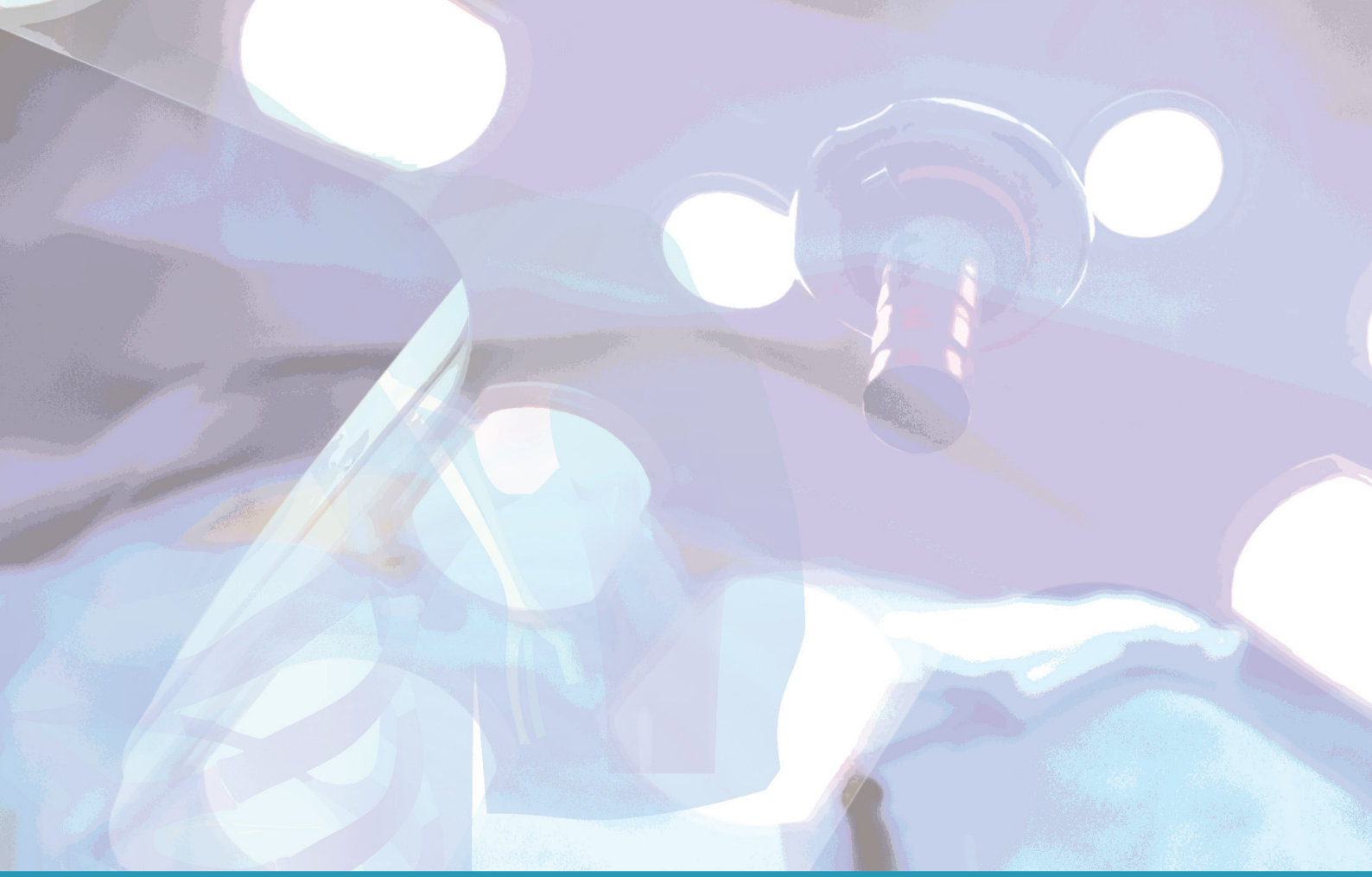
ANNUAL REPORT 2015

UZ Leuven Transplant Council

2015

UZ LEUVEN | RAAD VOOR TRANSPLANTATIE

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



ANNUAL REPORT 2015

UZ Leuven Transplant Council

Edited by: UZ Leuven transplant coordination

Final editing and layout:
UZ Leuven communications department

E-mail: transplantatiecoordinatie@uzleuven.be

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PREFACE

Dear Professor, Colleague, Sir, Madam,

We are proud to present the Transplant Council's 2015 annual report. This brochure provides a summary of donor activities and results of the various transplant care programmes undertaken during the past year, i.e. 2015, compared to previous years. I would like to thank all those involved in donation and transplantation activities for the preparation of this annual report. For the second time the annual report is available in English.

In 2015 we saw a significant increase (+15%) in the number of actual donors (115) compared to 2014 (99). These numbers accounts to 56% of the total number of registered potential donors (206 in 2015). Actual donors include those deceased following both brain death (heart-beating or DBD; increase from 69 to 81) and those after cardiocirculatory arrest (non-heart-beating or DCD; increase from 30 to 34). The proportion of donors originating from UZ Leuven was only 10% (compared to 23% in 2014). We are happy that we can still rely on our partner donor hospitals. In total 411 organs have been recovered from all donors. Nine living kidney donors came forward in 2015.

Activities involving tissue procurement were substantial with 1,203 femur head donations and 506 umbilical cord blood samples.

On the national level, we recorded an increase (+11,7%) from 282 to 315 effective donors in 2015. The Leuven Organ Donation Partnership (LSGO) accounts for 36.5% of all deceased donors in Belgium.

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 2015 a total of 313 solid organ transplants were performed at UZ Leuven involving an organ from a deceased or living donor (an increase with 17 compared to 2014) representing a 30.7% share of all transplantations (1,018) in Belgium: 140 (29.7%) kidney, 68 (27.1%) liver, 64 (56.1%) lung, 27 (32.9%) heart (lung), and 4 (44.4%) pancreas transplants. No small bowel transplant and also no tracheal transplant were performed in 2015 in Belgium. In addition, 5 patients received 9 beta-cell allografts in total at UZ Leuven.

With guidance from Professor (emer) Dr. Patrick Ferdinande, services to the referring donor hospitals were further developed. In accordance with the federal law, additional training was offered by our transplant centre to local donor coordinators in the donor hospitals that have signed an agreement with UZ Leuven for collaboration. This resulted in the fifth successful LSGO training day and official meeting of our internal transplant board on 4 February 2015, preceeding the annual donor and transplantation symposium. Our special thanks goes to Margriet Goedhuys for perfectly organizing this annual meeting.

Organ perfusion is increasingly being used at UZ Leuven for preservation, assessment and reconditioning of organs. Hypothermic perfusion has been conducted since many years for kidneys recovered from non-heart-beating donors. Unfortunately, no reimbursement by the RIZIV is foreseen for this technique despite a posttive advice in an official report from the Federal Agency for Knowledge in Health Care (KCE) to the health authorities in 2014. Recently, normothermic perfusion of lungs and livers was started at our center as part of ongoing studies. We hope that in 2016 cardiac normothermic perfusion will become available in our center to resuscitate hearts recovered from non-heart-beating donors.

We would like to express our gratitude to all those responsible in referring donor hospitals for the trust they place in UZ 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 hospital possible in 2015.

Speaking on behalf of all members of the Transplant Council, I would like to express our hope that we can continue our successful cooperation in 2016.

Yours faithfully,

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

TRANSPLANT BOARD MEMBERS

• Luc Ampe	tissue bank activity centre, tissue coordinator representative
• dr. Johan De Coster	anaesthesiology
• 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
• prof. dr. Steven De Vleeschouwer	neurosurgery
• dr. Didier Desruelles	emergency medicine
• 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. Evelyne Lerut	bio banking activity centre, coordinator, donor work group representative
• prof. dr. Johan Maertens	haematology, bone marrow 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. Filip Rega	cardiac surgery, heart transplant representative
• prof. dr. Peter Sinnaeve	cardiology
• prof. dr. Johan Van Cleemput	cardiology, heart transplant 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. Wim Van Paesschen	neurology
• prof. dr. Dirk Van Raemdonck	thorax surgery, chairman of the transplant council
• prof. dr. Robin Vos	pneumology, lung transplant representative
• prof. dr. Joost Wauters	general internal medicine

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: UZ Leuven and partner hospitals

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

TABLE 1.1 | evolution of number of potential donor registrations 2001 - 2015. DBD or heart-beating donors (DCD or non-heart-beating donors) (hospitals with at least one donor registration in the past fifteen years)

Centre		01	02	03	04	05	06	07	08	09	10	11	12	13	14	2015 DBD/(DCD)
Aalst	OLV ZH – campus Aalst	11	5	4	3	4	5 (1)	6	3	-	2	3 (1)	3	6	2	**5 (1)**
Antwerpen	ZNA Stuivenberg	-	-	-	-	-	-	-	-	-	-	1	1	-	-	**-**
Assebroek	AZ St-Lucas	1	4	1	1	1	2 (1)	2	2	-	2	3	3	2	2 (1)	**2**
Bonheiden	Imelda ZH	1	-	4	3	1	2 (2)	7	4	3	4	4	5	9	5 (1)	**8 (1)**
Brugge	AZ St-Jan	2	2	3	4	2	4	5	3	11	3	9	3	2 (3)	2 (2)	**7 (3)**
Brussel	Kliniek St-Jan	-	-	-	-	-	-	1	-	-	-	-	-	-	-	**-**
Deinze	St-Vincentius ZH	1	-	-	-	- (1)	1	-	-	-	1	-	-	-	-	**-**
Dendermonde	AZ St-Blasius	-	-	-	-	-	-	-	-	-	-	-	2	-	(1)	**-**
Diest	AZ Diest	-	-	1	-	-	-	-	-	-	-	-	-	-	1 (1)	**1**
Genk	ZOL – campus St-Jan	12	10 (1)	10	6	13 (1)	15 (2)	15 (1)	9	9	12 (1)	11 (2)	12 (1)	13	14 (3)	**13 (1)**
Gent	AZ Maria Middelares	-	-	-	-	-	-	- (1)	-	-	-	-	-	-	-	**-**
Gent	AZ St-Lucas	8	3	3 (1)	7 (1)	4 (2)	4	-	-	-	-	-	-	-	-	**-**
Halle	AZ St-Maria	-	-	-	-	-	-	-	-	-	-	-	-	-	1	**-**
Hasselt	Jessa ZH	15	3	8	5	7	6	9 (1)	7 (3)	11 (3)	10	11 (4)	9 (6)	12 (5)	9 (5)	**10 (8)**
Herentals	AZ Herentals	-	-	-	-	-	-	1	-	-	-	-	1	2	(2)	**3 (1)**
Heusden	St-Franciskus ZH	1	-	2	6	3	7 (1)	3	5	2	3	9 (1)	7 (1)	6	2	**4**
Ieper	Jan Yperman ZH	1	-	-	-	1	1	1	-	1	6	2 (1)	3 (1)	1	2 (1)	**(3)**
Izegem	St-Jozefskliniek	-	-	-	-	-	-	-	-	- (1)	-	- (1)	-	-	-	**-**
Knokke - Blankenberge	AZ Zeno	-	-	-	-	-	1	-	-	-	2	1 (1)	-	1 (1)	-	**2**
Kortrijk	AZ Groeninge	3	2	4	2	11	7	10	6	7 (1)	2	14	11	5 (1)	10 (2)	**12 (2)**
Lier	H. Hart ZH	3	2	5	2	3	7 (1)	7	6	4 (1)	3 (1)	8	4 (2)	6 (1)	8 (4)	**5 (3)**
Maaseik	ZH Maas en Kempen	-	-	-	-	-	-	-	-	-	-	-	-	-	1 (1)	**1**
Malle-Zoersel	AZ St-Jozef	-	2	-	1	2	1	-	1	(1)	1	1 (1)	-	-	1 (1)	**-**
Mechelen – Duffel	AZ St-Maarten	-	-	-	-	-	-	-	1	-	2	1	-	3	-	**2**
Menen	AZ Delta – campus Rijselstraat	3	1 (1)	1	-	1	2	-	-	-	1	-	-	1 (1)	(1)	**1**
Mol	H. Hart ZH	-	-	-	-	1 (1)	1	(1)	1	1	-	2	-	2 (1)	-	**-**
Oostende	AZ Damiaan	3	5	4	6	1	7	4 (1)	6 (2)	2 (1)	1	1	3 (1)	2 (2)	2 (3)	**2 (2)**
Overpelt	Maria ZH	-	-	-	-	-	-	(1)	1	1 (1)	-	(1)	(1)	-	(1)	**2**
Roeselare	AZ Delta – campus Wilgenstraat	14	16	12	19	13 (1)	14 (4)	13 (1)	10 (6)	12 (4)	15 (3)	9 (8)	15 (13)	18 (17)	18 (9)	**23 (11)**
Ronse	AZ Glorieux	1	-	-	-	-	-	-	-	-	-	-	-	-	1 (2)	**3 (1)**
St-Niklaas	AZ Nikolaas	5	5	3	4 (1)	-	-	3	3	1	2 (1)	3	1	2	2	**3**
St-Truiden	St-Trudo ZH	2	-	1	3	-	1	1	1	6	4	1	2	3	3	**2 (1)**
Tielt	St-Andries ZH	3	-	-	2	-	1	3	1	-	1	2	1	1	1	**2 (3)**
Tienen	Regionaal ZH H. Hart	-	-	-	-	1	-	-	-	-	-	-	-	-	(1)	**1**
Tongeren	AZ Vesalius	-	-	-	-	-	2	-	1	1	-	-	2	-	1 (3)	**-**
Torhout	AZ St-Rembert	-	-	-	-	-	2	-	1	-	2	1 (1)	1	-	(1)	**-**
Turnhout	AZ Turnhout	2	2	4	4	6	3	3 (3)	4	4	7	12	8	5 (1)	7	**2 (1)**
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)	**8 (4)**
Vilvoorde	AZ Jan Portaels	-	-	-	-	1	-	-	-	1	1	1	1 (2)	1	-	**1**
Waregem	OLV van Lourdes ZH	-	1	-	-	1	-	(1)	1	1 (1)	1	-	1	-	(2)	**-**
Zottegem	AZ St-Elisabeth	-	3	1	-	1	1	1	-	-	-	-	-	-	-	**-**
Leuven	UZ Leuven	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)	**22 (13)**
SUBTOTAL	DBD / heart-beating	**110**	**87**	**97**	**99**	**115**	**119**	**129**	**102**	**113**	**132**	**153**	**137**	**149**	**129**	**147**
SUBTOTAL	DCD / non-heart-beating	**-**	**2**	**2**	**4**	**10**	**12**	**18**	**27**	**27**	**32**	**47**	**46**	**62**	**72**	**59**
TOTAL		**110**	**89**	**99**	**103**	**125**	**131**	**147**	**129**	**140**	**164**	**200**	**183**	**211**	**201**	**206**

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

	2011	2012	2013	2014	2015
Actual donors	108 (54%)	101 (55,2%)	97 (46%)	99 (49,3%)	115 (55,8%)
Potential donors, of which were refused:	92 (46%)	82 (44,8%)	114 (54%)	102 (50,7%)	91 (44,2%)
Medical contra-indication, of which in situ refusal	56 (60,9%), 9 (9,8%)	44 (53,7%), 1 (1,2%)	65 (57%), 5 (4,4%)	57 (55,9%), 7 (6,9%)	50 (55%) 4 (4,4%)
'Not brain dead' and no potential DCD cat. II - III because of various factors (no DCD cat. III protocol in donor hospital – patient too old – precarious condition - . . .)	10 (10,9%)	19 (23,2%)	15 (13,2%)	16 (15,7%)	15 (16,5%)
Donor refusal (National register)	2 (2,2%)	1 (1,2%)	3 (2,6%)	4 (3,9%)	4 (4,4%)
Informal donor refusal (start registration 8/2015)	-	-	-	-	5 (5,5%)
Family refusal	22 (23,9%)	16 (19,5%)	28 (24,6%)	24 (23,5%)	16 (17,6%)
Refused by public prosecutor's office	2 (2,2%)	2 (2,4%)	-	-	1 (1,1%)
Legal contra-indication	-	-	3 (2,6%)	1 (1%)	-

TABLE 1.3 | evolution of the number of actual donors 2001 - 2015. DBD or heart-beating donors (DCD or non-heart-beating donors) (hospitals with at least one actual donor registration)

Centre		01	02	03	04	05	06	07	08	09	10	11	12	13	14	2015 DBD/(DCD)
Aalst	OLV ZH – campus Aalst	10	3	4	2	2	4	4	3	-	2	2 (1)	1	5	2	**5 (1)**
Antwerpen	ZNA Stuivenberg	-	-	-	-	-	-	-	-	-	-	1	-	-	-	**-**
Assebroek	AZ St-Lucas	-	3	1	-	-	-	2	1	-	2	3	3	-	1	**1**
Bonheiden	Imelda ZH	-	-	4	1	-	2	5	2	1	2	1	3	4	4	**6**
Brugge	AZ St-Jan	2	-	2	3	1	3	4	3	9	3	6	3	(3)	2 (2)	**5 (3)**
Deinze	St-Vincentius ZH	-	-	-	-	-	1	-	-	-	1	-	-	-	-	**-**
Dendermonde	AZ St-Blasius	-	-	-	-	-	-	-	-	-	-	-	1	-	-	**-**
Genk	ZOL – campus St-Jan	9	9	9	5	11	12 (1)	12 (1)	5	7 (1)	9 (1)	9 (1)	6 (1)	7	9	**9**
Gent	AZ Maria Middelares	-	-	-	-	-	-	(1)	-	-	-	-	-	-	-	**-**
Gent	AZ St-Lucas	6	1	2 (1)	5 (1)	2	4	-	-	-	-	-	-	-	-	**-**
Hasselt	Jessa ZH	12	2	5	4	3	3	4	5 (1)	5 (1)	9	7 (2)	5 (2)	6 (3)	4 (3)	**7 (6)**
Herentals	AZ Herentals	-	-	-	-	-	-	-	-	-	-	-	-	-	(2)	**2 (1)**
Heusden	St-Franciskus ZH	1	-	2	6	-	6 (1)	3	4	2	1	5	3	4	1	**3**
Ieper	Jan Yperman ZH	-	-	-	-	1	-	-	-	1	2	2	2	1	(1)	**(3)**
Kortrijk	AZ Groeninge	2	2	4	2	8	6	6	3	7	1	8	7	4 (1)	6 (1)	**6 (1)**
Lier	H. Hart ZH	1	1	4	2	3	4 (1)	3	4	2 (1)	2	8	4 (1)	2	6 (2)	**3 (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	-	**2**
Menen	AZ Delta – campus Rijselstraat	2	-	-	-	1	-	-	-	-	-	-	-	1 (1)	(1)	**1**
Mol	H. Hart ZH	-	-	-	-	-	-	-	-	1	-	2	-	1 (1)	-	**-**
Oostende	AZ Damiaan	3	5	-	2	-	4	2	4	1 (1)	-	-	2 (1)	(1)	1	**2 (1)**
Overpelt	Maria ZH	-	-	-	-	-	-	-	1	(1)	-	(1)	-	-	(1)	**1**
Roeselare	AZ Delta – campus Wilgenstraat	10	11	10	8	9	11	11 (1)	2 (1)	8 (2)	11	6 (3)	12 (6)	11 (4)	10 (2)	**13 (5)**
Ronse	AZ Glorieux	-	-	-	-	-	-	-	-	-	-	-	-	-	1 (1)	**-**
St-Niklaas	AZ Nikolaas	5	5	3	2 (1)	-	-	3	3	1	1	3	1	2	2	**3**
St-Truiden	St-Trudo ZH	1	-	1	3	-	-	1	-	3	4	1	1	3	1	**1 (1)**
Tielt	St-Andries ZH	1	-	-	-	-	-	1	1	-	1	2	-	-	-	**1 (2)**
Tienen	Regionaal ZH H. Hart	-	-	-	-	-	-	-	-	-	-	-	-	-	-	**1**
Tongeren	AZ Vesalius	-	-	-	-	-	1	-	-	1	-	-	1	-	(1)	**-**
Torhout	AZ St-Rembert	-	-	-	-	-	1	-	-	-	-	1 (1)	1	-	-	**-**
Turnhout	AZ Turnhout	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)	**2 (2)**
Vilvoorde	AZ Jan Portaels	-	-	-	-	1	-	-	-	-	-	1	- (2)	-	-	**1**
Waregem	OLV van Lourdes ZH	-	1	-	-	-	-	(1)	1	1 (1)	1	-	-	-	-	**-**
Zottegem	AZ St-Elisabeth	-	1	1	-	1	1	1	-	-	-	-	-	-	-	**-**
Leuven	UZ Leuven	14	11	19 (1)	14	17 (1)	10	16	9 (4)	9 (2)	10 (3)	13 (3)	14 (5)	19 (4)	13 (10)	**6 (6)**
SUBTOTAL	DBD - heart-beating	81	60	74	65	67	75	81	60	67	79	96	81	77	69	**81**
SUBTOTAL	DCD - non-heart-beating	-	-	2	2	1	3	5	8	16	11	12	20	20	30	**34**
TOTAL		81	60	76	67	68	78	86	68	83	90	108	101	97	99	**115**

115 actual donors were registered in 2015, an increase of 16% in comparison to 2014 (99 actual donors).

We would like to express our sincerest gratitude to the many colleagues of LSGO hospitals and UZ 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 UZ Leuven and partner hospitals 1996 - 2015

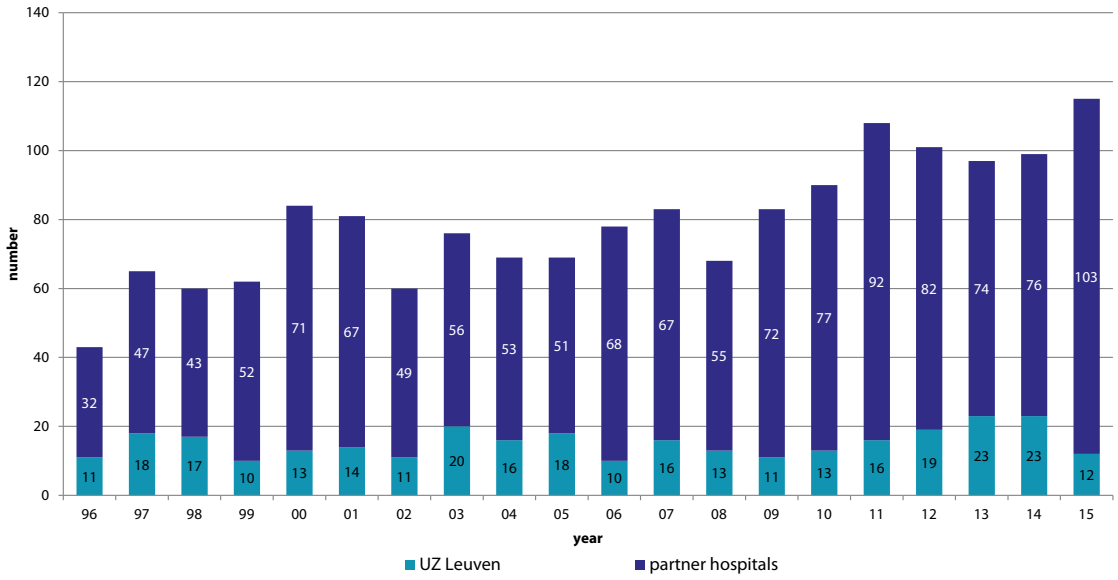


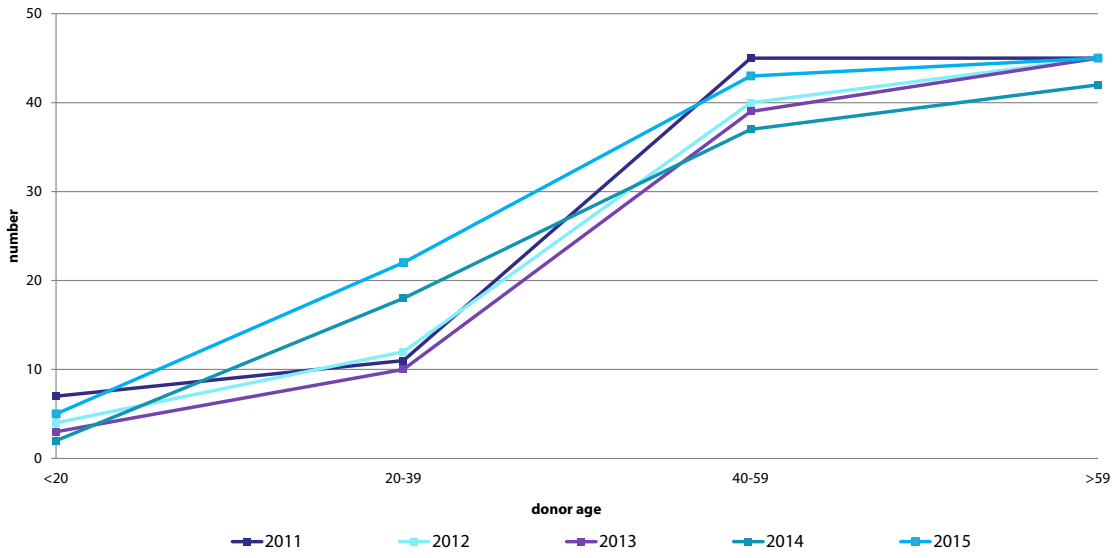
Table 1.4 illustrates the cause of death of potential donors (2001 - 2015): 68,5% died of cerebrovascular disease; 20,4% died due to trauma.

TABLE 1.4 | donor profile: cause of death (potential donors UZ Leuven and collaborating hospitals 2001-2015)

	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)	14 (n=201)	2015 (n=206)
Traumatic brain injury (traffic + other)	51%	26%	37%	40%	27%	32%	28%	35%	22,9%	25%	27,5%	20,7%	17,1%	20,9%	**20,4%**
Cerebrovascular disease:															
- spontaneous intra-cranial haemorrhage	39%	51%	41%	51%	50%	43%	41%	39%	32,9%	40,2%	34%	43,2%	38,4%	32,3%	**37,9%**
- cerebral infarction	4%	9%	5%	6%	5%	6%	6%	7%	12,1%	6,7%	13,5%	7,7%	9,9%	10%	**7,8%**
- anoxia	2%	2%	6%	2%	11%	14%	19%	14,5%	6,4%	18,3%	18%	18,6%	27,5%	22,9%	**22,8%**
Tumours	2%	-	1%	1%	1,5%	1,5%	1,5%	-	2,9%	2,4%	0,5%	1,1%	0,5%	1%	**0,5%**
Intoxication	-	3%	4%	-	3%	1,5%	1,5%	2,5%	1,4%	1,2%	0,5%	0,5%	0,5%	-	**1,9%**
Suicide	2%	6%	4%	-	1,5%	1%	1,5%	1%	0,7%	1,2%	5%	3,3%	4,3%	11,4%	**7,2%**
Bacterial meningitis	-	3%	2%	-	1%	1%	1,5%	1%	0,7%	1,2%	-	2,7%	-	-	**1%**
Euthanasia	-	-	-	-	-	-	-	-	0,7%	-	-	2,2%	0,5%	0,5%	**0,5%**

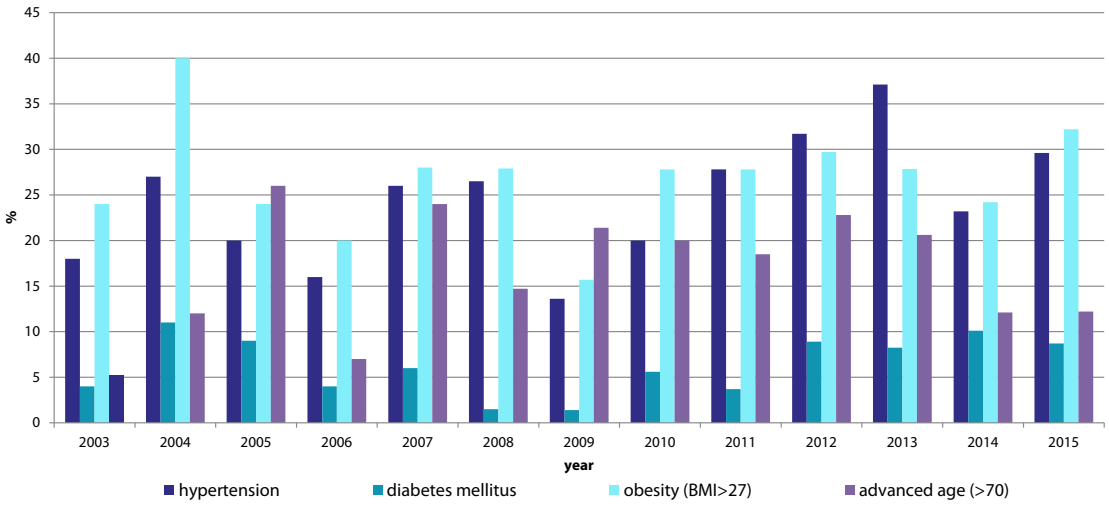
Figure 1.2 shows the classification into age categories of the actual donors in 2015 (compared to those in 2010, 2011, 2012, 2013 and 2014) which illustrates that the number of young donors (aged <20) slightly increased and the number of donors (20-39) has continued to increase to its highest level (in comparison to previous years). The number of 'older' donors (>59) remains the largest group.

FIGURE 1.2 | actual donor profile: age (UZ Leuven and partner hospitals 2010 - 2011 - 2012 - 2013 – 2014 vs 2015)



A remarkable part of the recorded donors are associated with co-morbidity (hypertension: 29.6%, diabetes mellitus: 8.7% and obesity: 32.2%) and advanced age (12.2%).

