Annual Report 2014

UZ Leuven Transplant Council

UZ LEUVEN | RAAD VOOR TRANSPLANTATIE

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

Annual Report 2014

UZ Leuven Transplant Council

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CONTENTS

PREFACE

Dear Professor, Colleague, Sir, Madam

We are proud to present the Transplant Council's 2014 annual report. This brochure provides a summary of donor activities and results of the various transplant care programmes undertaken over the past year, i.e. 2014, compared to previous years. I would like to thank all those involved in donation and transplantation activities for the preparation of this annual report. This annual report in English will facilitate its distribution amongst non-Dutch speaking colleagues and those from abroad. It will also help to spread the news of the outstanding results achieved in our transplant centre.

In 2013 we saw a slight increase (2%) in the number of actual donors (99) in comparison to 2013 (97). These numbers are approximately half of the total number of registered potential donors (201 in 2014 versus 211 in 2013). Actual donors include those deceased following both brain death (heart-beating or DBD; a decrease from 77 to 69) and those after cardiocirculatory arrest (non-heart-beating or DCD; an increase from 20 to 30). These changes follow the same trend of other European countries (e.g. United Kingdom, Netherlands). The proportion of donors originating from the University Hospitals Leuven was 23%. For the remaining donors (77%) we can still rely on our partner donor hospitals (LSGO – Leuven Organ Donation Partnership). Remarkably, 14 living kidney donors came forward in 2014.

Activities involving tissue procurement increased considerably (in comparison to 2013) up to 1206 (967) femur head donations (+24.7%) and 857 (533) umbilical cord blood samples (+60.8%).
We would like to thank the transplant coordinators (Dirk Claes, Karlien Degezelle, Bruno Desschans, Nele Grossen, and Glen Van Helleputte) and all tissue coordinators (Dimitri Aertgeerts, Luc Ampe, Henk Desplentere, Maarten Vanhaecke, and Bert Verduyckt) for their unstinting efforts.
In Belgium we recorded a slight drop (-7.9%) from 306 to 282 effective donors in 2014. The Leuven Organ Donation Partnership (LSGO) accounts for 35.1% of all deceased donors in Belgium.

In 2014 a total of 282 transplants were performed at the University Hospitals Leuven involving an organ from a deceased donor (a drop of 7 in comparison to 2013) representing a 33.3% share of all transplantations (846) in Belgium: 114 (27.5%) kidney, 72 (31.2%) liver, 58 (55.8%) lung, 28 (34.1%) heart (lung), 5 (45.5%) pancreas, 4 (100%) intestinal, and 1 (100%) trachea transplants. The 2014 activity in all transplant programmes was stable in comparison to 2013 with a slight decrease in liver transplants (from 86, the highest number ever in the University Hospitals Leuven to 72) and a remarkable increase in the number of pancreas (from 1 to 5) and in intestinal (from 0 to 4) transplants. In addition, 4 patients received 6 beta-cell allografts in total. The activities of the tissue bank also resulted in many tissue transplants in 2014.

With guidance from professor (em.) dr. Patrick Ferdinande, professor dr. Diethard Monbaliu and professor dr. Nadine Ectors and professional support of Stijn Dirix, services to the referring donor hospitals were developed in more detail. In accordance with federal law, our transplant centre offered additional training to local donor coordinators in the donor hospitals that signed an collaboration agreement with the University Hospitals Leuven. This resulted in the fifth successful LSGO training day and official meeting of our internal transplant board on 5 February 2014, preceding the annual donor and transplantation symposium. Our special thanks goes to Margriet Goedhuys for the perfect organisation of this annual meeting.

The mandate of representatives of our transplant centre in the National Council for Transplantation working within the Federal Governmental Service (FOD) of Health, came to an end on 31 December 2014. We look forward to the publication of a new Royal Decree by our Minister of Health, Maggie De Block, with the names of the new representatives in this forum. So far, there is no news on the start of a 'College of Doctors for Transplantation' as foreseen in the Royal Decree of 10 November 2012. We are still awaiting new initiatives by the federal authorities to adapt the Royal Decrees of 3 July 2012 and 10 November 2012 according to the comments forwarded by all Belgian Transplant Centres in order not to further decrease the number of potential donors and to organise current organ retrieval activities in accordance to the law.

We would like to express our gratitude to all those responsible in referring donor hospitals for the trust they put in the University Hospitals Leuven by signing 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 departments, intensive care units, surgical wards, and other hospital departments for their tireless efforts and commitment, which made the donor procedures in their hospitals possible in 2014.

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.

On behalf of all members of the Transplant Council, I would like to express our hope that we can continue our successful cooperation in 2015.

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

1 secretary
2 vice chair

TRANSPLANT COORDINATION

Head of department

prof. dr. Jacques Pirenne | abdominal transplant surgery and transplant coordination

Transplant coordinators

Dirk Claes

Karlien Degezelle

Bruno Desschans

Nele Grossen

Glen Van Helleputte

Stijn Dirix | Transplant Council

TISSUE COORDINATION

AC bio banking coordinator

prof. dr. Nadine Ectors | tissue and cell banks

Tissue coordinators

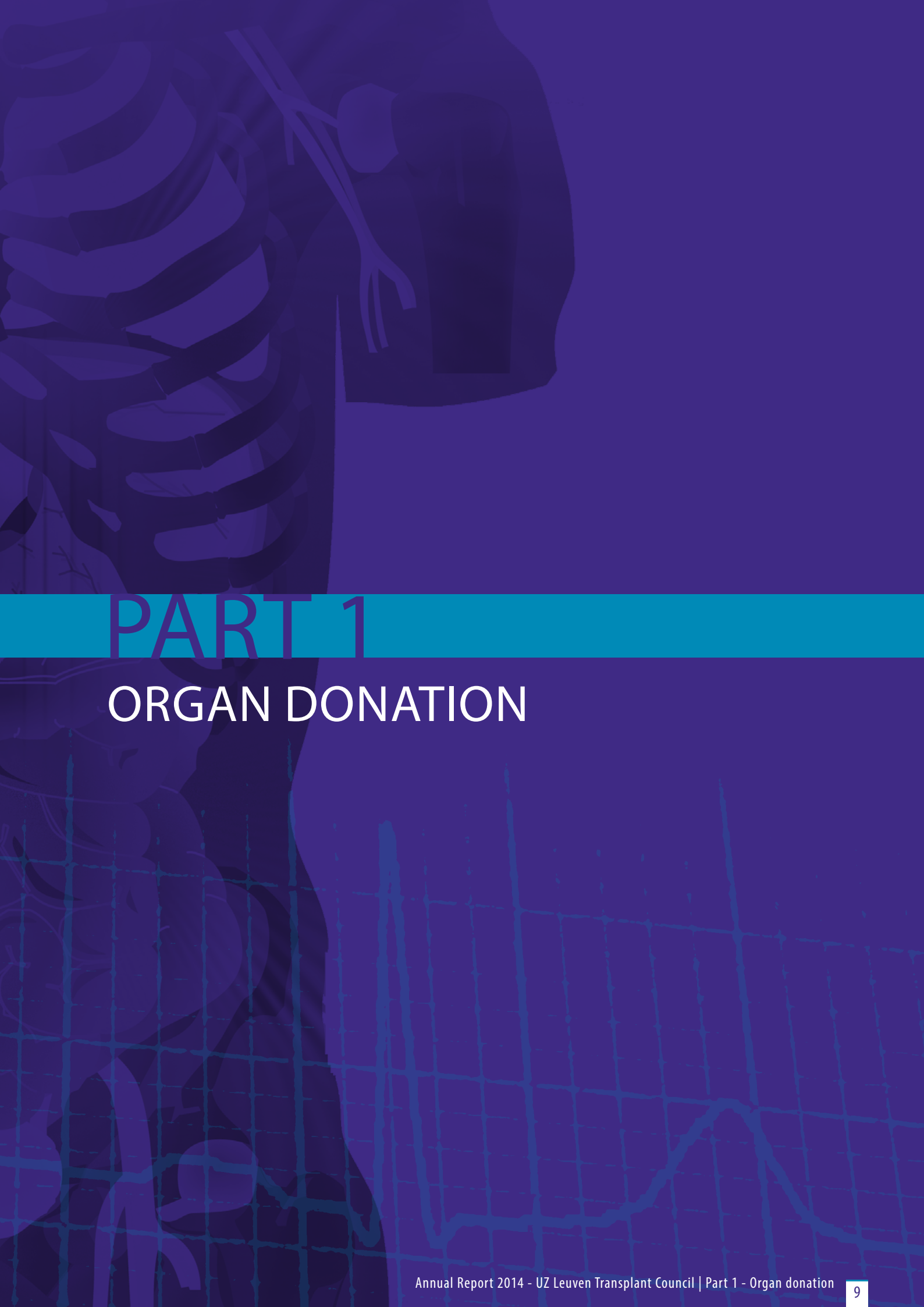
Dimitri Aertgeerts

Luc Ampe

Henk Desplentere

Maarten Vanhaecke

Bert Verduyckt



PART 1

ORGAN DONATION

Potential and effective donor registrations: University Hospitals Leuven and partner hospitals

Table 1.1 illustrates the annual evolution of donor potential in the group of partner donor hospitals and University Hospitals Leuven (LSGO - Leuven Organ Donation Partnership).

TABLE 1.1 | evolution of number of potential donor registrations 2000 - 2014. DBD or heart-beating donors (DCD or non-heart-beating donors) (hospitals with at least one donor registration in the past fifteen years)

Centre		'00	'01	'02	'03	'04	'05	'06	'07	'08	'09	'10	'11	'12	'13	2014 DBD/(DCD)
Aalst	OLV ZH – campus Aalst	11	11	5	4	3	4	5 (1)	6	3	-	2	3 (1)	3	6	2
Antwerpen	ZNA Stuivenberg	-	-	-	-	-	-	-	-	-	-	-	1	1	-	-
Assebroek	AZ St-Lucas	5	1	4	1	1	1	2 (1)	2	2	-	2	3	3	2	2 (1)
Bonheiden	Imelda ZH	4	1	-	4	3	1	2 (2)	7	4	3	4	4	5	9	5 (1)
Brugge	AZ St-Jan	4	2	2	3	4	2	4	5	3	11	3	9	3	2 (3)	2 (2)
Brussel	Kliniek St-Jan	-	-	-	-	-	-	-	1	-	-	-	-	-	-	-
Deinze	St-Vincentius ZH	1	1	-	-	-	- (1)	1	-	-	-	1	-	-	-	-
Dendermonde	AZ St-Blasius	-	-	-	-	-	-	-	-	-	-	-	-	2	-	(1)
Diest	AZ	-	-	-	1	-	-	-	-	-	-	-	-	-	-	1 (1)
Genk	ZOL – campus St-Jan	15	12	10 (1)	10	6	13 (1)	15 (2)	15 (1)	9	9	12 (1)	11 (2)	12 (1)	13	14 (3)
Gent	AZ Maria Middelares	-	-	-	-	-	-	-	- (1)	-	-	-	-	-	-	-
Gent	AZ St-Lucas	6	8	3	3 (1)	7 (1)	4 (2)	4	-	-	-	-	-	-	-	-
Halle	AZ St-Maria	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1
Hasselt	Jessa ZH – campus Virga Jesse	4	12	1	5	5	5	2	7	2 (3)	10 (3)	10	8 (3)	9 (6)	12 (5)	9 (4)
Hasselt	Jessa ZH – campus Salvator	3	3	2	3	-	2	4	2 (1)	5	1	-	3 (1)	-	-	(1)
Herentals	AZ St-Elisabeth	-	-	-	-	-	-	-	1	-	-	-	-	1	2	(2)
Heusden	St-Franciskus ZH	1	1	-	2	6	3	7 (1)	3	5	2	3	9 (1)	7 (1)	6	2
Ieper	Jan Yperman ZH	-	1	-	-	-	1	1	1	-	1	6	2 (1)	3 (1)	1	2 (1)
Izegem	St-Jozefskliniek	-	-	-	-	-	-	-	-	-	- (1)	-	- (1)	-	-	-
Knokke - Blankenberge	AZ Zeno	1	-	-	-	-	-	1	-	-	-	2	1 (1)	-	1 (1)	-
Kortrijk	AZ Groeninge	1	3	2	4	2	11	7	10	6	7 (1)	2	14	11	5 (1)	10 (2)
Lier	H. Hart ZH	5	3	2	5	2	3	7 (1)	7	6	4 (1)	3 (1)	8	4 (2)	6 (1)	8 (4)
Maaseik	ZH Maas en Kempen	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1 (1)
Malle-Zoersel	AZ St-Jozef	1	-	2	-	1	2	1	-	1	(1)	1	1 (1)	-	-	1 (1)
Mechelen – Duffel	AZ St-Maarten	-	-	-	-	-	-	-	-	1	-	2	1	-	3	-
Menen	AZ Delta – campus Rijselstraat	2	3	1 (1)	1	-	1	2	-	-	-	1	-	-	1 (1)	(1)
Mol	H. Hart ZH	-	-	-	-	-	1 (1)	1	(1)	1	1	-	2	-	2 (1)	-
Oostende	AZ Damiaan	2	3	5	4	6	1	7	4 (1)	6 (2)	2 (1)	1	1	3 (1)	2 (2)	2 (3)
Overpelt	Maria ZH	-	-	-	-	-	-	-	(1)	1	1 (1)	-	(1)	(1)	-	(1)
Roeselare	AZ Delta – campus Wilgenstraat	11	14	16	12	19	13 (1)	14 (4)	13 (1)	10 (6)	12 (4)	15 (3)	9 (8)	15 (13)	18 (17)	18 (9)
Ronse	AZ Glorieux	-	1	-	-	-	-	-	-	-	-	-	-	-	-	1 (2)
St-Niklaas	AZ Nikolaas	3	5	5	3	4 (1)	-	-	3	3	1	2 (1)	3	1	2	2
St-Truiden	Regionaal ZH St-Trudo	5	2	-	1	3	-	1	1	1	6	4	1	2	3	3
Tielt	St-Andries ZH	2	3	-	-	2	-	1	3	1	-	1	2	1	1	1
Tienen	Regionaal ZH H. Hart	-	-	-	-	-	1	-	-	-	-	-	-	-	-	(1)
Tongeren	AZ Vesalius	1	-	-	-	-	-	2	-	1	1	-	-	2	-	1 (3)
Torhout	St-Rembert ZH	1	-	-	-	-	-	2	-	1	-	2	1 (1)	1	-	(1)
Turnhout	AZ – campus St-Jozef	-	-	-	-	-	-	-	1 (2)	-	-	-	-	-	-	-
Turnhout	AZ – campus St-Elisabeth	2	2	2	4	4	6	3	2 (1)	4	4	7	12	8	5 (1)	7
Veurne	AZ St-Augustinus	-	-	2	1	2	3	1	3 (3)	8 (5)	7 (8)	13 (15)	8 (10)	8 (6)	10 (10)	7 (5)
Vilvoorde	AZ Jan Portaels	-	-	-	-	-	1	-	-	-	1	1	1	1 (2)	1	-
Waregem	OLV van Lourdes ZH	-	-	1	-	-	1	-	(1)	1	1 (1)	1	-	1	-	(2)
Zottegem	St-Elisabeth ZH	-	-	3	1	-	1	1	1	-	-	-	-	-	-	-
Leuven	UZ Leuven	22	18	19	25 (1)	19 (2)	34 (4)	21	31 (4)	17 (11)	28 (5)	31 (11)	35 (15)	30 (12)	36 (19)	27 (19)
SUBTOTAL	DBD / heart-beating	113	110	87	97	99	115	119	129	102	113	132	153	137	149	129
SUBTOTAL	DCD / non-heart-beating	-	-	2	2	4	10	12	18	27	27	32	47	46	62	72
TOTAL		113	110	89	99	103	125	131	147	129	140	164	200	183	211	201

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

	2010	2011	2012	2013	2014
Actual donors	90 (54,9%)	108 (54%)	101 (55,2%)	97 (46%)	99 (49,3%)
Potential donors, of which were refused:	74 (45,1%)	92 (46%)	82 (44,8%)	114 (54%)	102 (50,7%)
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%)	57 (55,9%), 7 (6,9%)
'Not brain dead' + age (average) and no potential DCD cat. II - III because of various factors (no DCD cat. III protocol in donor hospital – patient too old – precarious condition - . . .)	25 (33,8%) 77 yrs. (27-91)	10 (10,9%) 80 yrs. (54-87)	19 (23,2%) 71 yrs. (39-87)	15 (13,2%) 73,5 yrs. (38-84)	16 (15,7%) 75 yrs. (43-94)
Donor refusal (National register)	-	2 (2,2%)	1 (1,2%)	3 (2,6%)	4 (3,9%)
Family refusal	8 (10,8%)	22 (23,9%)	16 (19,5%)	28 (24,6%)	24 (23,5%)
Refused by public prosecutor's office	1 (1,4%)	2 (2,2%)	2 (2,4%)	-	-
Legal contra-indication	-	-	-	3 (2,6%)	1 (1%)

TABLE 1.3 | evolution of the number of actual donors 2000 - 2014. DBD or heart-beating donors (DCD or non-heart-beating donors) (hospitals with at least one actual donor registration)

Centre		'00	'01	'02	'03	'04	'05	'06	'07	'08	'09	'10	'11	'12	'13	2014 DBD/(DCD)
Aalst	OLV ZH – campus Aalst	10	10	3	4	2	2	4	4	3	-	2	2 (1)	1	5	2
Antwerpen	ZNA Stuivenberg	-	-	-	-	-	-	-	-	-	-	-	1	-	-	-
Assebroek	AZ St-Lucas	5	-	3	1	-	-	-	2	1	-	2	3	3	-	1
Bonheiden	Imelda ZH	3	-	-	4	1	-	2	5	2	1	2	1	3	4	4
Brugge	AZ St-Jan	3	2	-	2	3	1	3	4	3	9	3	6	3	(3)	2 (2)
Deinze	St-Vincentius ZH	1	-	-	-	-	-	1	-	-	-	1	-	-	-	-
Dendermonde	AZ St-Blasius	-	-	-	-	-	-	-	-	-	-	-	-	1	-	-
Genk	ZOL – campus St-Jan	11	9	9	9	5	11	12 (1)	12 (1)	5	7 (1)	9 (1)	9 (1)	6 (1)	7	9
Gent	AZ Maria Middelares	-	-	-	-	-	-	-	(1)	-	-	-	-	-	-	-
Gent	AZ St-Lucas	5	6	1	2 (1)	5 (1)	2	4	-	-	-	-	-	-	-	-
Hasselt	Jessa ZH – campus Virga Jesse	1	10	-	3	4	3	1	3	(1)	4 (1)	9	5 (1)	5 (2)	6 (3)	4 (2)
Hasselt	Jessa ZH – campus Salvator	3	2	2	2	-	-	2	1	5	1	-	2 (1)	-	-	(1)
Herentals	AZ St-Elisabeth	-	-	-	-	-	-	-	-	-	-	-	-	-	-	(2)
Heusden	St-Franciskus ZH	-	1	-	2	6	-	6 (1)	3	4	2	1	5	3	4	1
Ieper	Jan Yperman ZH	-	-	-	-	-	1	-	-	-	1	2	2	2	1	(1)
Knokke - Blankenberge	AZ Zeno	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Kortrijk	AZ Groeninge	1	2	2	4	2	8	6	6	3	7	1	8	7	4 (1)	6 (1)
Lier	H. Hart ZH	5	1	1	4	2	3	4 (1)	3	4	2 (1)	2	8	4 (1)	2	6 (2)
Maaseik	ZH Maas en Kempen	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1 (1)
Malle-Zoersel	AZ St-Jozef	-	-	1	-	1	-	1	-	1	(1)	1	-	-	-	1 (1)
Mechelen – Duffel	AZ St-Maarten	-	-	-	-	-	-	-	-	1	-	1	1	-	1	-
Menen	AZ Delta – campus Rijselstraat	2	2	-	-	-	1	-	-	-	-	-	-	-	1 (1)	(1)
Mol	H. Hart ZH	-	-	-	-	-	-	-	-	-	1	-	2	-	1 (1)	-
Oostende	AZ Damiaan	2	3	5	-	2	-	4	2	4	1 (1)	-	-	2 (1)	(1)	1
Overpelt	Maria ZH	-	-	-	-	-	-	-	-	1	(1)	-	(1)	-	-	(1)
Roeselare	AZ Delta – campus Wilgenstraat	7	10	11	10	8	9	11	11 (1)	2 (1)	8 (2)	11	6 (3)	12 (6)	11 (4)	10 (2)
Ronse	AZ Glorieux	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1 (1)
St-Niklaas	AZ Nikolaas	2	5	5	3	2 (1)	-	-	3	3	1	1	3	1	2	2
St-Truiden	Regionaal ZH St-Trudo	4	1	-	1	3	-	-	1	-	3	4	1	1	3	1
Tielt	St-Andries ZH	2	1	-	-	-	-	-	1	1	-	1	2	-	-	-
Tongeren	AZ Vesalius	-	-	-	-	-	-	1	-	-	1	-	-	1	-	(1)
Torhout	St-Rembert ZH	1	-	-	-	-	-	1	-	-	-	-	1 (1)	1	-	-
Turnhout	AZ – campus St-Elisabeth	2	2	2	2	3	5	1	1	3	3	5	9	7	3 (1)	2
Veurne	AZ St-Augustinus	-	-	2	1	2	2	-	2 (1)	4 (2)	5 (5)	10 (7)	5	4 (2)	3 (1)	2 (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	-	-	-	-	-	-	-
Leuven	UZ Leuven	13	14	11	19 (1)	14	17 (1)	10	16	9 (4)	9 (2)	10 (3)	13 (3)	14 (5)	19 (4)	13 (10)
SUBTOTAL	DBD - heart-beating	84	81	60	74	65	67	75	81	60	67	79	96	81	77	69
SUBTOTAL	DCD - non-heart-beating	-	-	-	2	2	1	3	5	8	16	11	12	20	20	30
TOTAL		84	81	60	76	67	68	78	86	68	83	90	108	101	97	99

99 actual donors were registered in 2014, a slight increase in comparison to 2013 (97 actual donors).
We would like to express our sincerest gratitude to the many colleagues of LSGO hospitals and the University Hospitals Leuven who made all this possible. Thanks to their efforts many transplant patients can enjoy a longer life.

FIGURE 1.1 | evolution of the number of actual donors University Hospitals Leuven and partner hospitals 1996 - 2014

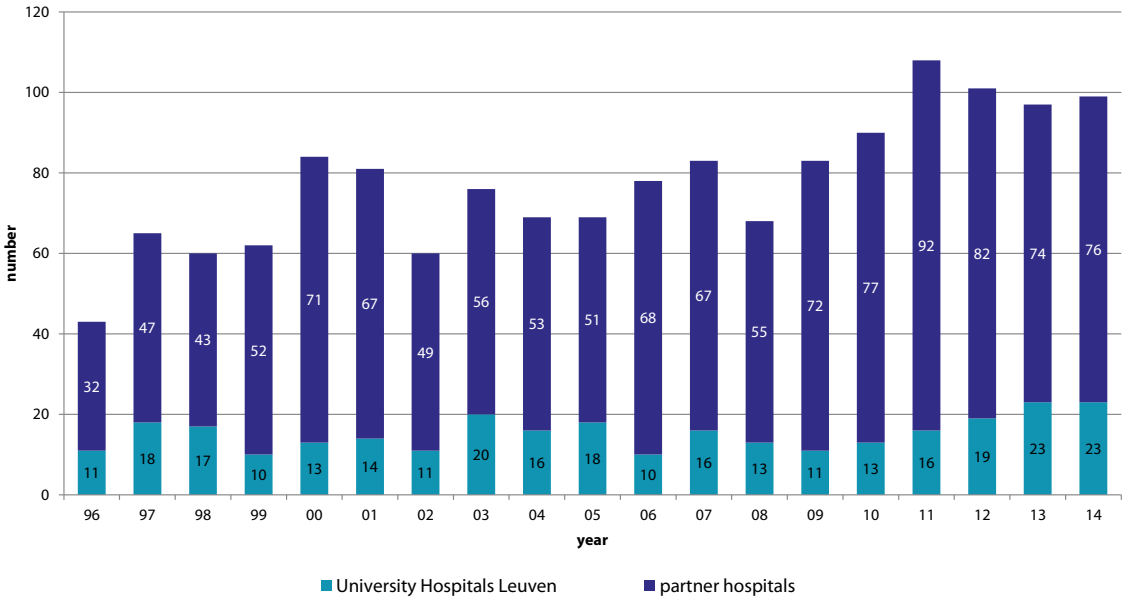


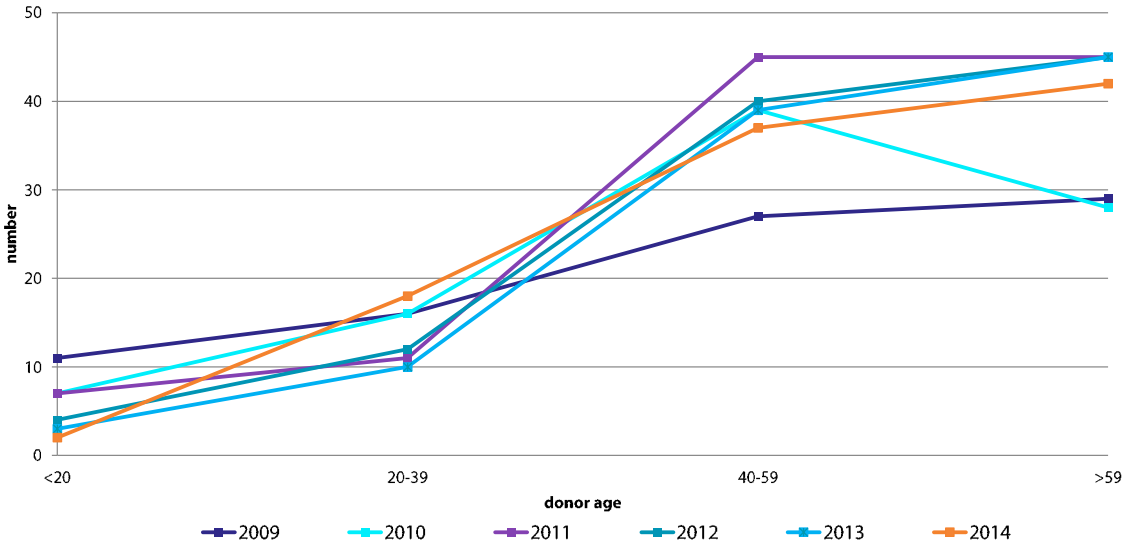
Table 1.4 illustrates the cause of death of potential donors (2000 - 2014): 65,2% died of cerebrovascular disease; 20,9% died as a result of trauma.

TABLE 1.4 | illustrates the cause of death of potential donors (2000 - 2014): 65,2% died of cerebrovascular disease; 20,9% died as a result of trauma.

	'00 (n=113)	'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)	'13 (n=211)	2014 (n=201)
Traumatic brain injury (traffic + other)	35%	51%	26%	37%	40%	27%	32%	28%	35%	22,9%	25%	27,5%	20,7%	17,1%	**20,9%**
Cerebrovascular disease:															
- spontaneous intra-cranial haemorrhage	43%	39%	51%	41%	51%	50%	43%	41%	39%	32,9%	40,2%	34%	43,2%	38,4%	**32,3%**
- cerebral infarction	4%	4%	9%	5%	6%	5%	6%	6%	7%	12,1%	6,7%	13,5%	7,7%	9,9%	**10%**
- anoxia	8%	2%	2%	6%	2%	11%	14%	19%	14,5%	6,4%	18,3%	18%	18,6%	27,5%	**22,9%**
Tumours	5%	2%	-	1%	1%	1,5%	1,5%	1,5%	-	2,9%	2,4%	0,5%	1,1%	0,5%	**1%**
Intoxication	2%	-	3%	4%	-	3%	1,5%	1,5%	2,5%	1,4%	1,2%	0,5%	0,5%	0,5%	**-**
Suicide	3%	2%	6%	4%	-	1,5%	1%	1,5%	1%	0,7%	1,2%	5%	3,3%	4,3%	**11,4%**
Bacterial meningitis	-	-	3%	2%	-	1%	1%	1,5%	1%	0,7%	1,2%	-	2,7%	-	**-**
Euthanasia	-	-	-	-	-	-	-	-	-	0,7%	-	-	2,2%	0,5%	**0,5%**

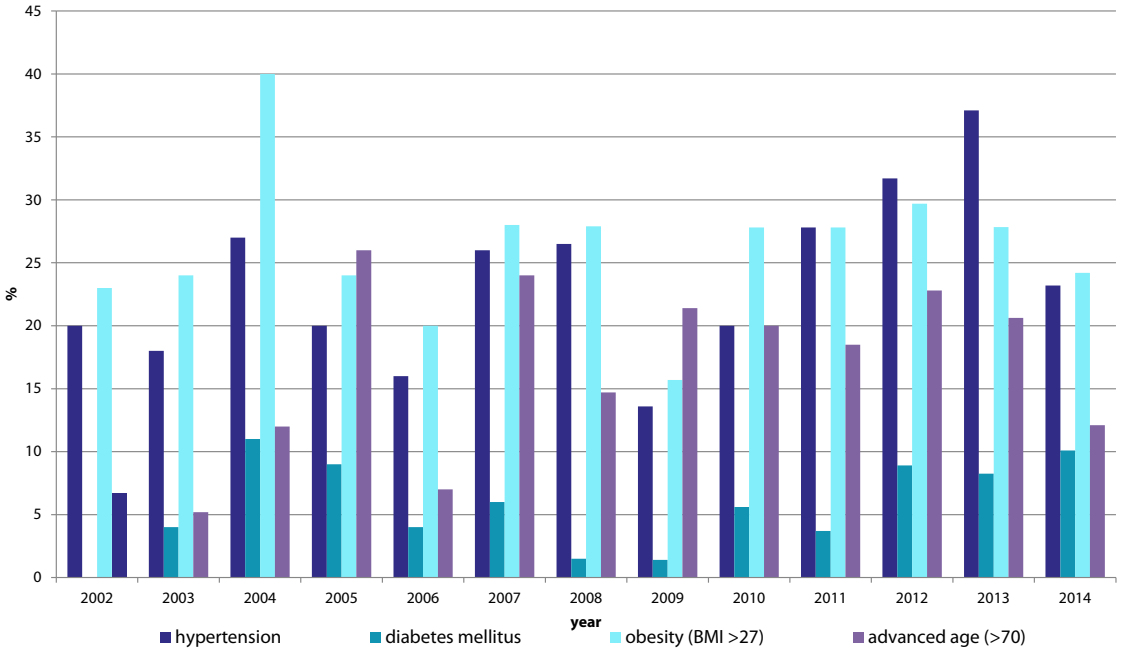
Figure 1.2 shows the classification into age categories of the actual donors in 2014 (compared to those in 2009, 2010, 2011, 2012 and 2013) which illustrates that the number of young donors (aged <20) and the number of middle aged donors (40-59) has continued to drop slightly in comparison to 2013. The number of donors aged between 20 and 39 has increased in comparison to previous years. The number of 'older' donors (> 59) remains the largest group in 2014.

FIGURE 1.2 | actual donor profile: age (University Hospitals Leuven and partner hospitals 2009 - 2010 - 2011 - 2012 - 2013 versus 2014)



A remarkable part of the recorded donors are associated with co-morbidity (hypertension: 23%, diabetes mellitus: 10% and obesity: 24%) and advanced age (12%).

