1	-	2	6	-	6 (1)	3	4	2	1	5	3	4
Ieper	Jan Yperman ZH	-	-	-	-	-	-	1	-	-	-	1	2	2	2	1
Knokke - Blankenberge	AZ Zeno	-	1	-	-	-	-	-	-	-	-	-	-	-	-	-
Kortrijk	AZ Groeninge	2	1	2	2	4	2	8	6	6	3	7	1	8	7	4 (1)
Lier	H. Hart ZH	-	5	1	1	4	2	3	4 (1)	3	4	2 (1)	2	8	4 (1)	2
Malle-Zoersel	AZ St-Jozef	-	-	-	1	-	1	-	1	-	1	(1)	1	-	-	-
Mechelen – Duffel	AZ St-Maarten	-	-	-	-	-	-	-	-	-	1	-	1	1	-	1
Menen	AZ Delta – campus Rijselstraat	1	2	2	-	-	-	1	-	-	-	-	-	-	-	1 (1)
Mol	H. Hart ZH	-	-	-	-	-	-	-	-	-	-	1	-	2	-	1 (1)
Oostende	AZ Damiaan	2	2	3	5	-	2	-	4	2	4	1 (1)	-	-	2 (1)	(1)
Overpelt	Maria ZH	-	-	-	-	-	-	-	-	-	1	(1)	-	(1)	-	-
Roeselare	AZ Delta – campus Wilgenstraat	14	7	10	11	10	8	9	11	11 (1)	2 (1)	8 (2)	11	6 (3)	12 (6)	11 (4)
St-Niklaas	AZ Nikolaas	-	2	5	5	3	2 (1)	-	-	3	3	1	1	3	1	2
St-Truiden	Regionaal ZH St-Trudo	-	4	1	-	1	3	-	-	1	-	3	4	1	1	3
Tielt	St-Andries ZH	-	2	1	-	-	-	-	-	1	1	-	1	2	-	-
Tongeren	AZ Vesalius	-	-	-	-	-	-	-	1	-	-	1	-	-	1	-
Torhout	St-Rembert ZH	1	1	-	-	-	-	-	1	-	-	-	-	1 (1)	1	-
Turnhout	AZ – campus St-Elisabeth	1	2	2	2	2	3	5	1	1	3	3	5	9	7	3 (1)
Veurne	AZ St-Augustinus	-	-	-	2	1	2	2	-	2 (1)	4 (2)	5 (5)	10 (7)	5	4 (2)	3 (1)
Vilvoorde	AZ Jan Portaels	-	-	-	-	-	-	1	-	-	-	-	-	1	(2)	-
Waregem	OLV van Lourdes ZH	-	-	-	1	-	-	-	-	(1)	1	1 (1)	1	-	-	-
Zottegem	St-Elisabeth ZH	1	-	-	1	1	-	1	1	1	-	-	-	-	-	-
Leuven	UZ Leuven	10	13	14	11	19 (1)	14	17 (1)	10	16	9 (4)	9 (2)	10 (3)	13 (3)	14 (5)	19 (4)
SUBTOTAL	DBD - heart-beating	59	84	81	60	74	65	67	75	81	60	67	79	96	81	77
SUBTOTAL	DCD - non-heart-beating	-	-	-	-	2	2	1	3	5	8	16	11	12	20	20
TOTAL		59	84	81	60	76	67	68	78	86	68	83	90	108	101	97

97 effective donors were registered in 2013, a slight drop compared to 2012 (101 effective donors). We would like to express our gratitude to the many colleagues of LSGO hospitals and UZ Leuven who made all this possible. Because of their efforts many transplant patients are able to enjoy a longer life.

FIGURE 1.1 | evolution of the number of effective donors UZ Leuven and partner hospitals 1996-2013

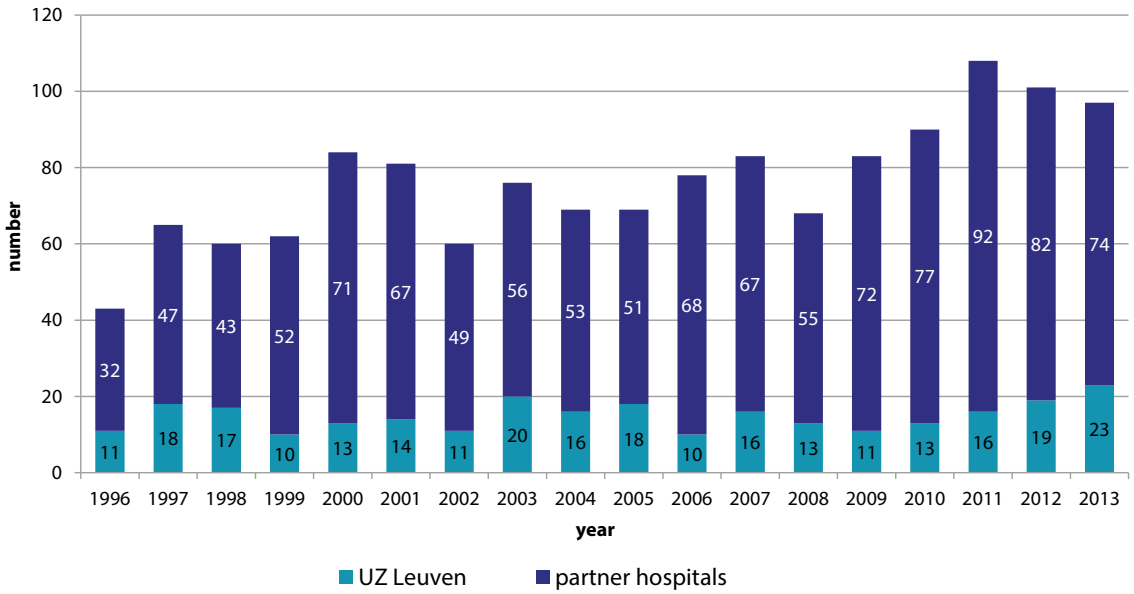


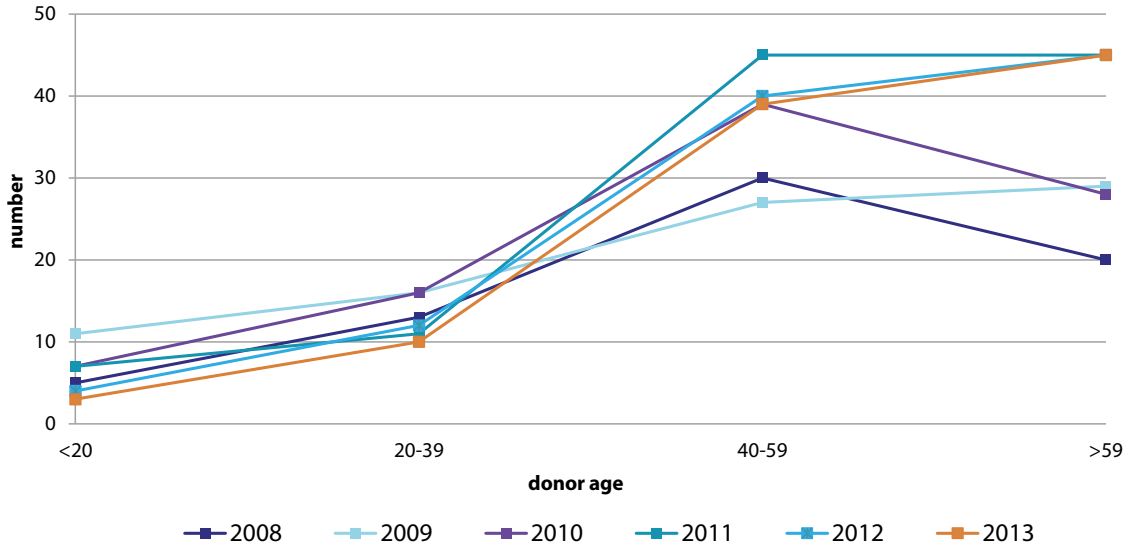
Table 1.4 illustrates the cause of death of potential donors (2001-2013): 75.8% died from cerebrovascular disease; 17.6% died as a result of trauma.

TABLE 1.4 | donor profile: cause of death (potential donors UZ Leuven and partner hospitals 2001-2013)

	'01 (n=109)	'02 (n=89)	'03 (n=98)	'04 (n=103)	'05 (n=125)	'06 (n=131)	'07 (n=147)	'08 (n=129)	'09 (n=140)	'10 (n=164)	'11 (n=200)	'12 (n=183)	2013 (n=211)
Traumatic brain injury (traffic + other)	51%	26%	37%	40%	27%	32%	28%	35%	22,9%	25%	27,5%	20,7%	**17,1%**
Cerebrovascular disease:													
- spontaneous intracranial hemorrhage	39%	51%	41%	51%	50%	43%	41%	39%	32,9%	40,2%	34%	43,2%	**38,4%**
- cerebral infarction	4%	9%	5%	6%	5%	6%	6%	7%	12,1%	6,7%	13,5%	7,7%	**9,9%**
- anoxia	2%	2%	6%	2%	11%	14%	19%	14,5%	6,4%	18,3%	18%	18,6%	**27,5%**
Tumours	2%	-	1%	1%	1,5%	1,5%	1,5%	-	2,9%	2,4%	0,5%	1,1%	**0,5%**
Intoxication	-	3%	4%	-	3%	1,5%	1,5%	2,5%	1,4%	1,2%	0,5%	0,5%	**0,5%**
Suicide	2%	6%	4%	-	1,5%	1%	1,5%	1%	0,7%	1,2%	5%	3,3%	**4,3%**
Bacterial meningitis	-	3%	2%	-	1%	1%	1,5%	1%	0,7%	1,2%	-	2,7%	**-**
Euthanasia	-	-	-	-	-	-	-	-	0,7%	-	-	2,2%	**0,5%**

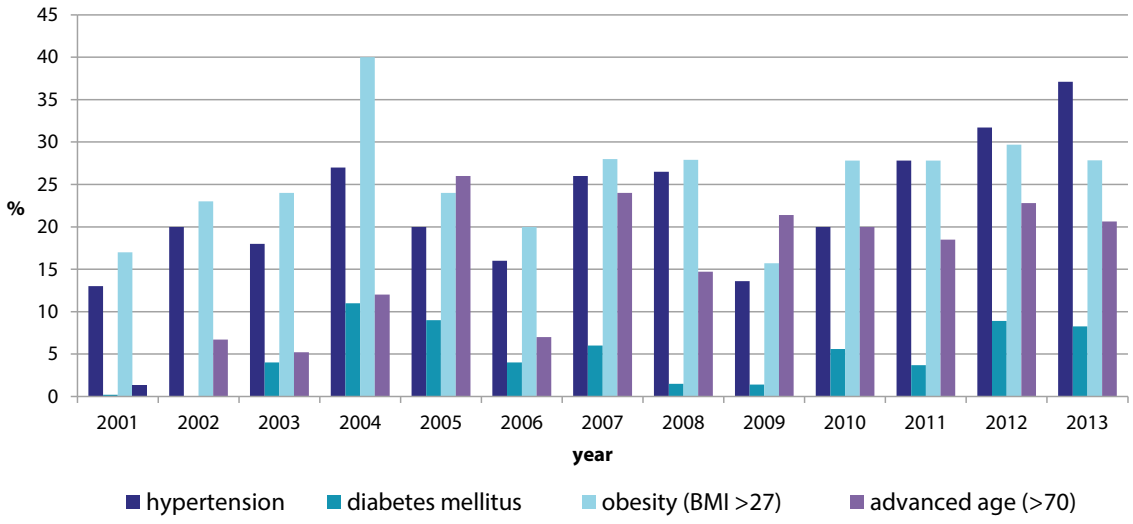
Figure 1.2 shows the classification into age categories of the effective donors in 2013 (compared to those in 2008, 2009, 2010, 2011 and 2012) which illustrates that the number of young donors (aged <20) and donors aged between 20 and 39 has continued to drop slightly compared to 2012. The number of middle aged donors (40-59) in 2013 is comparable to the number in 2012. The number of 'older' donors (> 59) is also the largest group in 2013.

FIGURE 1.2 | effective donor profile: age (UZ Leuven and partner hospitals 2008-2009-2010-2011-2012 versus 2013)



The donor profile shows a remarkable pattern, i.e. an increase in the prevalence of hypertension compared to the data for 2012. This increase has been noticeable for 4 consecutive years. In 2013 the average age of effective donors was 58 (5-90 age range), compared to an average age of 57 in 2012.

FIGURE 1.3 | donor profile: associated co-morbidity and advanced age (effective donors in UZ Leuven and partner hospitals 2001-2013)



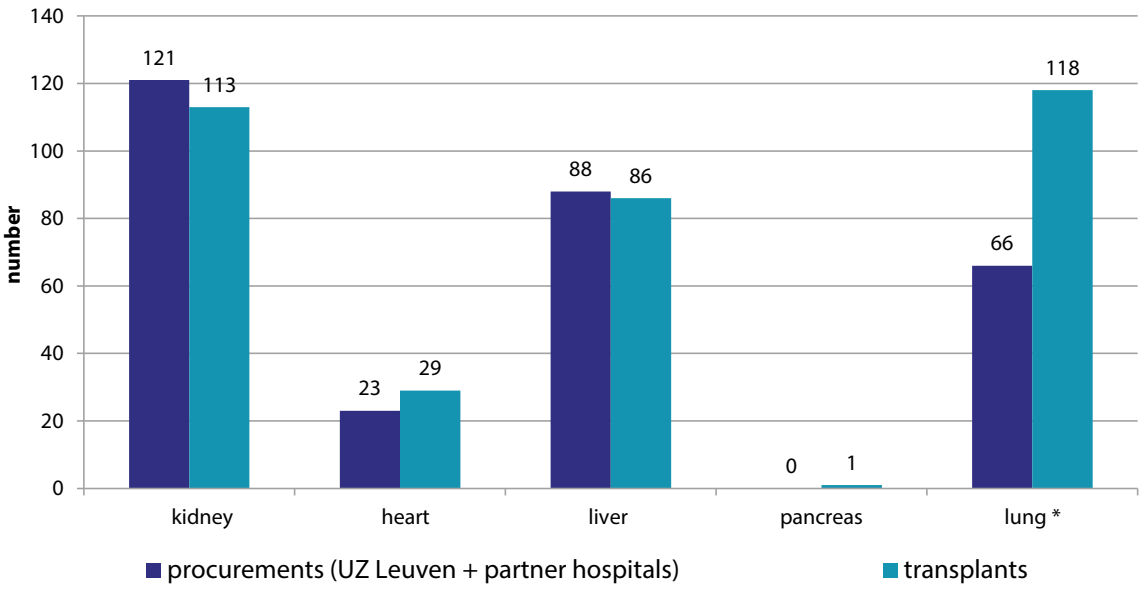
In 2013 an average of 3.07 organs (3.48 in 2012) were procured per donor.

TABLE 1.5 | type and number of procured organs UZ Leuven and partner hospitals 2000-2013

	'00	'01	'02	'03	'04	'05	'06	'07	'08	'09	'10	'11	'12	2013
Kidney (single)	153	144	87	125	111	80	102	132	103	135	130	142	147	**121**
Heart (± lung)	44	41	28	36	29	21	19	25 (1)	23	27	26	23	30	**23**
Liver (+ split-liver)	69	72	50	68	57	68	67	69 (3)	60	71	74 (6)	92 (4)	80 (6)	**84 (4)**
Pancreas	15	16	21	4	13	7	5	12	6	6	8	3	-	**-**
Lung (single)	48	46	35	51	46	49	59	52	45	66	75	77	88	**66**
Total	**329**	**319**	**221**	**284**	**256**	**225**	**252**	**294**	**237**	**305**	**319**	**341**	**351**	**298**

In 2013 more hearts (+3) and considerably more livers (+21), but fewer lungs (-22) were transplanted than in 2012. The number of kidney and pancreas transplants also decreased.

FIGURE 1.4 | number of organs (deceased donors only, UZ Leuven and partner hospitals) procured by UZ Leuven and number of (deceased donor) organ transplants at UZ Leuven in 2013



*** the number relates to the number of lungs: 32 double and 2 single lung procurements (n=66) and 59 double lung transplants (n=118).**

Organ donation in Belgium

In 2012 the effective donor number in Belgium was 320, which equates to 29.2 donors per million inhabitants (pmi) (figure 1.5). In 2013 we recorded 306 effective organ donors, a drop to 28 donors pmi.

FIGURE 1.5 | development of the number of effective donors (DBD + DCD) in Belgium 1996-2013

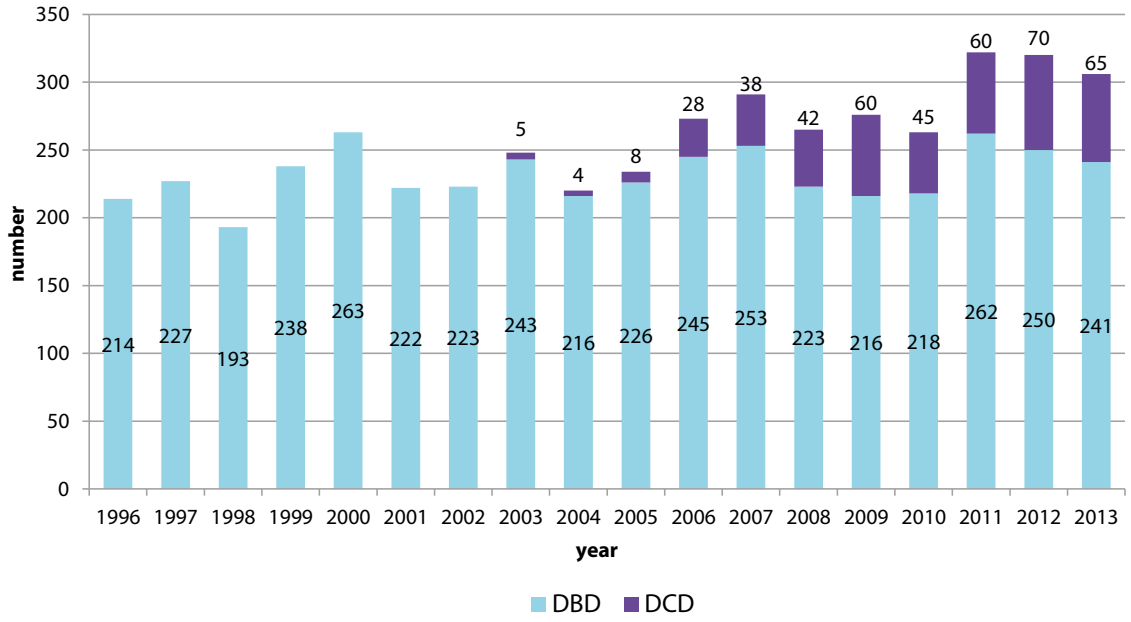


FIGURE 1.6 | type and number of procured organs in Belgium 2000-2013

PART 2

ABDOMINAL TRANSPLANTS

surgery
abdominal transplant surgery

internal medicine
endocrinology
gastroenterology
hepatology
nephrology

transplant coordination

transplant programmes
intestinal transplant
living donation of a kidney, hepatic lobe and intestines
liver transplant
kidney and pancreas transplant

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social work
Kathleen Remans

physiotherapy
Leen Schepers

psychological support
Tine Peeters

dietary advice
Nelle Pauwels

speech therapy
Sofie Van Craenenbroeck

Intestinal transplantation programme

For patients suffering from intestinal failure as a result of anatomical or functional loss of the small intestine, continuous administration of total parenteral nutrition is still the first treatment option. An intestinal transplant would undoubtedly be the first choice if the long term results were comparable to those of other organ transplants. However, even today there are various reasons why intestinal transplants remain a significant surgical, clinical and immunological challenge.

The main reason is that by definition the intestine is an infected organ, which is also highly sensitive to rejection and consequently requires high dose immunosuppression. Moreover, prior to the intestinal transplant, patients often already underwent various surgical procedures and are seriously undernourished. Factors such as these explain a global five year survival rate of only 55%, as reported by the international intestinal transplant registry.

The intestinal transplant programme for adults and children was launched at UZ Leuven in 2000, following a long preparatory experimental and clinical phase. The first successful intestinal transplant in the Benelux was carried out that same year in a 55 year old woman. Since then a total of 12 transplants were carried out, 2 involving children and 10 involving adults. One of the patients received an approximately 2 m long small intestine from a living donor. So far the five year patient survival rate (n=12) is 70%. Of the 12 patients, 10 (n=10) received an intestine from a deceased donor and were treated using a specific ´Leuven immunosuppressant protocol´ in order to inhibit the severe rejection associa-ted with the intestine. The five year survival rate in this group (n=10) is 90% with an early rejection in 1 patient (10%). All the survivors have a normally functioning intestine and were able to resume their day to day activities.

INTESTINAL TRANSPLANTATION

Until now 2887 intestinal transplants have been carried out worldwide – based on the latest report of the international intestinal transplant registry (2013). This amounts to only 0.4% of the total abdominal transplant activities. Intestinal transplants consequently remain delicate operations with global survival figures that are considerably below those for other organs.

The laboratory for abdominal transplant surgery has, therefore, developed a protocol to inhibit the extreme rejection response associated with intestinal grafts in conjunction with the laboratory for experimental transplantation.

This ´Leuven´ protocol is based on the following four principles: i) donor specific blood transfusion to the recipient at the time of transplantation results in better intestine graft acceptance; ii) avoidance of high doses of corticosteroids as they can inhibit the positive effect of the donor specific blood transfusion;
iii) avoidance of high doses of maintenance immune suppression – with its associated complications such as kidney failure, infections and tumour development – will paradoxically result in better intestine graft acceptance; and iv) limitation of inflammation in the intestine using colon cleansing medication in the donor and recipient, and highly selective choice of suitable donors.

Until now this protocol was used in UZ Leuven for 10 consecutive recipients involving the intestine of a deceased donor (18 months to 11 years and 10 months follow-up). The five year survival rate of this group (n=10) is 90%. The average age was 35, and 8 female patients were involved; 2 patients were children aged 2 and 9; 5 patients underwent a combined liver and intestine transplant, the other 5 received an isolated intestine transplant with an additional kidney transplant in two cases. The latter 2 patients suffered from enteric hyperoxaluria in which crystals develop in the kidneys as a result of intestinal failure. The crystals developed into stones and eventually led to terminal kidney failure.

Despite the fact that intestinal transplants are characterized by acute rejection, only 1 of these 10 patients (n=10), who suffered from Crohn's disease, developed early rejection (acute rejection within 3 months of the transplant) (10%). This patient and 2 other patients developed late rejection (rejection later than 3 months after the transplant) (30%). Following rejection 4 months post transplant, the first patient developed an aspergillus infection and died 8 months after the transplant from intracranial bleeding. With the second patient discontinuation of the anti-rejection medication (non- compliance) led to rejection at 46 months. Fortunately, the rejection process was reversed with high doses of steroids. The last patient to develop late rejection at 18 months was the one mentioned above with Crohn's disease. Crohn's disease could potentially be an additional risk factor. Fortunately, the rejection process was also reversed with high doses of steroids. 8 of the 10 patients are still alive today. They all have a functioning intestine and were able to resume their day to day activities. In addition to the above mentioned patient who died from rejection and aspergillus infection, our first transplant patient died in 2012 (12 years after the transplant) as a result of taking anti-inflammatory drugs (non steroid anti-inflammatory drugs) and various ulcerations of the intestinal wall via which bacteria were able to enter the blood stream, which led to a massive infection.

In addition to the 10 patients described above, 2 other patients underwent a small intestine transplant. The Leuven protocol could not be used for the first patient, a 43 year old male, because of a lack of donor specific blood. This patient underwent a combined liver, stomach, duodenum, pancreas and small intestine transplant from a deceased donor. The post transplant process was compromised by graft-versus-host disease and rejection. The patient died 4 months later from an aspergillus infection and intracranial bleeding. The other patient, a 34 year old female, differed from the group of 10 patients described above in that she received a partial intestinal graft (2 m distal small intestine) from a living donor, her mother. Churg-Strauss syndrome was the reason for the transplant. The donor is doing well. However, the transplanted graft had to be resected 7 months after the transplant because of refractory acute and chronic rejection. We were not able to continue to follow this patient because she went abroad. We were recently informed that she has died.

The five year patient survival rate in this series of 12 small intestine transplants (n=12) is 70%. This seems to be a favourable result compared to the results reported by the international intestinal transplant registry (55% five year patient survival rate following intestinal transplant).

At the beginning of 2014, there were 5 patients active on the waiting list: 3 were awaiting an isolated small intestine transplant, 1 a combined liver/intestine transplant and 1 a multi-visceral transplant. 3 of these patients received a transplant with favourable post operative progress during the first 4 months.

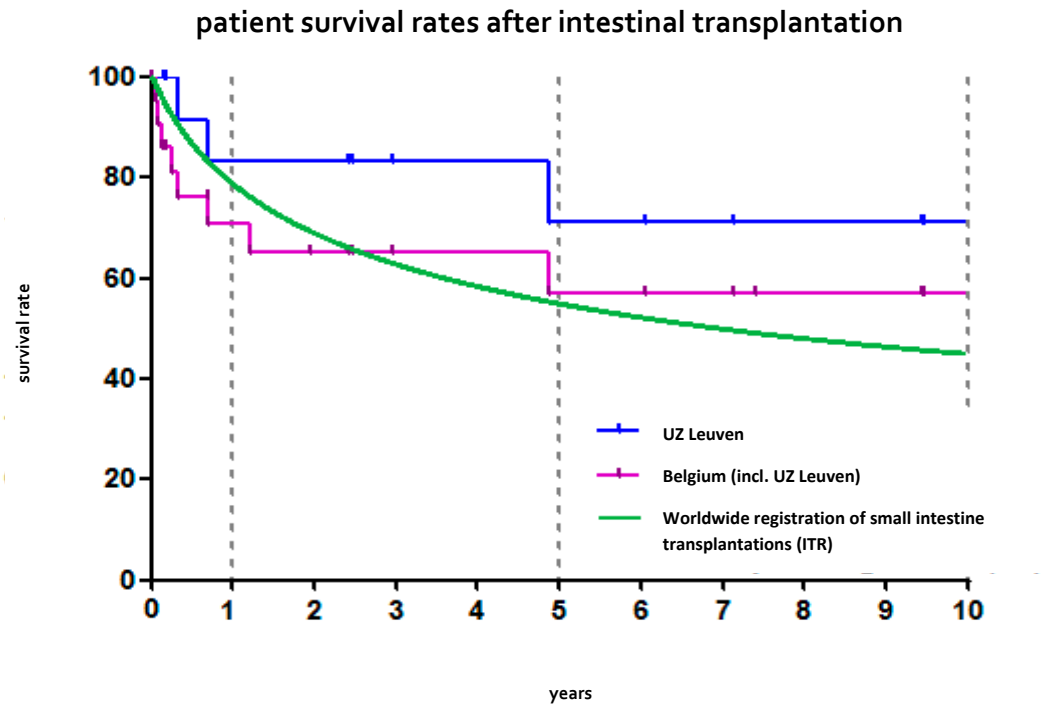
One of the most important pieces of information in the latest report of the international intestinal transplant registry (2013), which records approximately 95% of all intestinal transplants worldwide, was a significant drop in transplant activity. Whereas in 2007 approximately 250 transplants were carried out annually, by 2012 this figure had dropped to 100. Possible explanations for this remarkable decrease are the improvements in the development of parenteral nutrition and recent improvements in venous catheters to administer this nutrition, which probably explains why fewer patients develop liver failure and infections.

Multi-centre and international cooperation involving research in intestinal transplantation is, therefore, essential in the coming years in order to better understand and treat immunological barriers, improve results and thus extend the indications. This will also enable us to offer patients a place on the waiting list sooner and thus avoid having to wait until their clinical condition dramatically deteriorates.

That is why we took the initiative in the past year, in conjunction with the gastroenterology and pathological anatomy departments, to initiate an international study with colleagues in Beaujon (France), Birmingham (the UK) and Maastricht (the Netherlands). The objective of the study is to retrospectively check the biopsies of all our intestinal transplant patients in order to study the reaction of Paneth cells (a cell responsible for immune resistance in intestinal villi) to the transplant and their role in the rejection process. We are also investigating whether there is a correlation between the genetic risk factors associated with Crohn's disease and rejection.

We hope that this information will enable us to optimise the results of our intestinal transplant programme even further in the coming years.

FIGURE 2.1 | intestinal transplant survival curve UZ Leuven versus Belgium (including Leuven) versus ITR (Intestinal Transplant Registry)



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speech therapy
Sofie Van Craenenbroeck

Liver transplant care programme

We have seen a progressive increase in the number of liver transplants in our centre in recent years and last year we exceeded the threshold of 80 transplants in a single year. This resulted in a lower mortality rate on our waiting list.