FIGURE 1.3 | donor profile: associated co-morbidity and advanced age (actual donors in UZ Leuven and partner hospitals 2003 - 2015)



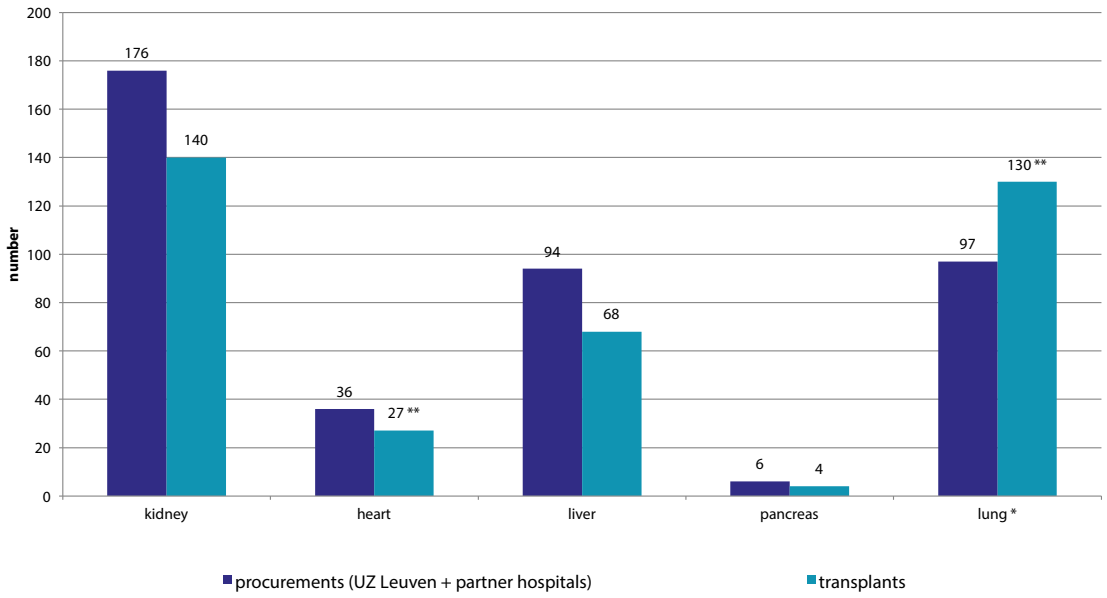
In 2015 an average of 3.57 organs (3,21 in 2014) was procured per donor.

TABLE 1.5 | type and number of procured organs UZ Leuven and partner hospitals 2003 - 2015

	03	04	05	06	07	08	09	10	11	12	13	14	2015
Kidney (single)	125	111	80	102	132	103	135	130	142	147	121	136	**176**
Heart (± lung)	36	29	21	19	25(1)	23	27	26	23	30	23	22	**36**
Liver (+ split-liver)	68	57	68	67	69(3)	60	71	74 (6)	92 (4)	80 (6)	84 (4)	77 (4)	**92 (4)**
Pancreas	4	13	7	5	12	6	6	8	3	-	-	1	**6**
Lung (single)	51	46	49	59	52	45	66	75	77	88	66	78	**97**
Total	**284**	**256**	**225**	**252**	**294**	**237**	**305**	**319**	**341**	**351**	**298**	**318**	**411**

In 2015 more kidneys (+26), more lungs (+12) but slightly less livers (-4) were transplanted. The number of heart and pancreas transplants remained more or less equal.

FIGURE 1.4 | number of organs (deceased donors only, UZ Leuven and partner hospitals) procured by UZ Leuven and number of (deceased donor) organ transplants at the UZ Leuven in 2015Leuven in 2015



* the number relates to the number of lungs: 47 double and 3 single lung procurements (n=97) and 64 double lung transplants (n=128)

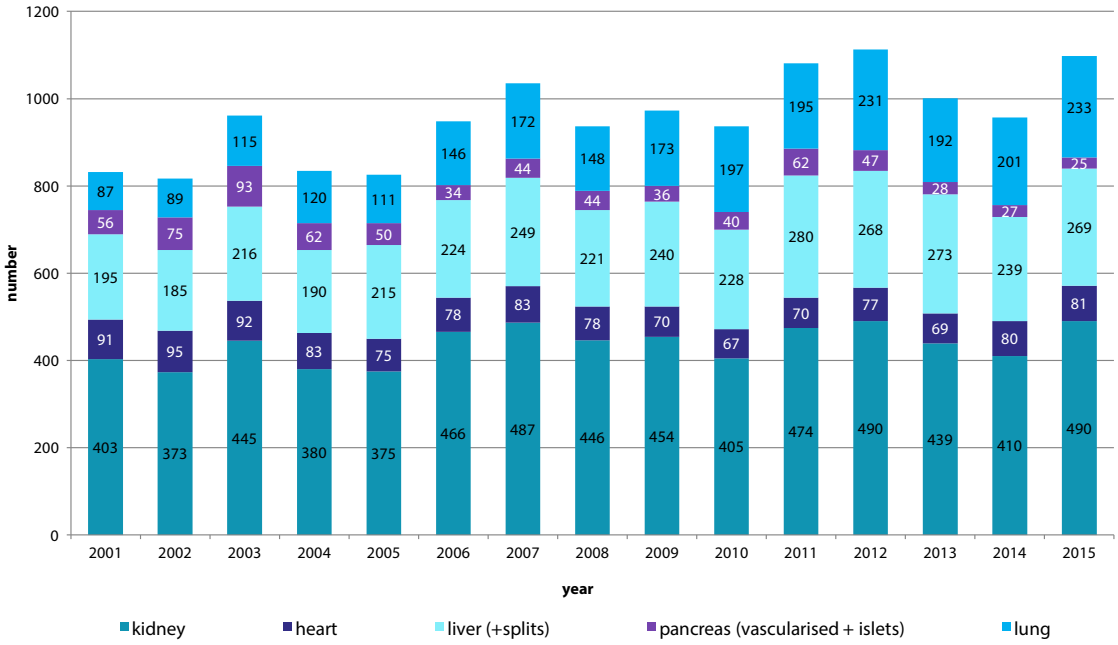
** heart-lung transplants included

Organ donation in Belgium

In 2014 the actual donor number in Belgium was 282, which equates to 25.2 donors per million inhabitants (pmi) *(figure 1.5)*. In 2015 we recorded 315 actual organ donors, an increase to 28 donors pmi (source Eurotransplant).

FIGURE 1.5 | evolution of the number of actual donors (DBD + DCD) in Belgium 1996 - 2015

FIGURE 1.6 | type and number of procured organs in Belgium 2001 - 2015



PART 2

ABDOMINAL TRANSPLANTS

surgery
abdominal transplant surgery

internal medicine
endocrinology
gastroenterology
hepatology
nephrology

transplant coordination

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

abdominal transplant surgery
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prof. dr. Diethard Monbaliu, prof. dr. Ina Jochmans

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

gastroenterology
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HILA
prof. dr. Marie-Paule Emonds

teams OR – ICU – hospitalisation
Liesbeth De Meyer, Magda Penninckx, Sus Vermeiren, Carine Breunig

nursing consultants
Mathilde Dehairs, Carine Breunig

transplant coordination
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

Small bowel and multivisceral transplant care program

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 an important surgical, clinical and immunological challenge.

The main reason is that by definition the intestine is an infected organ, which is highly sensitive to rejection and consequently requires high-dose immunosuppressive therapy. Moreover, prior to the intestinal transplantation, patients often already underwent various surgical procedures and were seriously undernourished. Factors such as these explain a global ten-year survival rate of 47%, as reported by the international intestinal transplant registry.

The small bowel transplant program for adults and children was launched at UZ 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 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 patient survival rate in this group (n=14) is 92% with an early (< 3 months after transplantation) acute rejection in 3 patients (21%), which was reversible in all with immunosuppression.

INTESTINAL TRANSPLANTATION

Until now 3 067 intestinal transplants have been carried out worldwide -based on the latest report of the international intestinal transplant registry (2015). 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 solid abdominal organs.

Therefore, the laboratory for abdominal transplant surgery has developed, in conjunction with the laboratory for experimental transplantation, 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 like 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 (Ceulemans et al. The Leuven immunomodulatory protocol promotes T-regulatory cells and substantially prolongs survival after first intestinal transplantation. Am J Transplant 2016).

Until now this protocol was applied at the University Hospitals of Leuven in 14 consecutive intestinal transplant recipients of a deceased donor (follow-up ranges from 1 to 13.5 years). The last 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. There were 8 female and 6 male patients transplanted and 3 patients were children aged 2, 3 and 9 years; 5 patients received an isolated intestinal transplant (with an additional kidney in three cases), 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 that 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 embolized the native arterial inflow to the stomach, liver, duodenum, pancreas and small bowel just prior to exenteration. A technique never reported before for this indication *(Figure 2.1)*.

Despite the fact that intestinal transplantation is characterized by acute rejection, only 3 of these 14 patients (n=14) developed early rejection (acute rejection within 3 months of the transplant) (21%), of which one suffered from Crohn´s disease. One of them and 2 other patients developed an episode of late rejection (rejection later than 3 months after transplantation) (21%). All rejections were reversible with high-dose of steroids. 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 also suffered from Crohn's disease. Crohn's disease, and its genetic background, could potentially have been an additional risk factor.

In addition to the above mentioned patient who died from an aspergillus infection, our first transplant patient died in 2012 (12 years after the transplant) as a result of non-steroidal anti-inflammatory drugs which led to diffuse ulcerations of the intestinal wall via which bacteria were able to enter the blood stream, which led to a massive inflammatory reaction and graft loss.

Twelve of the 14 patients are still alive today. Eleven of them have a successfully functioning intestine and were able to resume their day to day activities. The other patient lost her bowel graft due to a severe intestinal infection following a protocol biopsy. The patient required total parental nutrition and could safely return home.

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, 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 informed that she passed away in 2012 (almost 5 years after transplantation).

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 2016, 1 patients was actively listed for intestinal transplantation at our center, awaiting an isolated small intestinal transplant (in combination with an abdominal fascia and kidney transplant).

One of the most important aspects in the latest report of the international intestinal transplant registry (2015), 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 2014 this number had dropped to 100. Possible explanations for this recent 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 dramatically deterioration of the clinical condition pre-transplant.
That is why we, in Leuven, took the initiative in the past three years, in conjunction with the unit of gastroenterology and pathology, to initiate two international studies with colleagues from Beaujon (France), Birmingham (UK), Buenos Aires (Argentina) and Maastricht (the Netherlands). 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. With our increasing understanding of the importance of microbiota in transplantation and its effect on rejection, we launched – in collaboration with the unit of molecular bacteriology – a prospective follow-up of the microbiota of our intestinal transplant cohort.

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).

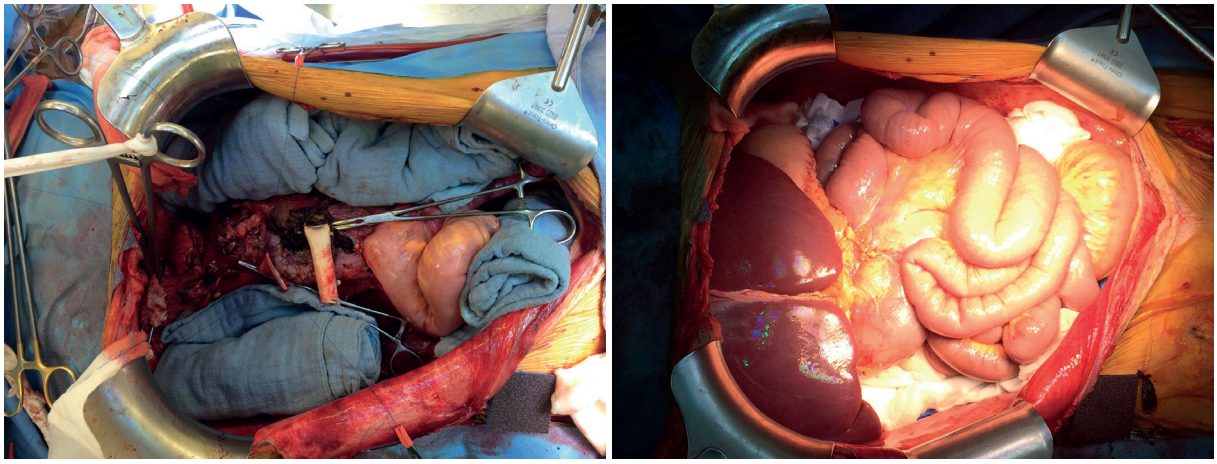
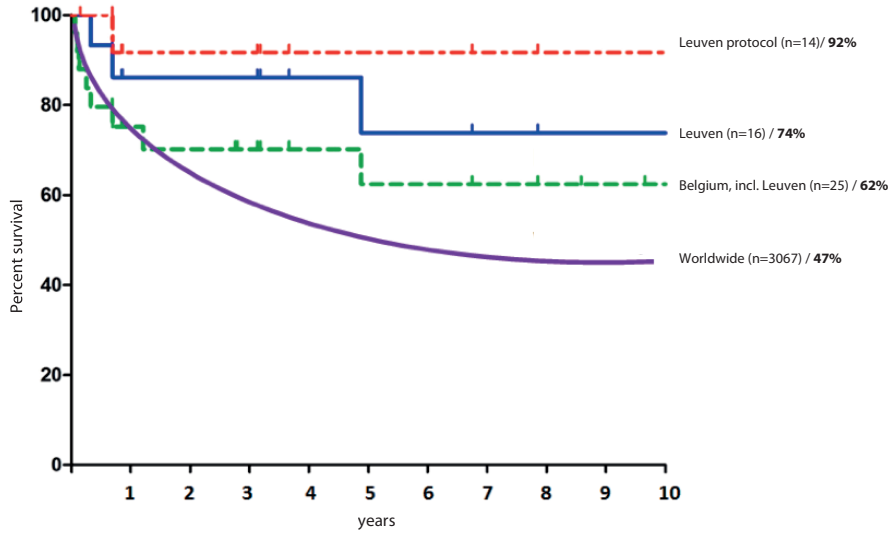


FIGURE 2.2 | survival curve intestinal transplantation UZ Leuven (protocol: n=14; and total experience: n=16) versus Belgium (including UZ Leuven; n=25) versus global experience (International Intestinal Transplant Registry; n= 3067).



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prof. dr. Frederik Nevens, prof. dr. Werner Van Steenbergen
prof. dr. Chris Verslype, prof. dr. David Cassiman
prof. dr. Wim Laleman, prof. dr. Schalk Van der Merwe

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

medical intensive care medicine
prof. dr. Alexander Wilmer, dr. Philippe Meersseman
prof. dr. Joost Wauters, prof. dr. Wouter Meersseman
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anaesthesiology
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teams OR – perfusion – ICU – hospitalisation
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nursing consultant
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dietary advice
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speech therapy
Sofie Van Craenenbroeck

Liver transplant care programme

Thanks to the use of DCD (Donation after Circulatory Death) donors, the number of liver transplantations remains stable in UZ Leuven. The survival rate at 5 years is 80%. This number also remains stable by the use of older donors (> 70 years). The outcome of transplant patients with these organs is similar to the outcome of patients transplanted with a liver from a younger donor.

More and more ill/sick patients are transplanted: patients with a MELD-score >30, meaning that >80% dies/ succumbs within 3 months without liver transplantation. The survival rate at 5 years for these patients remains 70%.

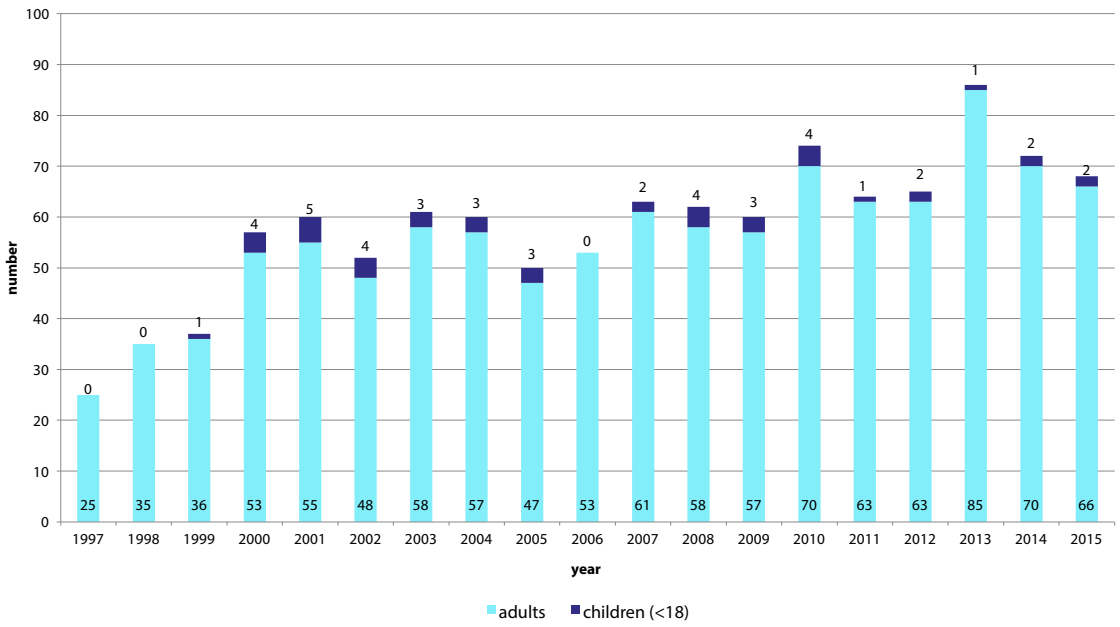
The combined transplant programme also remains very active with excellent results (11% of the transplant activity).

LIVER TRANSPLANTATION

Transplant activities

68 liver transplants were carried out in 2015, which fluctuates around the average number of liver transplants of the last 5 years (n=70). This is 30% of the total number of liver transplants carried out in our country. Since the department of abdominal transplant surgery was set up in 1997, a total number of 1103 liver transplants were performed. Before, from 1989 until 1996, 104 liver transplants were performed. This brings the total amount of liver transplants performed in UZ Leuven to 1207.

FIGURE 2.3 | number of liver transplants 1997-2015 UZ Leuven



Recipients

Etiology

Hepatocellular carcinoma (HCC) and post-alcohol cirrhosis are the most common indications for liver transplantation. The highest number of transplantation is performed in patients with a malignancy and/or complications of post-alcohol cirrhosis.

TABLE 2.1 | indication for liver transplantation 1997-2015 UZ Leuven (n=1103)

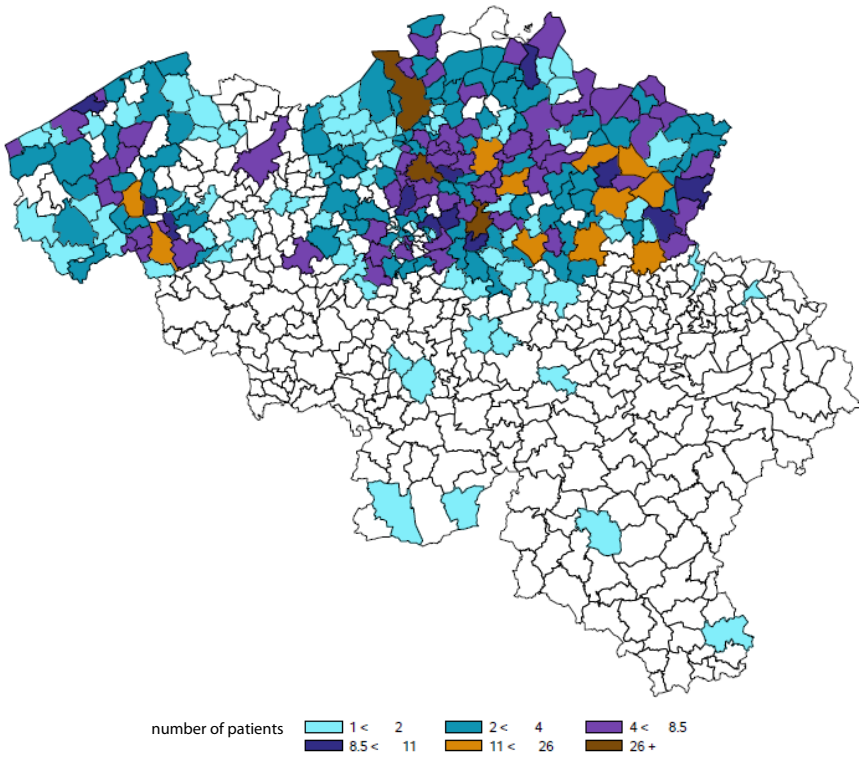
Indication	Number	%
Malignancy (HCC)	283	26%
Malignancy (other *)	16	1%
Viral hepatitis	181	16%
HCV without HCC	48	
HCV with HCC	78	
HBV without HCC	32	
HBV with HCC	23	
Post-alcohol	282	25%
without HCC	191	
with HCC	91	
Cholestatic	86	8%
PBC (primary biliary cirrhosis)	34	
PSC (primary sclerosing cholangitis)	52	

Indication	Number	%
Polycystosis	72	7%
Congenital/metabolic liver disease	87	8%
NASH	75	7%
without HCC	41	
with HCC	34	
Children < 18 year	43	4%
Acute liver failure	92	8%
Other (Budd Chiari, cryptogenic, auto-immune, benign tumors and other liver diseases)	98	9%
Re-transplantation	83	7%
Early (≤ 90 days after 1st tx)	28	
Late (> 90 days after 1st tx)	55	

*** Epithelioïd hemangioendothelioma, biliary tract carcinoma (Klatskin), …**

Geographic origin

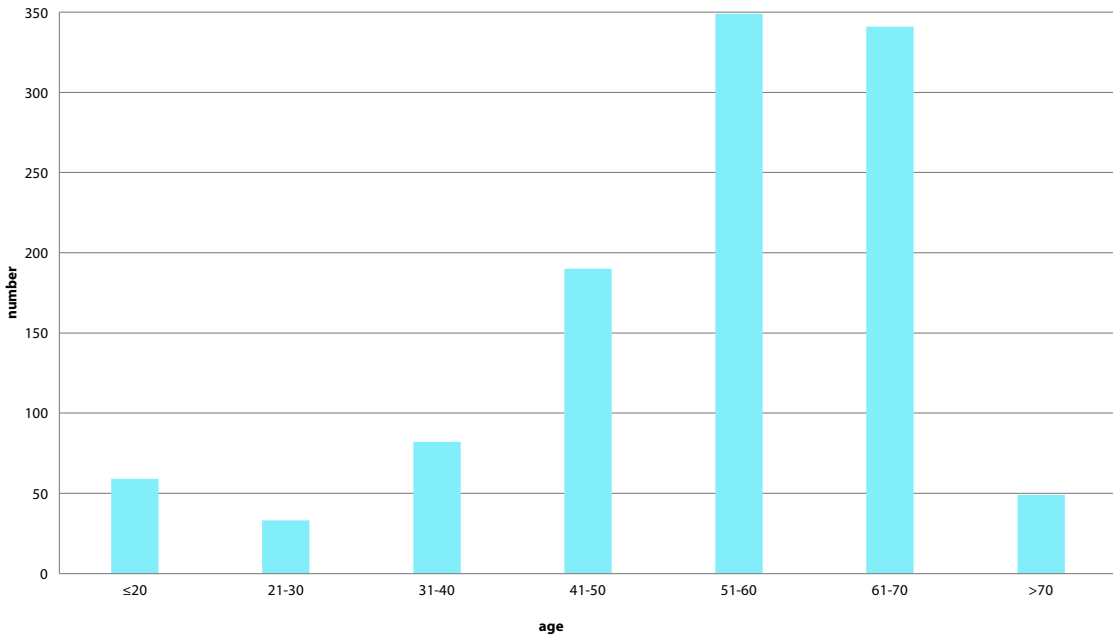
FIGURE 2.4 | geographic origin of liver recipients



Age distribution

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

FIGURE 2.5 | age distribution liver recipients 1997 to 2014

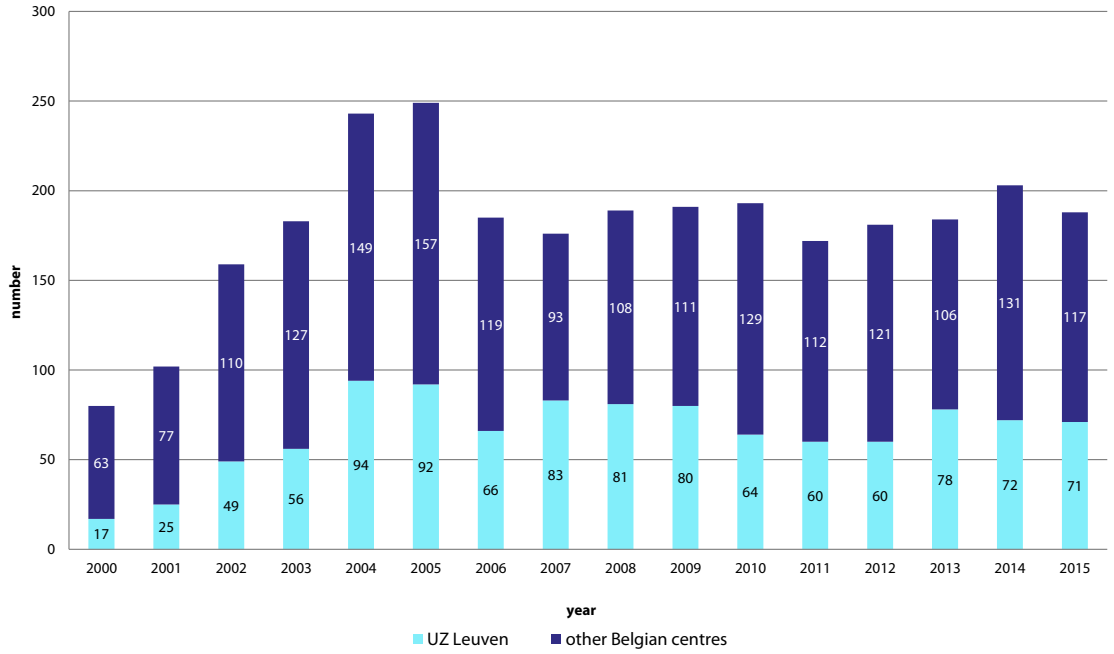


Waiting list data

Active waiting list in Belgium and UZ Leuven

At the end of 2015 the number of patients awaiting a liver transplant in Belgium was 188 patients, of which 71 patients (37%) from our center. The mean number of patients awaiting a liver transplant in our center in the last 5 years was 68/year.

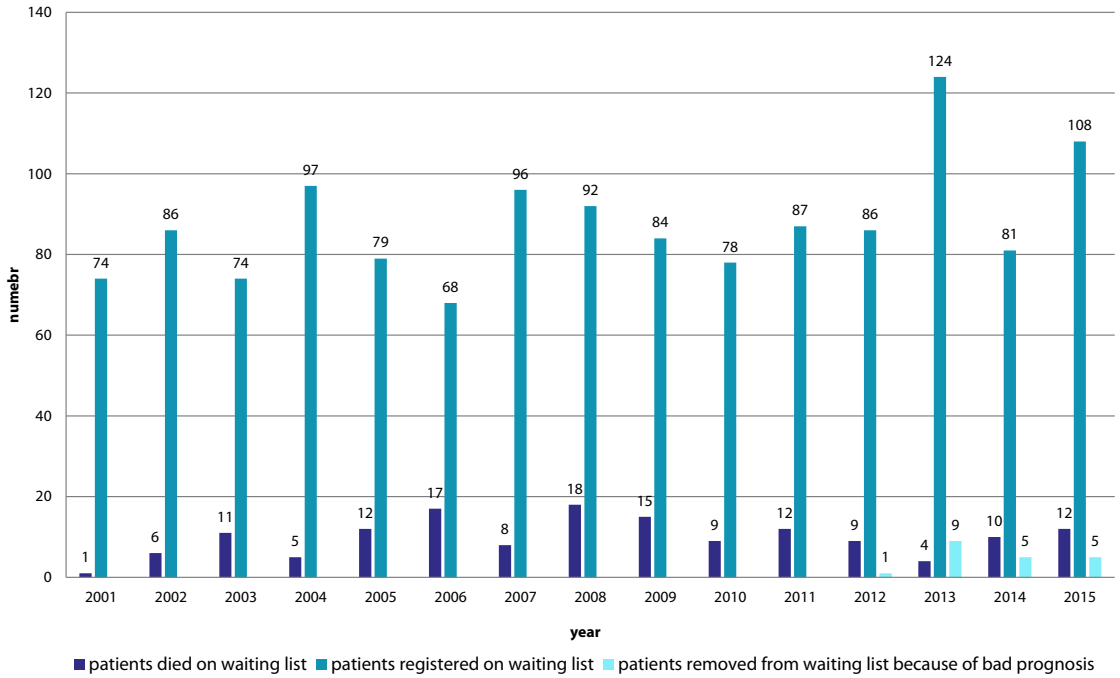
FIGURE 2.6 | evolution of the number of Belgian patients on the active Eurotransplant liver waiting list since 2000, UZ Leuven compared to the other liver transplant centers (number of transplant centers in Belgium n=6)



Registrations and deaths on the waiting list

In 2015, 108 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 97/year. Unfortunately twelve patients died on the waiting list and five patients were removed from the list mostly because of too bad prognosis (i.a. progression of HCC). Since 2012 the mean number of deaths on the waiting list is 13/year. This a mean drop out of 13% per 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 Eurotransplant 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: creatinine, bilirubin and protrombine-time (PT). 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 2015, 41% of our patients received a liver which was allocated based on the MELD score.
- In 2015, 29% of our patients received a liver which was allocated based on a standard exception (SE). The most common standard exception was HCC. Recipients must fulfill specific criteria before a standard exception can be granted.
  Some patients don 't fulfill these criteria. In that case a non-standard exception (NSE) can be requested. In 2015 ten patients (15%) received a liver which was allocated based on a NSE.
- In 2015 six livers were allocated to patients with acute liver failure (HU) (9%).
- Four liver transplantations (4%) were combined with a double lung transplantation. An 'approved combined organ' (ACO) can not be obtained for a combined liver kidney transplantation.

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%)
2015	28 (41%)	20 (29%)	10 (15%)	10 (15%)

The purpose of the liver allocation system is to give priority to the sickest patients.
This table shows that patients suffering from acute liver failure (HU) only wait a few days before receiving a liver transplant, and this for all blood types. For patients with an exception rule (SE or NSE) the median waiting time for all blood types is less than 1 year.

TABLE 2.3 | Waiting time in days (median) according to the blood group and status (HU – ACO – SE – NSE) 2011-2015 (n=355)

	HU	ACO	SE	NSE
A	4 (0-9) n= 11	101 (22-487) n=7	215 (2-1649) n=50	312 (156-1203) n=8
B	3 (2-5) n=4	(36-112) n=2	163 (21-2291) n=8	112 (98-137) n=3
0	3 (0-29) n=20	(82-492) n=2	169 (20-2255) n=52	329 (40-887) n=6
AB	-	(54-964) n=2	127 (81-201) n=4	-

The number of "center driven offers" has strongly increased over the last years. This is mainly due to the increasing number of DCD donors whose livers are always offered as center offers.