FIGURE 1.3 | donor profile: associated co-morbidity and advanced age
(actual donors in the University Hospitals Leuven and partner hospitals 2002 - 2014)



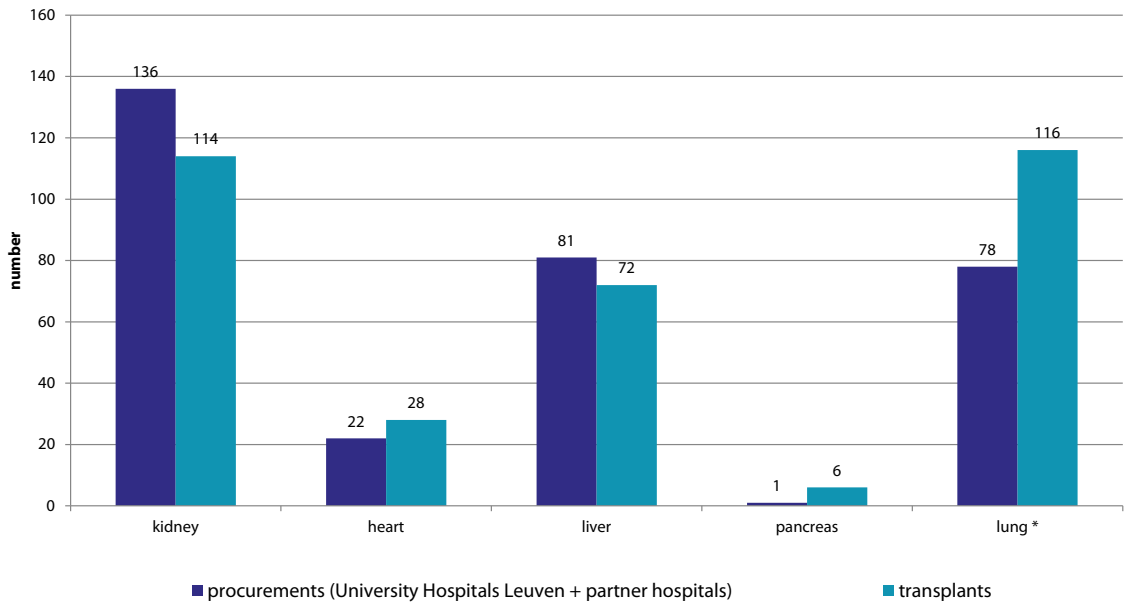
In 2014 an average of 3,21 organs (3,07 in 2013) was procured per donor.

TABLE 1.5 | type and number of procured organs University Hospitals Leuven and partner hospitals 2002 - 2014

	'02	'03	'04	'05	'06	'07	'08	'09	'10	'11	'12	'13	2014
Kidney (single)	87	125	111	80	102	132	103	135	130	142	147	121	**136**
Heart (± lung)	28	36	29	21	19	25(1)	23	27	26	23	30	23	**22**
Liver (+ split-liver)	50	68	57	68	67	69(3)	60	71	74 (6)	92 (4)	80 (6)	84 (4)	**77 (4)**
Pancreas	21	4	13	7	5	12	6	6	8	3	-	-	**1**
Lung (single)	35	51	46	49	59	52	45	66	75	77	88	66	**78**
Total	**221**	**284**	**256**	**225**	**252**	**294**	**237**	**305**	**319**	**341**	**351**	**298**	**318**

In 2014 more pancreata (+5) but considerably less livers (-14) were transplanted. The number of kidney, heart and lung transplants remained more or less equal.

FIGURE 1.4 | number of organs (deceased donors only, University Hospitals Leuven and partner hospitals) procured by the University Hospitals Leuven and number of (deceased donor) organ transplants at the University Hospitals Leuven in 2014



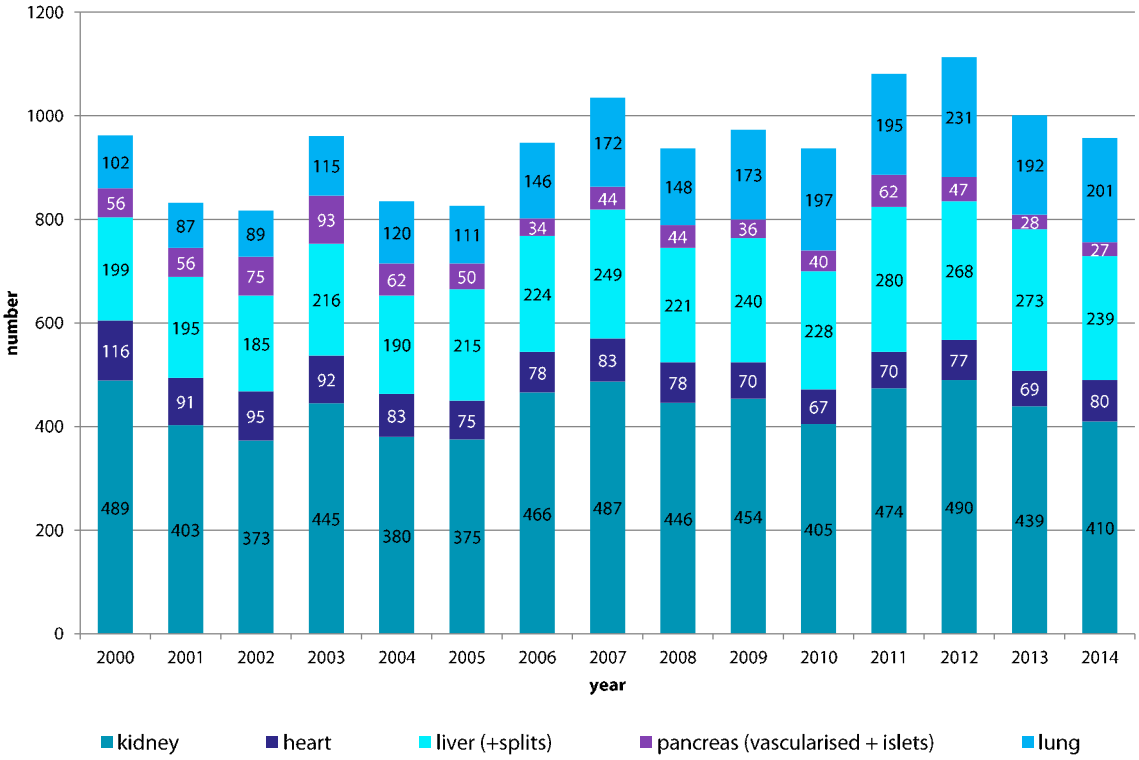
*** the number relates to the number of lungs: 38 double and 2 single lung procurements (n=78) and 58 double lung transplants (n=116).**

Organ donation in Belgium

In 2013 the actual donor number in Belgium was 306, which equates to 27.4 donors per million inhabitants (pmi) *(figure 1.5)*. In 2014 we recorded 282 actual organ donors, a drop to 25.2 donors pmi (source Eurotransplant).

FIGURE 1.5 | development of the number of actual donors (DBD + DCD) in Belgium 1996 - 2014

FIGURE 1.6 | type and number of procured organs in Belgium 2000 - 2014



PART 2

ABDOMINAL TRANSPLANTS

surgery
abdominal transplant surgery

internal medicine
endocrinology
gastroenterology
hepatology
nephrology

transplant coordination

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

abdominal transplant surgery
prof. dr. Jacques Pirenne, dr. Raymond Aerts
prof. dr. Diethard Monbaliu, prof. dr. Ina Jochmans

intensive care medicine
prof. dr. Geert Meyfroidt, prof. dr. Jan Gunst,
prof. dr. Dirk Vlasselaers*, dr. Lars Desmet *
*paediatric intensive care medicine

gastroenterology
prof. dr. Gert Van Assche, prof. dr. Martin Hiele, prof. dr. Severine Vermeire

paediatrics & transplantation
prof. dr. Elena Levtchenko, dr. Noël Knops, dr. Jean Herman,
prof. dr. Djalila Mekahli, prof. dr. Ilse Hoffman, prof. dr. Peter Witters

pathology
prof. dr. Gert De Hertogh

anaesthesiology
dr. Marleen Verhaegen

HILA
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Glen Van Helleputte, Bruno Desschans

social work
Kathleen Remans

physiotherapy
Leen Schepers

psychological support
Karine Van Tricht

dietary advice
Nelle Pauwels

speech therapy
Sofie Van Craenenbroeck

Intestinal and multivisceral transplant care 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 transplantation remains 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 immunosuppressive therapy. Moreover, prior to intestinal transplantation, patients often undergo various surgical procedures and are seriously undernourished. Factors such as these explain a global ten-year survival rate of ~ 50%, as reported by the international intestinal transplant registry.

The small intestine transplant programme for adults and children was launched at the University Hospitals Leuven in 2000, following a long preparatory experimental and clinical phase. The first successful small intestine transplant in the Benelux was carried out that same year in a 55-year-old woman. Since then, a total of 16 transplants were carried out, 3 involving children and 13 involving adults. One of the patients received an approximately 2 m long small intestinal graft from a living donor. So far the ten-year patient survival rate (n=16) is 74%. Of the 16 patients, 14 received an intestine from a deceased donor and were treated with a specific ´Leuven Immunomodulatory Protocol´ in order to inhibit the characteristic rejection associated with intestinal transplantation. The ten-year survival rate in this group (n=14) is 92% with an early (< 3 months after transplantation) acute rejection in 2 patients (13%). All the survivors have a normally functioning intestine and were able to resume their daily activities.

INTESTINAL TRANSPLANTS

Until now, 2,887 intestinal transplants have been carried out worldwide. This is based on the latest report of the international intestinal transplant registry (2013). This accounts for only 0.4% of the total global abdominal transplant activity. Intestinal transplantations consequently remain a delicate procedure with global survival rates that are considerably below those for other organs.

In conjunction with the laboratory for experimental transplantation, the laboratory for abdominal transplant surgery has therefore developed a protocol to inhibit the extreme rejection response towards the intestinal allograft.

This ´Leuven Immunomodulatory Protocol´ is based on the following four principles: i) donor specific blood transfusion to the recipient at the time of transplantation results in better intestinal allograft acceptance; ii) avoidance of high doses of steroids as they can inhibit the positive effect of the donor specific transfusion; iii) avoidance of high doses of maintenance immunosuppression with its associated complications such as kidney failure, infections and tumour development, will paradoxically result in better intestinal graft acceptance; and iv) limitation of the inflammatory response in the intestine by using small bowel decontamination in the donor and recipient as well as by a highly selective choice of suitable donors.

Until now this protocol was applied at the University Hospitals Leuven in 14 consecutive intestinal transplant recipients of a deceased donor (follow-up ranges from 9 months to 13 years). Four of these 14 patients received a new bowel in 2014. The ten-year survival rate of this group (n=14) is 92%. The average age was 38 years. 6 male and 8 female patients were transplanted; 3 patients were children aged 2, 3 and 9 years; 6 patients received an isolated intestinal transplant (in 3 cases with an additional kidney), 6 underwent a combined liver-intestinal transplantation and 2 patients received a multivisceral transplantation. The latter two received, apart from an entire small bowel graft, also a stomach, liver, duodenum and pancreas and one of them also underwent a simultaneous kidney transplantation. The indication for this en-bloc transplantation of almost the entire abdominal content was an extensive thrombosis of the entire venous splanchnic system that normally transports the blood from the intestine to the liver. Due to this obstruction, a diffuse network of collateral veins is formed. This poses an important risk towards bleeding (in particular during exenteration of the native organs at the moment of transplantation). In order to limit this risk, an interventional radiologist successfully embolised the native arterial inflow to the stomach, liver, duodenum, pancreas and small bowel just prior to exenteration. A technique which was never reported before for this indication *(Figure 2.1)*.

Despite the fact that intestinal transplantation is characterised by acute rejection, only 2 of the 14 patients (n=14) developed early rejection (acute rejection within 3 months of the transplant) (14%), one of which suffered from Crohn´s disease. Both were reversible with high-dose of steroids. One of them as well as 2 other patients developed an episode of late rejection (rejection later than 3 months after transplantation) (21%). Following anti-rejection therapy, the first patient developed an aspergillus infection and died 8 months after the transplant from an intracranial bleeding. In the second patient, discontinuation of the immunosuppressive therapy (non-compliance) led to rejection at 46 months. Fortunately, the rejection process was reversible with high-dose of steroids. The last patient to develop late rejection at 18 months was the above mentioned patient with Crohn's disease. Crohn's disease, and its genetic background, could potentially have been an additional risk factor. Fortunately, the rejection process was also reversed by high doses of steroids. 12 of the 14 patients are still alive today. They all have a successfully functioning intestine and were able to resume their day-to-day activities. In addition to the above patient who died from rejection and an 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) which led to diffuse ulcerations of the intestinal wall via which bacteria were able to enter the blood stream, leading to a massive inflammatory reaction and graft loss.

In addition to the 14 patients described above, 2 other patients underwent small bowel transplantation at our institution. The Leuven protocol could not be used for the first patient, a 43-year-old male, because of the lack of donor-specific blood. This patient underwent a combined liver, stomach, duodenum, pancreas and small bowel 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 14 patients described above in that she received a partial intestinal graft (2 meters of ileum) from a living donor, i.e. her mother. Intestinal Churg-Strauss syndrome was the reason for the transplant. The donor is doing well. However, the transplanted graft had to be resected 7 months later because of refractory acute and chronic rejection. We were not able to continue monitoring the patient because she went abroad. We were recently informed that she has died.

The ten-year patient survival rate in this series of 16 small intestine transplants (n=16) is 74%. This seems to be a favourable result compared to the results reported by the international intestinal transplant registry (47% ten-year patient survival rate following intestinal transplantation over the same time period) and the overall Belgian experience (n=25) (62%, including Leuven) *(Figure 2.2)*.

At the beginning of 2015, 2 patients were actively listed for intestinal transplantation at our centre. 1 awaiting an isolated small intestinal transplant (in combination with an abdominal wall transplant) and 1 for a combined pancreas-intestinal transplantation.

One of the most important aspects 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 annual 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 into 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 dramatical deterioration of the clinical condition pre-transplant.

That is why in the past two years we took the initiative in Leuven, to initiate two international studies with colleagues from Beaujon (France), Birmingham (UK), Buenos Aires (Argentina) and Maastricht (the Netherlands), and this in conjunction with gastroenterology and pathology unit. The objective of the first 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 immunological resistance in the intestinal wall) on the transplantation and their role in the rejection process. A second study aims to determine whether there is a correlation between the genetic risk factors associated with Crohn's disease and rejection after intestinal transplantation.

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 | multivisceral transplantation. Left panel: following resection of the native organs; right panel: following transplantation of the multivisceral bloc (stomach-liver-duodenum-pancreas-small bowel).

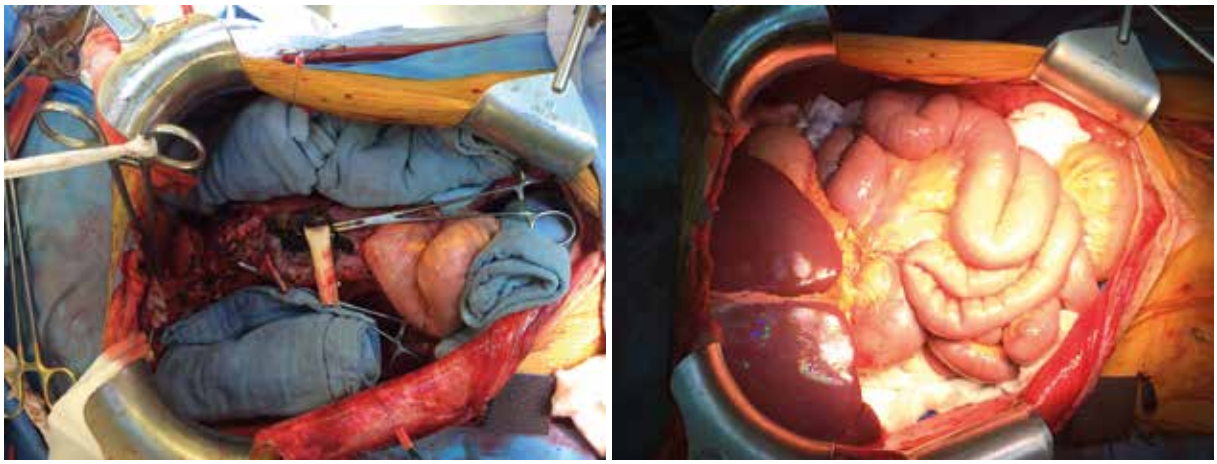
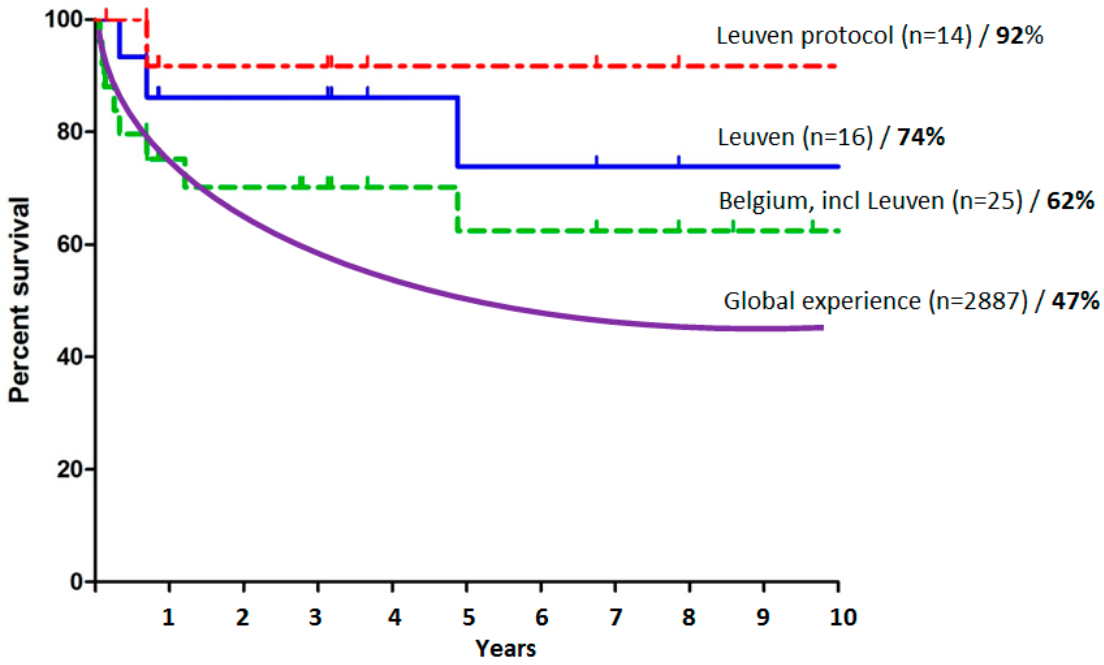


FIGURE 2.2 | survival curve intestinal transplantation University Hospitals Leuven (protocol: n=14; and total experience: n=16) versus Belgium (including Leuven; n=25) versus global experience (International Intestinal Transplant Registry; n= 2887).



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dietary advice
Nelle Pauwels

speech therapy
Sofie Van Craenenbroeck

Liver transplant care programme

There is a further progress in our liver transplant activity: as such an increase of 40% as observed over the last 10 years. This results in a total number of liver transplants of 1,139 at the end of 2014.

The survival rate stays excellent. The graft survival at 1 year is 18% better than the mean graft survival from other Eurotransplant centres and the early need of re-transplantation is only 3%.

Hepatocellular carcinoma has become an important indication for liver transplantation. There is no difference in survival the first 2 years but due to recurrence there is a difference in survival of 15% after 5 years. However, recently the recurrence rate has dropped to ≤ 5%.

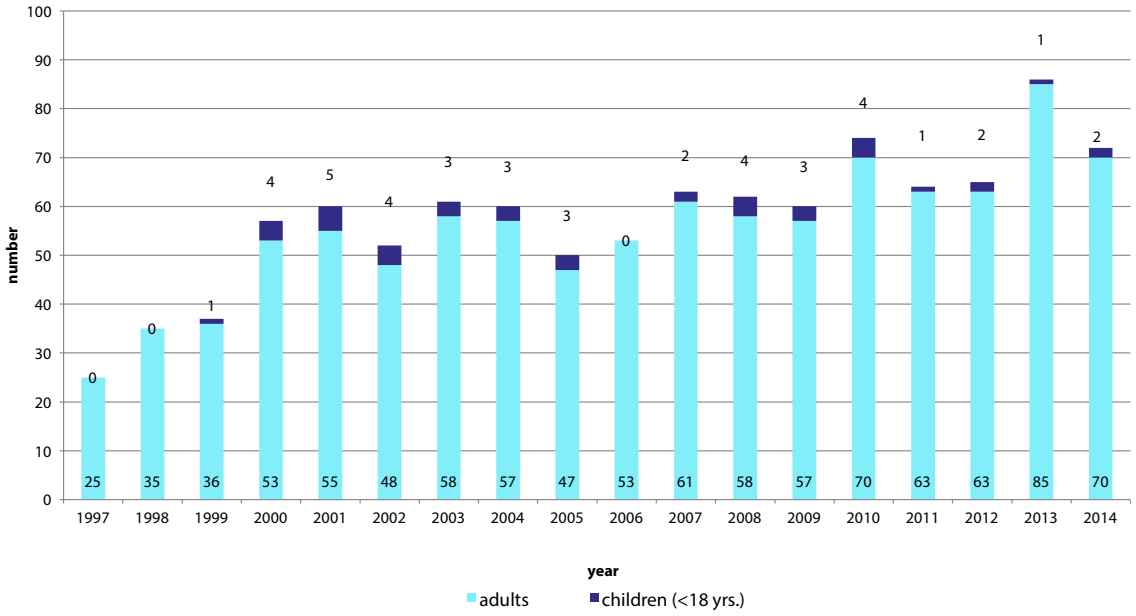
Organ shortage is increasingly compensated by the use of DCD livers (donation after circulatory death). These are livers prelevated mostly from donors who died in intensive care. In our centre, the outcome of transplanting patients with these organs is similar to transplantations with organs form heart-beating donors due to the short cold ischemic time.

LIVER TRANSPLANTS

Transplant activities

72 liver transplants were carried out in 2014, a figure which fluctuates around the average number of liver transplants of the last 5 years (n=70). A progressive increase of 40% is observed over the last 10 years. Since the department of abdominal transplant surgery was set up in 1997, 1,035 liver transplants were performed. Before, from 1989 until 1996, 104 liver transplants were performed. This brings the total amount of liver transplants performed in the University Hospitals Leuven to 1,139.

FIGURE 2.3 | number of liver transplants 1997-2014 University Hospitals Leuven



Recipients

Etiology

Malignancy (mostly HCC) and complications of post-alcohol cirrhosis are the most common indications for liver transplantation. The last 5 years NASH (non-alcoholic steatohepatitis) has become a more common cause for liver transplantation: before 2009 11 patients were transplanted for NASH, since 2009 this number has risen to 37.

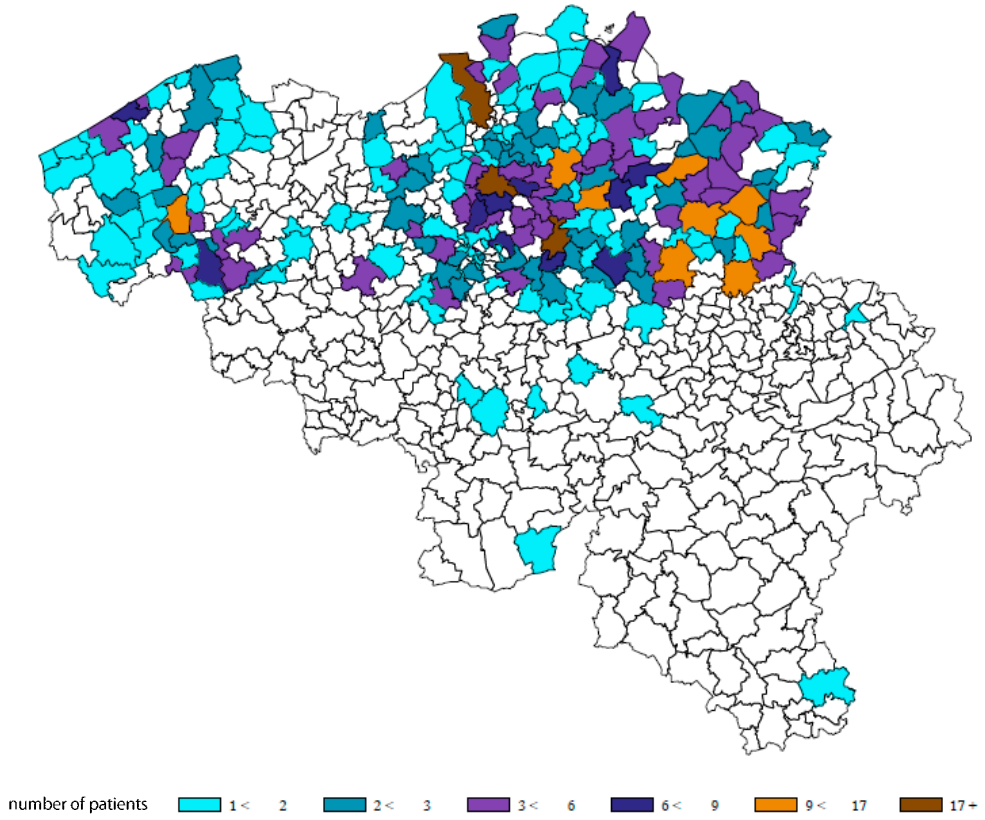
TABLE 2.1 | primary diagnosis for liver transplant 1997 - 2014 University Hospitals Leuven (n=1035)

Indication	Number	%
Malignancy (HCC)	264	26%
Viral hepatitis	183	18%
HCV without HCC	49	5%
HCV with HCC	74	7%
HBV without HCC	38	4%
HBV with HCC	22	2%
Post-alcohol	271	26%
Without HCC	185	18%
With HCC	86	8%
Cholestatic	77	7%
PBC (primary biliary cirrhosis)	32	3%
PSC (primary sclerosing cholangitis)	45	4%

Indication	Number	%
Polycystosis	72	7%
Congenital/metabolic liver disease	85	8%
NASH	50	5%
Without HCC	31	3%
With HCC	19	2%
Children < 18 year	41	4%
Acute liver failure	87	8%
Other (Budd Chiari, cryptogenic, auto-immune, benign tumors and other liver diseases)	86	8%
Re-transplantation	79	8%
Early (< 90 days after 1st tx)	27	3%
Late (> 90 days after 1st tx)	52	5%

Geographic origin

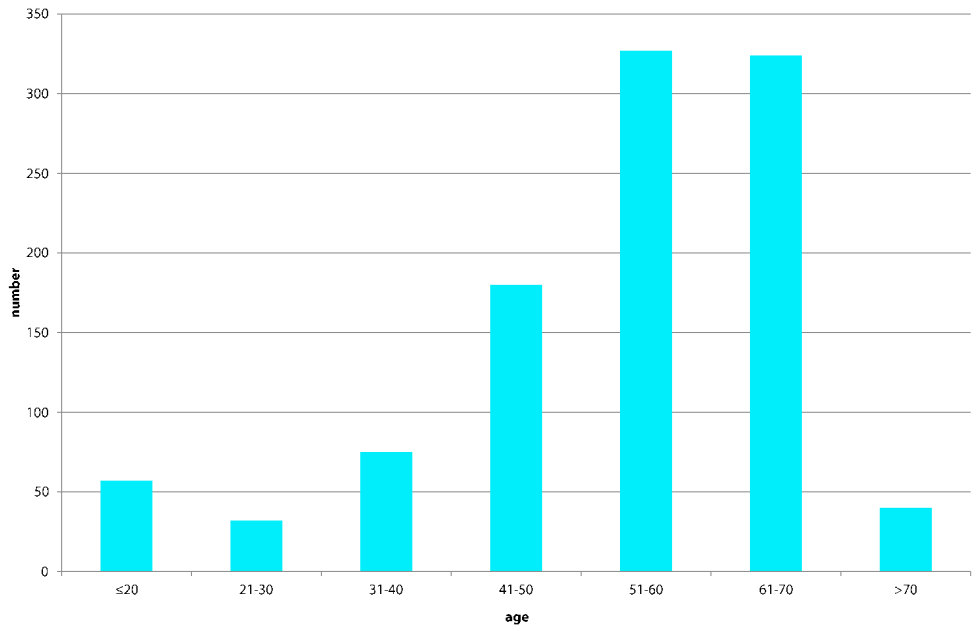
FIGURE 2.4 | geographic origin of liver recipients



Age distribution

The largest group consists of patients between the age of 51 and 70 years.

FIGURE 2.5 | age distribution liver recipients1997 to 2014

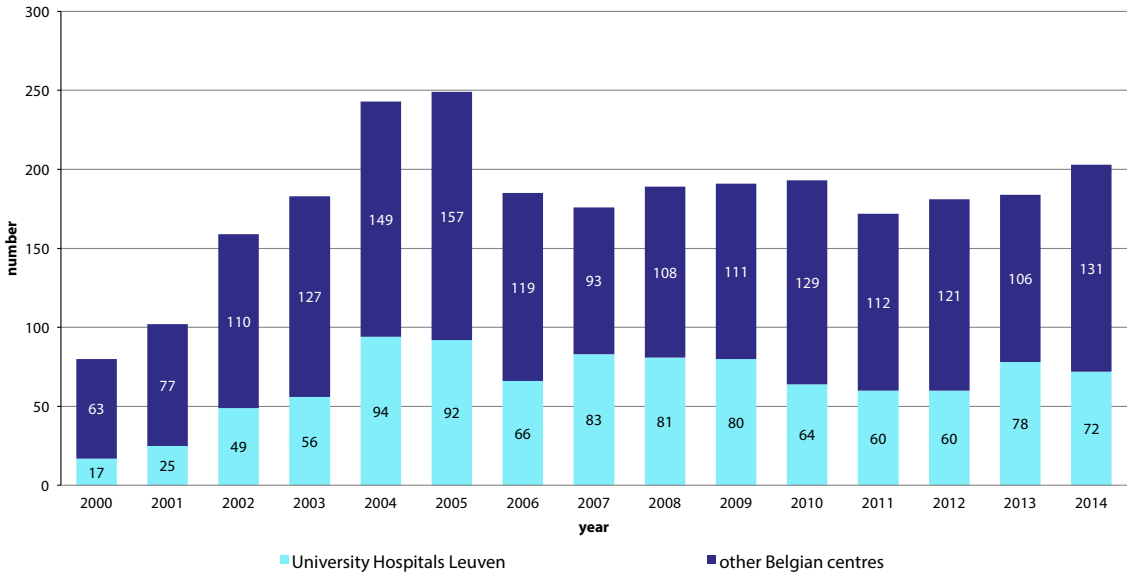


Waiting list data

Active waiting list in Belgium and the University Hospitals Leuven

At the end of 2014 the number of patients awaiting a liver transplant in Belgium was 203 patients, 72 of which (36%) from our centre. The mean number of patients awaiting a liver transplant in our centre in the last 5 years was 67 a year.

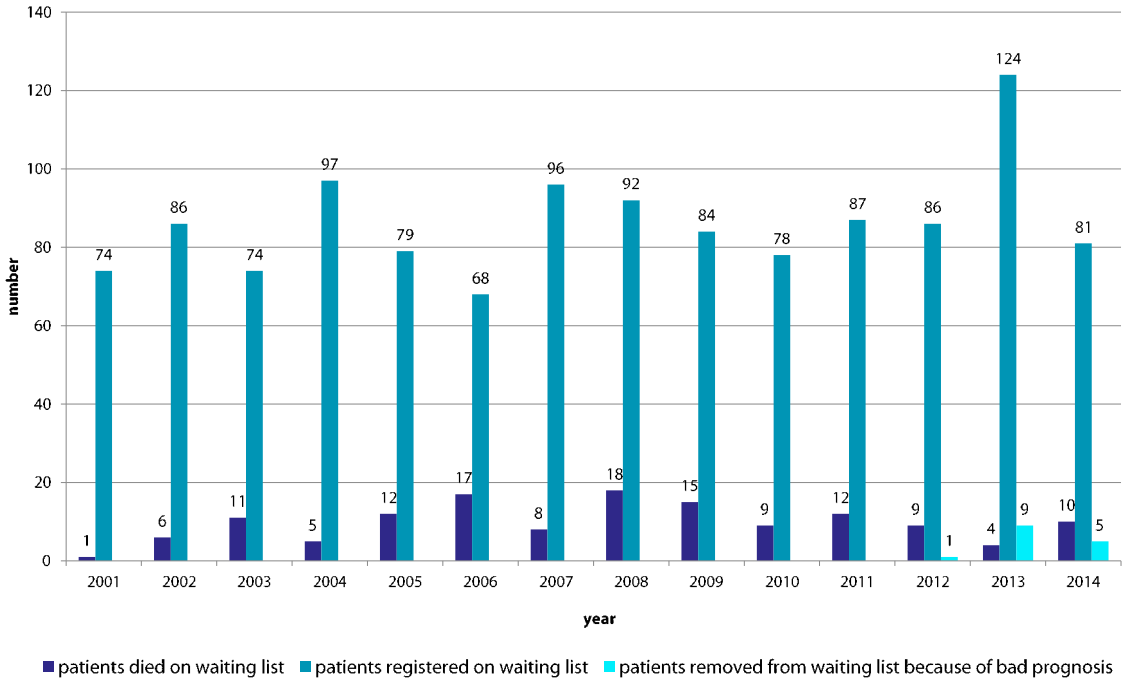
FIGURE 2.6 | evolution of the number of Belgian patients on the active Eurotransplant liver waiting list since 2000, University Hospitals Leuven versus other liver transplant centres (number of transplant centres in Belgium n=6)



Registrations and deaths on the waiting list

In 2014, 81 patients were registered on the waiting list for a liver transplant. The mean number of patients registered on the waiting list in the last 5 years is 91 a year. Ten patients died while on the waiting list and five patients were removed from the waiting list mostly because of progression of HCC. Since 2012 the mean number of deaths on the waiting list is 13 a year. This is a mean drop-out rate of 13% a year.