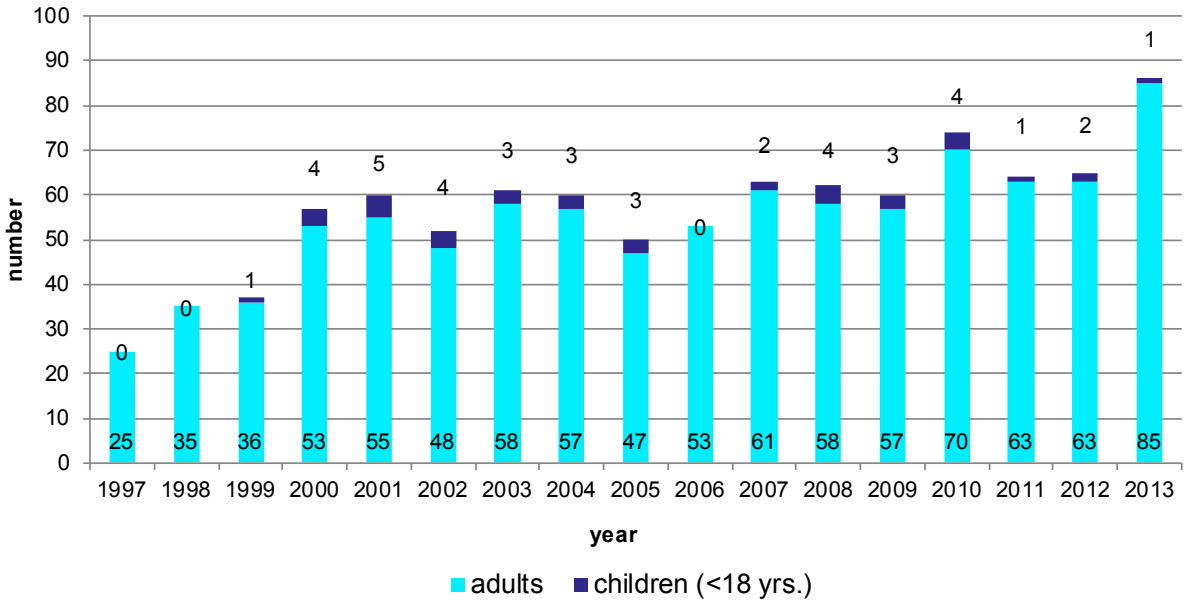
This increase in the number of transplants can partly be explained by the use of older livers for older patients and the use of so-called 'non-heart beating' organs from donors who die in intensive care. This is justified because in our centre no difference exists between the survival of these patients and others who received a liver from brain dead donors. In the past these livers were not used but the optimum cooperation between the hospitals that offer us these donors and our procurement and transplant team has made this possible.

Worldwide, and also in our centre, it has become clear that hepatocellular carcinoma is becoming a more frequent indication for liver transplantation. The risk of relapse is quite acceptable in our centre because of the selection of these patients. Similar to previous years, our centre has recorded excellent results. The immediate and long term patient and graft survival rate and the very low re-transplant rate remain better compared to the average results of Eurotransplant. This is explained by the extensive experience and commitment of all those involved in the liver transplant programme in Leuven.

Transplant activities

86 liver transplants were carried out in 2013, the largest number of transplants carried out in a single year in our hospital since the start of the liver transplant programme. We have now reached a total of 1068 transplants.

FIGURE 2.2 | number of liver transplants 1997-2013 UZ Leuven (n=961)



Recipients

Aetiology

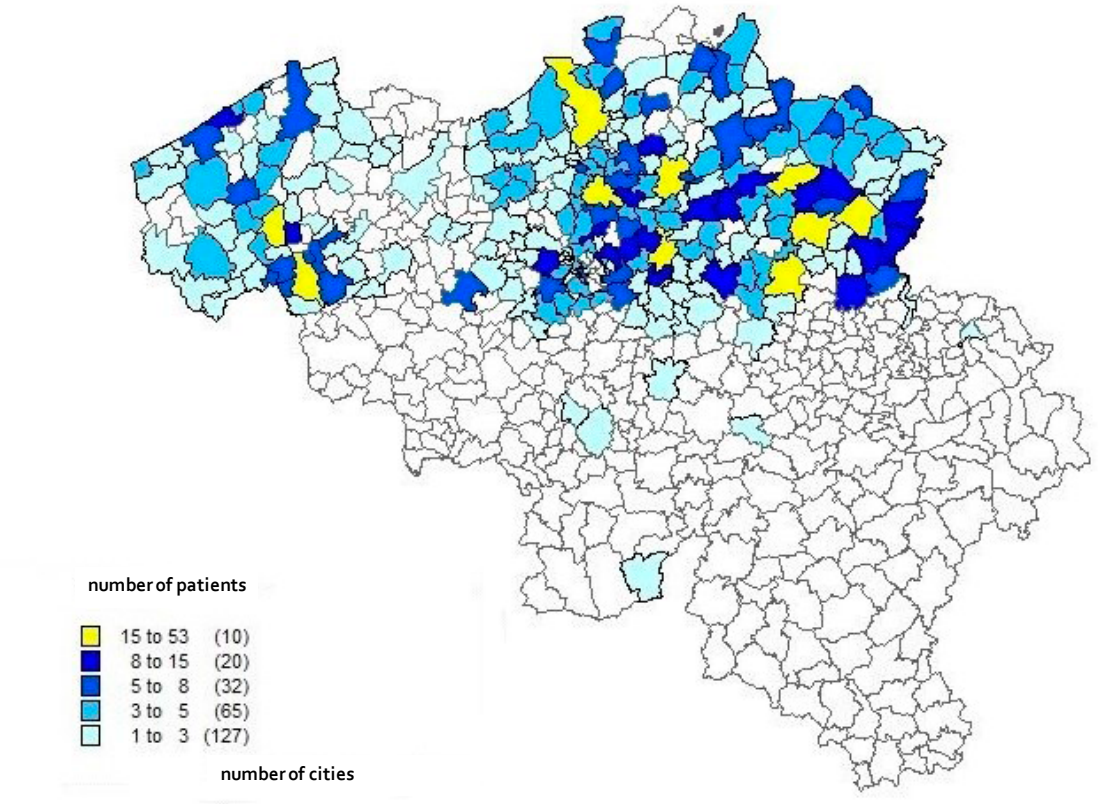
The following table shows the aetiology of liver disease in patients who underwent a liver transplant since 1997. Malignancy is the most frequent cause (24%) for a liver transplant (usually HCC).

TABLE 2.1 | primary diagnosis for liver transplantation n=964

Indication	1997 – 2013 n=964	%
Malignancy (HCC – hepatocellular carcinoma)	236	24%
Viral hepatitis (Hep.)		18%
Hep. C without HCC	47	5%
Hep. C with HCC	70	7%
Hep. B without HCC	38	4%
Hep. B with HCC	17	2%
Post alcohol		26%
Without HCC	171	18%
With HCC	76	8%
Cholestatic		7%
PBC (primary biliary cirrhosis)	32	3%
PSC (primary sclerosing cholangitis)	43	4%
Polycystosis	72	7%
Congenital/metabolic liver disease aged > 18	67	7%
Children ≤ 18	39	4%
Acute liver failure	81	8%
Other (Budd Chiari, Cryptogenic, Auto-immune,…)	77	8%
Re-transplantation	74	8%
Early (< 90 days after 1st tx)	26	3%
Late (> 90 days after 1st tx)	41	4%

Geographic origin

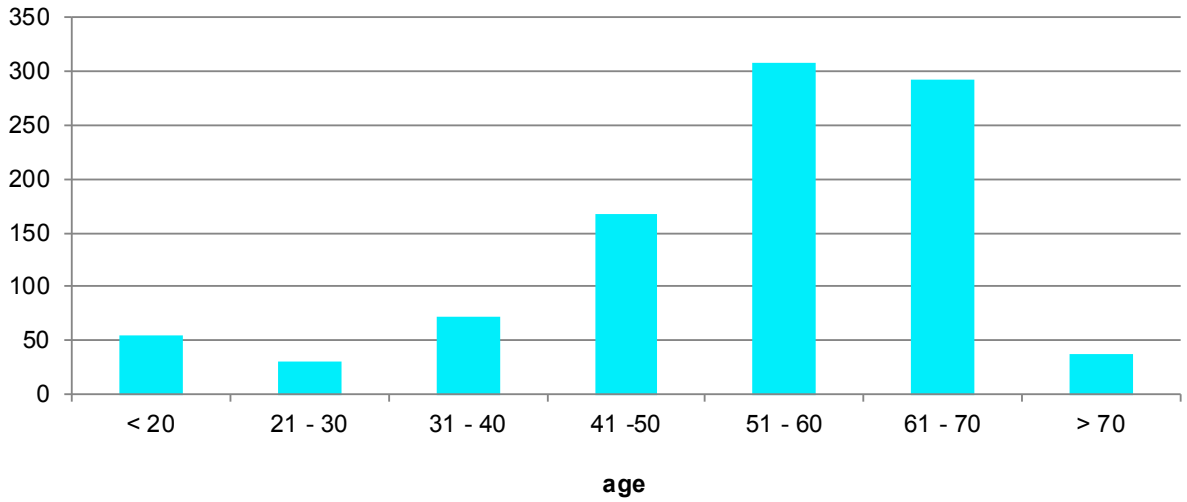
FIGURE 2.3 | geographic origin of liver recipients



Age distribution

This figure illustrates the age distribution at the time of transplant for all patients who underwent a transplant since 1997. The largest group consists of patients aged between 51 and 60 (32%).

FIGURE 2.4 | age distribution liver recipients 1997 to 2013

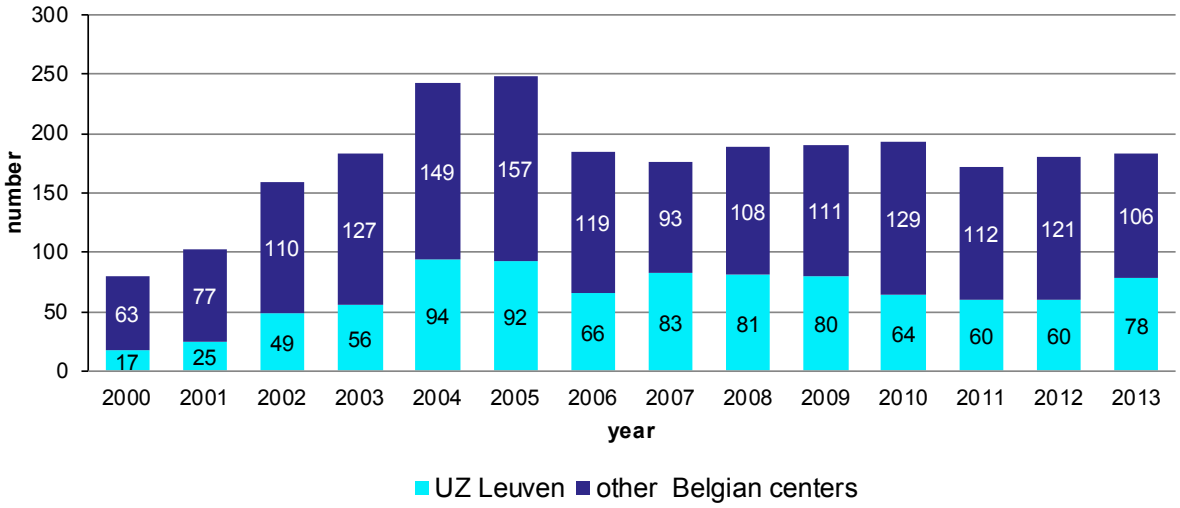


Waiting list data

Active waiting list in Belgium and UZ Leuven

The number of patients awaiting a liver transplant is fairly stable. In Belgium between 170 and 190 patients are awaiting a liver transplant. At the end of 2013 the waiting list included 78 patients (42%) from our centre.

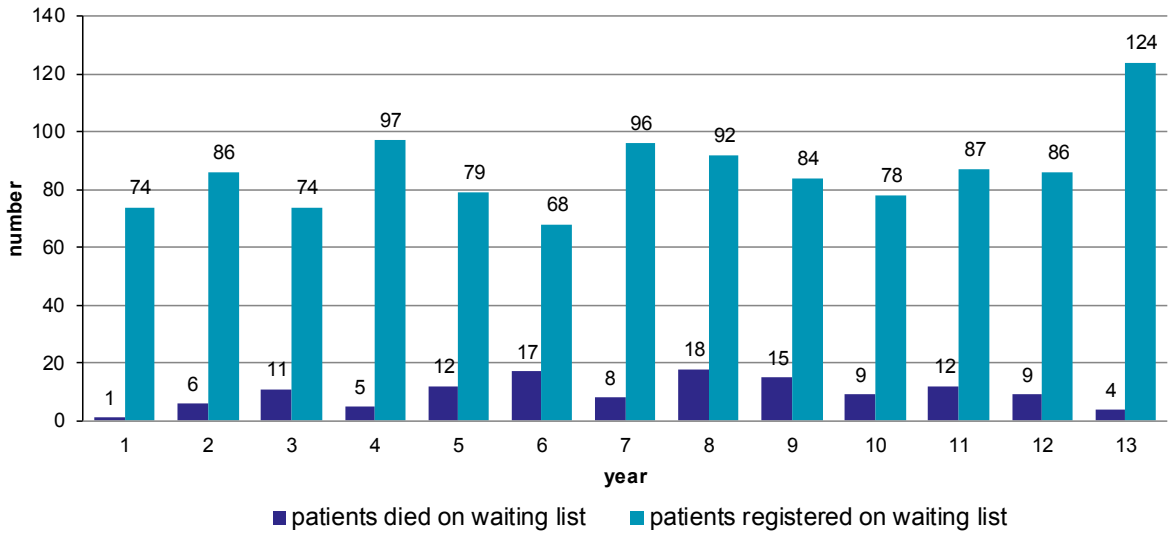
FIGURE 2.5 | evolution of the number of active patients on the Eurotransplant liver waiting list since 2000, UZ Leuven compared to the other liver transplant centres (n=5) in Belgium



Registrations and deaths on the waiting list

In 2013 the number of registrations for a liver transplant in our centre considerably increased (124 in 2013 as opposed 86 in 2012). The number of deaths on the waiting list was also reduced considerably (4 in 2013 as opposed to 9 deaths in 2012). 11 patients were removed from the waiting list, in most cases because their liver tumour had progressed or their general condition was too bad.

FIGURE 2.6 | number of patients registered on the waiting list and patients on the waiting list who died since 2001



MELD score system

Since 2007 Eurotransplant has allocated livers on the basis of the MELD score, an urgency code based on blood counts (LabMeld: creatinine, bilirubin and INR). Almost half of the livers were allocated to a specific patient on the basis of this system. The other livers were allocated to patients with acute liver failure (HU), patients with a standard exception (SE), such as HCCs, polycystosis, hepatopulmonary syndrome … These patients have to meet previously specified criteria in order to qualify for this type of exception. In some cases patients will not meet these criteria and an NSE (non standard exception) request can be submitted. 29 patients received an SE transplant in 2013, although the largest number (39) or 45% of patients received a transplant on the basis of their LabMeld score.

TABLE 2.2 | evolution of Eurotransplant liver allocation method
(HU = High Urgency; ACO = Approved Combined Organs; SE = Standard Exception; NSE = Non-Standard Exception; LabMeld)

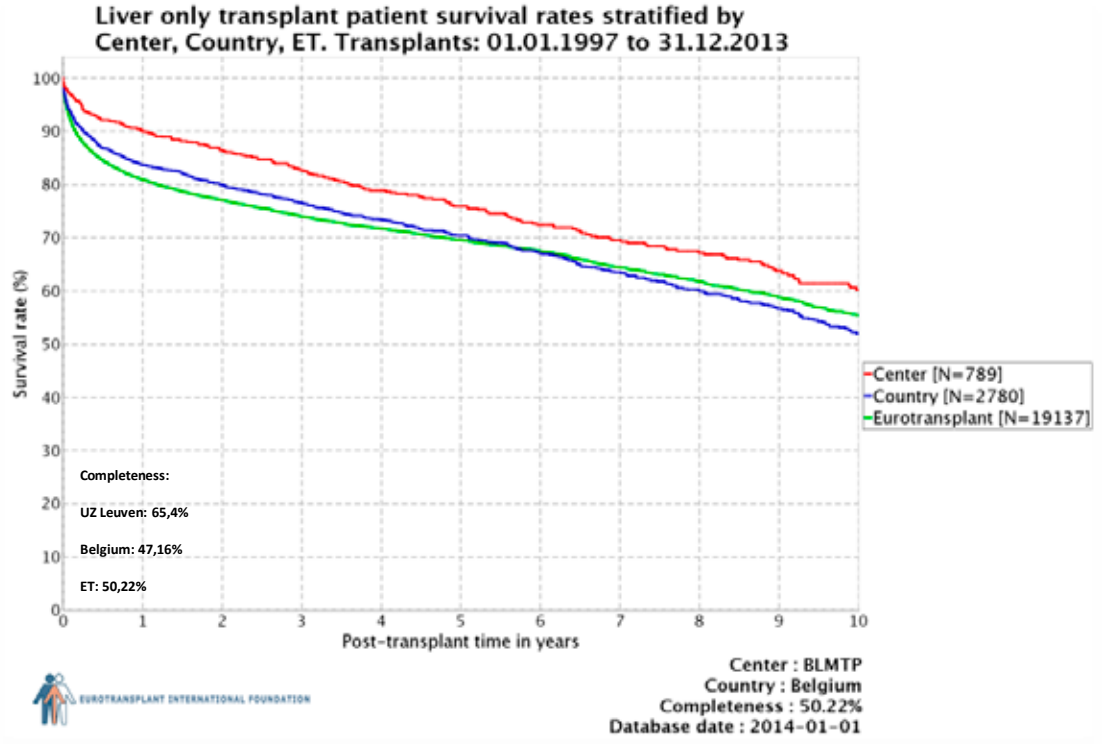
	HU/ACO	SE	NSE	LabMeld
2007	3	22 (35%)	8 (13%)	30 (48%)
2008	8	21 (34%)	5 (8%)	28 (45%)
2009	6	18 (30%)	6 (10%)	30 (50%)
2010	11	25 (34%)	6 (8%)	32 (43%)
2011	9	19 (30%)	6 (9%)	30 (47%)
2012	7	27 (41%)	5 (8%)	26 (40%)
2013	10	29 (34%)	8 (9%)	39 (45%)

Patient and graft survival

UZ Leuven versus Belgium and Eurotransplant

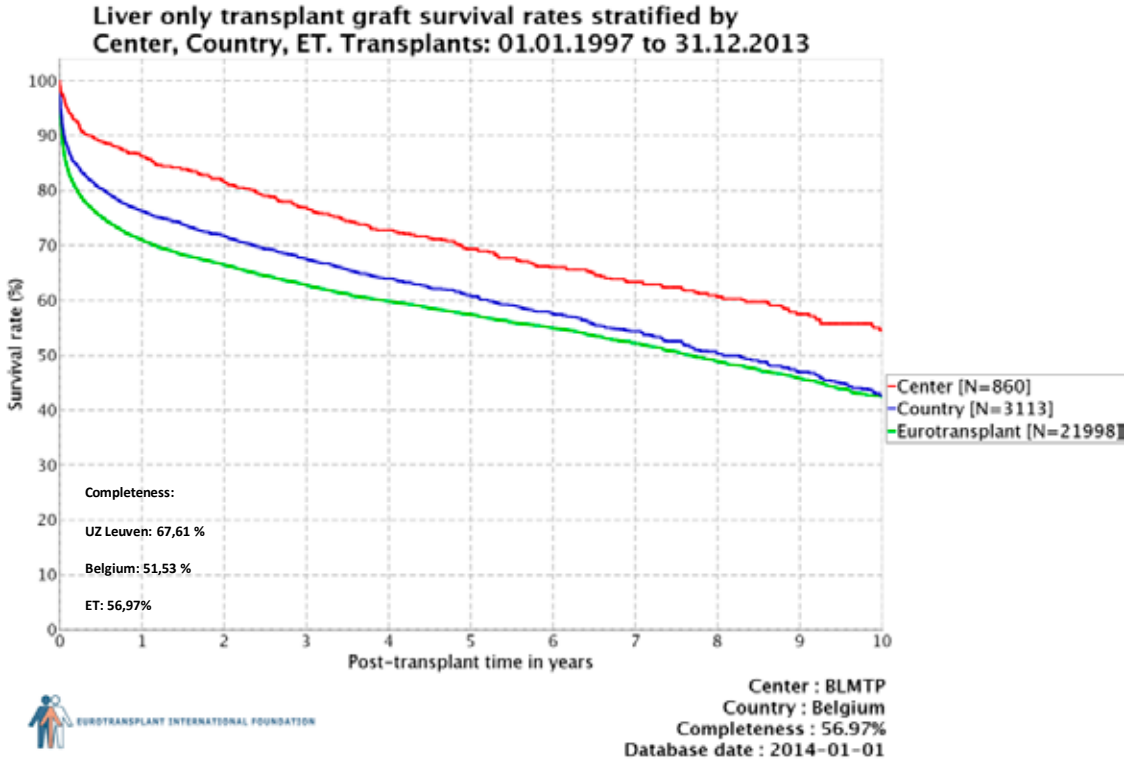
The figure below shows patient survival rates for all patients who underwent a liver only transplant in the period of 1997-2013. The actuarial patient survival rate in UZ Leuven is considerably higher when compared to the results of Eurotransplant and Belgium. These differences are immediately obvious during the post operative period.

FIGURE 2.7 | ten year patient survival rate (1997-2013 all indications – liver only transplants), UZ Leuven compared to Eurotransplant and Belgium (the figures for Belgium also include the results for UZ Leuven). Source: Eurotransplant



There is also a difference between our figures and those for Eurotransplant and Belgium for the graft survival.

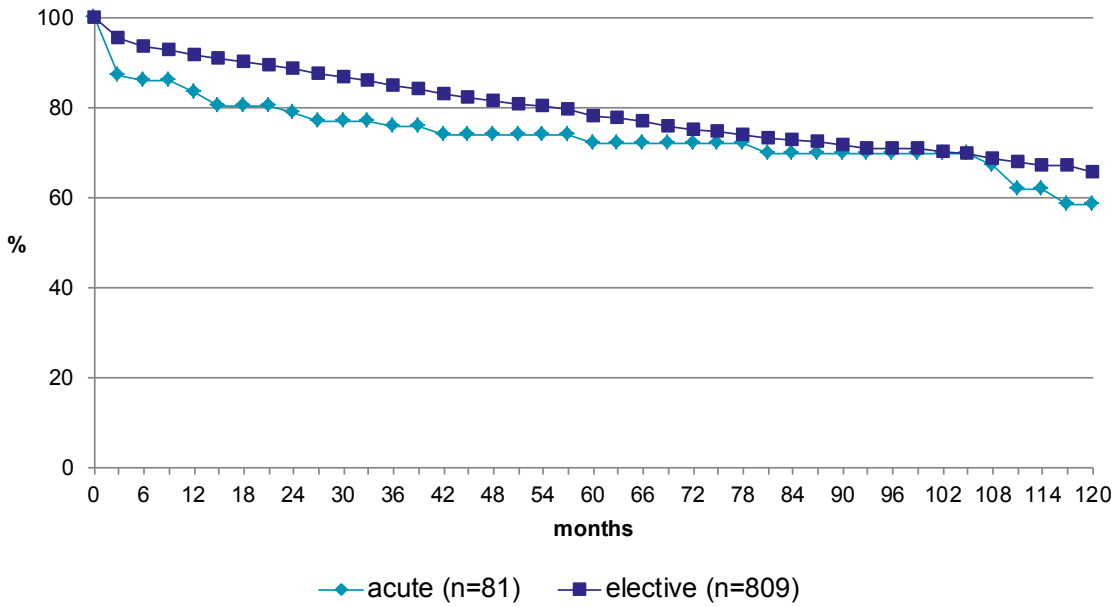
FIGURE 2.8 | ten year graft survival rate (1997-2013 all indications – liver only transplants), UZ Leuven compared to Eurotransplant and Belgium (the figures for Belgium also comprise the results for UZ Leuven). Source: Eurotransplant



'Acute' versus 'elective' liver transplantation

The 1 year survival rate following a liver transplant is 10% lower in case of acute liver failure compared to elective liver transplant. In the long term the results are virtually identical.

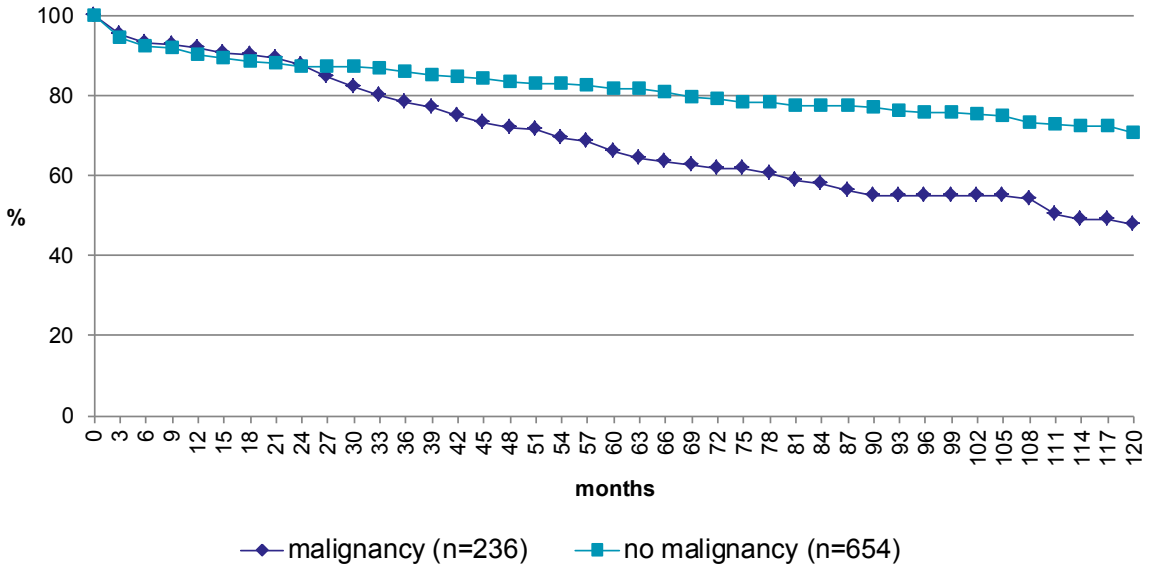
FIGURE 2.9 | ten year patient survival rate (1997-2013) for transplant due to acute liver failure versus elective liver transplant. Source: UZ Leuven database



Malignancy (HCC) versus no malignancy

Looking at the difference between patients who received a transplant with or without liver malignancy (usually HCC), there is no difference in the survival rate during the first 2 years. In the long term, however, there is a distinct difference (20% after 10 years) in survival between patients who underwent a transplant without malignancy and those with malignancy.

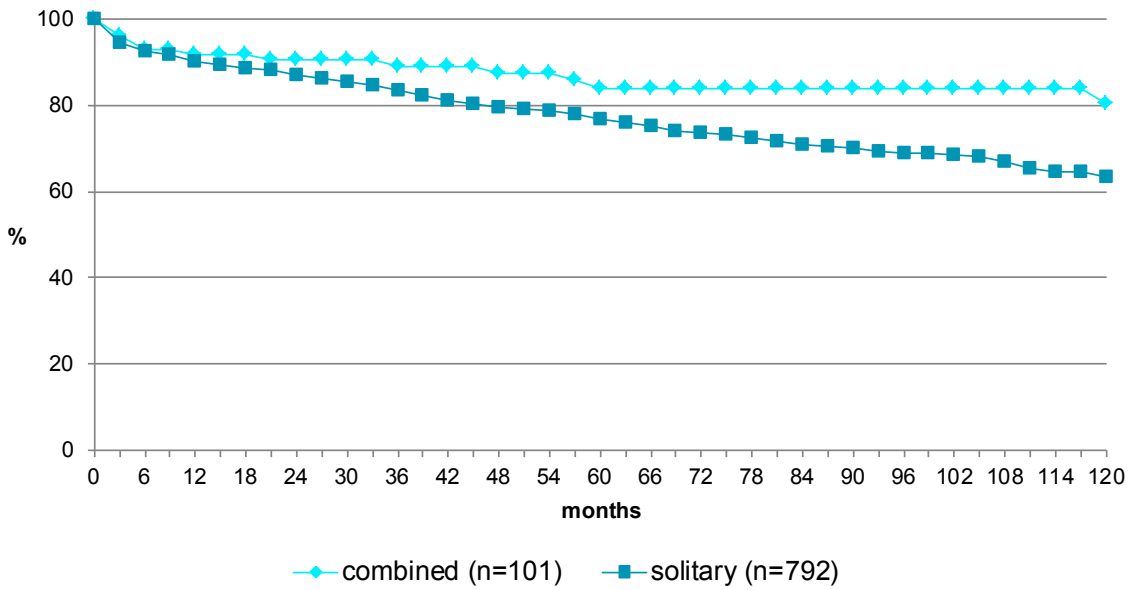
FIGURE 2.10 | ten years patient survival rate (1997-2013) for transplant due to malignancy or no malignancy.
Source: UZ Leuven database



Combined liver transplant (liver and other organ) versus liver only transplant

Our centre carries out approximately ten combined liver transplants each year, which brings the total of combined transplants since 1997 to 101. This is almost 10% of the total number of liver transplants carried out at our centre. The ten year survival rate of these patients is 80%.