TABLE 2.4 | number of patients transplanted via patient-driven allocation (match Meld) versus centre driven offer (2011-2015)

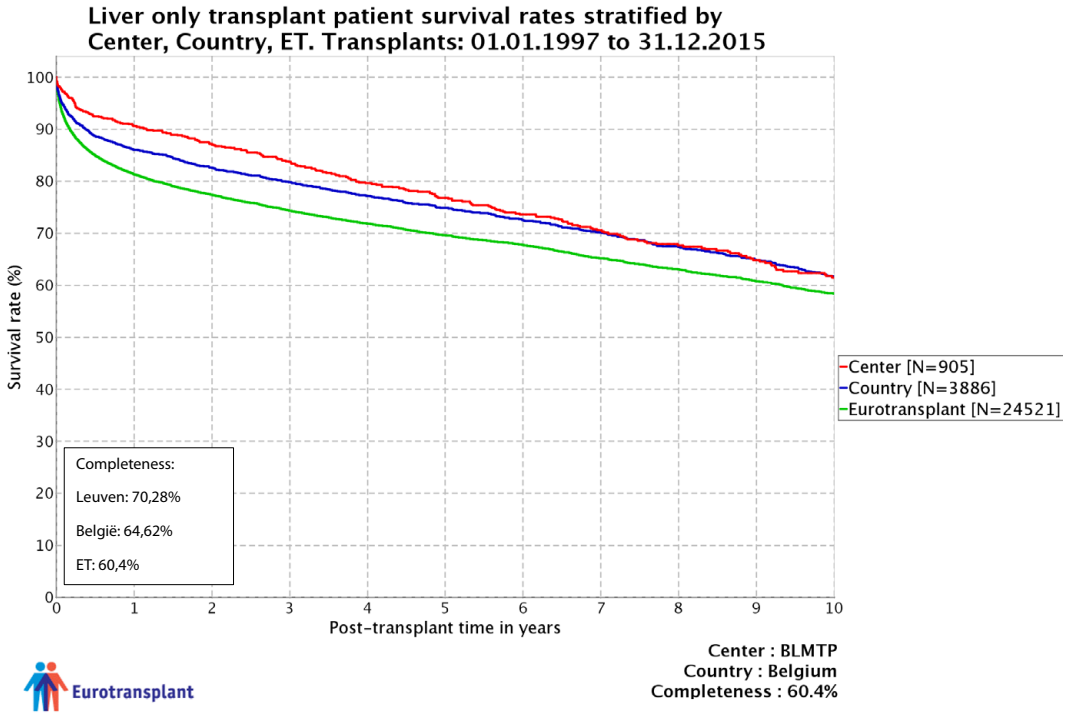
	patient-driven	centre-driven
2015	37 (54%)	31 (46%)
2014	51 (71%)	21 (29%)
2013	64 (74%)	22 (26%)
2012	48 (74%)	17 (26%)
2011	44 (69%)	20 (31%)

Patient and graft survival

UZ Leuven versus Belgium and Eurotransplant

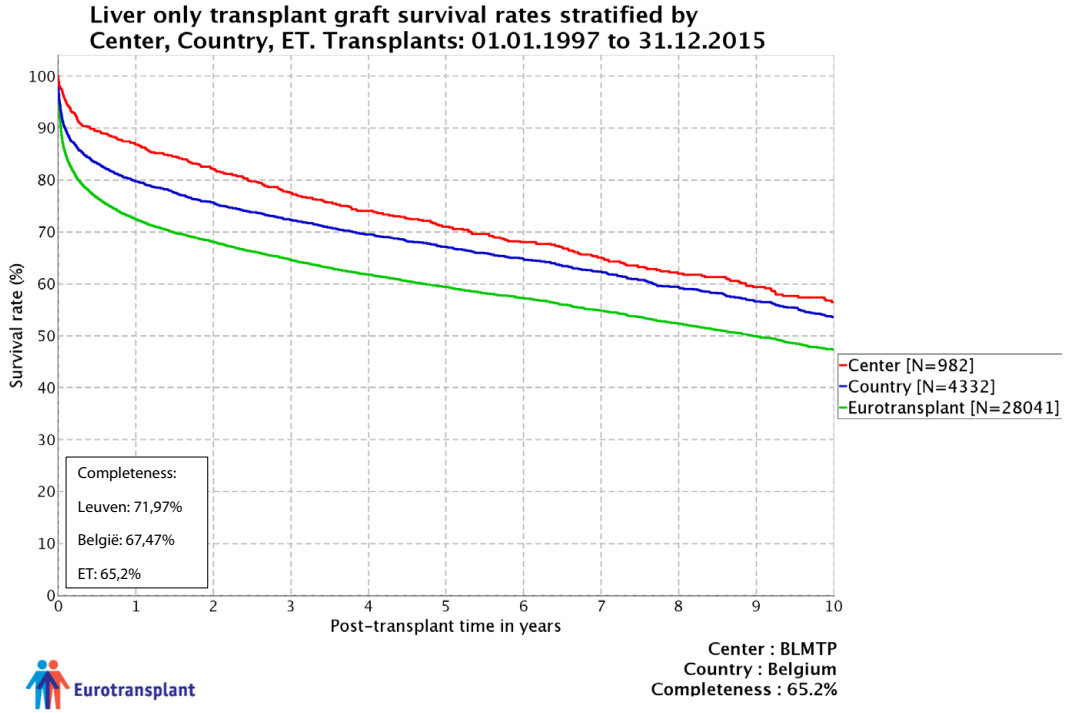
The figure below shows patient survival rates for all patients who underwent a solitary liver transplantation in the period of 1997-2015. The actuarial patient survival rate in UZ Leuven is considerably higher when compared to the results of Eurotransplant and Belgium. These differences are immediately obvious from the post operative period on.

FIGURE 2.8 | ten-year patient survival (1997-2015 all indications – liver only transplants), UZ Leuven in comparison to Eurotransplant and Belgium (the figures for Belgium also include the results for UZ Leuven). Source: Eurotransplant



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

FIGURE 2.9 | ten-year graft survival (1997-2015 all indications – liver only transplants), UZ Leuven in comparison to Eurotransplant and Belgium (the figures for Belgium also include the results for UZ Leuven). Source: Eurotransplant



Need for retransplantation

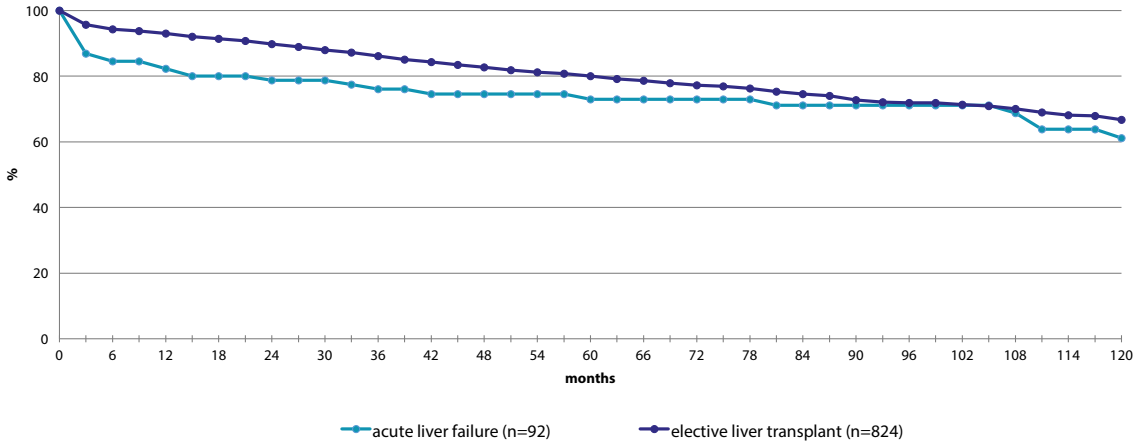
The need for early retransplantation (≤90 days) reflects the expertise of the procurement team and the competence of the surgical transplant team. In 2015 only one patient required early retransplantation due to thrombosis of the hepatic artery.

The need for late retransplantation (>90 days) in UZ Leuven was 4% (n=3) in 2015 and also remains low and stable. 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 results on long term are identical.

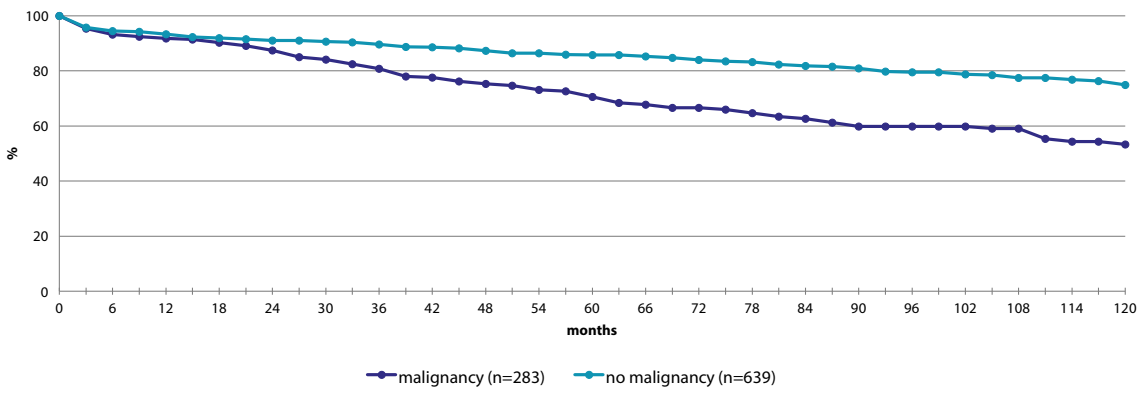
FIGURE 2.10 | ten-year patient survival (1997-2015) for transplant due to acute liver failure versus elective liver transplant (without combined transplants or retransplantations). Source: UZ Leuven database



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 the survival rate in the first 2 years. In the long term, however, there is a marked difference 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 patient survival (1997-2015) for transplant due to malignancy versus no malignancy (no retransplantations). Source: UZ Leuven database



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

In 2015, 10 combined liver transplants were carried out in UZ Leuven, which brings the total of combined liver transplants since 1997 to 125. This is more than 11% of the total number of liver transplants carried out at our center. In 2015 four livers were transplanted in combination with a double lung transplant and six livers were combined with a kidney transplant. The 10 year survival of these patients is excellent and amounts to 75%, comparable with patients who received a solitary liver transplant (without malignancy).

FIGURE 2.12 | ten-year patient survival (1997-2015) for combined liver transplants versus liver transplant only without malignancy (no retransplantations). Source: UZ Leuven database

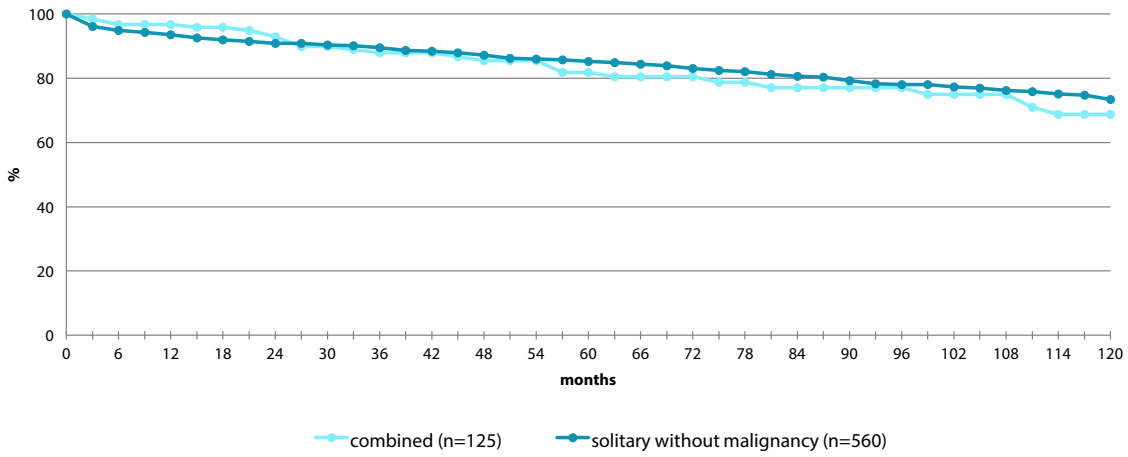


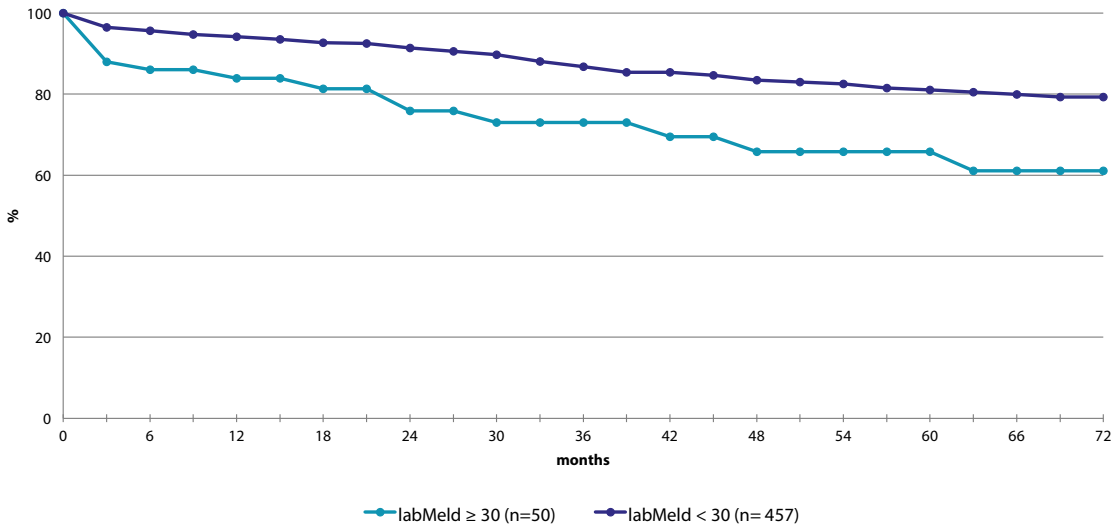
TABLE 2.5 | combined liver transplants (1997-2015)

Summary combined liver transplants	Total (n=125)	2015 (n=10)
Liver + kidney	95	6
Liver + small intestine	5	-
Liver + pancreas	6	-
Liver + small intestine + pancreas	1	-
Liver + small intestine + pancreas + colon	2	-
Liver + small intestine + pancreas + colon + kidney	1	-
Liver + pancreas + kidney	1	-
Liver + heart	3	-
Liver + heart + double lung	1	-
Liver + double lung	10	4

Survival following liver transplant on the basis of LabMELD

The LabMELD reflects the condition of the patient. The higher the score, the sicker the patient. This MELD system was introduced within Eurotransplant in 2007. The 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. Extremely ill/sick patients have a reduced, but still satisfactory chance for survival.

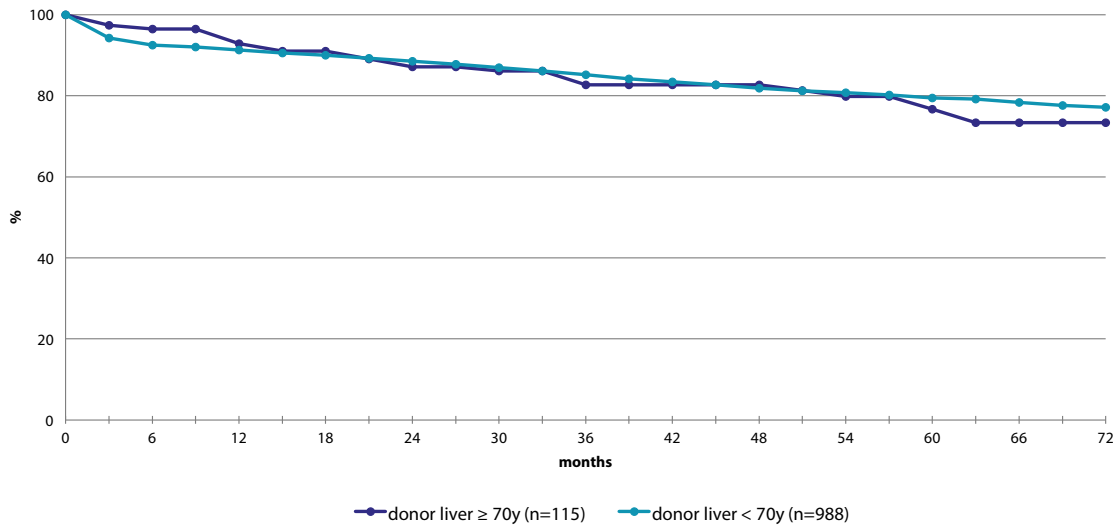
FIGURE 2.13 | six-year patient survival (2007-2015) for patients with a LabMELD of ≥30 versus patients with a LabMELD of <30.
Source: UZ Leuven database



Liver transplants with organs from 'extended criteria donors'

This curve demonstrates that the 6 year survival rate of transplant patients in our center who received an older liver is identical to that of patients who received a younger liver.

FIGURE 2.14 | six-year patient survival rate for patients who received a donor liver of ≥70 years old versus a donor liver of <70 years old.
Source: UZ 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 center acceptable with a 6 year patient survival of 79% and a 6 year graft survival of 73%.

FIGURE 2.15 | 14 six-year patient and graft survival for DCD donor livers. Source: UZ Leuven database

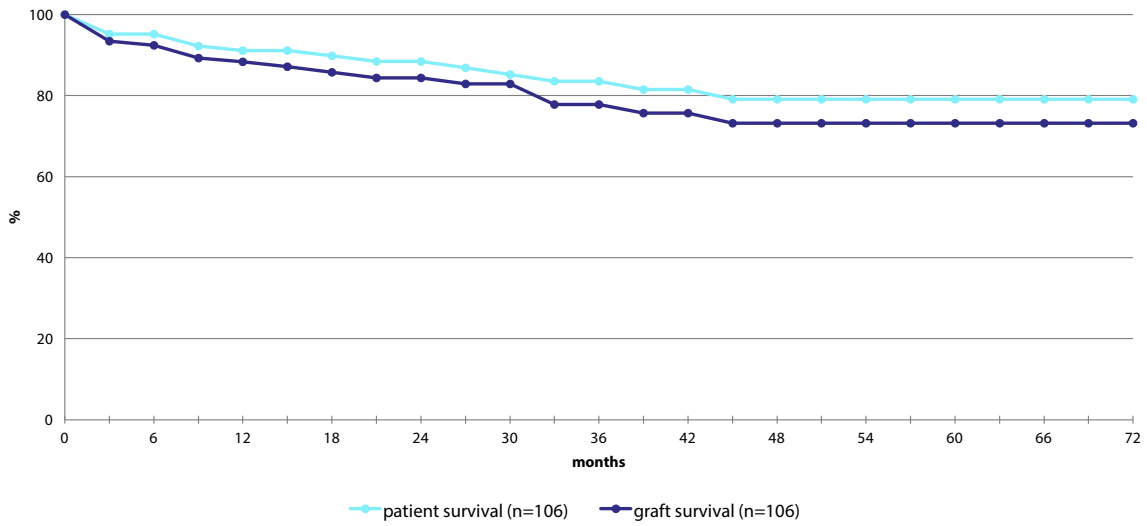


TABLE 2.6 | patients that received a liver of DCD donors in comparison to the total liver transplant activity

	number
2015	23 (34%)
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	0 (0%)
2005	3 (6%)
2004	1 (2%)
2003	2 (3%)

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prof. dr. Diethard Monbaliu, prof. dr. Ina Jochmans

general internal medicine
prof. dr. Steven Vanderschueren

nephrology
prof. dr. Dirk Kuypers, prof. dr. Maarten Naesens

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prof. dr. Marie-Paule Emonds

anaesthesiology
dr. Marleen Verhaegen

teams OR - hospitalisation
Liesbeth De Meyer, Gert Mees
Carine Breunig

transplant coordination
Glen Van Helleputte, Nele Grossen

social work
Glenda Vandevelde, Femke Hoebrechts

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.

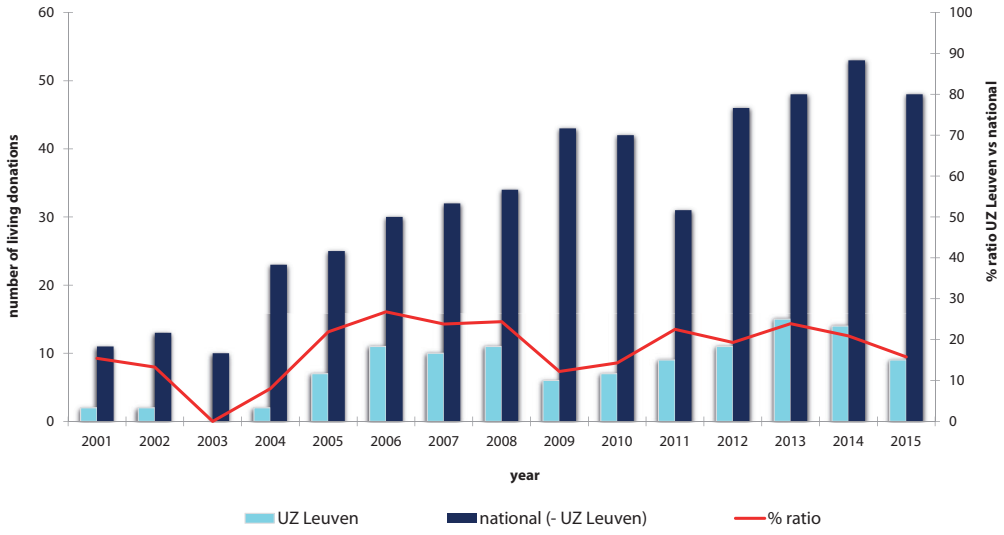
The living donation programme developed into a multidisciplinary care programme, which includes not only doctors and hospital workers involved in the screening process, but also the doctors treating the recipients, i.e. from the nephrology, hepatology and paediatric nephrology departments. Living donor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

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

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

A downward trend (national) is noticeable except for UCL where there was an increase in the number of living donations.

FIGURE 2.16 | ratio living donation transplants UZ Leuven versus national (number and percentage) 2001-2015



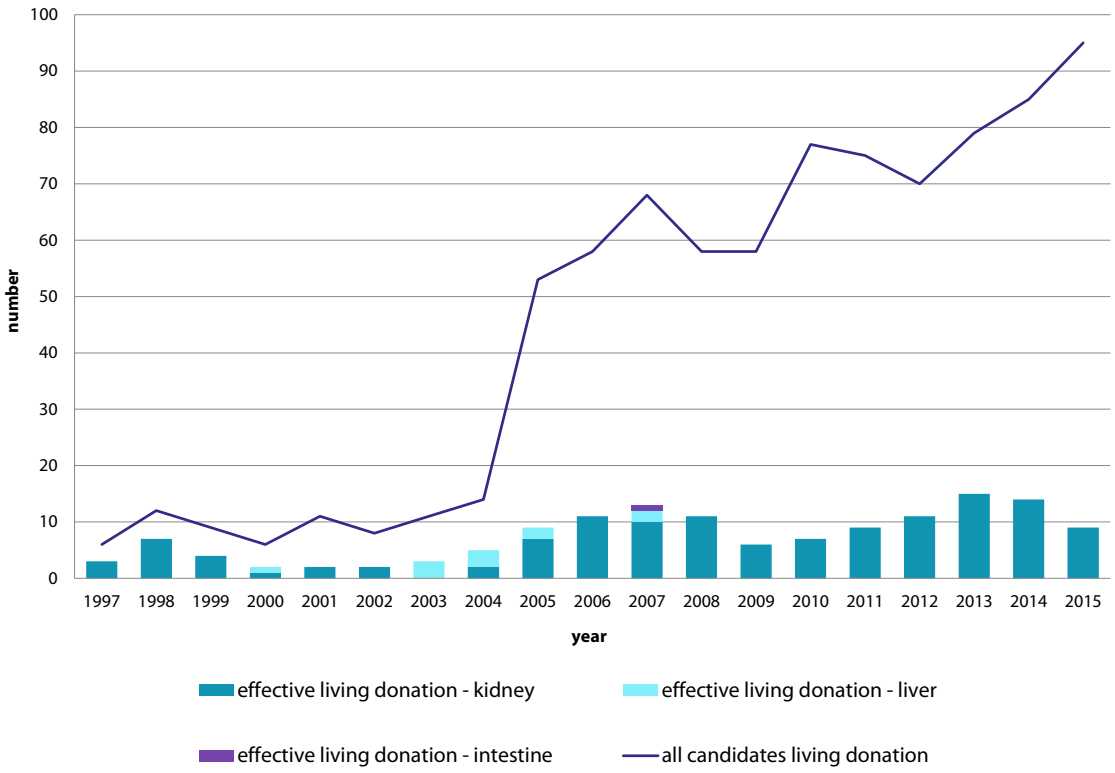
LIVING DONATION OF A KIDNEY, LIVERLOBE OR INTESTINE

Transplant activities

Since the start of the living donation programme at UZ Leuven – living kidney donation in 1997, living liver donation in 2000, living intestinal donation in 2007 – until the end of 2015, 809 candidate living donors (CLD) were screened for 530 candidate receptors (488 kidney recipients, 41 liver recipients and 1 small intestine recipient).

- 729 CLD kidney
- 79 CLD liver
- 1 CLD small intestine

FIGURE 2.17 | number of candidates and effective living donors: kidney, liver and intestine 1997-2015



In the period between May 1997 and end December 2015, 143 living donation organ transplants were carried out, of which 58 interventions (40%) in the past five years (131 living donation kidney transplants, 11 living donation liver transplants and 1 living donation intestinal transplant).

In 2015, 81 people volunteered to donate a living kidney; 13 candidacies were upheld, 9 interventions were completed. 42 candidacies were rejected, 35 candidacies were still under consideration.

14 people volunteered to be a living liver donor for 2 pediatric recipients. These candidates were referred in the context of a collaboration with UCL Saint-Luc.

Living donor profile

TABLE 2.7 | effective living donor profile by gender (1997-2015)

	Male	Female
Kidney	54	77
Liver	7	4
Intestine	-	1
Total	**61**	**82**

TABLE 2.8 | effective living donor profile based on age (1997-2015)

Age	Number of kidney donors	Number of liver donors	Number of intestine donors
18 – 30	8	8	-
31 – 40	29	2	-
41 – 50	40	-	1
51 – 60	37	1	-
61 – 70	17	-	-

TABLE 2.9 | effective living donor profile based on relationship with recipient (1997-2015)

	Genetically related donors	Emotionally related donors	Altruistic anonymous non directed donors
Kidney	80	50	1
Liver	11	-	-
intestine	1	-	-

TABLE 2.10 | LRD profile based on the relationship with the recipient (1997-2015)

LRD	Kidney	Liver	Intestine
GENETICALLY RELATED	**80**	**11**	**1**
Brother/sister	20	1	-
Father	20	1	-
Grandfather or -mother	-	1	-
Mother	31	3	1
Son/daughter	7	5	-
Nephew/niece	2	-	-
Uncle/aunt	-	-	-
EMOTIONALLY RELATED	**50**	**-**	**-**
Partner (Wife)	28	-	-
Partner (Husband)	17	-	-
Brother in law/sister in law	1	-	-
Father in law/mother in law	2	-	-
Friend	2	-	-
ALTRUISTIC anonymous non directed donors	**1**	**-**	**-**

412 candidacies (358 CLD kidney, 54 CLD liver) were rejected for various reasons *(see table 2.11)*.

TABLE 2.11 | | reason for rejection living kidney or liver donation candidates (1997-2015)

Reason for rejection candidacy	Number
Mismatches (n=63)	
ABO	23
Positive crossmatch	22
Size and/or age	18
Medical – psychosocial – surgical reasons	183
Donor withdrawal	56
Receptor withdrawal	20
Transplantation with organ from deceased donor during screening process living donation	46
Other reasons	44

For pairs in which blood group incompatibility or a positive HLA cross match are a contra-indication for kidney donation, the national multicentre LDEP (Living Donor Exchange Program) was set up in 2010, in which kidneys can still be donated and transplanted using cross donation. A case involving cross donation took place at UZ Leuven in 2013. In 2015 there were no cases involving cross donation. In case of blood group incompatibility, another possibility is the program of blood group incompatible living donation, which was performed in 2 patients in UZ Leuven. Both interventions took place in 2013.

Follow-up

At the start of the living donation transplant program it was decided that all living donors will be taken into follow-up for life. A specific protocol was developed for this purpose (consultations 1 month, 3 months, 6 months post operative and annually; 1 year after the donation renal exam (Cr - EDTA and CT with volumetry) is conducted) and follow-up data is stored in a databank.

27 living donors (20%) are no longer part of the follow-up scheme due to several reasons (eg stay abroad); the others are invited at least once a year to attend a consultation.

