Voordelen van levende niertransplantatie: Ontvanger

ORPADT 14.11.2023

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Inhoud:

- CKD en classificatie
- NBVN Cijfers voor niervervangende therapieën
- **Voordelen van levende niertransplantatie:**
  - Korte en lange termijn
- Nadelen van living donatie voor de ontvanger

Definitie van CKD:

Criteria for CKD (either of the following present for > 3 months)	
Markers of kidney damage (one or more)	Albuminuria (AER ⩾30 mg/24 h; ACR ⩾30 mg/g (⩾3 mg/mmol)) Urine sediment abnormalities Electrolyte and other abnormalities due to tubular disorders Abnormalities detected by histology Structural abnormalities detected by imaging History of kidney transplantation
Decreased GFR	GFR <60 ml/min per 1.73 m^2 (GFR categories G3a–G5)

Abbreviations: ACR, albumin-to-creatinine ratio; AER, albumin excretion rate; CKD, chronic kidney disease; GFR, glomerular filtration rate.

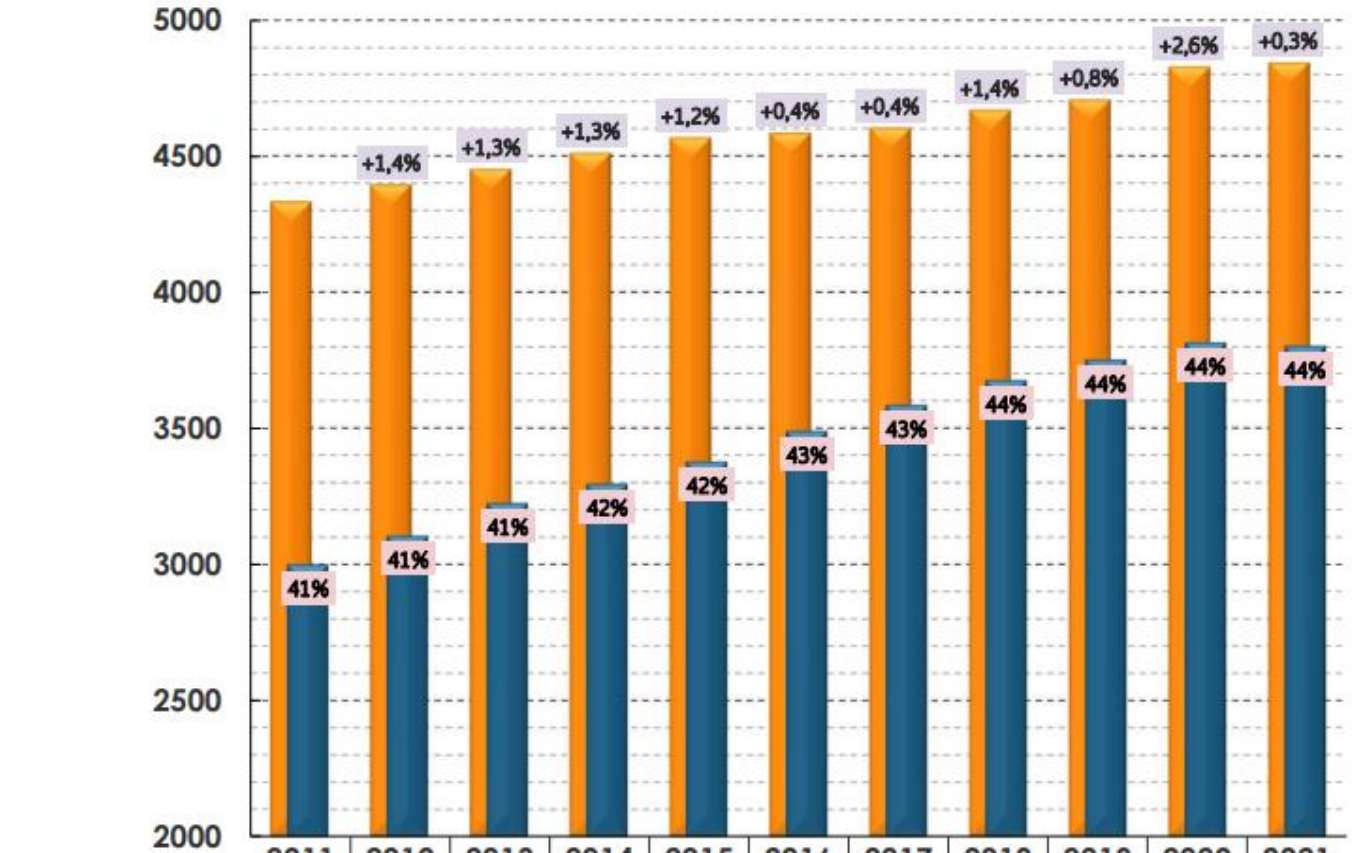
KDIGO Guidelines 2012

CKD-classificatie volgens KDIGO:

GFR category	GFR (mL/min/1.73 m²)	Terms
G1	≥90	Normal or high
G2	60–89	Mildly decreased
G3a	45–59	Mildly to moderately decreased
G3b	30–44	Moderately to severely decreased
G4	15–29	Severely decreased
G5	<15	Kidney failure

Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group.
Note: Data from KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. *Kidney Int Suppl.* 2013;3:1–150.[2]
Abbreviation: GFR, glomerular filtration rate.

KDIGO Guidelines 2012



	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
dialyse	4334	4396	4453	4513	4569	4587	4604	4670	4708	4829	4845
transplantatie	3000	3106	3226	3297	3378	3490	3586	3677	3753	3816	3803
Totaal in RRT	7334	7502	7679	7810	7947	8077	8190	8347	8461	8645	8648

PREVALENTIE – 2011-2021

Totaal aantal patiënten behandeld met nierfunctievervangende therapie [RRT] in NBVN