FIGURE 2.11 | ten year patient survival rate (1997-2013) for combined liver transplants versus liver only transplants for all indications.
Source: UZ Leuven database



Combined liver transplant (liver and other organ) versus liver only transplant without malignancy

FIGURE 2.12 | ten year patient survival rate (1997-2013) for combined liver transplants versus liver only transplants (without malignancy). Source: UZ Leuven database

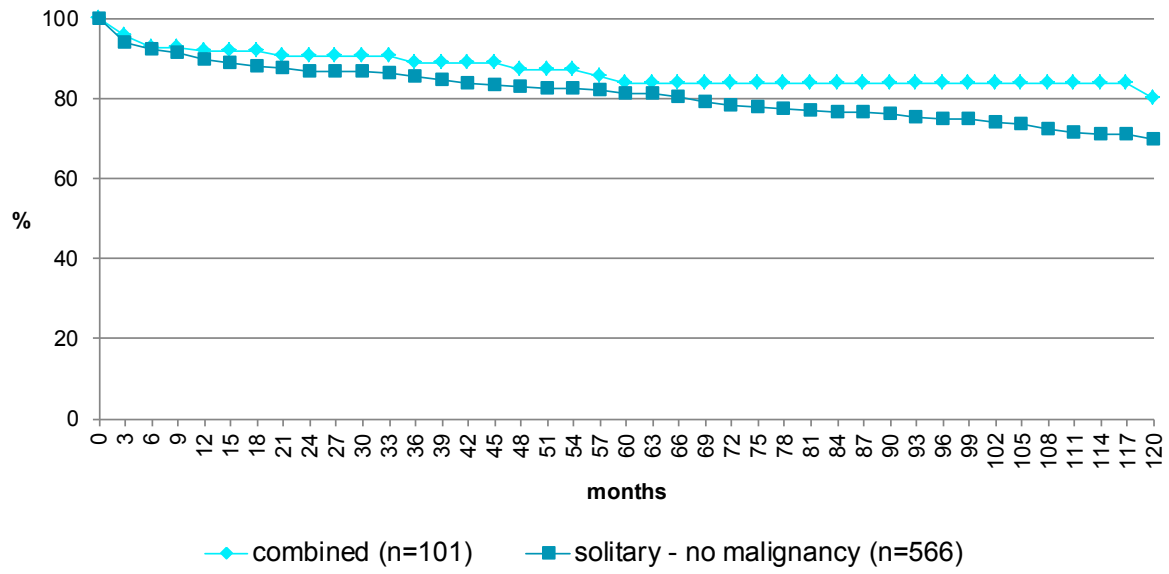


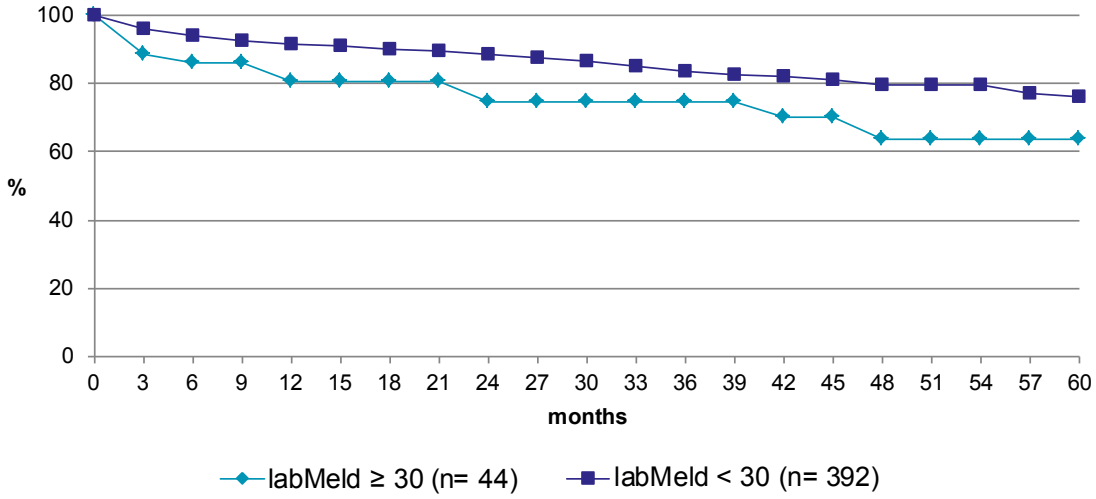
TABLE 2.3 | combined liver transplants (1997-2013)

Summary combined liver transplants (n=101)	Number
Liver + kidney	79
Liver + small intestine	5
Liver + pancreas	6
Liver + small intestine + pancreas + colon	1
Liver + heart	3
Liver + heart + double lung	1
Liver + double lung	5
Liver + pancreas + kidney	1

Survival following liver transplant on the basis of LabMeld

The LabMeld results usually reflect the patient's condition. The higher the score, the worse the patient's condition. This curve reflects the survival rate of our transplant patients with a LabMeld of at least 30 as opposed to transplant patients with a LabMeld below 30. Patients with acute liver failure (who usually have a very high LabMeld score) are not included here.

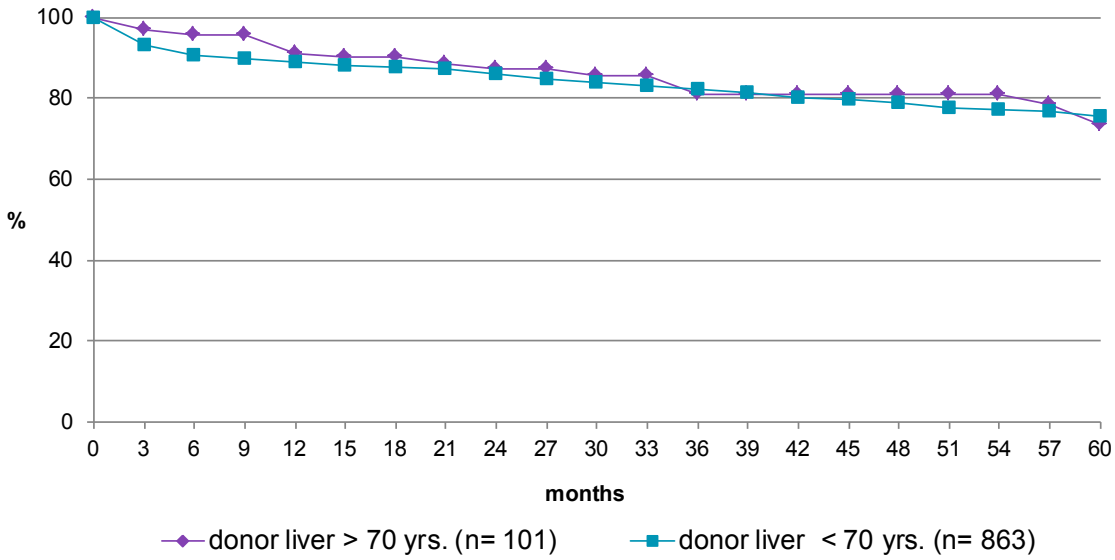
FIGURE 2.13 | ten year patient survival rate (1997-2013) for patients with a LabMeld of 30 or above as opposed to patients with a LabMeld of less than 30. Source: UZ Leuven-database



Liver transplants with organs from 'extended criteria donors'

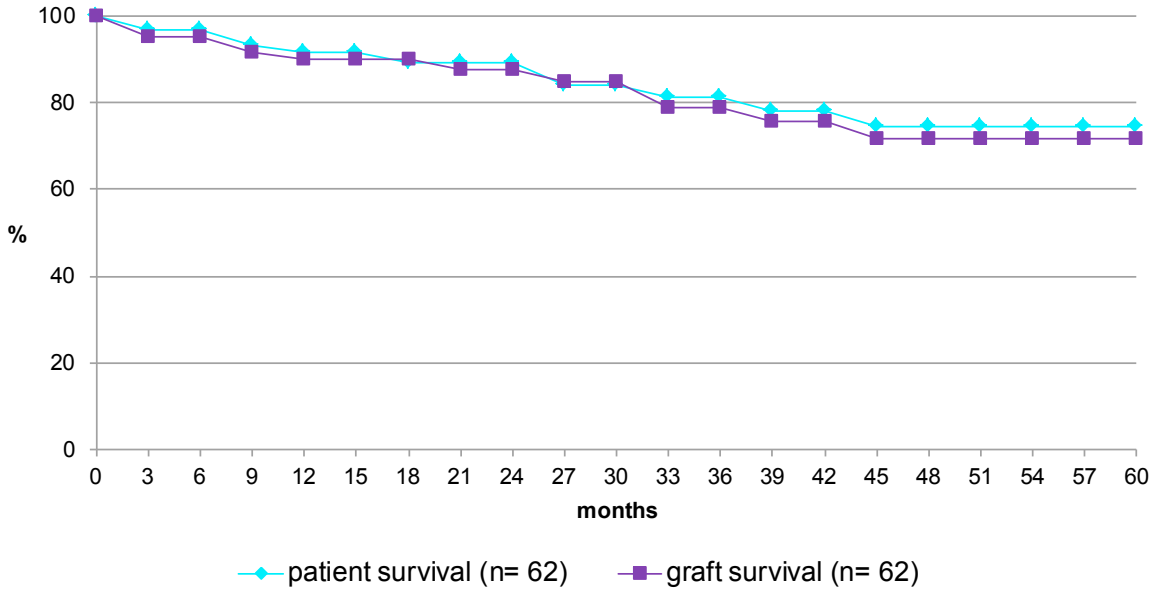
This curve demonstrates that the survival rate of transplant patients who received an older liver is identical to that of patients who received a younger liver.

FIGURE 2.14 | five year patient survival rate for transplant patients who received a donor liver of 70 years and above as opposed to a donor liver of less than 70 years old. Source: UZ Leuven database



In recent years livers from DCD (Non-Heart-Beating) donors are increasingly being used. The use of strict selection criteria in terms of both patient and donor makes the results of these liver transplants acceptable.

FIGURE 2.15 | five year patient and graft survival rate for DCD donor livers. Source: UZ Leuven database



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Living donation programme

The living kidney donation programme was initiated in 1997 following positive recommendations from the medical ethics commission.
The first living donation liver transplant was conducted in 2000 and the first living donation intestinal transplant took place in 2007.

The living donation programme developed into a multidisciplinary care programme, which includes not only doctors and hospital workers involved in the screening process, but also the doctors treating the recipients, i.e. from the nephrology, hepatology and paediatric nephrology departments. Living donor candidates are subject to multidisciplinary screening: biological, internal medical, psychological/psychiatric, social and surgical screening.

This meticulous screening process is coordinated by a clinical transplant coordinator.
An internal medicine specialist, who operates independently from the transplant team, represents the candidate donor throughout the entire screening process.
Living donors are followed up annually throughout their life.

The majority of candidate donors are related (genetically or emotionally). However, purely altruistic kidney donations are also an option.

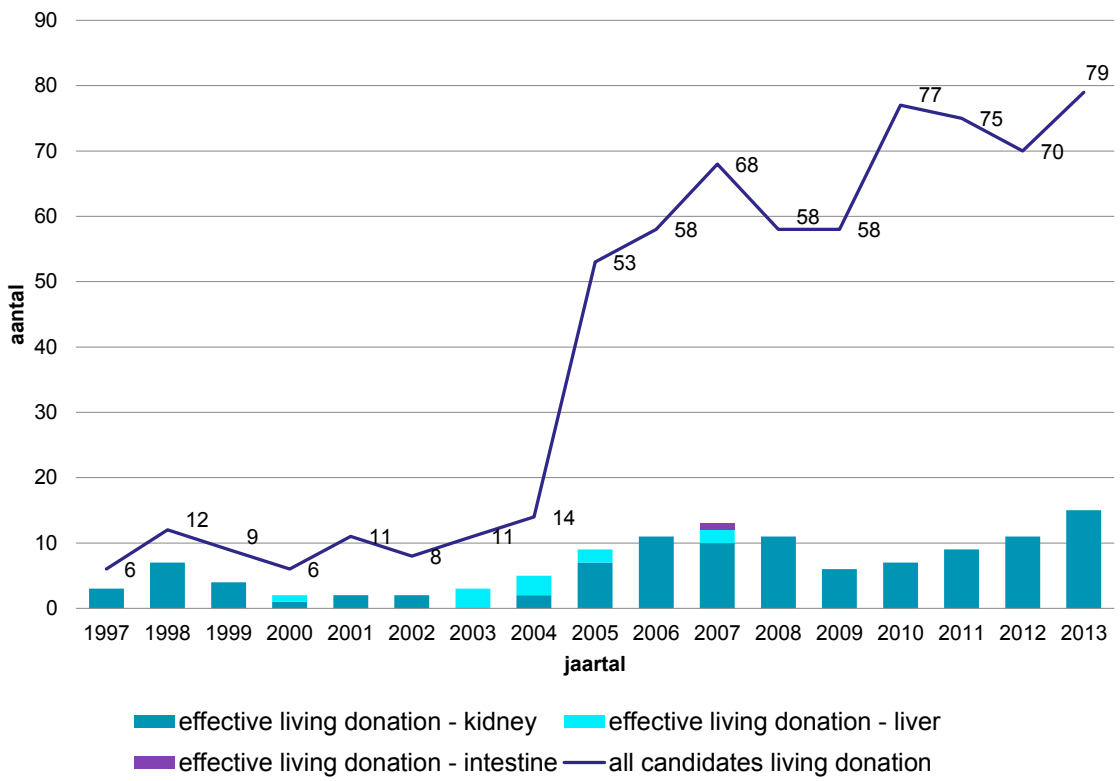
LIVING DONATION OF A KIDNEY, LIVER LOBE OR SMALL INTESTINE

Transplant activities

Since the start of the living donor programme at UZ Leuven – living kidney donation in 1997, living liver donation in 2000, living intestinal donation in 2007 – until the end of 2013, 629 candidate living donors (CLD) were screened for 419 candidate receptors (381 kidney recipients, 37 liver recipients and 1 small intestine recipient). This means that there were 1.5 candidate living donors available for each candidate recipient.

- 567 CLD kidney
- 61 CLD liver
- 1 CLD small intestine

FIGURE 2.16 | number of candidates and effective living donors kidney, liver and intestine 1997-2013



In the period between May 1997 and end December 2013, 120 living donation organ transplants were carried out, including 60 interventions (50%) during the past five years (108 living donation kidney transplants, 11 living donation liver transplants and 1 living donation intestinal transplant).

In 2013, 76 people volunteered to donate a living kidney; 16 candidacies were upheld, 15 interventions were completed. 30 candidacies were rejected, 30 candidacies were still under consideration.

3 people volunteered to be a living liver donor for 2 recipients. The 3 candidacies were rejected. 1 recipient received a transplant involving a liver from a deceased donor.

Living donor profile

TABLE 2.4 | effective living donor profile by gender (1997-2013)

	Male	Female
Kidney	48	60
Liver	7	4
Small intestine	-	1
Total	**55**	**65**

TABLE 2.5 | effective living donor profile based on age (1997-2013)

Age	Number of kidneys donors	Number of livers donors	Number of intestinal donors
18 – 30	7	8	-
31 – 40	22	2	-
41 – 50	36	-	1
51 – 60	29	1	-
61 – 70	14	-	-

TABLE 2.6 | effective living donor profile based on relationship with recipient (1997-2013)

	LRD[1] Genetically related	LURD [2] Emotionally related	LURD[3] Altruistic
Kidney	67	40	1
Liver	11	-	-
Small intestine	1	-	-

[1] LRD = Living Related Donor; blood relatives, genetically related

[2] LURD = Living Unrelated Donor; emotionally related

[3] LURD = Living Unrelated Donor; altruistic donor

TABLE 2.7 | LRD profile based on the nature of the relationship with the recipient (1997-2013)

LRD	Kidney	Liver	Intestine
GENETIC RELATIVE	**67**	**11**	**1**
Brother/sister	14	1	-
Father	17	1	-
Grandfather or grandmother	-	1	-
Mother	27	3	1
Son/daughter	7	5	-
Nephew/niece	2	-	-
Uncle/aunt	-	-	-
EMOTIONALY RELATED	**40**	**-**	**-**
Partner (wife)	23	-	-
Partner (husband)	14	-	-
Father in law or mother in law	2	-	-
Friendship	1	-	-
ALTRUISTIC	**1**	**-**	**-**

316 candidacies (266 CLD kidney, 50 CLD liver) were rejected for various reasons (see table 2.8).

TABLE 2.8 | reason for rejection living kidney or liver donation candidates (1997-2013)

Reason for rejection candidacy	Number
Mismatches (n=50)	
ABO	22
Positive crossmatch	14
Size and/or age	14
Medical – psychosocial – surgical reasons	147
Donor withdrawal	36
Recipient withdrawal	18
Transplant with organ from deceased donor during screening living donor	31
Other reasons	34

For pairs in which blood group incompatibility or a positive HLA cross match are a contraindication for kidney donation, the multicentre LDEP (Living Donor Exchange Program) was set up in 2010, in which kidneys can still be donated and transplanted using cross donation. A case involving cross donation took place at UZ Leuven in 2013.

Follow-up

At the start of the living donation transplant programme it was decided that all living donors would be followed up for life. A specific protocol was developed for this purpose (consultations 1 month, 3 months, 6 months post operative and annually) and follow-up data is stored in a databank.
30 living donors (27%) are no longer part of the follow-up scheme; the others are invited at least once a year to attend a consultation.

Results

Living donor kidney transplant

RECIPIENTS (n=108) (see figures 2.17)

- 14.8% child (< 16, n=15), 85.2% adult receptors (> 16, n=93)
- Delayed graft function (DGF) (dialysis requirement < 8 days post Tx): 1.0% (= 1 casus: factor rejection? DGF?)
- Primary Non Function (PNF): 0%
- Acute rejection: 20.3% (n=22); adult receptors: 23.6%, children: 0%
- 3 month and 6 month graft survival: 100%
- 1 year graft survival: 99% (n=107 kidney Tx). Reason for graft loss (1 patient): rejection as a result of non compliance with therapy.

DONORS (N=108)

- 0% peri-operative mortality
- Morbidity:
  - Peri-operative requirement for transfusion in 1 patient (0.9%)
  - 1 surgical revision on d0 for mild bleeding in 1 patient (0.9%)
  - 1 surgical revision due to wound infection (0.9%)
  - 3 patients (2.8%) with chronic pain
  - 1 patient (0.9%) with incisional hernia repair

Living donation liver transplant

RECIPIENTS (N=11)

- 91% 1 year graft survival
  (1 patient at 2 weeks post transplant 'acute cardiac death' with functioning graft)
- 91% 1 year patient survival
  (1 patient at 2 weeks post transplant 'acute cardiac death' with functioning graft)

DONORS (N=11)

- 0% mortality
- 1 revision for incisional hernia repair

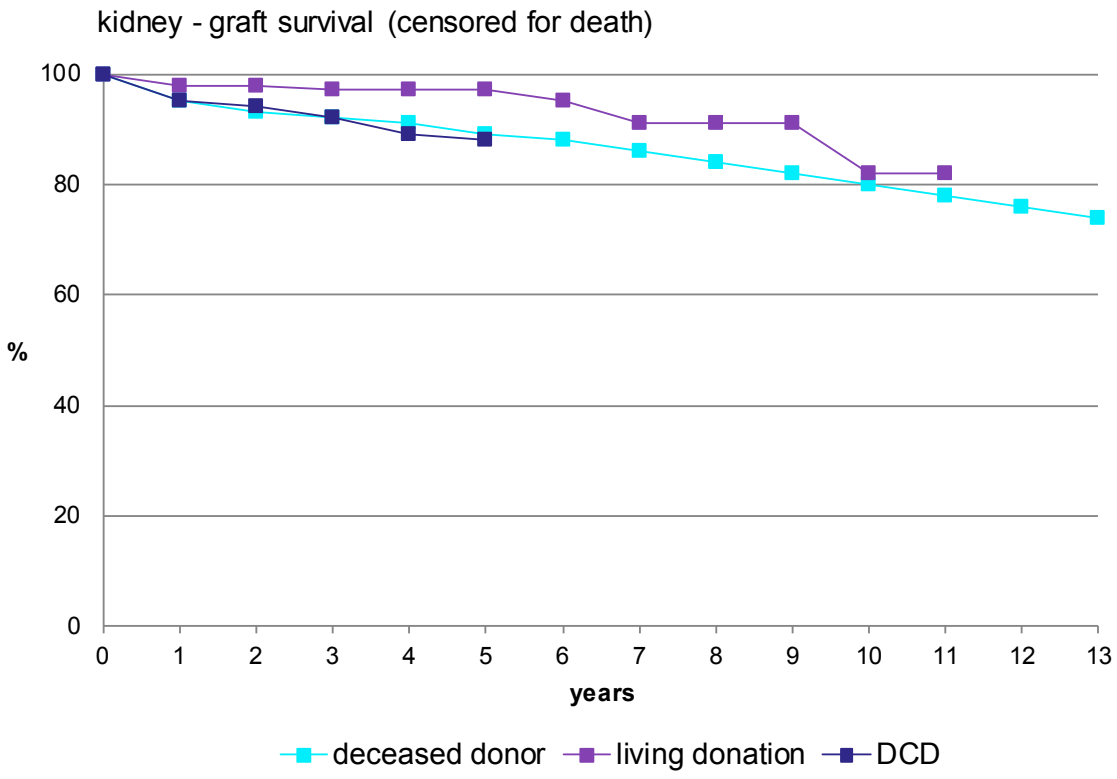
Living donation intestinal transplant

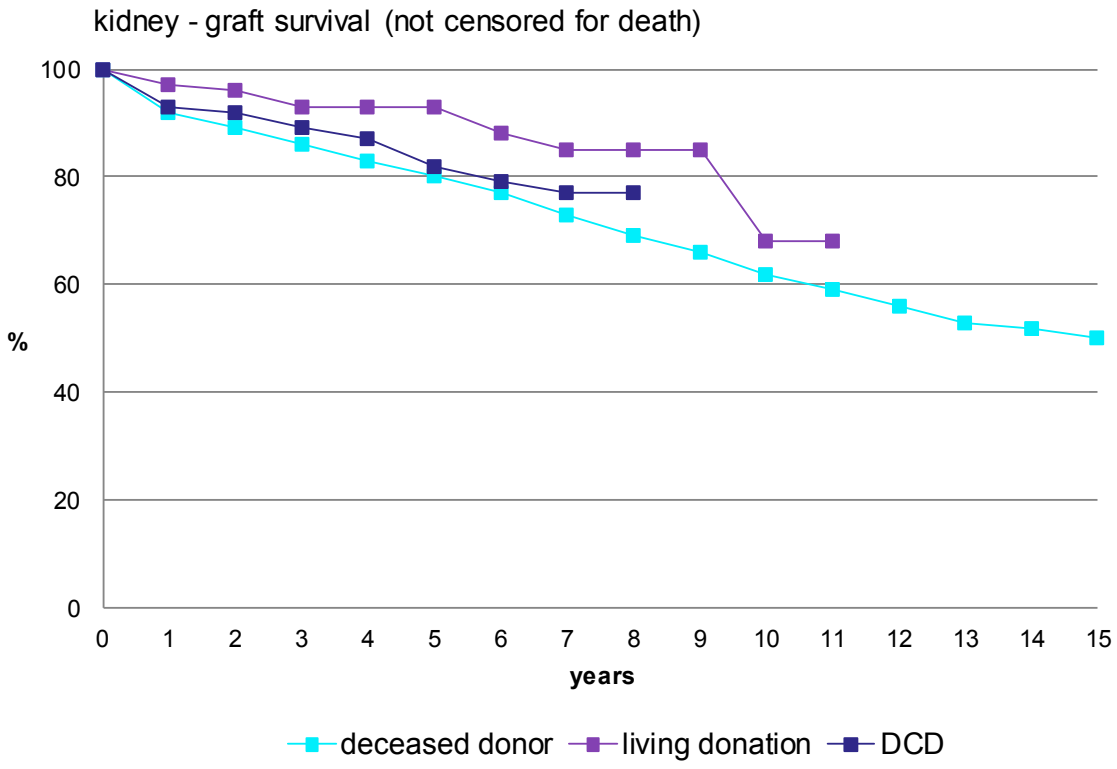
RECIPIENTS (N=1)

- Graft survival: graft loss as a result of refractory rejection
- Patient survival: the patient required a retransplant but was 'lost to follow up'. We found out that the patient died on 27 September 2012.

DONOR (N=1)

- no mortality
- no morbidity: positive effect on hypercholesterolaemia and bowel movement pattern


kidney - graft survival (censored for death)
100
80
60
%
40
20
0
0 1 2 3 4 5 6 7 8 9 10 11 12 13
years
deceased donor
living donation
DCD


kidney - graft survival (not censored for death)
100
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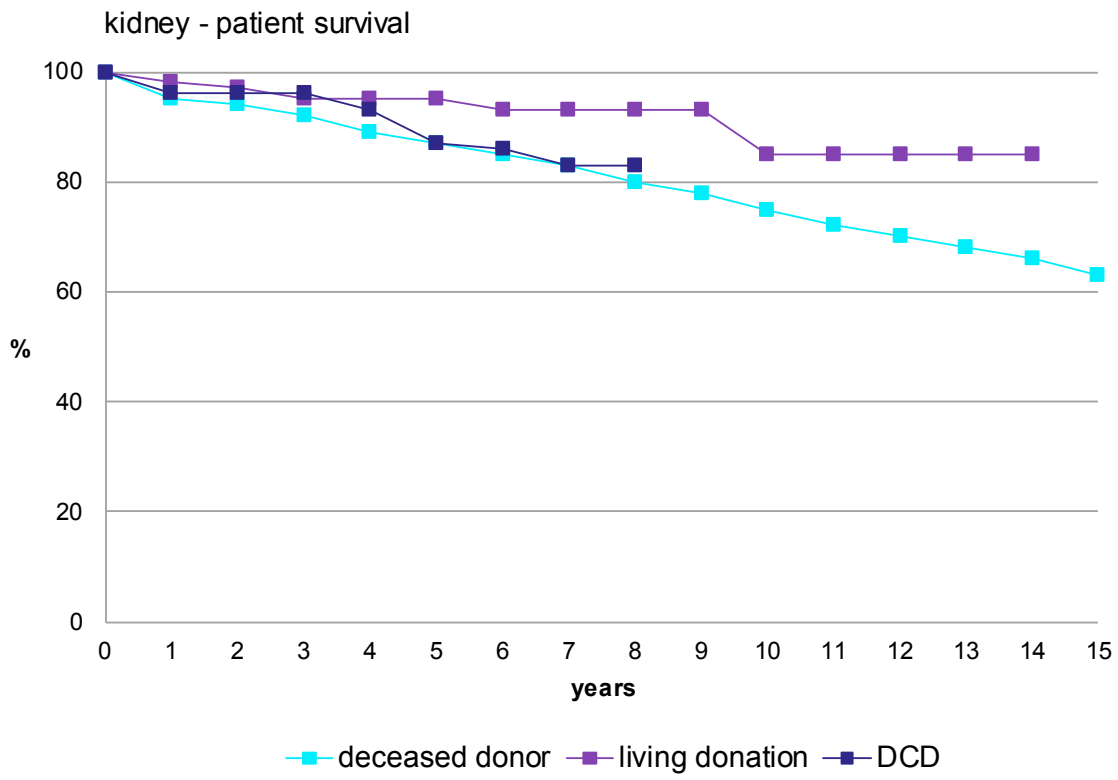
60
%
40
20
0
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
years
deceased donor
living donation
DCD


kidney - patient survival
100
80
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0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
years
deceased donor
living donation
DCD

nephrology
Professor Dr. Yves Vanrenterghem (†), Professor Dr. Dirk Kuypers, Professor Dr. Bert Bammens, Professor Dr. Björn Meijers, Professor Dr. Kathleen Claes, Professor Dr. Pieter Evenepoel, Professor Dr. Maarten Naesens, Professor Dr. Ben Sprangers

abdominal transplant surgery
Professor Dr. Jacques Pirenne, Professor Dr. Diethard Monbaliu, Professor Dr. Ina Jochmans

anaesthesiology
Dr. Marleen Verhaegen

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nursing consultant
Katleen De Bondt

post transplant consultation nurse
Cecile De Vlieghere

waiting list management
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social work
Christa De Baere

physiotherapy
Leen Schepers

psychological support
Tine Peeters

dietary advice
Veerle Resseler

speech therapy
Sofie Van Craenenbroeck

Kidney and kidney/pancreas transplant care programme

The five year kidney survival rate (censored for patient death) following a transplant involving a deceased donor is currently 91% at UZ Leuven and consequently one of the highest in the world. These are exceptional results, particularly when taking into account that 41% of donors are Extended Criteria Donors (ECD) or Donation after Cardiac Death (DCD) donors with a mean donor age of 48. It is also well known that the profile of the receptor has changed significantly over time; the mean recipient age is 54 (compared to 38 thirty years ago) and 21% of recipients are over 65 at the time of the transplant. It is clear that, amongst others, diabetes mellitus, cardiovascular problems and other co-morbidity factors represent significant additional challenges that corroborate a five year patient survival rate of 88% as excellent. With 15 kidney transplants following living donation, a record number of procedures were carried out in 2013, including 1 ABO blood group incompatible transplant. Decidedly personal monitoring of transplant patients has probably contributed to the increasing kidney and patient survival rates at UZ Leuven. During this process not only standard traditional clinical parameters are monitored. It also includes information on the histological condition of the transplant kidney, clinical alloimmunisation indicators and immunosuppressant medication dosages. Accurate and correct intake of the medication has a significant impact on the latter parameters and is consequently an important focus point in patient monitoring, together with a healthy diet and active lifestyle. Translational research conducted at UZ Leuven also looks for ways in which to reduce chronic transplant kidney damage, limit (allo) immunization and optimize immunosuppressive therapy. Improving organ quality during both storage and implantation also remains a vital area of clinical and scientific research at our hospital. We hope to celebrate the 4000th kidney transplant in 2014.