Results

Living donor kidney transplant

RECIPIENTS (n=131) *(see figures 2.18)*

- 13.8% child (< 16, n=18), 86.2% adult receptors (> 16, n=113)
- Delayed graft function (DGF) (dialysis requirement < 8 days post Tx): 2.2% (= 3 cases: factor rejection? DGF?)
- Primary Non Function (PNF): 0%
- Acute rejection: 25.9% (n=34); adult receptors: 30%, children: 0%
- 3 month and 6 month graft survival: 99.3%
- 1 year graft survival: 97.8% (n=131 kidney Tx). Reason for graft loss:
  - 1 patient: rejection as a result of non-compliance with therapy
  - 1 patient: recurrence of initial disease
  - 1 patient: arteria renalis trombosis

DONORS (n=131)

- 0% peri-operative mortality
- Morbidity:
  - Peri-operative requirement for transfusion in 1 patient (0.7%)
  - 1 surgical revision on d0 for mild bleeding in 1 patient (0.7%)
  - 1 surgical revision due to wound infection (0.7%)
  - 4 patients (3.0%) with chronic pain
  - 7 patients (5.3%) with incisional hernia repair

Living donation liver transplant

RECIPIENTS (n=11)

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

DONORS (n=11)

- 0% mortality
- 1 revision for incisional hernia repair

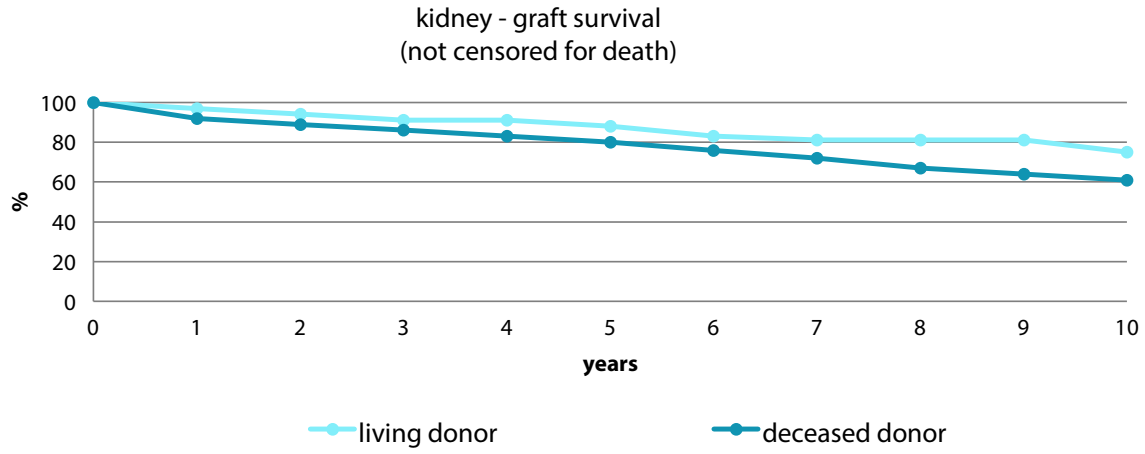
Living donation intestinal transplant

RECIPIENTS (n=1)

- Graft survival: graft loss as a result of refractory rejection
- Patient survival: the patient required a retransplant but this could not be done in Belgium due to non Belgian citizenship. Patient went back to her native country (Poland) and we were informed that – in the absence of a retransplantation (multivisceral) - 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
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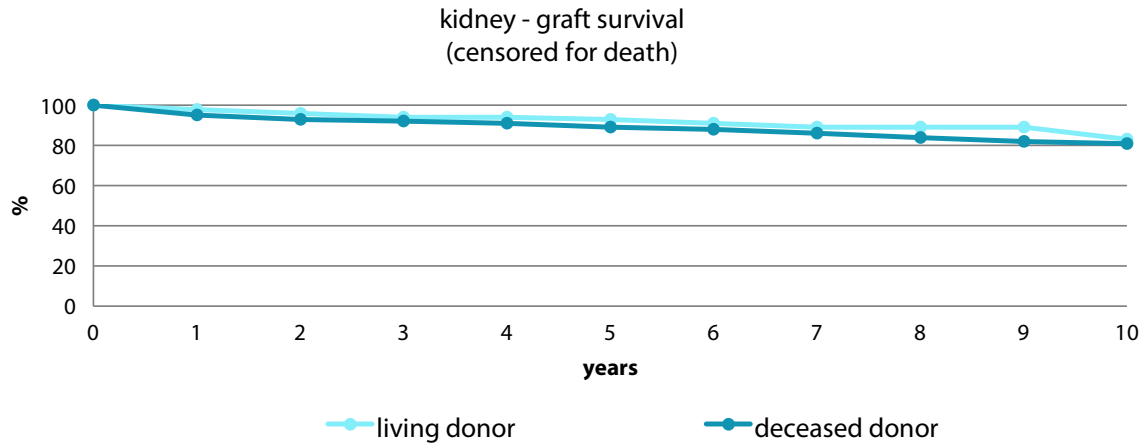
years
living donor
deceased donor


kidney - graft survival
(censored for death)
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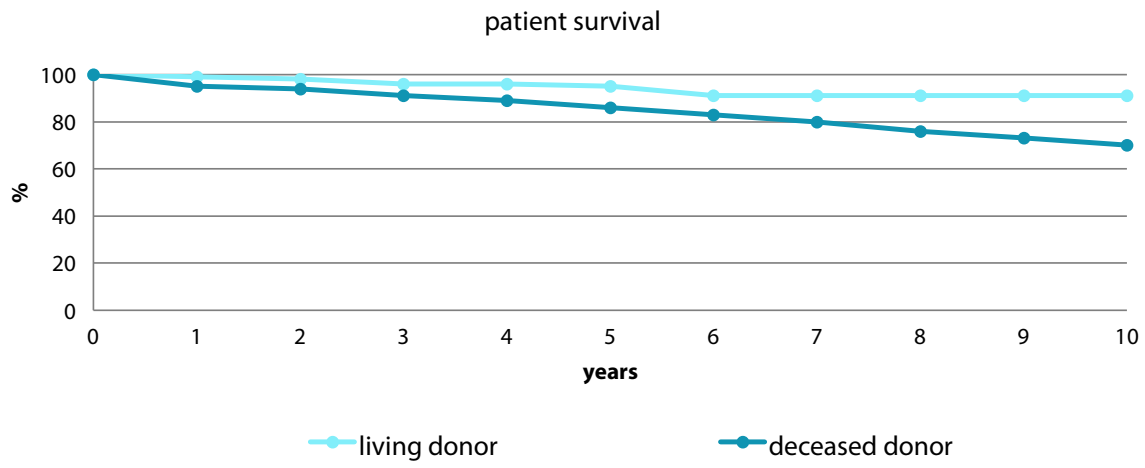
living donor
deceased donor


patient survival
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years
living donor
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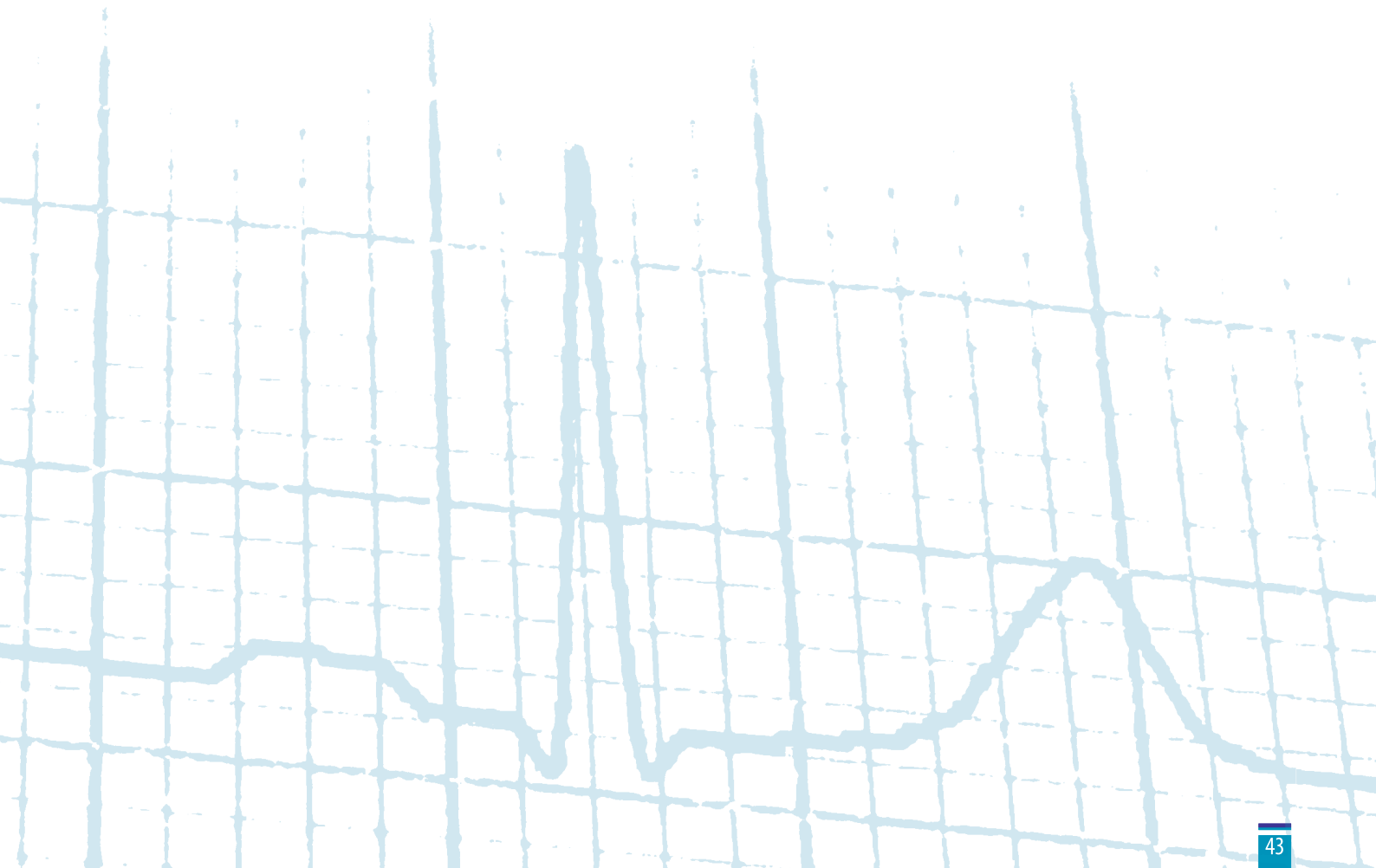

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prof. dr. Kathleen Claes, prof. dr. Maarten Naesens
prof. dr. Ben Sprangers

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

anaesthesiology
dr. Marleen Verhaegen

teams OR – hospitalisation
Liesbeth De Meyer, Magda Penninckx
Carine Breunig, Mathilde Dehairs

nursing consultant
Katleen De Bondt

post transplant consultation nurse
Cecile De Vlieghere

waiting list management
Joke Gorter

social work
Christa De Baere

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Kidney and kidney/pancreas transplant care programme

2016 was a very successfull year in renal transplantation with a total of 145 renal allografts transplanted. Both the short-term and the long-term outcome of our kidney transplants continues to improve. The latter is a consequence of a rather unique way of meticulous clinical follow-up of our transplant patients . Too often is is forgotten that death of the recipient of a renal allograft is still the most frequent cause of graft loss after successful transplantation. It is therefore of the utmost importance, and even after a very successful kidney transplantation, that clinicians stay aware for the associated diseases such as cardiovascular diseases, diabetes mellitus and also the consequences of chronic renal function impairment. Equally important is the intensive and pro-active follow up of typical transplant associated complications such as opportunistic infections and malignancies. In the Leuven kidney transplantation program routine clinical follow up includes at regular intervals the organization of gastrointestinal, gynaecological, urological, cardiovascular, skin and endocrinological assessments. Depending on the time after transplantation certain types of, mainly viral, infections are actively screened for such as for example cytomegalovirus, BK polyomavirus and the Ebstein-Barr virus. We also maintain a very intensive and active vaccination program in the prevention of viral and bacterial infections after kidney transplantation. The status of the kidney allograft is not only assessed om te basis of regular blood and urine examinations, but also by performing at regular intervals renal biopsies of the transplanted kidney. This strategy is actually quite unique and is only performed in a clinical setting in a few centers around the world. The use of protocol kidney biopsies allows us to identify certain pathological processes that are not detectable in an early stage in blood or urine examinations. For example on the routine protocol biopsy three months after transplantation, a subclinical acute rejection (incidence of approximately 8.3%) can be diagnosed and treated before even graft deterioration commences. Or on a routine biopsy a year after transplantation we can detect the undesired effects of certain immunosuppressive drugs on the kidney and consequently adapt our therapy. This form of personalised follow up is very work intensive but it also guarantees a regular critical and in-dept evaluation of the transplanted patient. We are convinced that it is this strategy that contributes to the extremely good long-term outcome as well as the quality of the clinic care program. In this way we ended 2015 with a record number of 145 renal transplants bringing us to a total of 4243 kidneys in UZ Leuven.

Transplant activities

The results shown here below reflect our activities in adult kidney transplantation. Pediatric transplantation will be shown in chapter 4 of this booklet.

In 2015 a total of 145 kidney transplantations were performed. 129 patient received their first kidney, 13 patients a second kidney and in 3 patients a third kidney was transplanted *(figure 2.19)*
The number of transplantations with a living donor slightly decreased in 2015. In 2011 9 patients were transplanted with a kidney from a living donor, in 2012 there were 11 patients and in 2013 the number increased to 15 patients. Already in 2014 we noticed a small drop in the number of patients transplanted with a living donor to 14 and in 2015 this number was further reduced to a total of 7 patients.
In 2015 the number of kidney transplants with kidneys coming from non-heart-beating donors (or DCD-donors, donation after circulatory death) increased strongly. Currently 1 in 5 transplants is performed by using a kidney from a DCD-donor.

FIGURE 2.19 | evolution in the number of kidney transplants 1992-2015

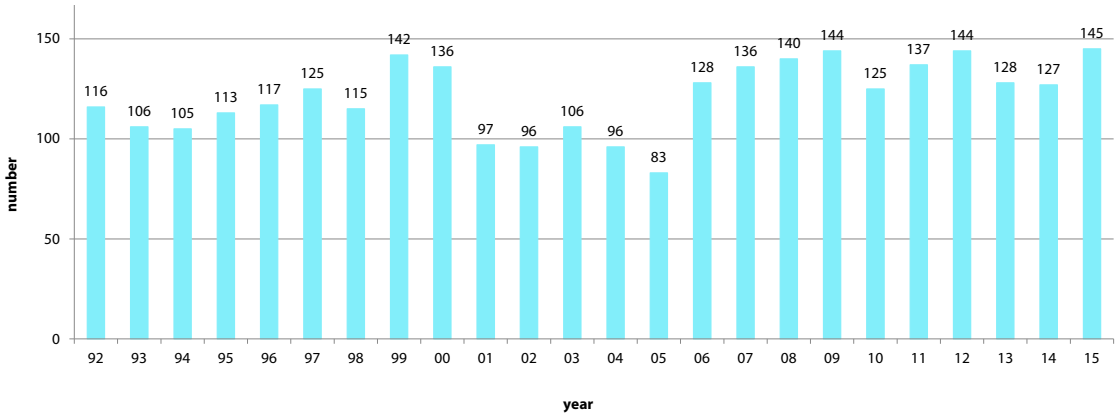
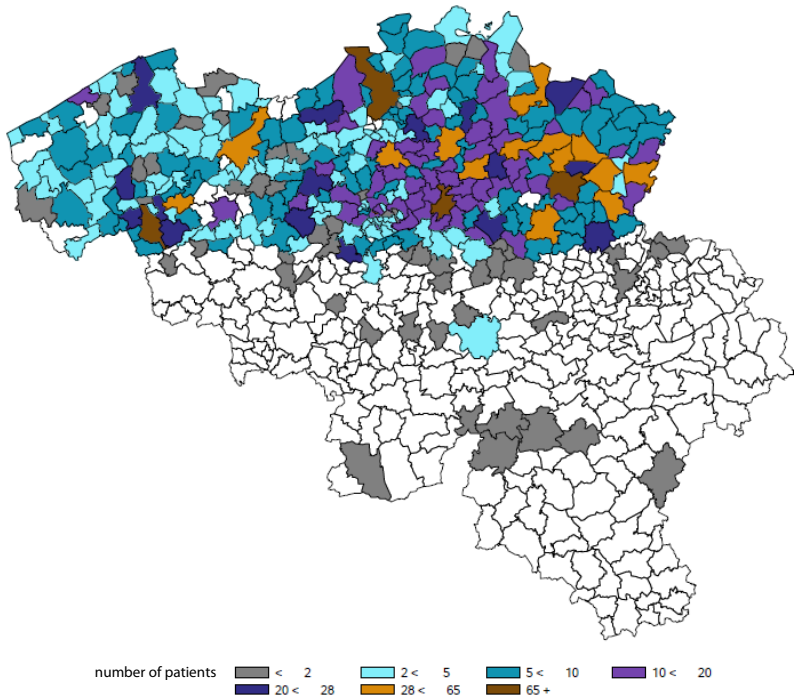


FIGURE 2.20 | geographical origin kidney recipients (1963-2015)

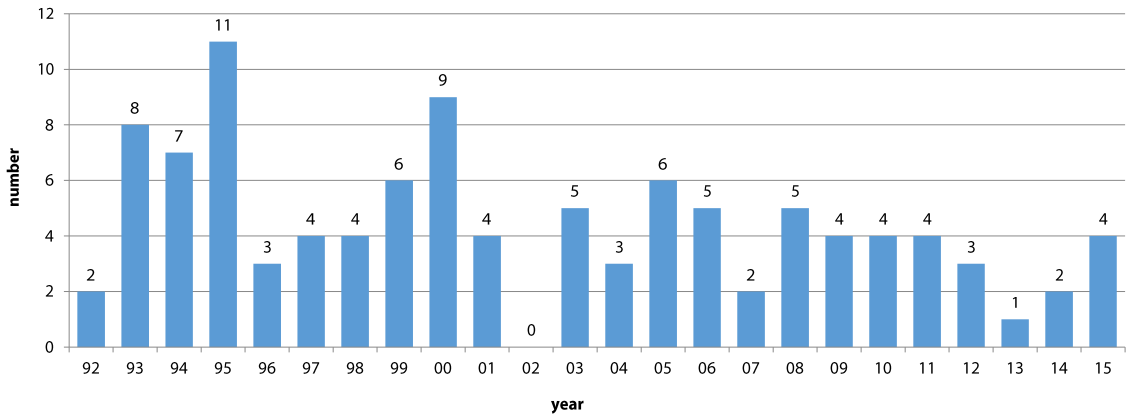


In 2015 the number of combined transplantations remained more or less at the same level as in the previous years. In 2013 we performed 6 combined transplantations, in 2014 this number increased to 15. This year a total of 13 combined kidney + other organ transplantations were performed: 6 combined kidney-liver transplantations, 4 kidney-pancreas transplantations *(figure 2.21)*, 1 kidney-heart transplantation and 1 combined kidney-lung transplantation *(table 2.12)*.

TABLE 2.12 | number of combined kidney transplants performed (2005-2015)

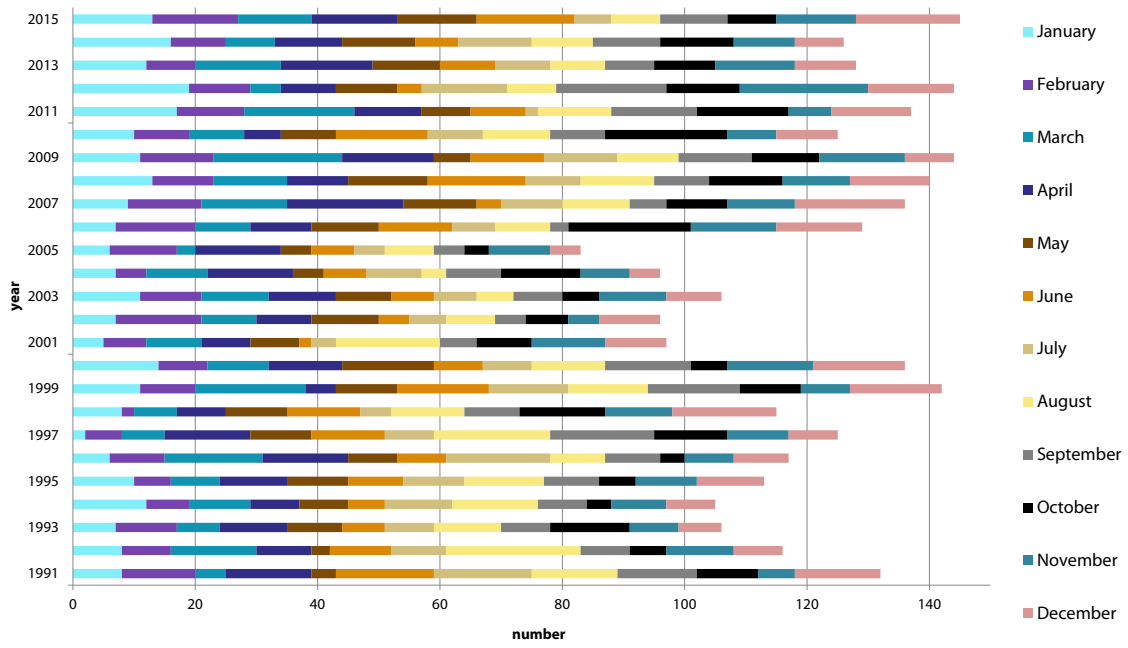
	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Kidney + liver	1	5	4	5	3	9	8	11	4	10	**6**
Kidney + heart	-	1	1	-	-	3	1	-	1	1	**1**
Kidney + lung	-	2	-	-	-	-	-	4	-	-	**1**
Kidney + pancreas	6	5	2	5	4	4	4	3	1	2	**4**
Kidney + intestine	-	-	1	-	-	-	1	-	-	2	-
Total	**7**	**13**	**8**	**10**	**7**	**16**	**14**	**18**	**6**	**15**	**12**

FIGURE 2.21 | number of combined kidney-pancreas transplants between 1992 and 2015



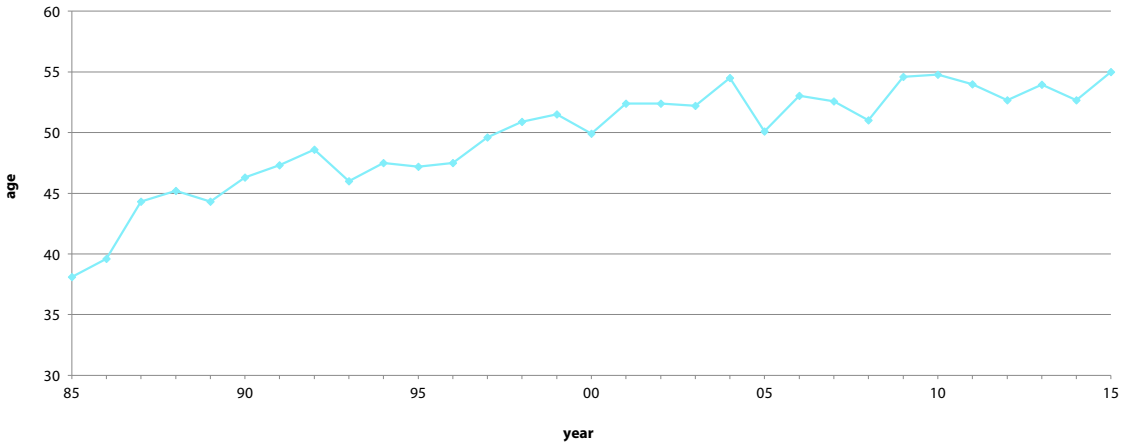
The transplantation activities in 2015 were quite evenly spread throughout the year. The largest number of transplantations (17) was performed in December. Months with lower activity were July and August as well as October with only 8 transplantations performed *(figure 2.22)*.

FIGURE 2.22 | evolution of the monthly number of kidney transplants over the past years



The mean age of patients at the time of transplantation is slowly stabilizing. In 2014 the mean receptor age was 52,7 years, in 2015 the mean age of the recipients was 55 years. *(figure 2.23)*.

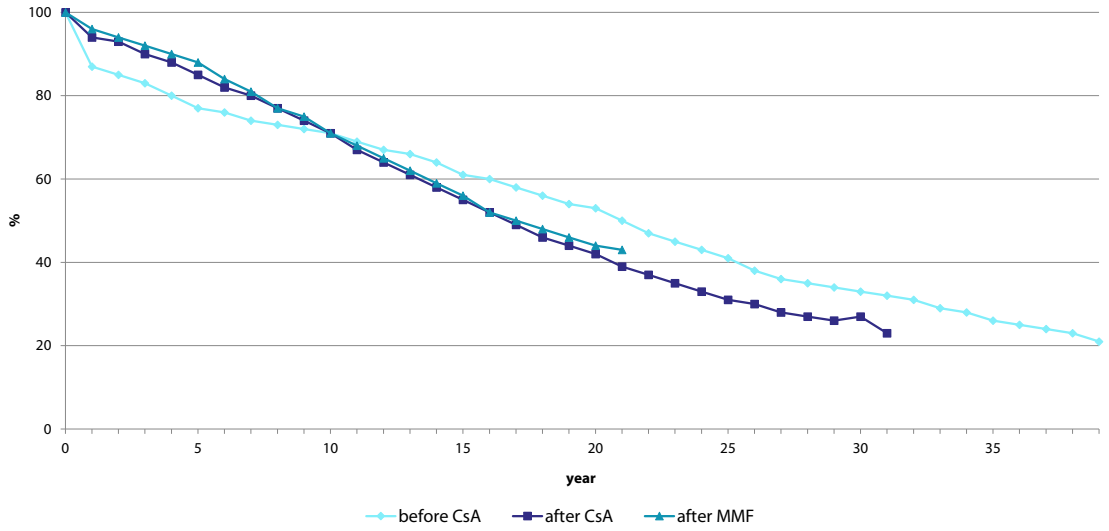
FIGURE 2.23 | evolution of the average receptor age since 1985



Results of patient survival

The actuarial patient survival before and after 1983 is shown in figure 2.24 (this was the year Cyclosporin was introduced). The patient survival is initialy significant better in the Cyclosporin treated group but at 12 years after grafting both curves seem to level around the same percentage of graft survival.
The actuarial patient survival after 1993 (the year Mycophenolate Mofetil (MMF) was introduced), is also shown. This survival curve is initialy somewhat better than the Cyclosporin treated group but eventually also the MMF treated patient survival runs parallel with that of other patient groups.

FIGURE 2.24 | actuarial patient survival rate before and after introduction of Cyclosporin (CsA) and Mycophenolate Mofetil (MMF)



The analysis of the actuarial patient survival since 1983 and calculated for equal time periods of 5 years, is shown in figure 2.25. Here we see that 5 year patient survival after 1992 slightly increases. These positive results seem to disappear again with longer follow-up.

FIGURE 2.25 | evolution of the actuarial patient surviva rate since 1983

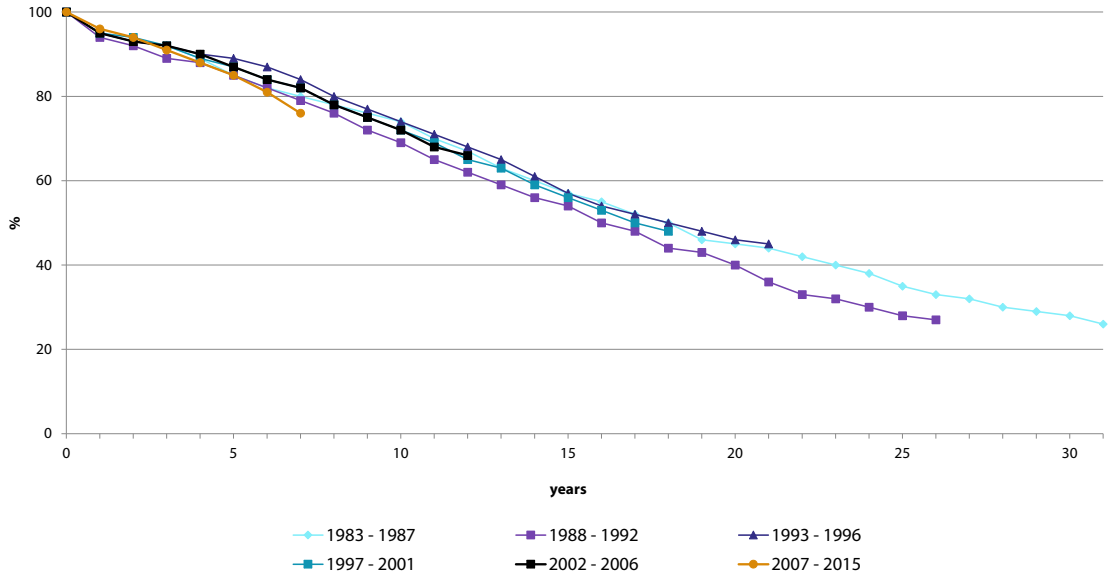


Figure 2.26 shows the effect of recipient age at time of transplantation on actuarial patient survival. As expected, patient survival is inversely related to the age of the receptor: after 25 years, 75% of the patients <30 years at the time of transplantation is still alive, while for recipients aged between 30 and 49 years this is 41% after 25 years. Patients transplanted at an older age (this means older than 60 years) 20 year survival is below 20%.

FIGURE 2.26 | actuarial patient survival rate on the basis of age

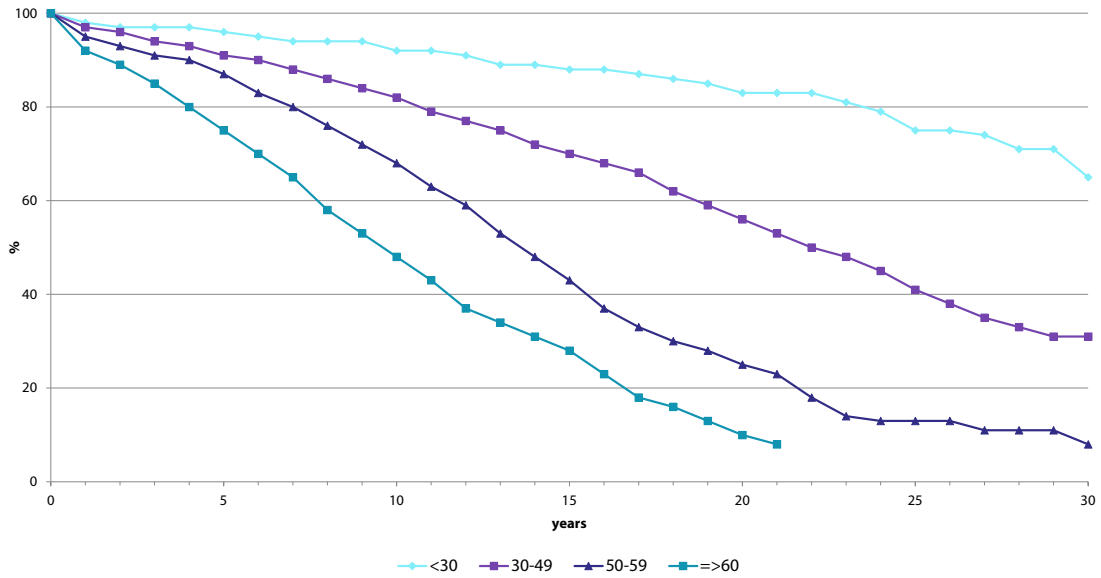
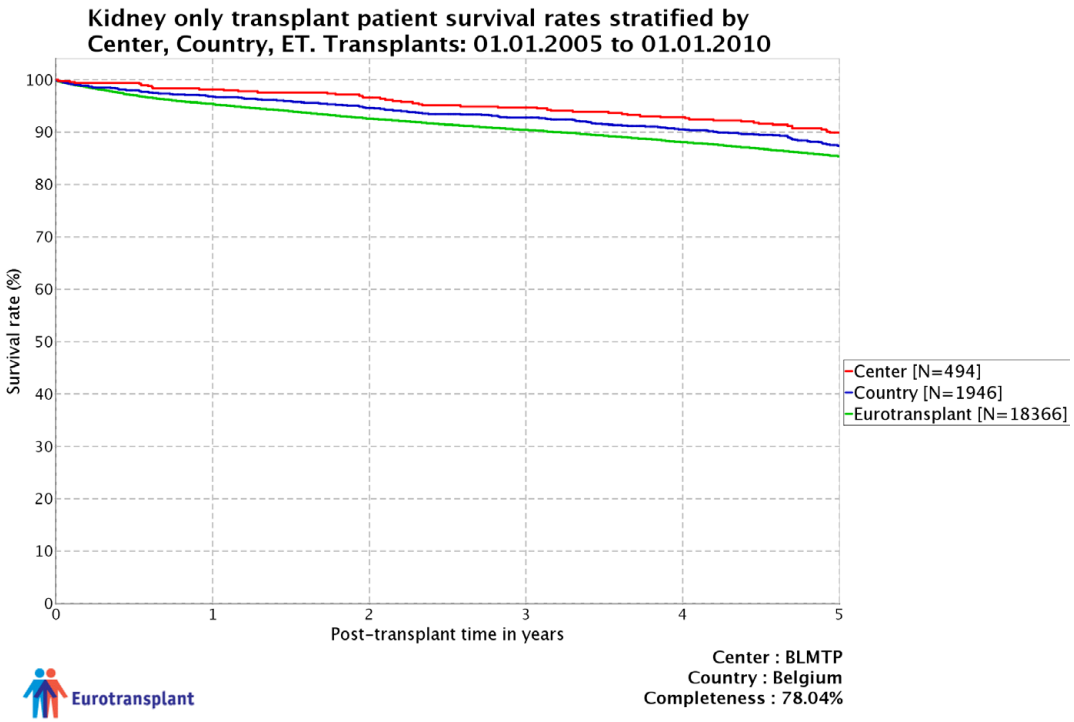


FIGURE 2.27 | five-year patient survival rate (2005-2010) kidney only transplants. UZ Leuven compared to Eurotransplant and Belgium (the figures for Belgium also include the results for UZ Leuven). Source: Eurotransplant



Results of graft survival

The actuarial graft survival not censored for death is shown in figure 2.28. The noticeable difference in graft survival in the initial years after transplantation between patients that were transplanted before or after the introduction of Cyclosporin is wel known. Both curves now almost run perfectly parallel. Striking is the fact that the survival curve of the patients transplanted after the introduction of Mycophenolate Mofetil (MMF) remains significantly higher (at 20 years 34% versus 25% and 28%).