FIGURE 2.7 | number of patients registered on the waiting list; patients on the waiting list who died (since 2001) and patients removed from the waiting list because of progressed HCC (since 2012).



Priority rules:

Since 2007, the allocation of livers in the Eurotranplant zone is based on the MELD score. MELD stands for "Model for End stage Liver Disease". This scoring system is based on three objective lab parameters: protrombine time, creatinine and bilirubin. It aims at stratifying recipients by their disease severity according to a score estimating the 3-month probability of death on the waiting list.

- In 2014, 42% of our patients received a liver which was allocated based on the MELD score.
- In 2014, 35% of our patients received a liver which was allocated based on a standard exception (SE). The most common standard exception applied in 2014 was HCC, followed by polycystosis and hepatopulmonary syndrome. Recipients must fulfill specific criteria before a standard exception can be approved.
  Patients who are not eligible for a SE can request a non-standard exception (NSE). In 2014 five patients (7%) received a liver which was allocated based on such a NSE.
- In 2014 eight livers were allocated to patients with acute liver failure (HU)(11%).
- Four liver transplantations (5,5%) were combined with another organ such as lung, intestine and/or pancreas. An 'approved combined organ' (ACO) can not be obtained for a combined liver kidney transplantation.

The number of patients in each category has not changed since 2002.

TABLE 2.2 | evolution of Eurotransplant liver allocation method (LabMELD, SE= Standard Exception, NSE= Non Standard Exception, HU= High Urgency, ACO= Approved Combined Organ)

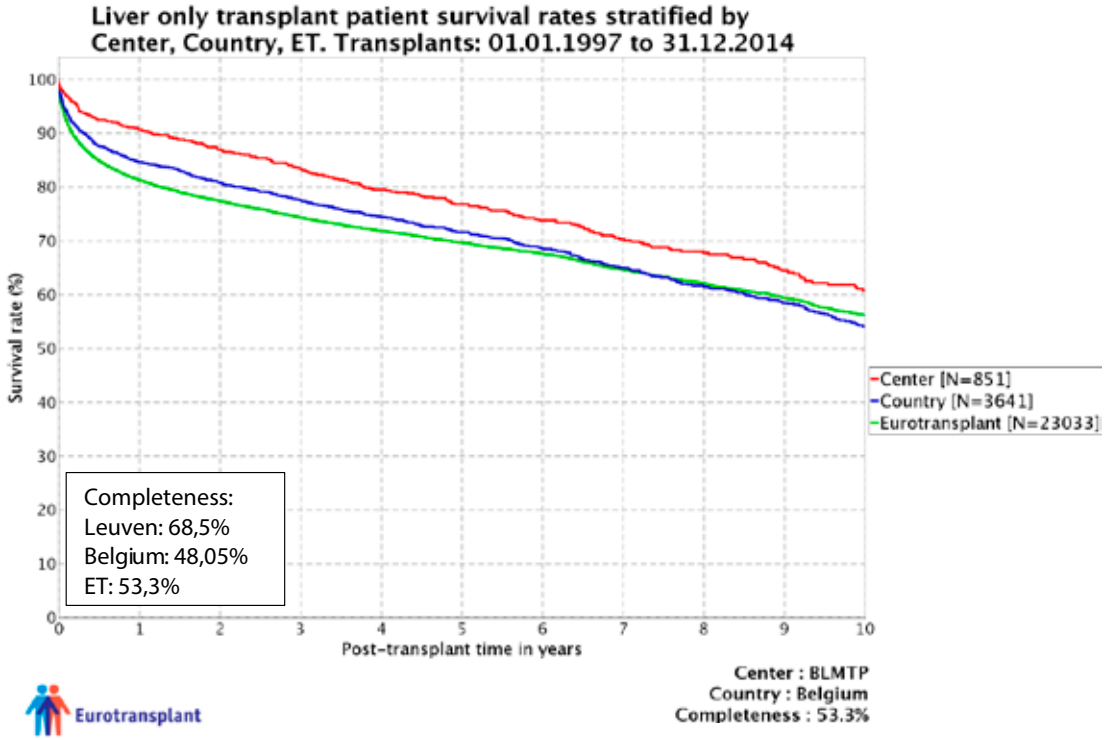
	LabMELD	SE	NSE	HU/ACO
2007	30 (48%)	22 (35%)	8 (13%)	3 (5%)
2008	28 (45%)	21 (34%)	5 (8%)	8 (13%)
2009	30 (50%)	18 (30%)	6 (10%)	6 (10%)
2010	32 (43%)	25 (34%)	6 (8%)	11 (15%)
2011	30 (47%)	19 (30%)	6 (9%)	9 (14%)
2012	26 (40%)	27 (41%)	5 (8%)	7 (11%)
2013	39 (45%)	29 (34%)	8 (9%)	10 (12%)
2014	30 (42%)	25 (35%)	5 (7%)	12 (17%)

Patient and graft survival

University Hospitals Leuven versus Belgium and Eurotransplant

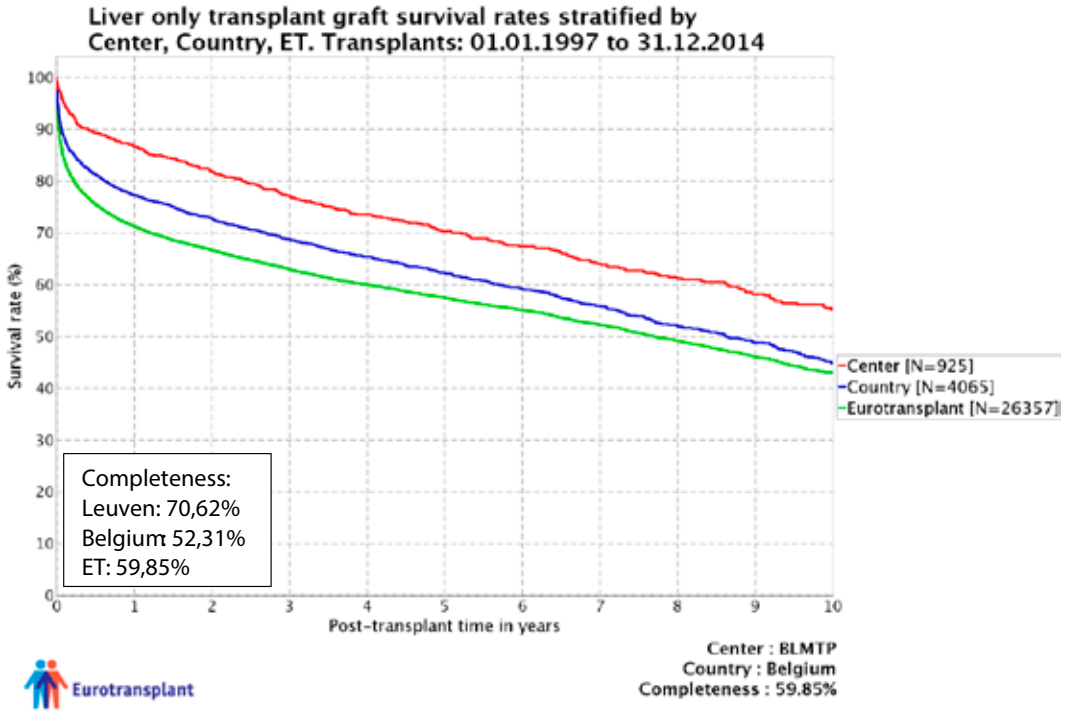
The figure below shows patient survival rates for all patients who underwent a liver-only transplant in the period of 1997 - 2014. The actuarial patient survival rate in the University Hospitals Leuven is considerably higher in comparison to the results of Eurotransplant and Belgium. These differences become immediately obvious from the post-operative period on.

FIGURE 2.8 | ten-year patient survival (1997 - 2014 all indications – liver-only transplants), University Hospitals Leuven compared to Eurotransplant and Belgium (the figures for Belgium also include the results for the University Hospitals Leuven). Source: Eurotransplant



There is also a difference in outcome between our centre versus those for Eurotransplant and Belgium for the graft survival.

FIGURE 2.9 | ten-year graft survival (1997 - 2014, all indications – liver-only transplants), University Hospitals Leuven in comparison to Eurotransplant and Belgium (the figures for Belgium also include the results for the University Hospitals Leuven). Source: Eurotransplant



Need for retransplantation

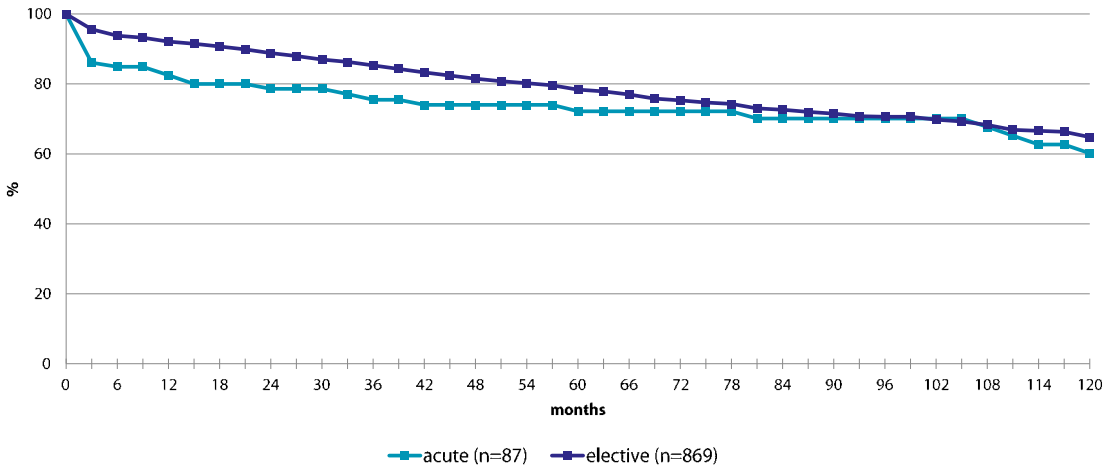
The need for early retransplantation (≤90 days) reflects the expertise of the procurement team and the competence of the surgical transplant team. In 2014 the mean need for early retransplantation in the University Hospitals Leuven was 3% (n=2) and remains extremely low.

The need for late retransplantation (>90 days) in the University Hospitals Leuven was 4% (n=3) in 2014 and also remains extremely low. This reflects for instance the occurrence of ischemic biliary strictures and relapse of the initial disease.

'Acute' versus 'elective' liver transplantation

The one-year survival rate following a liver transplant is 10% lower in case of acute liver failure compared to elective liver transplant. However, the long-term outcome for these mostly younger patients is better.

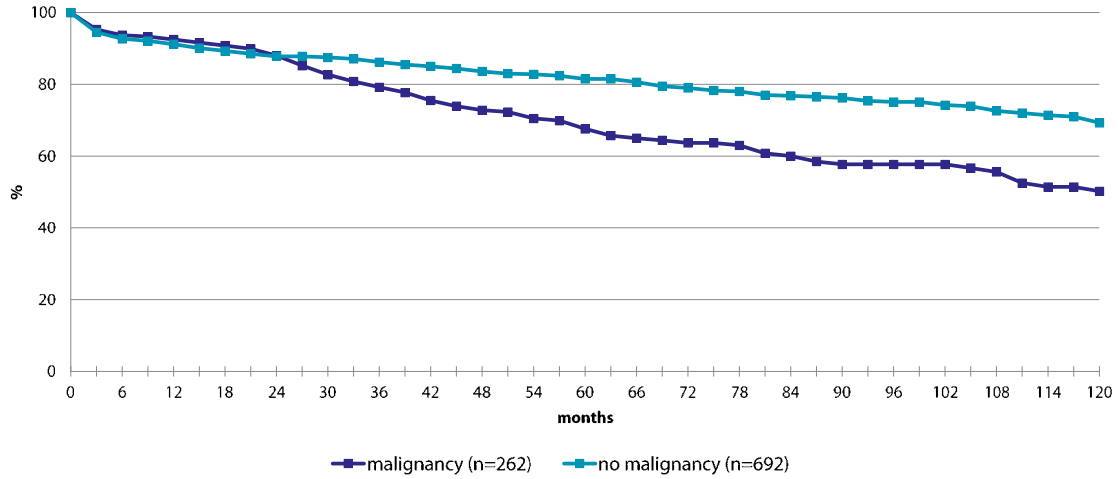
FIGURE 2.10 | ten-year patient survival (1997 - 2014) for transplant due to acute liver failure versus elective liver transplant. Source: University Hospitals Leuven database



Malignancy (HCC) versus no malignancy

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

FIGURE 2.11 | ten-year survival (1997 - 2014) for transplant due to malignancy or no malignancy.
Source: University Hospitals Leuven database



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

In 2014, 14 combined liver transplants were carried out in the University Hospitals Leuven, which brings the total of combined liver transplants since 1997 to 115. This is 11% of the total number of liver transplants carried out in our centre. With 75%, the ten-year survival of these patients is excellent and comparable with patients who received a liver-only transplant (without malignancy).

FIGURE 2.12 | Ten-year patient survival (1997 - 2014) for combined transplants versus solitary transplants (without malignancy).
Source: University Hospitals Leuven database

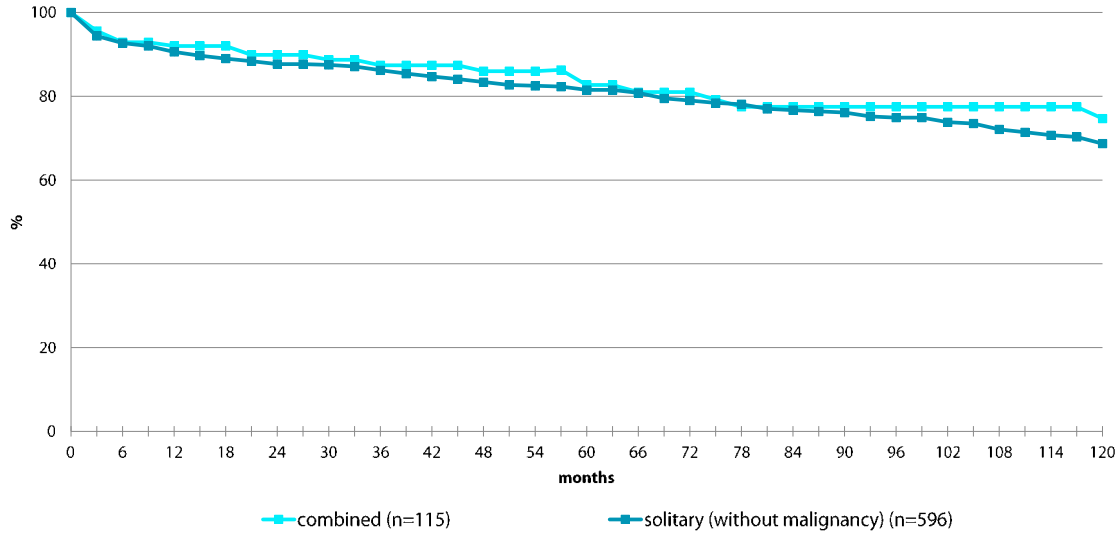


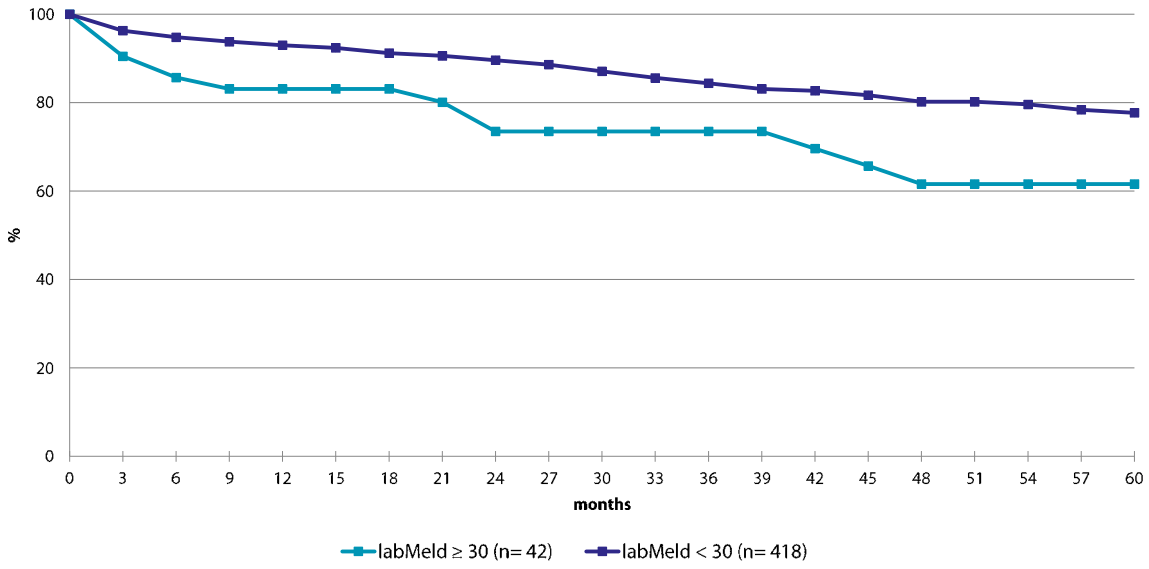
TABLE 2.3 | combined liver transplants (1997 - 2014)

Summary combined liver transplants	Total (n=115)	2014 (n=14)
Liver + kidney	89	10
Liver + small intestine	5	-
Liver + pancreas	6	-
Liver + small intestine + pancreas	1	1
Liver + small intestine + pancreas + colon	2	1
Liver + small intestine + pancreas + colon + kidney	1	1
Liver + pancreas + kidney	1	-
Liver + heart	3	-
Liver + heart + double lung	1	-
Liver + double lung	6	1

Survival following liver transplant on the basis of LabMELD

The LabMELD results reflects the condition of the patient. The higher the score, the sicker the patient. This curve shows the survival rate of our transplant patients with a score of ≥ 30 versus patients with a score < 30. Patients who already underwent a liver transplant in the past and patients with acute liver failure (who usually have a very high LabMELD score) are not included. As expected patients with a high labMELD have worse survival chances.

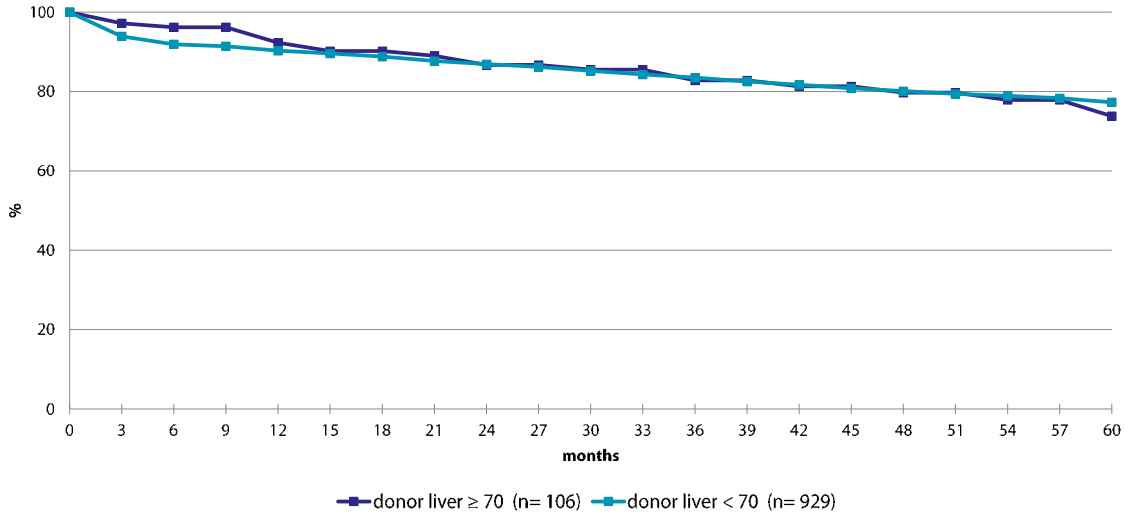
FIGURE 2.13 | five-year patient survival (2007 - 2014) for patients with a LabMELD of ≥ 30 versus patients with a LabMELD of < 30. Source: University Hospitals Leuven database



Liver transplants with organs from 'extended criteria donors'

This curve demonstrates that the survival of transplant patients in our centre 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 patients who received a donor liver of ≥70 years old versus a donor liver of < 70 years old. Source: University Hospitals Leuven database



In recent years livers from DCD (Donation after Circulatory Death) donors are increasingly being offered and transplanted. The use of strict selection criteria in terms of both patient and donor makes the results of these liver transplants in our centre acceptable with a five-year patient survival of 74% and a five-year graft survival of 67%.

FIGURE 2.15 | five-year patient and graft survival for DCD donor livers. Source: University Hospitals Leuven database

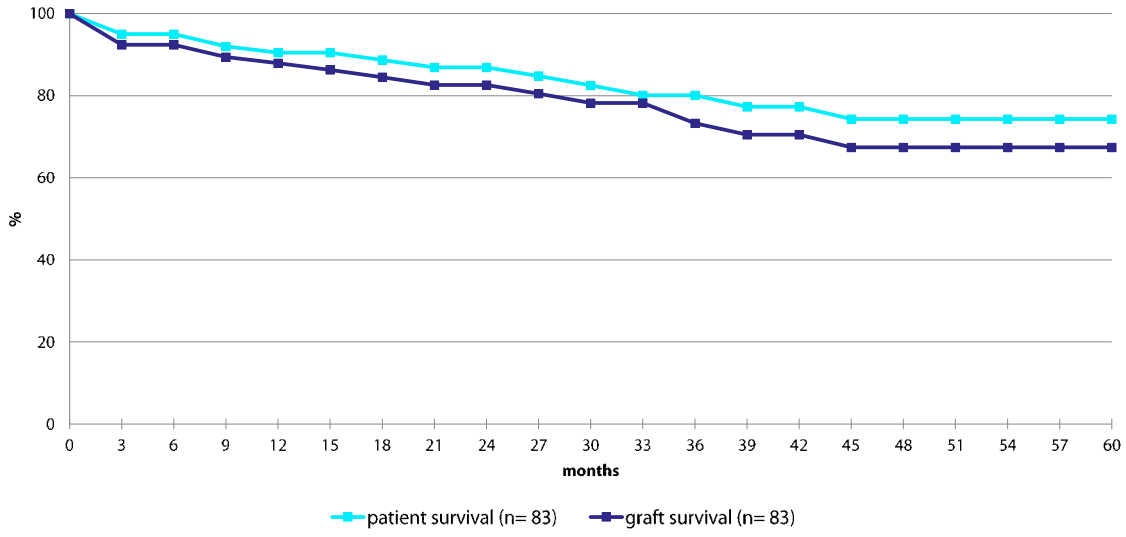


TABLE 2.4 | patients that received a liver of DCD donors in comparison to the total liver transplant activity

	Number
2014	21 (29%)
2013	15 (17%)
2012	10 (15%)
2011	7 (11%)
2010	6 (8%)
2009	12 (20%)
2008	4 (6%)
2007	2 (3%)
2006	-
2005	3 (6%)
2004	1 (2%)
2003	2 (3%)

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Living donation care 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 not only includes doctors and hospital workers involved in the screening process, but also 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.
Follow-up of living donors is done annually and throughout their life.

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

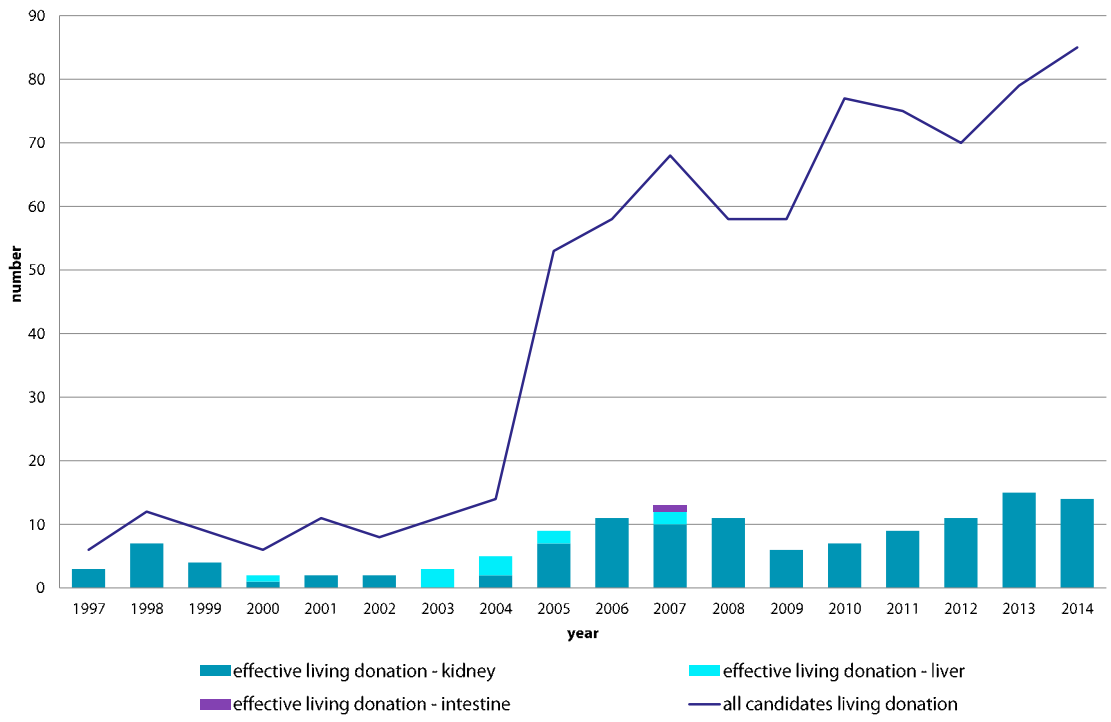
LIVING DONATION OF A KIDNEY, LIVER LOBE OR INTESTINE

Transplant activities

Since the start of the living donor programme at the University Hospitals Leuven – living kidney donation in 1997, living liver donation in 2000, living intestinal donation in 2007 – until the end of 2014, 714 candidate living donors (CLD) were screened for 478 candidate receptors (438 kidney recipients, 39 liver recipients and 1 small intestine recipient).

- 648 CLD kidney
- 65 CLD liver
- 1 CLD small intestine

FIGURE 2.16 | number of candidates and effective living donors kidney, liver and intestine 1997 - 2014



In the period between May 1997 and end December 2014, 134 living donation organ transplants were carried out, including 56 interventions (42%) over the past five years (122 living donation kidney transplants, 11 living donation liver transplants and one living donation intestinal transplant).
In 2014, 81 people volunteered to donate a living kidney; 14 candidates were upheld, 14 interventions were completed. 48 candidates were rejected, 19 candidates are still under consideration.
Four people volunteered to be a living liver donor for two recipients. The four candidates were rejected. One recipient received a transplant involving a liver from a deceased donor; and one recipient is still on the active waiting list for liver transplantation.

Living donor profile

TABLE 2.5 | effective living donor profile by gender (1997 - 2014)

	Male	Female
Kidney	52	70
Liver	7	4
Intestine	-	1
Total	**59**	**75**

TABLE 2.6 | effective living donor profile based on age (1997 - 2014)

Age	Number of kidney donors	Number of liver donors	Number of intestine donors
18 – 30	8	8	-
31 – 40	25	2	-
41 – 50	39	-	1
51 – 60	34	1	-
61 – 70	16	-	-

TABLE 2.7 | effective living donor profile based on relationship with recipient (1997 - 2014)

	Genetically related donors	Emotionally related donors	Altruistic
Kidney	74	47	1
Liver	11	-	-
Intestine	1	-	-

TABLE 2.8 | LRD profile based on the nature of the relationship with the recipient (1997 - 2014)

LRD	Kidney	Liver	Intestine
GENETICALLY RELATED	**74**	**11**	**1**
Brother/sister	18	1	-
Father	18	1	-
Grandfather or -mother	-	1	-
Mother	29	3	1
Son/daughter	7	5	-
Nephew/niece	2	-	-
Uncle/aunt	-	-	-
EMOTIONALLY RELATED	**47**	**-**	**-**
Partner (wife)	25	-	-
Partner (husband)	17	-	-
Brother-in-law or sister-in-law	1	-	-
Father-in-law or mother-in-law	2	-	-
Friendship	2	-	-
ALTRUISTIC	**1**	**-**	**-**

368 candidates (314 CLD kidney, 54 CLD liver) were rejected for various reasons *(see table 2.9)*.

TABLE 2.9 | reason for rejection living kidney or liver donation candidates (1997 - 2014)

REASON FOR REJECTION CANDIDACY	Number
Mismatches (n=58)	
ABO	23
Positive cross match	18
Size and/or age	17
Medical – psychosocial – surgical reasons	168
Donor withdrawal	49
Receptor withdrawal	19
Transplantation with organ from deceased donor during screening living donor	35
Other	39

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 Programme) in which kidneys can still be donated and transplanted using cross-donation was set up in 2010. A case involving cross-donation took place at the University Hospitals Leuven in 2013. In 2014, there were no cases involving cross-donation. Another possibility in case of blood group incompatibility is the programme of blood group incompatible living donation, which was performed in two patients in University Hospitals Leuven. Both interventions took place 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 (post-operative consultations one month, three months, six months and annually) and follow-up data is stored in a database.

29 living donors (21%) are no longer part of the follow-up scheme; the others are invited at least once a year to attend a consultation.

Results

Living donation kidney transplant

RECIPIENTS (n=122) (see figures 2.17)

- 14.8% child (< 16, n=16), 85.2% adult receptors (> 16, n=106)
- Delayed graft function (DGF) (dialysis requirement < 8 days post Tx): 1.6% (= 2 casus: factor rejection? DGF?)
- Primary Non Function (PNF): 0%
- Acute rejection: 22.1% (n=27); adult receptors: 25.5%, children: 0%
- Three month and six month graft survival: 100%
- One-year graft survival: 98.3% (n=122 kidney Tx).
  Reason for graft loss:
  - patient: rejection as a result of non-compliance with therapy.
  - 1 patient: recurrence of initial disease.