op 1 januari, 2011-2021

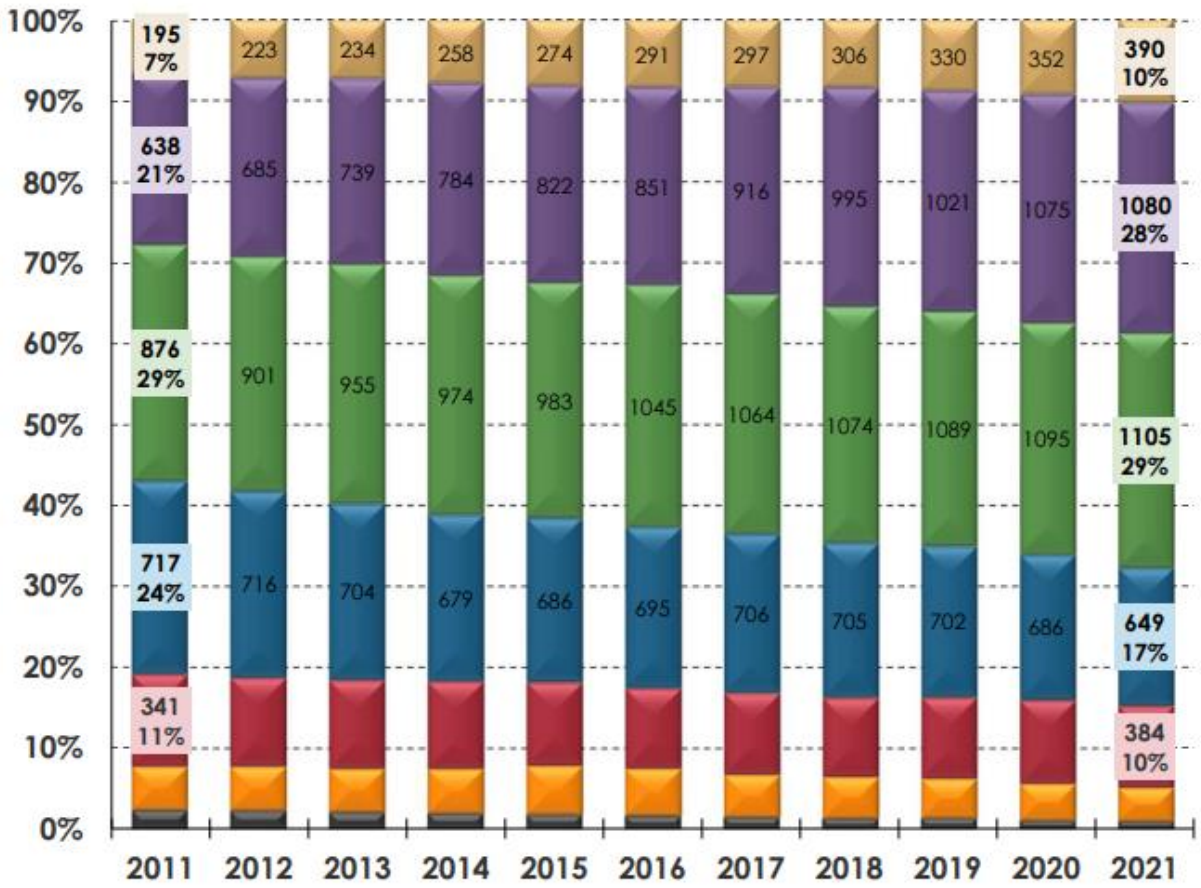
verdeling volgens dialyse en transplantatie

1 jan 2021, N= 8 648

Dialyse = 56%

Transplantatie = 44%

Jaarverslag NBVN 2021



PREVALENTIE – 2011-2021

Totaal aantal patiënten in NBVN met niertransplantaat

op 1 januari, 2011-2021

verdeling volgens leeftijdsklasse

- ≥75 jaar
- 65 - 74 jaar
- 55 - 64 jaar
- 45 - 54 jaar
- 35 - 44 jaar
- 25 - 35 jaar
- <25 jaar

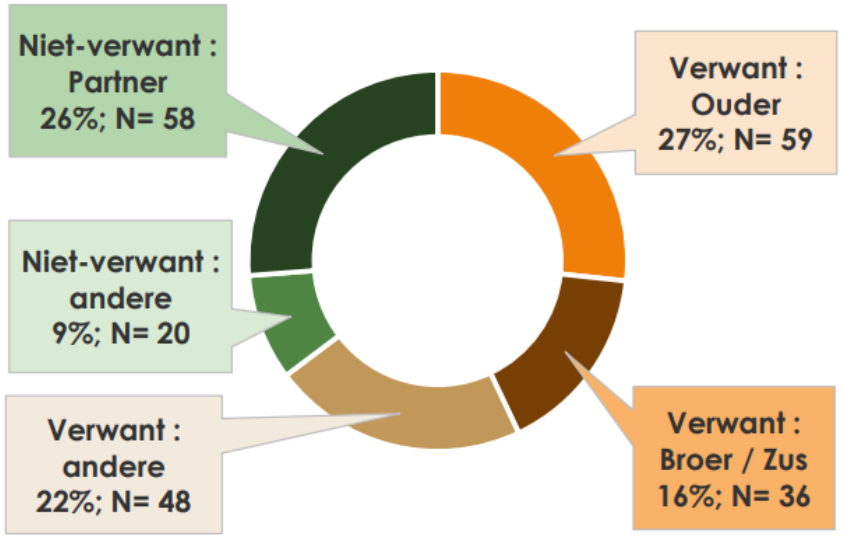
Totaal patiënten met nier-transplantaat	3000	3106	3226	3297	3378	3490	3586	3677	3753	3816	3803

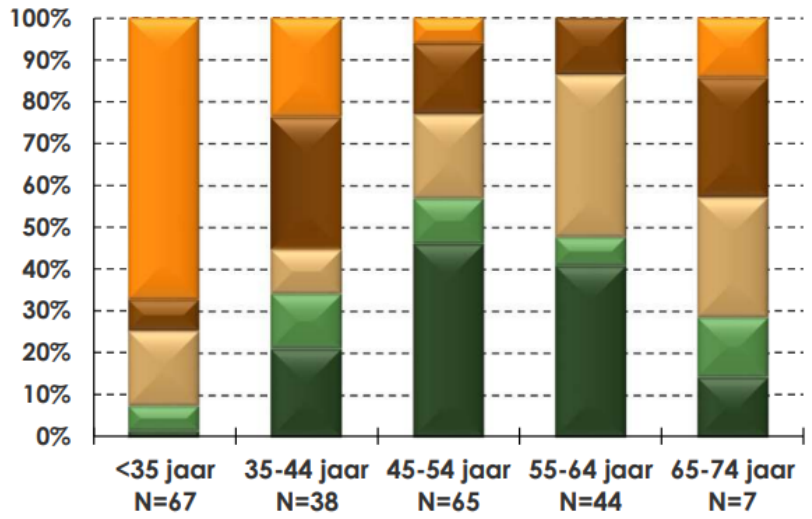
TRANSPLANTATIE – 2011-2020

Transplantatie met levende donoren bij NBVN patiënten

kalenderjaren
2011-2020
N= 221

Verwantschap donor, per leeftijdsklasse ontvanger





Kidney transplants per million population, by year, by country, by donor type

	Donor type	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
Austria	Deceased	41.1	44.1	41.5	42.1	40.9	39.0	34.8	32.7	29.6	31.3
	Living	8.6	8.3	7.2	7.7	7.9	7.9	8.8	5.1	4.7	6.1
Austria		**49.7**	**52.4**	**48.7**	**49.8**	**48.8**	**46.9**	**43.6**	**37.7**	**34.3**	**37.4**
Belgium	Deceased	39.2	37.0	41.9	40.0	42.7	41.6	33.9	28.3	31.0	36.4
	Living	5.7	6.0	5.1	5.9	5.5	5.0	3.9	3.2	5.1	4.7
Belgium		**44.9**	**43.0**	**47.0**	**46.0**	**48.3**	**46.6**	**37.8**	**31.5**	**36.1**	**41.1**
Croatia	Deceased	48.1	43.6	49.2	43.7	37.1	43.4	31.4	23.4	29.5	26.3
	Living	0.7	2.6	1.2	1.7	2.6	1.2	1.7	0.7	1.2	2.6
Croatia		**48.8**	**46.2**	**50.4**	**45.3**	**39.7**	**44.6**	**33.1**	**24.1**	**30.7**	**28.9**
Germany	Deceased	19.2	18.7	19.1	18.2	16.5	20.0	19.4	17.5	18.2	17.2
	Living	9.0	7.7	7.9	7.3	6.7	7.7	6.3	5.4	5.7	6.4
Germany		**28.2**	**26.3**	**27.0**	**25.5**	**23.3**	**27.7**	**25.7**	**23.0**	**24.0**	**23.6**
Hungary	Deceased	15.4	34.5	30.7	31.2	26.2	29.6	24.1	17.6	16.4	19.6
	Living	1.9	4.7	4.1	3.5	4.1	4.6	3.1	3.1	3.5	5.8
Hungary		**17.4**	**39.2**	**34.8**	**34.7**	**30.3**	**34.2**	**27.2**	**20.7**	**19.9**	**25.4**
Netherlands	Deceased	25.9	27.9	27.8	25.1	25.1	28.4	26.0	25.4	26.6	28.0
	Living	31.0	31.7	30.4	33.2	32.3	29.7	29.0	21.5	25.9	29.3
Netherlands		**56.9**	**59.7**	**58.2**	**58.3**	**57.4**	**58.1**	**55.1**	**46.9**	**52.5**	**57.3**
Slovenia	Deceased	29.1	26.7	31.0	21.3	22.3	26.1	18.3	21.9	24.2	24.2
	Living				1.0	1.0	1.0		0.5	0.5	0.9
Slovenia		**29.1**	**26.7**	**31.0**	**22.3**	**23.2**	**27.1**	**18.3**	**22.4**	**24.7**	**25.2**
All ET	Deceased	23.9	25.1	25.5	24.2	22.8	25.6	23.1	20.7	21.4	21.7
	Living	10.5	10.1	9.9	9.9	9.5	9.7	8.7	6.9	7.8	9.0
All ET		**34.4**	**35.2**	**35.4**	**34.1**	**32.3**	**35.3**	**31.8**	**27.6**	**29.2**	**30.6**