Transplant activities

128 kidney transplants were carried out in 2013. 113 patients underwent their first transplant, 12 patients underwent a second transplant and 3 patients received a third transplant (figure 2.18).
The number of transplants involving a kidney originating from a living donor has risen once again. 9 patients received a transplant with a kidney from a living donor in 2011. In 2012 the number was 11 and in 2013 it increased to 15 patients.
The number of transplants involving kidneys from non-heart-beating donors (or DCD donors, donation after circulatory death) remained stable in 2013. One in five transplants currently involves a kidney from a DCD donor.

FIGURE 2.18 | evolution of the number of kidney transplants 1992-2013

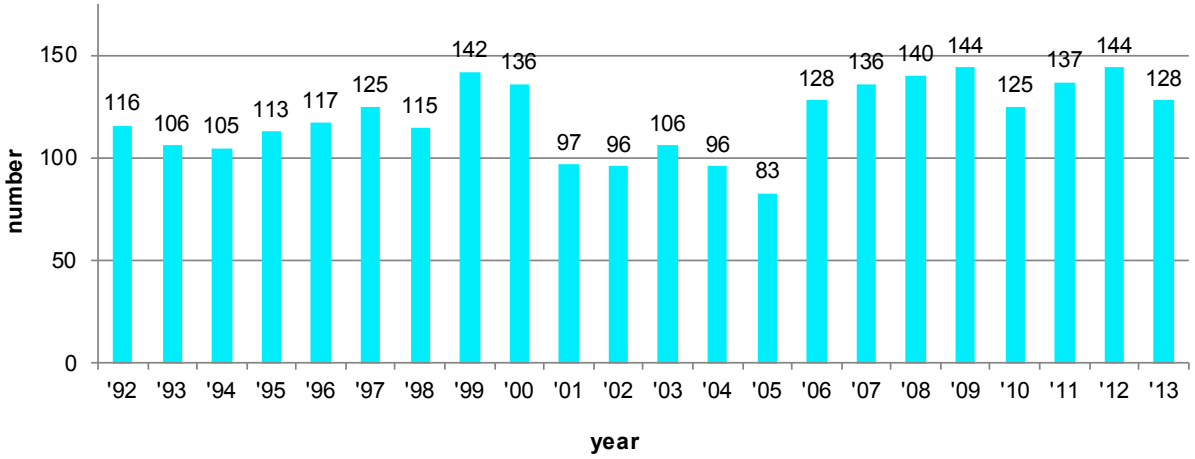
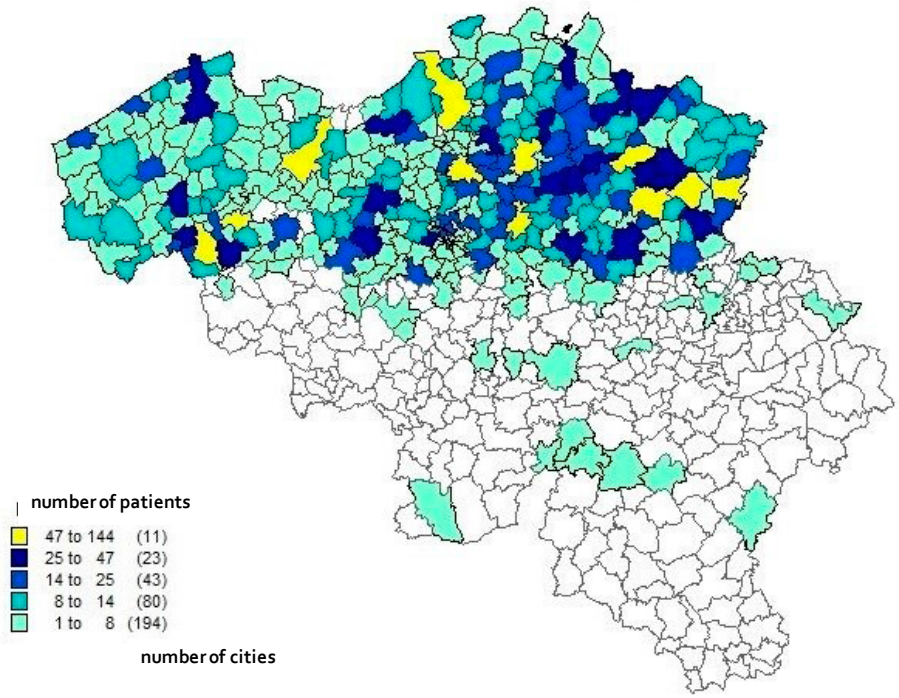


FIGURE 2.19 | geographic origin of kidney recipients (1963-2013)

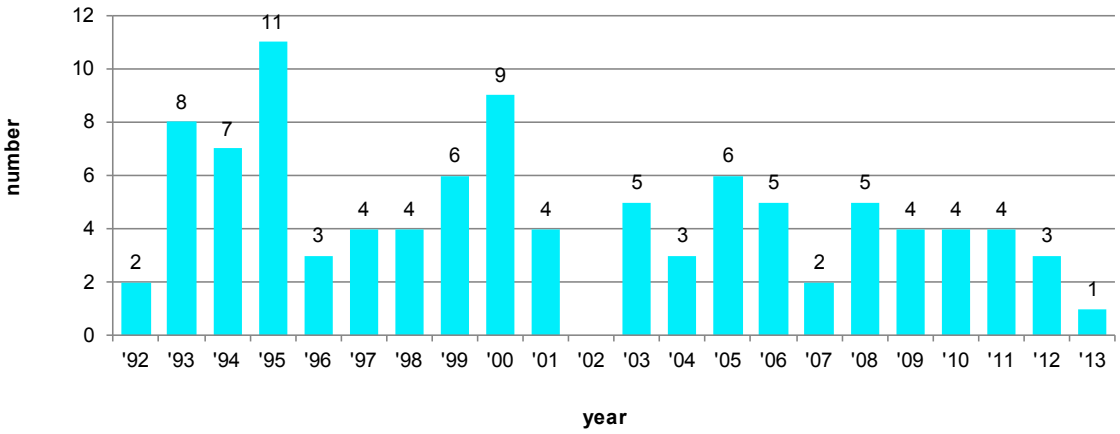


The number of combined transplants has decreased considerably. Only 6 combined transplants were carried out in 2013: 4 combined kidney/liver transplants, 1 kidney/pancreas transplant and 1 combined kidney/heart transplant (table 2.9).

TABLE 2.9 | number of combined kidney transplants carried out in 2013

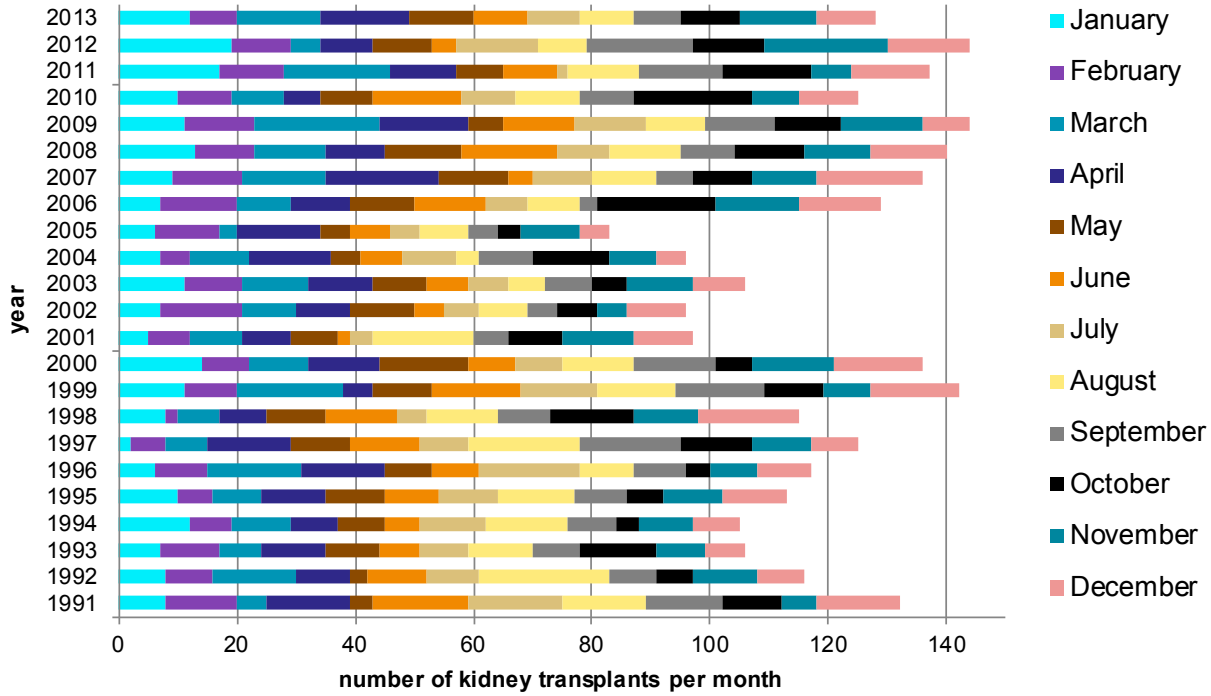
	2005	2006	2007	2008	2009	2010	2011	2012	2013
Kidney + liver	1	5	4	5	3	9	8	11	4
Kidney + heart		1	1			3	1		1
Kidney + lung		2						4	
Kidney + pancreas	6	5	2	5	4	4	4	3	1
Kidney + intestine			1				1		
Total	**7**	**13**	**8**	**10**	**7**	**16**	**14**	**18**	**6**

FIGURE 2.20 | annual number of combined kidney/pancreas transplants between 1992 and 2013



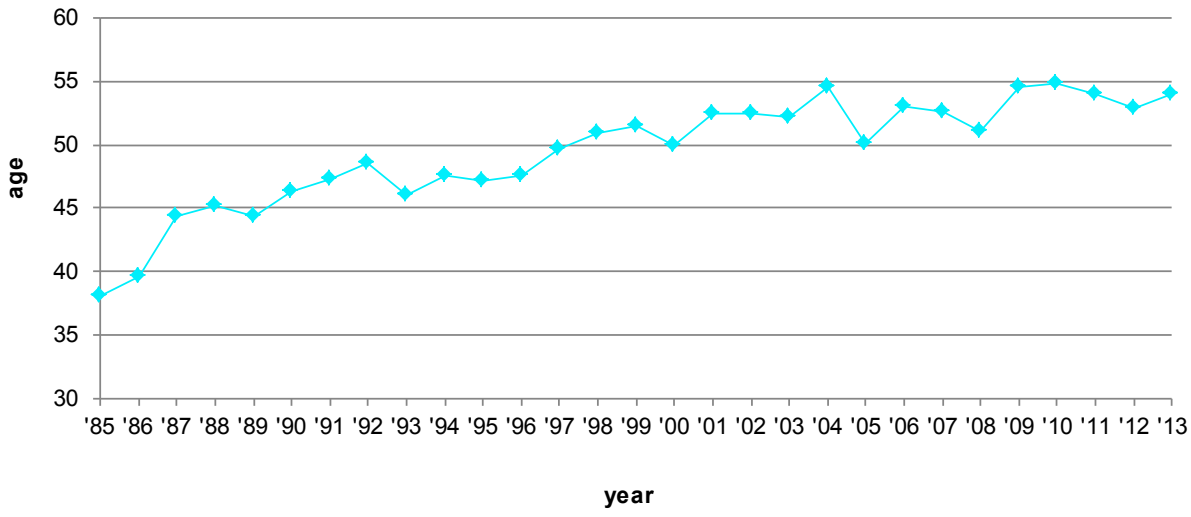
Transplant activities were spread more consistently in 2013 than in previous years. The largest number of transplants (15) were carried out in April. February and September were the quietest months with 8 kidney transplants (figure 2.21).

FIGURE 2.21 | evolution of the monthly number of kidney transplants in previous years



The average age of patients at the time of the transplant has stabilised in recent years. Last year the mean age was 52.82. Now the mean recipient age at the time of the transplant is 53.95 (figure 2.22).

FIGURE 2.22 | evolution of the mean recipient age since 1985



Patient survival results

Figure 2.23 shows the actuarial patient survival rate before and after 1983 (the year cyclosporin was introduced). Initially the patient survival rate is significantly better in the group that received a transplant after the introduction of cyclosporin (CsA), but from the 12th year after transplant both curves appear to coincide (Wilcoxon p=0.006 – log rank n.s.).
The actuarial patient survival rate after 1993 (the year Mycophenolate Mofetil (MMF) was introduced) is also shown. Initially the curve is slightly higher than the CsA curve, but eventually the MMF curve runs parallel with the curve for the other transplant patient groups.

FIGURE 2.23 | actuarial patient survival rate before and after the introduction of cyclosporin (CsA) and Mycophenolate Mofetil (MMF)

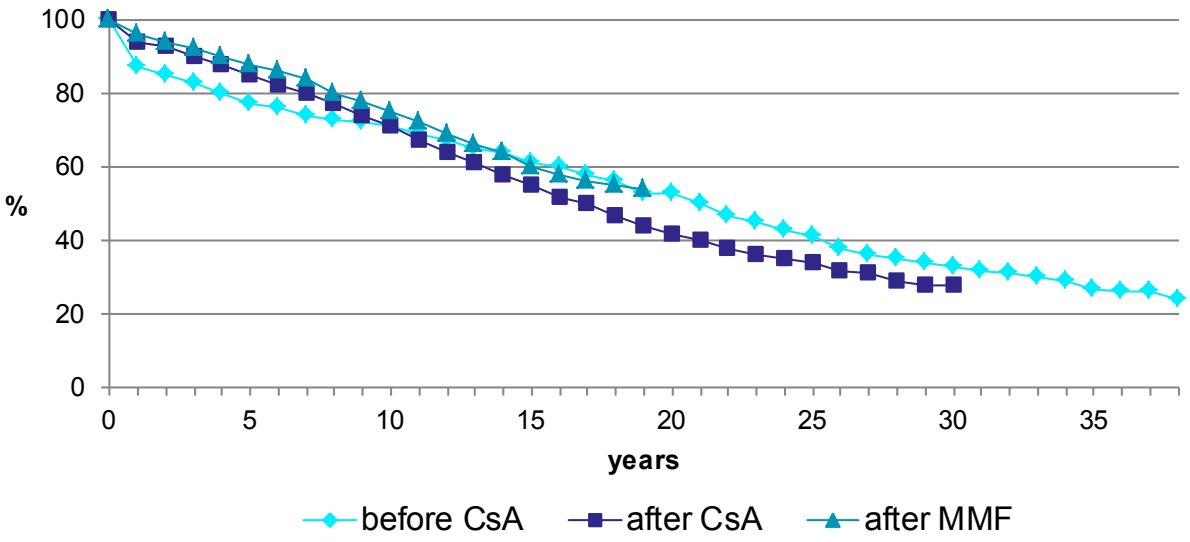
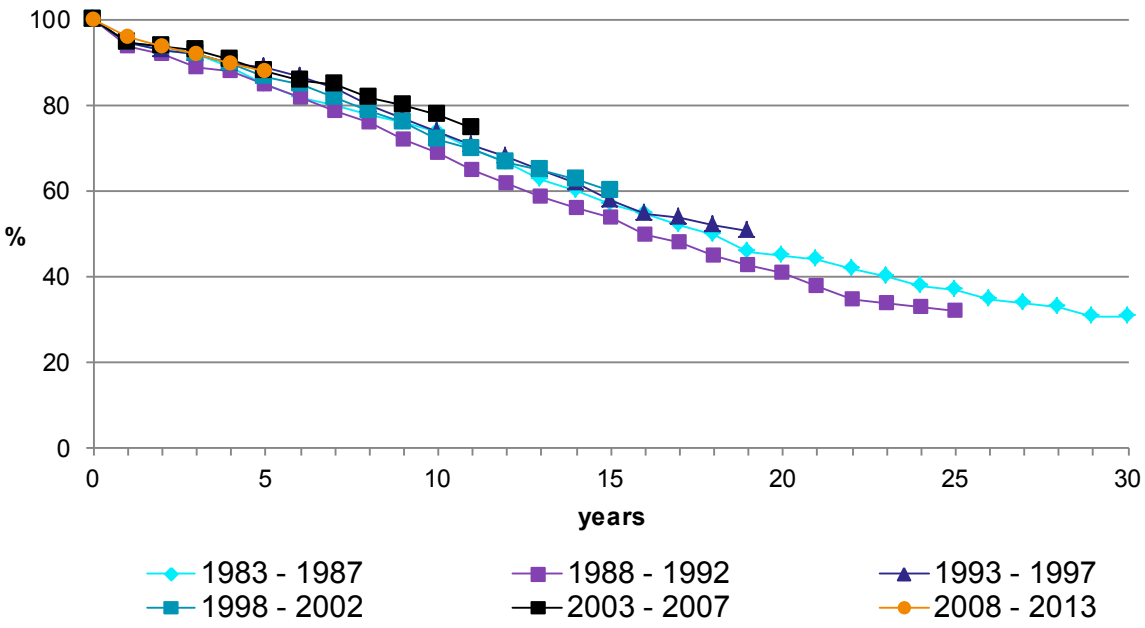


Figure 2.24 shows the analysis of the actuarial patient survival rate since 1983, calculated on the basis of consecutive 5 year periods. This demonstrates that after 1992 the five year survival rate increased from 85% to 88%. This positive result for the five year survival rate for groups transplanted after 2003 continues to increase.

FIGURE 2.24 | evolution of the actuarial patient survival rate since 1983



The effect of the recipient's age at the time of transplant on the actuarial patient survival rate (Wilcoxon p<0.0001) is shown in figure 2.25. Obviously survival is inversely proportional to the recipient's age: 75% after 25 years in the group aged below 30 and 44% in the group aged between 30 and 49. Understandably the patient survival rate after more than 20 years in patients transplanted at a later age (> 60) is below 20%.

FIGURE 2.25 | actuarial patient survival rate on the basis of age

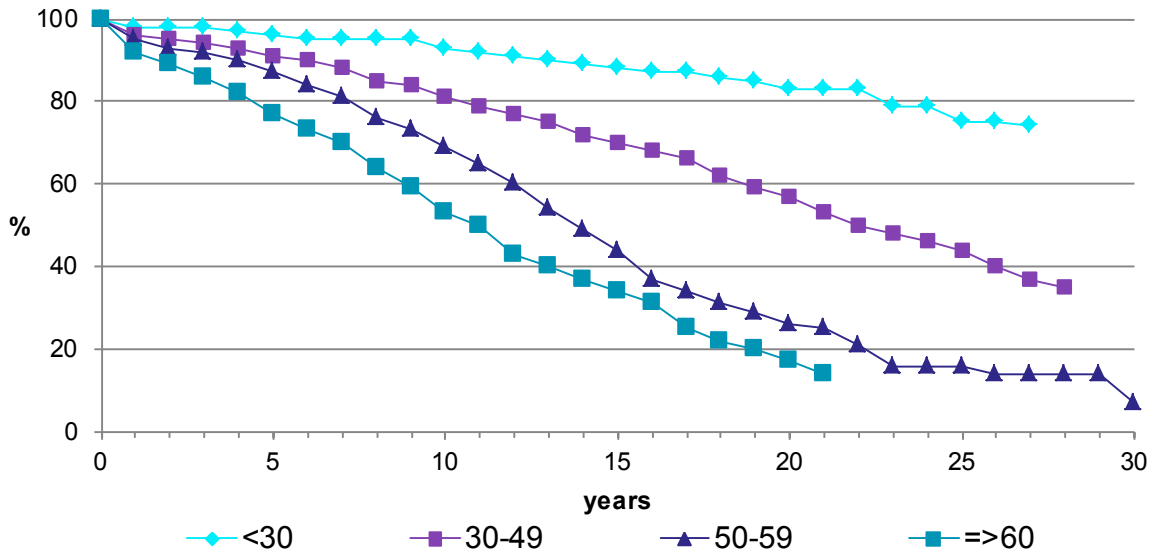
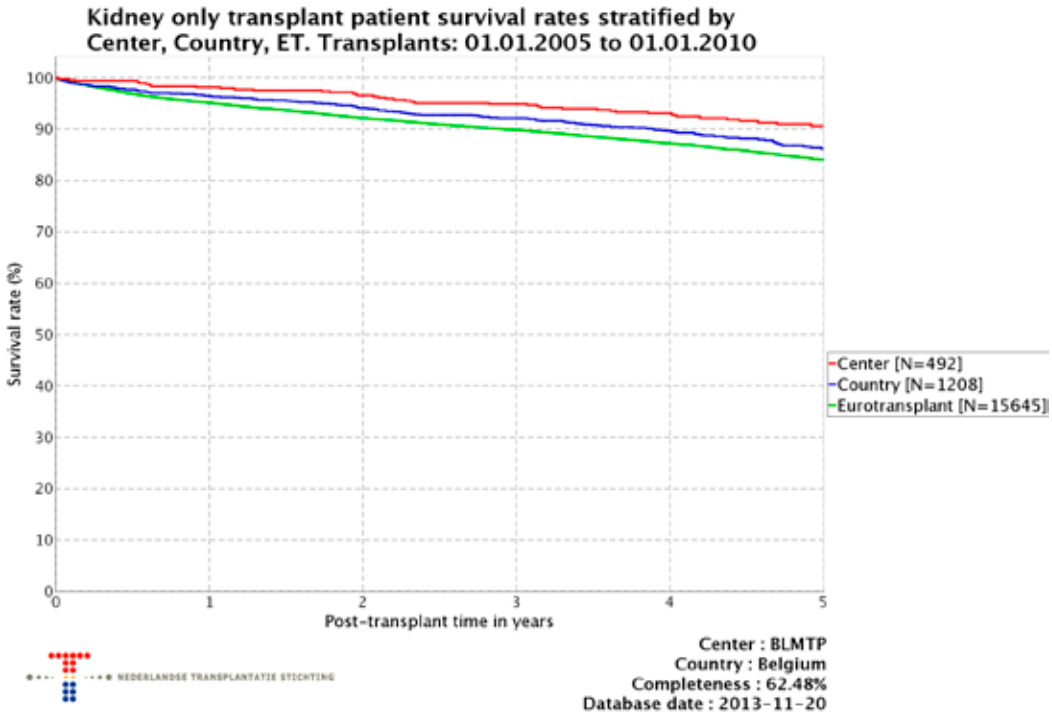


Figure 2.26 shows the Eurotranplant data (period 2005-2010) for patient survival (up to 5 years post operatively) in our kidney transplant programme compared to the global experience within the entire Eurotranplant region and the pooled results from all Belgian centres.

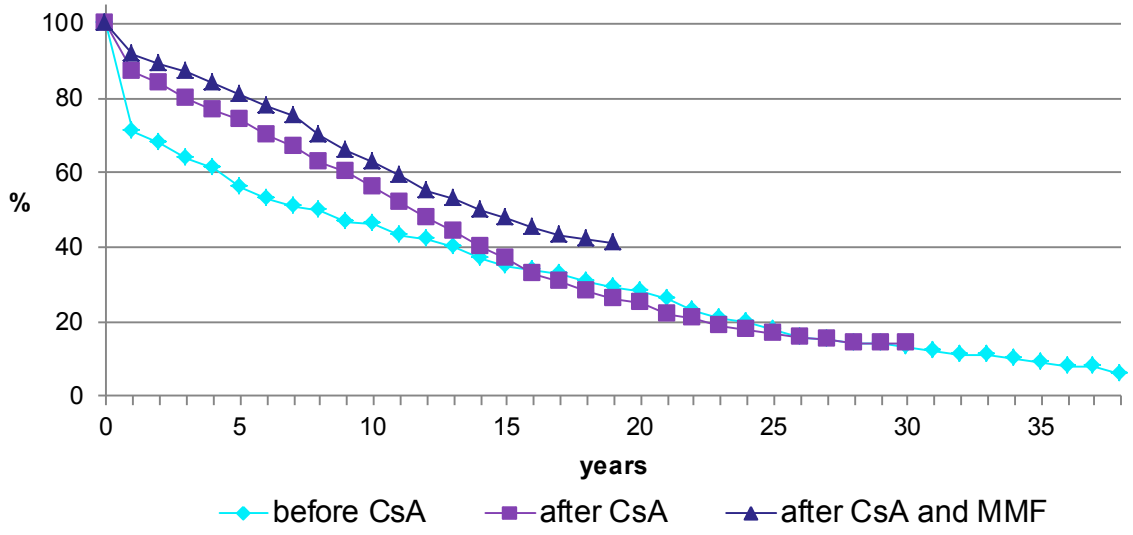
FIGURE 2.26 | five year patient survival rate (2005-2013) kidney only transplants), UZ Leuven compared to Eurotransplant and Belgium (the Belgian figures also include the results for UZ Leuven). Source: Eurotransplant



Kidney survival results

Figure 2.27 shows the actuarial kidney survival rate for which the death of patients with a functional graft is considered the end point (not censored for death). The remarkable difference at the start of the initial years following transplant between patients transplanted before and after the introduction of cyclosporine is well known. Both curves now almost perfectly coincide. What remains notable, however, is that the curve for patients transplanted after the introduction of Mycophenolate Mofetil is considerably higher (in 19 years 41% as opposed to 26% and 29%).

FIGURE 2.27 | actuarial kidney survival rate before and after CsA (not censored for death)



Looking at the actuarial kidney survival rate, but excluding patients who die with a functional graft (censored for death), it is again notable that patients who received a transplant following the introduction of Mycophenolate Mofetil are doing significantly better than those who received a transplant before the introduction (18 years after the transplant 68%, 56%, 52% respectively) (figure 2.28).