DONORS (n=122)

- 0% peri-operative mortality
- Morbidity:
  - Peri-operative requirement for transfusion in 1 patient (0.8%)
  - One surgical revision on d 0 for mild bleeding in one patient (0.8%)
  - One surgical revision due to wound infection (0.8%)
  - Three patients (2.4%) with chronic pain
  - Four patients (3.2%) with incisional hernia repair

Living donation liver transplant

RECIPIENTS (n=11)

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

DONORS (n=11)

- 0% mortality
- One revision for incisional hernia repair

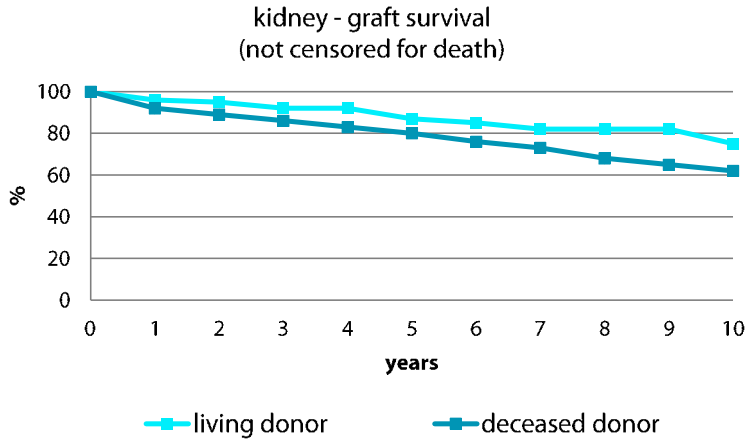
Living donation intestinal transplant

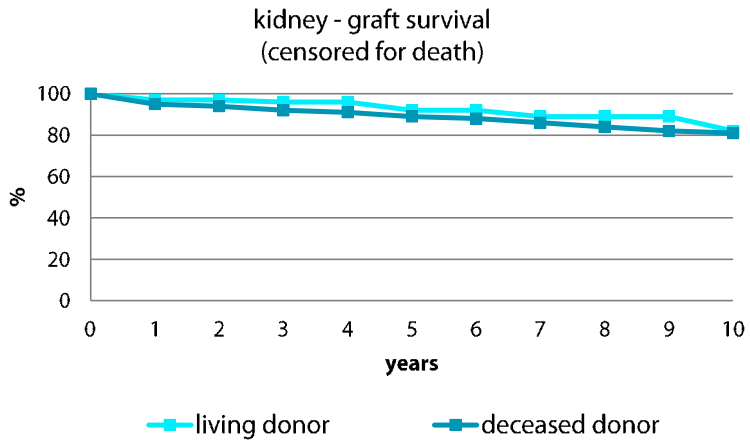
RECIPIENTS (n=1)

- 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
(not censored for death)
100
80
60
40
20
0
%
0 1 2 3 4 5 6 7 8 9 10
years
living donor
deceased donor


kidney - graft survival
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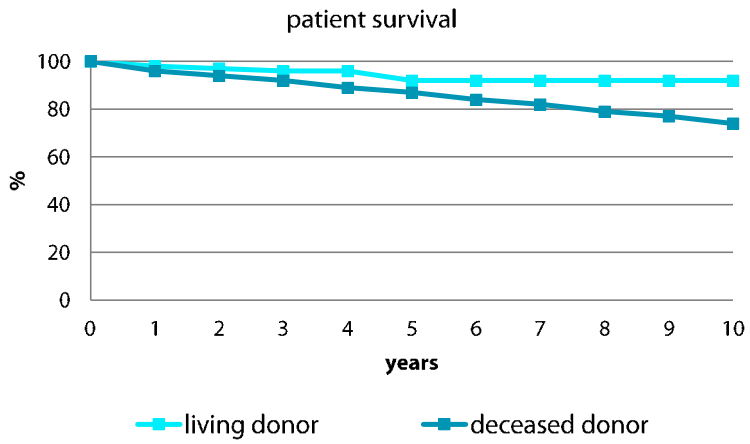
patient survival
100
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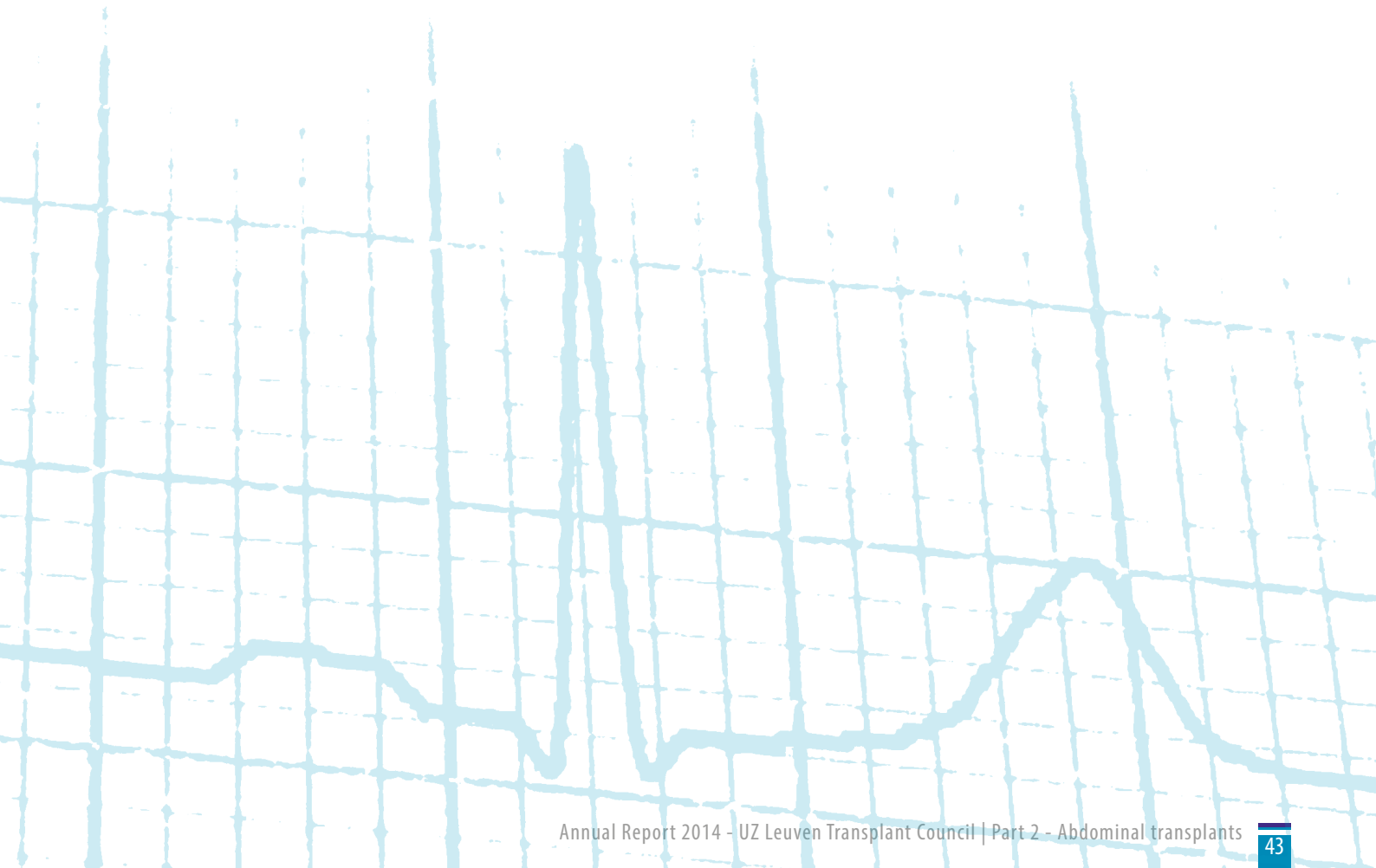

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Kidney and kidney/pancreas transplant care programme

On Thursday 6 March 2014 the University Hospitals Leuven celebrated its 4,000th kidney transplant. This milestone allowed us to proudly look back on more than 50 years of experience in kidney transplantation but also to critically reflect on the future. The successes in organ transplantation have expanded the boundaries of possibilities to help more patients with a diversity of complex medical conditions. The progressive increase in mean organ recipient age is just a partial reflection of this evolution. Patients with a severe pre-existing cardiovascular, urological and even oncological pathology form an important part of the 170 formal pre-transplantation evaluations that take place in the University Hospitals Leuven each year. The numbers of combined transplantations (kidney-liver, kidney-pancreas, kidney-heart/lung) illustrate in a different way the increasing complexity of organ transplantation. Also from an immunological standpoint the challenges are numerous – as reflected by the number of re-transplantations, the number of highly-sensitised patients, the importance of donor-specific antibodies and the need for ABO-incompatible transplantations and desensitisation programs. In addition, the persistent organ shortage and the shift in type of donors to DCD and ECD donors becomes more apparent as illustrated by our own data. The future challenges include the search for, and the development of, novel efficient therapeutic molecules that not only allow us to prolong intrinsic graft survival but also to provide long-term safety for our patients and enable us to counter immunological and non-immunological injuries to the graft. The latter requires prolonged and high-technological clinical and translational research in partnership with national and international transplant centres and pharmaceutical partners. Concurrently, optimisation of the different donor organ types in the initial phase of transplantation plays a central role in ensuring an optimal start for the graft. Finally, current organ allocation rules are reviewed and evaluated for achieving the optimal combination of waiting time, recipient age, donor age and organ quality to create circumstances for obtaining maximal estimated graft survival.

Even though the counter showed 4,098 kidney transplantations on 31 December 2014, the challenges are bigger and more diverse than ever!

Transplant activities

In 2014, 127 kidney transplants were performed: 108 patients underwent their first transplant, and 17 patients underwent a second transplant. In addition, one patient received a third transplant and one patient even received a fourth transplant (figure 2.18).

There was a slight decline in the number of transplants performed with kidneys from living donors . In 2011, nine patients received a kidney from a living donor. In 2012 the amount increased to eleven and in 2013 it increased even to fifteen patients. In 2014, fourteen patients were transplanted with a kidney from a living donor.

The number of transplants performed with kidneys from non-heart-beating donors (or DCD donors, donation after circulatory death) also remained stable in 2014. Currently almost one in five kidney transplants received a kidney from a DCD donor.

FIGURE 2.18 | evolution amount of kidney transplants 1992 - 2014

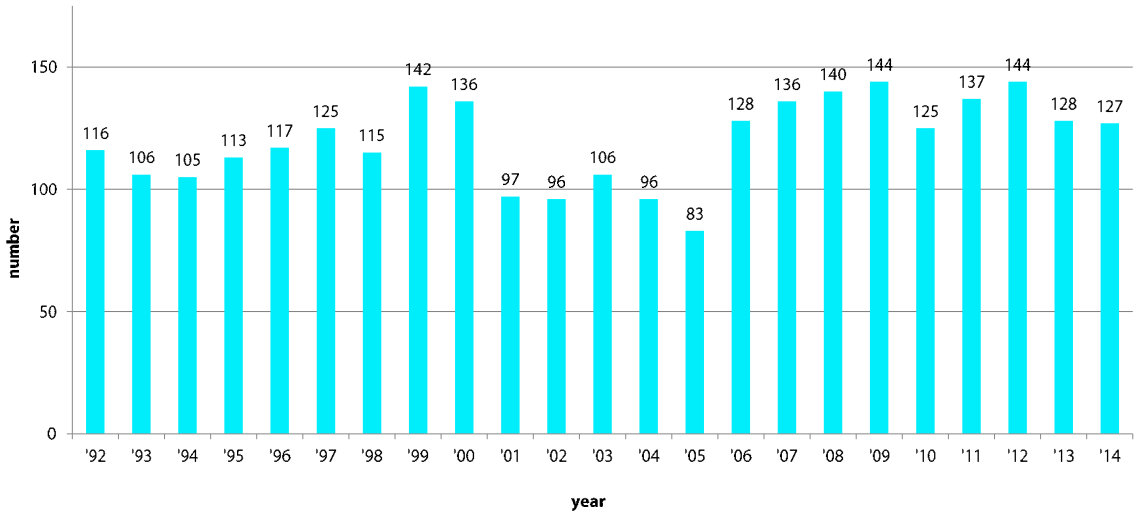
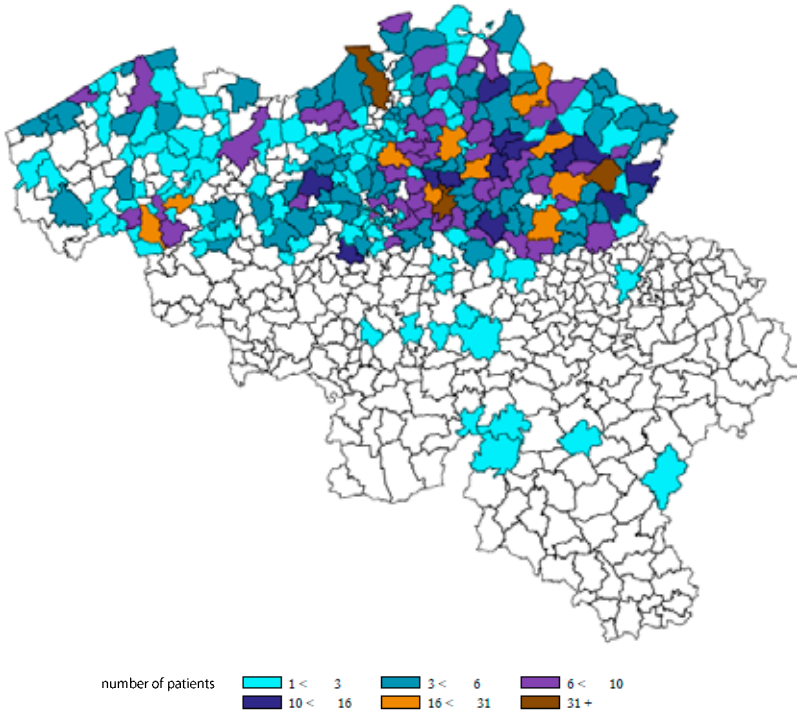


FIGURE 2.19 | geographical origin kidney recipients (1963 - 2014)

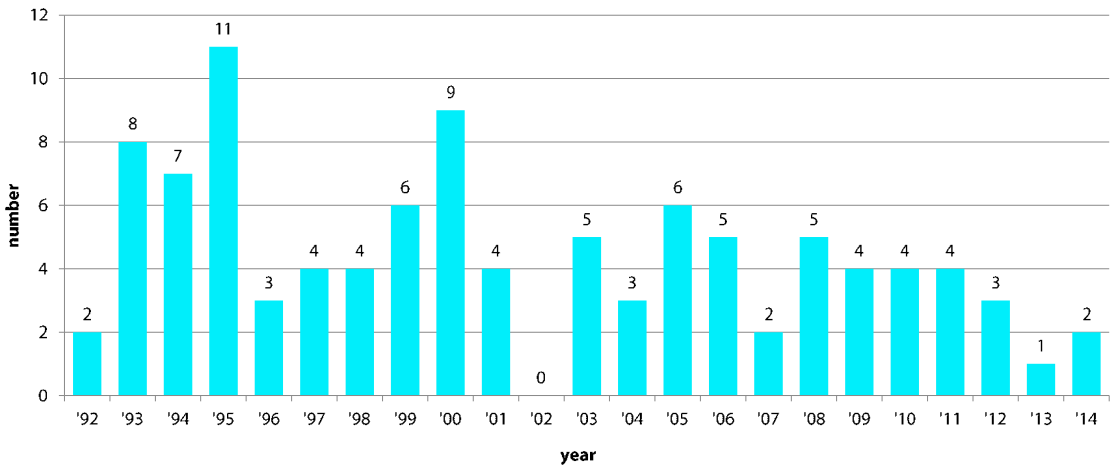


The number of combined transplants returned to the level of previous years. In 2013, only six combined transplants were performed, but in 2014, this number increased back to fifteen. There were ten combined kidney-liver transplants, two kidney-pancreas transplants, one combined kidney-heart transplant and two intestinal transplants with an additional kidney *(table 2.10)*.

TABLE 2.10 | number of combined kidney transplants performed in 2014

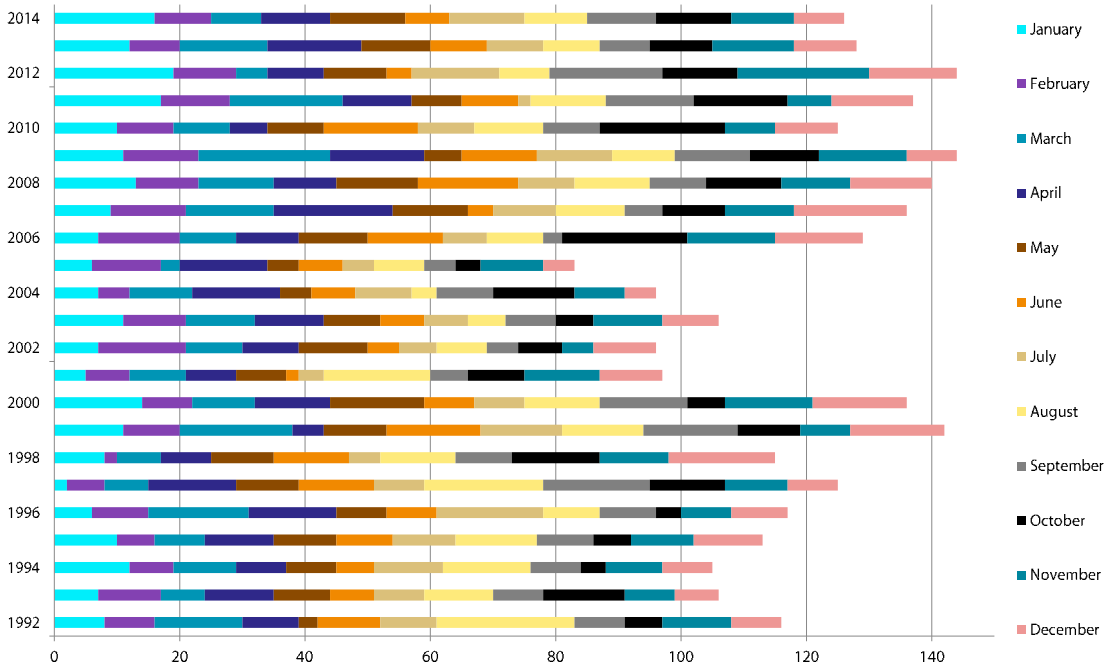
	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
Kidney + liver	1	5	4	5	3	9	8	11	4	**10**
Kidney + heart	-	1	1	-	-	3	1	-	1	**1**
Kidney + lung	-	2	-	-	-	-	-	4	-	**-**
Kidney + pancreas	6	5	2	5	4	4	4	3	1	**2**
Kidney + intestine	-	-	1	-	-	-	1	-	-	**2**
Total	**7**	**13**	**8**	**10**	**7**	**16**	**14**	**18**	**6**	**15**

FIGURE 2.20 | number of combined kidney-pancreas transplants between 1992 and 2014



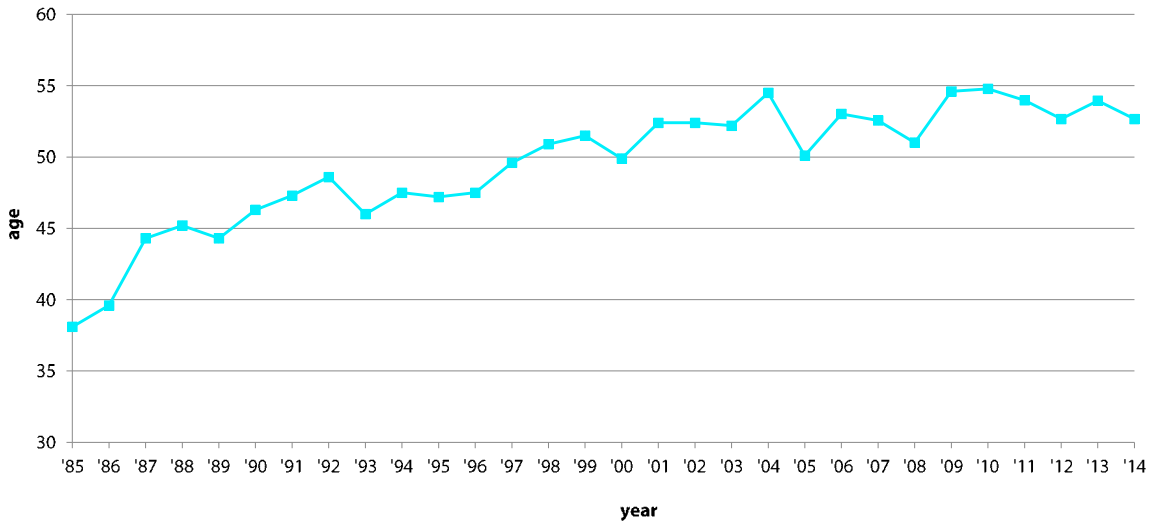
The transplant activity in 2014 was spread evenly. The largest number of transplants (16) was carried out in January. There was less activity in June when only seven transplants were performed *(figure 2.21)*.

FIGURE 2.21 | evolution of the monthly number of kidney transplants over the past years



The average age of patients at the time of the transplant has stabilised in recent years. Last year, the average age was 53.95 and now we see an average age of 52.67 years at the time of transplant *(figure 2.22)*.

FIGURE 2.22 | evolution of the average receptor age since 1985



Patient survival results

Figure 2.23 shows the actuarial patient survival rate before and after 1983 (the year in which cyclosporin was introduced). Initially the patient survival rate is significantly better in the group which received a transplant after the introduction of cyclosporin (CsA), but as of the 12th year after transplant both curves appear to coincide (Wilcoxon p=0.006 – log rank n.s.).
The actuarial patient survival rate after 1998 (the year in which 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 from the other transplant patient groups.

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

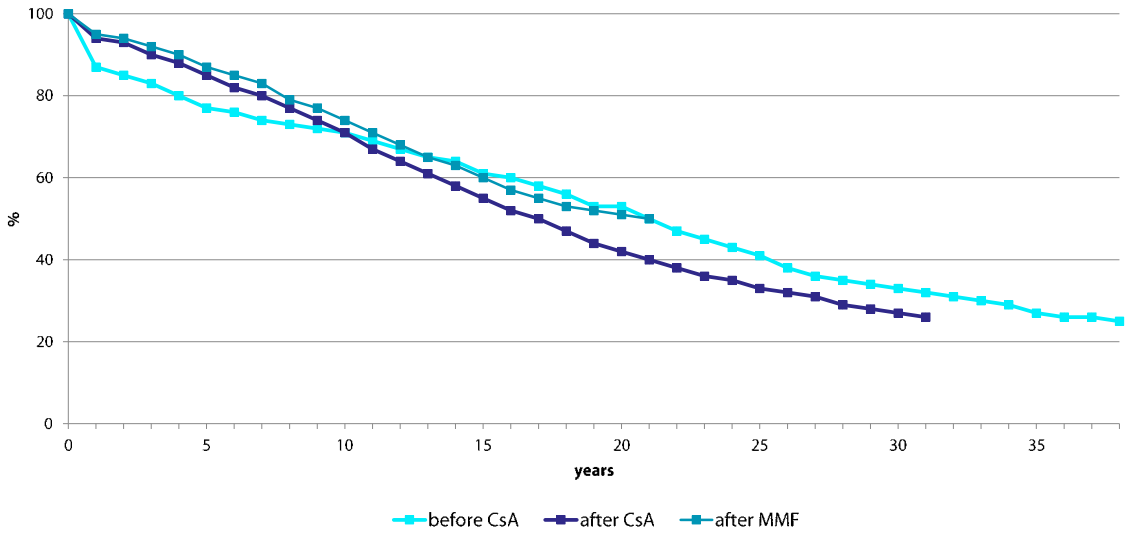
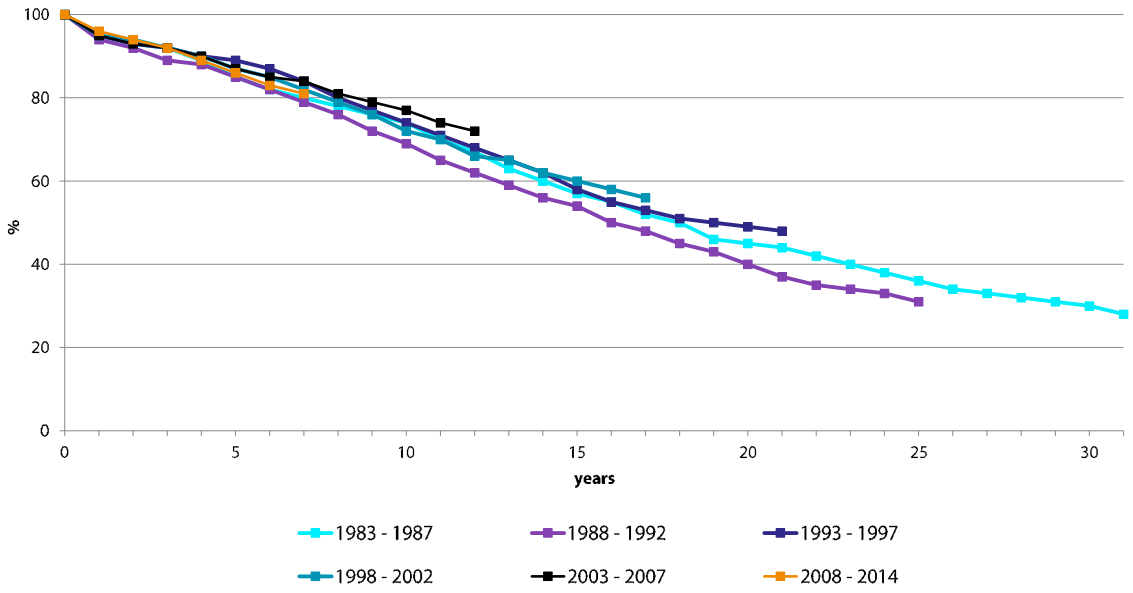


Figure 2.24 shows the analysis of the actuarial patient survival rate since 1983, calculated on the basis of consecutive 5 year periods. This demonstrates that after 1992 the five-year survival rate increased. This positive result for the five-year survival rate for groups transplanted after 2003 continues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

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



The effect of the recipients' 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 recipients' age: 76% after 25 years in the group aged below 30 and 43% in the group aged between 30 and 49. It's understandable that 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

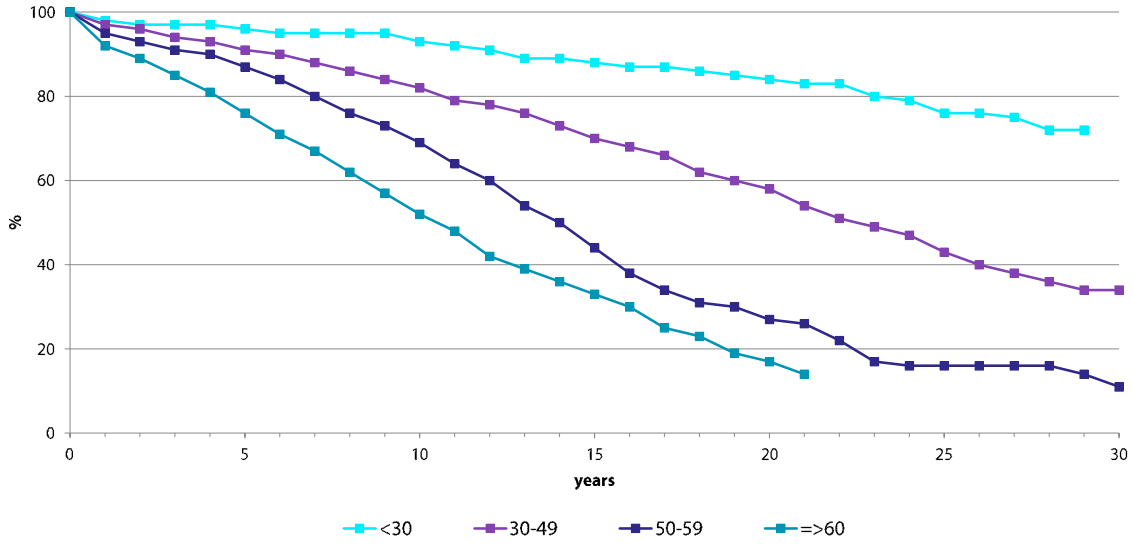
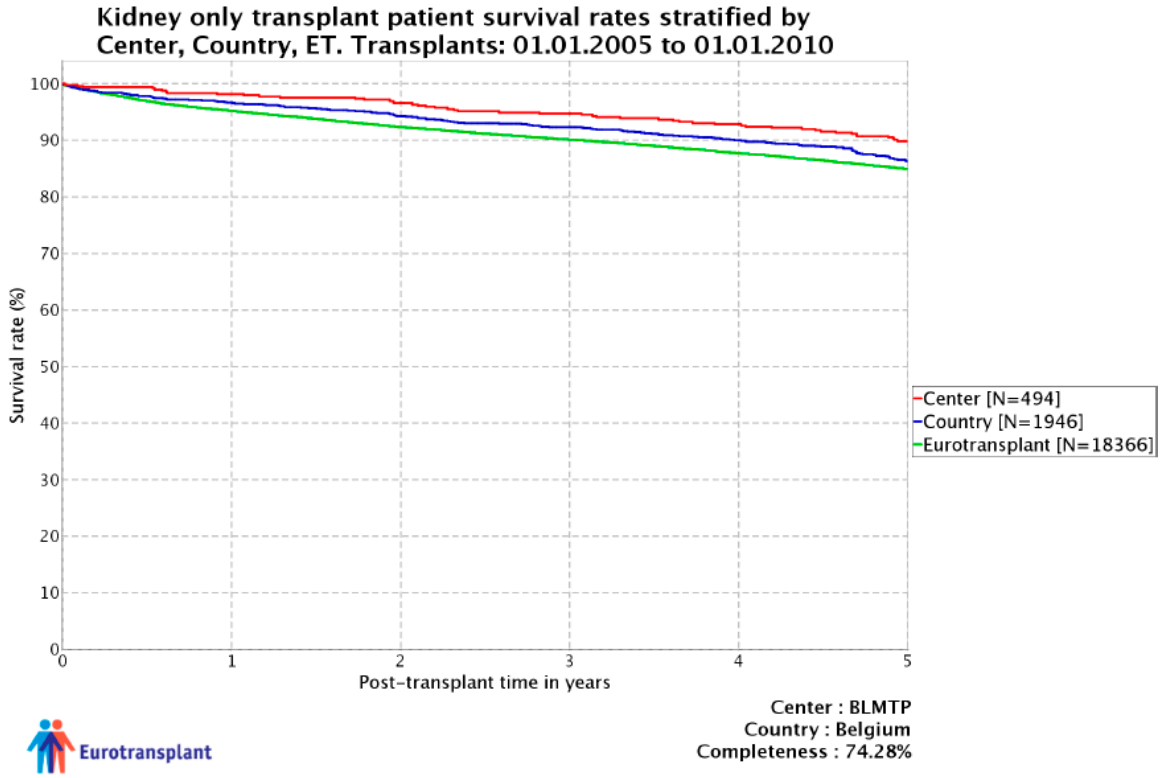


Figure 2.26 shows the Eurotranplant data (period 2005 - 2010) for patient survival (up to five years post-operatively) in our kidney transplant programme compared to the global experience within the entire Eurotransplant region and the pooled results from all Belgian centres.

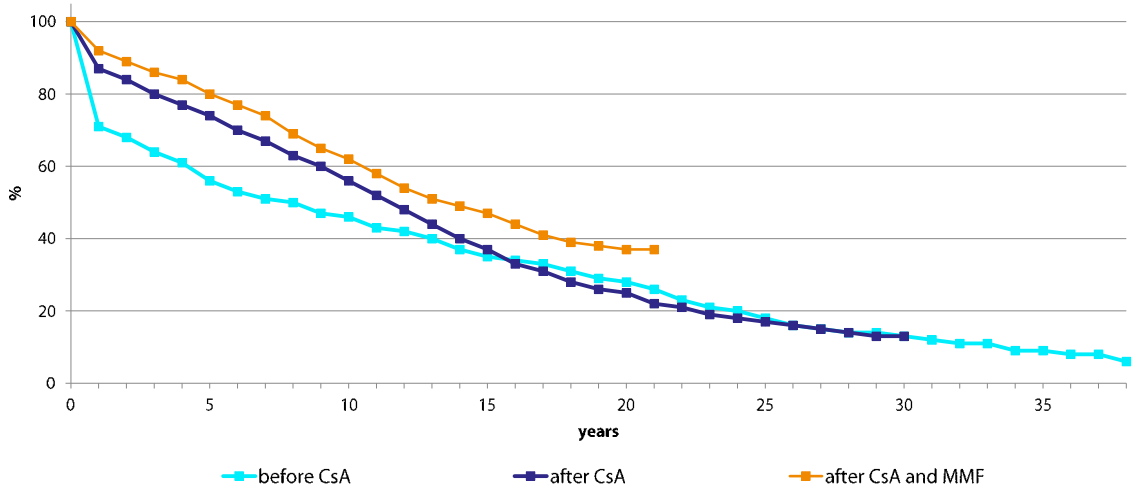
FIGURE 2.26 | five-year patient survival rate (2005 - 2010) kidney only transplants. University Hospitals Leuven compared to Eurotransplant and Belgium (the Belgian figures also include the results for the University Hospitals Leuven). Source: Eurotransplant.



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 coincide almost perfectly. What remains notable, however, is that the curve for patients transplanted after the introduction of Mycophenolate Mofetil is considerably higher (in 20 years 37% as opposed to 25% and 28%).

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 (nineteen years after the transplant 67%, 55%, 51% respectively) *(figure 2.28)*.