statistics.eurotransplant.org : 2270P_kidney : 08.02.2023 : based on population at start of year

NierTx vs Dialyse:

Tonelli et al.

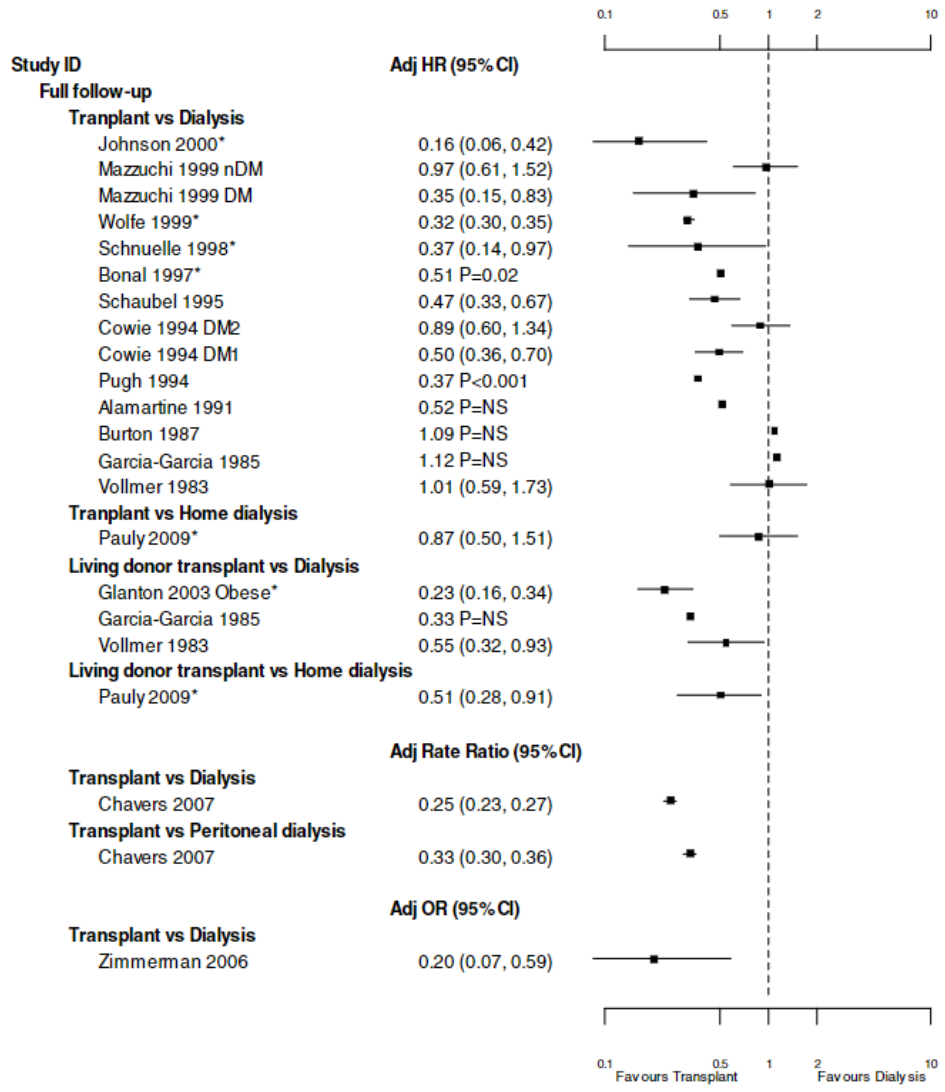
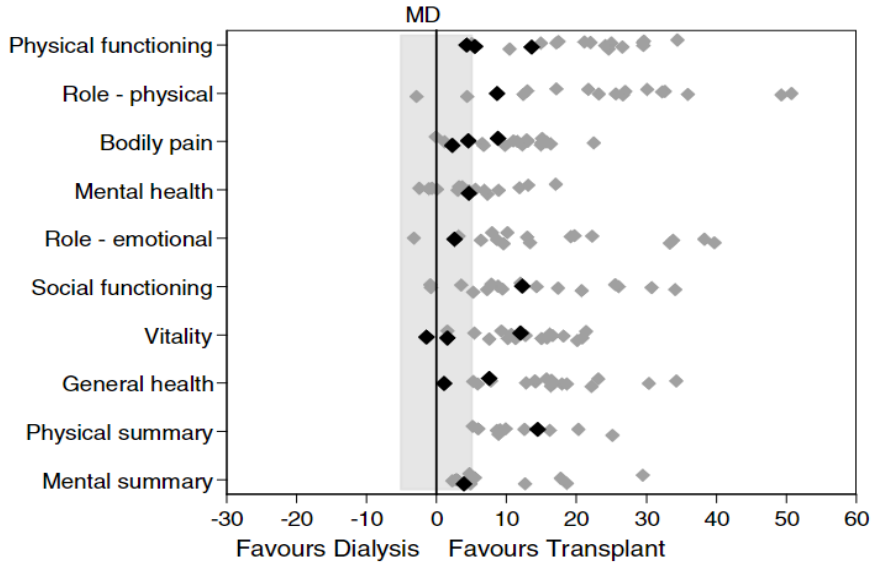
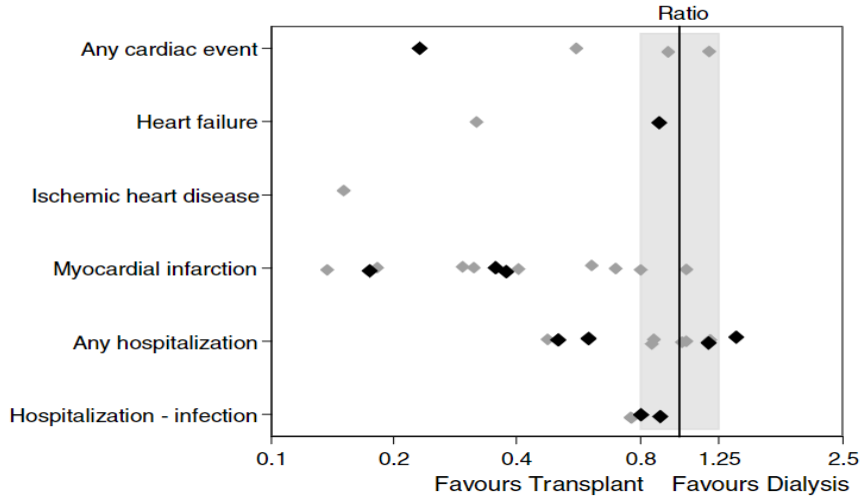


Figure 3: Continued.

