



Medical Use Case Nephrology

Borchert, Dr. Schapranow
Data Management for Digital Health
Winter 2023

Agenda

Pillars of the Lecture

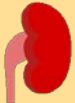
Medical Use Cases



Biology Recap



Oncology



Nephrology



Infectious
Diseases

Technology Foundation



Data
Sources



Data
Formats



Processing and
Analysis



Software
Architectures

Machine Learning

Data



Refine



Evaluate



Prediction +
Probability

Medical Use Case Nephrology

Data Management for
Digital Health, Winter
2023
2

Agenda

Pillars of the Lecture

Medical Use Cases



Biology Recap



Oncology



Nephrology



Infectious
Diseases

Technology Foundation



Data
Sources



Data
Formats



Processing and
Analysis



Software
Architectures

Machine Learning

Data



Refine



ML



Evaluate

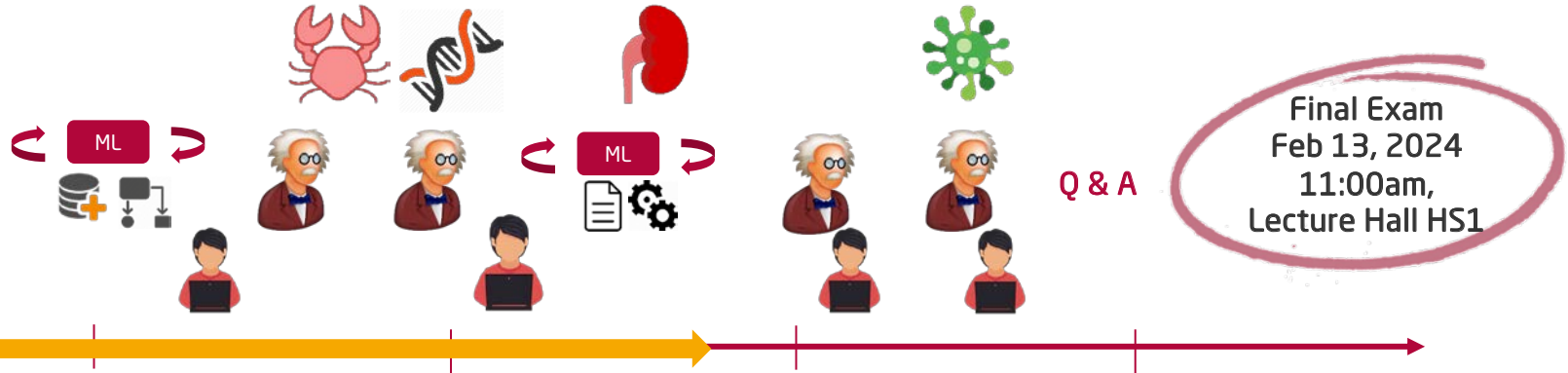


Prediction +
Probability

Medical Use Case Nephrology

Data Management for
Digital Health, Winter
2023

Lecture Schedule



Nov

Dec

Jan

Feb

- Lecture Kickoff
- Actors in Healthcare
- Digital Health Data

- Machine Learning (ML) Foundations
- Use Case Oncology
- Biology Recap

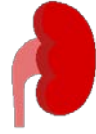
- Natural Language Processing
- Use Case Nephrology & Intensive Care
- Supervised ML & Deep Learning

- Use Case Infectious Diseases
- Unsupervised ML

Medical Use Case Nephrology

Data Management for Digital Health, Winter 2023

Agenda



- Facts you should know
- Kidney diseases
- Treatments options
 1. Dialysis
 2. Transplantation
 - Organ donation strategies
 - Donor-recipient matching
 - The role of the immune system
 3. Brew your own Organ



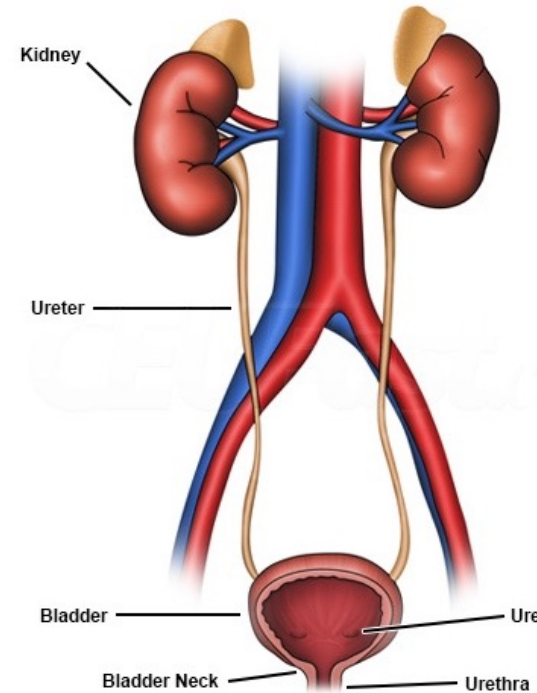
Medical Use Case Nephrology

Data Management for
Digital Health, Winter
2023

What are Tasks of your Kidneys?

<< QUIZ >>

- What do you think are the tasks of the kidneys?
 - A. Leveling, e.g. water volume and pH levels
 - B. Remove toxic waste from the body
 - C. Regulation, e.g. red blood cells production and blood pressure
 - D. Production of hormones, e.g. erythropoietin

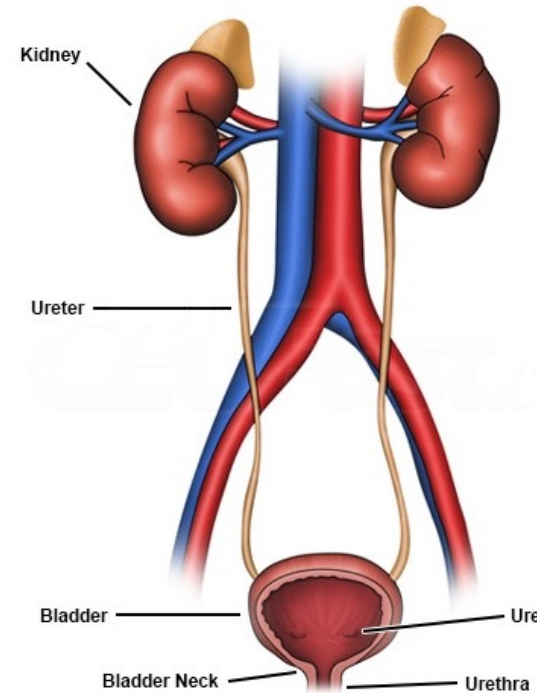


**Medical Use Case
Nephrology**
Data Management for
Digital Health, Winter
2023

What are Tasks of your Kidneys?

<< QUIZ >>

- What do you think are the tasks of the kidneys?
 - A. Leveling, e.g. water volume and pH levels
 - B. Remove toxic waste from the body
 - C. Regulation, e.g. red blood cells production and blood pressure
 - D. Production of hormones, e.g. erythropoietin

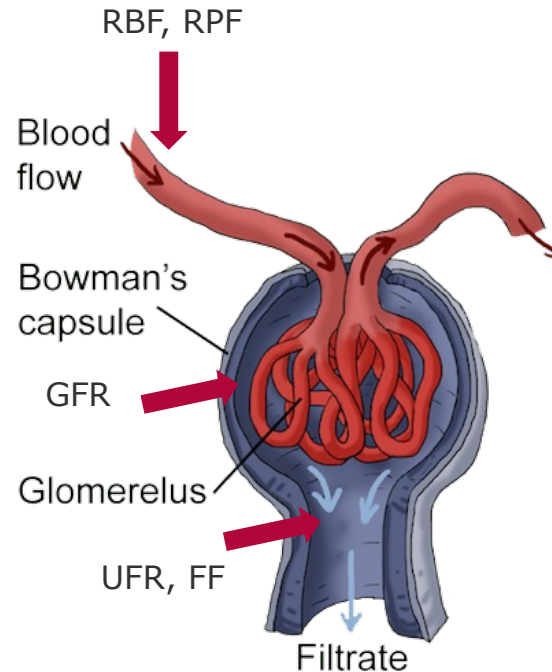


**Medical Use Case
Nephrology**
Data Management for
Digital Health, Winter
2023

Numbers You Should Know

<< QUIZ >>

- Renal Blood Flow (RBF)
 - Renal Plasma Flow (RPF)
 - Glomerular Filtration Rate (GFR)
 - Urine Flow Rate (UFR)
 - Filtration Fraction (FF)
-
- Choose options wisely:
1,440l/d, 1,000l/d, 864l/d,
333l/d, 173l/d, 1.4l/d,
30%, 20%, 10%



http://media1.shmoop.com/images/biology/biobook_animdig_graphik_14.png



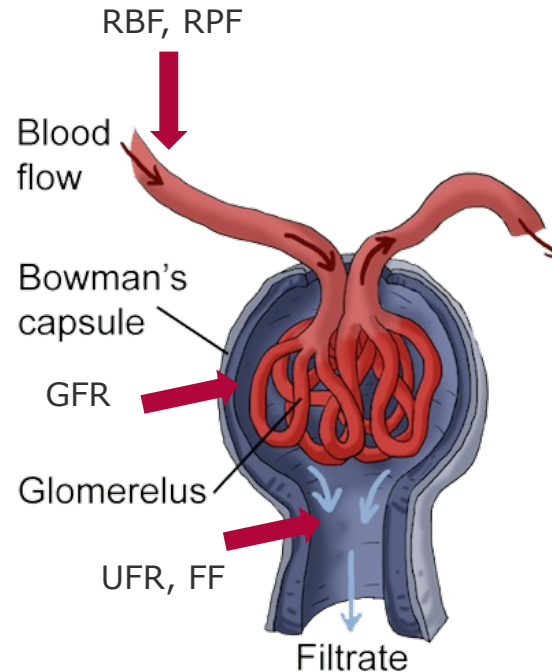
Medical Use Case Nephrology

Data Management for
Digital Health, Winter
2023

Numbers You Should Know

<< QUIZ >>

- Renal Blood Flow (RBF) = 1l/min
- Renal Plasma Flow (RPF) = 600ml/min
- Glomerular Filtration Rate (GFR) = 120ml/min
- Urine Flow Rate (UFR) = 1ml/min
- Filtration Fraction (FF) = GFR/RPF