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

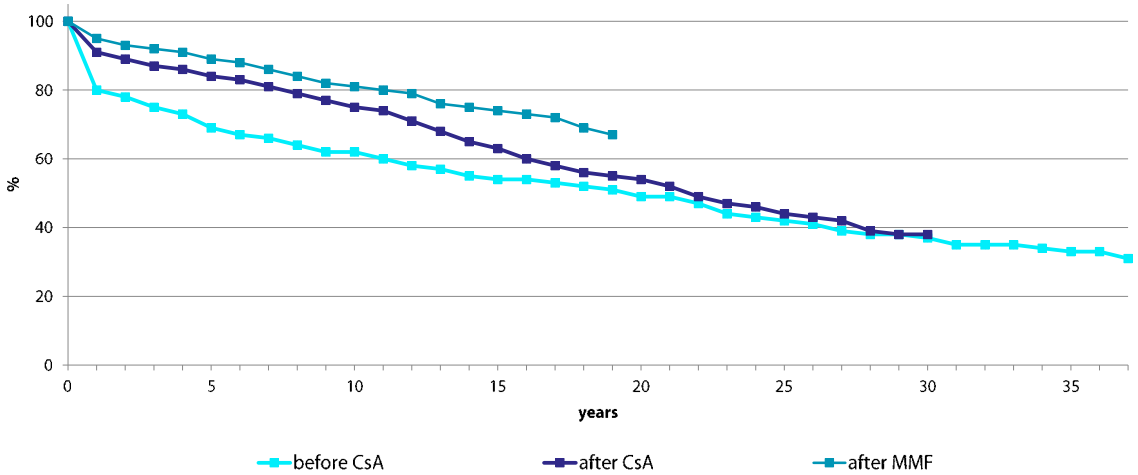
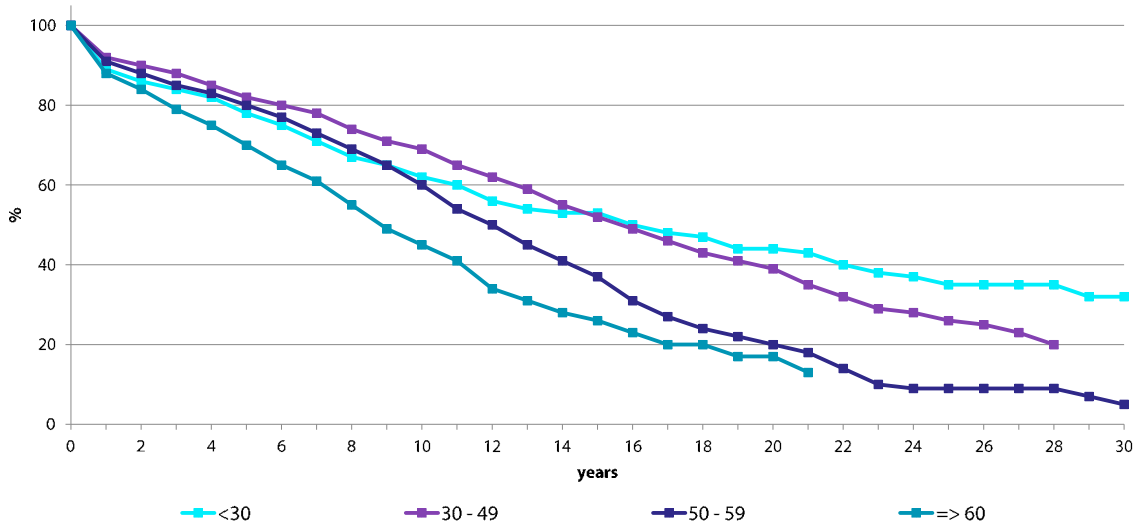


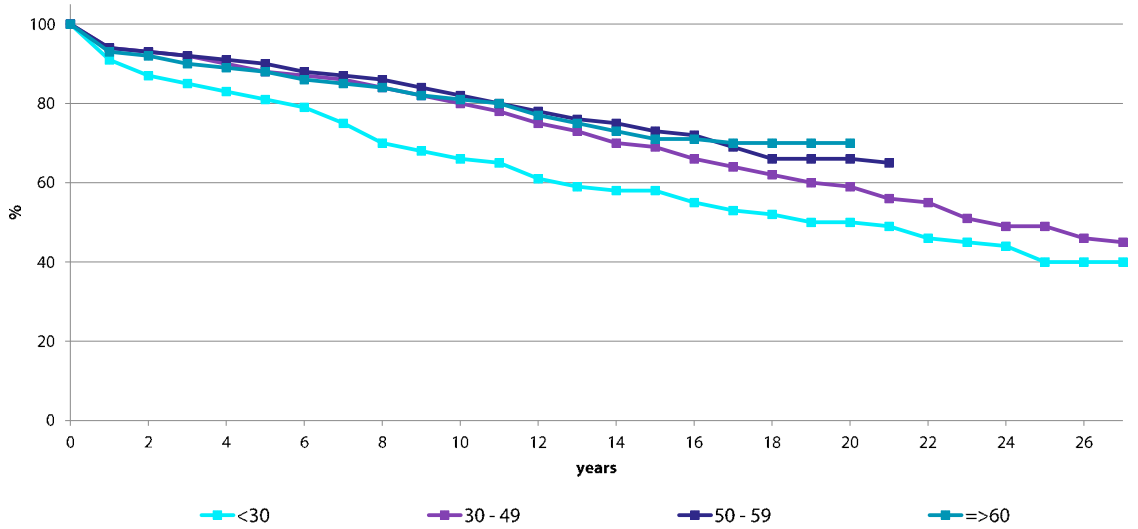
Figure 2.29 shows the actuarial kidney survival rate. Taking into account the recipients' age there are notably large differences between younger and older recipients.

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



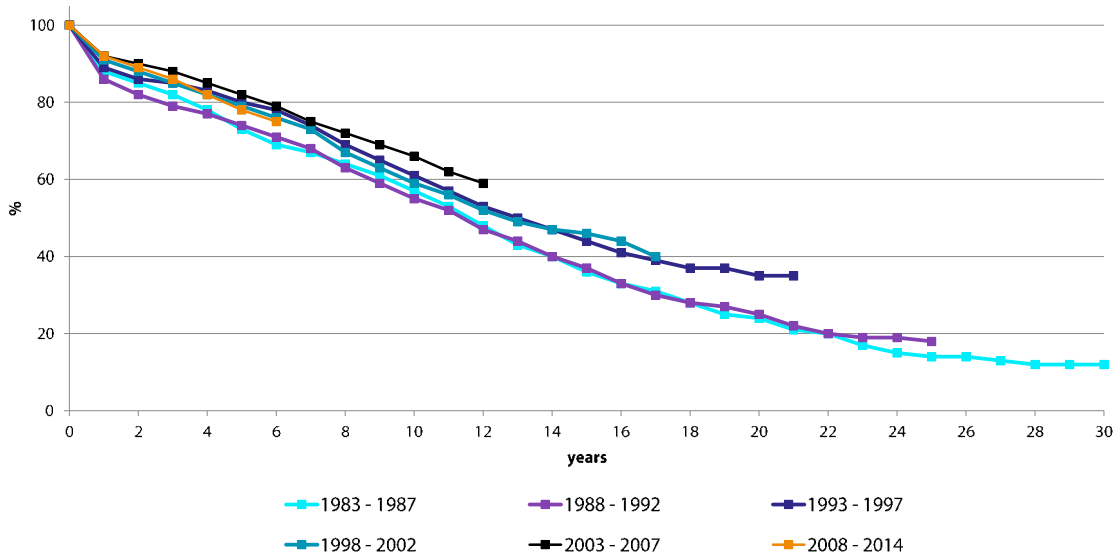
If the recipient's death is also taken into account (censored for death), it is safe to say that the loss of the transplanted kidney in the >60 year-old recipient category is largely due to the recipient's death. Consequently, the older age category has a better intrinsic kidney survival rate than the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

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



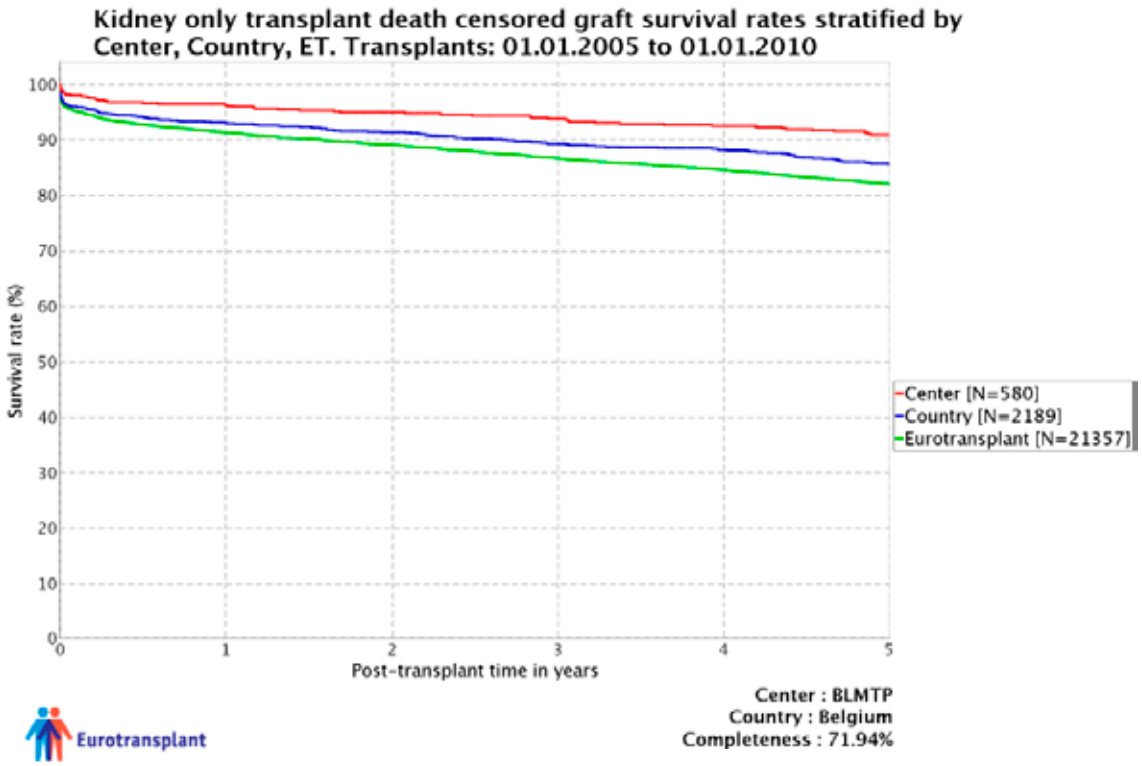
Kidney survival has continued to improve in recent years and the downward percentage based trend is also decreasing. The five-year survival rate for patients who received a transplant in the period between 1983 and 1987 was 73%. For patients who received a transplant in the period after 2008 the five-year survival rate increases but in a more restricted extent than the cohort of patients transplanted between 2003 and 2007 *(figure 2.31)*.

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



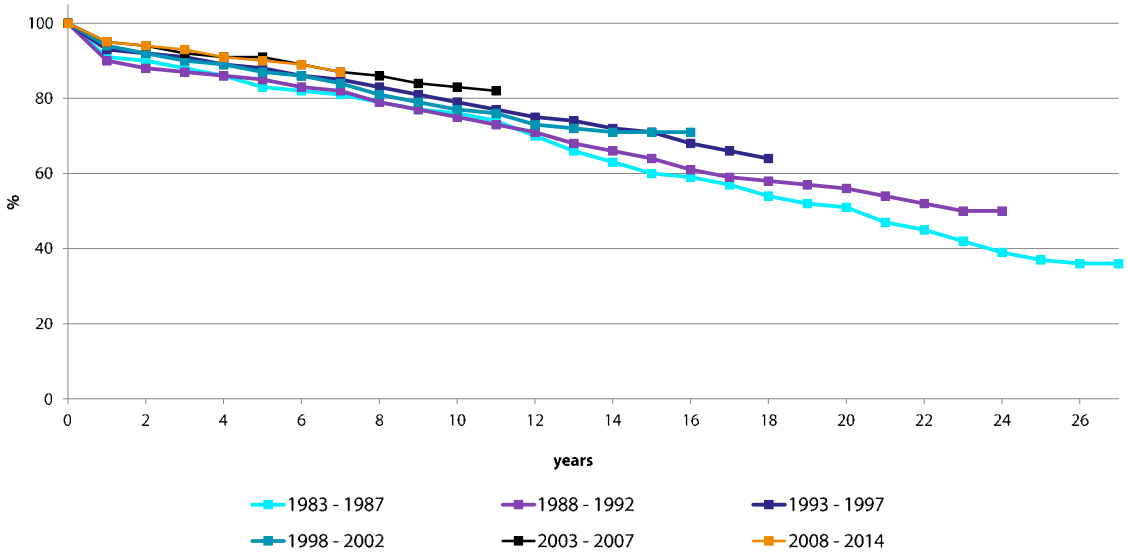
There is also a difference between the figures for the University Hospitals Leuven and those for Eurotransplant and Belgium for graft survival rate.

FIGURE 2.32 | five-year graft survival rate (2005 - 2010) (death censored) kidney only transplants, University Hospitals Leuven compared to Eurotransplant and Belgium (the Belgian figures also include the results for the University Hospitals 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 - 2014) is no less than 7% higher (90% as opposed to 83%).

FIGURE 2.33 | evolution of the actuarial kidney survival rate (censored for death) since 1983



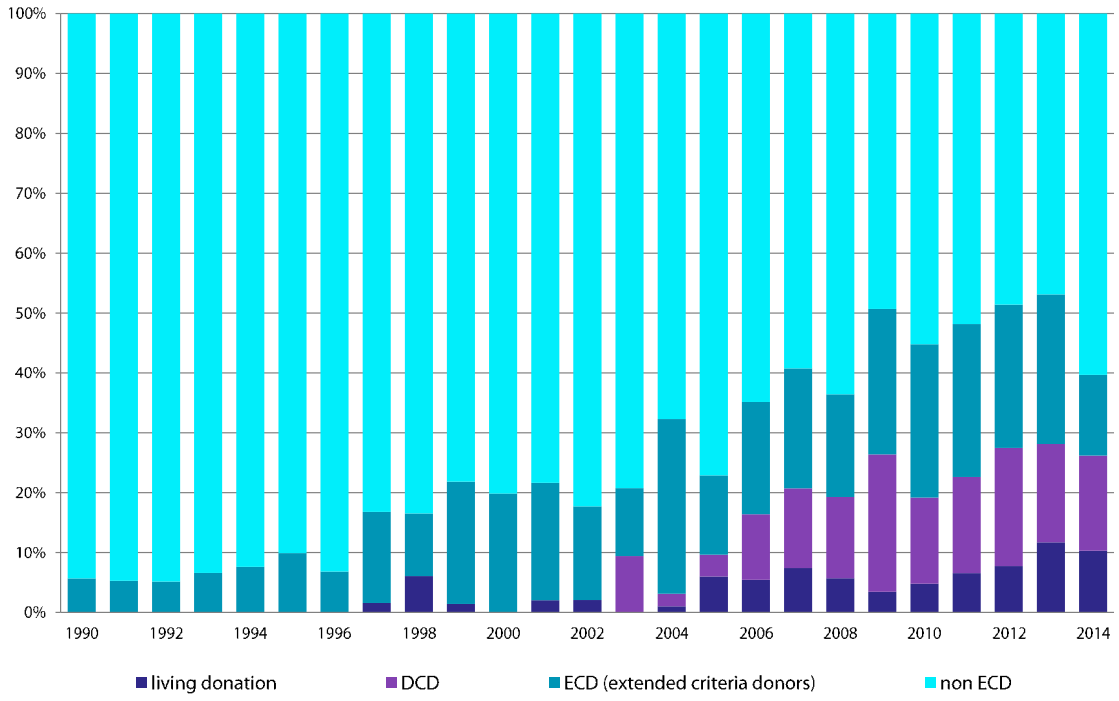
Donor type development

Since the early '90's there has been a downward trend in the number of suitable organs from deceased donors. Obviously the number of completed transplants initially followed this downward trend.

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.

It is remarkable that the past year much less kidneys were transplanted from ECD-donors, which, with a stable number of DCD-donors, the combined share of ECD- and DCD-donors LD fell below 50% in 2014.

FIGURE 2.34 | kidney transplant percentage on the basis of donor type 1990 - 2014



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

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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 took off on 1 September 1987. Since then 626 transplants were performed in 596 patients (status on 25 February 2015 – excluding heart/lung transplants). These patients originate from across Flanders (figure 3.1). Care providers who are currently involved in the heart transplant programme are listed alongside. Even a fairly extensive list fails to do justice to many colleagues and co-workers in cardiology, cardiac surgery and other disciplines, in primary care and in other hospitals, whose input – although less obvious – is by no means less important. Also the co-workers from the early days, at all levels and in all disciplines, have had a major input in the way the heart transplant programme currently operates.

HEART TRANSPLANTS

Transplant activities

In our centre the number of heart transplants has somewhat increased in recent years *(figure 3.2)*: on average there were 26 procedures per year over the past five years, which represents 30 to 40% of the total number of heart transplants in Belgium (with seven active heart transplant centres), and 50 to 60% of the heart transplant activity in Flanders. This trend deviates a little from the status quo in heart transplant numbers on a broader scale, nationally *(figure 3.3)* as well as in the Eurotransplant region and globally.

Over the past decade the waiting list has doubled in length, both locally *(figure 3.4)* and in the whole Eurotransplant region. The rate of increase however seems to have waned, and numbers have been fairly stable over the past 5 years. The median waiting time is seven to ten months *(figure 3.5)*, but with the help of the Eurotransplant 'high urgency' programme, we continue to provide a donor heart within a much shorter period of time in case of exceptional urgent need. Also, the use of mechanical circulatory support systems (VAD - ventricular assist device) as a bridge to transplantation has been a clinical reality for a number of years now. About half of the newly transplanted patients needed a 'heart pump' to bridge the waiting time *(figure 3.6)*.

The age of heart donors continues to rise *(figure 3.7)*. Over the past ten years three quarters of donor hearts were procured in collaborating Belgian hospitals *(figure 3.8)*.

FIGURE 3.1 | Geographic origin of our heart transplant patients

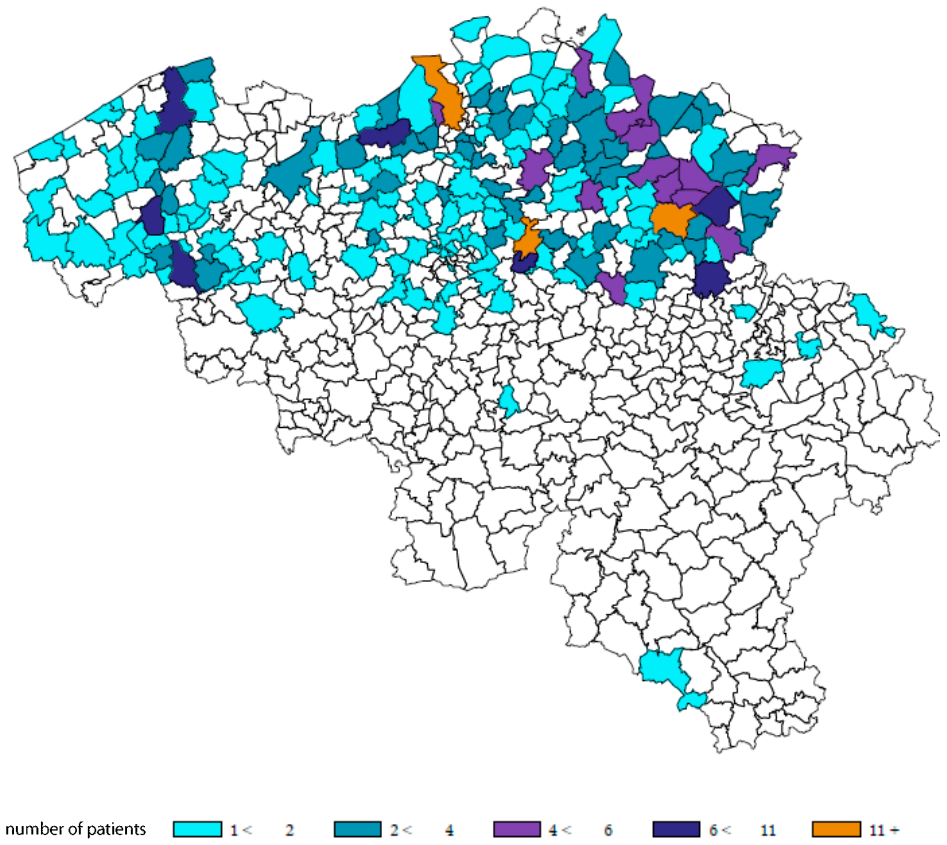


FIGURE 3.2 | number of heart transplants in the University Hospitals Leuven

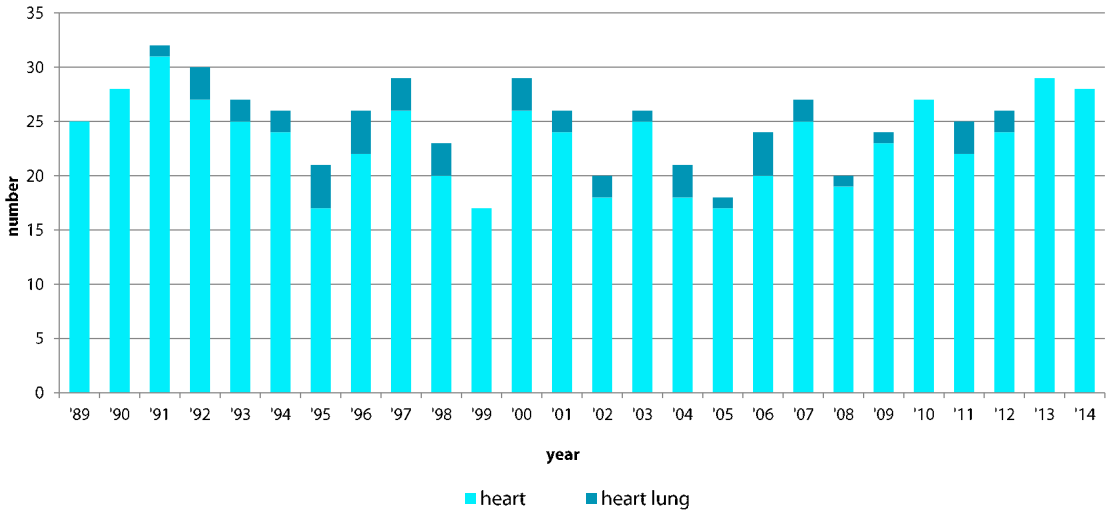


FIGURE 3.3 | number of heart transplants in Belgium

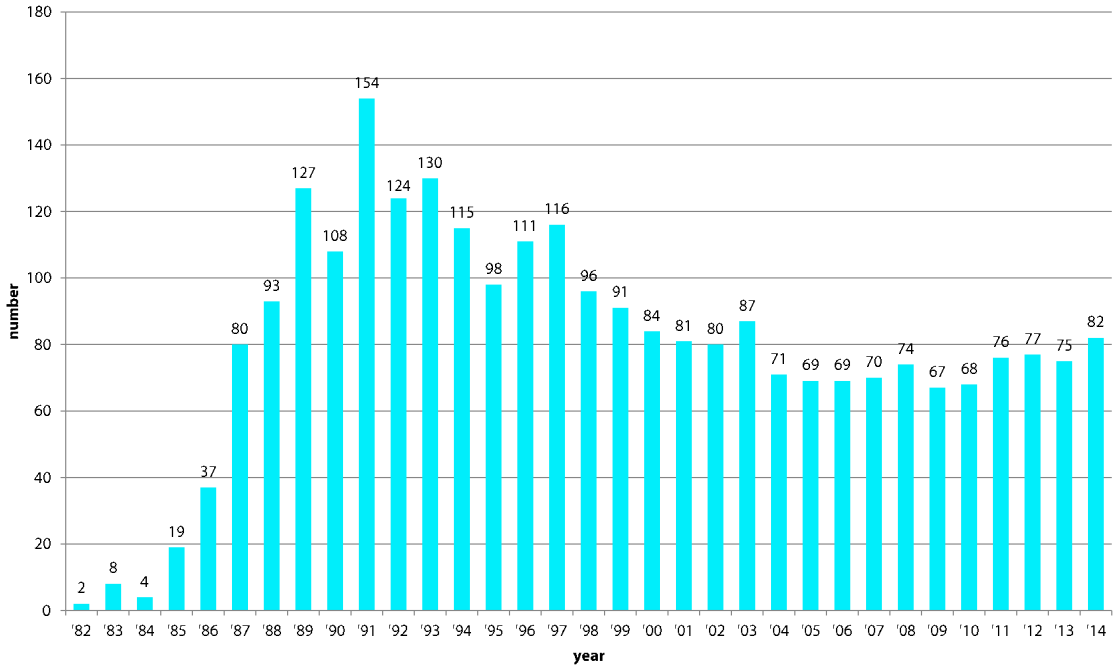


FIGURE 3.4 | waiting list at year's end

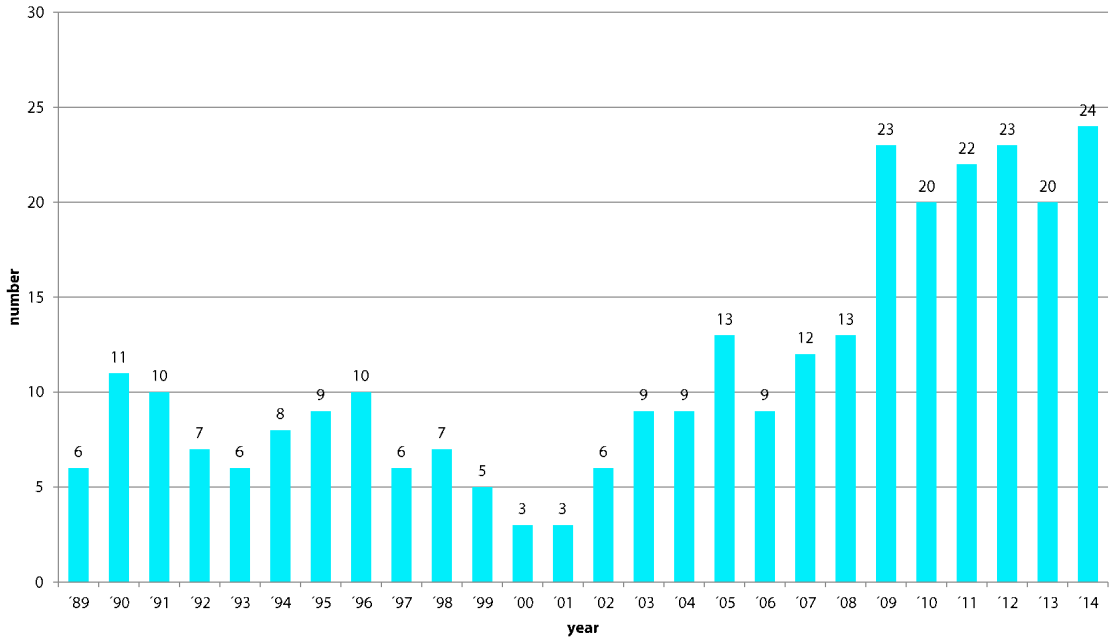


FIGURE 3.5 | median waiting time for heart transplants

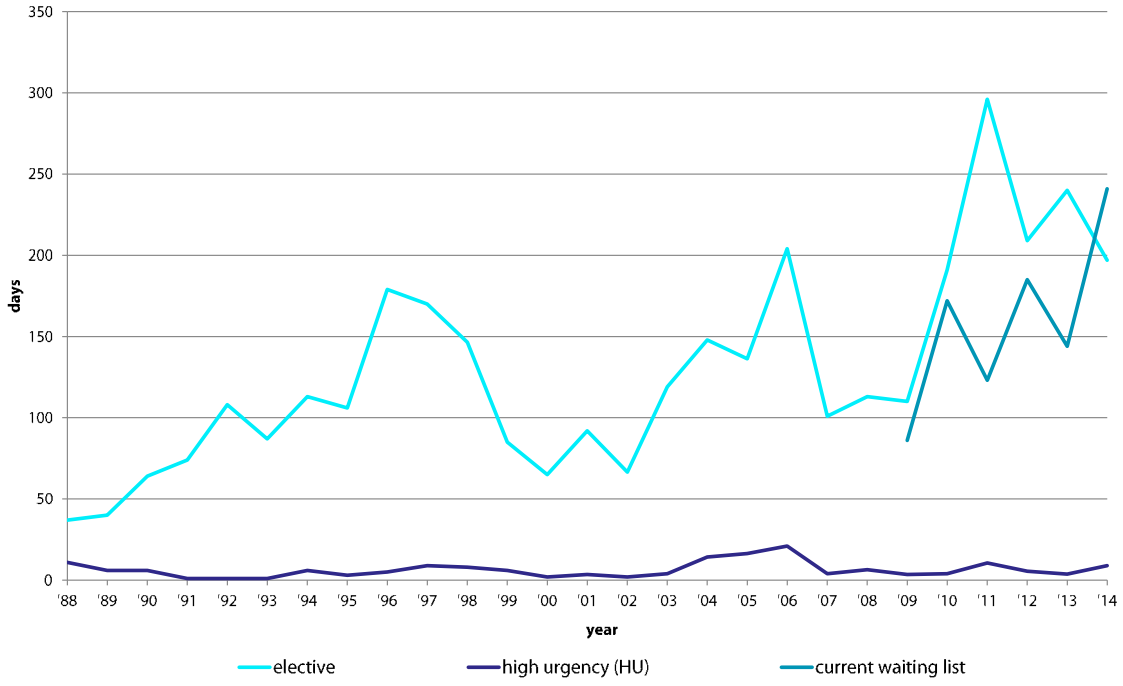


FIGURE 3.6 | percentage of patients who received a heart transplant involving mechanically supported circulation (bridge-to-transplant)

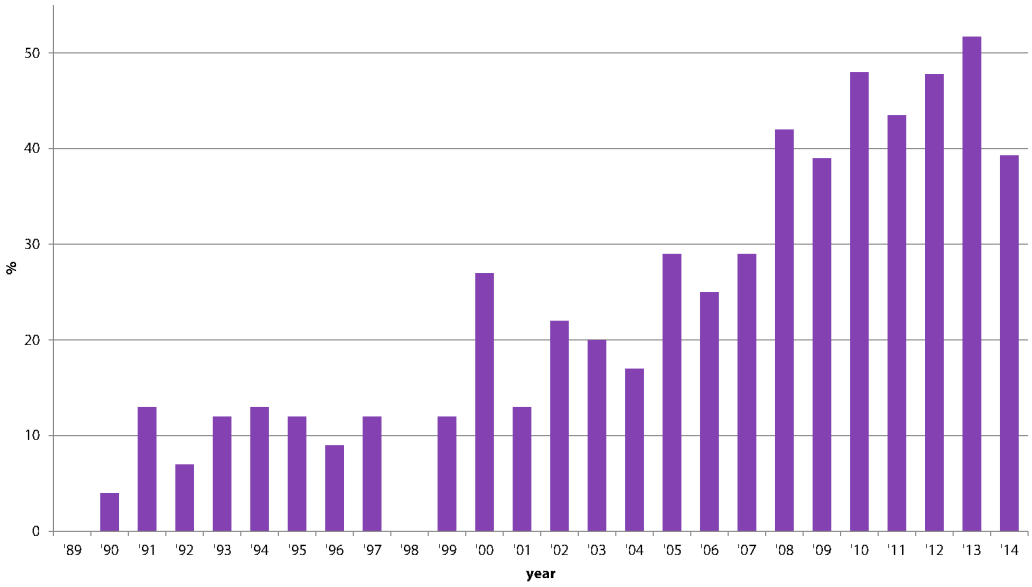


FIGURE 3.7 | average age of the heart donors

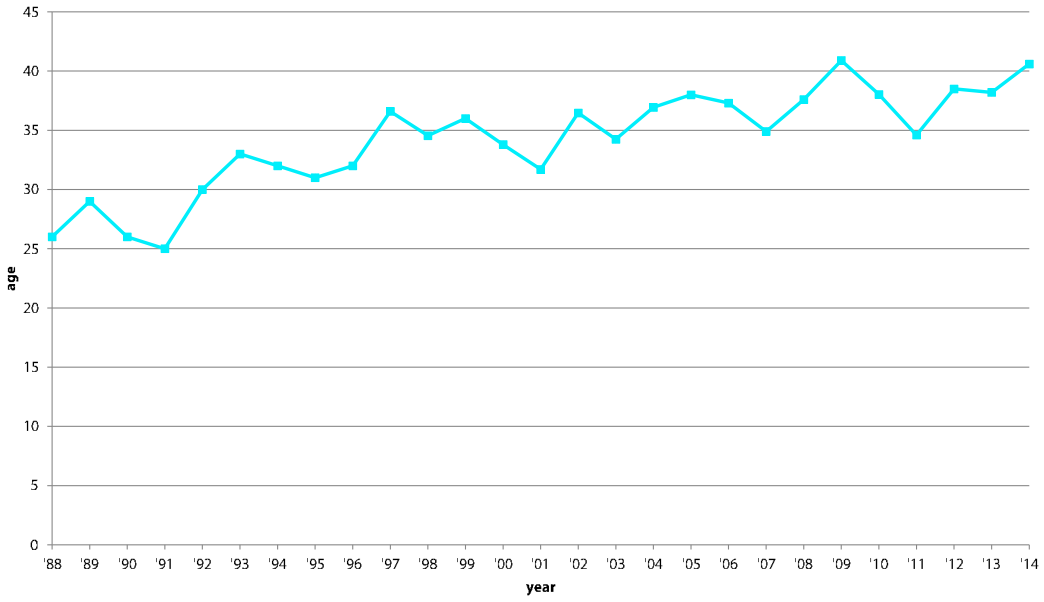


FIGURE 3.8 | donor heart origin

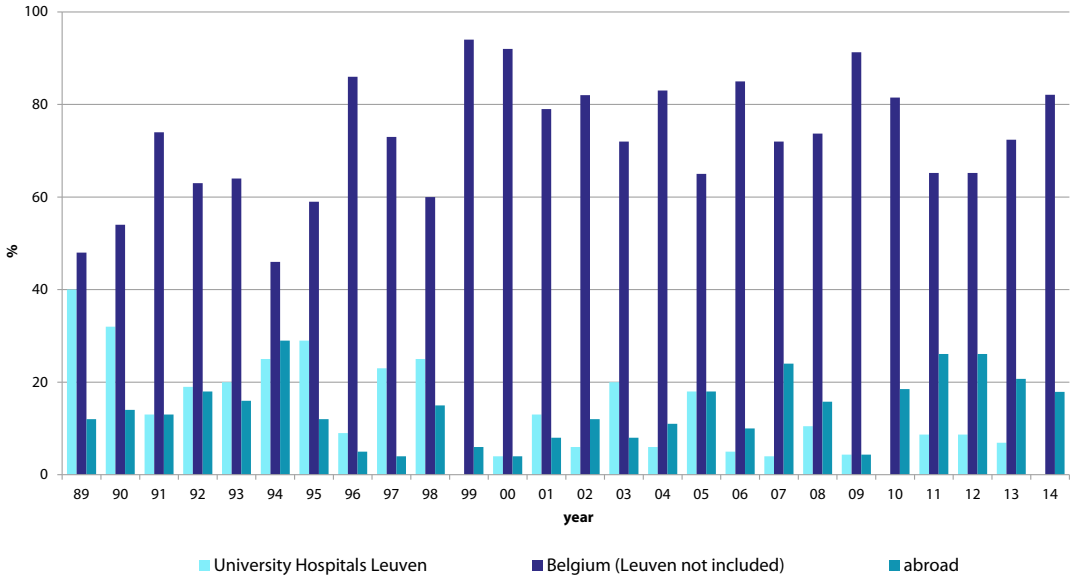
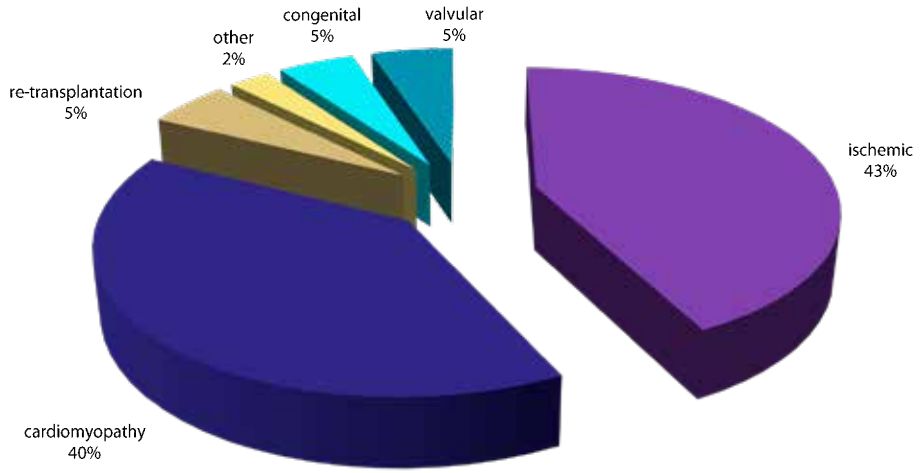


FIGURE 3.9 | heart disease resulting in transplantation



Transplant results

Patient survival was calculated for the total patient group until the end of 2014: 622 heart transplantations in 592 patients, including 22 combined heart/kidney transplants and 3 combined heart/liver transplants (this does not include the results of 47 heart/lung transplants which can be found in the section entitled '(Heart) Lung transplant care programme'). Figure 3.10 compares the actuarial patient survival rate in our programme with the aggregate results in the global Registry of the International Society for Heart and Lung Transplantation (ISHLT). The ten-year survival rate in Leuven currently stands at 75% as opposed to 52% in the ISHLT Registry.