FIGURE 2.28 | actuarial kidney survival rate before and after CsA (not censored for death)

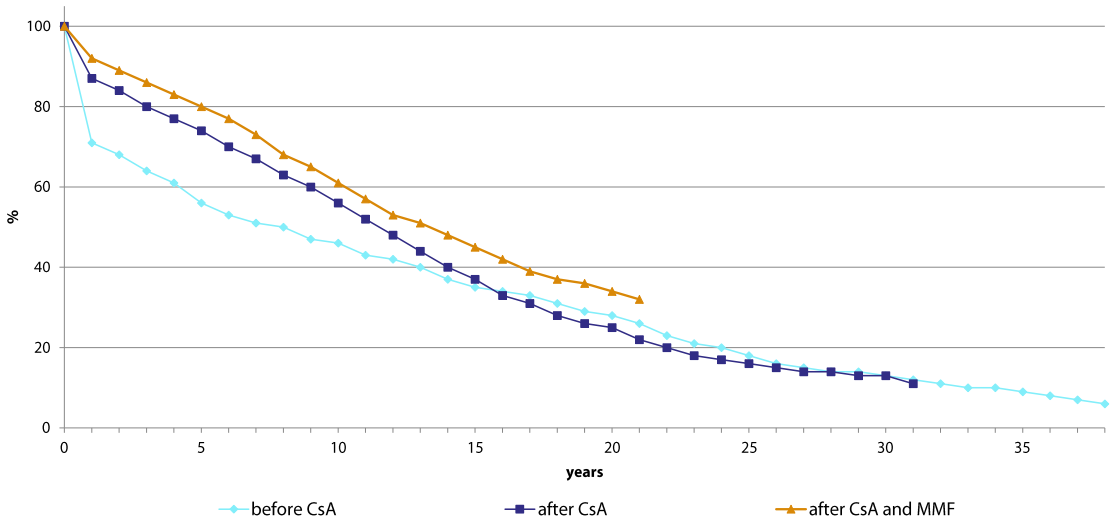
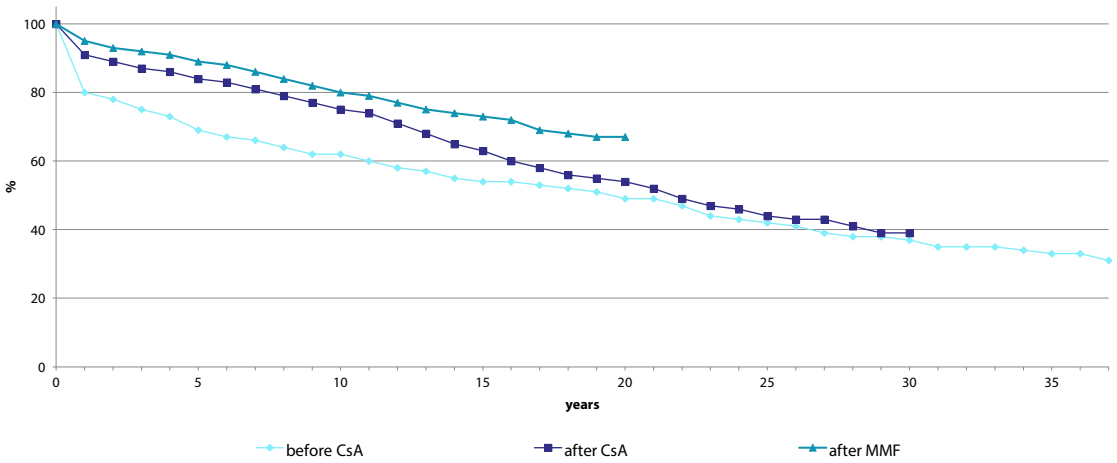


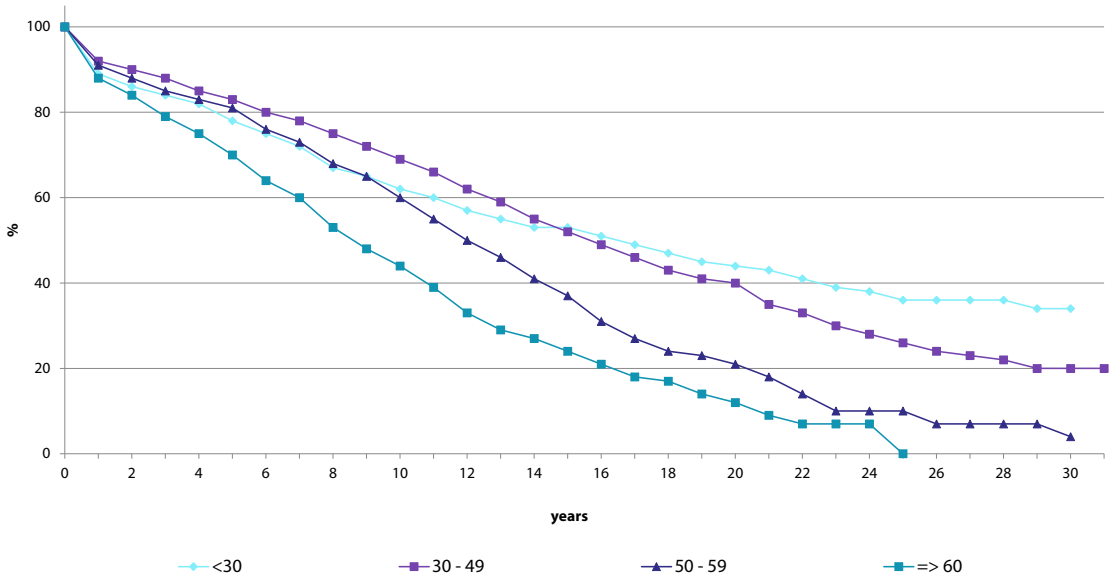
Figure 2.29 shows the actuarial graft survival censored for death. Again it is quite striking that patients transplanted after the introduction of MMF are significantly better than those who were transplanted before the introduction (20 year graft survival: 67%, 54% and 49% respectively).

FIGURE 2.29 | actuarial kidney survival rate classified into before and after the introduction of Cyclosporin (CsA) and Mycophenolate Mofetil (MMF) (censored for death)



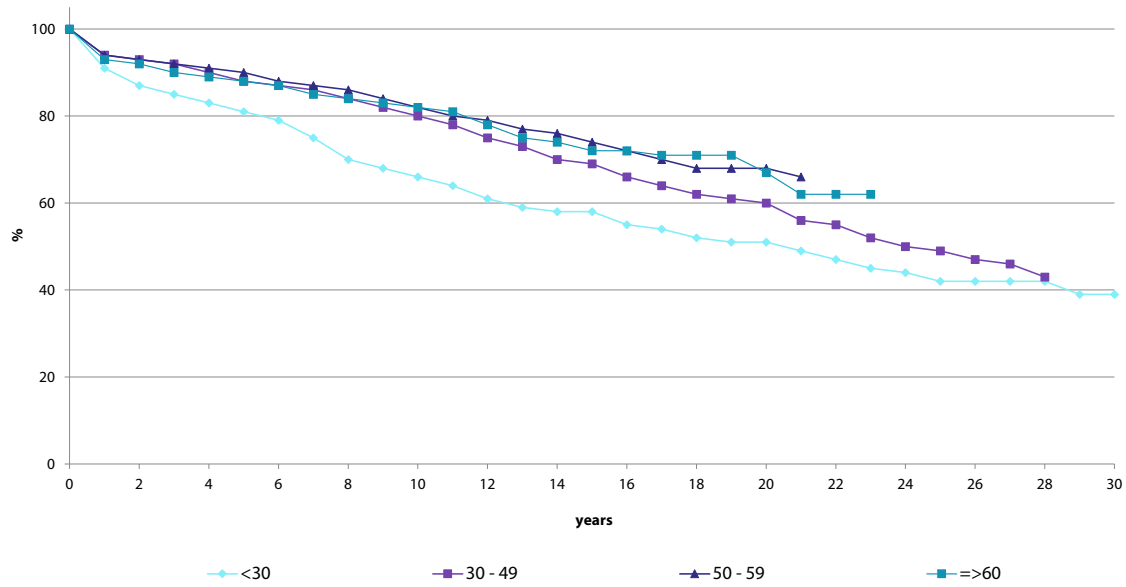
The actuarial graft survival is shown in figure 2.30. If one takes into account the recipient age, striking differences are observed between young and elderly recipients.

FIGURE 2.30 | actuarial kidney survival rate (not censored for death) on the basis of age



When one takes into account graft survival 'censored for death', figure 2.31 shows that older age categories have a better intrinsic graft survival than youger age categories. This is based on the fact that loss of a transplanted kidney in a patient older than 60 years would off course be strongly related to death of the recipient.

FIGURE 2.31 | actuarial kidney survival rate (censored for death) on the basis of age



The graft survival 'censored for death' improves when we compare transplantations before and after 1993. 5-year graft survival for patients who were transplanted between 1983 and 1987 was 73%. In patients who were transplanted after 1993 5-year graft survival improves while in the group of patients transplanted between 2008 and 2015 graft survival was 78%, which means that the difference with prior time periods becomes smaller. *(figure 2.32)*.

FIGURE 2.32 | evolution of the actuarial kidney survival rate (not censored for death) since 1983

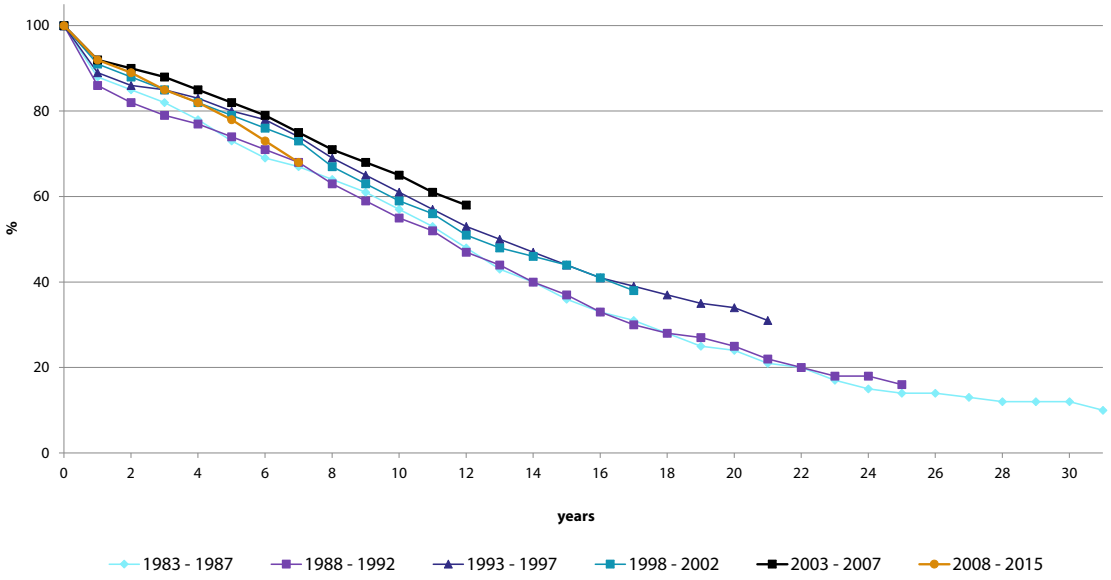


FIGURE 2.33 | five-year graft survival rate (2005-2010) (death censored) kidney only transplants. UZ Leuven compared to Eurotransplant and Belgium (the figures for Belgium also include the results for UZ Leuven). Source: Eurotransplant

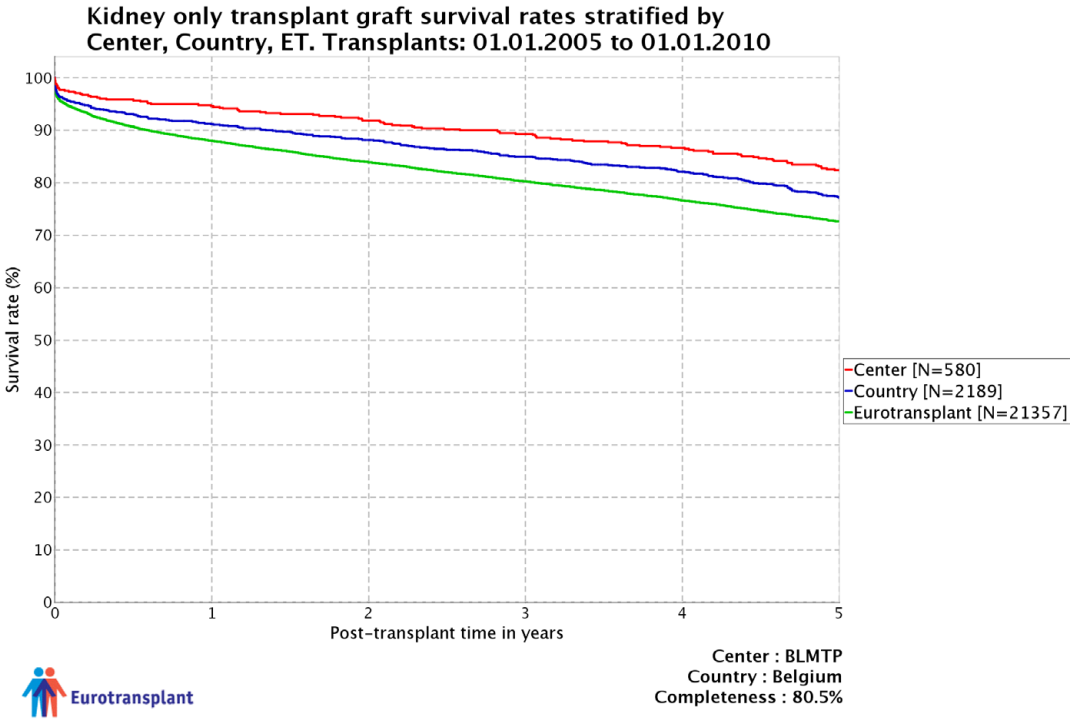
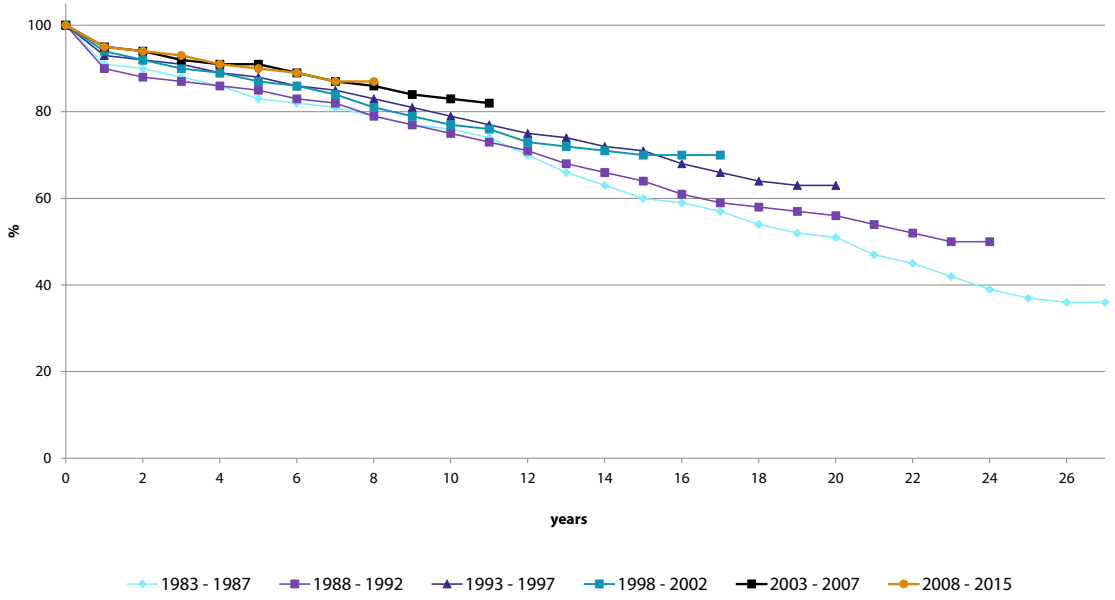


Figure 2.34 shows graft survival that is 'censored for death'. 5 year graft survival in patient transplanted between 2008 and 2015 is 7% higher compared to previous periods (90% vs 83%).

FIGURE 2.34 | evolution of the actuarial kidney survival rate (censored for death) since 1983

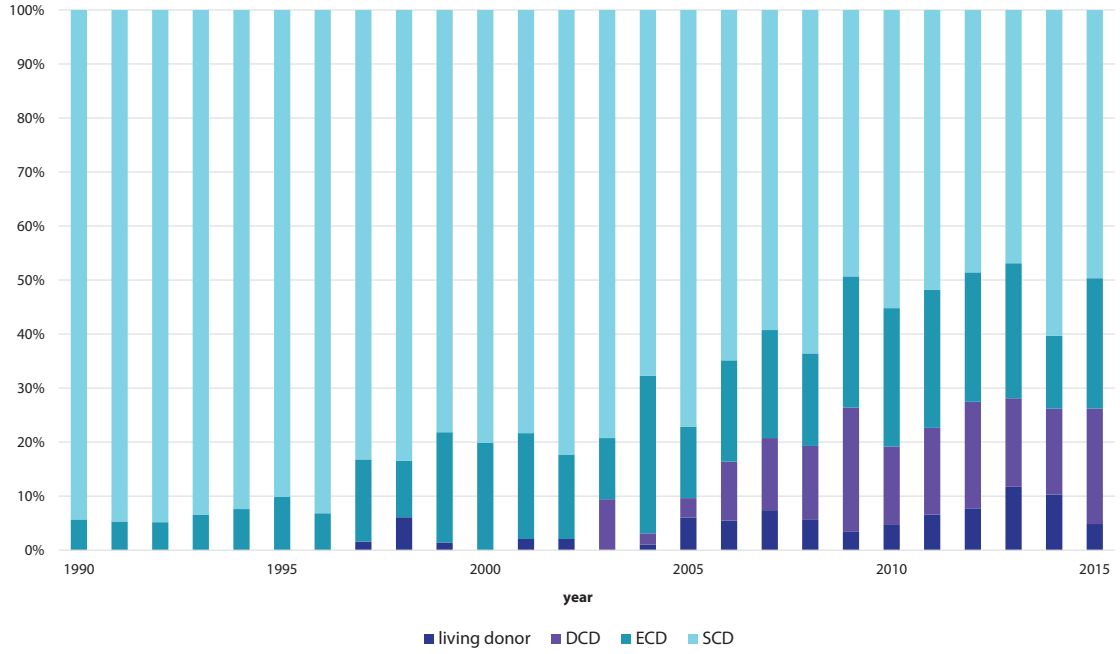


Evolution donor types

The downward trend in the number of available organs from deceased donors, starting in the beginning of the nineties, has changed (improved) due to the use of kidneys from ECD donors (extended criteria donors) and also kidneys from DCD donors as well as living donation.

In 2014 fewer kidneys were transplanted from ECD donors. In 2015 however the number of ECD donors was back equal to the number of 2013. This brings the combined proportion of patients that receive kidneys from ECD, DCD and living donation back above 50%. *(figure 2.35)*

FIGURE 2.35 | kidney transplant percentage on the basis of donor type 1990-2015



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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Katrien Vandersmissen, Jean Driesen

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Theophiel Claes, Bart Peeters

psychological support
Marijke Potargent

dietary advice
Nelle Pauwels, Kathleen Gerits

HEART TRANSPLANT CARE PROGRAMME

The heart transplantation program took off on September 1, 1987. Since that time 619 patients underwent a total of 650 heart transplantations (as of February 26, 2016; heart-lung transplantations not included). The patients come from all over the Flemish region (figure 3.1). The health care professionals who are currently and directly involved in the program are listed on the facing page. Even this rather extensive list doesn't do justice to many colleagues and coworkers from the cardiology and cardiac surgery departments, from other disciplines, from primary health care and from other hospitals, whose input may have been less direct but nonetheless equally important. Also the collaborators from the early days have contributed considerably to the heart transplantation program as it stands today.

HEART TRANSPLANTS

Transplant activities

The number of heart transplantations in Leuven has increased in recent years *(figure 3.2)*: over the last 6 years there were on average 26 new transplants per year. That is about 30 to 40 percent of the total annual volume in our country (with 7 heart transplant centers that are active), and about 50 to 60 percent of the heart transplantations in the Flemish region. This trend is somewhat in contrast with the status quo of transplant procedures on a wider scale, i.e. nationally *(figure 3.3)* as well as within the Eurotransplant region and worldwide.

The number of patients on the waiting list has doubled against before, both locally *(figure 3.4)* and in the whole Eurotransplant region. This major increase seems to be over now; numbers have been stable for the past 5 years. The average waiting time for a heart transplantation is 7 to 10 months *(figure 3.5)*, but thanks to the Eurotransplant high-urgency program a donor heart can become available in a much shorter time when the need is extremely urgent. Furthermore the use mechanical circulatory support (VAD or ventricular assist device) as a bridge to transplantation has been a clinical reality for several years now: almost half of the newly transplanted patients had a heart pump on board to bridge the waiting time *(figure 3.6)*.

Donor age continues to rise *(figure 3.7)*. Over the past decade 70% of the donor hearts came from collaborating Belgian hospitals *(figure 3.8)*.

FIGURE 3.1 | geographical origin of heart transplant patients

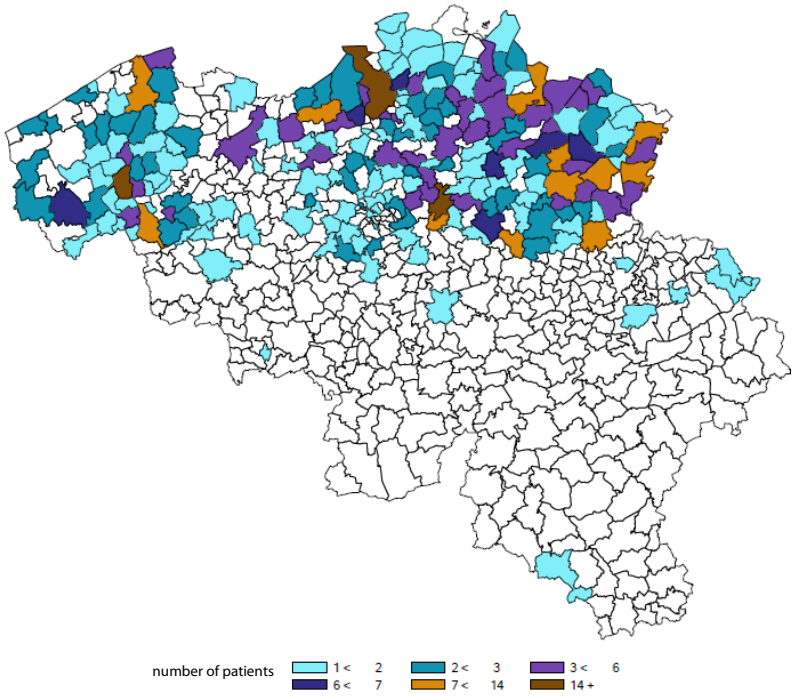


FIGURE 3.2 | annual heart transplant volume in UZ Leuven (1989-2015)

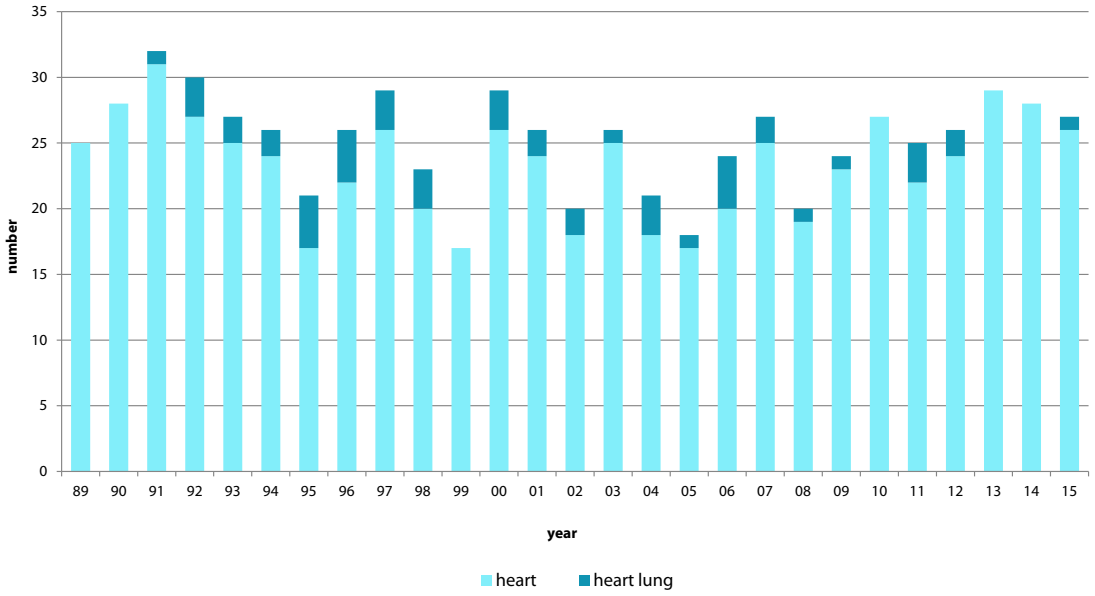


FIGURE 3.3 | annual heart transplant volume in Belgium (1982-2015)

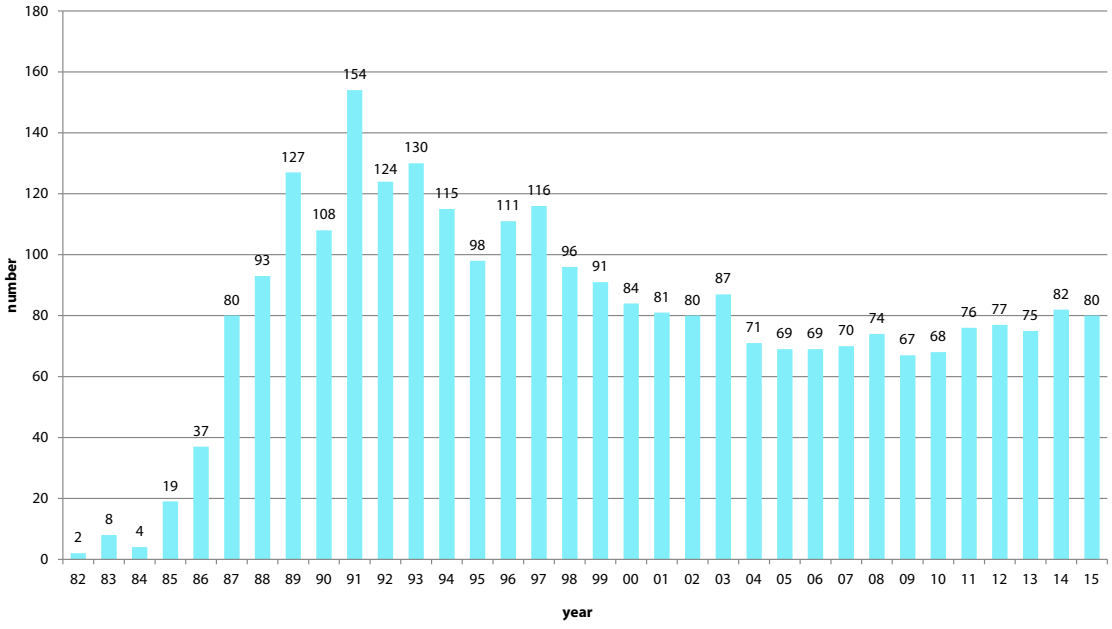


FIGURE 3.4 | patients on the waiting list at year's end

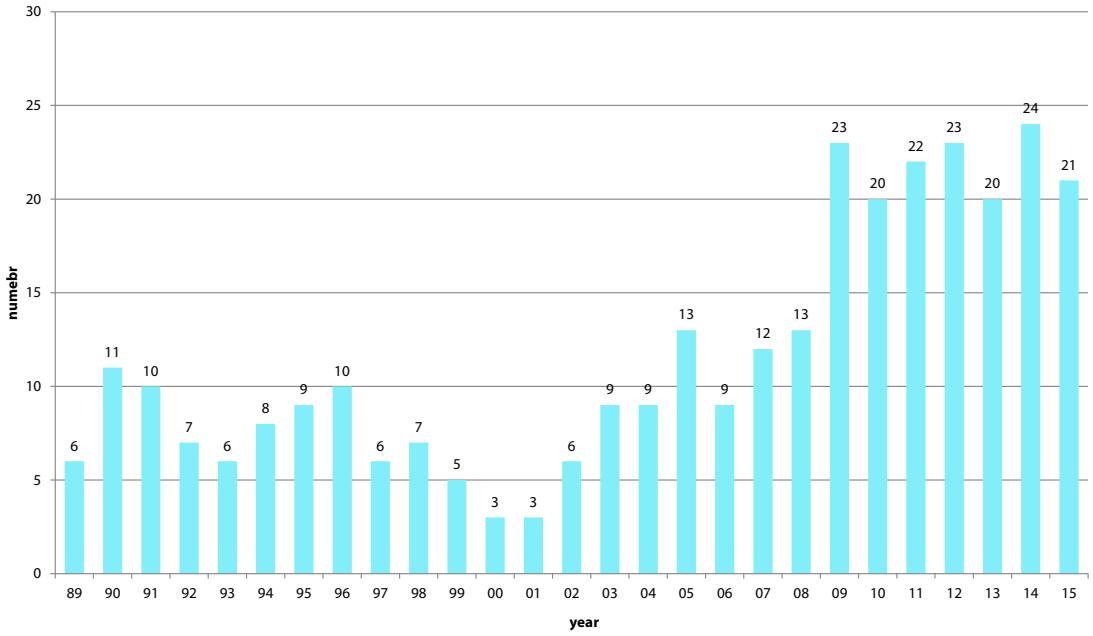


FIGURE 3.5 | average waiting time (days)