http://media1.shmoop.com/images/biology/biobook_animdig_graphik_14.png

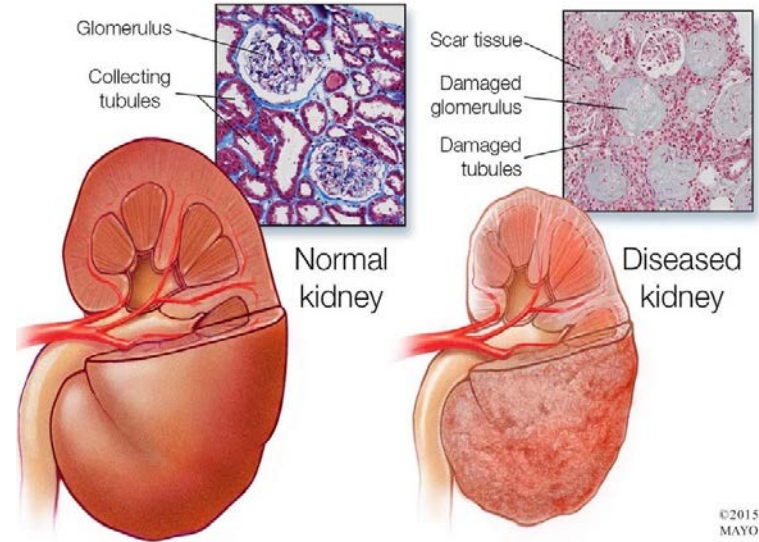


Medical Use Case Nephrology

Data Management for
Digital Health, Winter
2023

Kidney Diseases: What If a Kidney Fails?

- Est. 800M people affected by end-stage kidney disease worldwide
- Kidney Disease
 - Worldwide deaths (2019): place 10 or 17.3 / 100k [1]
 - German deaths (2019): place 8 or 27.3 / 100k [1]
- Categories of kidney diseases
 - Acute kidney injury (AKI)
 - Chronic kidney disease (CKD)



Medical Use Case Nephrology

Data Management for
Digital Health, Winter
2023
10

[1] <https://www.who.int/data/gho/data/themes/mortality-and-global-health-estimates/ghe-leading-causes-of-death>

URINE TEST

BLOOD TEST

UACR



eGFR



Kidney Diseases: Glomerular Filtration Rate

- Measuring GFR (mGFR) is complex → Estimated Glomerular Filtration Rate (eGFR) is good approximation for the kidney's function and cleaning quality
- eGFR depends on multiple factors, e.g. age, sex, ethnicity, etc.
- $eGFR = 141 \times \min(Scr/\kappa, 1)^\alpha \times \max(Scr/\kappa, 1)^{-1.209} \times 0.993 \text{ Age} \times 1.018 \text{ [if female]} _ 1.159 \text{ [if African American]} \text{ [1]}$
 - with Scr = serum creatinine,
 - κ is 0.7 for females, 0.9 for males,
 - α is -0.329 for females, -0.411 for males,
 - the minimum of Scr/ κ or 1, and
 - the maximum of Scr/ κ or 1.

Medical Use Case Nephrology

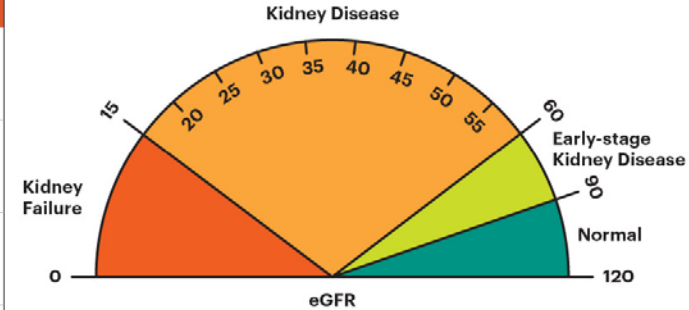
Data Management for
Digital Health, Winter
2023

12

Kidney Diseases: Glomerular Filtration Rate (cont'd)

Age [years]	Avg. eGFR [ml/min/1.73m ²]
0	1.5
1	30
10	70
20-29	116
30-39	107
40-49	99
50-59	93
60-69	85
70+	75

Stage	Description	eGFR	Kidney Function
1	Possible kidney damage (e.g., protein in the urine) with normal kidney function	90 or above	90-100%
2	Kidney damage with mild loss of kidney function	60 to 89	60-89%
3a	Mild to moderate loss of kidney function	45 to 59	45-59%
3b	Moderate to severe loss of kidney function	30 to 44	30-44%
4	Severe loss of kidney function	15 to 29	15-29%
5	Kidney failure	Less than 15	Less than 15%



https://www.kidney.org/sites/default/files/egfr_speedometer_v2-09.jpg

- eGFR can be a reliable indicator for the presence of a kidney disease
- Test yourself: https://www.kidney.org/professionals/kdoqi/gfr_calculator

Medical Use Case Nephrology

Data Management for
Digital Health, Winter
2023
13

Kidney Diseases: Acute vs. Chronic Kidney Disease



Acute Kidney disease

Chronic Kidney disease

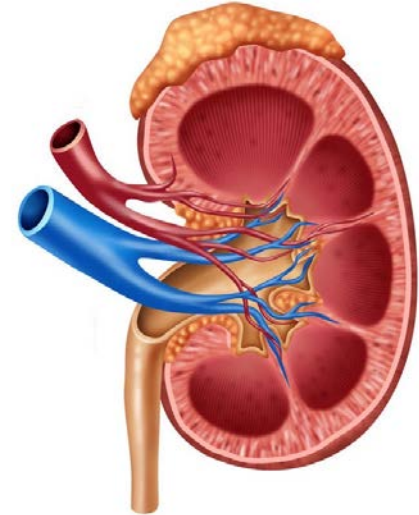
System Human Body

**Medical Use Case
Nephrology**

Data Management for
Digital Health, Winter
2023
14

Acute Kidney Injury (AKI) / Acute Renal Failure

- Sudden and severe drop of renal function
- → Decreased urine output / fluid overflow
- Affects between 7 and 18% of hospital patients [1]
- Reasons:
 - Issues with blood flow
 - Direct damage to the kidney itself
 - Blockage of urine tract



Medical Use Case Nephrology

Data Management for
Digital Health, Winter
2023
15

Acute Kidney Injury (AKI) / Acute Renal Failure: Treatment Options

- Requires immediate medical treatment
- Monitoring of kidney function in an intensive care unit
- Dialysis may help to release stress from kidney and assist kidney function
- Drugs for controlling blood pressure and adjusting electrolytes
- Strict fluid management



Source: Armed Forces Institute of Cardiology & National Institute of Heart Diseases (Pakistan)

Medical Use Case Nephrology

Data Management for
Digital Health, Winter
2023
16

Kidney Disease: Acute vs. Chronic Kidney Disease



Acute Kidney disease

Chronic Kidney disease

System Human Body

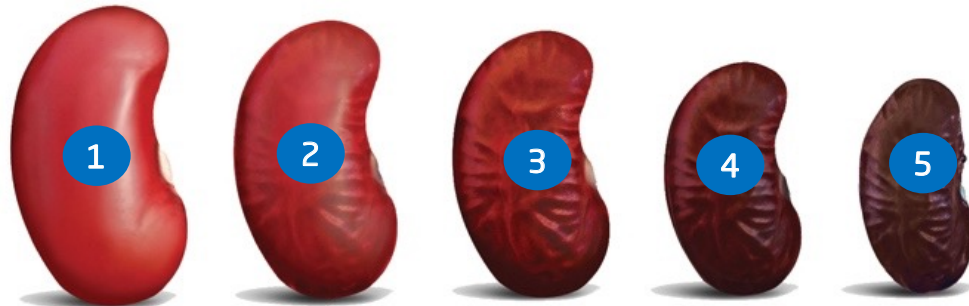
**Medical Use Case
Nephrology**

Data Management for
Digital Health, Winter
2023
17

Chronic Kidney Disease (CKD)

- Prolonged, sustained loss of renal function for 3+ months
- Typically, no symptoms until in an advanced stage of the disease
- Risk factors: age, sex, diabetes, hypertension, heart disease, obesity

Absence of specific symptoms for stages 1..3



CKD stages: 1 - 5
based on GFR values

**Medical Use Case
Nephrology**

Data Management for
Digital Health, Winter
2023
18

Chronic Kidney Disease (CKD): Treatment Options

- For stages I-IV:
 - Special diets recommendations
 - Reduction of impact of existing comorbidities, e.g. high blood pressure, diabetes mellitus
- For Stage V:
 - Dialysis
 - Renal replacement therapy



Image by Mohamed Hassan from Pixabay

Medical Use Case Nephrology

Data Management for
Digital Health, Winter
2023
19

Kidney Disease: Acute vs. Chronic Kidney Disease



Chronic Kidney disease

Acute Kidney disease

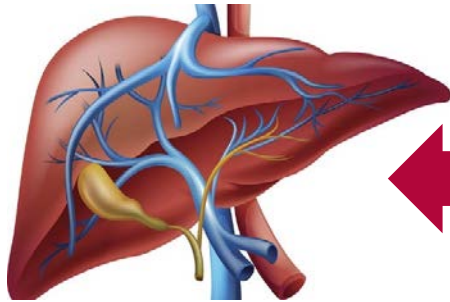
System Human Body

**Medical Use Case
Nephrology**

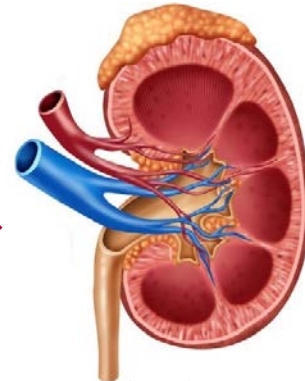
Data Management for
Digital Health, Winter
2023
20