The short- and medium-term results for consecutive periods have remained at a high level, despite increasing technical complexity and relaxation of both the recipient and donor criteria. This also seems to indicate that the use of mechanical circulatory support systems during the time on the waiting list has no detrimental effect on the outcome of the transplantation itself. Survival continues to improve over the long-term and in the most recent cohorts the five- and ten-year survival rates are 90 and 78% respectively *(figure 3.11)*.

At the end of 2014 there were 370 heart transplant patients in active follow-up *(figure 3.12)*, which resulted in 1,800 outpatients visits over the course of last year *(figure 3.13)*.

FIGURE 3.10 | patient survival

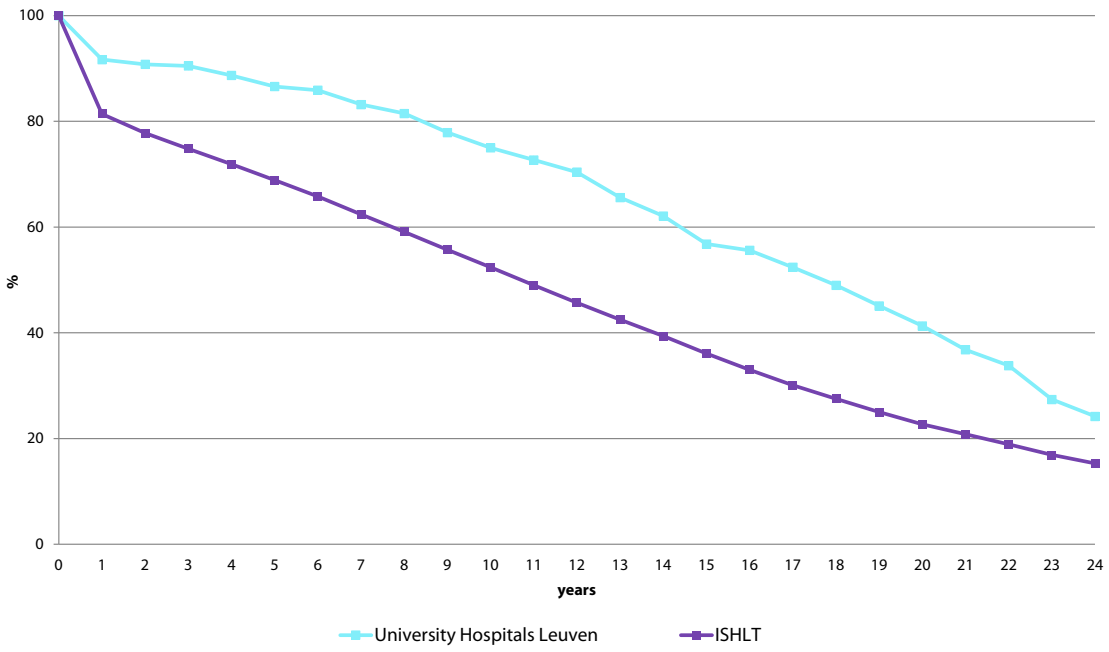


FIGURE 3.11 | patient survival in successive eras

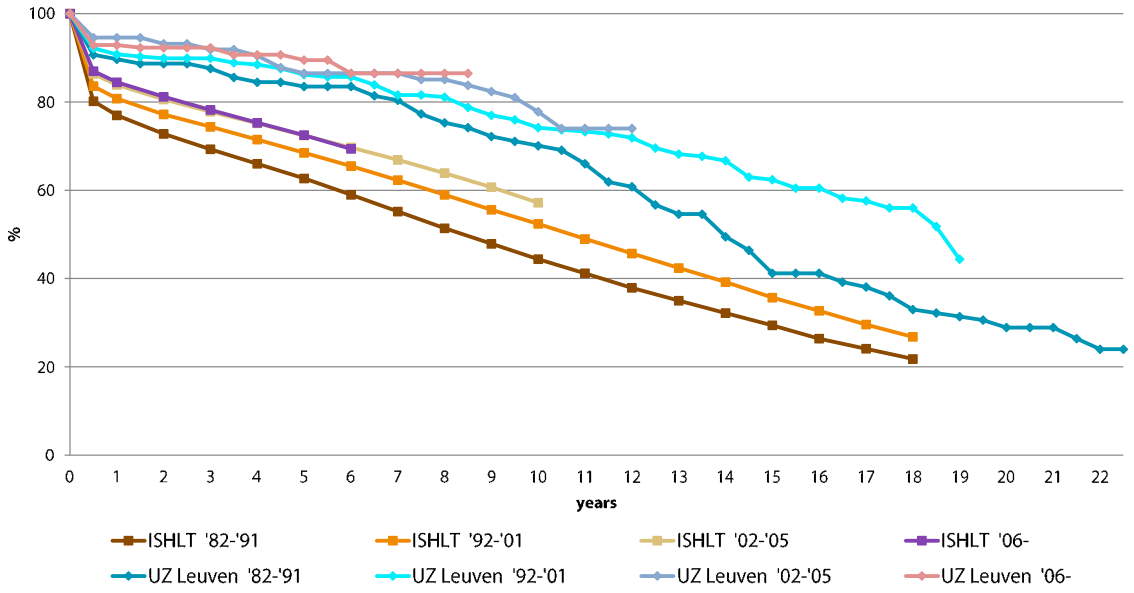


FIGURE 3.12 | number of patients in active follow-up

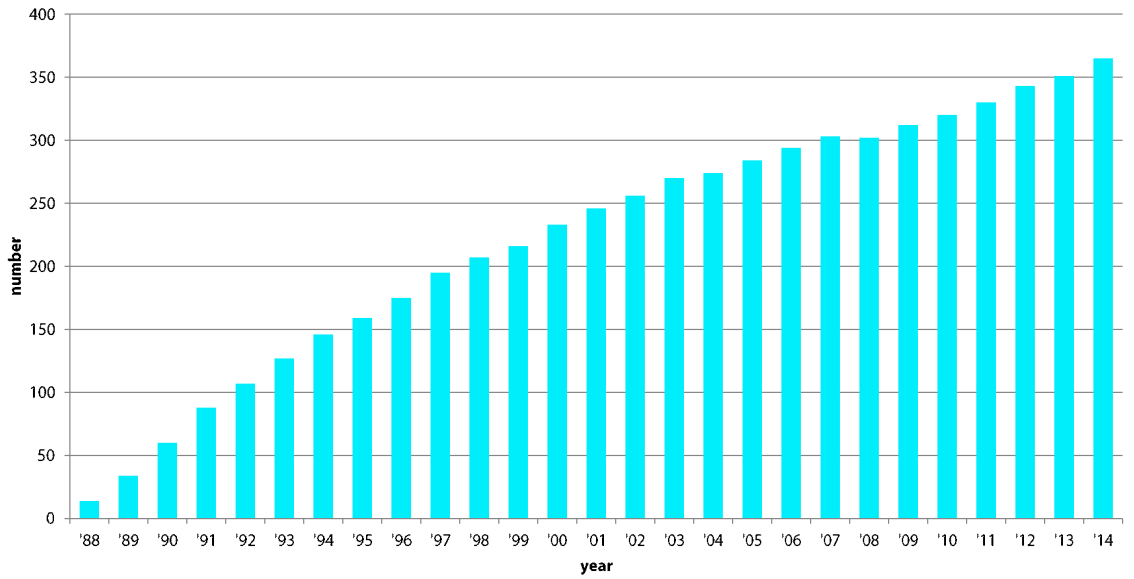
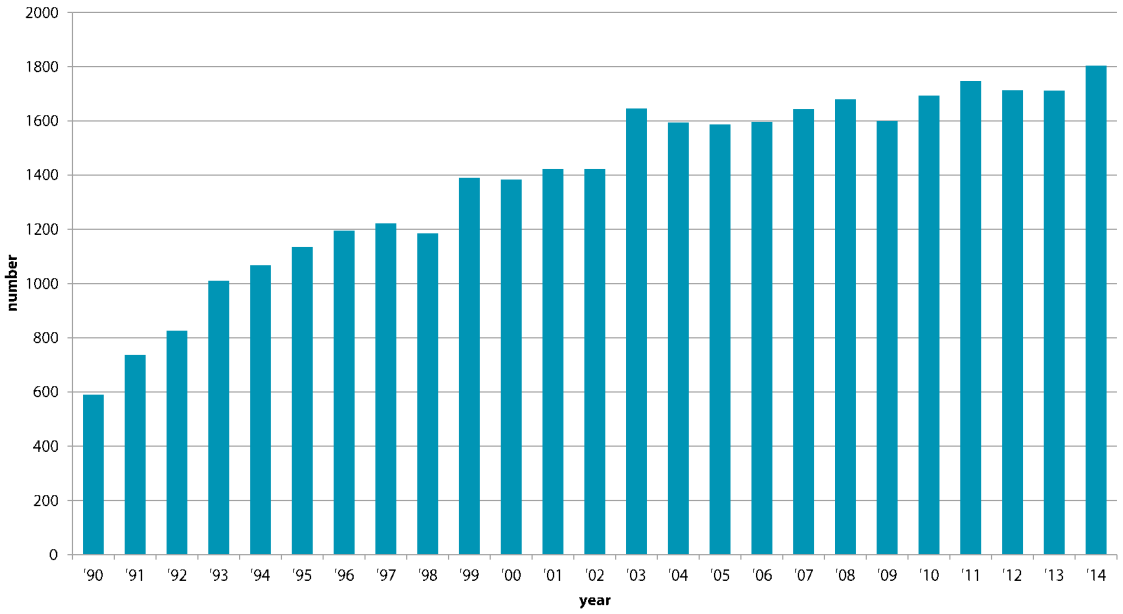


FIGURE 3.13 | number of outpatient visits



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(Heart) lung transplant care programme

The Leuven lung and heart-lung transplant programme was initiated in 1991. During the last years, we perform a mean of 58 procedures per year, which makes Leuven the third largest centre in Europe (after Hannover and Vienna). In Belgium, approximately 110 (heart)-lung transplantations are performed annually. With 58 procedures per year, Leuven is the biggest centre in Belgium. The most important indications for lung transplantation are COPD, pulmonary fibrosis, cystic fibrosis and pulmonary arterial hypertension. Over the past years there is a steadily growth in the number of transplantations performed for pulmonary fibrosis, which reflects the increasing referral rate for this condition. The five-year survival is remarkably better compared to the ISHLT registry database (77% versus 55%). This can be explained by the growing experience of our team, but also by the shift from single to a standard double lung transplantation, resulting in a superior survival rate.

(HEART-)LUNG TRANSPLANTS

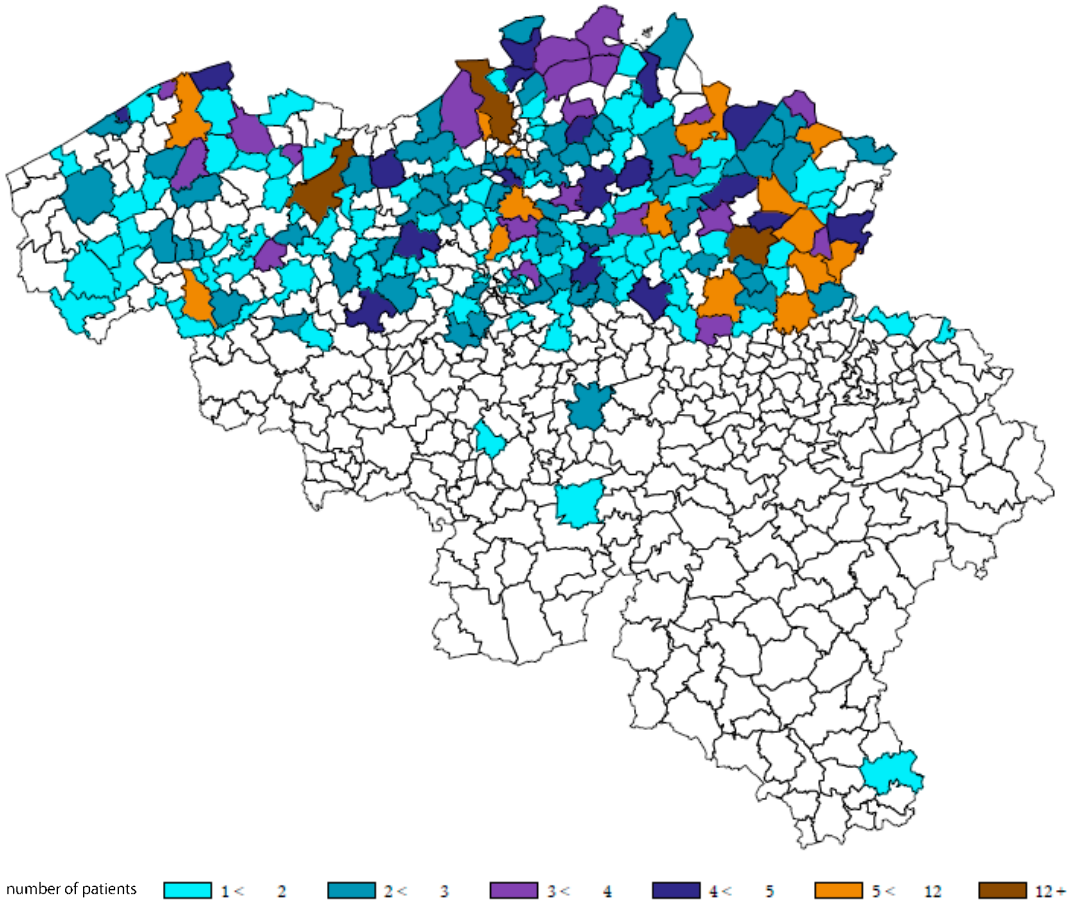
Transplant activities

With 58 lung transplantations in 2014, the number remains comparable to the year 2013. Only double-lung and no heart-lung transplantations were performed.

TABLE 3.1 | number of lung transplantations in the University Hospitals Leuven (1995 - 2014)

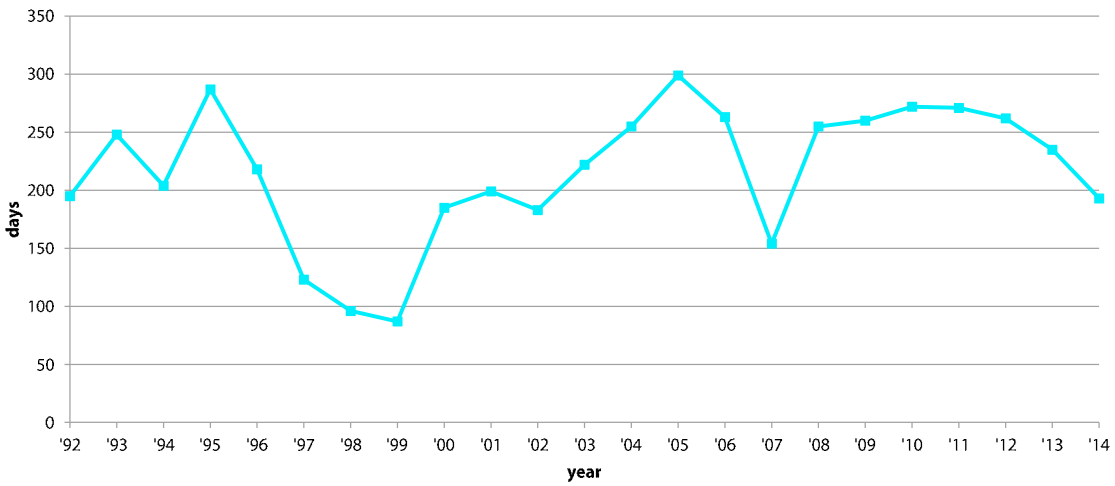
	'95	'96	'97	'98	'99	'00	'01	'02	'03	'04	'05	'06	'07	'08	'09	'10	'11	'12	'13	'14
Heart-lung	4	4	3	3	-	3	2	2	1	3	1	4	2	1	1	-	3	2	-	-
Unilateral	7	5	6	2	8	4	10	10	15	14	9	19	7	8	4	7	1	-	-	-
Bilateral	1	3	4	8	4	13	20	21	27	22	29	34	44	40	42	51	58	79	59	**58**
Total	12	12	13	13	12	20	32	33	43	39	39	57	53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

FIGURE 3.14 | geographic origin of the (heart) lung transplant patients



The mean waiting time in 2014 further decreased to 193 days (variation between 4 – 871 days), compared to 235 days in 2013. Mortality on the waiting list remains low (<5%).

FIGURE 3.15 | mean waiting time from 1992 on



The indications for lung transplantation remain identical and are shown in figure 3.16. The most current indications are COPD/emphysema, pulmonary fibrosis and cystic fibrosis. There is a progressive increase in the number of patients with pulmonary fibrosis, mainly due to the increase in referrals for idioparthic pulmonary fibrosis (IPF). In 2014, 3 redo lung transplantations were performed for chronic rejection (5%).

FIGURE 3.16 | Indications for lung transplantation in 2014

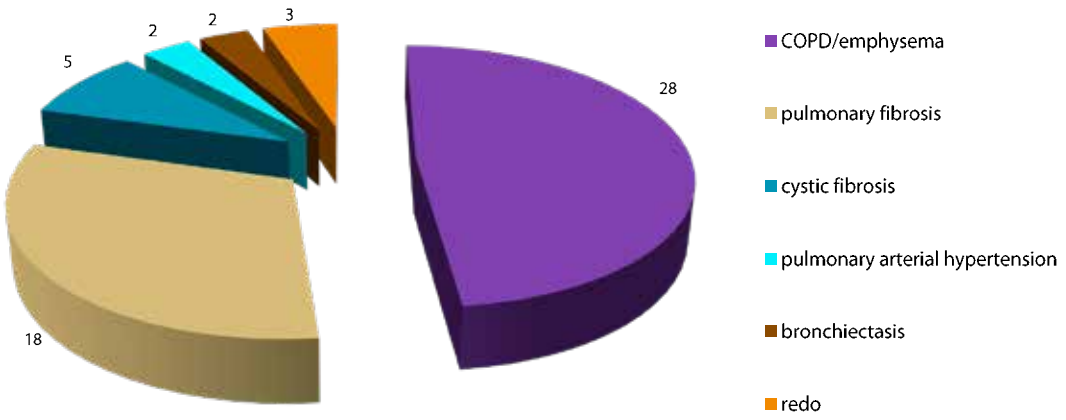
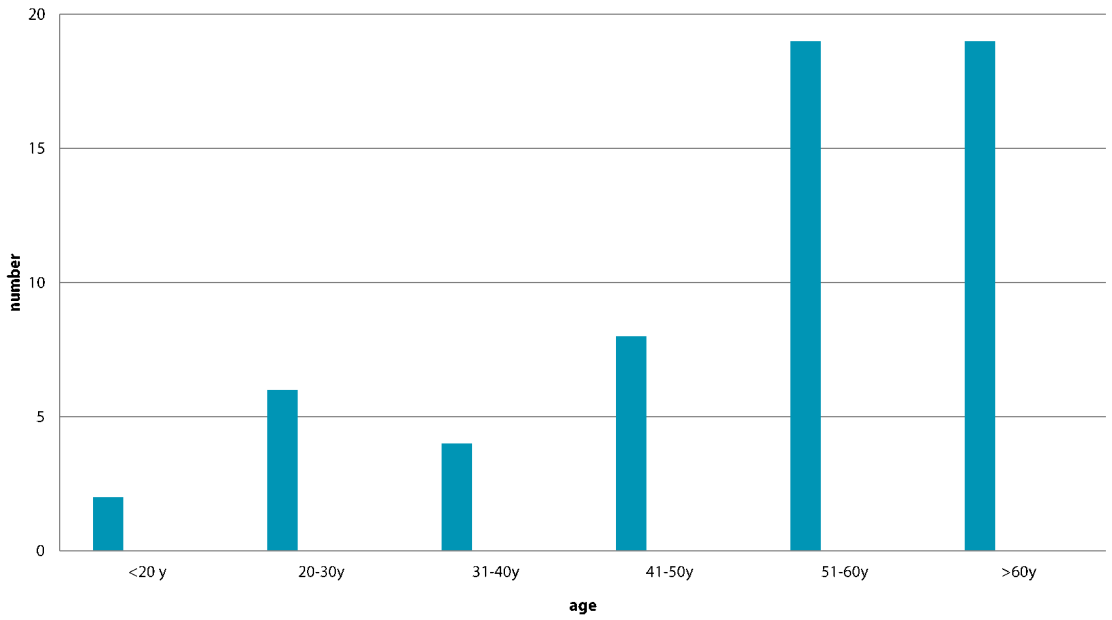


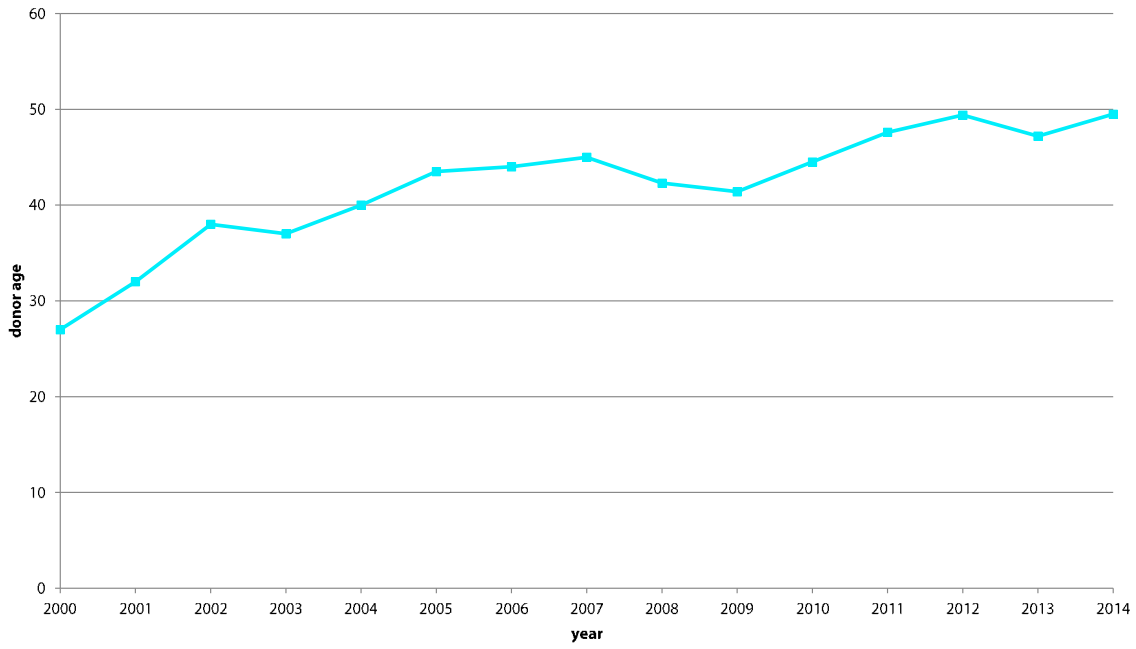
Figure 3.17 gives an overview of the receptor age, which again remains comparable to previous years, and reflects the most common transplant indications: emphysema and pulmonary fibrosis.

FIGURE 3.17 | distribution of receptor age in 2014



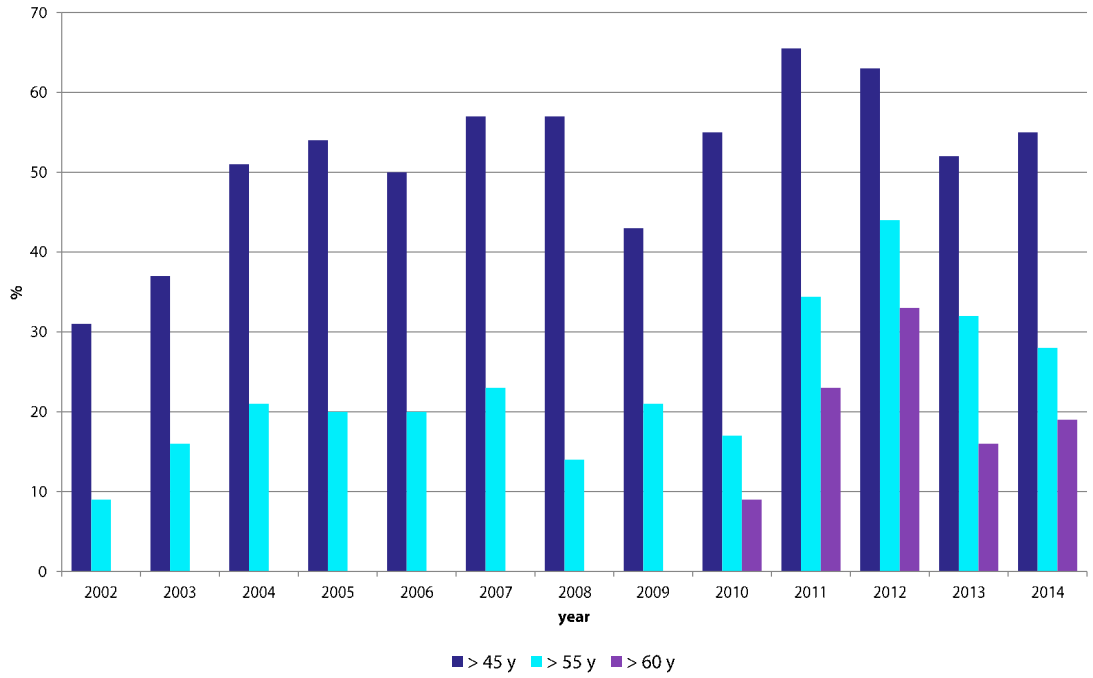
In figure 3.18 the mean donor age is shown since 2000. There is a minor increase in donor age compared to 2013 (mean 49.5 years, 12-79 versus 47.2 years old in 2013.

FIGURE 3.18 | mean donor age over the years



The number of donors above 55 years further decreased from 44% in 2012, to 32% in 2013 and 28% in 2014. On the other hand, the percentage of donors > 60 years increased to 19%. There were 16% donors above 65 years *(Figure 3.19)*.

FIGURE 3.19 | percentage of donors according to age during the last 13 years



Transplant results

In figure 3.20, the actuarial survival between January 2005 and December 2014 (n=548) in the Leuven programme is displayed and compared with the figures from the ISHLT registry database during a comparable time period. Survival in Leuven is better at every point in time with a current five-year survival of 77% (55% in ISHLT registry database), and a median survival half-life of 114 months.