Tonelli et al.



Systematic Review of Kidney Transplantation



Systematic Review: Kidney Transplantation Compared with Dialysis in Clinically Relevant Outcomes; M.Tonelli et al

Korte historie van levende Tx in de mens:

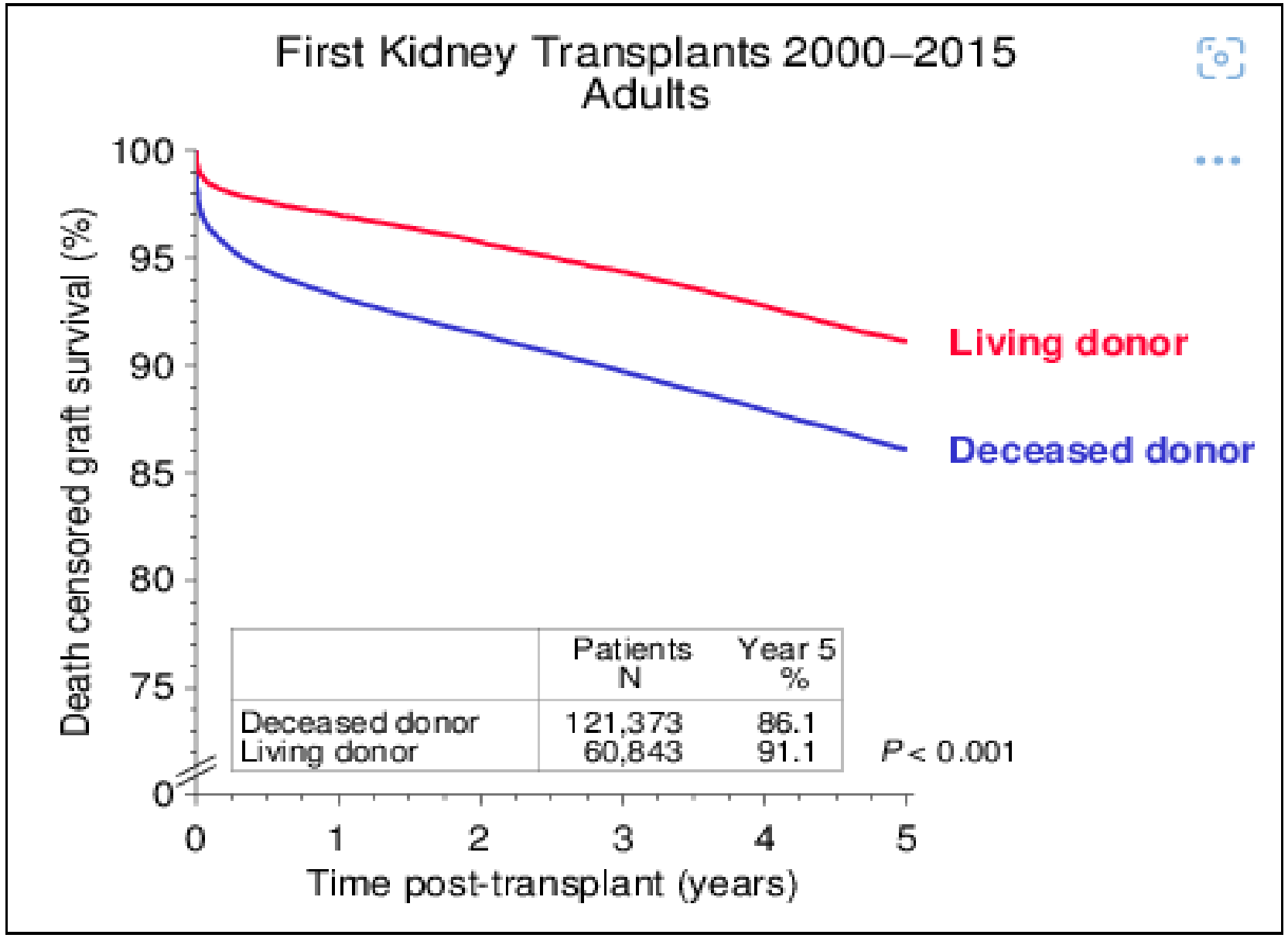
- De eerste lange termijn levende niertransplantatie werd in **1954** uitgevoerd
  - Tussen eeneiige tweeling (bij de Peter Bent Birmingham Hospital in Boston)
  - Immunologisch perspectief was o.b.v. genetisch identiteit door geboorte akte, Skingraft vooraf aan transplantatie
- De donor heeft daarna 56 jaar geleefd zonder problemen
- Eerst levende transplantatie was in 1906
  - Xenotransplantatie

Voordelen van levende nierTx:

- Korte wachttijd
- Betere kwaliteit nier een en nierfunctie
- Langere overleving van transplantnier
- Langere overleving van patiënt
- Goede kwaliteit van leven

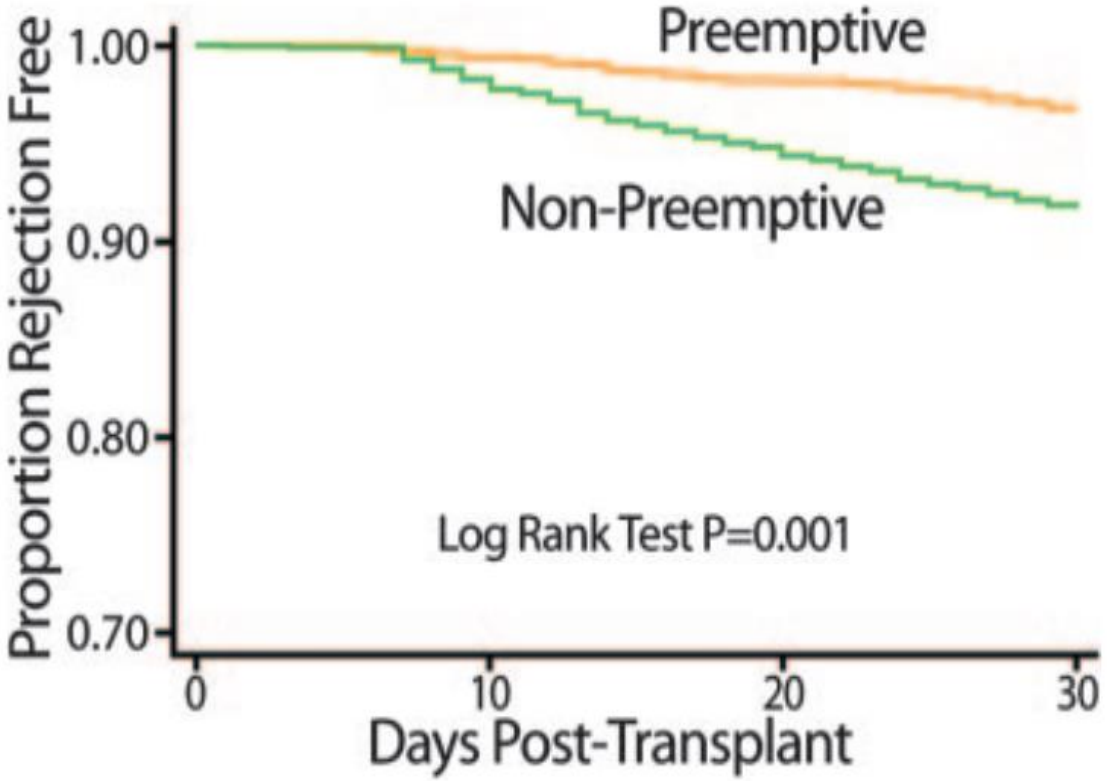
Voordelen van levende Niertransplanatie:

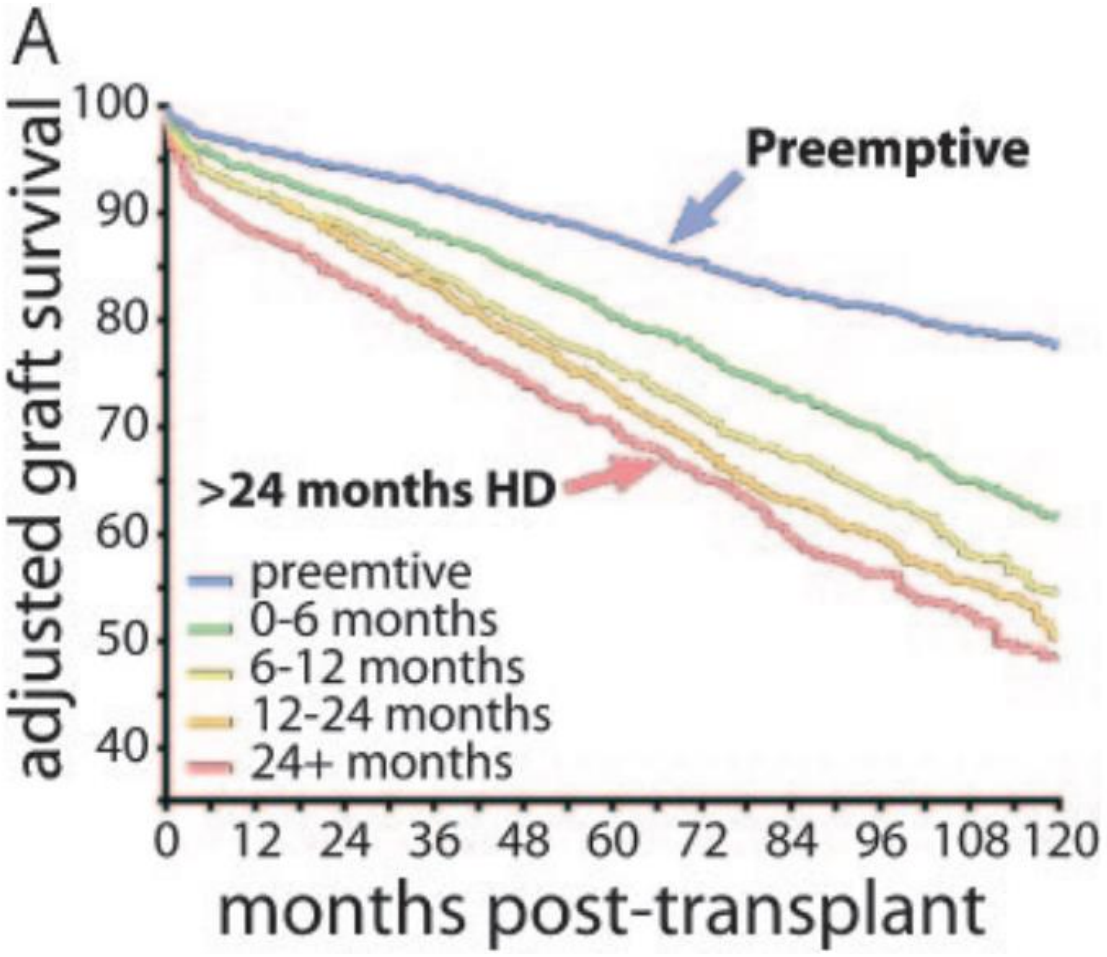
- Pre-emptieve living transplantatie is geassocieerd met de beste patiënt en greffe overleving
- Virtual afwezigheid van Delayed Graft Functie (DGF)
  - DGF is geassocieerd met verhoogd risico op acute afstoting en chronische allogreffe nefropathie
- Levende nierTx is op alle tijdspunten beter t.o.v. postmortale nierTx
  - 5 jaar overleving >85% vs en 75%
- Langere gemiddelde overleving
  - 15.3 jaar vs 12,5 jaar
- Minder peri en postoperatieve complicaties
- Geen strikte noodzaak voor HLA-matchting
  - Slechte match bij levende donatie is nog steeds beter dan PM nier
- Bloedgroep incompatibiliteit hoeft geen belemmerende factor te zijn



Collaborative Transplant Study, Newsletter May 2017

Pre-emptieve NierTx:





OPTARN Registry

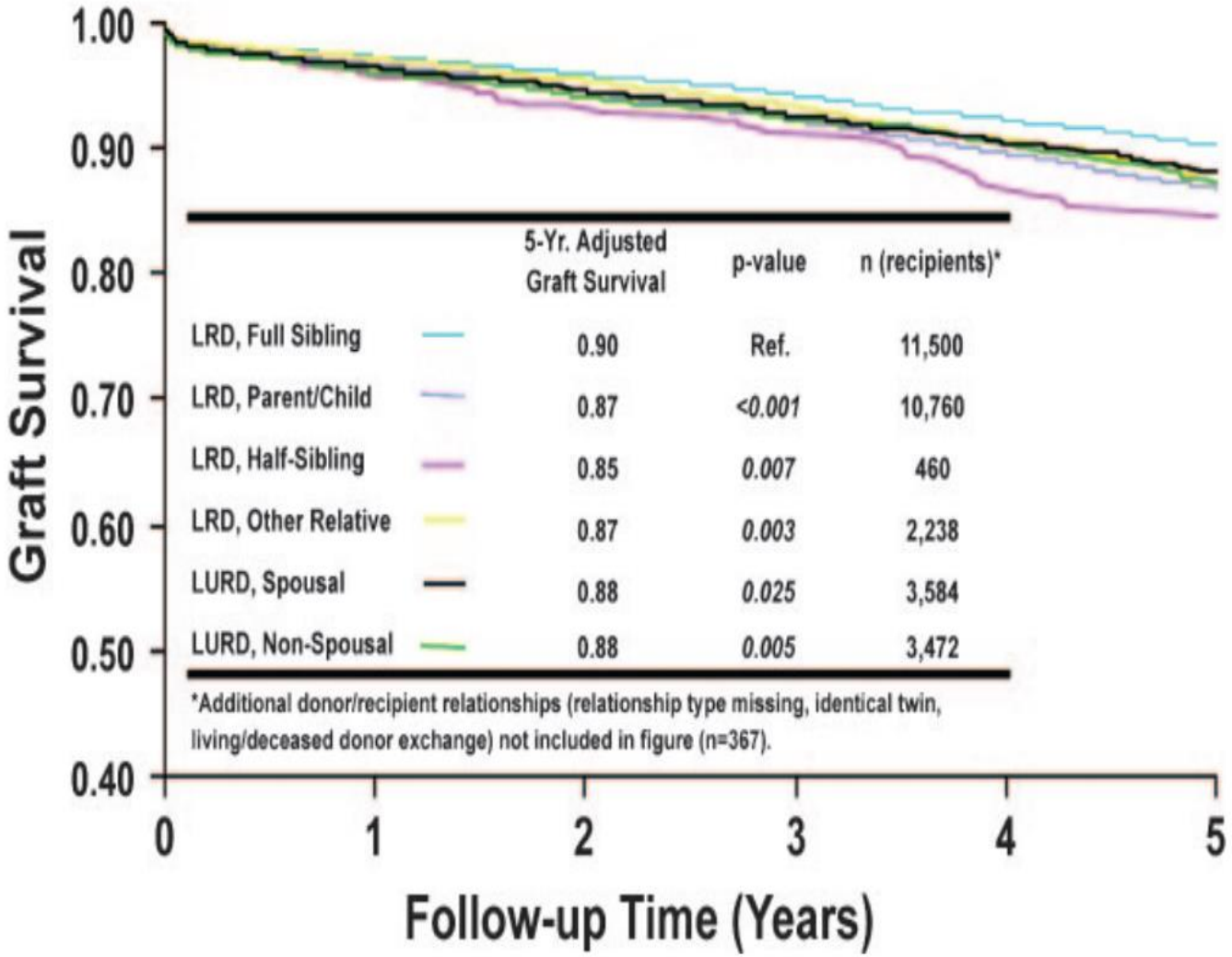


Figure 5. Five-year graft survival according to donor relationship to the recipient. OPTN/SRTR database, Annual Report as of August 1, 2003, Table 5.9b.

OPTARN Registry

Delayed graft functie(DGF):

- DGF:
  - Noodzaak tot dialyse binnen de eerste 7 dagen na niertransplantatie
- Frequentie: Afhankelijk van studies
  - 4-10% in levende donatie
  - 25-30.8% in DBD donatie
  - 45-55% in DCD donatie
- Oorzaken: Divers, maar de twee meest belangrijke
  - Ischemie Reperfusie Schade (IRI)
  - Immunologisch respons op het transplant

Panel 1: Risk factors for delayed graft function

Procurement
- Kidneys from non-heart-beating donor
- Inotropic support of the donor
- Cold storage preservation
- Cold ischaemia time

Donor
- Age (>55 years)
- Marginal kidneys from diabetic or hypertensive donors

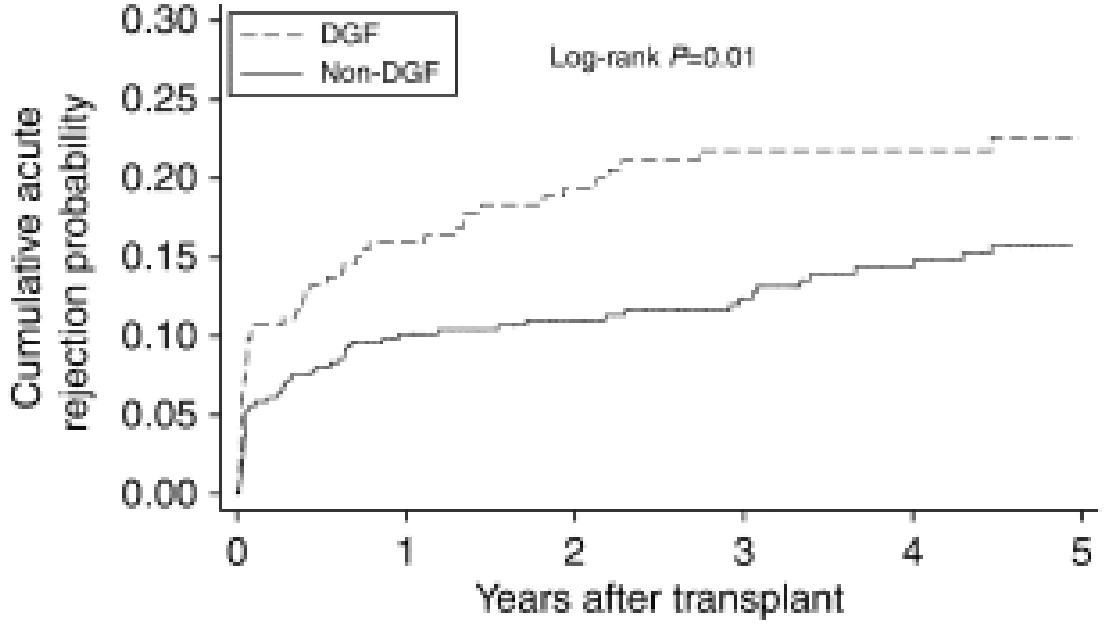
Recipient

Prerenal
- Recipient hypovolaemia
- Intraoperative albumin administration
- Nocturnal haemodialysis
- Haemodialysis with ultrafiltration within 24 h before Tx
- Recipient or donor bodyweight
- Number of previous transplants

Renal
- Inherited thrombophilia
- Factor V Leiden mutation
- OKT3 monoclonal antibody therapy
- Antiphospholipid antibodies
- Preformed antidonor antibodies
- Acute tubular necrosis
- Ciclosporin nephrotoxicity

Postrenal
- Ureteral leakage
- Ureteral obstruction

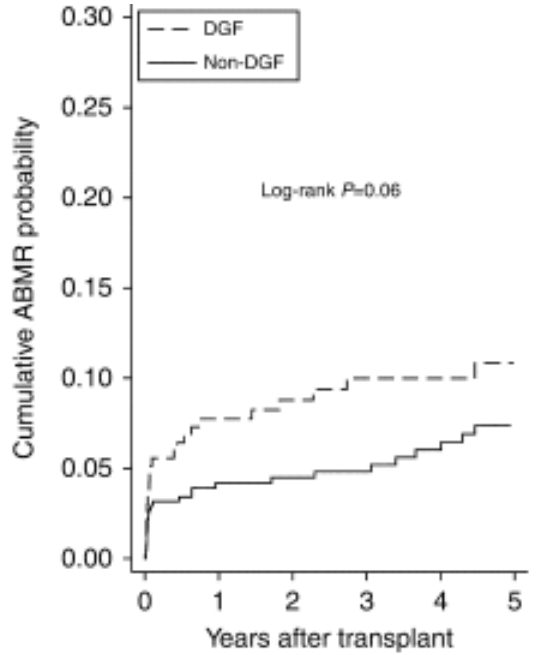
Delayed graft function and the risk of acute rejection in the modern era of kidney transplantation; W.Kelly Wu et al; Kidney International 2015
Delayed graft function in kidney transplantation; Disha Bahl et al: Current opinion
Delayed fraf function in kidney transplantation; Norberto Perico et al; Lancet



Number at risk

DGF	234	180	143	122	103	82
Non-DGF	411	332	284	230	199	163

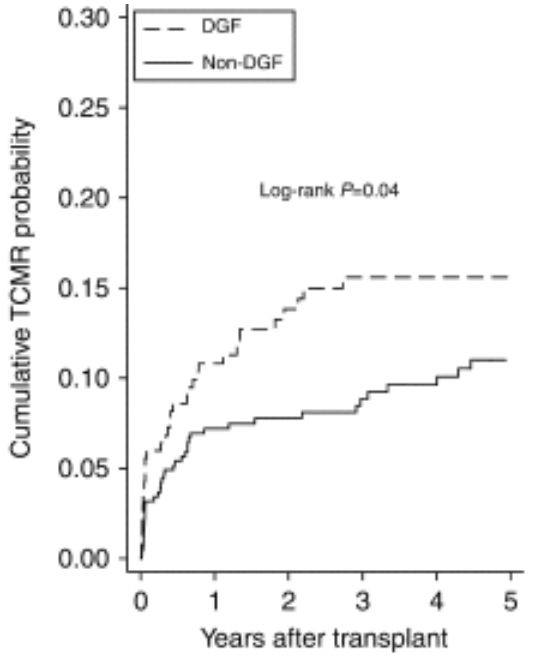
Note: based on standard definition of DGF.