How does the Liver affect the Kidneys? Hepatorenal Syndrome

- Complication of liver cirrhosis (severe liver disease)
- Decrease in renal blood flow and GFR
- A progressive rise in serum creatinine
- Increase in hepatic injury further deteriorated kidney function



<https://share.upmc.com/2015/09/what-does-the-liver-do-for-the-body/>



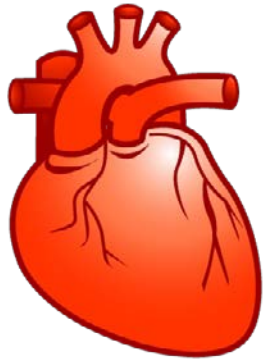
https://edc2.healthtap.com/ht-staging/user_answer/reference_image/3694/large/Kidney.jpeg

Medical Use Case Nephrology

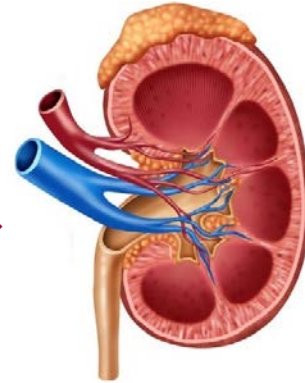
Data Management for
Digital Health, Winter
2023
21

How does the Heart affect the Kidneys? Cardiorenal Syndrome

- Dysfunction of one organ may induce dysfunction of the other, e.g. reduced heart function might impact the kidney function and vice versa
- Low cardiac output reduces renal perfusion (blood supply)



https://www.iconfinder.com/icons/44842/cardiology_heart_icon

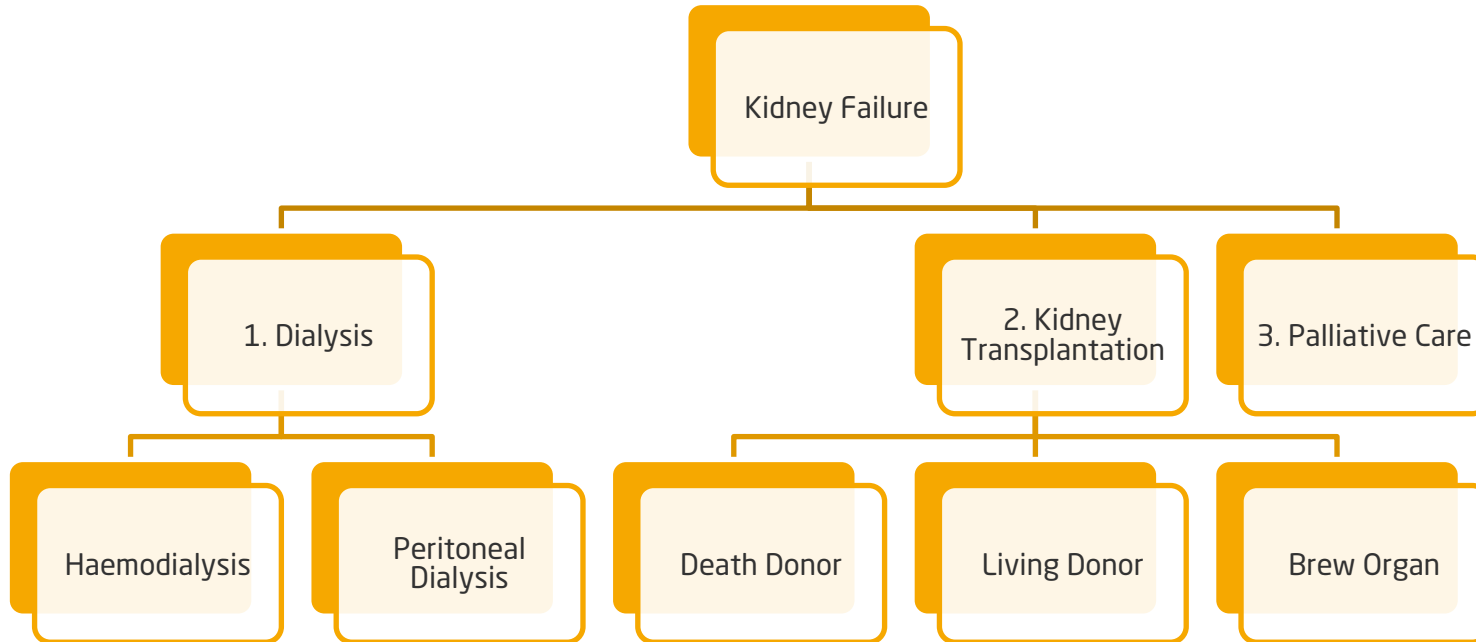


https://edc2.healthtap.com/ht-staging/user_answer/reference_image/3694/large/Kidney.jpeg

**Medical Use Case
Nephrology**

Data Management for
Digital Health, Winter
2023
22

Treatment Options for Kidney Failure



Medical Use Case Nephrology

Data Management for
Digital Health, Winter
2023
23

Treatment Options:

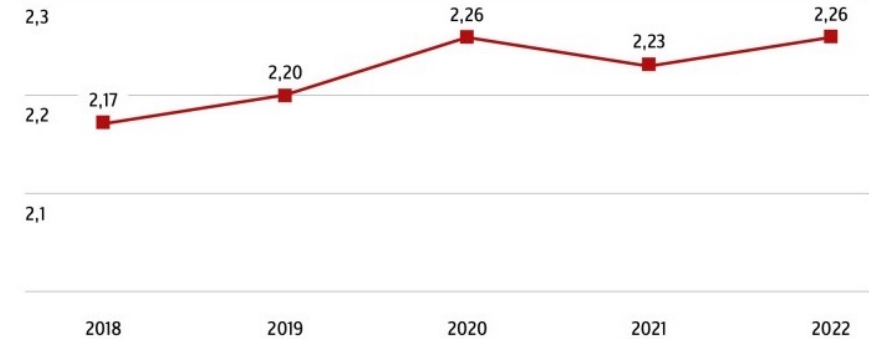
1. Dialysis in Germany

- 93k patients required dialysis in 2019 [1]
- Approx. 950 dialysis centers in 2023
- Costs for regular dialysis approx. 30-50k EUR p.a. and patient



<https://www.br.de/nachrichten/bayern/dialysezentren-bundesweit-unter-wirtschaftlichem-druck,TlHqmxp>

Costs for dialysis per year in [billion EUR]



Darstellung: GKV-Spitzenverband; Quelle: Amtliche Statistik KJ 1

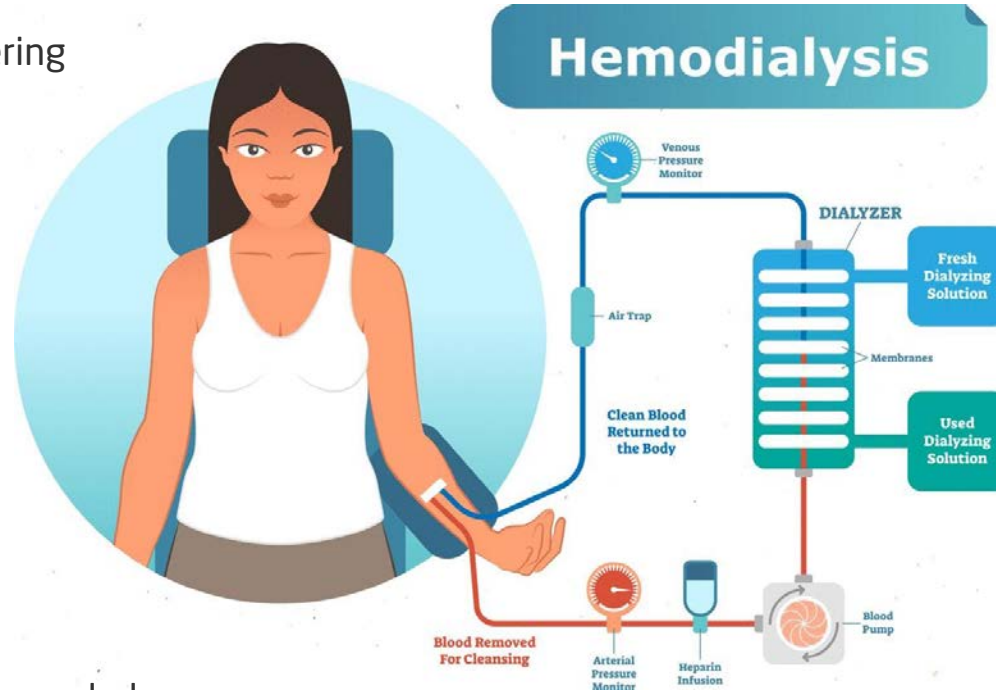
Medical Use Case Nephrology

Data Management for
Digital Health, Winter
2023
24

Treatment Options:

1. Dialysis: Hemodialysis

- Aim: Support kidney's filtering function
- Location: Dialysis centers
- Intervals: 1-3 times per week
- Duration: Hours
- Cons: Patients have to
 - Avoid certain foods
 - Reduce consumption of liquids
 - Travel to dialysis center regularly



<https://www.dialysisready.com/understand-more-about-kidney-dialysis/>

Medical Use Case Nephrology

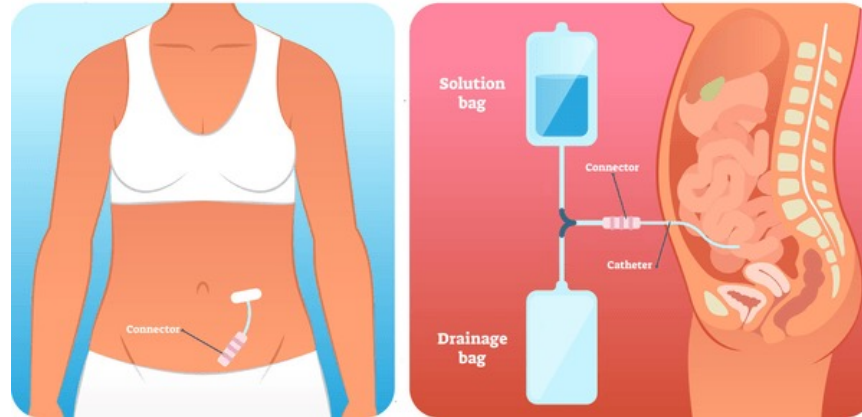
Data Management for
Digital Health, Winter
2023
25