FIGURE 2.28 | actuarial kidney survival rate classified into before and after the introduction of cyclosporin (Cs) and Mycophenolate Mofetil (MMF) (censored for death)

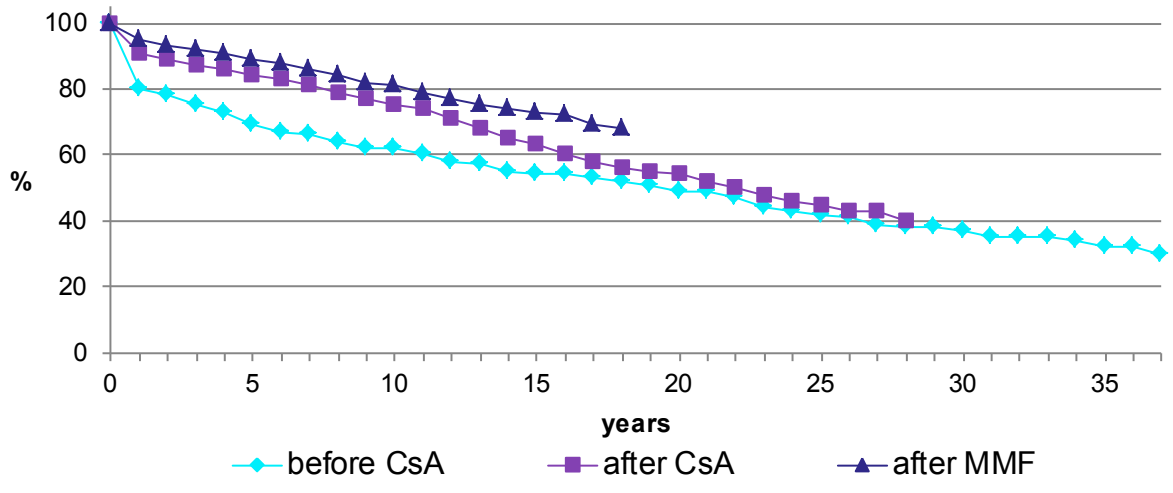
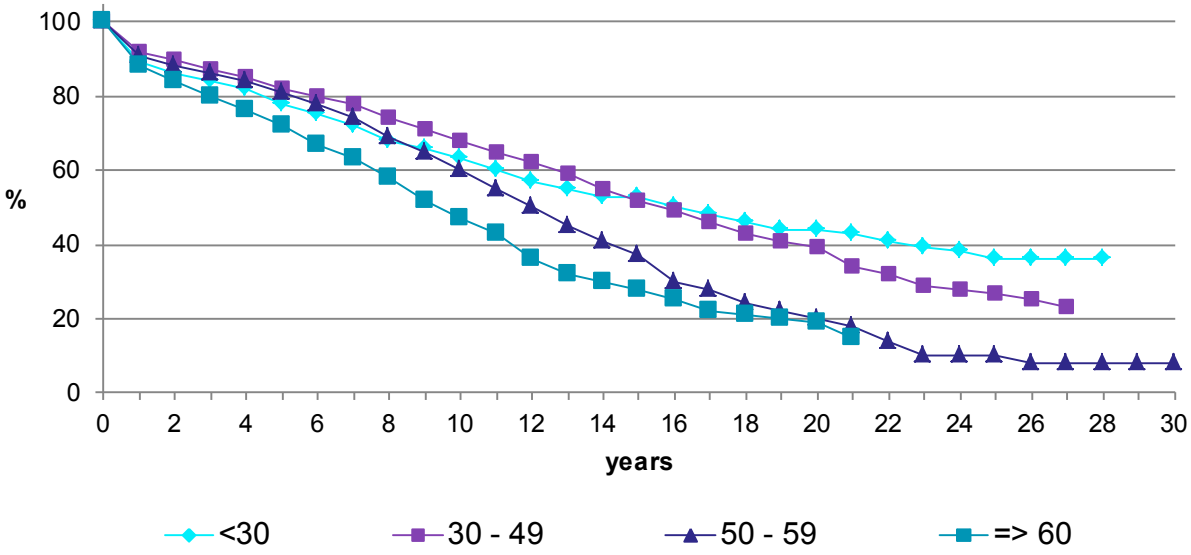


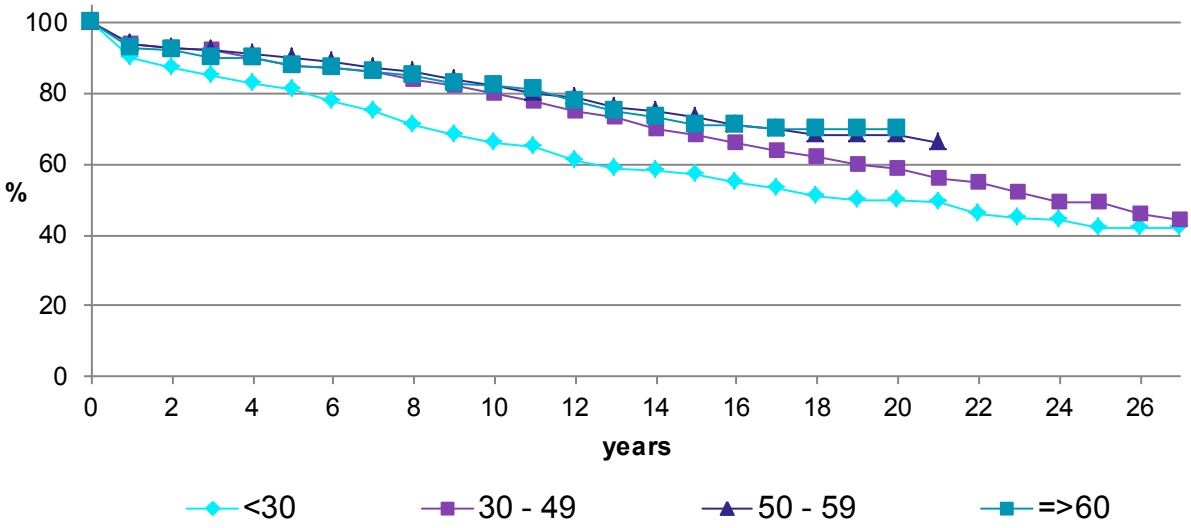
Figure 2.29 shows the actuarial kidney survival rate. Taking into account the recipient's age there are notably large differences between younger and older recipients.

FIGURE 2.29 | actuarial kidney survival rate (not censored for death) on the basis of age



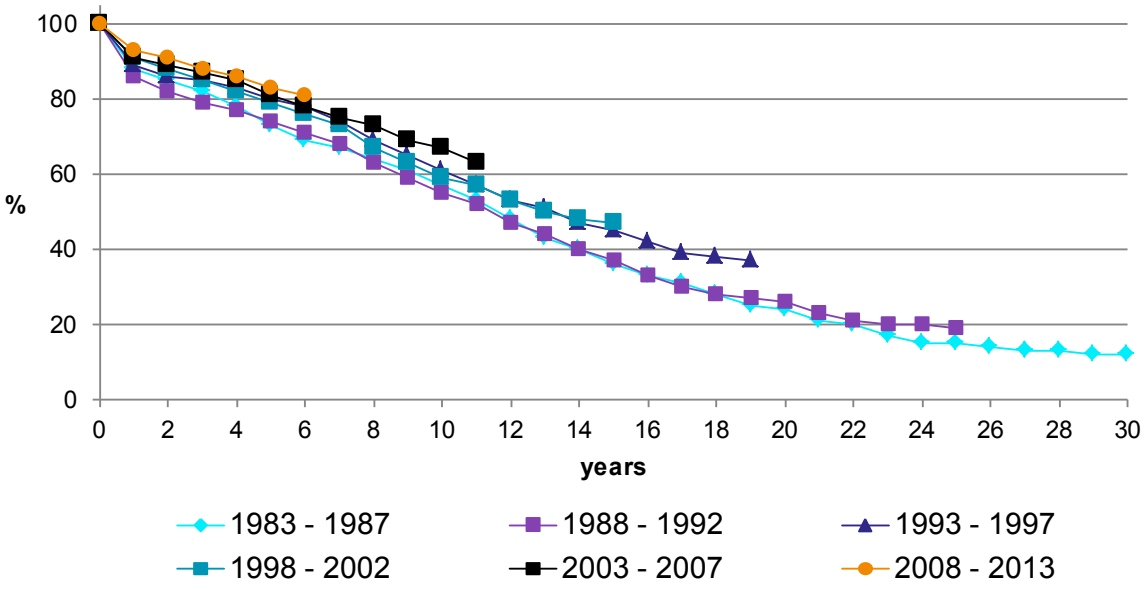
If the recipient's death is also taken into account (censored for death), it is safe to say that the loss of the transplanted kidney in the > 60y old recipient category is largely due to the recipient's death. The older age category consequently has a better intrinsic kidney survival rate than the younger groups.

FIGURE 2.30 | actuarial kidney survival rate (censored for death) on the basis of age



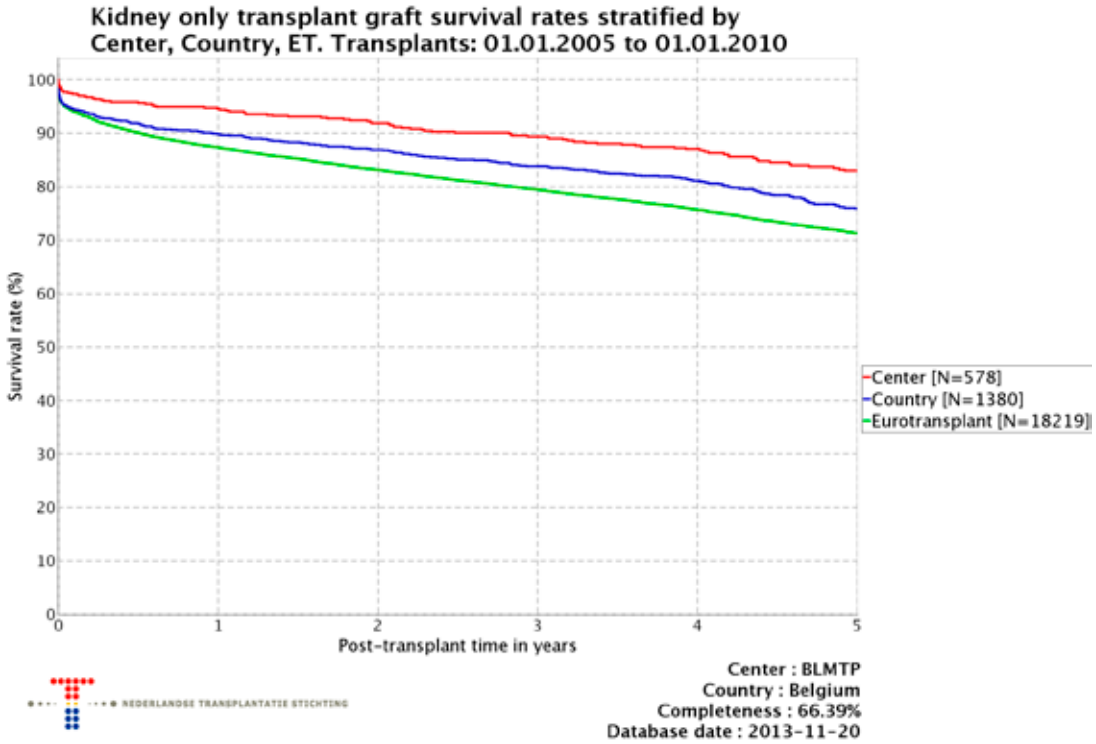
Kidney survival has continued to improve in recent years. The five year survival rate for patients who received a transplant in the period between 1983 and 1987 was 73%. For patients who received a transplant in the period after 2008 the five year survival rate increases by 10% to 83% (figure 2.31).

FIGURE 2.31 | evolution of the actuarial kidney survival rate (not censored for death) since 1983



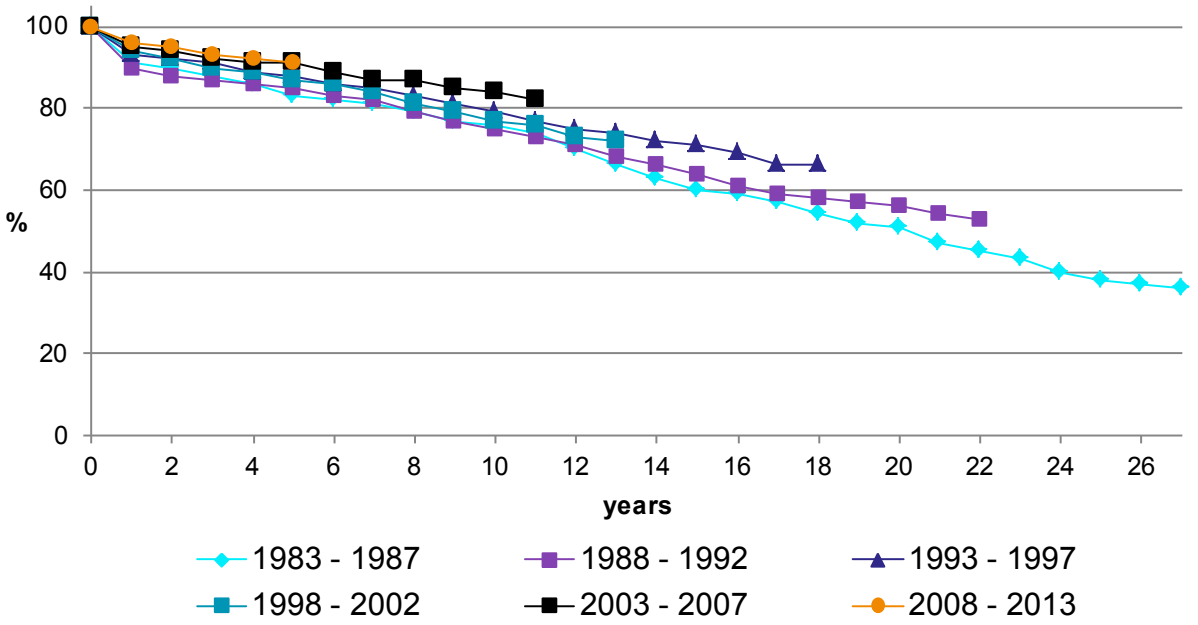
There is also a difference between the figures for UZ Leuven and those for Eurotransplant and Belgium for graft survival rate.

FIGURE 2.32 | five year graft survival rate (2005-2013) kidney only transplants, UZ Leuven compared to Eurotransplant and Belgium (the Belgian figures also include the results for UZ Leuven). Source: Eurotransplant



Finally, figure 2.33 shows the kidney survival rate with a functional transplant kidney at the time of the patient's death as the end point (censored for death). This obviously confirms the previous finding. The five year survival rate in the latter group (2008-2013) is no less than 8% higher (91% as opposed to 83%).

FIGURE 2.33 | evolution of the actuarial kidney survival rate (not censored for death) since 1983



Donor type development

There has been a downward trend in the number of suitable organs from deceased donors since the early nineties (red line). Obviously the number of completed transplants initially followed this downward trend (blue line). Fortunately, this downward trend in the number of transplants could be corrected early on by using kidneys originating from ECD donors (extended criteria donors), by transplanting kidneys from DCD donors and by conducting living donor kidney transplants.

The number of these types of donors is currently more than 50%.

FIGURE 2.34 | evolution of the number of kidney transplants on the basis of donor type 1992-2013

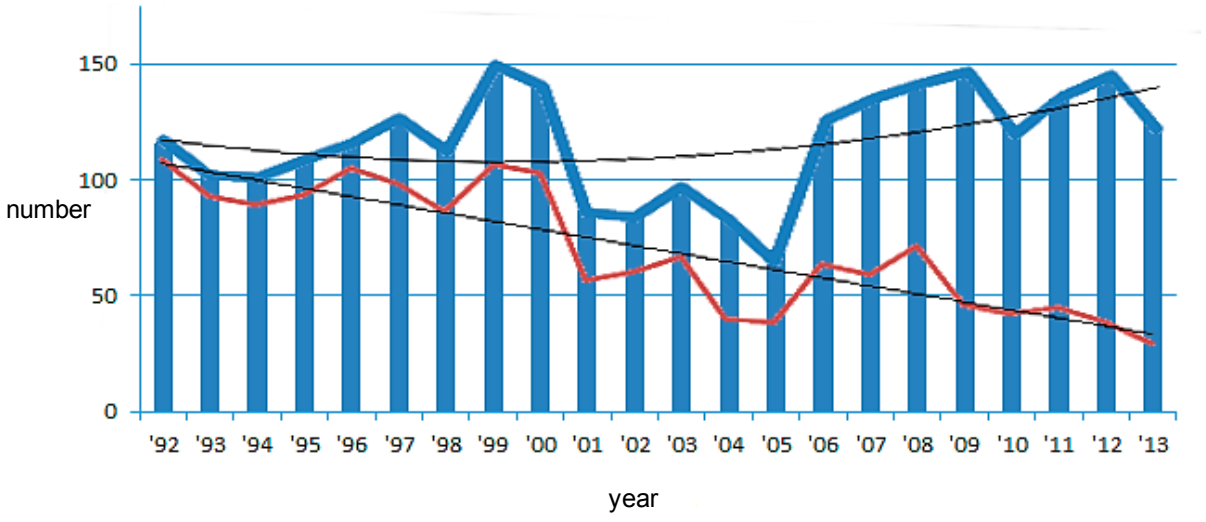
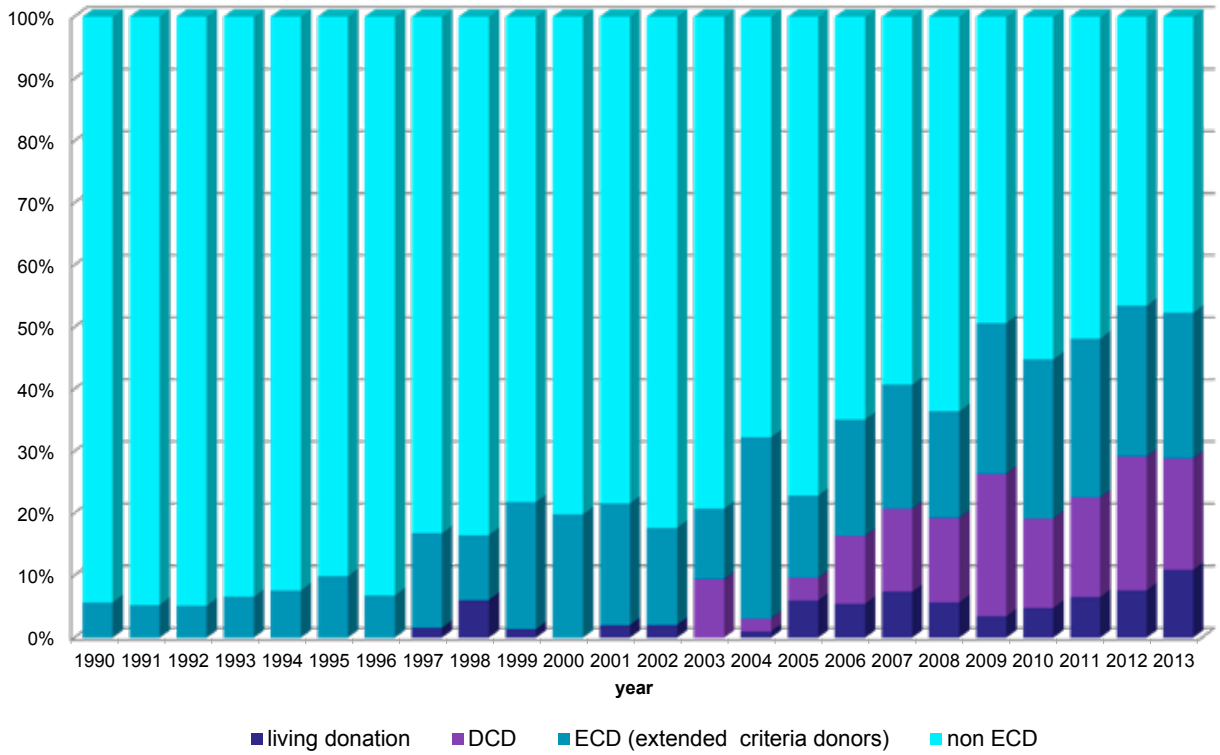


FIGURE 2.35 | kidney transplant percentage on the basis of donor type 1990-2013



PART 3

THORACIC TRANSPLANTS

surgery
cardiac surgery
thoracic surgery
ear, nose & throat disease, facial and neck surgery
plastic and reconstructive surgery

internal medicine
cardiology
pneumology

transplant coordination

transplant programmes
heart transplant
lung transplant
combined heart/lung transplant
trachea transplant

cardiology
Professor Dr. Johan Vanhaecke, Professor Dr. Johan Van Cleemput, Dr. Walter Droogne, Dr. Gabor Vörös

cardiac surgery
Professor Dr. Bart Meyns, Professor Dr. Paul Herijgers, Professor Dr. Bart Meuris, Professor Dr. Filip Rega

anaesthesiology
Professor Dr. Jan Van Hemelrijck, Dr. Gert Poortmans, Dr. Layth Al Tmimi, Professor Dr. Steffen Rex, Professor Dr. Carlo Missant

intensive medicine
Professor Dr. Maria Schetz, Professor Dr. Sophie Van Cromphaut, Professor Dr. Dirk Vlasselaers, Dr. Lars Desmet

teams OR – perfusion - ICU – hospitalisation
Luc Hoppenbrouwers, Eddy Vandezande, Nancy Vandenbergh, Koen Vanhonsebrouck, Sabine Gryp, Suzanna Mijten, Hilde Bollen

specialist nurse
Nathalie Duerinckx

day room nurse
Dominica Kums, Kristof Aussloos

transplant coordination
Dirk Claes, Nele Grossen

social work
Karen Niclaes, Sabine Vanoost

physiotherapy
Theophiel Claes, Bart Peeters

psychological support
Marijke Potargent

dietary advice
Rita Lenaerts, Kristine Bessemans, Kathleen Gerits

Heart transplant care programme

The heart transplant programme was initiated on 1 September 1987. Since then 604 transplants were carried out on 575 patients (status on 29 April 2014 – excluding heart/lung transplants). These patients originate from across Flanders (fig. 3.3). Care providers who are currently directly involved in the heart transplant programme are listed alongside. Even a fairly extensive list does not truly reflect the many colleagues and employees of the cardiology, cardiac surgery and other disciplines, from primary services and from other hospitals, whose input may be less obvious but by no means less important. Also those colleagues who were involved in the early days, at all levels and in all disciplines, have had a major input in the way the heart transplant programme currently operates.

Transplant activities

In the Eurotransplant region – and globally – the number of heart transplants has decreased by approximately a quarter between 1990 and 2005. In Belgium it even dropped by 44% (figure 3.1), in Leuven by 24% (figure 3.2). This development is in sharp contrast to other organ disciplines and initially coincided with shorter waiting lists and fewer fatalities on the waiting list. This remarkable combination of trends was probably caused mainly by a spectacular improvement in other treatment options for heart failure. However, the impact of this improved heart failure therapy is now waning and falling behind. Since 2003 the heart transplant waiting list at Eurotransplant has been increasing again. We have also noticed the impact of this development: the number of patients on the waiting list the past five years has been double that for previous years (figure 3.4). The increased use of mechanical support as a 'bridge to transplantation' could possibly also play a part: the number of patients receiving a transplant 'from a heart pump' continues to rise and for the first time amounted to more than 50% of new transplants last year (figure 3.5). The number of heart transplants in Belgium has stabilised again since the middle of the past decade and it remains to be seen whether we will be able to achieve a further increase. If not, this will have an adverse effect on waiting list mortality. In any case, the lack of donors remains problematic.

FIGURE 3.1 | heart transplants in Belgium (1982-2013)

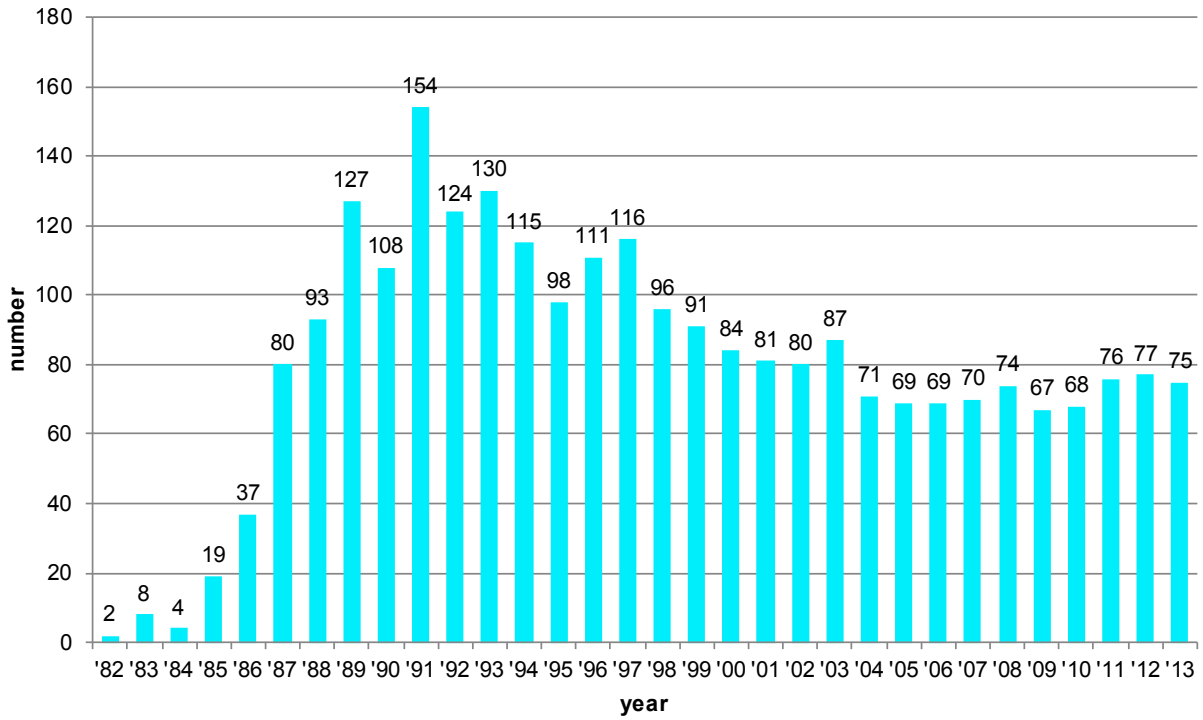


FIGURE 3.2 | heart transplants at UZ Leuven

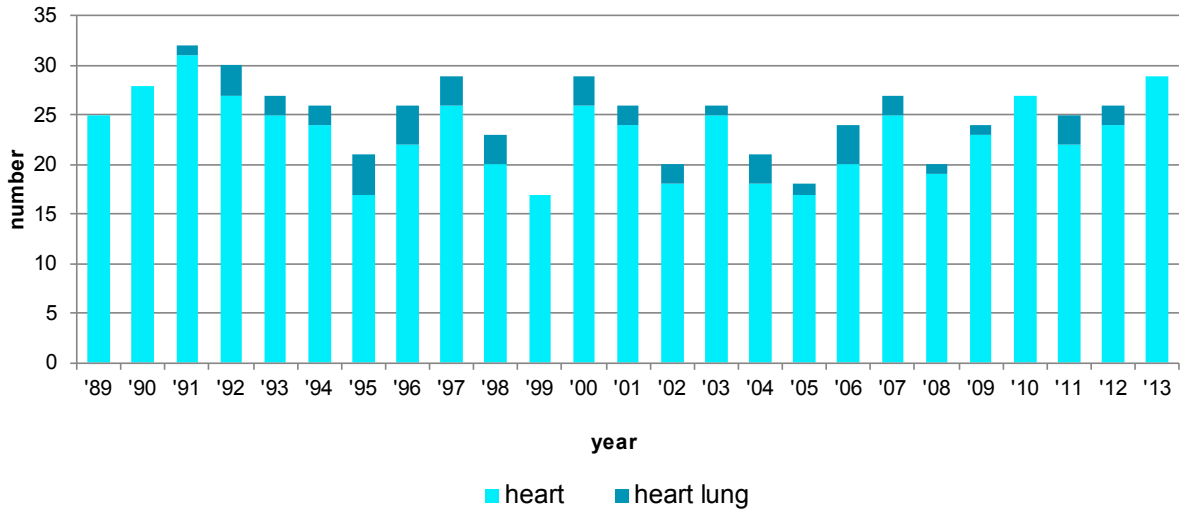


FIGURE 3.3 | geographic origin of patients who underwent a heart transplant

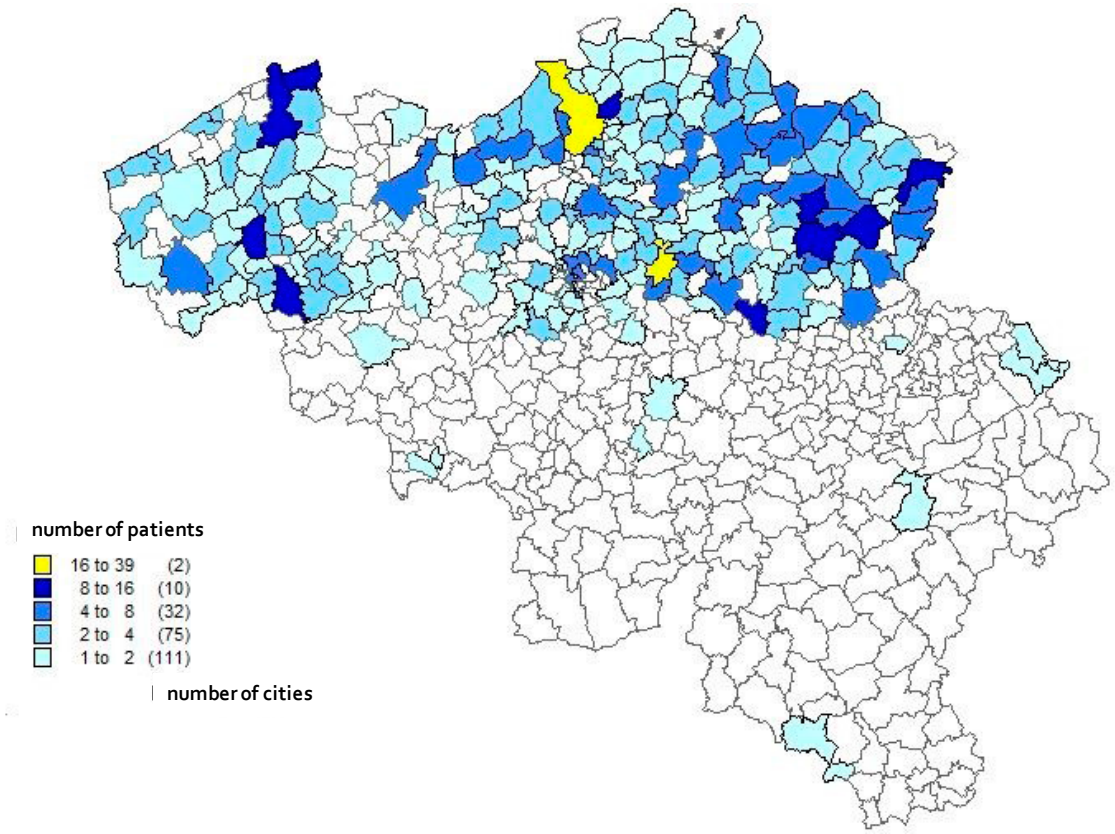


FIGURE 3.4 | evolution of the number of patients on the waiting list on 31 December each year