Number at risk

DGF	234	197	162	137	116	93
Non-DGF	411	354	305	251	215	179

Note: based on standard definition of DGF.

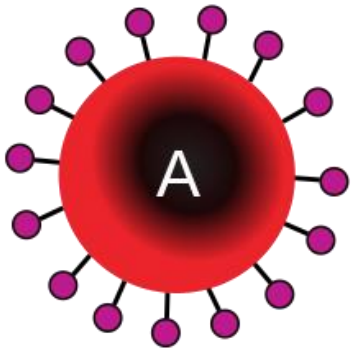
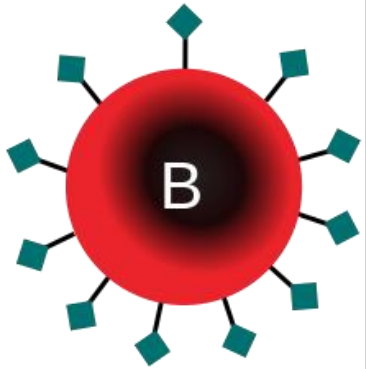
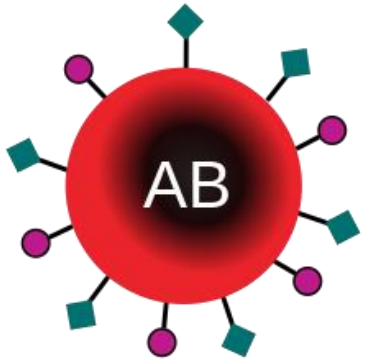
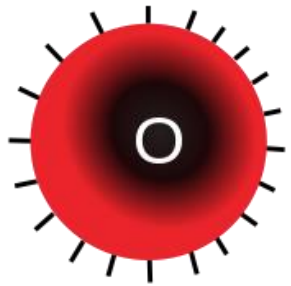
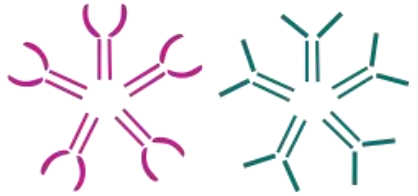


Number at risk

DGF	234	190	152	130	108	86
Non-DGF	411	341	293	239	206	167

Note: based on standard definition of DGF.

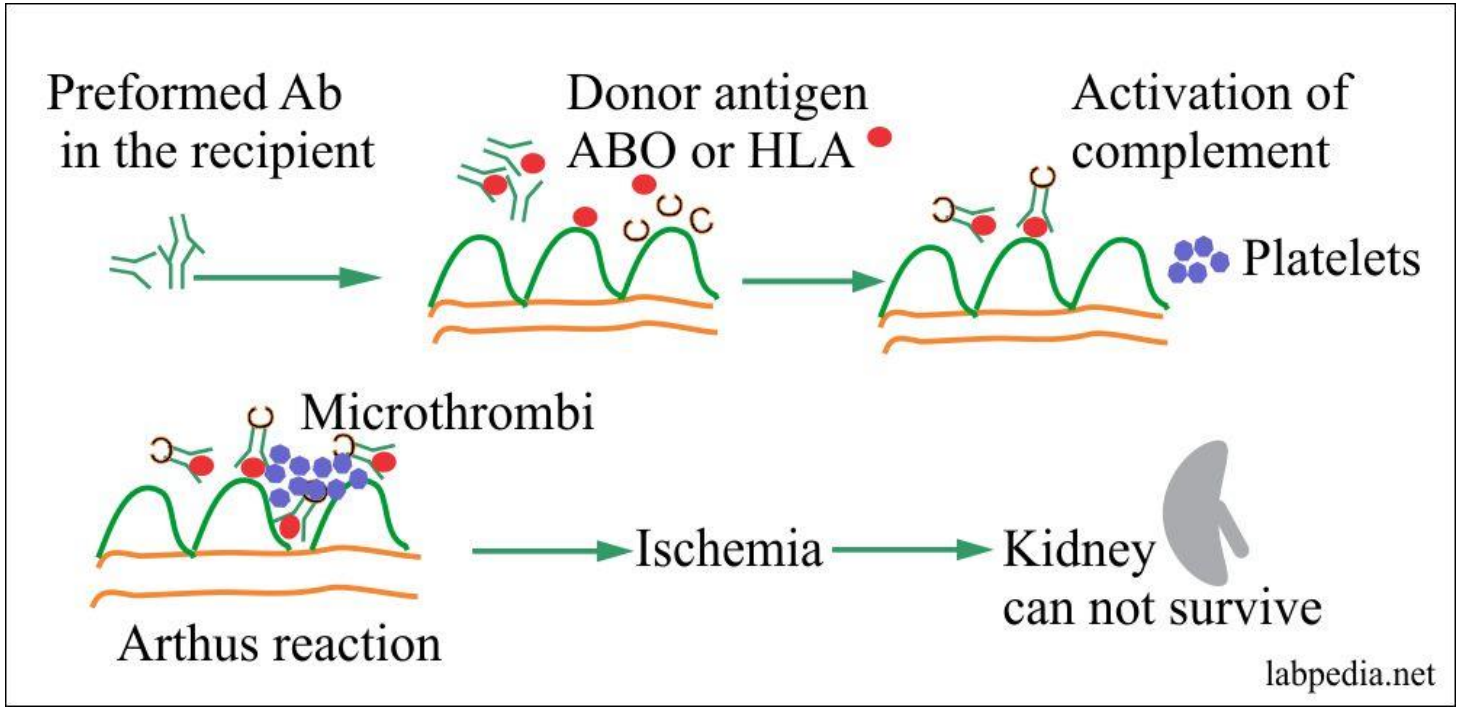
Delayed graft function and the risk of acute rejection in the modern era of kidney transplantation; W.Kelly Wu et al; Kidney International 2015

	Group A	Group B	Group AB	Group O
Red blood cell type				
Antibodies in plasma	 Anti-B	 Anti-A	None	 Anti-A and Anti-B
Antigens in red blood cell	 A antigen	 B antigen	 A and B antigens	None

If you have blood type...	You can normally receive a kidney from a donor with the blood type:	You can normally donate a kidney from a donor with the blood type:
O	O	O, A, B, AB
A	A, O	A, AB
B	B, O	B, AB
AB	O, A, B, AB	AB

Hyperacute rejectie:

- Binnen minuten tot uren na de transplantatie
- Vooraf aanwezigheid van antistoffen:
  - **ABO-incompatibiliteit**
  - **Donor Specifieke Antistoffen**
- **Nier is niet te redden**