Treatment Options:

1. Dialysis: Peritoneal Dialysis

- Aim: Support kidney's filtering function + improving quality of life
- Location: At home
- Intervals: Daily
- Pros:
 - Continuously performed compared to hemodialysis
 - Less accumulation of potassium, sodium and fluids
 - Allows more flexible diet
- Con: Not for obese patients or patients having abdominal scarring

Peritoneal Dialysis



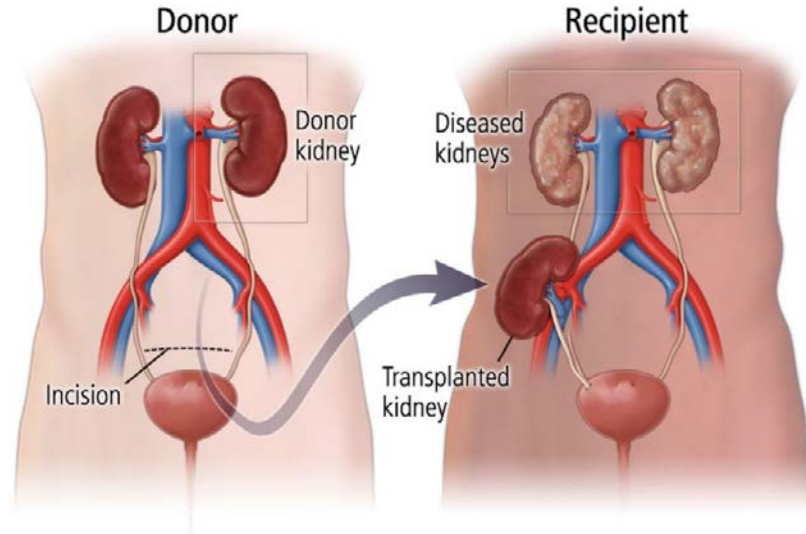
<https://www.dialysisready.com/understand-more-about-kidney-dialysis/>

Medical Use Case Nephrology

Data Management for
Digital Health, Winter
2023
26

Treatment Options:

2. Organ Transplantation

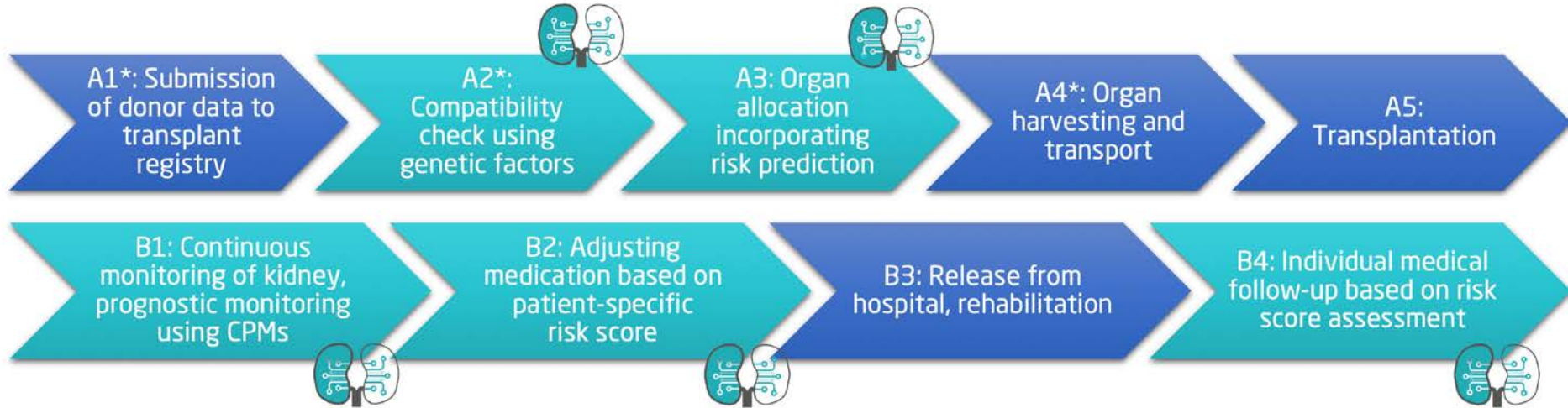


<https://www.templehealth.org/services/transplant/kidney-transplant/living-kidney-donation>

Medical Use Case Nephrology

Data Management for
Digital Health, Winter
2023
27

Treatment Options: Simplified Organ Donation Process

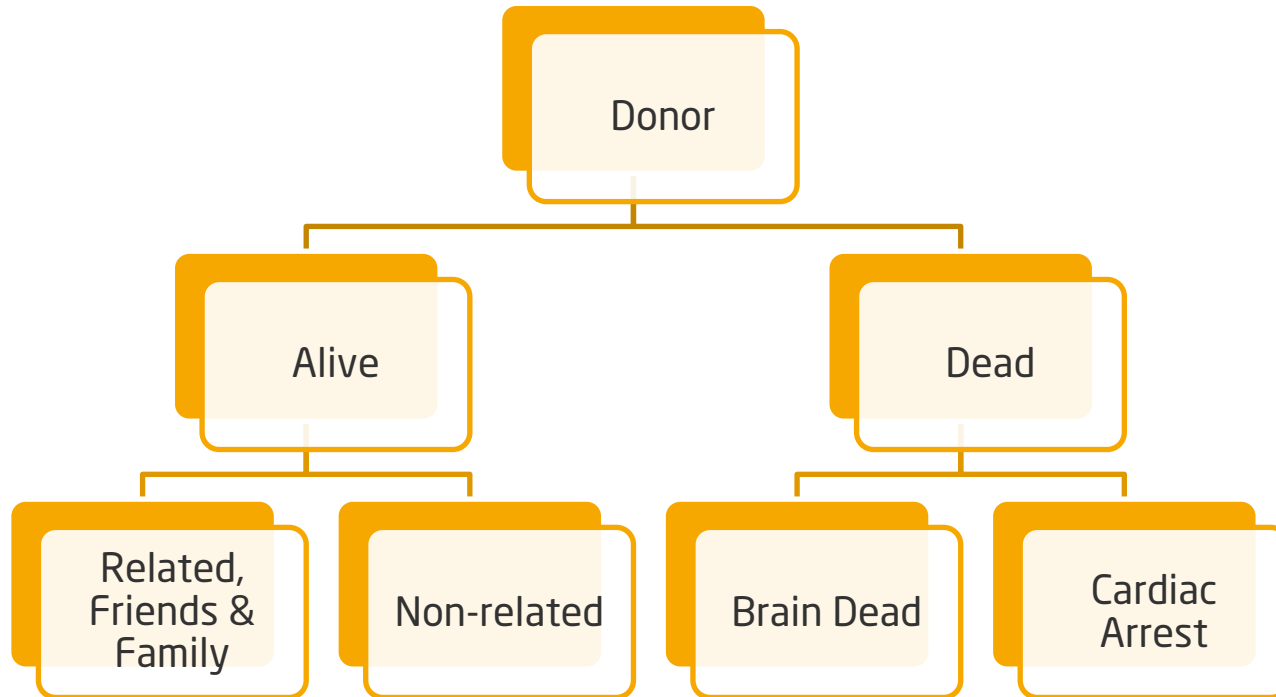


* only required for non-living organ donations

**Medical Use Case
Nephrology**

Data Management for
Digital Health, Winter
2023
28

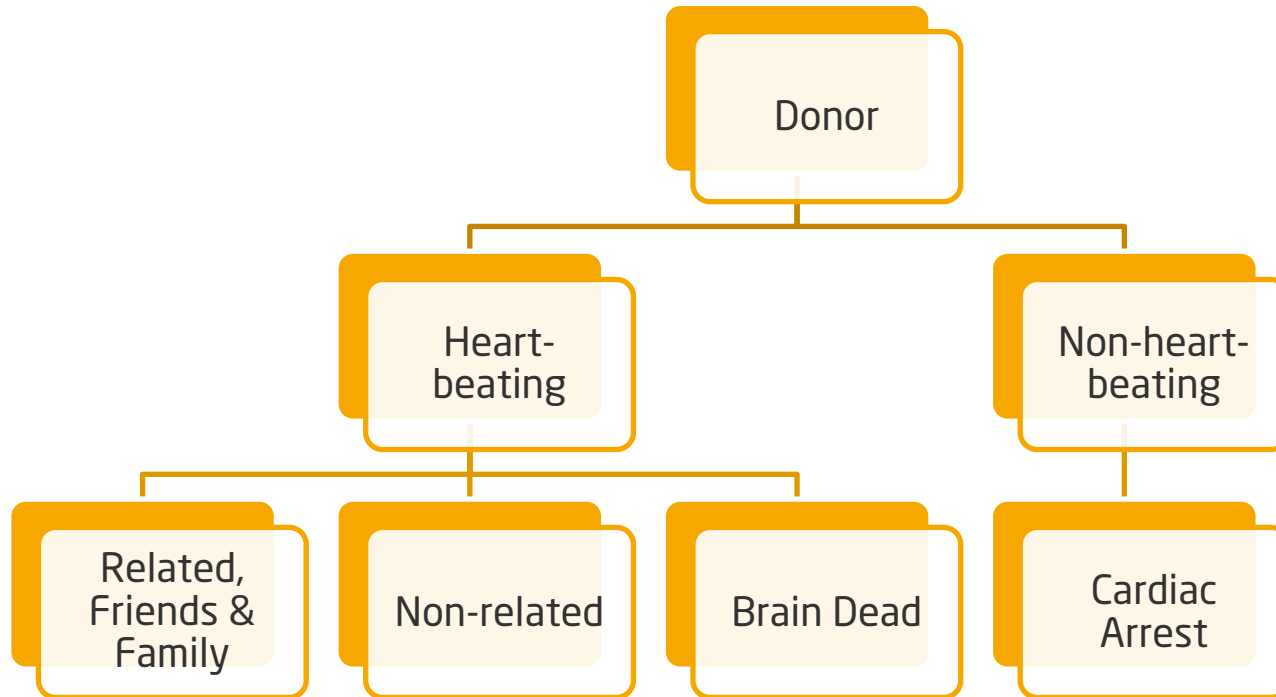
Treatment Options: Organ Transplantation by Type