FIGURE 3.20 | actuarial survival in Leuven compared to ISHLT registry database

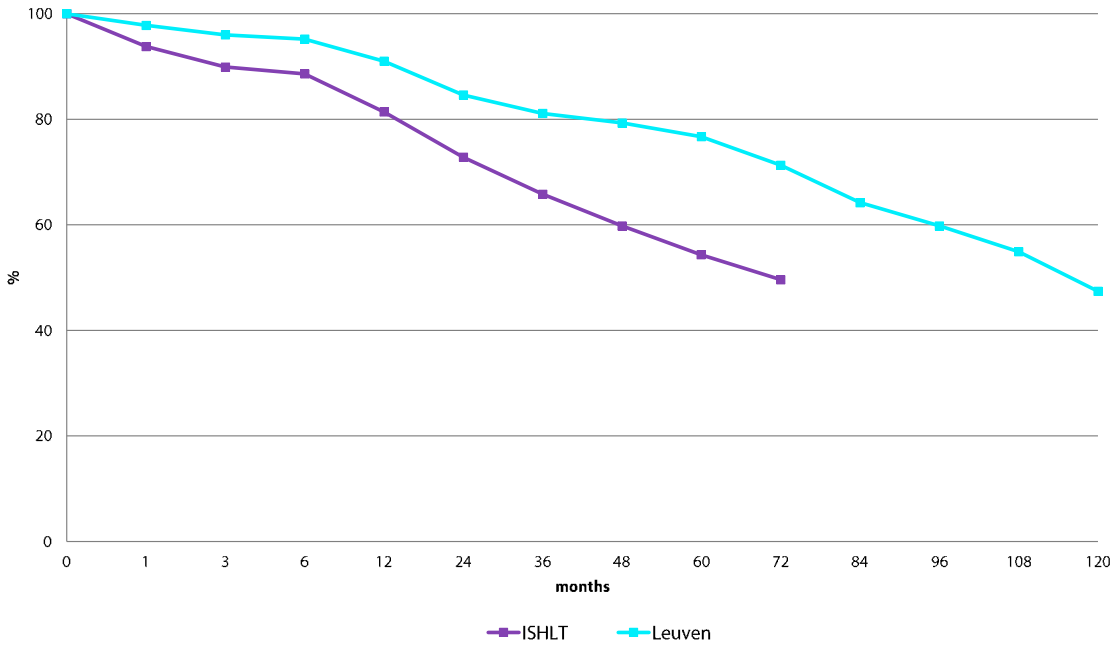


Figure 3.21 demonstrates survival curves according to underlying diagnosis between January 2005 and December 2014 (n=548) showing a significant difference (p<0.0001). The actuarial five-year survival is 85.6% for CF (cystic fibrosis, n=68), 83 % for Brect (bronchiectasis, n=13), 82% for COPD (n=264), 67% for PAHT (pulmonary arterial hypertension, n=22), 63% for ILD (interstitial lung disease, n=124), and 51% for retransplantations (n=32). The corresponding figures in the ISHLT registry database are 59,6% for CF, 54% for COPD, 48% for ILD and 51% for PAHT.

FIGURE 3.21 | survival in the Leuven programme according underlying diagnosis (COPD, ILD, CF, Brect, PAHT and redo transplants)

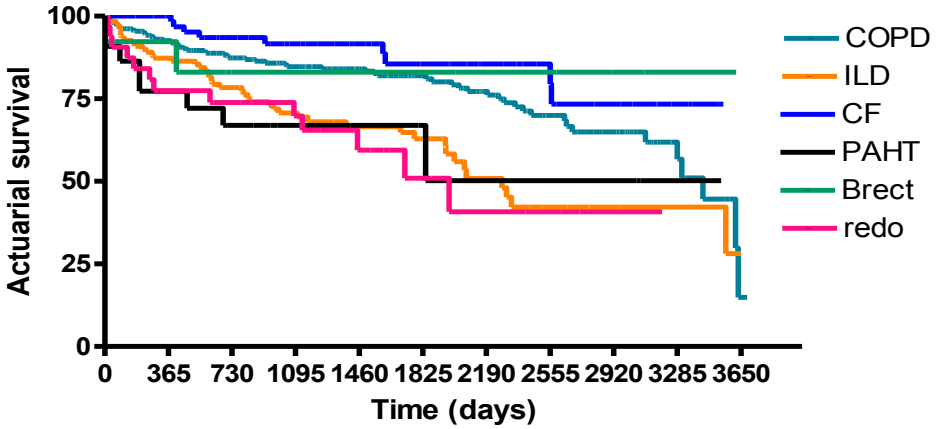


Figure 3.22 demonstrates the number of patients in actual follow-up. There is an exponential increase, causing a huge effort to continuously evaluate all these patients. This is also demonstrated in figure 3.23 which shows the number of outpatient clinic contacts over the years. This number remains stable now as we have reached the maximum number of patients we can evaluate on a yearly basis. This was achieved by increasing the time between visits in the stable patients who are at least 5 years out.

FIGURE 3.22 | cumulative number of patients in active follow-up

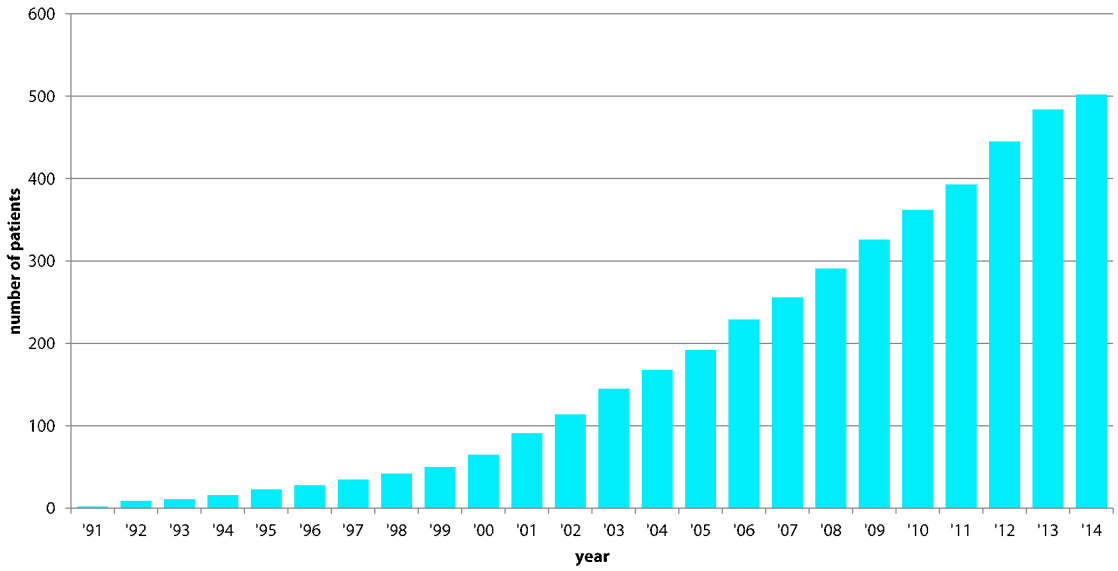
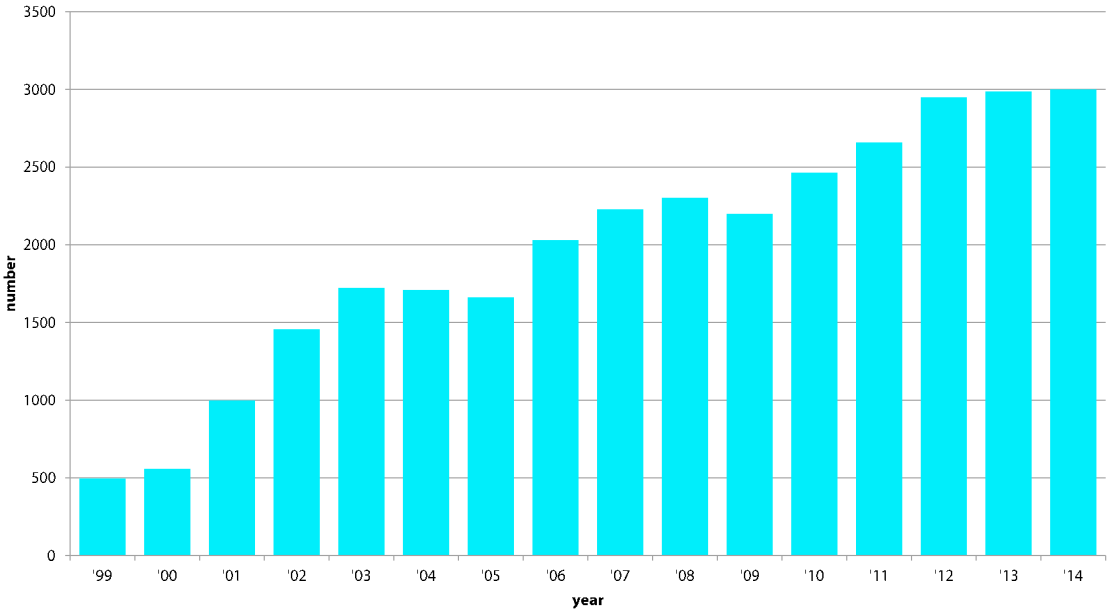


FIGURE 3.23 | number of outpatient visits per year from 1999 on



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Trachea transplant care programme

A tracheal transplant is a `composite tissue allotransplant'. Tracheal allotransplantation has been developed to repair difficult tracheal defects, which could not be treated by conventional techniques. Both the experimental and the clinical aspects were developed within the University Hospitals Leuven.

An important aspect is the possibility to withdraw the immunosuppressive medication.

TRACHEAL TRANSPLANTS

Tracheal allotransplantation is a new technique that allows for repair of pathological airway segments (post-traumatic, post-intubation, rare tumoral) with a length of more than 4 cm, which cannot be treated by conventional techniques.

The principle is based on an urgent implantation of the trachea at the recipient's forearm. Immunosuppressive drugs are those of the lung transplantation protocol. At the forearm, the transplant will undergo a slow revascularisation and remucosalisation. Complete revascularization and respiratory mucosal regeneration is reached after 2-5 months. Controls of the transplant can be done on an outpatient basis.

Important for tracheal transplants is the withdrawal of immunosuppressive drugs after full revascularisation. The cartilaginous framework (the 'unique part' of the tracheal allotransplant) will preserve its viability after the withdrawal of immunosuppressive therapy (chondrocytes are protected within the cartilaginous lacunae).

The first (worldwide) vascularised tracheal transplant was performed at the University Hospitals Leuven.

Case 1 November 2007: heterotopic transplantation at the forearm;
September 2008: orthotopic transplantation after withdrawal of immunosuppressants.

Case 2 3 June 2009: heterotopic transplantation;
16 July 2009: orthotopic transplantation after withdrawal of immunosuppressive drugs.

Case 3 5 March 2010: heterotopic transplantation;
31 March 2010: orthotopic transplantation after withdrawal of immunosuppressive drugs.

Case 4 5 September 2010: heterotopic transplantation, withdrawal of immunosuppressive drugs.

Case 5 22 March 2011: heterotopic transplantation;
4 July 2011: orthotopic transplantation after withdrawal of immunosuppressive drugs.

Case 6 22 February 2012: heterotopic transplantation;
25 June 2012: orthotopic transplantation after withdrawal of immunosuppressive drugs.

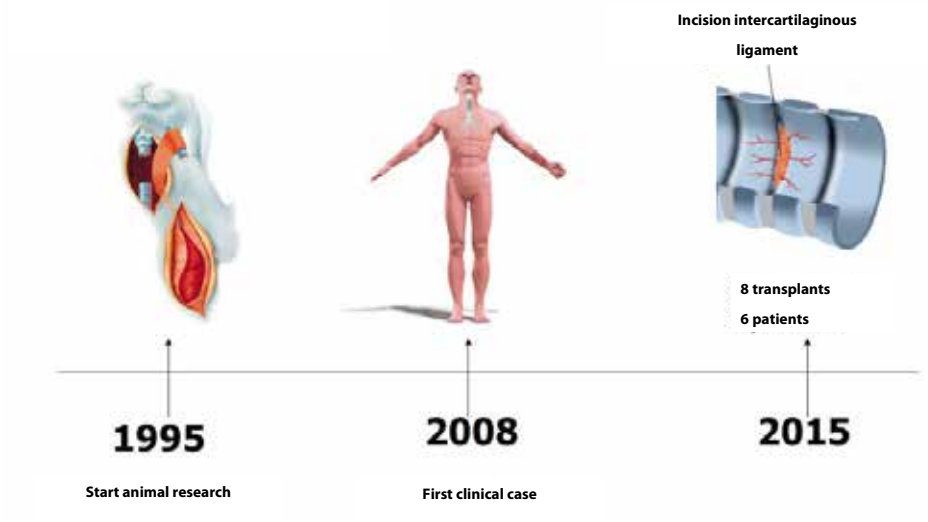
Case 7 13 April 2012: heterotopic transplantation. Withdrawal of immunosuppressive drugs.
4 February 2013: orthotopic transplantation.

Case 8 10 December 2013: heterotopic transplantation. Withdrawal of immunosuppressive drugs.
20 October 2014: orthotopic transplantation.

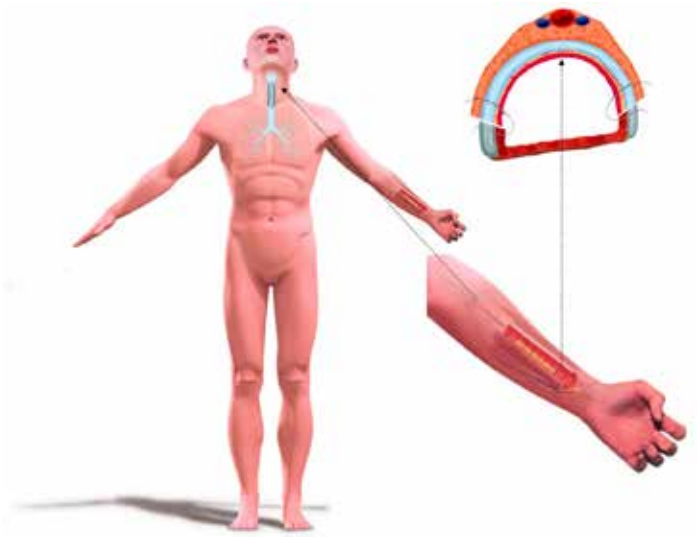
All indications were post-traumatic strictures. Only patient 5 concerned a low-grade chondrosarcoma.

Timeline of tracheal transplantation

Since 2008, six patients were treated with eight tracheal allografts. Two transplants (case 2 and 4) were lost after terminating the immunosuppressive therapy. Incision of the intercartilaginous ligaments is necessary to enable a safe reduction of immunosuppressants (ref. 2). Four patients are in good clinical condition without tracheostomy. Two patients are in good clinical condition with the presence of a tracheostoom. Immunosuppressive therapy was stopped in all patients.



The tracheal transplant is placed at the forearm after making the skin flaps. The trachea is wrapped with the subcutaneous tissue and fascia of the forearm. After several months, the transplant is completely revascularised and ready for orthotopic transplantation to the airway on the radial artery and veins.



Additional information on the clinical experience of tracheal transplantation:

1. Tracheal allotransplantation after withdrawal of immunosuppressive therapy. Delaere P, Vranckx J, Verleden G, De Leyn P, Van Raemdonck D, Leuven Tracheal Transplant Group. N Engl J Med 2010; 362: 138-145.
2. Learning curve in tracheal allotransplantation. Delaere P, Vranckx J, Meulemans J, Vander Poorten V, Segers K, Van Raemdonck D, De Leyn P, Decaluwé H, Dooms C, Verleden G. Am J Transpl 2012; 12: 2538-45.
3. Tracheal allograft after withdrawl of immunosuppressive therapy. Delaere P, Vranckx J, Den Hondt M, Leuven Tracheal Transplant Group. N Engl J Med 2014; 370: 1568-70.

PART 4

PAEDIATRIC TRANSPLANTS

surgery
abdominal transplant surgery

transplant coordination

internal medicine
paediatrics - paediatric transplantation
gastroenterology
hepatology
nephrology

paediatric nephrology & transplantation
dr. Noël Knops, dr. Jean Herman, dr. Maria Van Dyck
prof. dr. Djalila Mekahli, prof. dr. Elena Levtchenko

abdominal transplant surgery
prof. dr. Jacques Pirenne, dr. Raymond Aerts
prof. dr. Diethard Monbaliu, prof. dr. Ina Jochmans

anaesthesiology
dr. Marleen Verhaegen
prof. dr. Jan Van Hemelrijck, dr. Gert Poortmans
dr. Layth Al Tmimi, prof. dr. Arne Neyrinck

paediatric intensive care medicine
prof. dr. Dirk Vlasselaers, dr. Lars Desmet

teams OR – perfusion – ICU – hospitalisation
Liesbeth De Meyer, Magda Penninckx
Luc Hoppenbrouwers
Eddy Vandezande
Koen Vanhonsebrouck
Lucia Vandueren, Johan Rombouts, Miet Neyens

nurse specialist
Laura Moyens

transplant coordination
Bruno Desschans, Nele Grossen

social work
Carolien Cooreman

psychological support
Lore Willem

dietary advice
Katrien Van der Vaerent

Paediatric transplant care programme

The paediatric transplant programme covers kidney, liver and intestinal transplants. It was initiated in 1980, when the transplantation procedure was initially carried out at the Université Catholique de Louvain (UCL) (kidney transplants). Since 1986 transplants have been conducted at the University Hospitals 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 prof. dr. Peter Witters of the paediatric gastroenterology department.

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

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

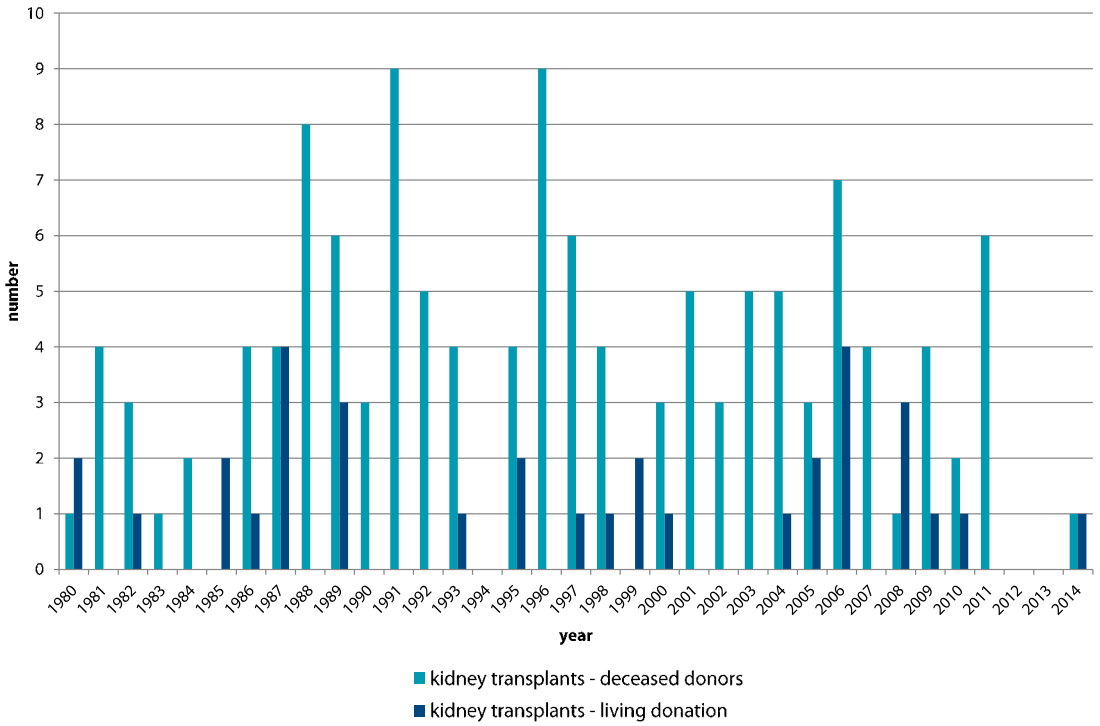
Moreover, for quite some time research has been conducted into the pharmacokinetics of immunosuppressants during childhood (initiated by em. prof. dr. Rita van Damme-Lombaerts), problems associated with compliance during childhood and transition (Loes Decorte, in cooperation with prof. Fabienne Dobbels).

PAEDIATRIC KIDNEY TRANSPLANTS

In 2014 we performed two renal transplants in children, including one from a living donor. Both children were younger than four years at the time of transplantation and are currently doing well.

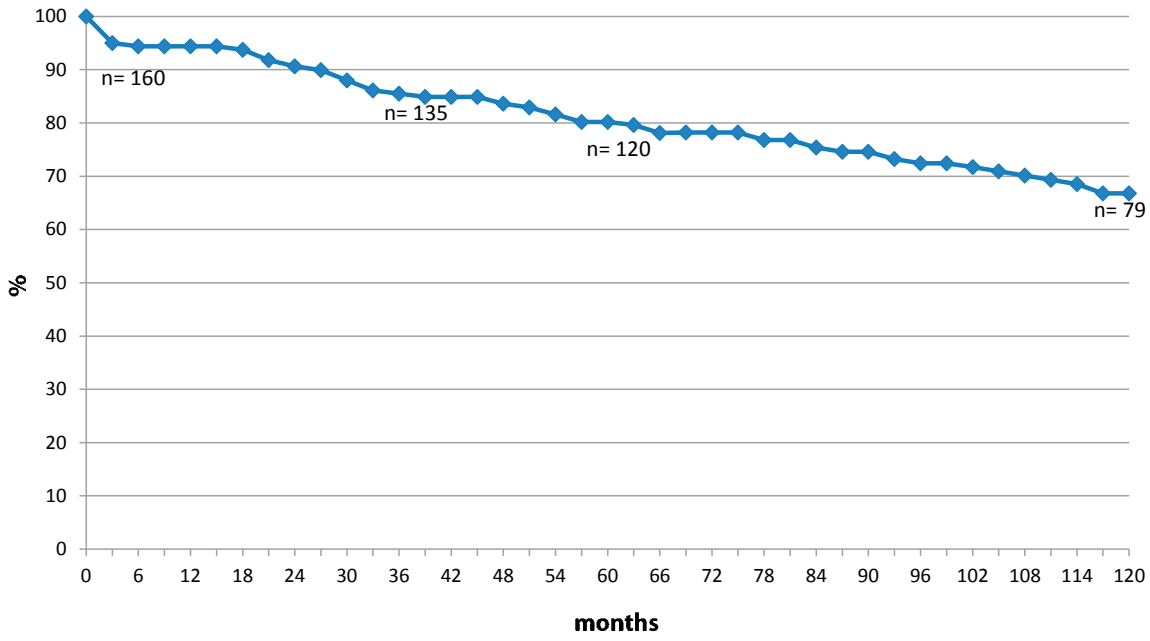
At the end of 2014 there were four children on the active waiting list. One of them is listed for a combined kidney-pancreas transplantation. There are five children in dialysis, two of which are currently not eligible for renal transplantation. No children lost their renal allograft in 2014.

FIGURE 4.1 | number of renal transplants performed in children since 1980



Since 1980 we performed 160 renal transplants in 144 children (85 boys en 59 girls) with an average age of 10.7 years (+/- 4.9) at transplantation. Allograft survival for the entire cohort: one-year: 94%, three-year: 86%, five-year: 80% and ten-year: 67% *(Figure 4.2)*. The percentage of living donations procedures is 21% (n=34).

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



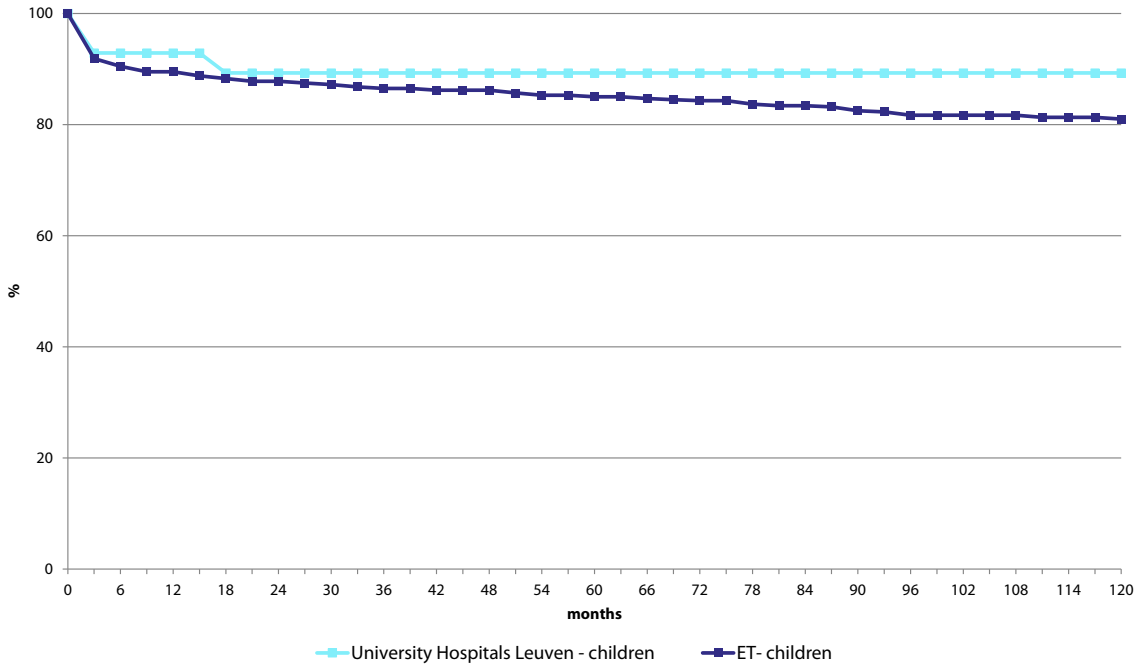
PAEDIATRIC LIVER AND INTESTINAL TRANSPLANTS

In 2014 no isolated liver transplantation procedures in children were performed.

The total number of paediatric liver transplants in our programme remains at 40 in 40 children (< 18 years) (one person underwent a re-transplant at the age of adulthood). There was no mortality on the waiting list, nor allograft failure during follow-up.

At the start of 2015 four children are listed for a liver transplant (including one for a combined pancreas-liver graft). Below, you'll find the patient survival curve for our cohort of paediatric liver transplant recipients.

FIGURE 4.3 | patient survival rate 120 months – paediatric liver transplants (1999 - 2014), University Hospitals Leuven versus ET



We performed one successful combined liver-small bowel transplant in 2014 (in a patient with microvillous inclusion disease). In the meantime parental nutrition (PN) was stopped and he is on full enteral (tube) feeding. Only one child remains listed for a small bowel transplant (megacystis-microcolon hypoperistalsis syndrome). He is largely dependent on PN, but has suffered no severe-life threatening complications recently and is growing well.

This amounts to three children that have now received a successful combined intestinal transplantation in our programme, all with a relatively good outcome thus far.

PART 5

CELL AND TISSUE BANKS

banks for human bodily material

AC Biobanking / cell and tissue banks

transplant programmes

Bank for grafts of musculo-skeletal system
- Orthopaedic surgery
- Neurosurgery
- Traumatology
- Oto-rhino-laryngology, head and neck surgery
- Stomatology and dentistry

Bank for skin grafts
- Intensive medicine: centre for burns
- Plastic, reconstructive and aesthetic surgery

Bank for tympano-ossicular grafts
- Oto-rhino-laryngology, head and neck surgery

Bank for placental membranes
- Intensive medicine: centre for burns
- Dermatology
- Vascular center
- Eye-surgery

Bank for ophthalmic tissues
- Eye-surgery

Bank for keratinocytes
- Intensive medicine: centre for burns
- Dermatology
- Vascular center

Umbilical cord blood bank
- Hematology

Hematopoietic stem cell bank
- Hematology

Mesenchymal stem cell bank
- Hematology

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, Maarten Vanhaecke, 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: prof. 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
weefseltechnologen: Daniël Carels, Inge Daris, Katrien Smaers

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

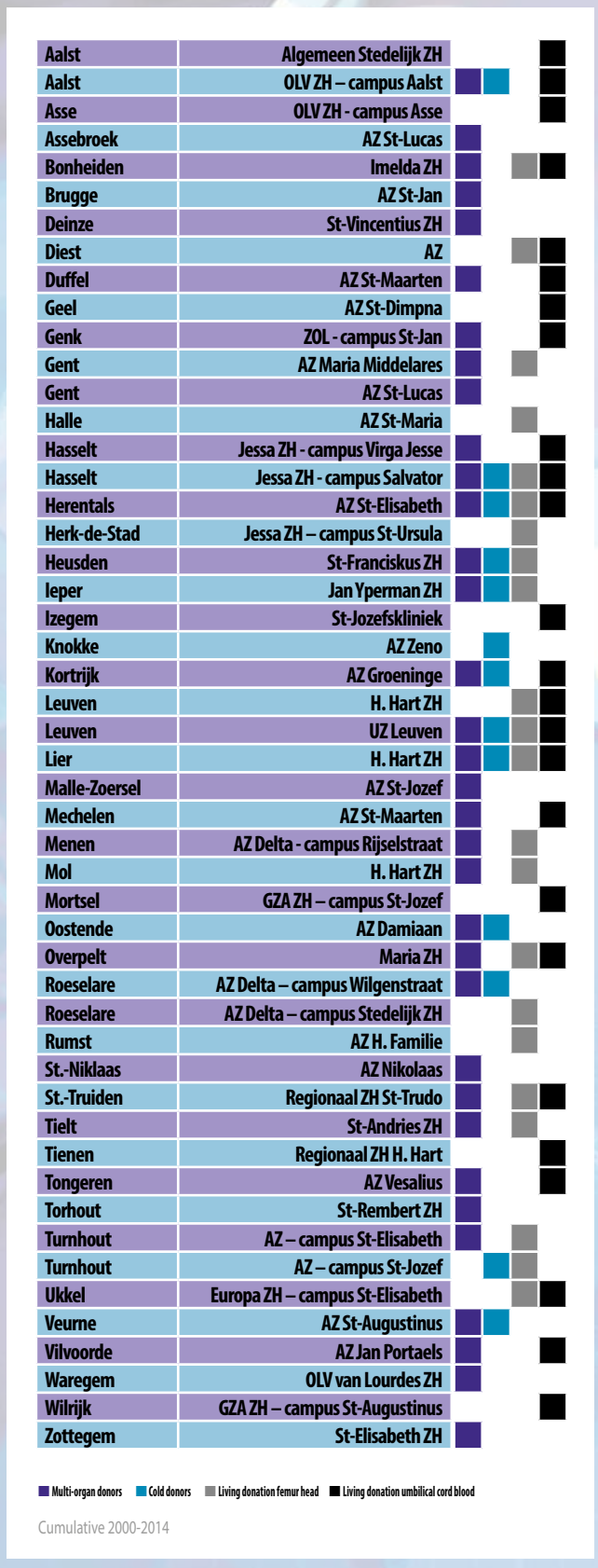
Mesenchymal stem cells
staff members: prof. dr. Timothy Devos
tissue technologists: Ann Van Campenhout, Lore Swinnen

Quality assurance
Johan Klykens, Franky Sinap

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

Managers
em. prof. dr. Marc Boogaerts (umbilical cord blood bank),
prof. dr. Gregor Verhoef (haematopoietic stem cells, mesenchymal stem cells),
prof. dr. Nadine Ectors (other banks)

Biobanking Activity Centre



Cumulative 2000-2014

The University Hospitals Leuven-KU Leuven tissue and cell banks endeavour to develop a high quality service 'from and for' 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.

Living donors

Within cell and tissue banks this type of procurement covers different domains. The patient is informed through an informed consent form which is handed over by his/her treating physician. Based on predefined criteria the same physician decides whether the patient qualifies for donation. Subsequently, after patient consent, the following biological tests are performed: anti-HIV 1 and 2, HBsAg, anti-HBc, anti-HCV, anti-HTLV1 and 2, and a test for the detection of syphilis. In addition a nucleic acid amplification test (NAT) for HIV (Human immunodeficiency virus), HBV (Hepatitis B virus) and HCV (Hepatitis C virus) are performed on the blood sample.

Femoral head donation

Femoral heads are collected from living donors who undergo hip replacement surgery after trauma or for coxarthrosis. After procurement a microbiological culture is taken from the tissue, serological tests are performed, and the femoral head is double packed in a sterile way and frozen. When all legal conditions are met, the femoral head is released for processing and subsequently for transplantation. The tissue bank collects femoral head allografts (1206 in 2014, +19.8% compared to 2013) under increasingly stringent regulations (current legislation: law of 19 December 2008 and implementing royal decrees end 2009). Femoral heads were donated in 15 Flemish hospitals (one of which was a newcomer).