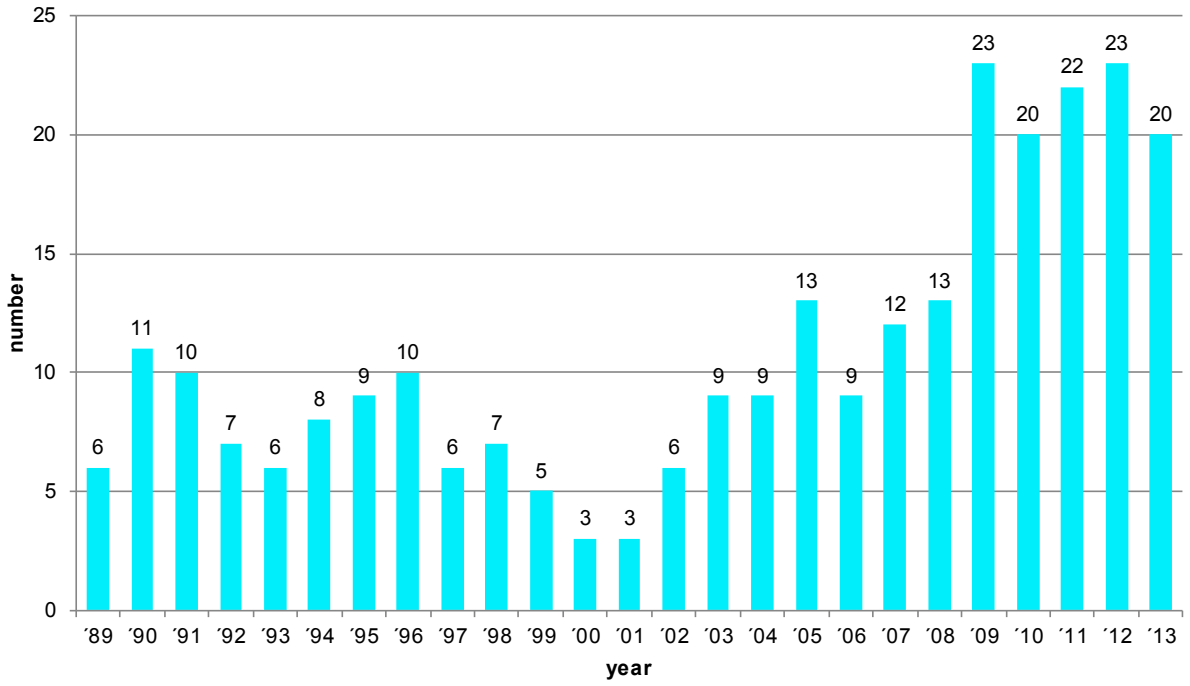


FIGURE 3.5 | percentage of patients who received a transplant involving mechanically supported circulation (bridge-to-transplantation)

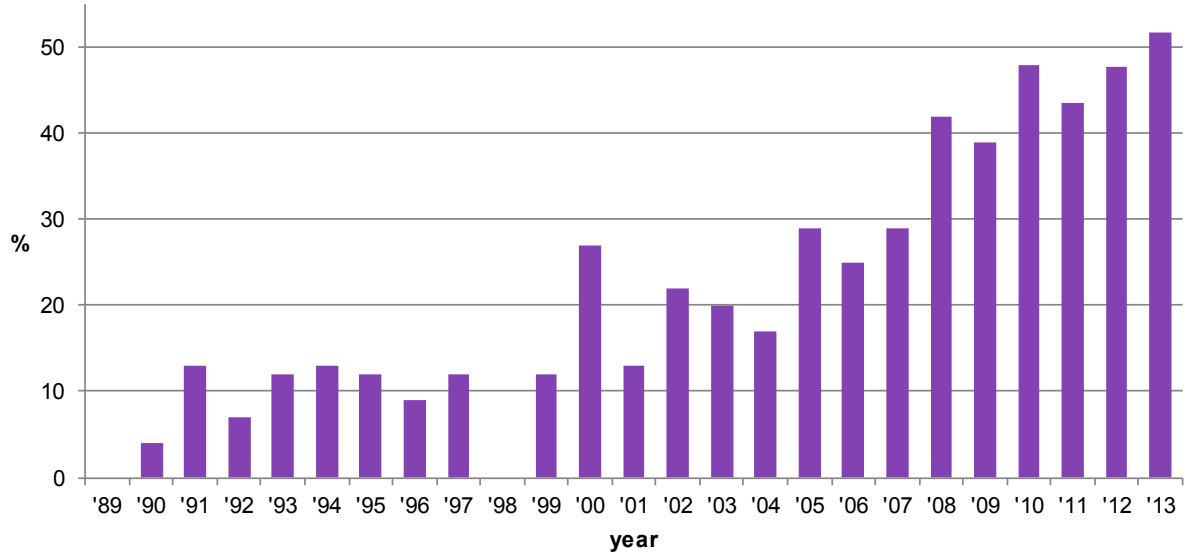


FIGURE 3.6 | patients in active follow-up

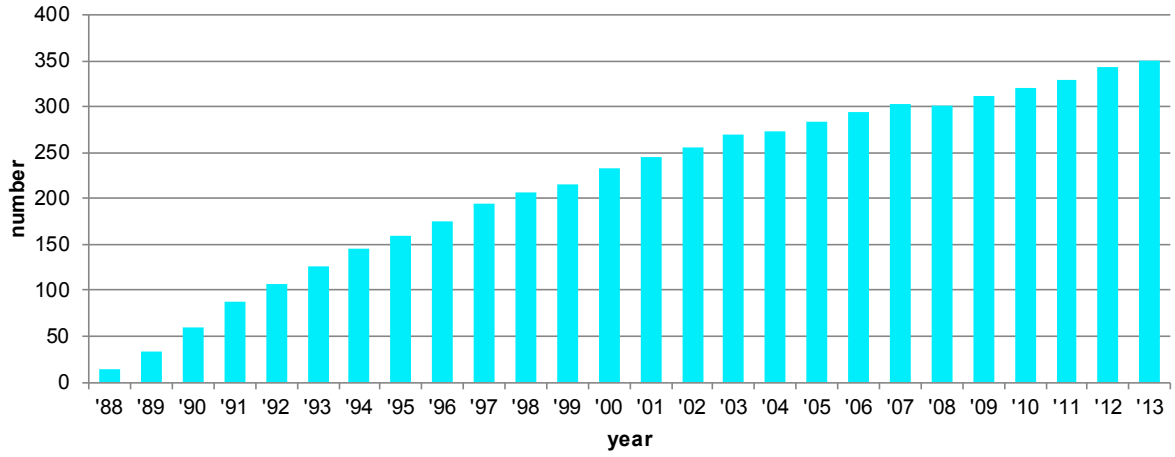


FIGURE 3.7 | average age of heart transplant recipients

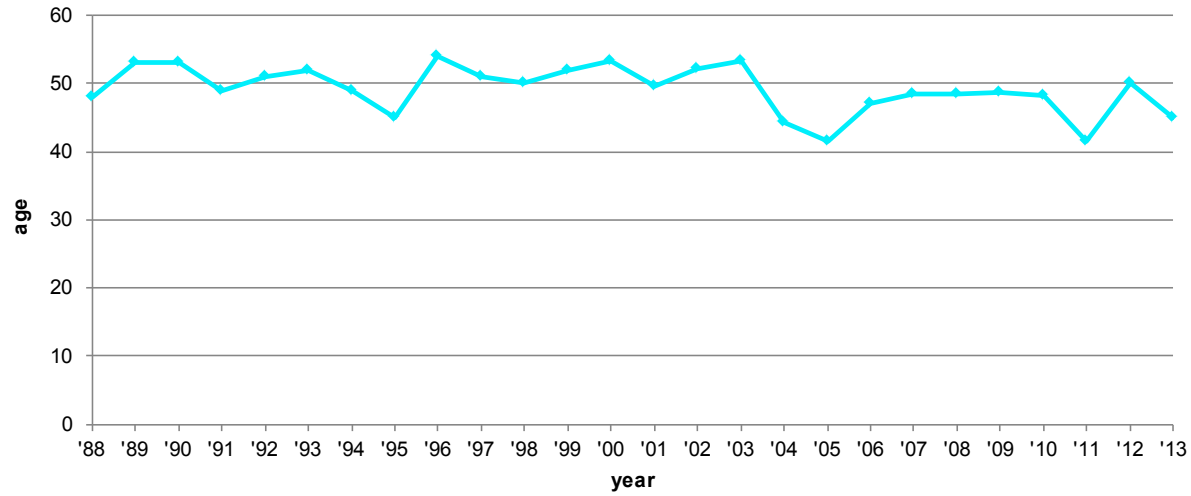


FIGURE 3.8 | average age of heart transplant donor

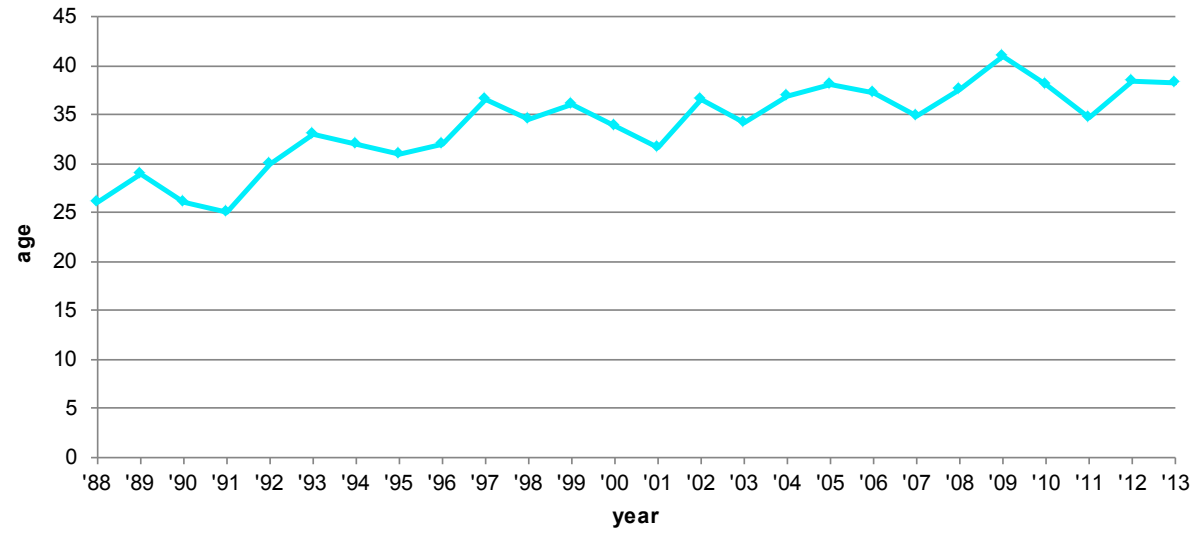


FIGURE 3.9 | reason for transplant

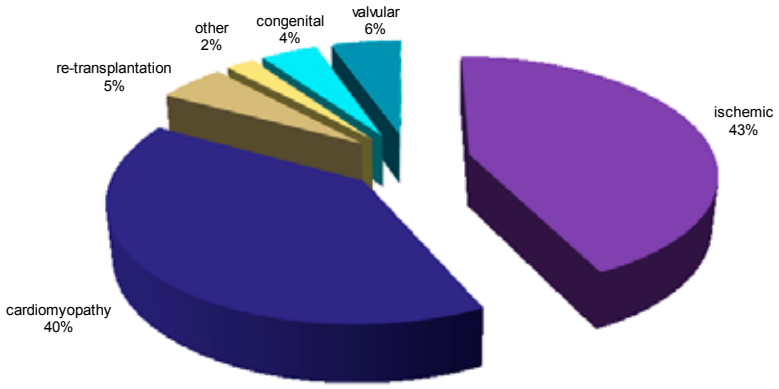


FIGURE 3.10 | average waiting time for a heart transplant

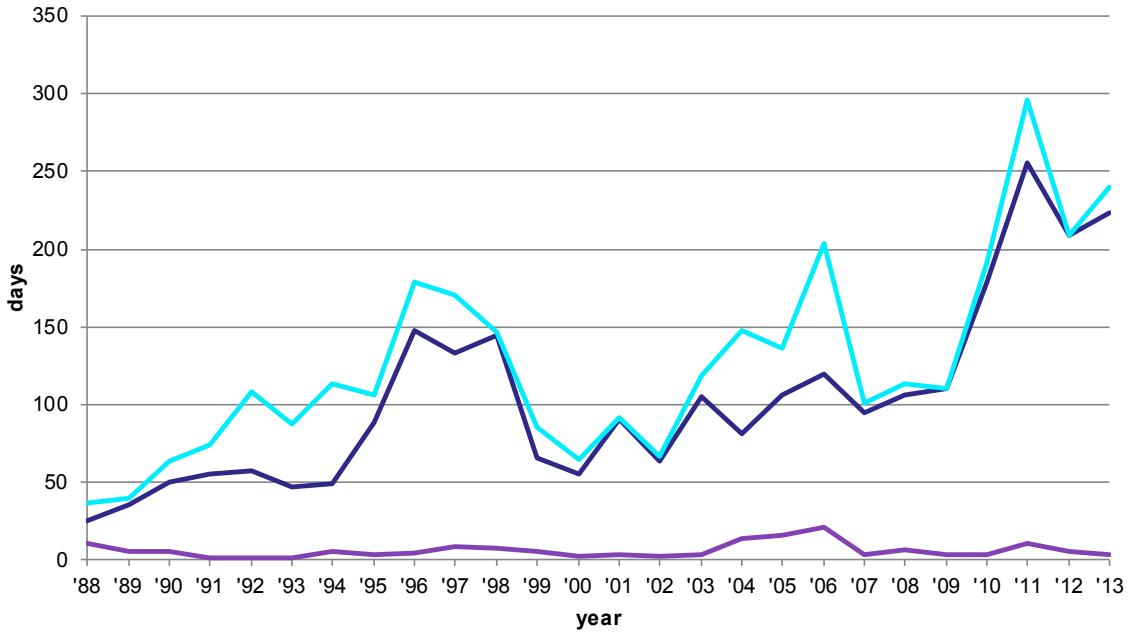
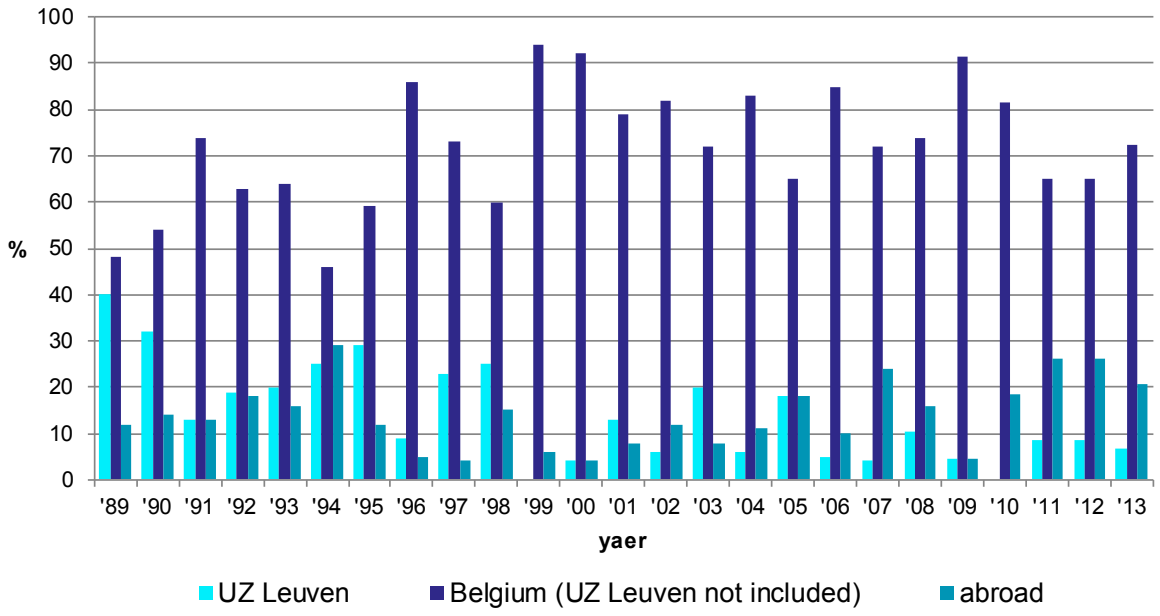


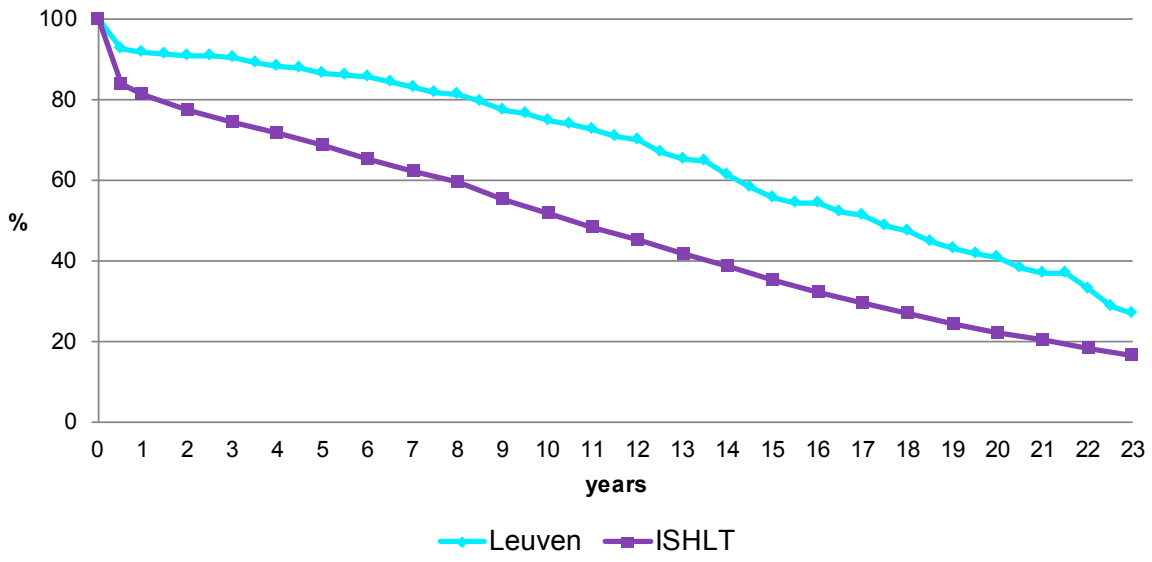
FIGURE 3.11 | donor heart origin



Transplant results

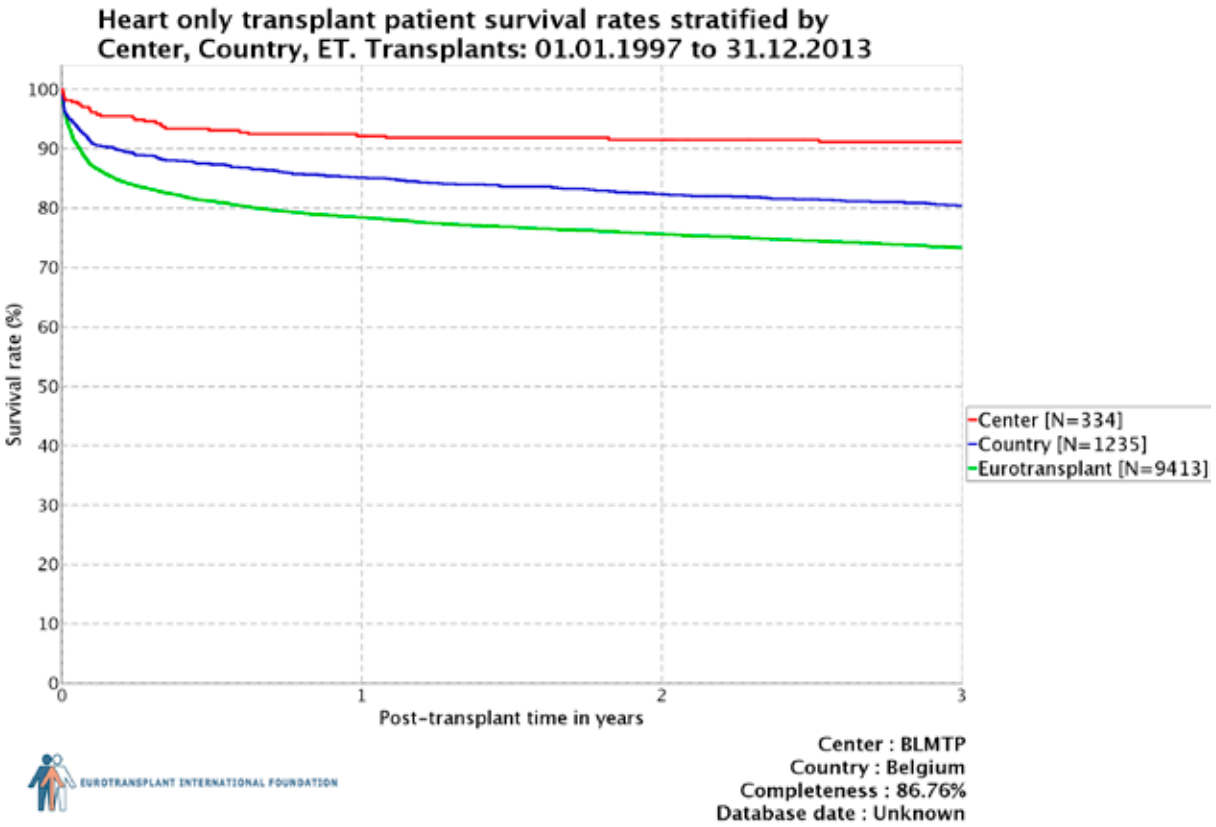
Survival results were calculated on the basis of our overall experience until end 2013: 594 hearts transplants on 565 patients, including 21 combined heart/kidney transplants and 3 combined heart/liver transplants (this does not include the results of 47 heart/lung transplants, they can be found in the section entitled 'Lung transplantation'). Figure 3.12 compares the actuarial patient survival rate with the combined results in the global Registry of the International Society for Heart & Lung Transplantation (ISHLT). The ten year survival rate for patients in Leuven currently stands at 74.9% as opposed to 51.8% in the ISHLT Registry.

FIGURE 3.12 | heart transplant patient survival rate



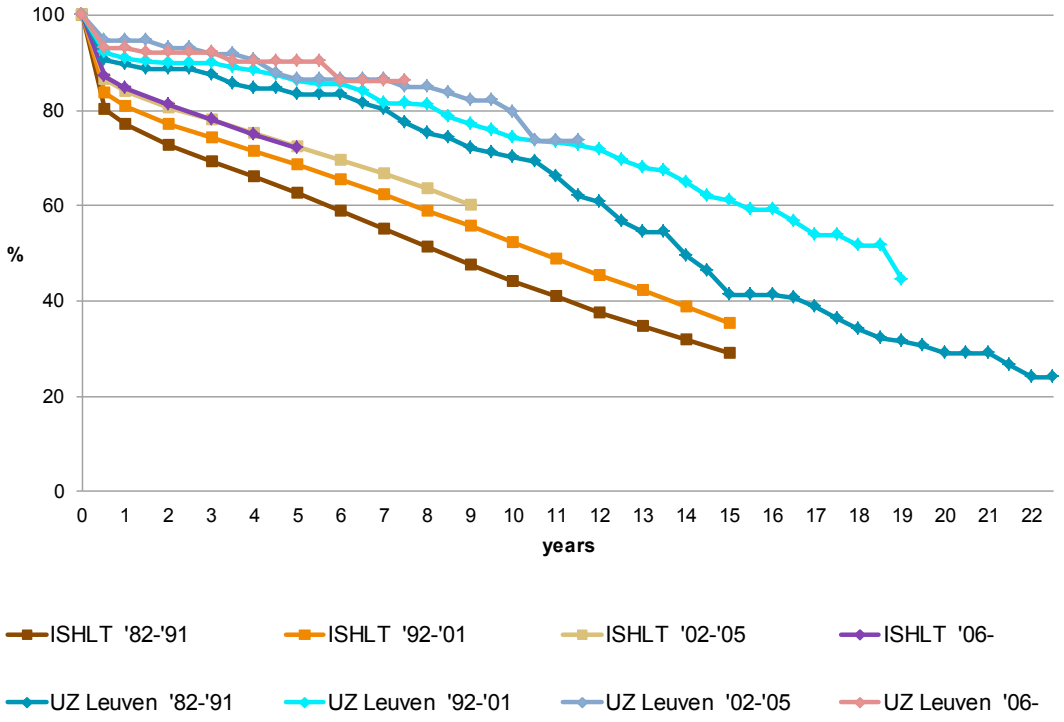
Using the available Eurotranplant data we can also compare patient survival rates (up to 3 years post operatively) for our programme with the overall experience within the entire Eurotranplant region and with the pooled results for all Belgian centres for the period 1997-2013.

FIGURE 3.13 | three year patient survival rates (1997-2013 heart only transplants), UZ Leuven compared to Eurotransplant and Belgium (the figures for Belgium also include the results for UZ Leuven). Source: Eurotransplant



The short and medium term results for consecutive periods have remained at a high level, despite increasing complexity and the relaxation of both the recipient and donor criteria. Survival rates continue to improve over the long term and in the most recent cohort studies the five and ten year survival rates are 90 and 80% respectively (figure 3.14).

FIGURE 3.14 | heart transplant patient survival per period



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(Heart) lung transplant care programme

The lung and heart/lung transplant programme which was initiated in UZ Leuven in 1991, reverted back to its normal number of 59 in 2013 following a record number of 81 procedures in 2012. This merely appears to be the result of fewer lung donor registrations in the past year. Nevertheless, our more flexible approach to lung donors remains in place and the number of 'marginal lung donors' and DCD (donation after circulatory death) donors consequently continues to rise with good results. The main indications for a lung transplant continue to be COPD, pulmonary fibrosis, cystic fibrosis and pulmonary hypertension. The five year survival rate following a lung transplant, which remains markedly better than in the 'International Registry for Heart and Lung Transplantation', is stable around 75%.

Transplant activities

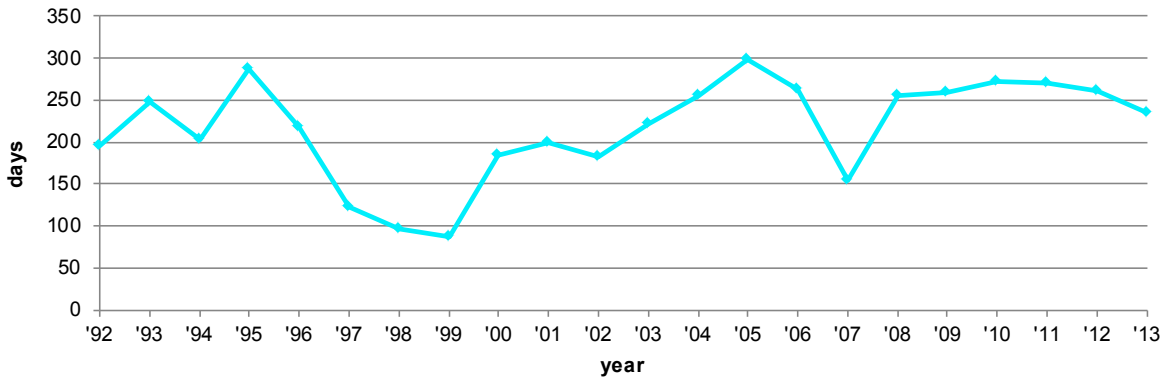
Compared to 2012 the number of interventions has decreased to 59 procedures, which is closer to our normal annual number. Only double lung transplants were carried out; one patient underwent a combined double lung and liver transplant. No heart/lung transplants were conducted in 2013.

TABLE 3.1 | number of (heart) lung transplants UZ Leuven (1994-2013)

	'94	'95	'96	'97	'98	'99	'00	'01	'02	'03	'04	'05	'06	'07	'08	'09	'10	'11	'12	'13
Heart-lung	2	4	4	3	3	-	3	2	2	1	3	1	4	2	1	1	-	3	2	-
Unilateral	9	7	5	6	2	8	4	10	10	15	14	9	19	7	8	4	7	1	-	-
Bilateral	2	1	3	4	8	4	13	20	21	27	22	29	34	44	40	42	51	58	79	**59**
Total	13	12	12	13	13	12	20	32	33	43	39	39	57	53	49	47	58	62	81	**59**

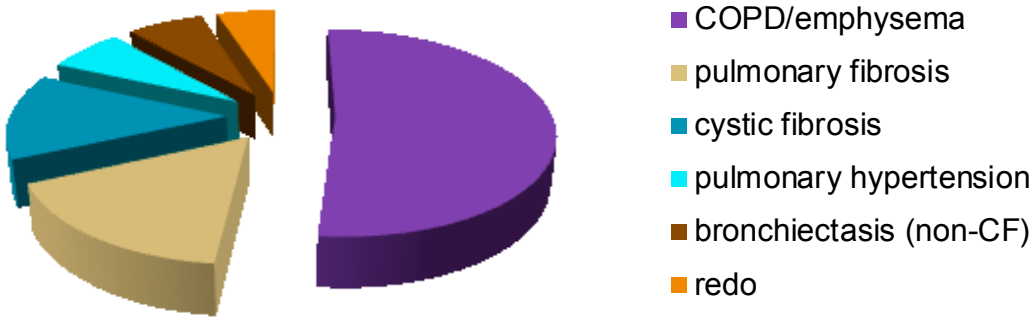
The number of candidate lung transplant patients on the active waiting list remains stable between 35 and 45. The average waiting time has dropped further (235 days, variation 23-953 days) versus 262 in 2012. Waiting list mortality remains low (< 5%).