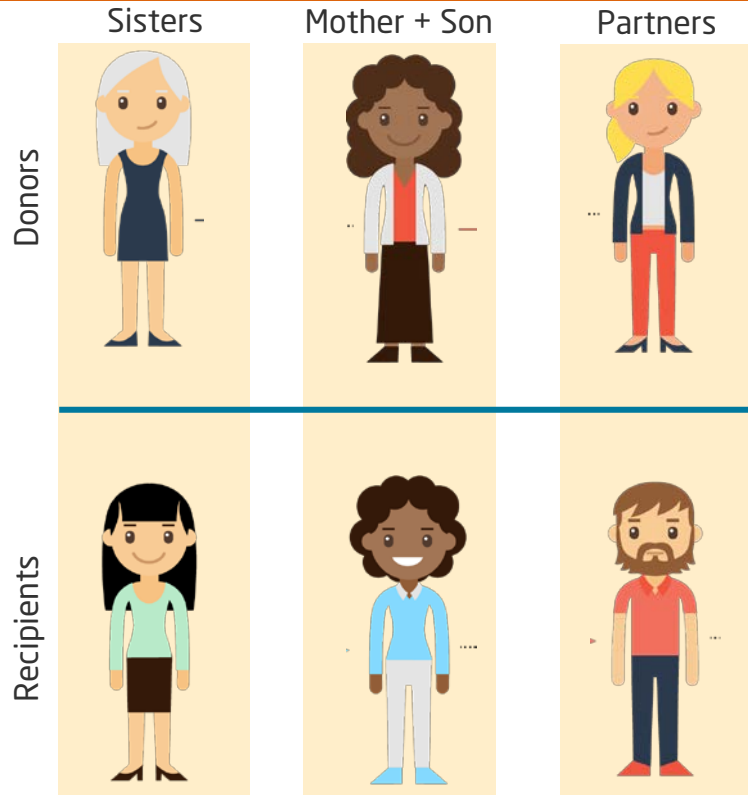
Medical Use Case Nephrology

Data Management for
Digital Health, Winter
2023
29

Treatment Options: Organ Transplantation by Type (former)



Transplantation Strategies: Related, Family & Friends Donations

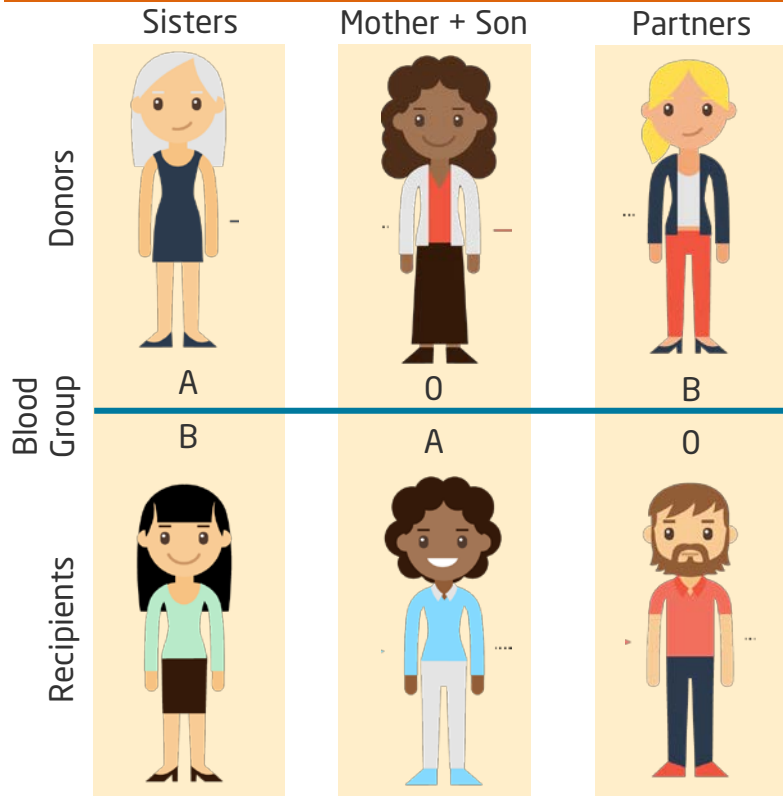


 Not a match for kidney transplant
People in the above illustration were Designed by Freepik

Medical Use Case Nephrology

Data Management for
Digital Health, Winter
2023
31

Transplantation Strategies: Related, Family & Friends Donations (cont'd)



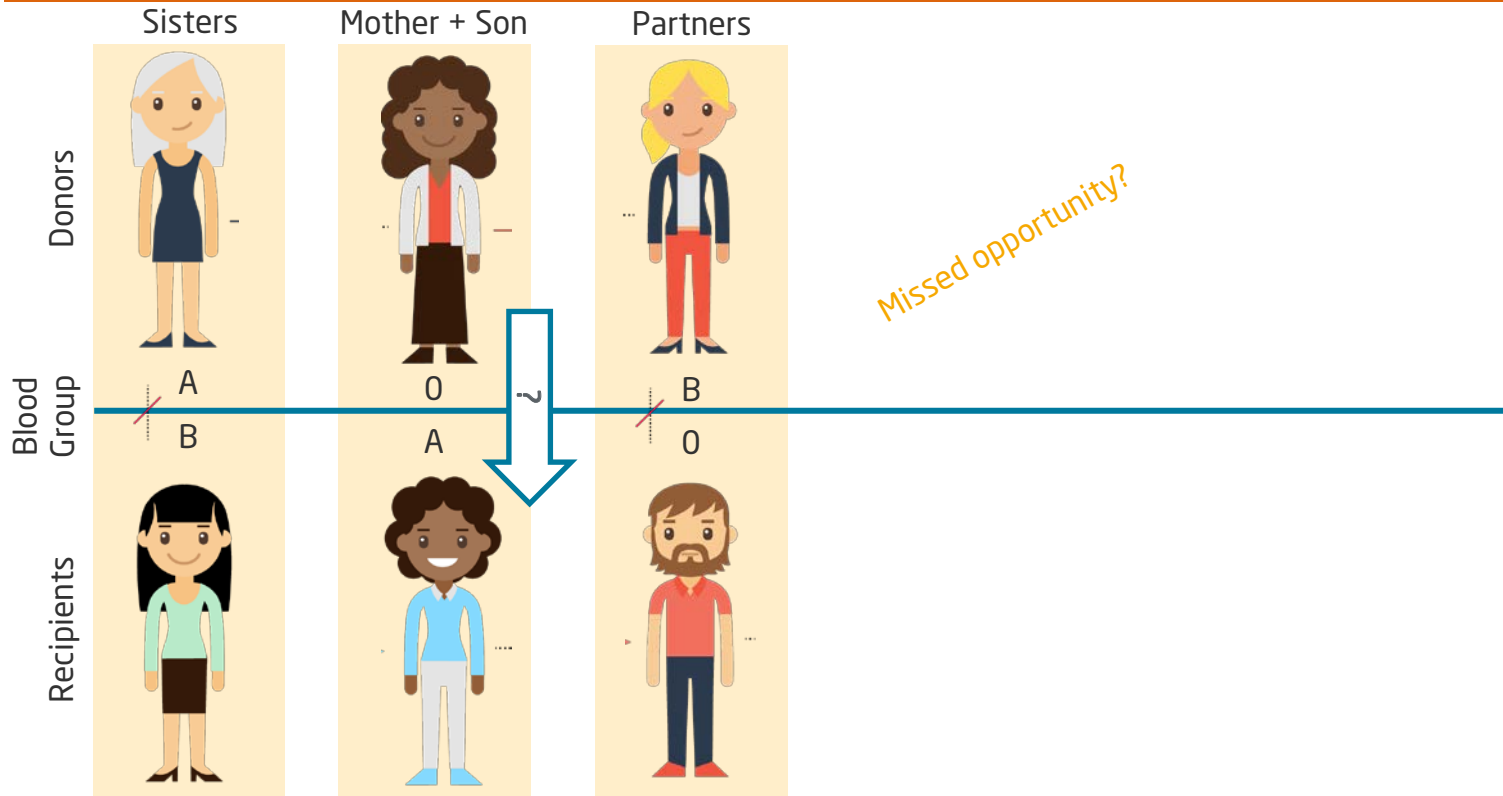
Blood Group	Receive from	Donate to
O	O	O, A, B, AB
A	O, A	A, AB
B	O, B	B, AB
AB	O, A, B, AB	AB

 Not a match for kidney transplant
People in the above illustration were Designed by Freepik

**Medical Use Case
Nephrology**
Data Management for
Digital Health, Winter
2023
32

Adapted from <https://www.med.unc.edu/surgery/kidney-transplant-a-chain-of-events-that-saves-lives/>

Transplantation Strategies: Related, Family & Friends Donations (cont'd)



Blood Group	Receive from	Donate to
O	O	O, A, B, AB
A	O, A	A, AB
B	O, B	B, AB
AB	O, A, B, AB	AB

~~Not a match for kidney transplant~~
People in the above illustration were Designed by Freepik