TABLE 5.1 | evolution donor hospitals ~ femoral head donations 2004 - 2014

Centre		'04	'05	'06	'07	'08	'09	'10	'11	'12	'13	'14
Bonheiden	Imelda ZH	-	-	-	-	-	-	56	136	155	167	168
Diest	AZ	-	21	10	18	13	10	21	18	25	32	56
Gent	AZ Maria Middelares	-	-	-	-	-	-	-	-	5	1	-
Halle	AZ St-Maria	22	15	19	17	22	29	48	59	64	57	75
Hasselt	Jessa ZH – campus Salvator	-	-	-	-	72	83	93	88	-	-	-
Herentals	AZ St-Elisabeth	-	-	-	-	-	-	-	3	27	68	114
Herk-de-stad	Jessa ZH – campus St-Ursula	50	62	56	14	-	-	-	-	-	-	-
Heusden	St-Franciskus ZH	-	-	-	-	-	-	-	-	-	-	6
Ieper	Jan Yperman ZH	-	-	-	-	-	-	-	-	-	56	113
Leuven	H. Hart ZH	41	58	65	57	79	35	71	62	72	66	86
Leuven	orthopaedics UZ Leuven	91	71	31	82	105	122	147	143	134	97	95
Leuven	traumatology UZ Leuven	37	33	16	7	8	2	1	2	1	-	-
Lier	H. Hart ZH	-	-	-	-	-	-	157	193	151	134	102
Menen	AZ Delta – campus Rijselstraat	18	18	-	-	-	-	-	-	-	-	-
Mol	H. Hart ZH	-	-	-	-	-	67	73	74	55	51	57
Overpelt	Maria ZH	-	16	47	48	47	39	29	11	-	-	-
Roeselare	AZ Delta – campus Stedelijk ZH	-	-	-	-	-	-	-	-	-	106	174
Rumst	AZ H. Familie	34	22	11	23	3	23	3	29	10	12	14
St-Truiden	Regionaal ZH St-Trudo	40	35	36	31	23	22	47	39	59	70	81
Tielt	St-Andries ZH	-	-	-	-	-	-	-	8	24	50	57
Turnhout	AZ Turnhout	-	-	-	-	3	-	-	-	-	-	8
Ukkel	Europa ZH – campus St-Elisabeth	-	-	-	-	11	11	17	14	-	-	-
Total		333	351	291	297	386	443	763	879	782	967	1206

Placental membranes donation

Amnion and chorion grafts are collected during normal deliveries in collaboration with the umbilical cord blood bank of the University Hospitals Leuven. These grafts are used as a bandage to cover skin defects as well as defects form the surface of the eye. The seven donations in 2014 were obtained via the obstetrics department of the University Hospitals Leuven.

Keratinocyte donation

Keratinocytes are isolated from the epidermis, the superficial part of the skin. They are preferably obtained from the skin of very young donors, for example during circumcision or breast reduction surgery (surgical residue). The cells are cultured and distributed as dermatological treatment to cover and heal difficult to treat skin defects. Typical 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 needed.

Umbilical cord blood donation

Blood is collected from the umbilical cord immediately after the baby is born and the umbilical cord has been transected. This umbilical cord blood is of special interest because it has been shown that a high number of blood producing or haematopoietic stem cells are circulating herein. The blood 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. In 2014, 857 samples were frozen at the Leuven Umbilical Cord Blood Bank. On 1 January 2015, 8,769 samples were available for transplantation internationally. The umbilical cord blood originated from maternity units at the following locations:

TABLE 5.2 | evolution donor hospitals ~ umbilical cord donations 2011 - 2014

Centre		'11	'12	'13	'14
Aalst	Algemeen Stedelijk ZH	-	-	-	4
Aalst	OLV ZH – campus Aalst	58	36	24	31
Asse	OLV ZH – campus Asse	-	-	15	25
Bonheiden	Imelda ZH	65	40	35	43
Diest	AZ	36	20	34	23
Duffel	AZ St- Maarten	-	-	15	17
Genk	ZOL – campus St-Jan	106	62	45	89
Hasselt	Jessa ZH – campus Salvator	6	2	-	-
Hasselt	Jessa ZH – campus Virga Jesse	29	35	38	87
Herentals	AZ St-Elisabeth	46	47	50	42
Izegem	St-Jozefskliniek	33	28	28	29
Kortrijk	AZ Groeninge	-	-	-	64
Leuven	H. Hart ZH	77	49	53	54
Leuven	UZ Leuven	57	34	55	46
Lier	H. Hart ZH	-	-	-	57
Mechelen	AZ St-Maarten	-	-	20	19
Mortsel	GZA ZH – campus St-Jozef	-	-	-	18
Overpelt	Maria ZH	-	-	-	45
St-Truiden	Regionaal ZH St-Trudo	25	29	15	14
Tienen	Regionaal ZH H Hart	52	34	41	25
Tongeren	AZ Vesalius	41	28	31	49
Vilvoorde	AZ Jan Portaels	34	30	29	34
Wilrijk	GZA ZH – campus St- Augustinus	-	-	5	31
Family		-			11
Total - frozen		665	474	533	857

Hematopoietic stem cell (HSC) donation

HSC are collected using apheresis technology (peripheral stem cell collection) or bone marrow collection. These 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). Using similar techniques stem cells are collected from healthy donors (related or unrelated) and administered to the patient (without being frozen) the same or the next day.

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 University Hospitals Leuven MSCP (Mesenchymal Stem Cell Programme) was accredited as a cell bank by FAMHP (the Federal Agency for Medication and Health Products - FAGG).

Deceased donors

Among deceased donors a distinction has to be made between 'cold' donors and 'multi-organ donors'.

'Cold' donors

'Cold' donors are deceased donors, who might qualify for donation in case they fulfill the legal criteria. Procurement is performed both in and outside the University Hospitals Leuven (Table 5.3). In 2014 this type of donation accounted for 3 donors (all multi-tissue donors). It remains an important underuse of the number of potential donors, and motivates us to keep looking for external partners to extend the donor supply. We are therefore extremely pleased and grateful that even in very difficult circumstances tissue donation is considered.

TABLE 5.3 | evolution donor hospitals ~ tissue donation 'cold' donors 2004 - 2014

Centre		'04	'05	'06	'07	'08	'09	'10	'11	'12	'13	'14
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	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	-
Tielt	St-Andries ZH	-	-	-	-	-	-	-	-	-	-	1
Turnhout	AZ – campus St-Jozef	-	-	-	1	-	-	-	-	-	-	-
Veurne	AZ St-Augustinus	-	-		1	-	-	1	5	4	2	2
Total		26	26	17	9	28	17	6	6	11	9	3

Multi-organ donors

Multi-organ donation is a high-impact issue for the patient's close relatives. For many receptor patients a donor organ is their last option. It is therefore obvious that tissue donation cannot at all interfere with the process of organ donation, as the latter are live-saving donations. Tissue donation on the other hand results in a decrease of morbidity for the receptor. It might occur that relatives selectively refuse tissue donation. Their wishes are extensively discussed with the transplant coordinators in advance and obviously respected.

In multi-organ donors tissue procurement starts immediately after organ procurement has been finished. The procurement always takes place in the sterile conditions of the operating theatre. Donor screening assessment is done by the transplant coordinators. After three months, secondary screening is indirectly performed through screening of the organ receptor (back-screening). This results in a very safe procedure and guarantees safety and quality for the tissue recipients. This type of donors lends itself to a large number of tissue donations: cortical bone (complete or partial bone fragments), spongious bone, cartilage, tendons, menisci, skin, corneas, scleras and tympano-ossicular allografts. These procurements are spread over the whole Flemish region. In 2014, tissue was procured from 67 donors in 21 Flemish hospitals (three of which were newcomers). For deceased donors similar stringent legislation is applicable as for living donors (same law of 19 December 2008 and implementing decisions end 2009).

TABLE 5.4 | evolution donor hospitals ~ multi-organ donors 2004 - 2014

Centre		'04	'05	'06	'07	'08	'09	'10	'11	'12	'13	'14
Aalst	OLV ZH – campus Aalst	2	1	4	4	3	-	2	2	1	5	1
Assebroek	AZ St-Lucas	-	-	-	2	1	-	2	1	2	-	-
Bonheiden	Imelda ZH	1	-	2	4	2	1	2	-	1	3	3
Brugge	AZ St-Jan	-	-	1	-	-	1	1	1	-	-	3
Deinze	St-Vincentius ZH	-	1	-	-	-	-	1	-	-	-	-
Duffel	AZ St-Maarten	-	-	-	-	-	-	1	-	-	-	-
Genk	ZOL – campus St-Jan	5	4	11	10	5	4	5	7	4	4	6
Gent	AZ Maria Middelares	-	-	-	1	-	-	-	-	-	-	-
Gent	AZ St-Lucas	4	2	2	-	-	-	-	-	-	-	-
Hasselt	Jessa ZH – campus Salvator	-	1	2	1	1	-	-	2	-	-	-
Hasselt	Jessa ZH – campus Virga Jesse	4	2	1	3	5	5	10	3	6	7	6
Herentals	AZ St-Elisabeth	-	-	-	-	-	-	-	-	-	-	2
Heusden	St-Franciskus ZH	5	-	6	3	3	2	1	4	3	2	1
Ieper	Jan Yperman ZH	-	1	-	-	-	1	3	1	2	-	1
Kortrijk	AZ Groeninge	1	6	4	5	3	4	-	7	4	4	3
Leuven	UZ Leuven	13	13	8	13	7	5	10	10	11	7	15
Lier	H. Hart ZH	2	1	5	2	3	3	1	7	2	2	6
Maaseik	ZH Maas en Kempen	-	-	-	-	-	-	-	-	-	-	2
Malle-Zoersel	AZ St-Jozef	1	-	1	-	1	1	1	-	-	-	2
Mechelen	AZ St-Maarten	-	-	-	-	-	-	-	1	-	-	-
Menen	AZ Delta – campus Rijselstraat	-	-	-	-	-	-	-	-	-	1	-
Mol	H. Hart ZH	-	-	-	-	-	1	-	2	-	1	-
Oostende	AZ Damiaan	2	-	3	-	4	2	-	-	2	1	2
Overpelt	Maria ZH	-	-	-	-	1	1	-	1	-	-	1
Roeselare	AZ Delta – campus Wilgenstraat	3	6	6	5	1	3	5	5	6	7	6
Ronse	AZ Glorieux	-	-	-	-	-	-	-	-	-	-	1
St.-Niklaas	AZ Nikolaas	3	-	-	2	3	1	1	2	1	1	1
St.-Truiden	Regionaal ZH St- Trudo	2	-	-	1	-	-	2	1	1	2	1
Tielt	St-Andries ZH	-	-	-	-	1	-	1	2	-	-	-
Tongeren	AZ Vesalius	-	-	-	-	-	-	-	-	1	-	-
Torhout	St-Rembert ZH	-	-	1	-	-	-	-	1	1	-	-
Turnhout	AZ – campus St-Elisabeth	4	4	1	1	2	2	2	3	5	1	2
Veurne	AZ St-Augustinus	2	2	-	3	4	8	11	3	5	2	2
Vilvoorde	AZ Jan Portaels	-	1	-	-	-	-	-	-	1	-	-
Waregem	OLV van Lourdes ZH	-	-	-	1	1	-	1	-	-	-	-
Zottegem	St-Elisabeth ZH	-	-	-	1	-	-	-	-	-	-	-
Total		54	45	58	62	51	45	63	66	59	50	67

A further professionalisation of the process of tissue donation and procurement, a dedicated team of tissue coordinators, and not in the least a clear, efficient and professional communication between the tissue bank, donor hospitals (physicians, nurses, social and pastoral services) and transplant coordinators remains the cornerstone for the existence of the tissue bank. Moreover all this would be impossible without extreme solidarity and a sense of altruism.

Grafts supplied

A medical doctor with the necessary know-how and expertise in the relevant fields and activities performed in the bank is responsible for leading and organising a cell and tissue bank. According to the existing legal framework the responsible person takes care of

- ensuring that, in the establishment which that person is responsible for, human cells and tissues are procured, tested, processed, stored and distributed in accordance with the national framework. He is responsible for the traceability.
- respecting the technical, ethical and administrative rules relating to these activities.
- the relation with the procurement sites and teams outside the bank and with the transplantation departments and teams.
- the redaction of an annual report concerning the activities of the bank which he will address to the Minister in respect of confidentiality of the data about donors and receptors.
- the notification to the relevant competent authorities of all 'serious adverse events' and 'serious adverse reactions' as well as the preparation of a report analysing causes and important consequences.

The release of tissues and cells is dependent on the evaluation of the proof of conformity of the cells and tissues with the regulatory and legal requirements as well as the requested specifications related to quality and safety. From that moment onwards cells and tissues can be distributed. The release of tissues and cells is the responsibility of the person responsible. Distribution can be requested based on a medical prescription written by the person in charge of the implantation or on request of a recognised institution.

Numerous (allo/auto)grafts are made available by the cell and tissue banks of the University Hospitals Leuven but also in numerous other, mainly Belgian, hospitals.

Bank for musculo-skeletal allografts

From the point of view of basic material, types of products, sorts of manipulations and care programs, this bank is the most complex.

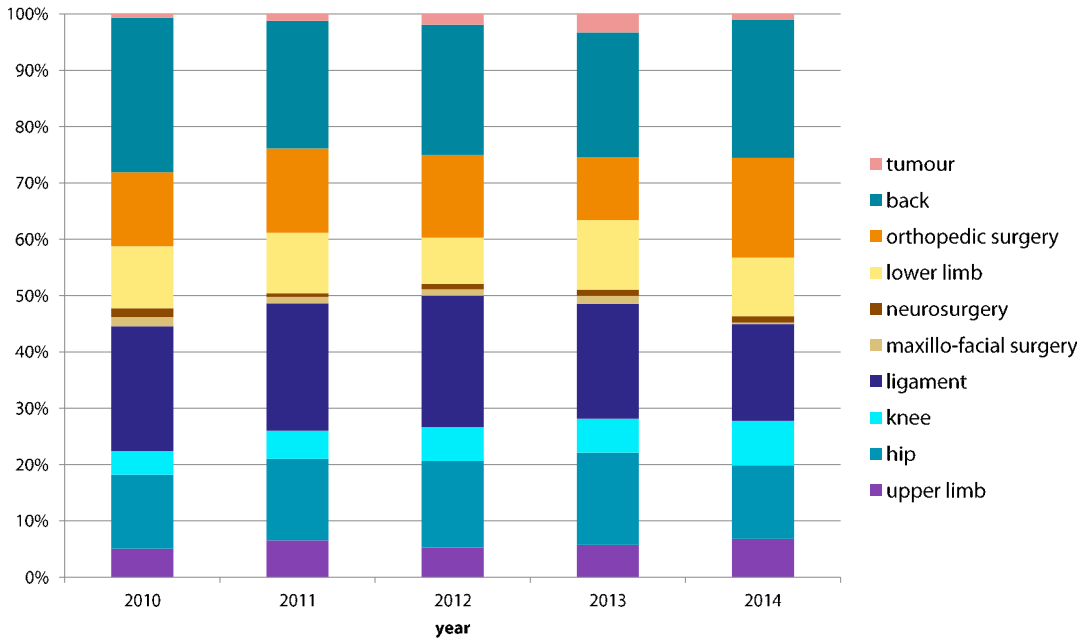
The tissues originate from living, 'cold' and multi-organ donors. The so-called 'soft tissues' can – for safety reasons – only be obtained from multi-organ donors. In contrast, the 'bones' can originate from living donors, 'cold' donors and multi-organ donors.

The manipulation and conservation can be based on lyophilisation and irradiation, freezing and cold storage (+4°C). Purely based on the reimbursement by the National Institute for Health and Disability Insurance (NIHDI, RIZIV, INAMI) 37 different products are reimbursed. In practice this consists of frozen 'soft tissues' (e.g. tendons, fascia, menisci …), frozen long bone fragments or articulations, fragments of spongy bones, cortical bone powder, demineralised cortical bone (DBM), fresh cartilage fragments …

Orthopaedic surgeons and neurosurgeons are the principal users, other less frequent users are the oto-rhino-laryngologist, head and neck surgeons, stomatology and dentistry, abdominal surgery …

Many of the indications for implantation relate to replacement of bone, tendons, cartilage or menisci or otherwise the filling of defects (mainly to stabilise prosthesis, implants …) and occasionally reinforcement (e.g. fascia's). The next figure demonstrates the variability of users and indications.

FIGURE 5.1 | use of grafts of the musculo-skeletal system in function of indication (area) from 2010 until 2014

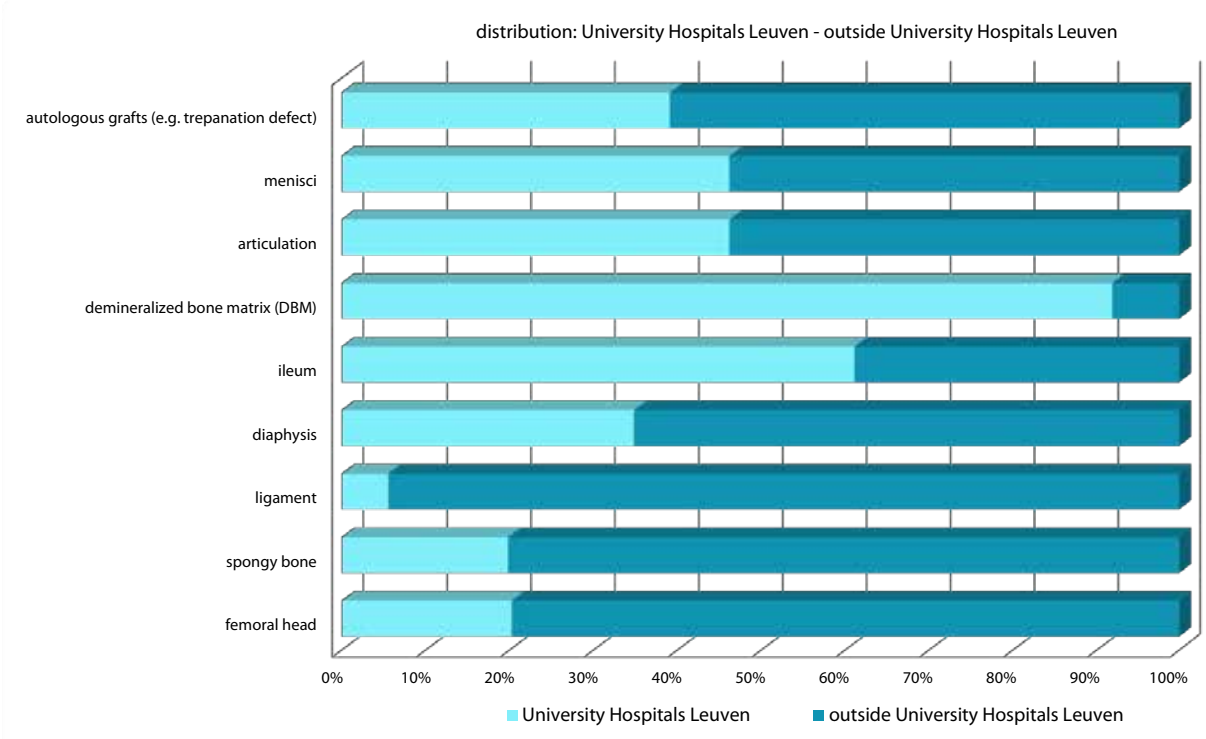


The type of grafts used depends on the medical discipline but also on the patient, the underlying condition, the techniques used. All this is reflected in different uses in different hospitals *(figure 5.2)*.

Every year thousands of patients can be helped with grafts of the musculoskeletal system delivered by our bank.

As indicated earlier these tissues originate from living, cold and multi-organ donors, and these donors originate from numerous hospitals. Therefore we endorse the following aim: "the cell and tissue banks of the University Hospitals Leuven-KU Leuven aim to provide a high-quality service towards the collaborating hospitals, according to the latest medical developments, under circumstances as optimal as possible, and in conformity with the current legislation and ethical norms. Our organisation sets itself as goal to optimise donation, procurement, preservation, storage and distribution of human tissues, for which it has obtained accreditation of the Federal Public Service of Health, to ensure that each patient, wherever in Belgium, is able to profit of this unique gift." It is fundamental to help all our partners in donation.

FIGURE 5.2 | distribution of use of grafts of the musculoskeletal system within the University Hospitals Leuven versus in other hospitals; in function of the type of grafts used.



Skin bank – bank for placental membranes – keratinocyte bank

In the University Hospitals Leuven the skin grafts are processed and stored in glycerol at room temperature. When needed we can obtain frozen skin through agreements with other banks. There is a high degree of solidarity between the different skin banks which is very important since large amounts of skin can be needed when major catastrophes occur. In 2014 skin was delivered for 111 interventions.

The placental membranes are lyophilised and irradiated (amnion membranes, chorion membranes) and are stored at room temperature. The keratinocytes are frozen and stored at -196°C (liquid nitrogen). The most important indications for the use of these grafts are skin defects due to chronic lower leg ulcers, diabetic feet, trauma, arterial/venous ulcers, scleroderma, pyoderma gangrenosum, oncological pathology, epidermolysis bullosa, burns …). The clinical departments requesting these grafts are dermatology, the vascular centre, the burns unit and traumatology. In 2014 placental membranes and keratinocytes were provided for 65 and 90 interventions respectively.

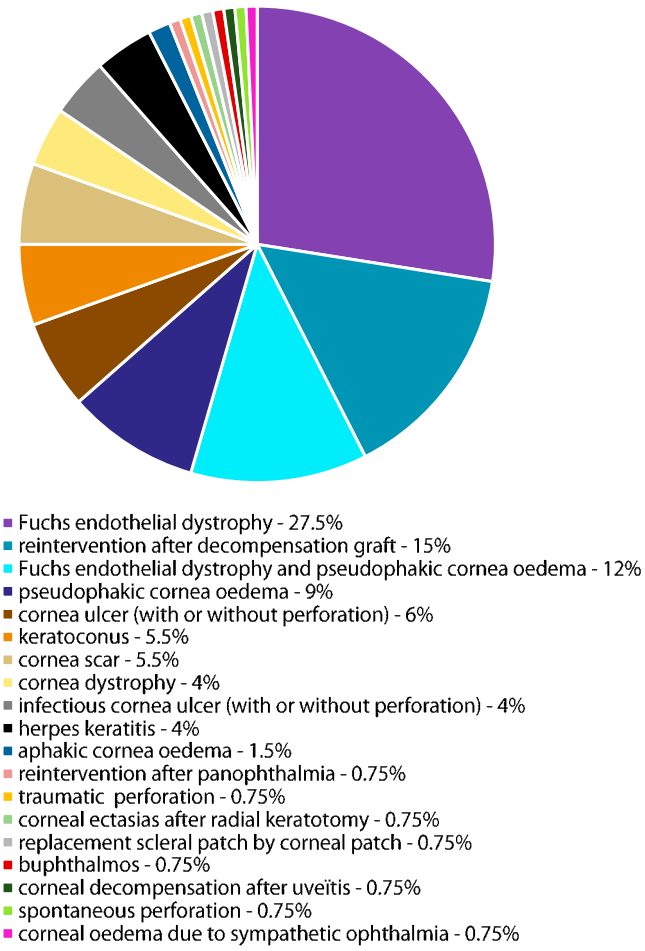
Bank for ophthalmic tissues

Ophthalmic allografts are cornea, sclera or other ocular tissue. As a rule, in Belgium, the eye is removed in total, is enucleated. After decontamination the corneoscleral part is resected from the eye, which can be split lateron manually or via automated methods using lasers. The sclera is prepared after dissection of the cornea. Both types of tissue are used for transplantation.

A large number of circumstances can result in cornea damage hindering vision. Figure 5.3 shows these different conditions in relative proportion.

FIGURE 5.3 | indications for corneal transplantation in 2014

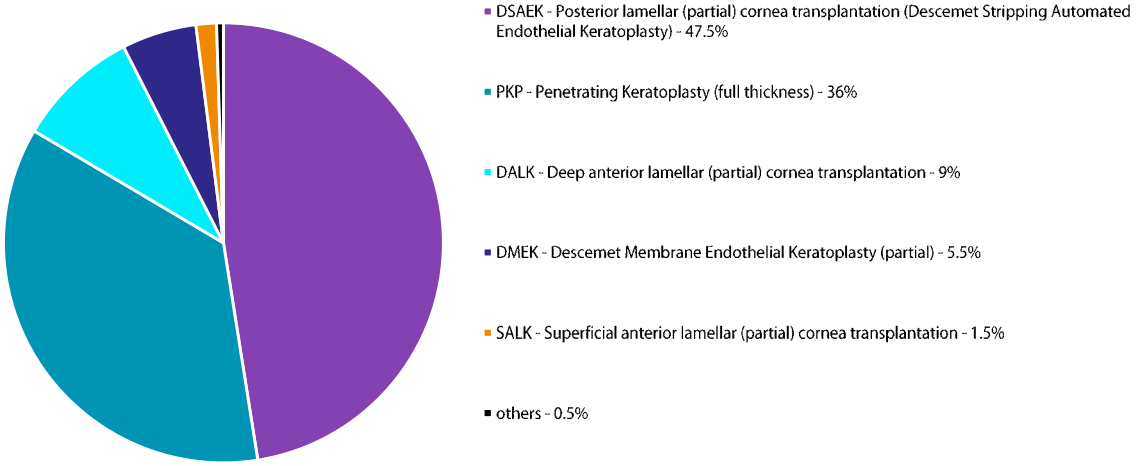
Indication for cornea transplantation 2014 - %



Damage to the cornea can be corrected through different types of surgical interventions.

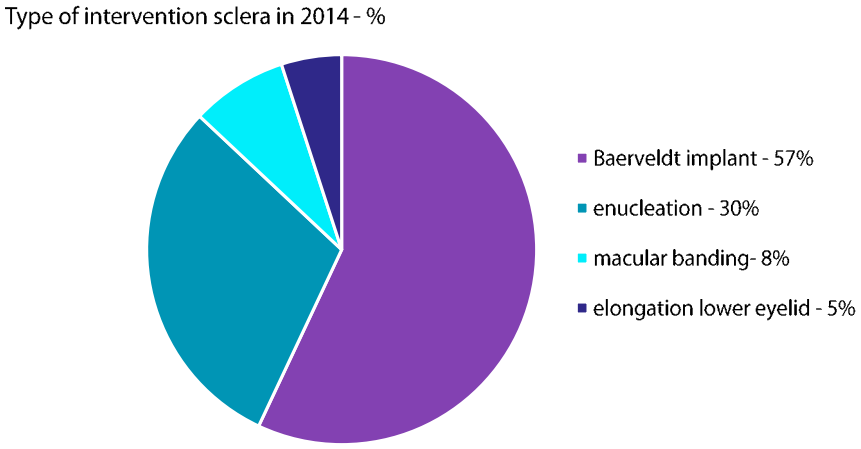
FIGURE 5.4 | types of interventions for which cornea transplantation can restore vision

Type of intervention cornea in 2014 - %



The most important indication for the use of a scleral graft is the surgical treatment of glaucoma by means of an implant (Baerveldt).

FIGURE 5.5 | indications for sclera transplantation in 2014



In 2014 ophthalmic tissues were delivered for approximately 200 surgical interventions.

Umbilical cord blood – Hematopoietic stem cells – mesenchymal stem cells

These types of grafts are mainly used in hematological patients.

In 2014, thirteen umbilical cord bloods were transferred to stem cell transplantation centres abroad.

In 2014 the University Hospitals Leuven Hematopoietic Stem Cell Bank prepared 143 transplants, including 57 autologous and 86 allogeneic transplants (35 sibling, 46 MUD (=matched unrelated donor), 5 haploidentical). The applied hematopoietic stem cells were obtained via peripheral stem cell collection (134), bone marrow procurement (6) or from umbilical cord blood (3).

In 2014 one patient was treated with MSC because of graft failure, in collaboration with the University of Liège (CHU).

Attached to these three banks a number of other agreements have been introduced in 2014 in order to allow clinical trials. In the near future the clinical trials will be a major challenge from different perspectives e.g. variability of questions, international/multicentric context, numbers, staffing needs ….

Other tissues and cells

Tympano-ossicular grafts may correspond to the tympanic membrane, membrane with 1 or more ossicles or isolated ossicles as hammer, anvil and stirrup. Because of the CJD issues all procurements are performed through the ear conduit. As a consequence only isolated ossicles can be obtained.

The cell and tissue banks have an agreement with the European Homograft bank for the procurement of heart valves and blood vessels.

PART 6

ISLET TRANSPLANTS

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Islet transplant care programme

A multicenter project is currently active in Belgium, in which the University Hospitals 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.

This unique clinical 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. The first protocol involved stable kidney transplant recipients and was initiated at UZ Brussels under the supervision of prof. dr. Daniel Pipeleers and prof. dr. Bart Keymeulen in 1994 (= islet-after-kidney). From 1998 onwards, islet transplants were mainly performed in patients with early diabetic complications and frequent hypoglycaemic episodes (often with underlying hypoglycaemic unawareness) (= islets transplantation alone) *(see figure 6.1)*.

Since the end of 2001, the University Hospitals Leuven have become active as an implant centre and in the screening and follow-up of patients. Since then 39 type 1 diabetic patients received a total of 72 allografts in Leuven, almost exclusively islet transplants (n=38 patients). Patients were referred by participating university and non-academic centres. The main indications for islet transplantation currently include the presence of frequent serious hypoglycaemic episodes (often coinciding with hypoglycaemic unawareness) and progressive diabetic complications, despite maximal intensive insulin therapy.

Since a few years a new implant site (peritoneum 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.

ISLETS TRANSPLANTS

Activity in 2014 of the multicentric programme

Four patients received transplants with a total of six β-cell allografts in 2014. 53% of the processed and transplanted Belgian organs in 2014 originated from the University Hospitals Leuven donor centre. Allografts were transplanted into the liver (n=5) or in the omentum (n=1). Immunosuppression consisted of ATG induction therapy and maintenance 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 or > 0.15 nmol/l) was present in three out of four recipients. Restoration of endogenous insulin secretion resulted in a reduction in the hypoglycaemia risk, insulin requirement and an HbA1c up to < 7.0 %. Two patients became insulin independent. Post-transplantation none of the patients suffered from severe hypoglycemia or diabetic ketoacidosis.

Patient and graft survival from 2001 to 2014

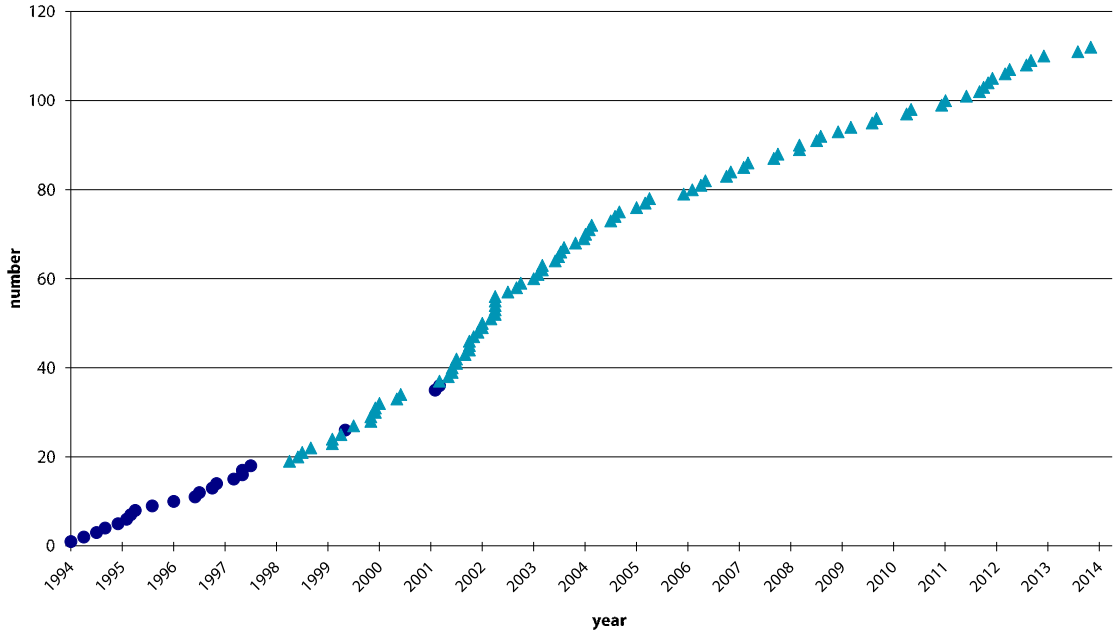
The outcome of type 1 diabetes patients who received a transplant with sufficient cells (= ≥ 2 X 10^6 per kg body weight per transplant) between 2001 (start of first JDRF protocol) and December 2014 are as follows:

After 1 year
- Patient survival: 98%
- Graft survival (= C-peptide of ≥ 0.5 ng/ml or > 0.15 nmol/l): 79%

After 3 year
- Patient survival: 95%
- Graft survival (= C-peptide of ≥ 0.5 ng/ml or > 0.15 nmol/l): 51%

After 5 year
- Patient survival: 93%
- Graft survival (= C-peptide of ≥ 0.5 ng/ml or > 0.15 nmol/l): 25%

FIGURE 6.1 | islet graft recipients at the 'JDRF centre for Beta Cell Therapy in Diabetes' between 1994 and 2014. 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).



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UZ LEUVEN | RAAD VOOR TRANSPLANTATIE

IN COLLABORATION WITH LSGO
(Leuven Organ Donation Partnership)