FIGURE 3.15 | average waiting time since 1992



The indications for lung transplantation remain comparable and are illustrated in figure 3.16. Emphysema, followed by pulmonary fibrosis and cystic fibrosis, continue to be the main indications. Only 3 re-transplants were carried out in 2013 (5% compared to 7.4% in 2012), all as a result of serious chronic rejection.

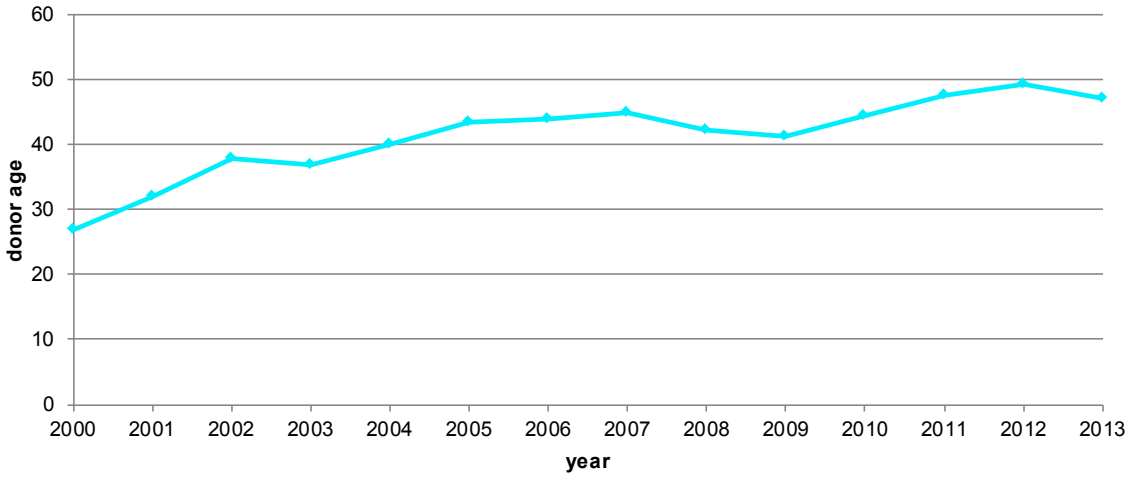
FIGURE 3.16 | indications for (heart) lung transplantation in 2013



The age distribution of recipients remains comparable to previous years, with most patients aged between 50 and 60, reflecting the most frequent indications, emphysema and lung fibrosis.

Figure 3.17 shows the average age of donors since 2000, indicating a slight reduction compared to last year (average age 47.2; min. 18, max. 77 compared to an average of 49.4 in 2012).

FIGURE 3.17 | average donor age per annum



The number of donors over the age of 55 has dropped again (from 44% in 2012 to 32% in 2013). The number of donors over the age of 60 has also dropped to 16%. 16% of donors were over 65.

FIGURE 3.18 | percentage of donors on the basis of age over the past 12 years

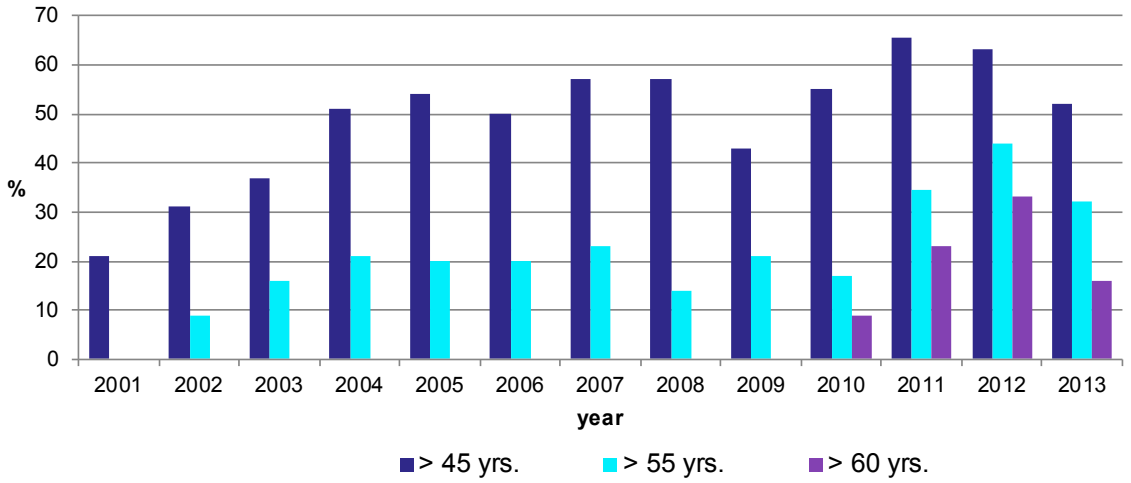


Figure 3.19 illustrates the survival rates over different time periods from the start of our programme in 1991. Compared to the data of the International Registry for Heart and Lung Transplantation (ISHLT) for these periods we are clearly systematically performing better. The survival rate at UZ Leuven is better at all times. The 30 day mortality rate at UZ Leuven remains very low (3.3%).

FIGURE 3.19 | actuarial survival at UZ Leuven versus ISHLT

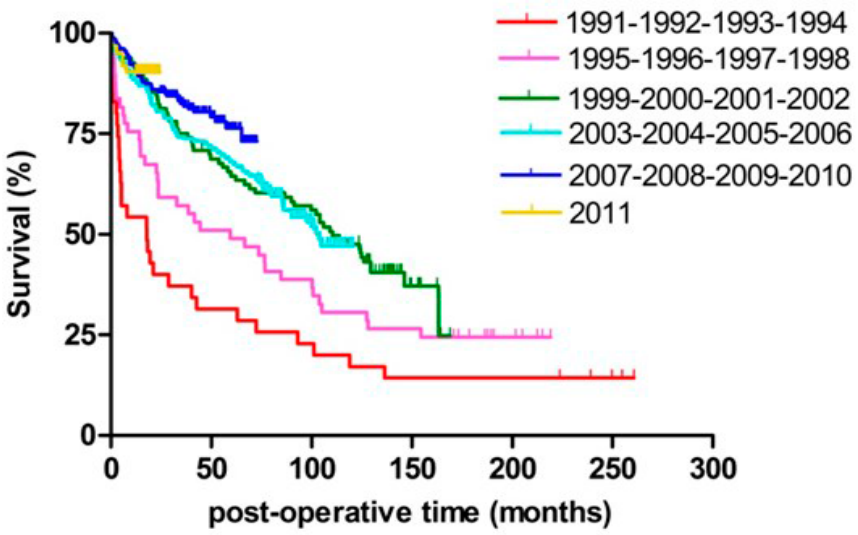


Figure 3.20 shows the survival rates at UZ Leuven (n=494) and in the ISHLT registry database.
The results at UZ Leuven are clearly better at any time, with a current five year survival rate of 76%.

FIGURE 3.20 | survival rate at UZ Leuven (2005-present) compared to the ISHLT registry database (2005-2011)

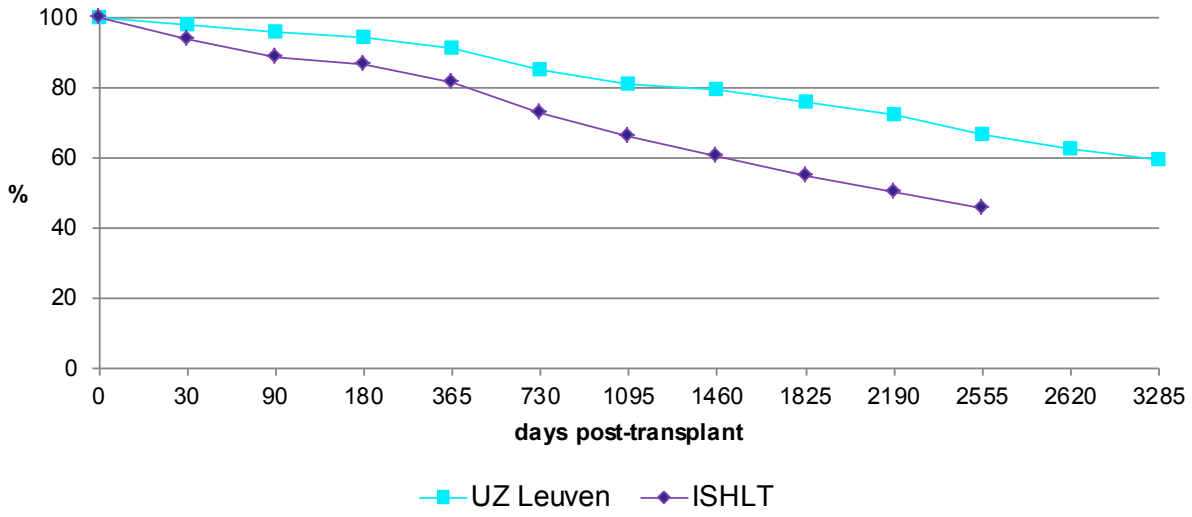


Figure 3.21 provides a summary of the number of transplant patients in active follow-up. The exponential increase results in continually high workloads associated with these check-ups, as illustrated in figure 3.21. The number of consultations has remained the same because, amongst other reasons, stable patients 5 years after the transplant need not be seen so frequently, which leaves room to see new patients more frequently.

FIGURE 3.21 | cumulative number of patients in follow-up

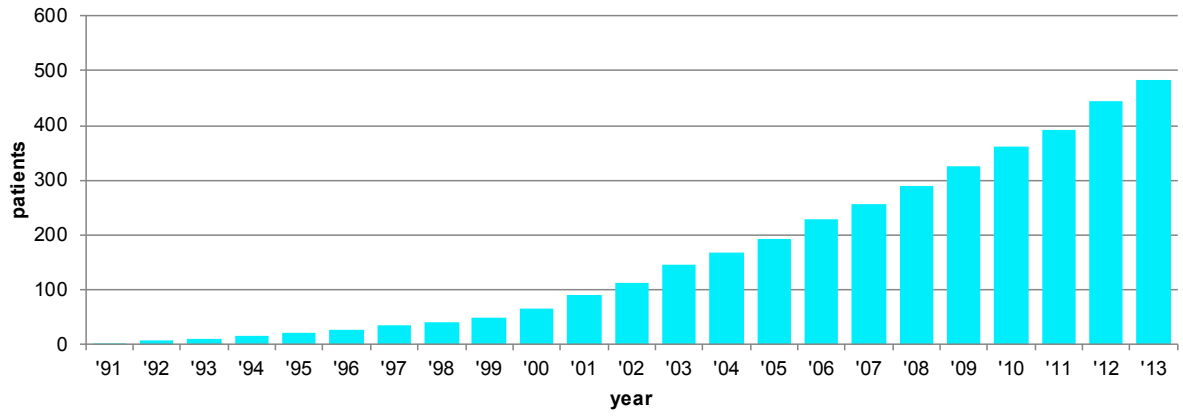
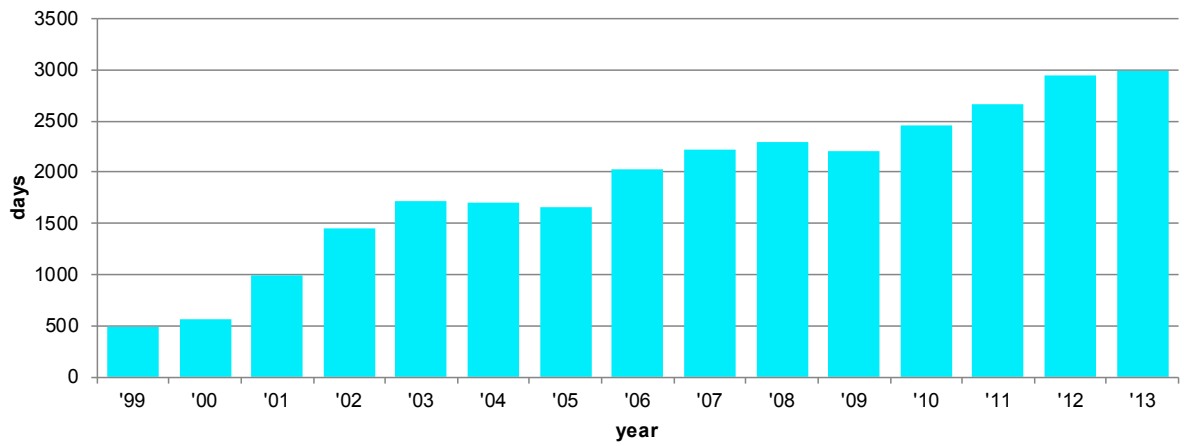


FIGURE 3.22 | number of ambulant consultations for lung transplant patients since 1999



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Trachea transplantation care programme

TRACHEA TRANSPLANTS

Tracheal allotransplantation is a new technique to repair pathological airway segments (post traumatic, post intubation, rarely tumoral) of more than 4 cm long that cannot be treated using conventional techniques.
The principle is based on an urgent (similar to lung) implant of the trachea on the recipient's forearm. Immunosuppressants are similar to those for the lung transplant protocol. Revascularization and remucosalization of the trachea occurs gradually on the forearm. Full revascularization and remucosalization is achieved after 1 to 3 months. The transplant is monitored on an ambulant basis. With a trachea transplant the use of immunosuppressants needs to be phased down during a second stage. This is possible when the donor mucosal lining has been replaced by the recipient's mucosal lining. The cartilage framework (the 'unique component' of the tracheal allotransplant) is known to be low or non immunogenic (chondrocytes are protected inside the cartilage lacunae).

The first (global) vascularized trachea transplant took place at UZ Leuven.

1. November 2007: heterotopic transplant on the forearm;
   September 2008: orthotopic transplant following cessation of immunosuppressants
   (New England Journal of Medicine, 2010).

   Following case studies:

2. 3 June 2009: heterotopic transplant;
   16 July 2009: orthotopic transplant followed by cessation of immunosuppressants.

3. 5 March 2010: heterotopic transplant;
   31 March 2010: orthotopic transplant followed by cessation of immunosuppressants.

4. 5 September 2010: heterotopic transplant, cessation of immunosuppressants.

5. 22 March 2011: heterotopic transplant;
   04 July 2011: orthotopic transplant followed by cessation of immunosuppressants.

6. 22 February 2012: heterotopic transplant;
   25 June 2012: orthotopic transplant followed by cessation of immunosuppressants.

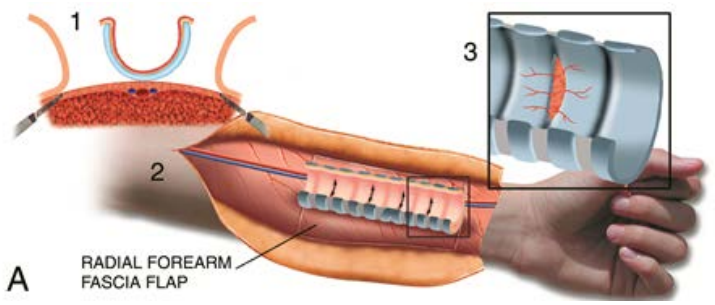
7. 13 April 2012: heterotopic transplant. Cessation of immunosuppressants.
   4 February 2013: orthotopic transplant.

8. 10 December 2013: heterotopic transplant.

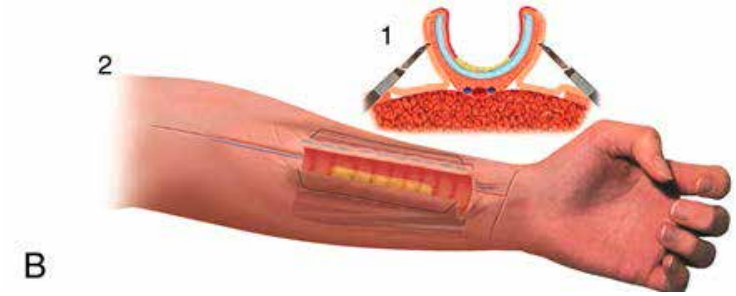
The indication for the first 4 patients was post traumatic narrowing. With the 5th patient we were dealing with low grade chondrosarcoma. With patients 6 and 7 post traumatic narrowing was again an indication for transplantation.

The current procedure (learning curve patient 1 to 5; Am J Transpl, 2012) is summarized in the figure below.

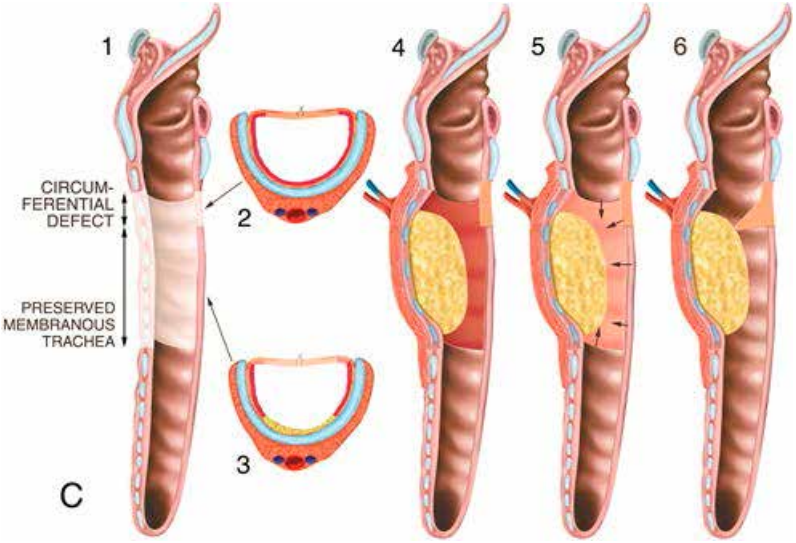
- The trachea transplant is applied to the forearm following the creation of skin flaps (1). Incisions are made in about four places on the intercartilaginous ligaments to promote ingrowth of the recipient's blood vessels (3). Forearm subcutaneous tissue and fascia is wrapped around the trachea.



- The transplant is revascularized after 2 months and the central portion of the donor mucosal lining is replaced with the recipient's buccal mucosa (yellow colour). After 3 months the transplant (1, 2) is ready for orthotopic transplantation onto the radial vein and artery.



- The tracheal defect (1) is repaired with the trachea transplant (2: circular, 3: patch). The transplant is a chimera consisting of donor and recipient tissue (4). When immunosuppression ceases the recipient blood vessels and recipient membrane at the suture with the 'native trachea' (arrows with 5) are repopulated. 6 illustrates the situation following complete cessation of immunosuppressants.



PART 4

PAEDIATRIC TRANSPLANTS

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transplant coordination

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Katrien Van der Vaerent

Paediatric transplant care programme

The paediatric transplant programme covers kidney, liver and intestinal transplants. It was initiated in 1980, when initially the transplantation procedure was carried out at the Université Catholique de Louvain (UCL) (kidney transplants). Since 1986 transplants have been conducted at UZ Leuven.

The haemodialysis programme for children was initiated in 1976 and peritoneal dialysis in 1984. Since 2013 the follow-up of children post liver transplant has been run in conjunction with Dr. Peter Witters of the paediatric gastroenterology department.

In 2006 Dr. Jean Herman defended his thesis on 'Renal transplantation in children'.

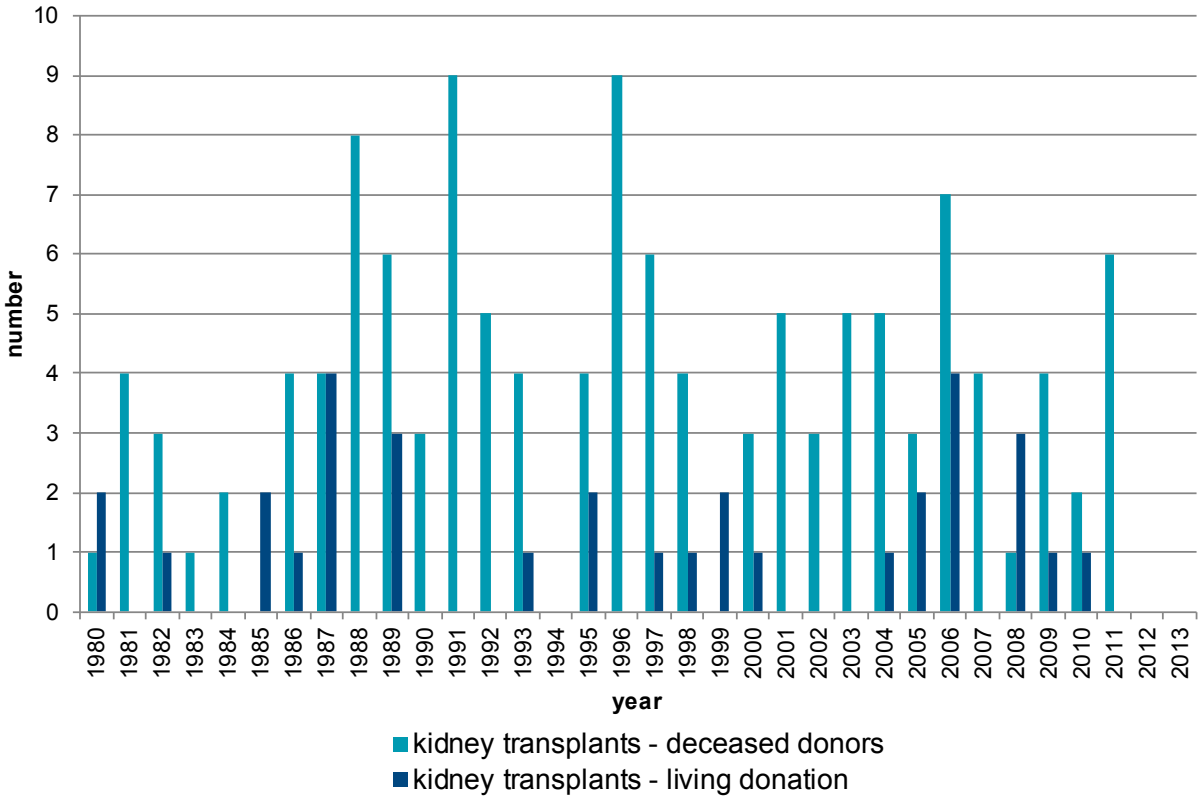
Dr. Noël Knops is currently working on a thesis entitled 'Pharmacogenetic determinants of calcineurin-inhibitor- induced nephrotoxicity (CNIT): translational mechanisms in conditionally immortalized human proximal tubule cells (ciPTEC) from adult and paediatric renal allograft recipients', in conjunction with Professor Dr. Dirk Kuypers of the internal medicine/ nephrology department.

Moreover, for quite some time research has been conducted into the pharmacokinetics of immunosuppressants during childhood (initiated by Professor (emer) Dr. Rita van Damme-Lombaerts), problems associated with compliance during childhood and transition (Loes Decorte, in cooperation with Professor Fabienne Dobbels).

PAEDIATRIC KIDNEY TRANSPLANTS

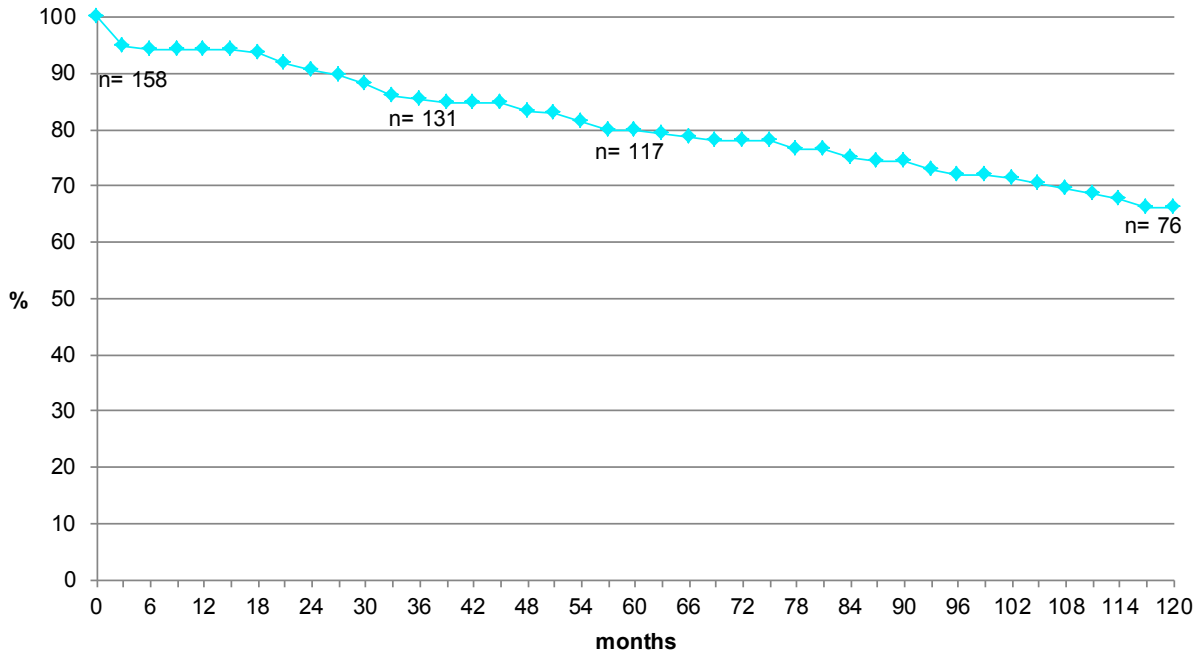
Following a productive 2011, no kidney transplants were carried out on children in 2012 and 2013. 4 children were on the waiting list at the end of 2013. 3 of them are undergoing dialysis because of congenital nephrotic syndrome (aged 2-5). 1 child was placed on the waiting list for a combined liver/kidney transplant as a pre-emptive measure. None of the children lost their transplant kidney.

FIGURE 4.1 | number of kidney transplants in children from 1980



Since 1980, 158 transplants were carried out involving 142 children (84 boys and 58 girls) with an average age of 10.8 (+/- 4.8) at the time of the transplant. The survival of the allograft for the entire group is 94% after 1 year, 86% after 3 years, 80% after 5 years and 66% after 10 years (figure 4.2). The number of living donations for the entire transplant patient group is 21% (n=33).

FIGURE 4.2 | graft survival rate (n= number of grafts 'at risk' at 0, 3, 5 and 10 years).

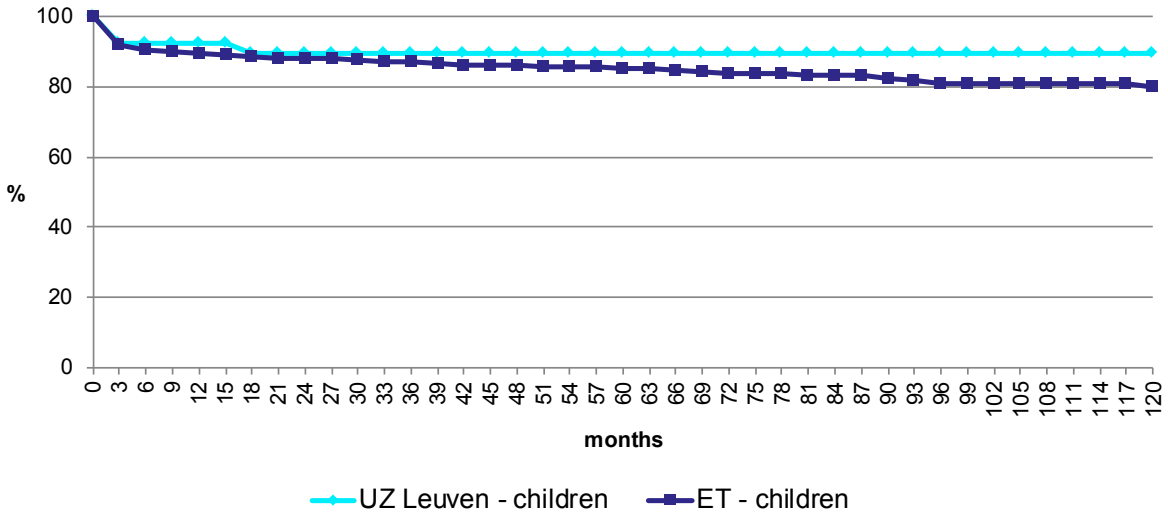


PAEDIATRIC LIVER AND INTESTINE TRANSPLANTS

1 child underwent a liver transplant in 2013. The patient suffered from Shwachman- Diamond syndrome, liver cirrhosis complicated by hepatorenal syndrome.
This brings the overall total to 40 liver transplants in 40 children (aged <18) in Leuven (1 child underwent a re-transplant as an adult).