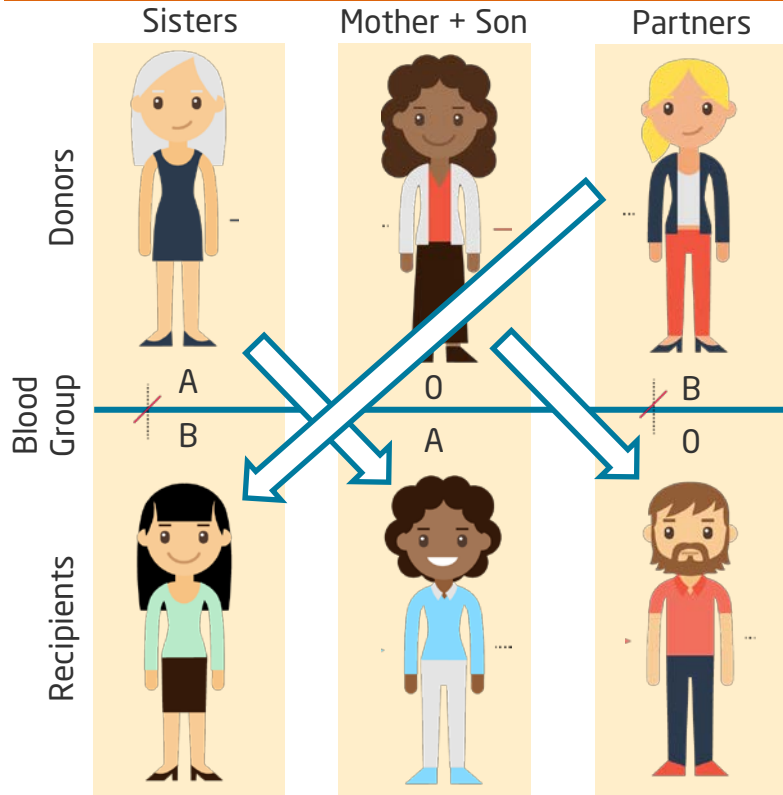
**Medical Use Case
Nephrology**

Data Management for
Digital Health, Winter
2023

33

Adapted from <https://www.med.unc.edu/surgery/kidney-transplant-a-chain-of-events-that-saves-lives/>

Transplantation Strategies: Non-related Donation, Kidney Swap



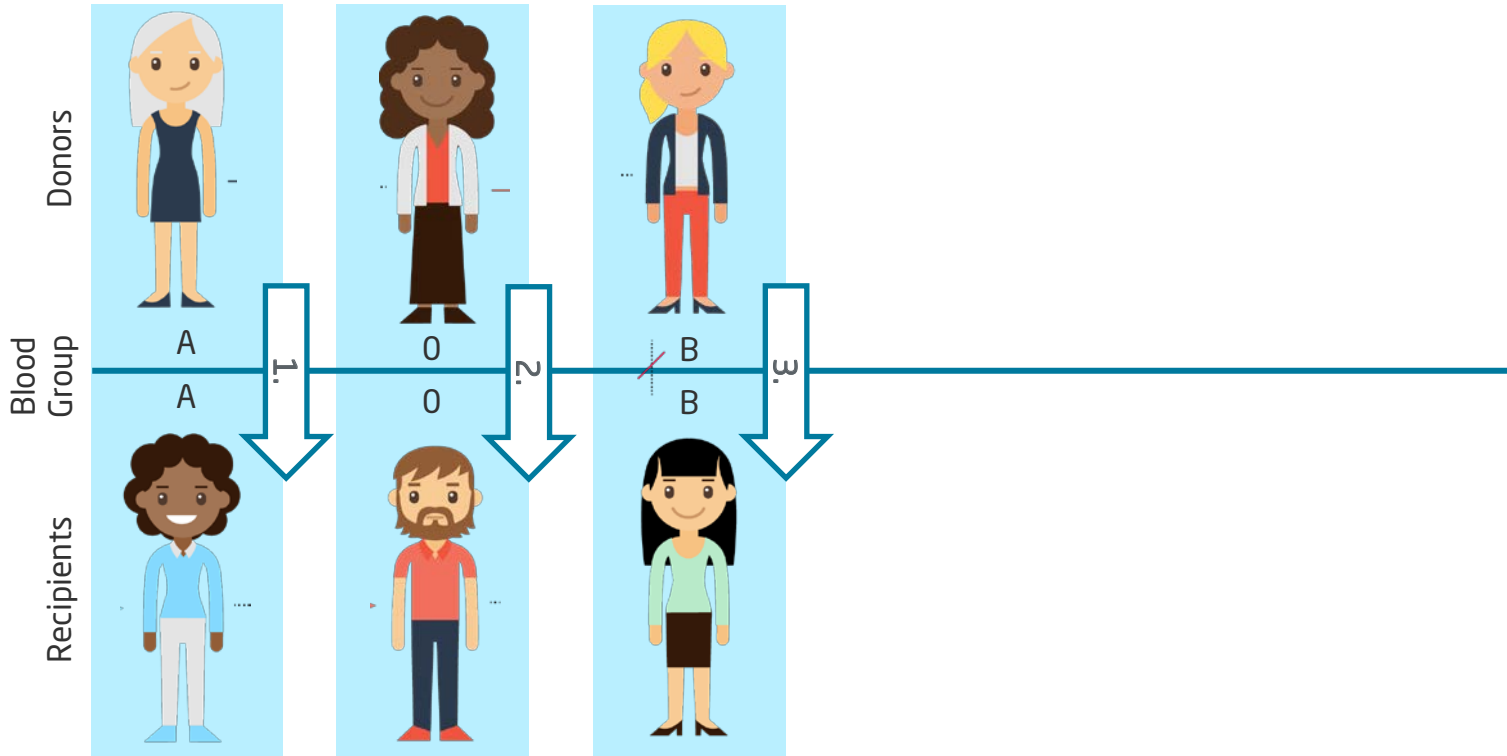
Blood Group	Receive from	Donate to
O	O	O, A, B, AB
A	O, A	A, AB
B	O, B	B, AB
AB	O, A, B, AB	AB

 Not a match for kidney transplant
People in the above illustration were Designed by Freepik

Medical Use Case Nephrology

Data Management for
Digital Health, Winter
2023
34

Transplantation Strategies: Non-related Donation, Kidney Swap (cont'd)



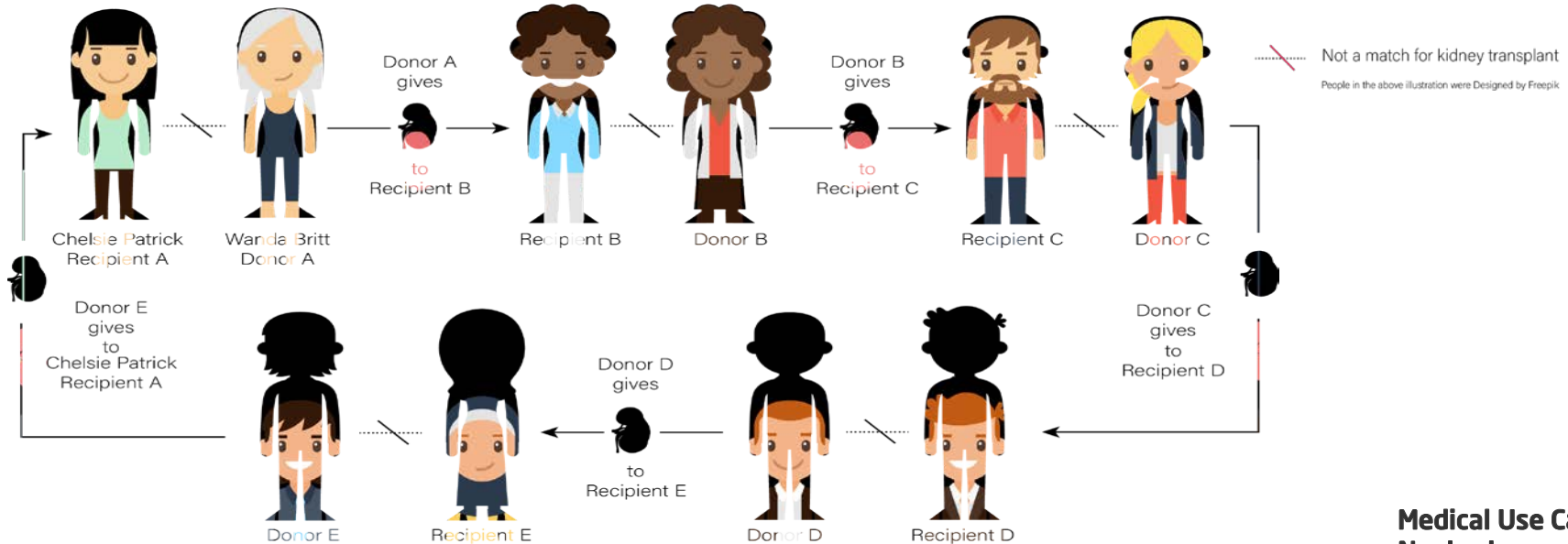
Blood Group	Receive from	Donate to
O	O	O, A, B, AB
A	O, A	A, AB
B	O, B	B, AB
AB	O, A, B, AB	AB

 Not a match for kidney transplant
People in the above illustration were Designed by Freepik

Medical Use Case Nephrology

Data Management for
Digital Health, Winter
2023
35

Transplantation Strategies: Non-related Donation, Kidney Chain



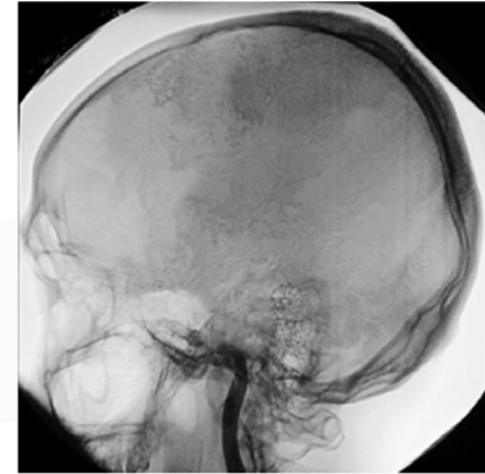
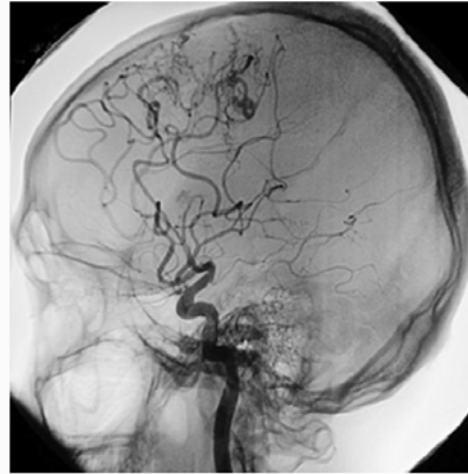
Kidney Chain Illustration