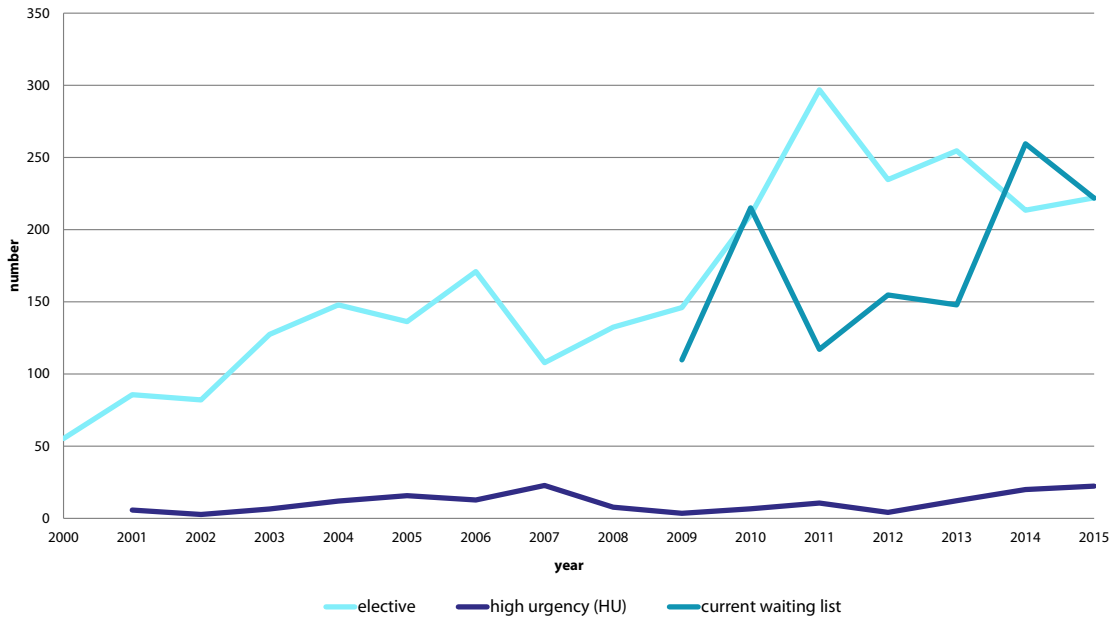


FIGURE 3.6 | mechanical circulatory support as a bridge-to-transplantation (percentage of patients)

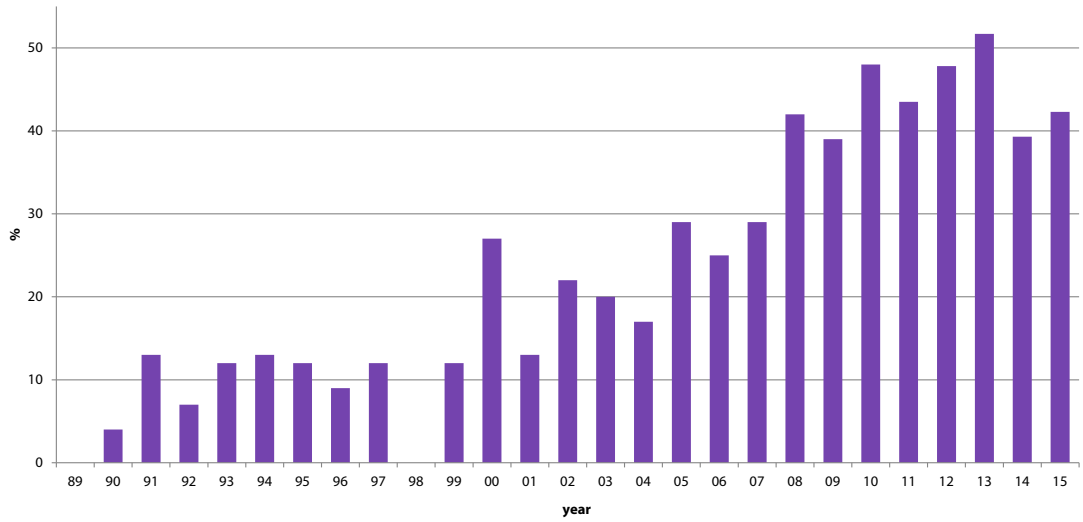


FIGURE 3.7 | average donor age

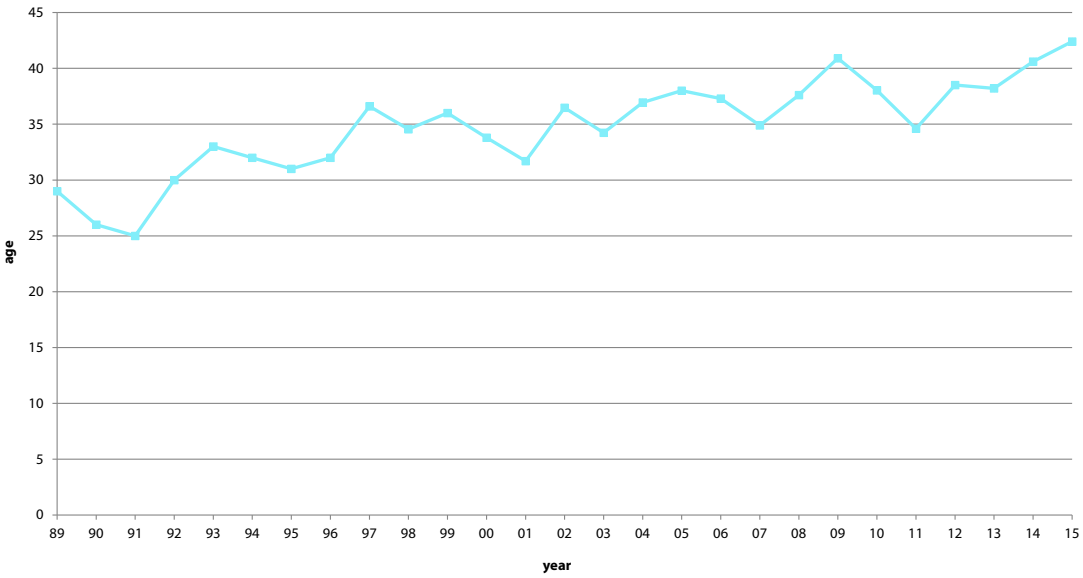


FIGURE 3.8 | donor heart origin

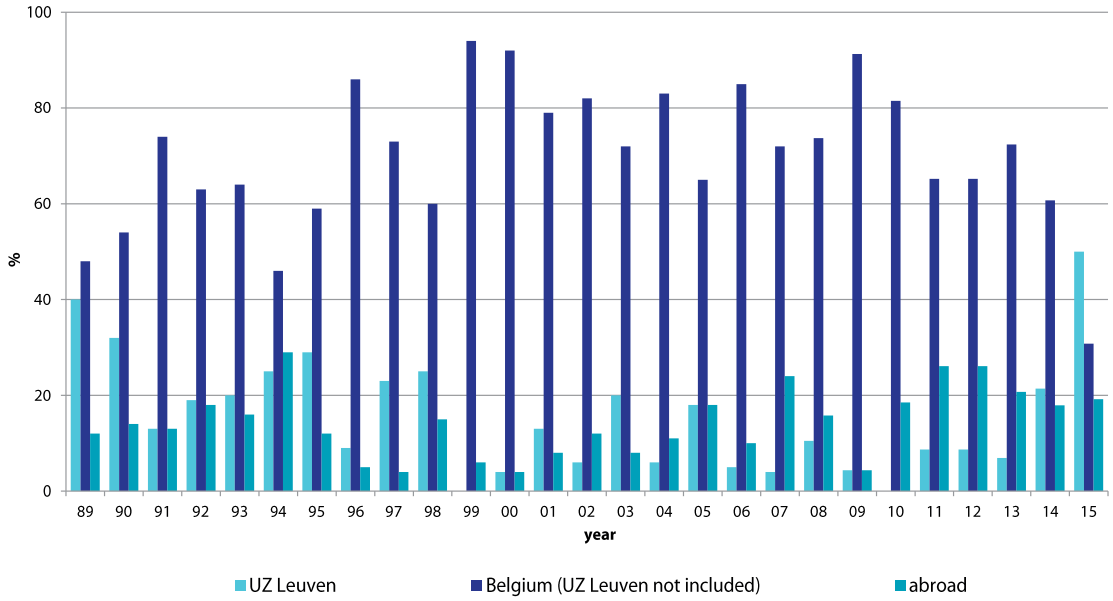
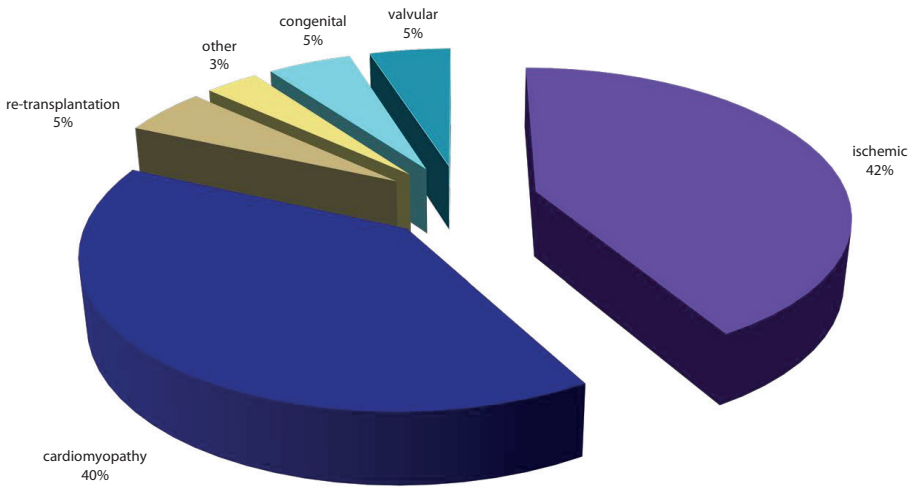


FIGURE 3.9 | reason for heart transplantation



Transplant results

Patient survival as of December 31, 2015 was calculated for the total Leuven heart transplantation experience: 648 heart transplantations in 617 patients, including 23 combined heart-kidney transplants and 3 combined heart-liver transplants (the results of 48 heart-lung transplants are not included but can be found in the section on lung transplantation). In figure 3.10 we compare our actuarial patient survival with that in the worldwide registry of the International Society for Heart and Lung Transplantation (ISHLT). Ten year survival for the entire Leuven cohort stands at 75 percent versus 52 percent in the ISHLT registry.

Short- and mid-term results in successive eras continued at a high level despite an increasing surgical complexity and increasingly liberal donor and recipient criteria. This also seems indicative of a lack of deleterious effect on posttransplant survival of the frequent use of pretransplant mechanical circulatory support. Long-term survival continues to improve and in the most recent patient cohorts 5 and 10 year survival stands at 91 and 78 percent respectively *(figure 3.11)*.

At the end of 2015 we had 386 heart transplant patients in active follow-up *(figure 3.12)*; among other things this resulted in 1800 outpatient visits over the year *(figure 3.13)*.

FIGURE 3.10 | overall patient survival (UZ Leuven vs ISHLT)

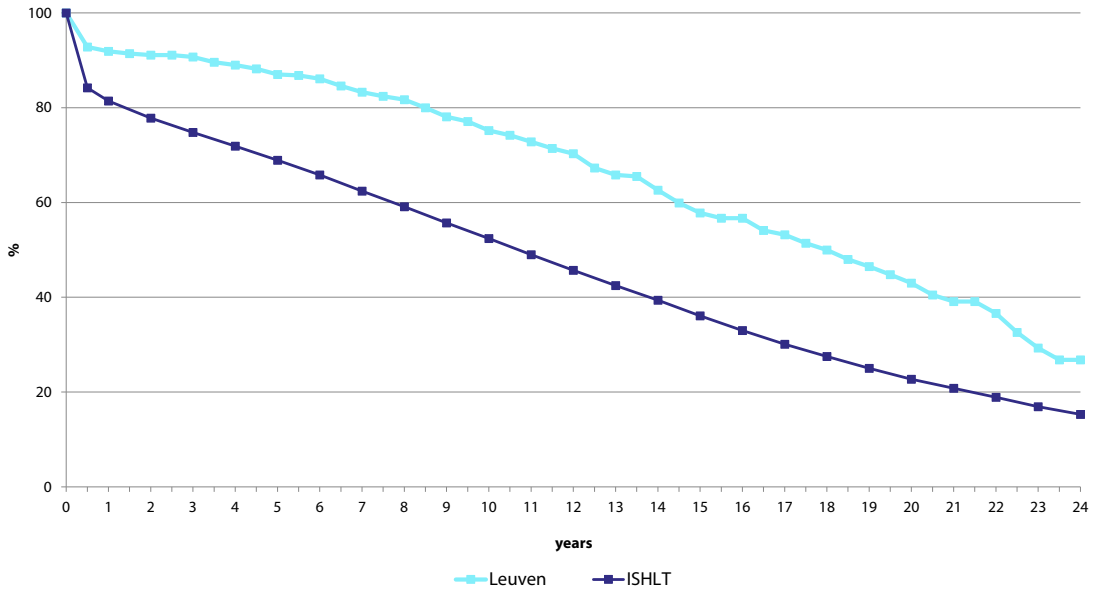


FIGURE 3.11 | patient survival in successive eras (UZ Leuven vs ISHLT)

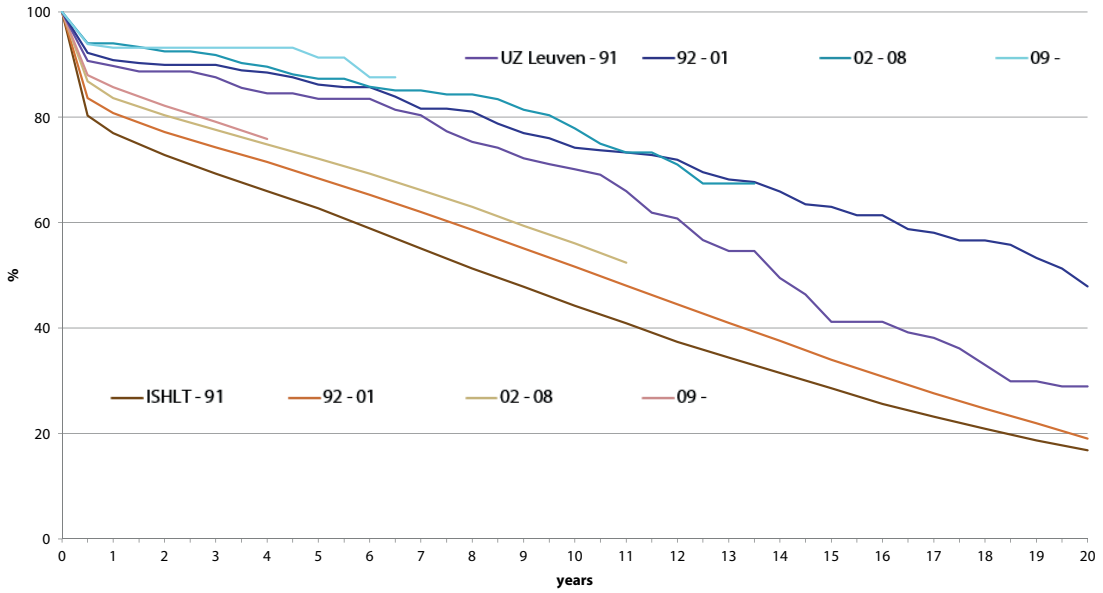


FIGURE 3.12 | patients in active follow-up

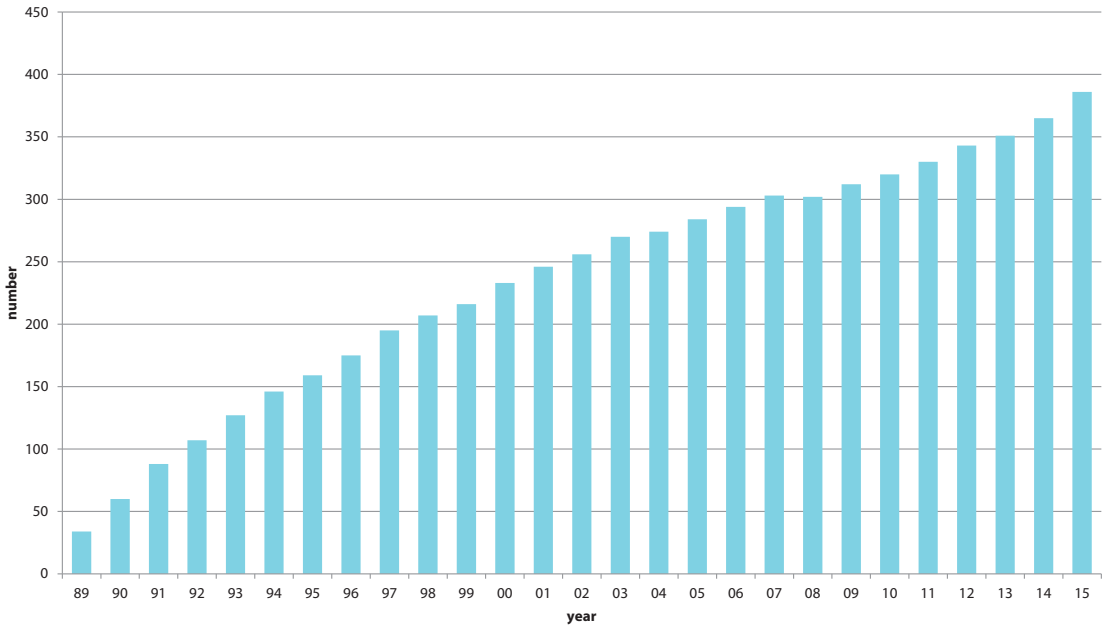
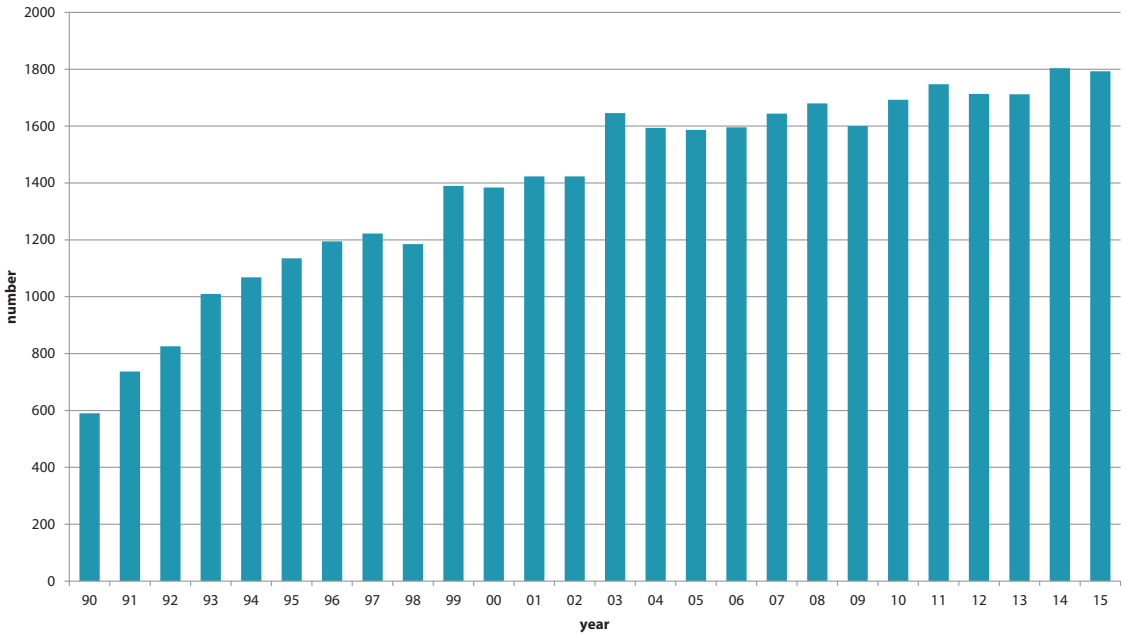


FIGURE 3.13 | outpatient visits



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prof. dr. Maria Schetz, prof. dr. Sophie Van Cromphaut
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*paediatric intensive care medicine

teams OR – perfusion - ICU – hospitalisation
Magda Penninckx, Luc Hoppenbrouwers
Eddy Vandezande
Nancy Vandenbergh, Petra Janssens
Annemieke Schoonis, Sabine Gryp

nurse specialist lung transplants
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outpatient clinic lung transplants
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physiotherapy
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psychological support
Karine Van Tricht, Marijke Potargent

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(Heart) lung transplant care programme

The lung and heart-lung transplantation programme was initiated in 1991 in the university hospitals of Leuven. Over the last 5 years, a mean of 63 procedures has annually been performed. Within Eurotransplant, Leuven remains number 3, after Vienna and Hannover. In Belgium, some 110 (heart)-lung transplantations are annualy performed in 3 active centers. With over 60 procedures per year, Leuven is by far the biggest center of the Benelux. The most important indications to perform a lung transplantation are end-stage emphysema (COPD), cystic fibrosis and pulmonary fibrosis, with IPF as the most important indication amonst those. Indeed the number of patients with pulmonary fibrosis that undergo a lung transplantation is gradually increasing as a consequence of an increased referral policy. At the moment, our 5-y survival reaches 80%, which is remarkably better than the 55% recorded in the registry of the 'International Society for Heart and Lung Transplantation'. This may be explained on the one hand by the experience our team has gained over the years, and on the other hand by the progressive shift from single to double lung transplantation, resulting in a better survival.

(HEART) LUNG TRANSPLANT

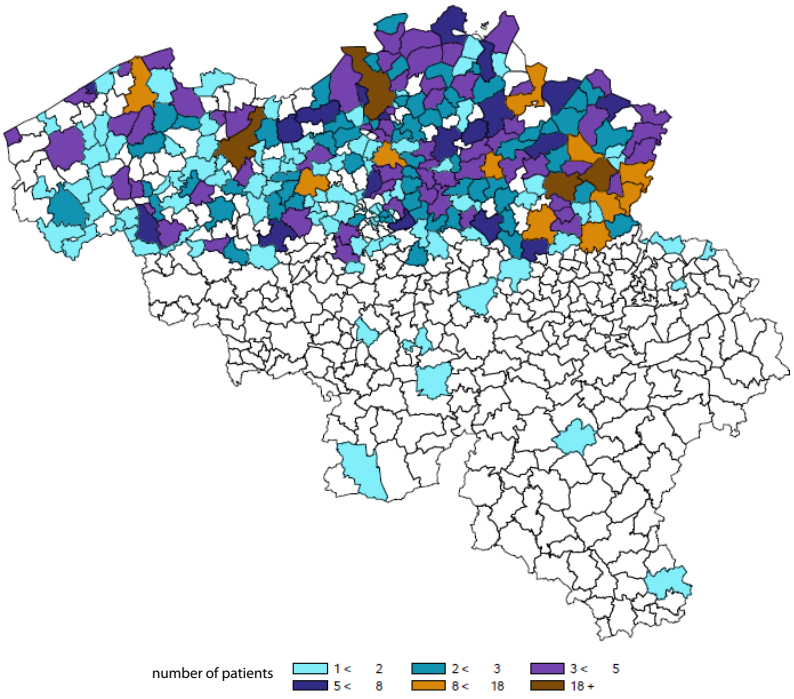
Transplant activities

Compared to 2014, the number of procedures has increased from 58 to 65. Except for 1 heart-lung transplantation, only double lung transplantation procedures were performed.

TABLE 3.1 | number of (heart) lung transplants in UZ Leuven (1995-2015)

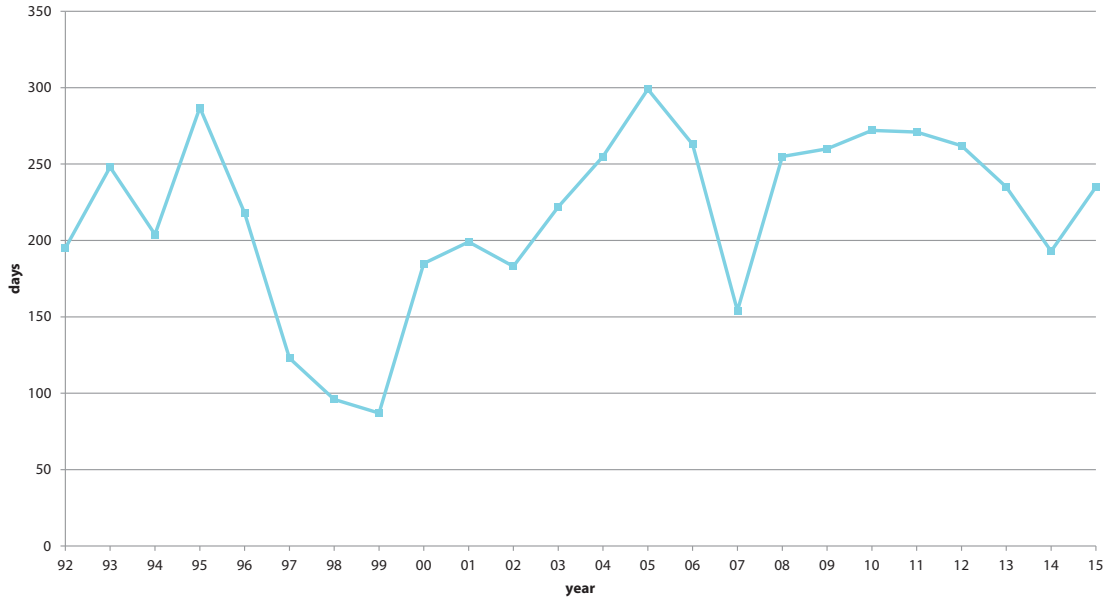
	95	96	97	98	99	00	01	02	03	04	05	06	07	08	09	10	11	12	13	14	15
Heart-lung	4	4	3	3	-	3	2	2	1	3	1	4	2	1	1	-	3	2	-	-	**1**
Unilateral	7	5	6	2	8	4	10	10	15	14	9	19	7	8	4	7	1	-	-	-	**-**
Bilateral	1	3	4	8	4	13	20	21	27	22	29	34	44	40	42	51	58	79	59	58	**64**
Total	**12**	**12**	**13**	**13**	**12**	**20**	**32**	**33**	**43**	**39**	**39**	**57**	**53**	**49**	**47**	**58**	**62**	**81**	**59**	**58**	**65**

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



The mean waiting time is increased to 235 days (variation 4 - 835 days), compared to 193 in 2014. The mortality on the waiting list remains very low (< 5%).

FIGURE 3.15 | mean time on the waiting list since 1992



The indications for lung transplantation remain comparable to the previous years and are shown in figure 3.16. COPD/emphysema, cystic fibrosis and pulmonary fibrosis are the major indications. There is a progressive increase in the number of lung transplantations for cystic fibrosis (9% in 2014, 20% in 2015). In 2015, 3 retransplant procedures for end-stage chronic rejection were performed (4,6% of the total number), which is again comparable to the previous year. Also 3 combined double-lung/liver, 1 combined double-lung/kidney and 1 heart-lung transplantation were performed in 2015.

FIGURE 3.16 | indications for lung transplant in 2015

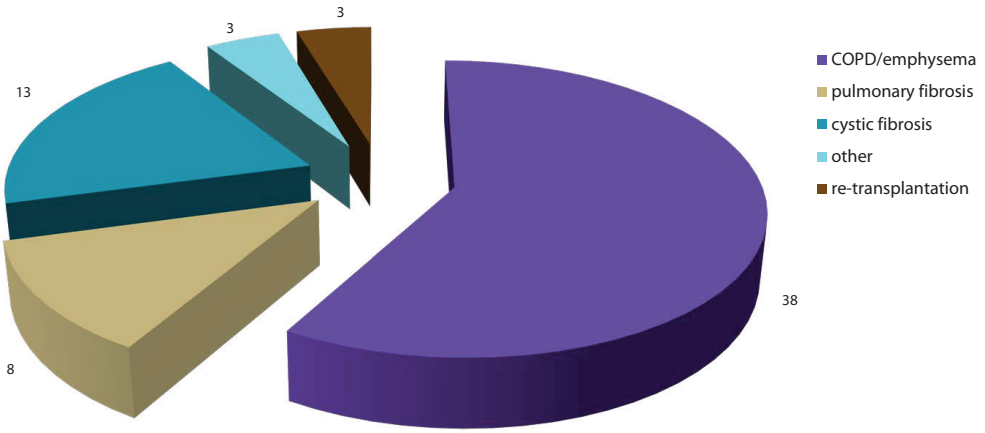


Figure 3.17 describes the age distribution of the patients transplanted in 2015. The vast majority of patients is between 50 and 60 years old, which reflects the most frequent indications for lung transplantation, being COPD/ emphysema and pulmonary fibrosis. There is also an increase towards younger patients, as a consequence of a growing number of transplantations for cystic fibrosis.