At the start of 2014 there were 6 children on the waiting list for a liver transplant, including 1 child for a combined liver/kidney transplant, 1 child for a combined liver/pancreas transplant and 1 child for a combined liver/intestine transplant. Survival curves were calculated since the start of the paediatric liver transplant programme.

FIGURE 4.3 | patient survival rate 120 months – paediatric liver transplant (1999-2013), UZ Leuven versus ET



No intestinal transplants were carried out on children in 2013. At the start of 2014 there were still 2 children on the waiting list (1 patient with microvillous inclusion disease and 1 patient with megacystis-microcolon hypoperistalsis syndrome). Both are dependent upon total parenteral nutrition but, considering the circumstances, are in a satisfactory condition.

The 2 children who underwent a combined liver/intestine and liver/intestine/pancreas transplant in 2004 and 2008 respectively are both doing fairly well. They both are independent of parenteral nutrition, have a normal oral diet and attend school.

PART 5

TISSUE AND CELL BANKS

bodily material banks

AC bio banking/tissue and cell banks

transplant programmes

bank for the musculoskeletal system
- orthopaedics
- traumatology
- neurosurgery
- ear, nose & throat diseases, facial and neck surgery

skin bank
- intensive medicine: burns centre plastic, reconstructive and aesthetic surgery

tympano-ossicular bank
- ear, nose & throat diseases, facial and neck surgery

amnion bank
- dermatology

ophthalmic tissue bank
- eye disease

keratinocyte bank
- dermatology

umbilical cord blood bank
- haematology

haematopoietic stem cell bank
- haematology

BANKS FOR HUMAN BODILY MATERIAL

Allografts for the musculoskeletal system
tissue coordinators: Dimitri Aertgeerts, Luc Ampe, Henk Desplentere, Bert Verduyckt

Skin grafts
tissue coordinators: Dimitri Aertgeerts, Luc Ampe, Henk Desplentere, Bert Verduyckt

Ophthalmic tissues
tissue coordinators: Dimitri Aertgeerts, Luc Ampe, Henk Desplentere, Bert Verduyckt
tissue technologists: Daniël Carels, Gerda Mahy

Tympano-ossicular grafts
tissue coordinators: Dimitri Aertgeerts, Luc Ampe, Henk Desplentere, Bert Verduyckt

Placental membranes
tissue technologists: Inge Daris, Katrien Smaers

Umbilical cord blood
staff members: Professor Dr. Timothy Devos, Dr. Helene Schoemans
tissue technologists: Marianne Boogaerts, Eline Cosemans, Julie De Louker, Louise Lauweryns, Werner Scheers, Sarah Van Diest, Veerle Verslegers

Keratinocytes
tissue technologists: Daniël Carels, Inge Daris, Katrien Smaers

Haematopoietic stem cells
staff members: Professor Dr. Michel Delforge, Professor Dr. Timothy Devos
tissue technologists: Marianne Boogaerts, Eline Cosemans, Julie De Louker, Louise Lauweryns, Werner Scheers, Sarah Van Diest, Veerle Verslegers

Mesenchymal stem cells
staff members: Professor Dr. Timothy Devos
tissue technologists: Ann Van Campenhout, Lore Swinnen

Quality assurance
Johan Klykens, Franky Sinap

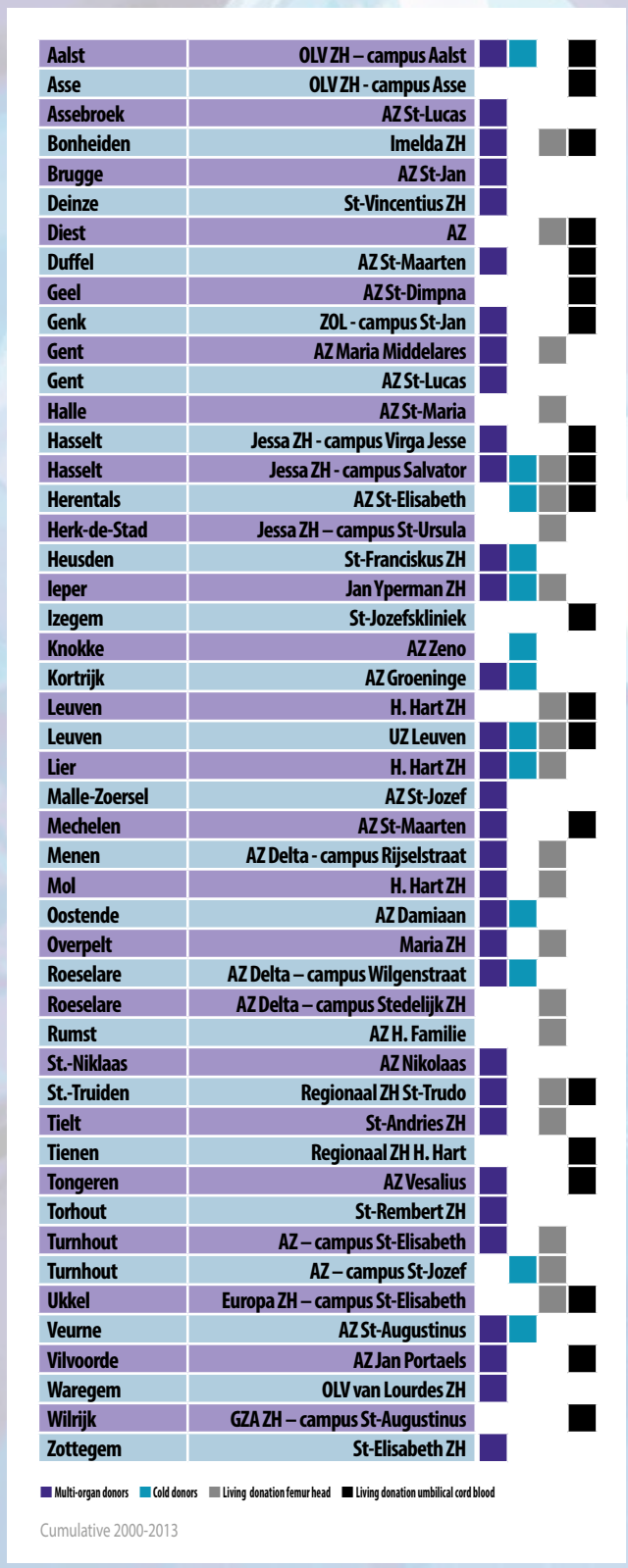
Administrative support / coordination
Carla Collijs, Diane Reggers, Sandra Van Effen

Managers
Professor (emer) Dr. Marc Boogaerts (umbilical cord blood bank),
Professor Dr. Gregor Verhoef (Haematopoitic stem cells, Mesenchymal stem cells),
Professor Dr. Nadine Ectors (other banks)

Biobanking Activity Centre

The UZ Leuven-KU Leuven tissue and cell banks endeavour to develop a high quality service 'from and for' the partner hospitals, in the best possible circumstances and in accordance with the latest medical developments and applicable legal and ethical standards.

Our organisation aims to optimise the donation, procurement, preservation, storage and distribution of human tissue, with approval from the Ministry for Public Health, to ensure that 'any' patient – anywhere in Belgium – can benefit from this unique human gift.



Cumulative 2000-2013

Living donors

Procurements of this type within the tissue and cell banks involve various domains. The patient is notified via an informed consent form submitted by the treating physician. This physician also decides on the basis of predetermined criteria whether the patient qualifies for donation. The following biological tests are also carried out subject to approval from the patient: anti-HIV 1,2; HBsAg; anti-HBc; anti-HCV; anti-HTLV1,2 and a test to detect syphilis. Finally, the blood sample is used to carry out a nucleic acid amplification test (NAT) for HIV *(Human immunodeficiency virus)*, HBV *(Hepatitis B-virus)* and HCV *(Hepatitis C-virus)*.

Femural head donors

Femural heads are collected from living donors who require a hip prosthesis as a result of trauma or osteoarthritis. Once removed from the body a tissue culture is taken, the serology is determined and the femural head is placed in sterile double packaging and frozen. Providing all legal requirements are met, the femural head will become available for processing and subsequent transplantation. Femural heads (967 in 2013, + 23.7% compared to 2012) are collected by the tissue bank in spite of increasingly stringent legislation (new legislation: law dated 19 December 2008 with implementation decrees end 2009). Femural heads were donated in 14 hospitals (including 3 newcomers) across Flanders.

TABLE 5.1 | evolution of donor hospitals ~ femural head donations 2003–2013

Centre		'03	'04	'05	'06	'07	'08	'09	'10	'11	'12	'13
Bonheiden	Imelda ZH	-	-	-	-	-	-	-	56	136	155	167
Diest	AZ	-	-	21	10	18	13	10	21	18	25	32
Gent	AZ Maria Middelares	-	-	-	-	-	-	-	-	-	5	1
Halle	AZ St-Maria	7	22	15	19	17	22	29	48	59	64	57
Hasselt	Jessa ZH – campus Salvator	-	-	-	-	-	72	83	93	88	-	-
Herentals	AZ St-Elisabeth	-	-	-	-	-	-	-	-	3	27	68
Herk-de-stad	Jessa ZH – campus St-Ursula	46	50	62	56	14	-	-	-	-	-	-
Ieper	Jan Yperman ZH	-	-	-	-	-	-	-	-	-	-	56
Leuven	H. Hart ZH	-	41	58	65	57	79	35	71	62	72	66
Leuven	orthopedie UZ Leuven	74	91	71	31	82	105	122	147	143	134	97
Leuven	traumatologie UZ Leuven	46	37	33	16	7	8	2	1	2	1	-
Lier	H. Hart ZH	-	-	-	-	-	-	-	157	193	151	134
Menen	AZ Delta – campus Rijselstraat	19	18	18	-	-	-	-	-	-	-	-
Mol	H. Hart ZH	-	-	-	-	-	-	67	73	74	55	51
Overpelt	Maria ZH	-	-	16	47	48	47	39	29	11	-	-
Roeselare	AZ Delta – campus Stedelijk ZH	-	-	-	-	-	-	-	-	-	-	106
Rumst	AZ H. Familie	28	34	22	11	23	3	23	3	29	10	12
St-Truiden	Regionaal ZH St-Trudo	-	40	35	36	31	23	22	47	39	59	70
Tielt	St-Andries ZH	-	-	-	-	-	-	-	-	8	24	51
Turnhout	AZ – campus St-Elisabeth	-	-	-	-	-	3	-	-	-	-	-
Ukkel	Europa ZH – campus St-Elisabeth	-	-	-	-	-	11	11	17	14	-	-
Total		220	333	351	291	297	386	443	763	879	782	968

Amnion donors

Amnion and chorion grafts are collected during normal deliveries in collaboration with the UZ Leuven umbilical cord blood bank. These grafts are used as bandages for skin and eye surface defects. Amnion and chorion grafts (6 donations in 2013) were collected by the tissue bank at the UZ Leuven obstetrics department.

Keratinocyte donors

Keratinocytes are preferably collected from very young donors, whereby keratinocytes are isolated from epidermis (surgery residue) released during circumcision or breast reduction operations. They are cultured and distributed as dermatological treatment for difficult to treat skin defects. Inherent to this production process is the fact that many grafts can be produced from a single skin biopsy, which means that donors are less frequently required.

Umbilical cord blood donors

Blood is collected from the umbilical cord immediately after the baby is born and the umbilical cord has been transsected, because it was established that a high number of blood producing or haematopoietic stem cells are circulating in the umbilical cord. The samples need to be processed in the laboratory within 48 hours of collection (volume reduction, addition of cryoprotectant, quality testing) and frozen to -196 °C (liquid nitrogen). These samples are a source of haematopoietic stem cells for stem cell transplantation. 533 samples were frozen at the Leuvense Navelstrengbloedbank (Leuven Umbilical Cord Blood Bank) in 2013. On 1 January 2014 we had 8319 samples available for transplantation internationally. The umbilical cord blood originated from maternity units at the following locations:

TABLE 5.2 | evolution of donor hospitals ~ umbilical cord blood 2009-2013

Centre		'09	'10	'11	'12	'13
Aalst	OLV ZH – campus Aalst	31	55	58	36	**24**
Asse	OLV ZH – campus Asse	-	-	-	-	**15**
Bonheiden	Imelda ZH	22	46	65	40	**35**
Diest	AZ	6	7	36	20	**34**
Duffel	AZ St- Maarten	-	-	-	-	**15**
Geel	AZ St-Dimpna	6	-	-	-	**-**
Genk	ZOL – campus St-Jan	78	77	106	62	**45**
Hasselt	Jessa ZH – campus Salvator	1	3	6	2	**-**
Hasselt	Jessa ZH – campus Virga Jesse	16	10	29	35	**38**
Herentals	AZ St-Elisabeth	44	55	46	47	**50**
Izegem	St-Jozefskliniek	12	20	33	28	**28**
Leuven	H. Hart ZH	74	44	77	49	**53**
Leuven	UZ Leuven	23	31	57	34	**55**
Mechelen	AZ St-Maarten	-	-	-	-	**20**
St-Truiden	Regionaal ZH St-Trudo	19	30	25	29	**15**
Tienen	Regionaal ZH H. Hart	29	39	52	34	**41**
Tongeren	AZ Vesalius	21	29	41	28	**31**
Ukkel	Europa ZH – campus St-Elisabeth	-	5	-	-	**-**
Vilvoorde	AZ Jan Portaels	19	26	34	30	**29**
Wilrijk	GZA ZH – campus St-Augustinus	-	-	-	-	**5**
Total - frozen		*401*	*477*	*665*	**474**	**533**

16 umbilical cord blood samples were sent to stem cell transplantation centres in Belgium and abroad in 2013.

Haematopoietic stem cells (HSC)

HSC are collected using apheresis technology (peripheral stem cell collection) or bone marrow collection. They can be frozen for autologous use in patients suffering from a haematological disease (stem cell collection following chemotherapy and several months of reinfusion of stem cells with an autologous stem cell transplant). With healthy donors (related or not related) stem cells are collected using the same techniques and administered to the patient (without being frozen) the same or the next day. In 2013 the UZ Leuven Haematopoietic Stem Cell Bank prepared 138 transplants, including 53 autologous and 85 allogeneic transplants (25 sibling, 56 MUD (=matched unrelated donor), 4 haploidentical). The applied haematopoietic stem cells were obtained via peripheral stem cell collection (129), bone marrow procurement (5) or from umbilical cord blood (4).

Mesenchymal stem cells (MSC)

MSC are immunomodulating and are administered to treat corticosteroid-refractory acute graft-versus-host disease (GvHD) following allogeneic stem cell transplantation or if the graft fails following allogeneic stem cell transplantation. In September 2011 the UZ Leuven MSCP (Mesenchymal Stem Cell Programme) was recognized as a cell bank by FAMHP (the Federal Agency for Medication and Health Products - FAGG). Between February 2008 and the end of 2013, 13 MSC infusions were administered for acute GvHD and 8 MSC infusions as a result of graft failure by the UZ Leuven haematology department, in conjunction with the University of Liège (CHU). 11 MSC end products were frozen at UZ Leuven in 2013. 1 of these MSC end products was used for quality control purposes. The other 10 MSC end products bring the total of frozen MSC end products suitable for patient use to 26. In addition, and as part of the clinical study in cooperation with Liège, 1 patient was treated at UZ Leuven with MSC produced in Liège (because of graft failure).

Deceased donors

Deceased donors are classified into 'cold' donors and 'multi organ donors.

'Cold' donors

'Cold' donors are donors who have died and may qualify for donation providing legal requirements are met. Procurement is carried out both in UZ Leuven and externally (see table). Tissue was procured this way from 9 donors (all multi tissue donors) in 2013. This remains a significant underuse of the number of potential donors. This is why we are still looking for external partners to supplement the number of available donors. We are, therefore, very pleased and extremely grateful that, sometimes in very difficult circumstances, the tissue bank is not forgotten.

TABLE 5.3 | evolution of donor hospitals ~ 'cold' donor registrations 2003-2013

Centre		'03	'04	'05	'06	'07	'08	'09	'10	'11	'12	'13
Aalst	OLV ZH – campus Aalst	-	2	1	2	1	2	-	-	-	-	-
Hasselt	Jessa ZH – campus Salvator	-	-	-	-	2	-	-	-	-	1	-
Herentals	AZ St-Elisabeth	-	-	-	-	-	-	-	-	-	-	1
Heusden	St-Franciskus ZH	-	-	1	-	-	-	-	-	1	-	-
Ieper	Jan Yperman ZH	-	-	-	-	-	-	-	-	-	-	1
Knokke	AZ Zeno	-	-	-	-	-	-	-	1	-	1	-
Kortrijk	AZ Groeninge	-	-	-	-	-	-	1	1	-	-	-
Leuven	UZ Leuven	38	24	24	15	3	25	13	2	-	2	2
Lier	H. Hart ZH	-	-	-	-	1	-	-	-	-	-	-
Oostende	AZ Damiaan	-	-	-	-	-	1	-	-	-	-	-
Roeselare	AZ Delta – campus Wilgenstraat	-	-	-	-	-	-	3	1	-	3	3
Turnhout	AZ – campus St-Jozef	-	-	-	-	1	-	-	-	-	-	-
Veurne	AZ St-Augustinus	-	-	-		1	-	-	1	5	4	2
Total		38	26	26	17	9	28	17	6	6	11	9

Multi organ donors

Multi organ donation is an important event for the patient's close family members. For many recipients donated organs represent a final chance. It is obvious that tissue donation must not in any way affect organ donation, as these are 'life saving' donations as opposed to tissue donations which generate a significant morbidity improvement for recipients. Sometimes family members will selectively oppose donation of specific tissues. These wishes are discussed in advance with transplant coordinators and are obviously respected.

With multi organ donors tissues are procured immediately after completion of the organ procurement procedure, in the sterile conditions of an operating theatre. The entire donor screening process is managed by the transplant coordinator. Secondary screening is conducted indirectly, after 3 months, via the organ recipient screening process. This makes it a very secure procedure, which provides important quality guarantees for tissue recipients. These donors are suitable for an extensive number of tissue donations: cortical bone (complete or fragmented bones), spongious bone, cartilage, tendons, menisci, skin, corneas, scleras and, where applicable, tympano-ossicular allografts. These procurements occur across Flanders. Tissue was procured from 50 donors in 2013.

Increasingly stringent regulations also apply to deceased donors (same recent legislation: law of 19 December 2008 with implementation decrees end 2009). These types of tissue procurements were performed in 16 hospitals across Flanders.

TABLE 5.4 | evolution of donor hospitals ~ multi organ donor registrations 2003-2013

Centre		'03	'04	'05	'06	'07	'08	'09	'10	'11	'12	'13
Aalst	OLV ZH – campus Aalst	2	2	1	4	4	3	-	2	2	1	**5**
Assebroek	AZ St-Lucas	1	-	-	-	2	1	-	2	1	2	**-**
Bonheiden	Imelda ZH	4	1	-	2	4	2	1	2	-	1	**3**
Brugge	AZ St-Jan	1	-	-	1	-	-	1	1	1	-	**-**
Deinze	St-Vincentius ZH	-	-	1	-	-	-	-	1	-	-	**-**
Duffel	AZ St-Maarten	-	-	-	-	-	-	-	1	-	-	**-**
Genk	ZOL – campus St-Jan	7	5	4	11	10	5	4	5	7	4	**4**
Gent	AZ Maria Middelares	-	-	-	-	1	-	-	-	-	-	**-**
Gent	AZ St-Lucas	1	4	2	2	-	-	-	-	-	-	**-**
Hasselt	Jessa ZH – campus Salvator	2	-	1	2	1	1	-	-	2	-	**-**
Hasselt	Jessa ZH – campus Virga Jesse	3	4	2	1	3	5	5	10	3	6	**7**
Heusden	St-Franciskus ZH	1	5	-	6	3	3	2	1	4	3	**2**
Ieper	Jan Yperman ZH	-	-	1	-	-	-	1	3	1	2	**-**
Kortrijk	AZ Groeninge	3	1	6	4	5	3	4	-	7	4	**4**
Leuven	UZ Leuven	17	13	13	8	13	7	5	10	10	11	**7**
Lier	H. Hart ZH	4	2	1	5	2	3	3	1	7	2	**2**
Malle-Zoersel	AZ St-Jozef	-	1	-	1	-	1	1	1	-	-	**-**
Mechelen	AZ St-Maarten	-	-	-	-	-	-	-	-	1	-	**-**
Menen	AZ Delta – campus Rijselstraat	1	-	-	-	-	-	-	-	-	-	**1**
Mol	H. Hart ZH	-	-	-	-	-	-	1	-	2	-	**1**
Oostende	AZ Damiaan	-	2	-	3	-	4	2	-	-	2	**1**
Overpelt	Maria ZH	-	-	-	-	-	1	1	-	1	-	**-**
Roeselare	AZ Delta – campus Wilgenstraat	4	3	6	6	5	1	3	5	5	6	**7**
St-Niklaas	AZ Nikolaas	2	3	-	-	2	3	1	1	2	1	**1**
St-Truiden	Regionaal ZH St-Trudo	1	2	-	-	1	-	-	2	1	1	**2**
Tielt	St-Andries ZH	-	-	-	-	-	1	-	1	2	-	**-**
Tongeren	AZ Vesalius	-	-	-	-	-	-	-	-	-	1	**-**
Torhout	St-Rembert ZH	-	-	-	1	-	-	-	-	1	1	**-**
Turnhout	AZ Turnhout – campus St-Elisabeth	2	4	4	1	1	2	2	2	3	5	**1**
Veurne	AZ St-Augustinus	-	2	2	-	3	4	8	11	3	5	**2**
Vilvoorde	AZ Jan Portaels	-	-	1	-	-	-	-	-	-	1	**-**
Waregem	OLV van Lourdes ZH	-	-	-	-	1	1	-	1	-	-	**-**
Zottegem	St-Elisabeth ZH	-	-	-	-	1	-	-	-	-	-	**-**
Total		**56**	**54**	**45**	**58**	**62**	**51**	**45**	**63**	**66**	**59**	**50**

Further professionalization of tissue donation and procurement, a dedicated team of tissue coordinators and particularly more transparent, efficient and professional communications between tissue banks, donor hospitals (doctors, nurses, social and pastoral services) and transplant coordinators remain the foundation for a successful tissue bank. Most importantly, all this is only possible if approached with all-embracing solidarity and altruism.

PART 6

ISLET TRANSPLANTS

endocrinology

Professor Dr. Pieter Gillard, Professor Dr. Chantal Mathieu,
Dr. Da hae Lee (doctorate student)

abdominal transplant surgery - procurement

Professor Dr. Jacques Pirenne, Professor Dr. Diethard Monbaliu,
Professor Dr. Ina Jochmans

abdominal surgery

Dr. Matthias Lannoo

radiology – intraportal injection islet graft

Professor Dr. Geert Maleux, Professor Dr. Sam Heye

hospitalisation team

Kristien Van Avermaet

study coordination

Hilde Morobé en team

diabetes education

Rudi Caron, Monique Robyn, Brigitta Swennen
Nadine Pardon, Tinne Wouters

Islet transplant care programme

A multicentre project is currently active in Belgium, in which UZ Leuven has joined forces with various other university centres (UZ Brussels, UZA, ULB, UZ Ghent and the Leiden University Medical Centre) to work on a clinical islet transplant programme.

The islet transplant programme became operational in 1990 (under the name Beta Cell Transplant) involving the isolation of human β-cells from pancreases from deceased donors to be used for clinical transplantation. The first protocol involving stable kidney transplant recipients was initiated at UZ Brussels under the supervision of Professor Dr. Daniel Pipeleers and Professor Dr. Bart Keymeulen in 1994 (= islet following kidney). From 1998 islet transplants mainly involved patients with incipient chronic and hypoglycaemic unawareness (= islets only) (see figure 6.1).

Since the end of 2001 UZ Leuven has also been active as an implant centre and screened and followed up patients. Since then 38 patients have received 70 graft transplants in UZ Leuven. Almost all patients underwent islet transplants alone (n=37 patients). Patients originate from university centres or have been referred by peripheral centres. The main indication for transplant is currently frequent serious hypoglycaemic episodes (often coinciding with hypoglycaemic unawareness), despite intensive insulin therapy.

Since June 2011 a new implant site (intraperitoneal space and subcutis) and a new matrix (encapsulated islets) are being tested. An additional indication for this type of transplant involves patients with failure of their first intraportal grafts.

ISLET TRANSPLANTS

Traditional activities in the multicentre programme

4 patients received transplants with a total of 8 β-cell allografts in 2013 (2 transplants per patient). 50% of the processed and 50% of the transplanted Belgian organs in 2013 originated from the UZ Leuven donor centre. Allografts were transplanted into the liver using percutaneous transhepatic puncture (UZ Leuven) or laparoscopic procedure (UZ Brussels). Immunosuppression was based on ATG induction therapy (plus Basiliximab in 2 patients). Maintenance therapy is based on a combination with MMF (Cellcept® 1000-2000 mg per day) and Tacrolimus (trough levels 8-10 ng/dl). Survival of the β-cell allograft (C-peptide > 0.5 ng/dl) was present in all recipients. This reinstatement of endogenous insulin secretion resulted in a reduction of the risk for serious hypoglycaemia, less insulin requirement and an HbA1c up to < 7.0 % in all patients.

Alternative implant area

A new implant site (intraperitoneal/omentum and subcutaneous) and a new alginate matrix are being are being tested in anticipation of the future use of cells of different origin rather than organs from deceased donors. New techniques are currently being investigated in preclinical studies. We anticipate they will be used in a new group of patients in the course of 2014.

Patient and graft survival since 2001

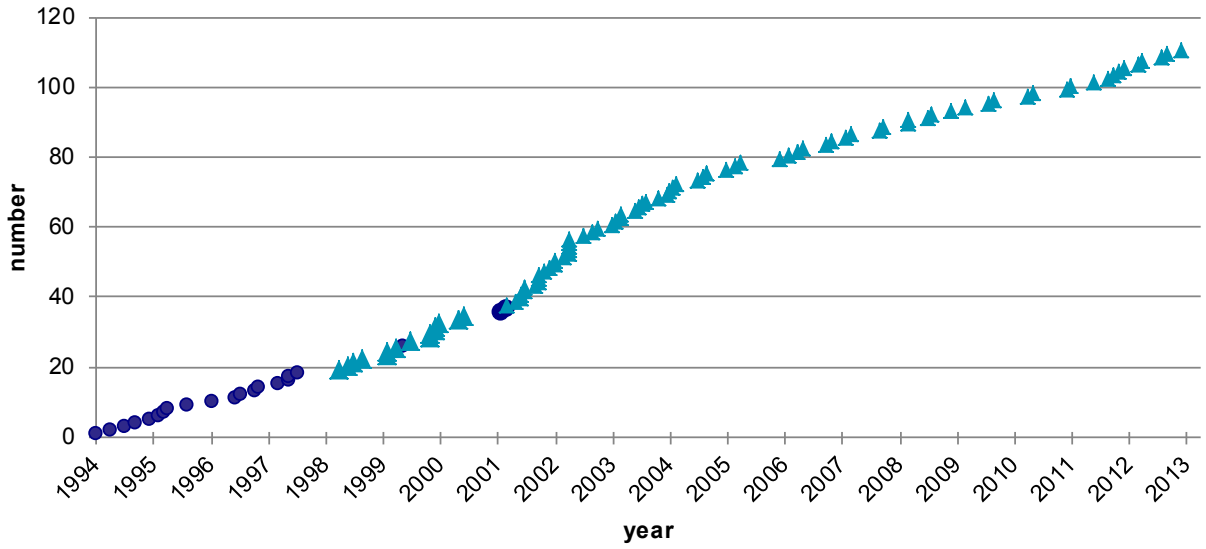
The results of type 1 diabetic patients who received a transplant with sufficient cells (= ≥ 2 X 106 per kg body weight per transplant) between 2001 and December 2013 are as follows:

After 1 year
- Patient survival: 99%
- Graft survival (= C-peptide of ≥ 0.5 ng/ml): 79%

After 3 years
- Patient survival: 96%
- Graft survival (= C-peptide of ≥ 0.5 ng/ml): 43%

After 5 years
- Patient survival: 91%
- Graft survival (= C-peptide of ≥ 0.5 ng/ml): 28%

Figure 6.1 | islet graft recipients at the 'JDRF centre for Beta Cell Therapy in Diabetes' between 1994 and 2013. During the initial 4 years islet transplants were only used in type 1 diabetic patients who had already undergone a kidney transplant (dark blue circles). From 1998 islet transplants alone were mainly carried out in non-uremic patients (light blue triangles). The number of patients in this case makes us the largest centre in Europe, and second in the world (after Edmonton).



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UZ LEUVEN | RAAD VOOR TRANSPLANTATIE

IN COLLABORATION WITH LSGO
(Leuven Organ Donation Partnership)