All Benefits Identified by Interview Participants

Tangible Benefits	Nontangible Benefits
Health and well-being benefits	Help or save recipient
Donor more proactive about health	Sense of life purpose
Reduced stress/worry postdonation	Emotional or mental health benefits
Improved donor quality of life	Sense of pride, satisfaction
Waitlist priority for donor	Learn about organ donation and kidney disease
Reduced dietary restrictions	Gratefulness, perspective
Time and financial benefits	Donor as a role model to children
Reduced caregiving burden	Recipient avoided dialysis (preemptive transplant)
Ability to travel	Contributing to research
Return to normalcy	Fulfill familial duty
Recipient's return to work	Recipient discontinued dialysis
Career benefits	Return favor to parents
Increased donor's free time	Receive/expect high quality healthcare
Financial benefits	Appreciation of support system
Interpersonal benefits	Belief in karma
Closer relationships with recipient and family	Legacy of donation
Involvement in donation advocacy	Regain control of situation
Spiritual/religious benefits	Relationship with exchange recipient family
Preserve family unit	
Recognition or appreciation	
Sense of courage/confidence/resilience	
Avoiding guilt of not donating	
Increased independence	
Community of other living donors	
Improved household dynamics	
Improved marital quality	
Recipient or donor able to see children grow/age	
Improve donor's social life	
Donor and recipient ability to have children	

The tangible Benefits of Living Donation; Sarah E, Van Pilsum

Absolute and Relative Contraindications to Living Kidney Donation

	Absolute	Relative
Age	Less than 18 years	Over 65 excluded from many programs
Informed consent	Impaired ability to make an autonomous decision because of mental or psychiatric condition	
Substance abuse	Active substance abuse	
Hypertension	Multiple agents or high doses of single agents for control Evidence of end-organ damage End-organ injury Additional strong risk factors for cardiovascular disease	Borderline or control with single agents
Diabetes	Diabetes mellitus	Impaired glucose tolerance
Obesity	Morbid obesity (BMI >35) with comorbid conditions	Obesity (BMI >30) with comorbid conditions
Renal disease	Evidence of renal disease with reduced creatinine clearance (GFR <80 mL/min), proteinuria (>250 mg), or hematuria	Borderline creatinine clearance, microscopic hematuria low levels of proteinuria (<30 mg/24 h)
Renal stones	Multiple or recurrent renal calculi of a metabolic condition that predisposes to the recurrence of renal calculi	Single renal stone
Inherited renal disease	ADPKD, SLE, Alport's syndrome, IgA nephropathy	TBMD, mutations in APOL1
Infection	HIV, hepatitis B, hepatitis C, West Nile virus, Chagas' disease	Hepatitis B core antibody
Cancer	Cancer current or treated but at significant risk for recurrence	
Cardiovascular disease	Coronary or peripheral vascular disease, or heart valve disease	
Renal anatomic abnormalities	Significant discrepancy in the kidney sizes	Vascular anomalies (see Figs. 7.1 to 7.4)

ADPKD, adult polycystic kidney disease; *APOL1*, apolipoprotein L1; *BMI*, body mass index; *GFR*, glomerular filtration rate; *HIV*, human immunodeficiency virus; *IgA*, immunoglobulin A; *SLE*, systemic lupus erythematosus; *TBMD*, thin basement membrane disease.

Modified from kidney transplantation, 7th ed., Chapter 7, MacConmara and Newell.

Kidney Transplantation Principels and Practice; Living kidney donation

Risico’s voor de donor:

- Verhoogd risico op het ontwikkelen van ESRD na donatie
  - 7-11 keer meer risico hierop
- Verhoogd risico op proteïnurie
- 30% donoren ontwikkelen CKD (eGFR<60ml/min/1.73)
- Zwangerschap: geen toegenomen maternaal of foetaal complicaties
  - Verhoogd risico op zwangerschap hypertensie en pre-eclampsie
- Verhoogd risico op opname binnen de eerste 3 jaar na donatie
- Risico factoren voor het ontwikkelen van bovenstaande zijn o.a.:
  - Hypertensie vooraf aan nier donatie (verhoogd systolisch/diastolisch bloeddruk)
  - Oudere donor
  - Verhoogd BMI

Kidney Transplantation Principels and Practice; Living kidney donation

Donor Complication Risks

	Risk (Percentage of Donations Unless Stated)
Mortality	0.02–0.03
Major Complication	
Bleeding	2.2
Bowel obstruction	1.0
Vascular injury	0.27
Open conversion	0.7–1.1
Reoperation	0.52
Blood transfusion	0.4
Wound infection	2.1
Urinary tract infection	4.5
Readmission (including nausea, vomiting, gastroenteritis, abdominal pain, ileus, bowel obstruction)	2–5
Hernia repair	0.8
End-stage renal failure	Hazard ratio 11.38 Additional risk in obese, elderly, and African American donors
Hypertension	15–25

Data from OPTN/SRTR 2015 Annual Data Report. In: Scientific registry of transplant recipients 2017; Mjøen G, Hallan S, Hartmann A, et al. Long-term risks for kidney donors. Kidney Int 2014;86:162–7; Lam NN, Lentine KL, Levey AS, et al. Long-term medical risks to the living kidney donor. Nat Rev Nephrol 2015;11:411–9.

Kidney Transplantation Principels and Practice; Living kidney donation

Conclusie:

- Levende niertransplantatie heeft alleen voordelen voor de ontvanger
- Minimale nadelen voor de donor

Literatuur:

- Sri G, Yarlagadda et al: Association between DGF and allograft and patient survival; systematic review and meta-analysis
- Collaborative Transplant Study, Newsletter May 2017 and May 2020
- Connie L Davis et al: Living-Donor Kidney Transplantation; A review of the Current practices for Live Donor
- Kidney Transplantation; Principels and Practice

GFR Stages	GFR (mL/min/1.73 m^2)	Terms
G1	>90	Normal or high
G2	60–89	Mildly decreased
G3a	45–59	Mildly to moderately decreased
G3b	30–44	Moderately to severely decreased
G4	15–29	Severely decreased
G5	<15	Kidney failure

Albuminuria Stages	AER or ACR (mg/24 h or mg/g)	Terms
A1	<30	Normal to mildly increased
A2	30–299	Moderately increased
A3	≥300	Severely increased

Abbreviations: ACR, albumin-to-creatinine ratio; AER, albumin excretion rate (24 hours).

Causes of CKD

1. Presence or absence of systemic disease and
2. Location within kidney of observed or presumed pathologic-anatomic findings such as glomerular diseases, tubulointerstitial diseases, vascular diseases, cystic and congenital diseases.

Data from Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. Kidney Inter Suppl 2013;3:1–150.

KDIGO Guidelines 2012

De verschillende typen greffe:

- **Autogreffe**:
  - Transplantatie van een deel van het lichaam naar een andere deel bij hetzelfde individu
- **Isogreffe**:
  - Tussen genetisch identiek individuelen van hetzelfde soort (bijv. tussen eeneiige tweeling)
- **Allogreffe:**
  - **Tussen niet genetisch identiek individuelen van hetzelfde soort**
- **Xenogreffe**:
  - Tussen individuelen van verschillende species

Classic and current Opninions in Human Organ and Tissue Transplantation; Angus N Oli et al

Kidney Transplantation Principels and Practice:

Type donoren:

- **Levende donoren** – ongeveer 10-15% in België
  - Living related donor (LR)
  - Living onrelated (LUR)
- **Postmortale/Lijkennier donoren**
  - Donation after Brain death (DBD)
  - Donation after Circulatory Arrest (DCD)