FIGURE 3.17 | age distribution of the recipients in 2015 (n=65)

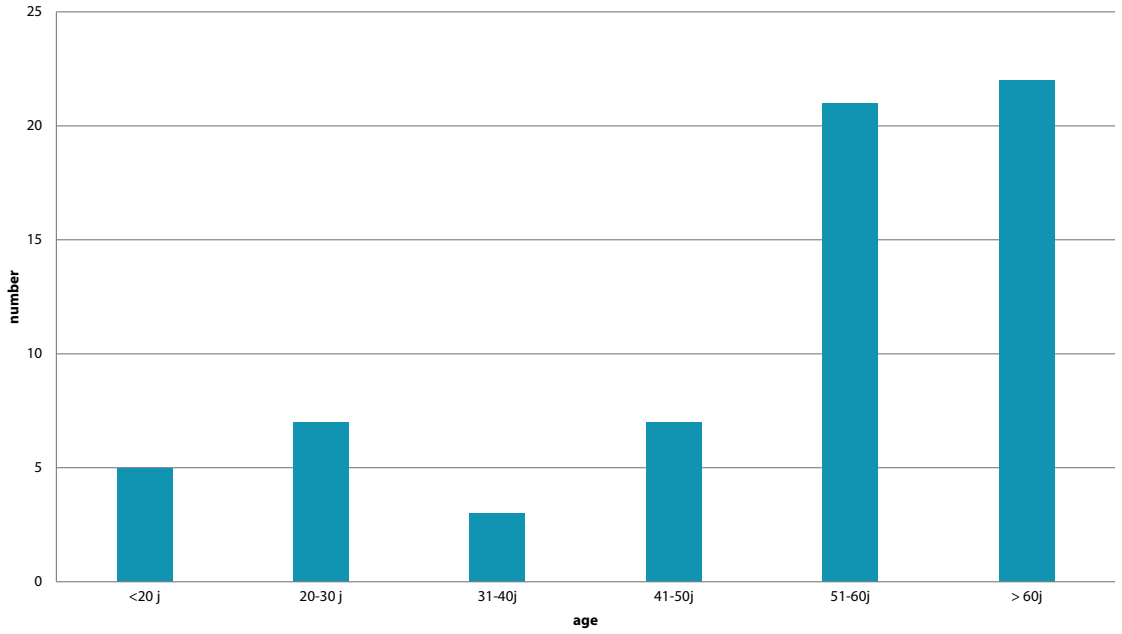
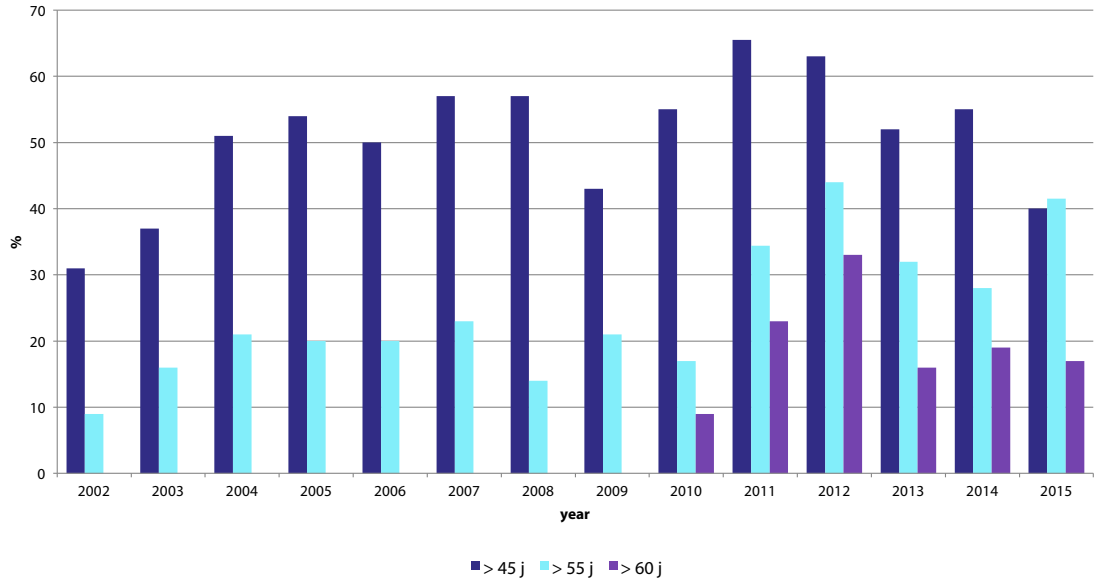


Figure 3.18 describes the mean donor age since 2000. There is a minor decrease in mean age compared to last year: 48,9 y (min. 14, max. 79) in 2015, compared to 49,5 y in 2014.

FIGURE 3.18 | mean donor age over the years

The percentage of donors older than 55 y is again increased (from 32% in 2013; 28% in 2014 to 41.5% in 2015). The percentage of donors >60 y remains rather stable (19% in 2014 and 17% in 2015); 15% of all donors are aged above 65 y.

FIGURE 3.19 | percentage of donors in relation to their age over the last 14 years



Transplant results

The actuarial 6-months survival of the 65 patients transplanted in 2015 is 100%. Peroperative mortality is 0%. Figure 3.20 describes the actuarial survival in Leuven from January 2010 till December 2015 (n=353), compared to the survival as registered by the ISHLT (International Society for Heart & Lung Transplantation) over a comparable time span (2009-2013). At each point in time, the survival in Leuven is better, with a current 5-y survival of 80% (compared to 55% in the ISHLT-registry).

FIGURE 3.20 | actuarial survival rate in UZ Leuven vs ISHLT

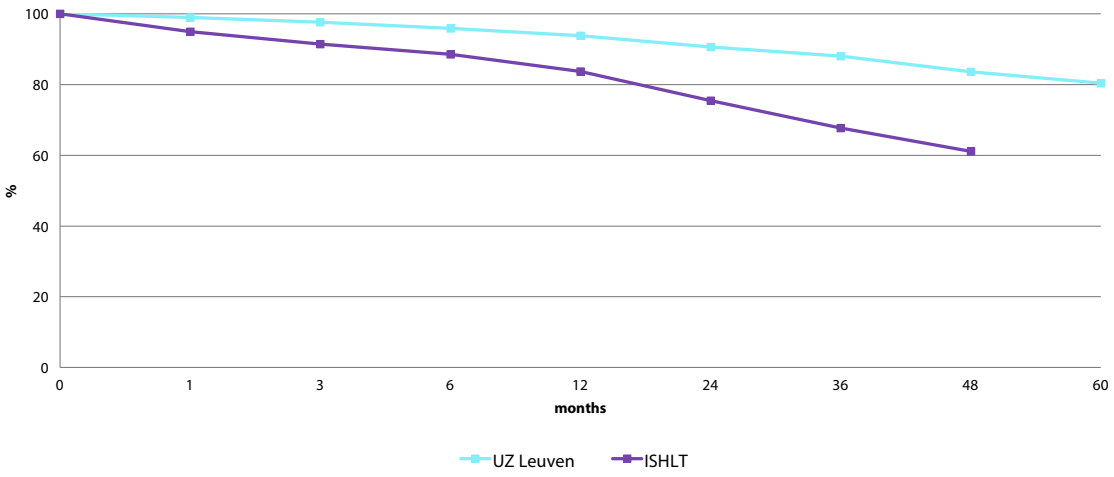


Figure 3.21 depicts a recent update of our transplant survival in cystic fibrosis patients.

FIGURE 3.21 | post transplant survival rate of CF patients (n=116). There is a trend to an improved rate over the last 11 years, compared to an earlier period.

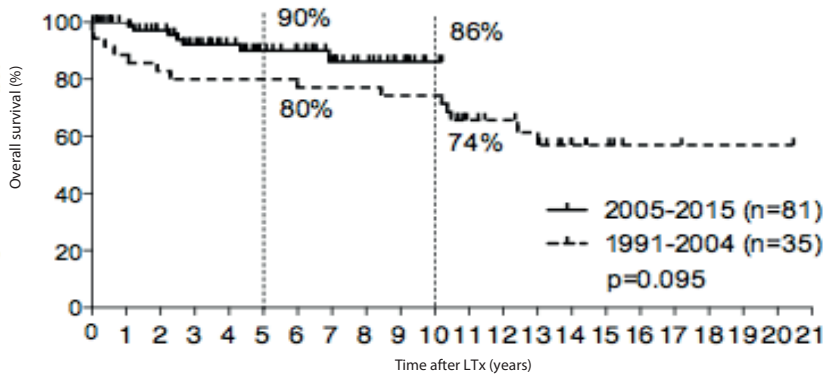


Figure 3.22 summarizes the number of lung transplant patients, actively followed in Leuven. There is an exponential increase in the number of patients, which leads to increased workload in ambulatory follow up as illustrated in in figure 3.23, illustrating the number of outpatients per year, which is again increased with 6%.

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

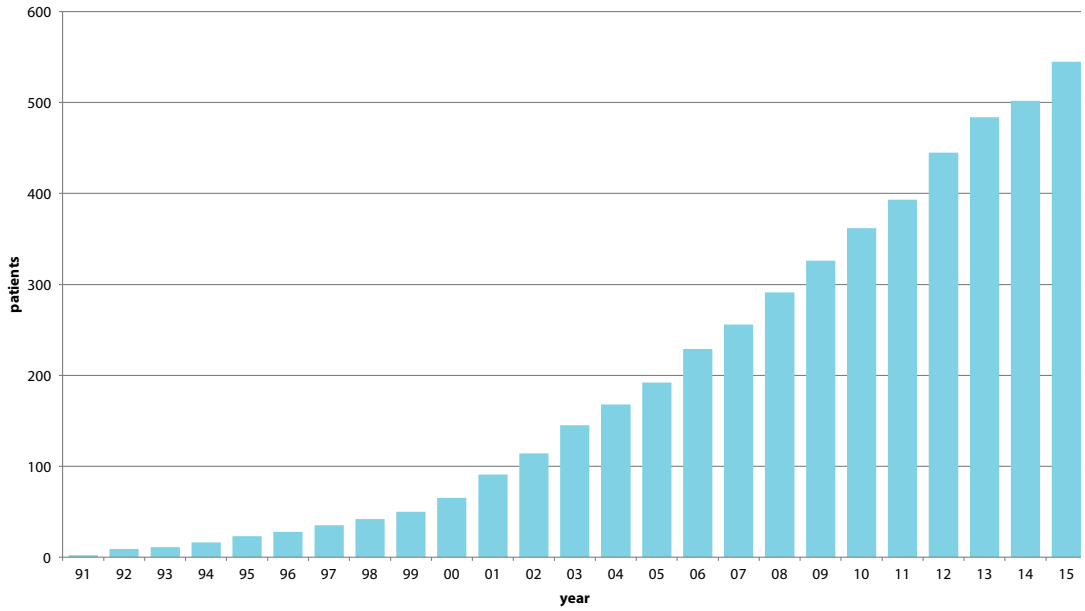
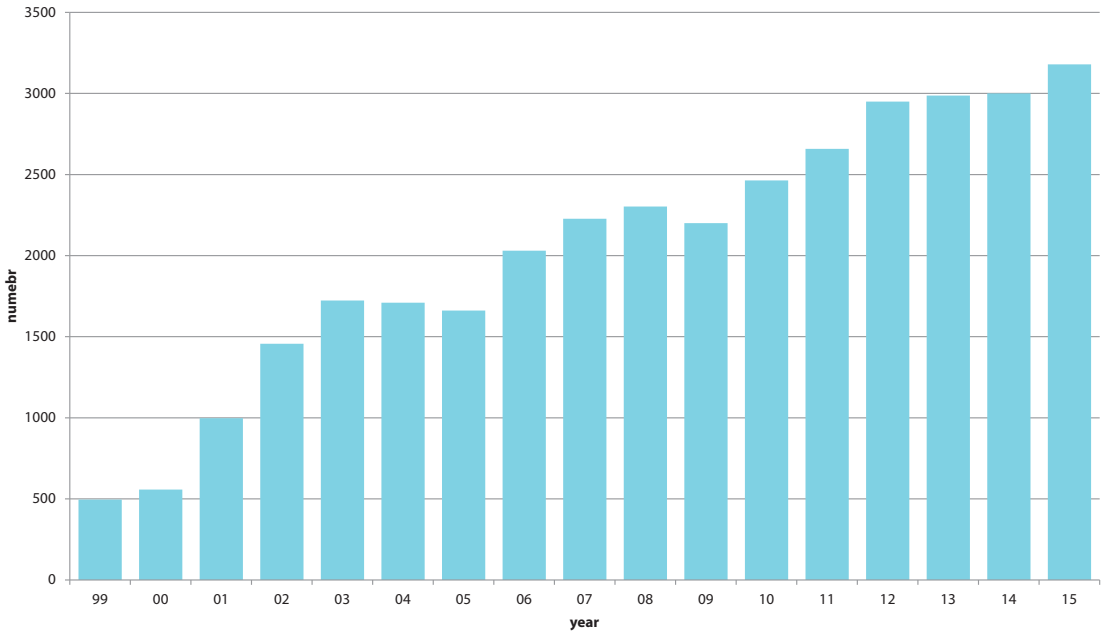


FIGURE 3.23 | number of outpatient visits per year since 1999



ear, nose & throat diseases, head and neck surgery
prof. dr. Pierre Delaere

pneumology
prof. dr. Geert Verleden, prof. dr. Christophe Dooms, prof. dr. Robin Vos
dr. Jonas Yserbyt

plastic, reconstructive and aesthestic surgery
prof. dr. Jan Vranckx, dr. Katarina Segers

thoracic surgery
prof. dr. Paul De Leyn, prof. dr. Dirk Van Raemdonck
dr. Philippe Nafteux, dr. Herbert Decaluwé

anaesthesiology
dr. Luc Veeckman

intensive care medicine
prof. dr. Sophie Van Cromphaut

teams OR – ICU – hospitalisation
Alexandra Meeus
Sus Vermeiren
Annemieke Schoonis, Leen Backaert

nurse specialist lung transplants
Veronique Schaevers

transplant coordination
Dirk Claes, Karlien Degezelle

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.

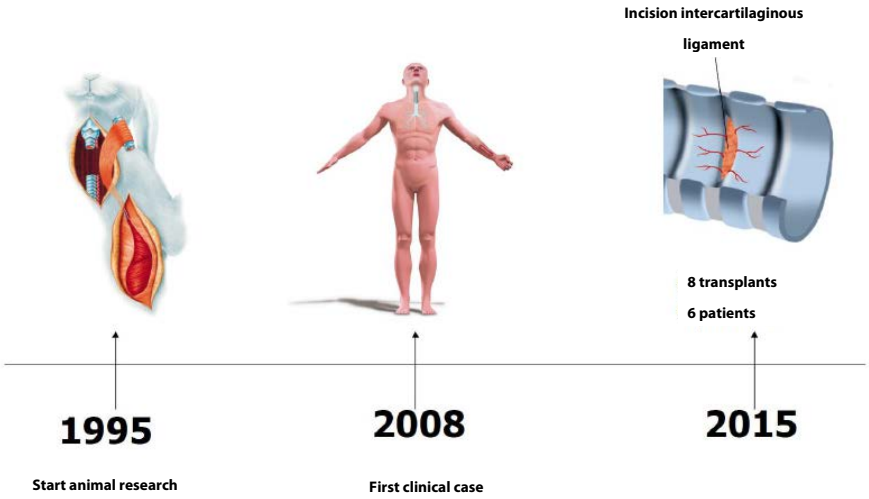
Case 7 13 April 2012: heterotopic transplantation. Withdrawal of immunosuppressive drugs.
4 February 2013: orthotopic transplantation.

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

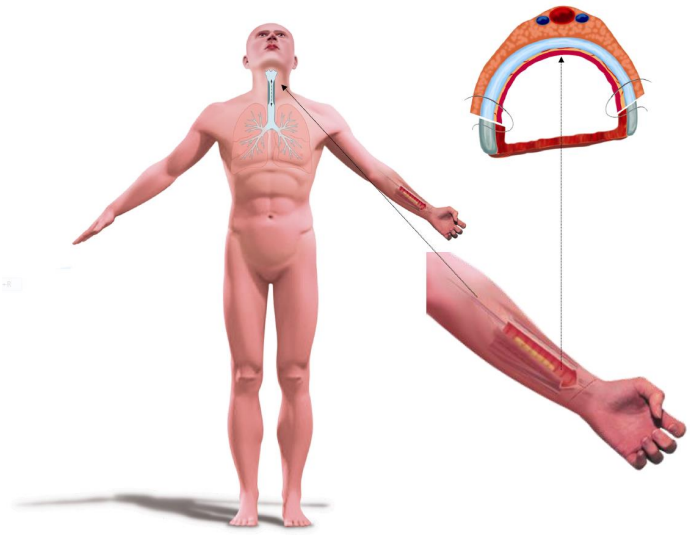
All indications were post-traumatic strictures. Only patient 5 concerned a low-grade chondrosarcoma.

Timeline of trachealtransplantation

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
prof. dr. Peter Witters*

* paediatric gastroenterology

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, prof. dr. Steffen Rex

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 program for pediatric solid organ transplantation includes kidney, liver and intestinal transplantation. The program for pediatric hemodialysis was initiated in 1976 and for peritoneal dialysis in 1984. The program for pediatric kidney transplantation was started in 1980, when initially the transplantation operative procedure was performed in Brussels (in the hospital of the "Université Catholique de Louvain (UCL)"). Since 1986 all activities take place in the university hospitals of Leuven (UZ Leuven).

In 1997 the first pediatric liver transplant was performed. Since 2013 the follow-up after liver transplantation is performed in collaboration with prof. dr. Peter Witters of the departement for pediatric gastroenterology and metabolic diseases.

Currently, dr Noël Knops is working on a PhD project entitled: "Pharmacogenetic determinants of calcineurin-inhibitor-induced nephrotoxicity: translational mechanisms in conditionally immortalized human proximal tubule cells (ciPTEC) from adult renal allograft recipients" in collaboration with prof. dr. Dirk Kuypers of the department of internal medicin and nephrology.

In addition, there has been a longstanding tradition of research in the field of pharmacokinetics and effects of exposure of immunosuppressives during childhood (started by prof.dr. Rita van Damme-Lombaerts*). Issues of compliance with therapy during childhood and the transition to adult care is another focus of attention (prof. Fabienne Dobbels).

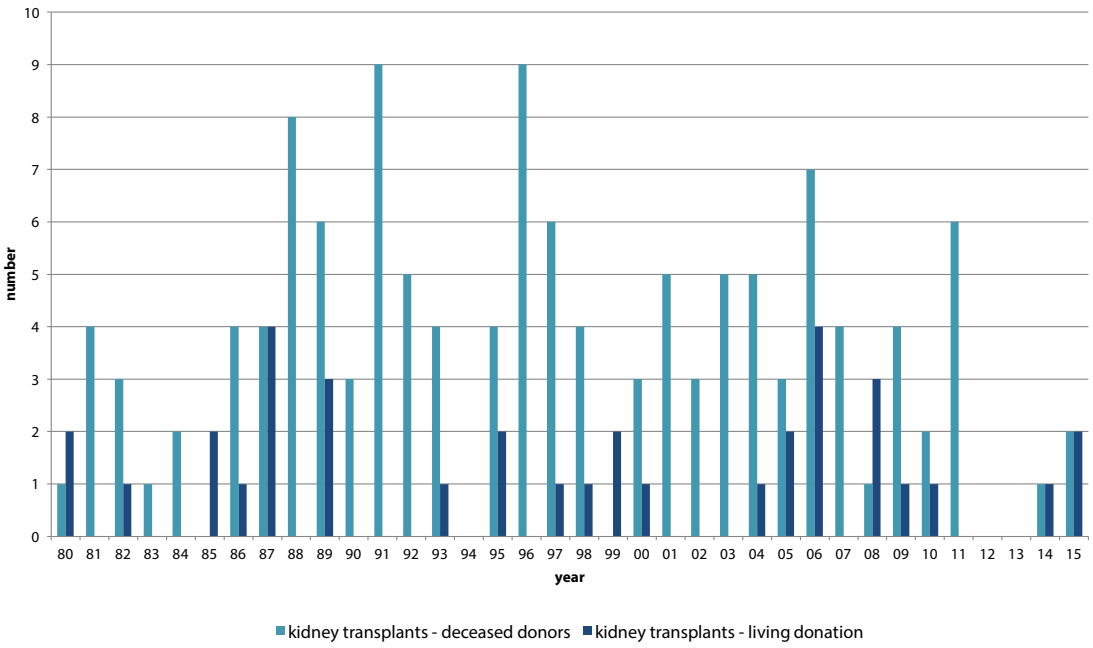
*emeritus

PAEDIATRIC KIDNEY TRANSPLANTS

In 2015, we performed four pediatric kidney transplantations, two of which with a living-related donor. One of the latter was complicated by acute renal artery thrombosis within the first week after transplantation and eventually a transplantectomy had to be performed.

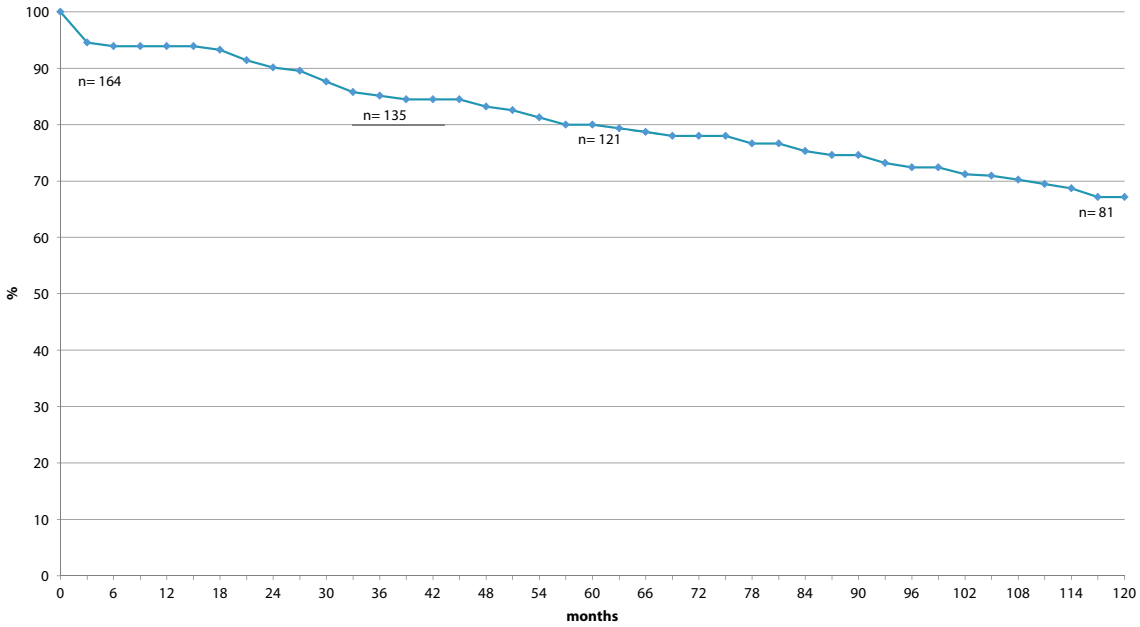
At the end of 2015, four children were active on the Eurotransplant waiting list for a deceased donor kidney. Seven children were on dialysis, three of whom were not eligible for transplantation at that time.

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



Since 1980 we performed 164 kidney transplantations in 148 children (86 boys and 62 girls) with a mean age of 10.7 years (±4.9) at transplantation. The total (=entire cohort) 1-year allograft survival is 94%; 3-year: 85%; 5-year: 80% and after 10 year: 67% *(figure 4.2)*. Twenty-two percent of all procedures were performed with a kidney derived from a living donor (n=36) .

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



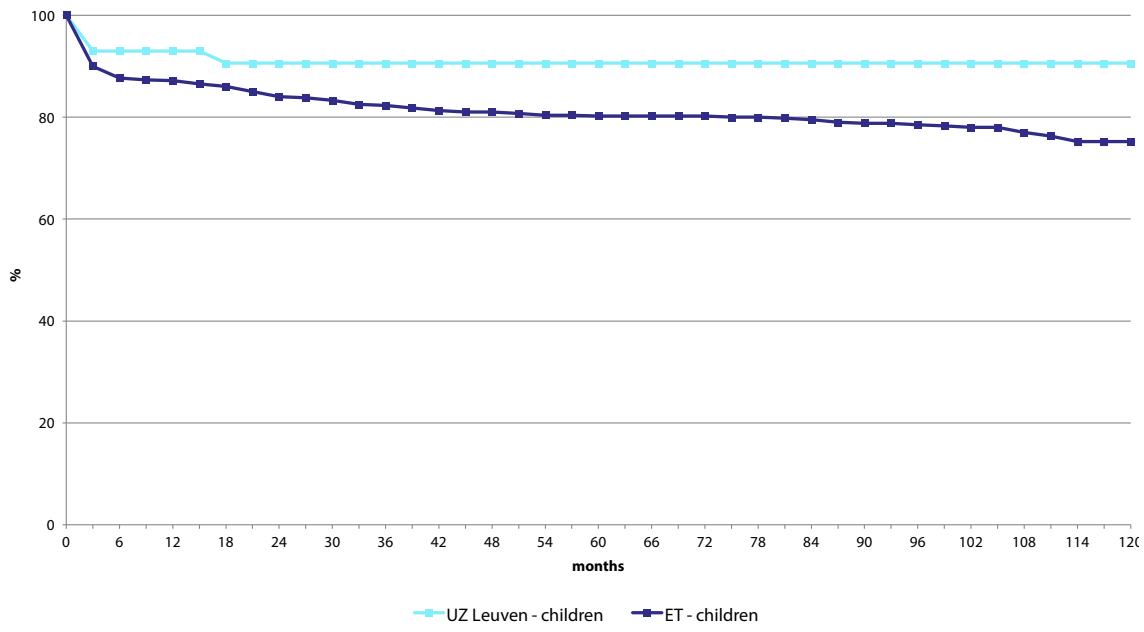
PAEDIATRIC LIVER AND INTESTINAL TRANSPLANTS

In 2015, we performed 2 liver transplantations in adolescent recipients. One patient suffered from auto-immune hepatitis with liver cirrhosis. The other patient had cystic fibrosis and received a combined liver-lung transplant.

This brings us to a total of 42 liver transplantation in 42 children (<18 year) performed in Leuven.

At the end of 2015 we have 5 children on the Eurotransplant waitinglist for a deceased donor liver (one in combination with a pancreas transplantation). We calculated the patient survival curve since the start of our program for pediatric liver transplantation and plotted this together with the survival data available from Eurotransplant. *(figure 4.3)*

FIGURE 4.3 | patient survival rate 120 months – paediatric liver transplants (1997-2015), UZ Leuven vs ET



In 2015, no pediatric intestinal transplantations were performed.

The three children who received a multivisceral transplantation in 2004, 2008 and 2014 are in good condition. They are able to tolerate full oral feeds and go to school.

PART 5

TISSUE AND CELL BANKS

banks for human bodily material

AC Biobanking / cell and tissue banks

Transplantation program

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

Bank for skin grafts
- Intensive medicine : center for burns
- Plastic, reconstructive and esthetic surgery

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

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

Bank for ophthalmic tissues
- Eye-surgery

Bank for keratinocytes
- Intensive medicine : center 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
Maarten Vanhaecke, Bert Verduyckt

skin grafts
tissue coordinators: Dimitri Aertgeerts, Luc Ampe, Henk Desplentere
Maarten Vanhaecke, Bert Verduyckt

ophtalmic tissues
tissue coordinators: Dimitri Aertgeerts, Luc Ampe, Henk Desplentere
Maarten Vanhaecke, Bert Verduyckt
tissue technologists: Gerda Mahy

tympano-ossicular grafts
tissue coordinators: Dimitri Aertgeerts, Luc Ampe, Henk Desplentere
Maarten Vanhaecke, 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, Julie De Louker
Louise Lauweryns, Werner Scheers, Sarah Van Diest, Veerle Verslegers

keratinocytes
tissue technologists: Inge Daris, Katrien Smaers

haematopoietic stem cells
staff members: prof. dr. Michel Delforge, prof. dr. Timothy Devos
tissue technologists: Marianne Boogaerts, 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, Malicorne Buysse

quality assurance
Johan Klykens, Franky Sinap

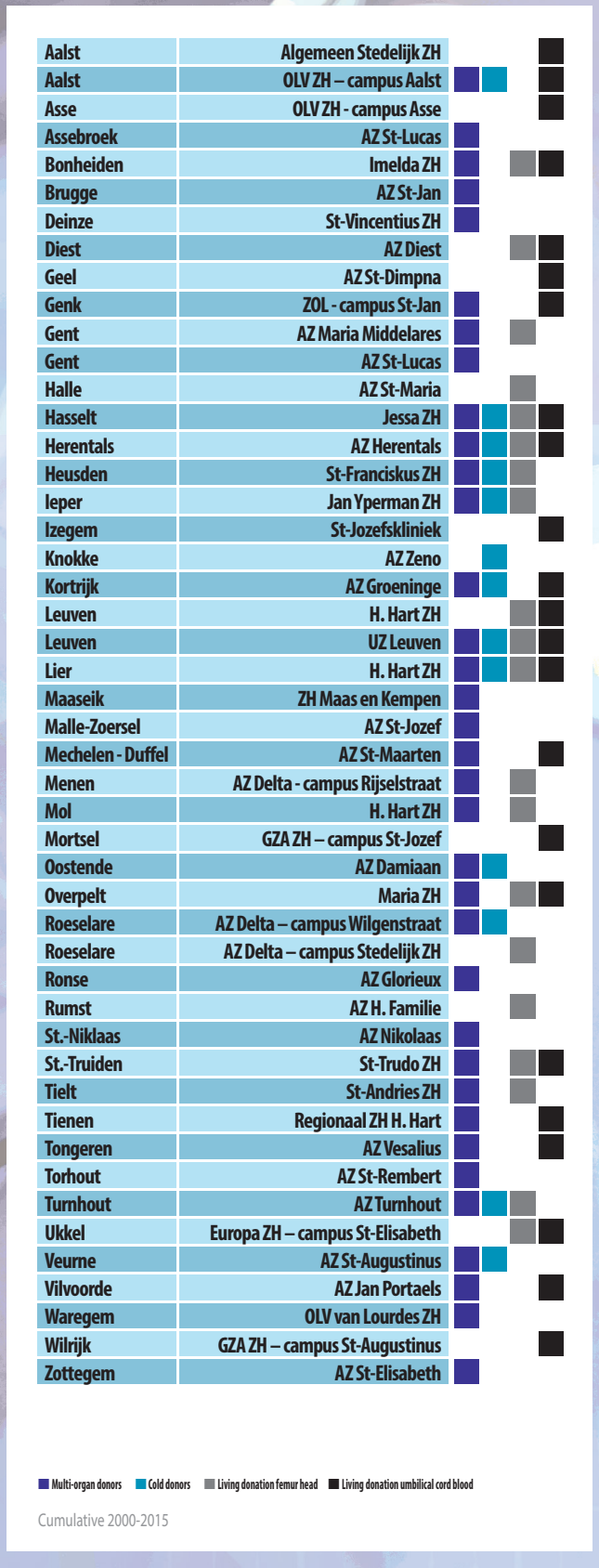
administrative support / coordination
Carla Collijs, Diane Reggers, Sandra Van Effen

managers
prof. dr. em. 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

The cell and tissue banks of UZ 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 organization sets itself as goal to optimize 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.