Medical Use Case Nephrology

Data Management for
Digital Health, Winter
2023
36

Transplantation Strategies: Dead Donor: Donation after Brainstem Dead

- Donation after Brain(stem) Dead (DBD) /
 - Donor typically hospitalized
 - Absolutely no brain activity + it is not expected to return
 - Donor undergoes a series of tests by multiple physicians
 - Dead happens controlled, i.e. stopping live-prolonging measures
 - Organ testing and matching can be conducted less time-sensitive



<https://donatelifecalifornia.org/education/how-donation-works/what-is-brain-death/>

Medical Use Case Nephrology

Data Management for
Digital Health, Winter
2023
37

Transplantation Strategies: Dead Donor: Donation after Circulatory/Cardiac Dead

Cat.	Description	Kind	Tissues and Organs
I	Brought in dead	Uncontrolled	Only tissues, e.g. heart valve, cornea
II	Unsuccessful resuscitation	Uncontrolled	Kidneys only after tissue testing
III	Awaiting cardiac arrest	Controlled	Almost all organs depending on health status of the patient, expect heart; liver and lung only from cat. III.
IV	Cardiac arrest after brain-stem death	Uncontrolled	
V	Cardiac arrest in a hospital inpatient	Uncontrolled	

- Donation after Circulatory Death a.k.a. Cardiac Dead (DCD), Non-heart-beating Donation (NHBD) introduced after brain death definition in the 1970s
- Maastricht Protocol est. in 1980s defines five categories of DCD since 1980s
- Problems:
 - Hard time-constraints after cardiac arrest
 - Ethical equivalence of 10+ mins cardiac death with DBD?

DCD in Germany:

- Since 1998 MDs argued against DCD organs
- DCD is not permitted, also not “imported” via Eurotransplant

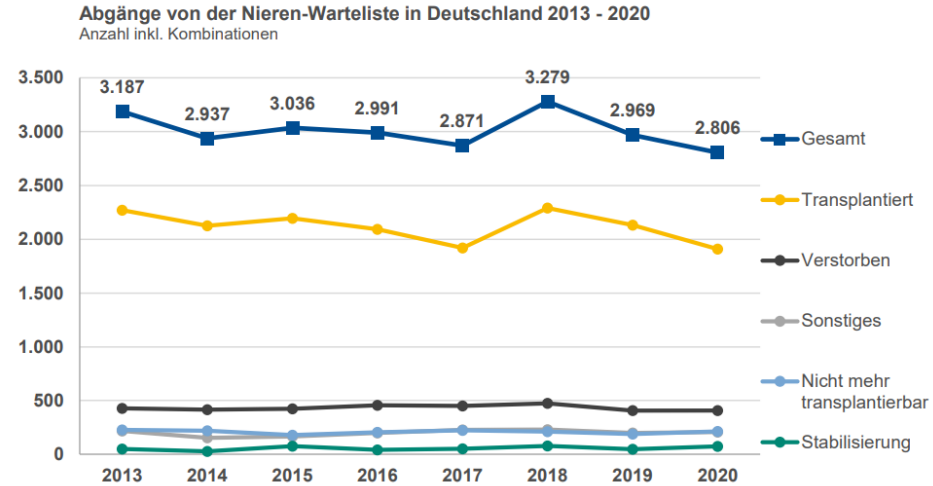
Medical Use Case Nephrology

Data Management for
Digital Health, Winter
2023

- German Organ Procurement Organization (DSO)
- Eurotransplant runs the following allocation programs:
 - Acceptable Mismatch Program (AM),
 - Eurotransplant Kidney Allocation System (ETKAS), and
 - Eurotransplant Senior Programme (ESP).
- Organ Donation Organization (ODOs) in each province of Canada

Kidney Transplantations in Germany: Patients on the Waiting List

- Number of performed transplantations decreased over the past years
- Gap b/w required and available organs
- Waiting time for an adequate donor organ can last up to ten years
- Approx. 500 patients p.a. die while on waiting list



<https://dso.de/BerichteTransplantationszentren/Grafiken%20%202020%20Niere.pdf>

Medical Use Case Nephrology

Data Management for
Digital Health, Winter
2023
40

Transplants in Germany by year, by donor type, by organ type

Deceased donor	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
heart	313	304	286	297	257	318	344	339	329	358
kidney	1,547	1,508	1,551	1,497	1,364	1,653	1,612	1,459	1,517	1,431
lung	371	352	295	328	309	375	361	344	283	254
liver	801	789	788	753	686	746	712	702	695	664
split liver	83	90	58	73	74	74	64	72	85	42
pancreas	128	120	105	97	72	95	94	92	65	44
pancreatic islets	1									
Total	3,244	3,163	3,083	3,045	2,762	3,261	3,187	3,008	2,974	2,793

Living donor	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
kidney	725	619	645	597	557	638	520	451	475	535
lung			1							
liver	3	4	3	8	2	5	1			1
split liver	83	58	45	54	61	52	54	52	54	41
Total	811	681	694	659	620	695	575	503	529	577

Total all organs	4,055	3,844	3,777	3,704	3,382	3,956	3,762	3,511	3,503	3,370
-------------------------	--------------	--------------	--------------	--------------	--------------	--------------	--------------	--------------	--------------	--------------

Medical Use Case Nephrology

Data Management for
Digital Health, Winter
2023

41

Active waiting list (at year-end) in 2022, by country, by organ

Active waiting list	A	B	D	H	HR	NL	SLO	Total
kidney	587	1,189	6,683	764	196	938	16	10,373
heart	40	83	699	44	23	128	27	1,044
lung	35	111	286	7	8	127	4	578
liver	57	130	841	67	150	41	7	1,293
pancreas	11	34	326	32	8	29	1	441
Total patients	716	1,504	8,505	877	375	1247	52	13,276

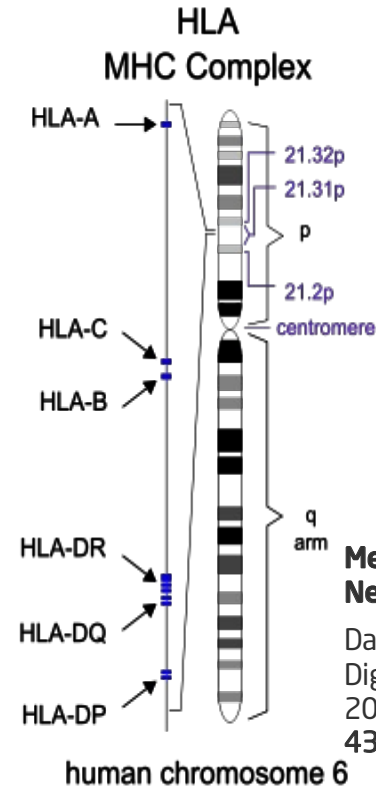
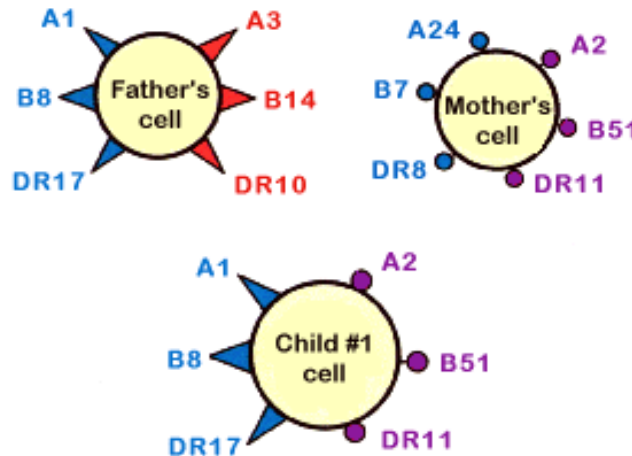
Medical Use Case Nephrology

Data Management for
Digital Health, Winter
2023

42

Kidney Transplantation: Organ Matching

- Aim: Reduce risk of post-transplant organ rejection through the recipient's immune system
- Procedure: Histocompatibility assessment, i.e. compatibility check with regards to Human Leukocyte Antigens (HLA) exposed by organ cells
- HLA excurses:
 - 200+ genes form the HLA family
 - HLA location on chr 6.

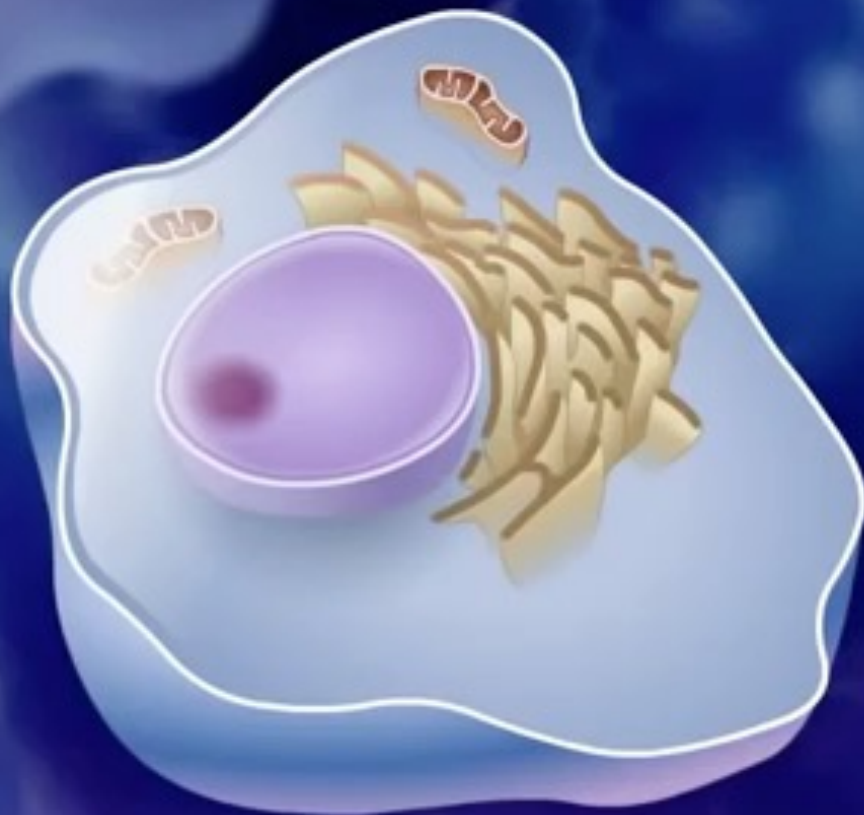


Medical Use Case Nephrology

Data Management for
Digital Health, Winter
2023
43

Kidney Transplantation: Organ Matching (cont'd)

- ABO blood group compatibility is critical for solid organ transplants
- HLA typing of donor and recipient
- Screening of recipient for presence of donor-specific antibodies (DSA)
- Currently, a minimum of 6 HLA markers need to match
- HLA-A, HLA-B and HLA-DR are in the focus for kidney transplantations

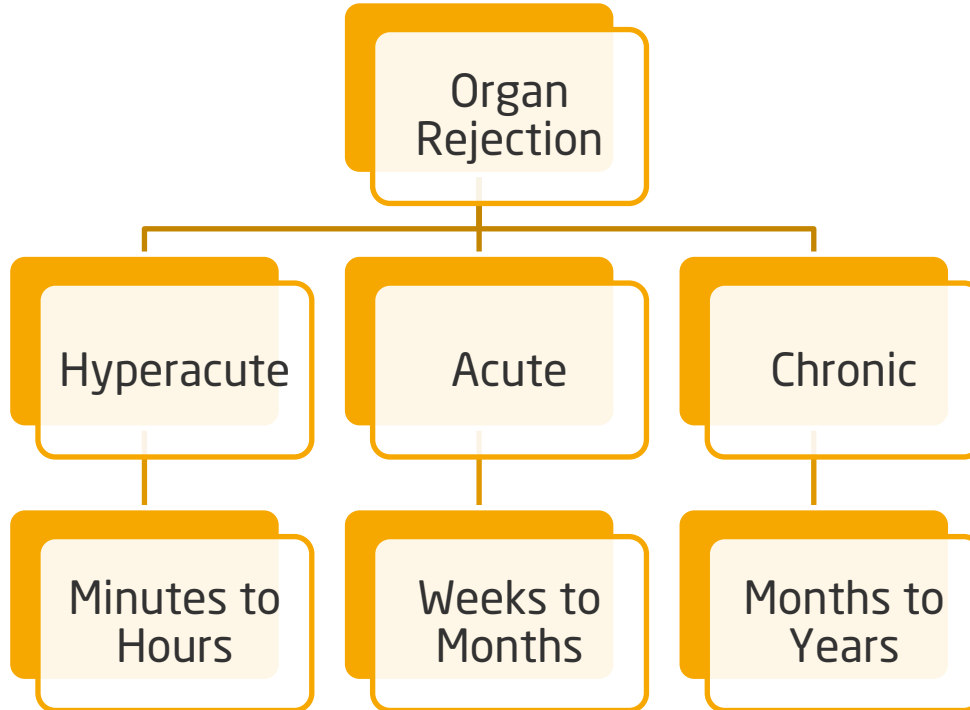


<https://www.youtube.com/watch?v=AucZivEv29Y>

Medical Use Case Nephrology

Data Management for
Digital Health, Winter
2023

Organ Rejection: By Type



Medical Use Case Nephrology

Data Management for
Digital Health, Winter
2023

Organ Rejection: Hyperacute

- **Timeframe:** Minutes to hours post-transplant
- **Cause:** Pre-existing DSAs in the recipient, e.g. ABO blood groups
- **Effects:**
 - Humoral, antibody-mediated rejection
 - Irreversible damage, e.g. thrombosis + necrosis
- **Result:** pre-mature organ failure



Photo by Ocean Ng

Medical Use Case Nephrology

Data Management for
Digital Health, Winter
2023

Organ Rejection: Acute

- **Timeframe:** Weeks to months post-transplant
- **Cause:** Immune systems recognize HLAs as foreigners
- **Effect:** T-Cell-Mediated Rejection (TCMR)
 - Direct → acute cellular rejection, i.e. lymphocytes induce apoptosis
 - Indirect → acute humoral rejection, i.e. B-cells create DSAs
- **Result:**
 - Use of immunosuppressants to reduce activity of immune system
 - Singular episodes of acute rejection should not compromise the transplant



Photo by Behnam Norouzi

Medical Use Case Nephrology

Data Management for
Digital Health, Winter
2023
48

Organ Rejection: Chronic

- **Timeframe:** Months to years post-transplant
- **Cause:** Not completely identified, but ideas, e.g.
 - Possible prior acute rejection might be a trigger
 - Vascular damage
 - Interstitial Fibrosis and Tubular Atrophy (IFTA)
- **Result:**
 - Slow, but ongoing allograft destruction



Photo by Anne Nygård

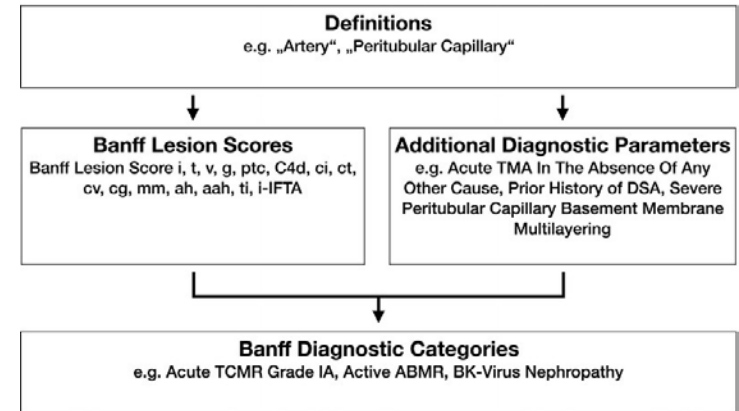
Medical Use Case Nephrology

Data Management for
Digital Health, Winter
2023

Organ Rejection: Biopsy for Validation of Kidney Rejection

- **Banff Lesion Scores:** Assess the presence and the degree of histopathological changes in the different compartments of renal transplant biopsy
- **Banff Diagnostic Categories:** Mapping to reasons for graft rejection:
 - 1: Normal
 - 2: Antibody-mediated
 - 3: Suspicious/ for acute TCMR
 - 4: TCMR
 - 5: IFTA
 - Other changes

Content of the Banff Classification of Renal Allograft Pathology



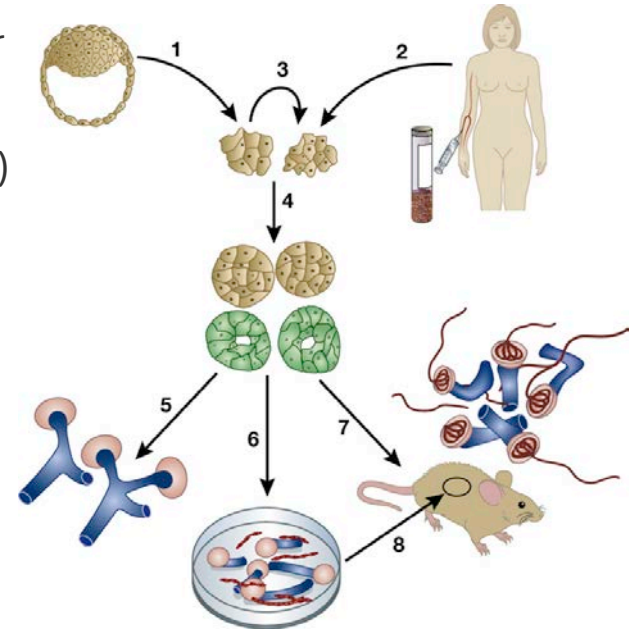
Medical Use Case Nephrology

Data Management for
Digital Health, Winter
2023
50

Treatment Options:

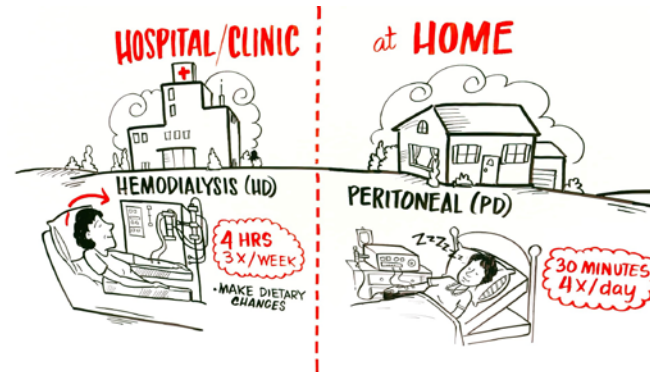
3. Brew Your Own Kidney

- Human pluripotent stem cells (PSCs) from early human embryos (1.) or mature blood, skin, or urine cells, etc. (2.)
- 4. Differentiate into mesoderm-like cells expressing molecules (green) → kidney precursor cells (KPC)
- KPC can be maintained:
 - 5. in 2D culture forming “tubule-like” structures (blue) and primitive nephrons (pink)
 - 6. as 3D organoids forming tubules (blue) and avascular glomeruli (pink)
 - 7. Implanted into immune-deficient mice
 - 8. Implant PSC-derived kidney organoids to immune-deficient mice (similar effect as 7)



What to Take Home?

- Your kidneys filters about 20-25% of the heart volume output every day
- Kidney failure is a “silent” disease requiring immediate action
- Treatment options vary from dialysis to transplantation
- Prevent kidney failure by eating fruits and vegetables, workout, stay hydrated
- Kidney failure and treatment options in a nutshell:
<https://www.youtube.com/watch?v=mi34xCfmLhw>



Medical Use Case Nephrology

Data Management for
Digital Health, Winter
2023
52