Cumulative 2000-2015

Living donors

Within cell and tissue banks this type of procurement covers different domains. The patient is informed through an informed consent 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 (1203 in 2015, status quo compared to 2014) under increasingly stringent regulations (current legislation: law of December 19, 2008 and implementing royal decrees end 2009). Femoral heads were donated in 14 Flemish hospitals.

TABLE 5.1 | evolution donor hospitals ~ femoral head donations 2005 – 2015

Centre		05	06	07	08	09	10	11	12	13	14	15
Bonheiden	Imelda ZH	-	-	-	-	-	56	136	155	167	168	**196**
Diest	AZ Diest	21	10	18	13	10	21	18	25	32	56	**66**
Gent	AZ Maria Middelares	-	-	-	-	-	-	-	5	1	-	**-**
Halle	AZ St-Maria	15	19	17	22	29	48	59	64	57	75	**69**
Hasselt	Jessa ZH	62	56	14	72	83	93	88	-	-	-	**-**
Herentals	AZ Herentals	-	-	-	-	-	-	3	27	68	114	**129**
Heusden	St-Franciskus ZH	-	-	-	-	-	-	-	-	-	6	**2**
Ieper	Jan Yperman ZH	-	-	-	-	-	-	-	-	56	113	**183**
Leuven	H. Hart ZH	58	65	57	79	35	71	62	72	66	86	**66**
Leuven	orthopedie UZ Leuven	71	31	82	105	122	147	143	134	97	95	**92**
Leuven	traumatologie UZ Leuven	33	16	7	8	2	1	2	1	-	-	**-**
Lier	H. Hart ZH	-	-	-	-	-	157	193	151	134	102	**84**
Menen	AZ Delta – campus Rijselstraat	18	-	-	-	-	-	-	-	-	-	**-**
Mol	H. Hart ZH	-	-	-	-	67	73	74	55	51	57	**32**
Overpelt	Maria ZH	16	47	48	47	39	29	11	-	-	-	**-**
Roeselare	AZ Delta – campus Stedelijk ZH	-	-	-	-	-	-	-	-	106	174	**125**
Rumst	AZ H. Familie	22	11	23	3	23	3	29	10	12	14	**14**
St-Truiden	St-Trudo ZH	35	36	31	23	22	47	39	59	70	81	**103**
Tielt	St-Andries ZH	-	-	-	-	-	-	8	24	50	57	**42**
Turnhout	AZ Turnhout	-	-	-	3	-	-	-	-	-	8	**-**
Ukkel	Europa ZH – campus St-Elisabeth	-	-	-	11	11	17	14	-	-	-	**-**
Total		351	291	297	386	443	763	879	782	967	1206	1203

Placental membranes donation

Amnion and chorion grafts are collected during normal deliveries in collaboration with the umbilical cord blood bank of UZ Leuven. The 6 donations in 2015 were obtained via the obstetrics department of UZ Leuven. These grafts are used as a bandage to cover skin defects as well as defects form the surface of the eye.

Keratinocyte donation

Keratinocytes are isolated from the epidermis, the superficial part of the skin. They are preferably obtained from skin from 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. In 2015 no new donor was needed.

Umbilical cord blood donation

Blood is collected from the umbilical cord immediately after the baby is born and the umbilical cord has been transsected. 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 2015 506 samples were frozen at the Leuvense Navelstrengbloedbank (Leuven Umbilical Cord Blood Bank). On the 1st of January 2016 10 899 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 – 2015

Centre		11	12	13	14	15
Aalst	Algemeen Stedelijk ZH	-	-	-	4	10
Aalst	OLV ZH – campus Aalst	58	36	24	31	12
Asse	OLV ZH – campus Asse	-	-	15	25	9
Bonheiden	Imelda ZH	65	40	35	43	21
Diest	AZ Diest	36	20	34	23	12
Genk	ZOL – campus St-Jan	106	62	45	89	46
Hasselt	Jessa ZH	35	37	38	87	40
Herentals	AZ Herentals	46	47	50	42	23
Izegem	St-Jozefskliniek	33	28	28	29	11
Kortrijk	AZ Groeninge	-	-	-	64	41
Leuven	H. Hart ZH	77	49	53	54	27
Leuven	UZ Leuven	57	34	55	46	21
Lier	H. Hart ZH	-	-	-	57	36
Mechelen - Duffel	AZ St-Maarten	-	-	35	36	34
Mortsel	GZA ZH – campus St-Jozef	-	-	-	18	17
Overpelt	Maria ZH	-	-	-	45	37
St-Truiden	St-Trudo ZH	25	29	15	14	15
Tienen	Regionaal ZH H. Hart	52	34	41	25	14
Tongeren	AZ Vesalius	41	28	31	49	38
Vilvoorde	AZ Jan Portaels	34	30	29	34	13
Wilrijk	GZA ZH – campus St- Augustinus	-	-	5	31	24
Familiaal		-			11	5
Total - frozen		665	474	533	857	506

Hematopoietic stem cell (HSC) donation

HSC are collected using apheresis technology (peripheral stem cell collection) or bone marrow collection. They can be frozen for autologous use in patients suffering from a haematological disease (stem cell collection following chemotherapy and several months of reinfusion of stem cells with an autologous stem cell transplant). Using similar techniques stem cells are collected from healthy donors (related or not related) 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 UZ Leuven MSCP (Mesenchymal Stem Cell Programme) was accredited as a cell bank by FAMHP (the Federal Agency for Medication and Health Products - FAGG). In collaboration with the University of Liège (CHU) the department of hematology of UZ Leuven administered, in the period from February 2008 till end of 2015, 15 MSC infusions in the setting of GvHD and 9 because of graft failure.

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 as well in as outside UZ Leuven *(Table 5.3)*. In 2015 this type of donation accounted for 6 donors (all multi-tissue donors). It remains an important underuse of the number of potential donors, and motivates us to keep on 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 2005 - 2015

Centre		05	06	07	08	09	10	11	12	13	14	15
Aalst	OLV ZH – campus Aalst	1	2	1	2	-	-	-	-	-	-	-
Hasselt	Jessa ZH	-	-	2	-	-	-	-	1	-	-	-
Herentals	AZ Herentals	-	-	-	-	-	-	-	-	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	15	3	25	13	2	-	2	2	-	1
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 Turnhout	-	-	1	-	-	-	-	-	-	-	-
Veurne	AZ St-Augustinus	-	-	1	-	-	1	5	4	2	2	5
Total		26	17	9	28	17	6	6	11	9	3	6

Multi-organ donors

Multi-organ donation is a high-impact matter for the patient' s close relatives. For many recipients 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 happen that relatives selectively refuse tissue donation. Their wishes are extensively discussed with the transplant coordinators in advance and -of course- 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 3 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 2015 tissues were procured from 68 donors in 22 Flemish hospitals (of which 1 newcomer). For deceased donors similarly stringent legislation is applicable as for living donors (same law of December 19, 2008 and implementing decisions end 2009).

TABLE 5.4 | evolution donor hospitals ~ multi-organ donors 2005 - 2015

Centre		05	06	07	08	09	10	11	12	13	14	15
Aalst	OLV ZH – campus Aalst	1	4	4	3	-	2	2	1	5	1	**5**
Assebroek	AZ St-Lucas	-	-	2	1	-	2	1	2	-	-	**1**
Bonheiden	Imelda ZH	-	2	4	2	1	2	-	1	3	3	**4**
Brugge	AZ St-Jan	-	1	-	-	1	1	1	-	-	3	**7**
Deinze	St-Vincentius ZH	1	-	-	-	-	1	-	-	-	-	**-**
Genk	ZOL – campus St-Jan	4	11	10	5	4	5	7	4	4	6	**4**
Gent	AZ Maria Middelares	-	-	1	-	-	-	-	-	-	-	**-**
Gent	AZ St-Lucas	2	2	-	-	-	-	-	-	-	-	**-**
Hasselt	Jessa ZH	3	3	4	6	5	10	5	6	7	6	**7**
Herentals	AZ Herentals	-	-	-	-	-	-	-	-	-	2	**1**
Heusden	St-Franciskus ZH	-	6	3	3	2	1	4	3	2	1	**2**
Ieper	Jan Yperman ZH	1	-	-	-	1	3	1	2	-	1	**1**
Kortrijk	AZ Groeninge	6	4	5	3	4	-	7	4	4	3	**5**
Leuven	UZ Leuven	13	8	13	7	5	10	10	11	7	15	**6**
Lier	H. Hart ZH	1	5	2	3	3	1	7	2	2	6	**3**
Maaseik	ZH Maas en Kempen	-	-	-	-	-	-	-	-	-	2	**-**
Malle-Zoersel	AZ St-Jozef	-	1	-	1	1	1	-	-	-	2	**-**
Mechelen - Duffel	AZ St-Maarten	-	-	-	-	-	1	1	-	-	-	**1**
Menen	AZ Delta – campus Rijselstraat	-	-	-	-	-	-	-	-	1	-	**1**
Mol	H. Hart ZH	-	-	-	-	1	-	2	-	1	-	**-**
Oostende	AZ Damiaan	-	3	-	4	2	-	-	2	1	2	**3**
Overpelt	Maria ZH	-	-	-	1	1	-	1	-	-	1	**1**
Roeselare	AZ Delta – campus Wilgenstraat	6	6	5	1	3	5	5	6	7	6	**8**
Ronse	AZ Glorieux	-	-	-	-	-	-	-	-	-	1	**-**
St.-Niklaas	AZ Nikolaas	-	-	2	3	1	1	2	1	1	1	**3**
St.-Truiden	St-Trudo ZH	-	-	1	-	-	2	1	1	2	1	**1**
Tielt	St-Andries ZH	-	-	-	1	-	1	2	-	-	-	**2**
Tienen	Regionaal ZH H. Hart	-	-	-	-	-	-	-	-	-	-	**1**
Tongeren	AZ Vesalius	-	-	-	-	-	-	-	1	-	-	**-**
Torhout	AZ St-Rembert	-	1	-	-	-	-	1	1	-	-	**-**
Turnhout	AZ Turnhout	4	1	1	2	2	2	3	5	1	2	**-**
Veurne	AZ St-Augustinus	2	-	3	4	8	11	3	5	2	2	**-**
Vilvoorde	AZ Jan Portaels	1	-	-	-	-	-	-	1	-	-	**1**
Waregem	OLV van Lourdes ZH	-	-	1	1	-	1	-	-	-	-	**-**
Zottegem	AZ St-Elisabeth	-	-	1	-	-	-	-	-	-	-	**-**
Total		**45**	**58**	**62**	**51**	**45**	**63**	**66**	**59**	**50**	**67**	**68**

A further professionalization of the process of tissue donation and procurement, a dedicated team of tissue coordinators, but not at least a clear, efficient and professional communication between tissue bank, donor hospitals (physicians, nurses, social and pastoral services) and transplant coordinators remains the cornerstone for the existence of the tissue bank. Above all this is impossible without an extreme solidarity and altruism.

Tissue and cell Banks - 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 the leading and organization of a cell and tissue bank. According to the existing legal framework the responsible person takes care of

- ensuring that, in the establishment for which that person is responsible, human cells and tissues are procured, tested, processed, stored and distributed in accordance with the national framework. He/she 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/she will address to the Minister in respect of confidentiality of the data relating to donors and receptors.
- the notification to the relevant competent authorities of all 'serious adverse event' and 'serious adverse reactions' as well as the preparation of a report analyzing 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 responsible person. Distribution can be requested based on a medical prescription written by the person in charge of the implantation or on request of a recognized institution.

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

Bank for musculo-skeletal allografts

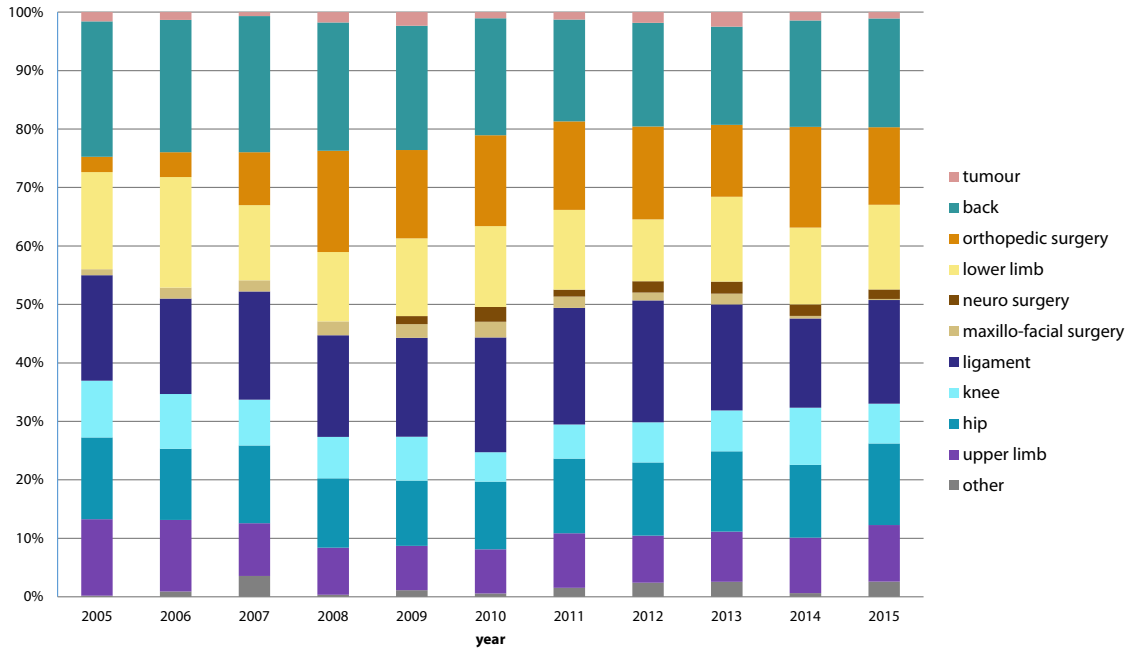
This bank is the most complex as well from point of view of basic material, types of products, sorts of manipulations and care programs.

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 lyophilization and irradiation, freezing, 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, demineralized cortical bone (DBM), fresh cartilage fragments, …

Orthopedic 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 stabilize prosthesis, implants, …) and occasionally reinforcement (e.g. fascia's). Figure 5.1 demonstrates the variability of users and indications.

FIGURE 5.1 | use of grafts of the musculo-skeletal system in function of indication (area) from 2005 until 2015



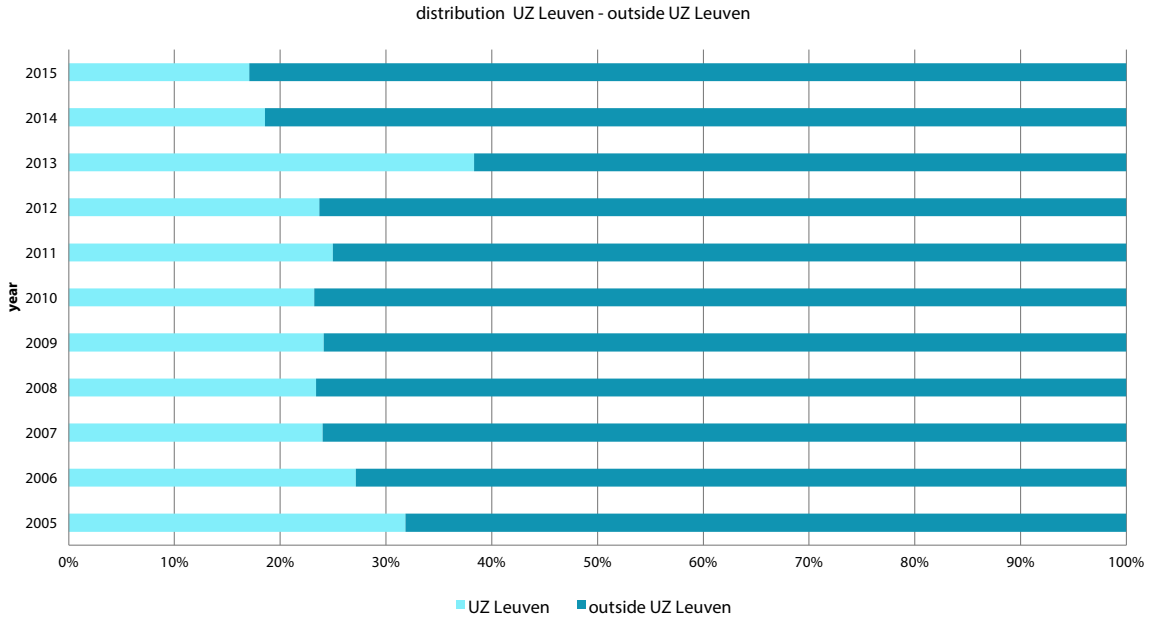
(The analysis is based on data retrieved from the medical prescriptions ; when rather non-specific information is obtained the information is regrouped under for example orthopaedics, upper limb, neurosurgery, lower limb, not otherwise specified.)

The type of grafts used differs on the one hand in function of the medical discipline but also the patient, the underlying condition, the used techniques. Al this is reflected in a different use in different hospitals *(figure 5.2)*.

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

As indicated earlier on these tissues originate from living, cold and multi-organ donors, these donors originate from numerous hospitals. Therefore our ultimate aim is: 'the UZ Leuven-KU Leuven tissue and cell banks 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 organization sets itself as goal to optimize 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 al our partners in donation.

FIGURE 5.2 | distribution of use of grafts of the musculoskeletal system within UZ Leuven vs other hospitals from 2005 until 2015



Skin bank – bank for placental membranes – keratinocyte bank

In UZ 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 in between the different skin banks which is very important since large amounts of skin can be needed when major catastrophes occur. In 2015 skin was delivered for 85 interventions.

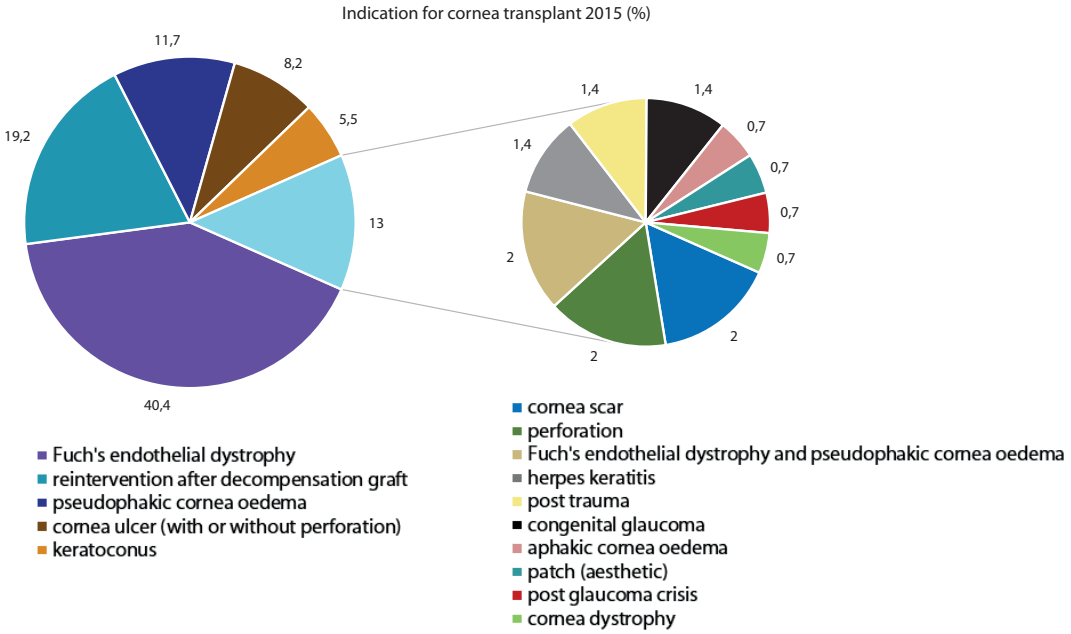
The placental membranes are lyophilized and irradiated (amnion membranes, chorion membranes) and are stored at room temperature. The keratinocytes are frozen and stored at -196°C (liquid nitrogen). The most important indications for the use of these grafts are skin defects due to chronic lower leg ulcers, diabetic feet, trauma, arterial/venous ulcers, sclerodermia, pyoderma gangrenosum, oncological pathology, epidermolysis bullosa, burns, …) The clinical departments requesting these grafts are dermatology, vascular center, burns and traumatology. In 2015 placental membranes and keratinocytes were provided for 70 and 4 interventions respectively.

Bank for ophthalmic tissues

Ophthalmic allografts are cornea, sclera or other ocular tissue. As a rule, in Belgium, the eye is enucleated in total. After decontamination the corneo-scleral 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.

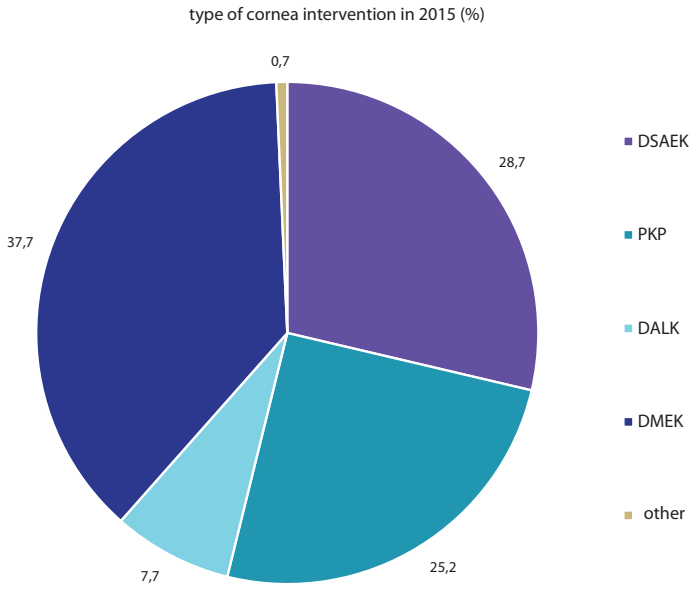
A large number of circumstances can result in a damage of the cornea hindering vision. Figure 5.3 shows these different conditions in relative proportion.

FIGURE 5.3 | indications for corneal transplantation in 2015



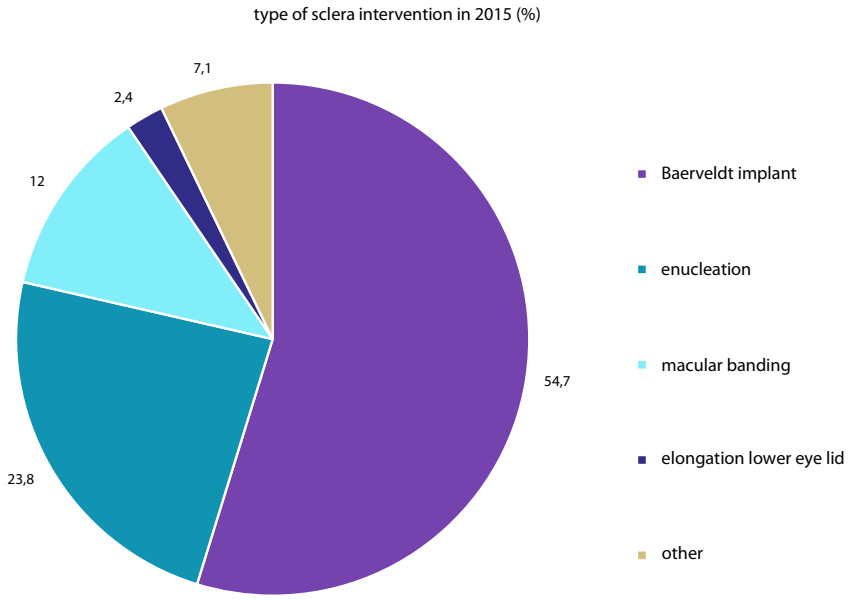
The damage to the cornea can be corrected through different types of surgical interventions *(figure 5.4)*.

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



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)*.

FIGURE 5.5 | indications for sclera transplantation in 2015



In 2015 ophthalmic tissues were delivered for approximate 200 surgical interventions.

Umbilical cord blood – Hematopoietic stem cells – mesenchymal stem cells

These types of grafts are mainly used in hematological patients.

In 2015 6 umbilical cord bloods were transferred to stem cell transplantation centers abroad.

In 2015 the UZ Leuven Hematopoietic Stem Cell Bank prepared 131 transplants, including 47 autologous and 84 allogeneic transplants (28 sibling, 48 MUD (=matched unrelated donor), 8 haploidentical). The applied hematopoietic stem cells were obtained via peripheral stem cell collection (120) and bone marrow procurement (11).

In 2015 2 patients were treated with MSC (1 for acute GvHD and 1 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 2015 in order to allow clinical trials. In the near future the clinical trials will be the major challenge from different perspectives e.g. variability of questions, international/multicentric context, numbers, need in personnel, ….

Other tissues and cells

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

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

PART 6

ISLET TRANSPLANTS

endocrinology

prof. dr. Pieter Gillard

prof. dr. Chantal Mathieu

dr. Da Hae Lee (PhD student)

abdominal transplant surgery - procurement

prof. dr. Jacques Pirenne, prof. dr. Diethard Monbaliu

prof. dr. Ina Jochmans

abdominal surgery

dr. Matthias Lannoo

radiology – intraportal injection islet graft

prof. dr. Geert Maleux, prof. dr. Sam Heye

dr. Sandra Cornelissen

team hospitalisation

Vicky Hooyberghs and team 642

diabetes educators

Rudi Caron, Nadine Pardon

Brigitta Swennen, Anna Vereertbrugghen

study coordination

Hilde Morobé and team

Islet transplant care programme

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

This unique clinical islet transplant program 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 Professor Dr. Daniel Pipeleers and Professor 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 hypoglycemic unawareness) (= islets transplantation alone) (*see figure 6.1*).

Since the end of 2001, UZ Leuven became active as an implant center and in the screening and follow-up of patients. Since then 42 type 1 diabetic patients received in total 75 allografts in Leuven, almost exclusively islet transplants alone (n=41 patients). Patients were referred by participating university and non-academic centers. The main indications for islet transplantation currently are 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. The reason for using this new sites is to explore sites that might be used to implant cells from other sources such as stem- or xenocells.

ISLETS TRANSPLANTS

Activity in 2015 of the multicentric programme

In 2015, 5 patients received transplants with a total of 9 β-cell allografts. More than 50% of the processed and transplanted Belgian organs were procured by the UZ Leuven donor center.

Allografts were transplanted into the liver (n=6) or in the omentum (n=3) . 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 4 out of 5 recipients. Restoration of endogenous insulin secretion resulted in a reduction in the hypoglycaemia risk, insulin requirement and an HbA1c up to < 7.0 %. Posttransplantation none of the patients suffered from severe hypoglycemia or diabetic ketoacidosis.

Patient and graft survival from 2001 to 2015

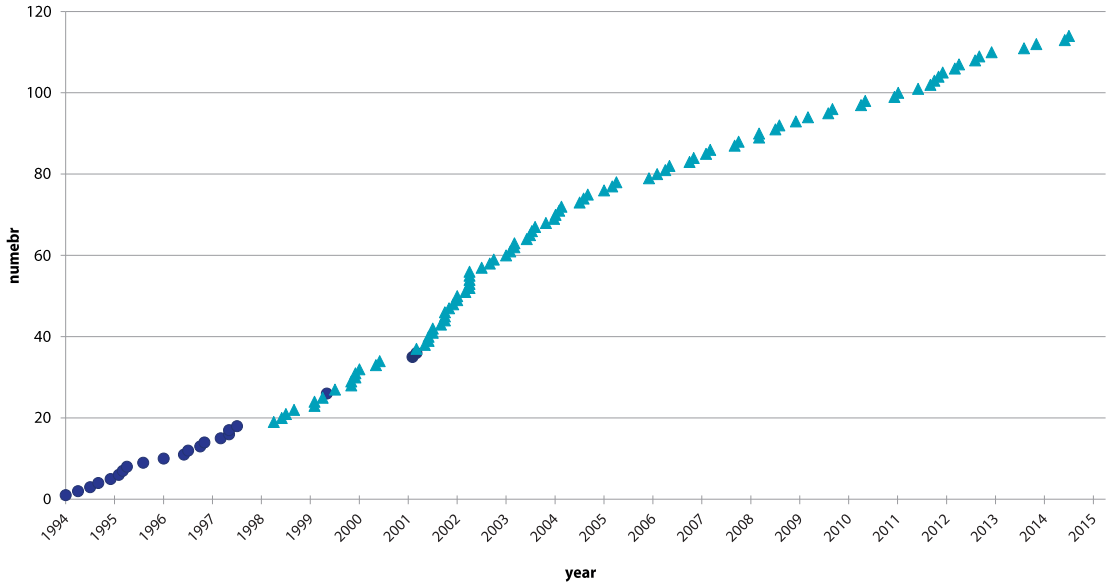
The outcome of type 1 diabetes patients who received a transplant with sufficient cells (= ≥ 2 X 10^6 per kg body weight per transplant) between 2001 (start of first JDRF protocol) and December 2015 are as follows:

After 1 year
- Patient survival: 99%
- Graft survival (= C-peptide of ≥ 0.5 ng/ml or > 0.15 nmol/l): 80%

After 3 years
- Patient survival: 97%
- Graft survival (= C-peptide of ≥ 0.5 ng/ml or > 0.15 nmol/l): 49%

After 5 years
- Patient survival: 97%
- Graft survival (= C-peptide of ≥ 0.5 ng/ml or > 0.15 nmol/l): 23%

FIGURE 6.1 | islets graft recipients in Belgium between 1994 and 2015. 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 on islet transplants were mainly carried out in non-uremic patients (light blue triangles).



UZ Leuven
Transplant Council
Herestraat 49
3000 Leuven

www.uzleuven.be/txsurgery
transplantatiecoordinatie@uzleuven.be

Design and production: communication service University Hospitals Leuven

UZ LEUVEN | RAAD VOOR TRANSPLANTATIE

IN COLLABORATION WITH LSGO
(Leuven Organ Donation Partnership)