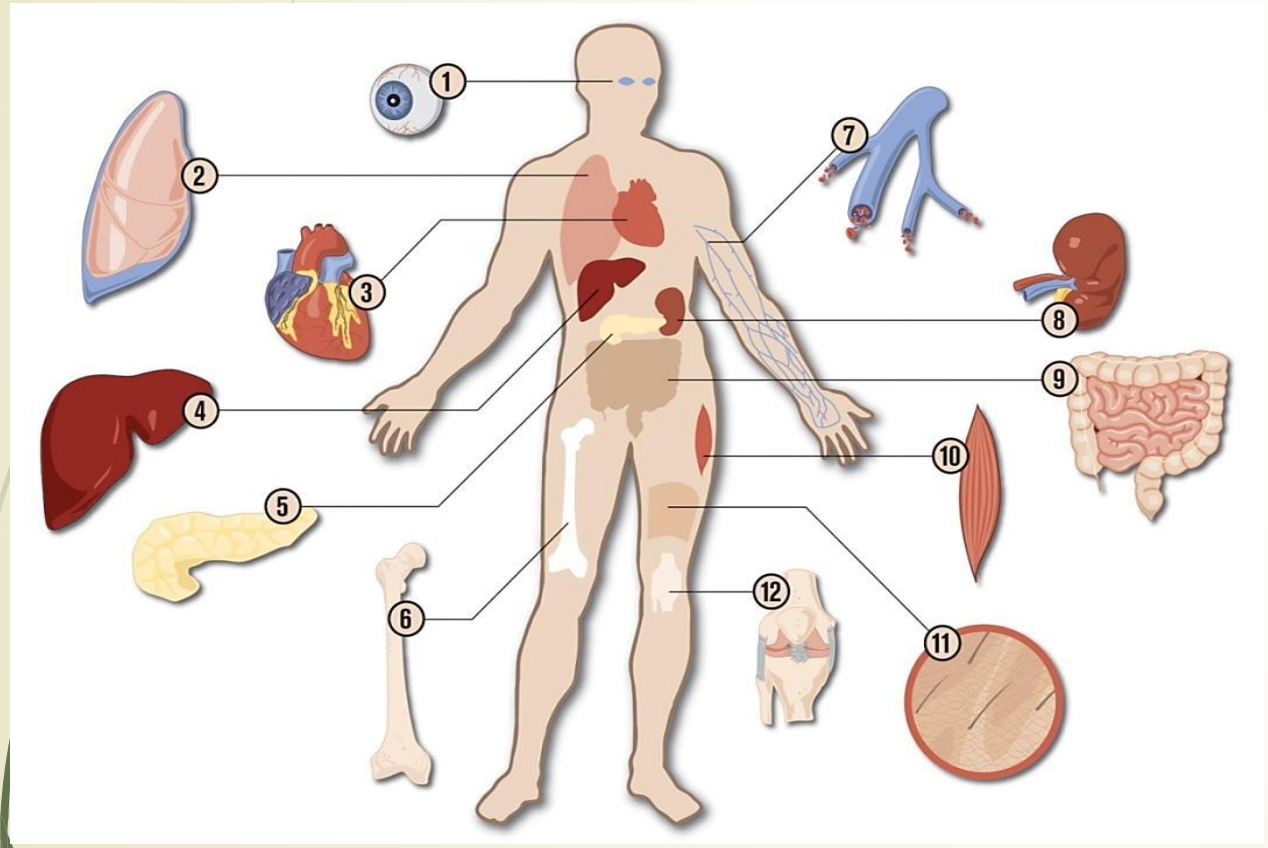

بسم الله الرحمن الرحيم

Allocation of Deceased Kidney Donors

Ali Momeni, Nephrologist

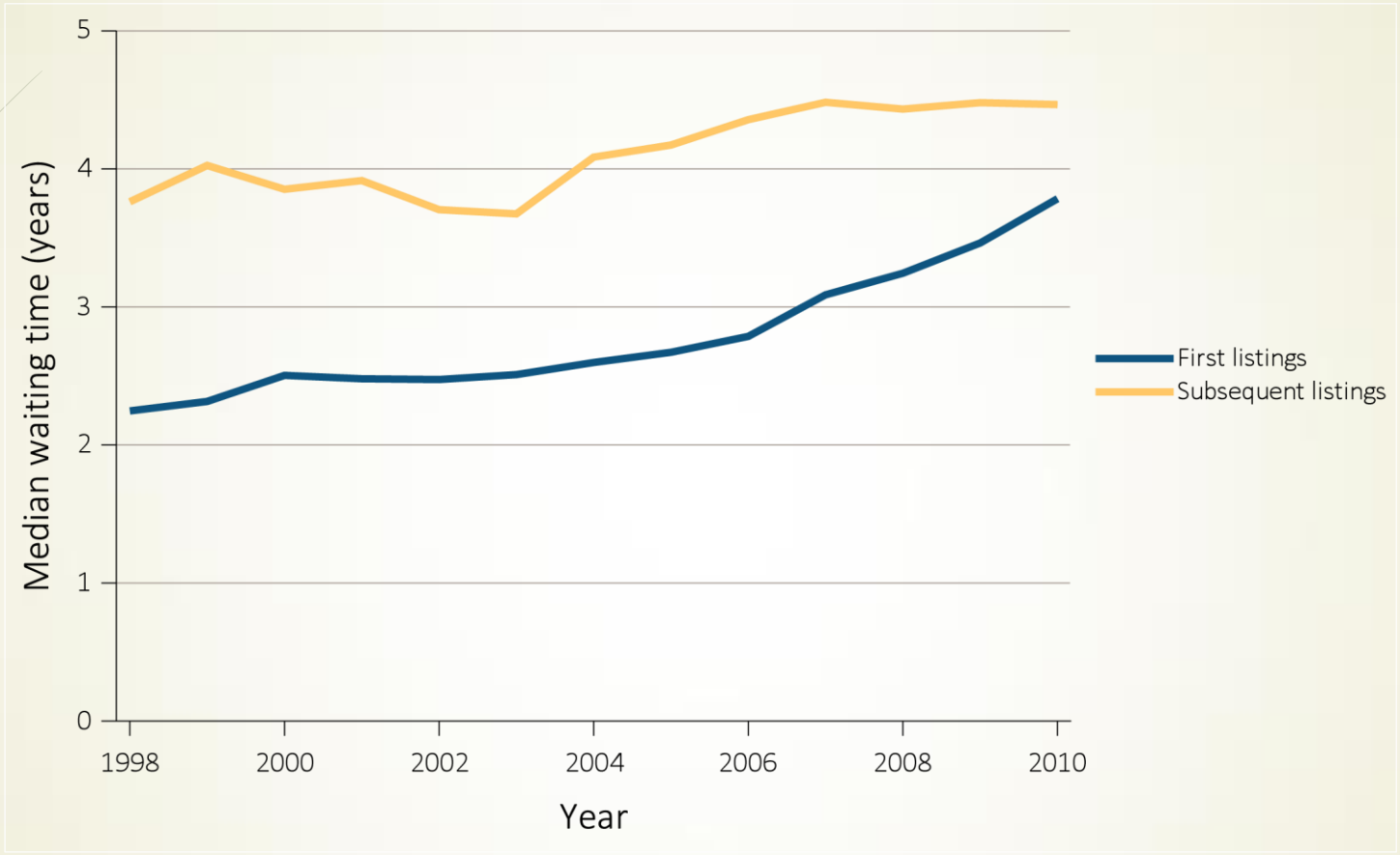
Shahrekord University of medical Sciences

DONATION POTENTIAL



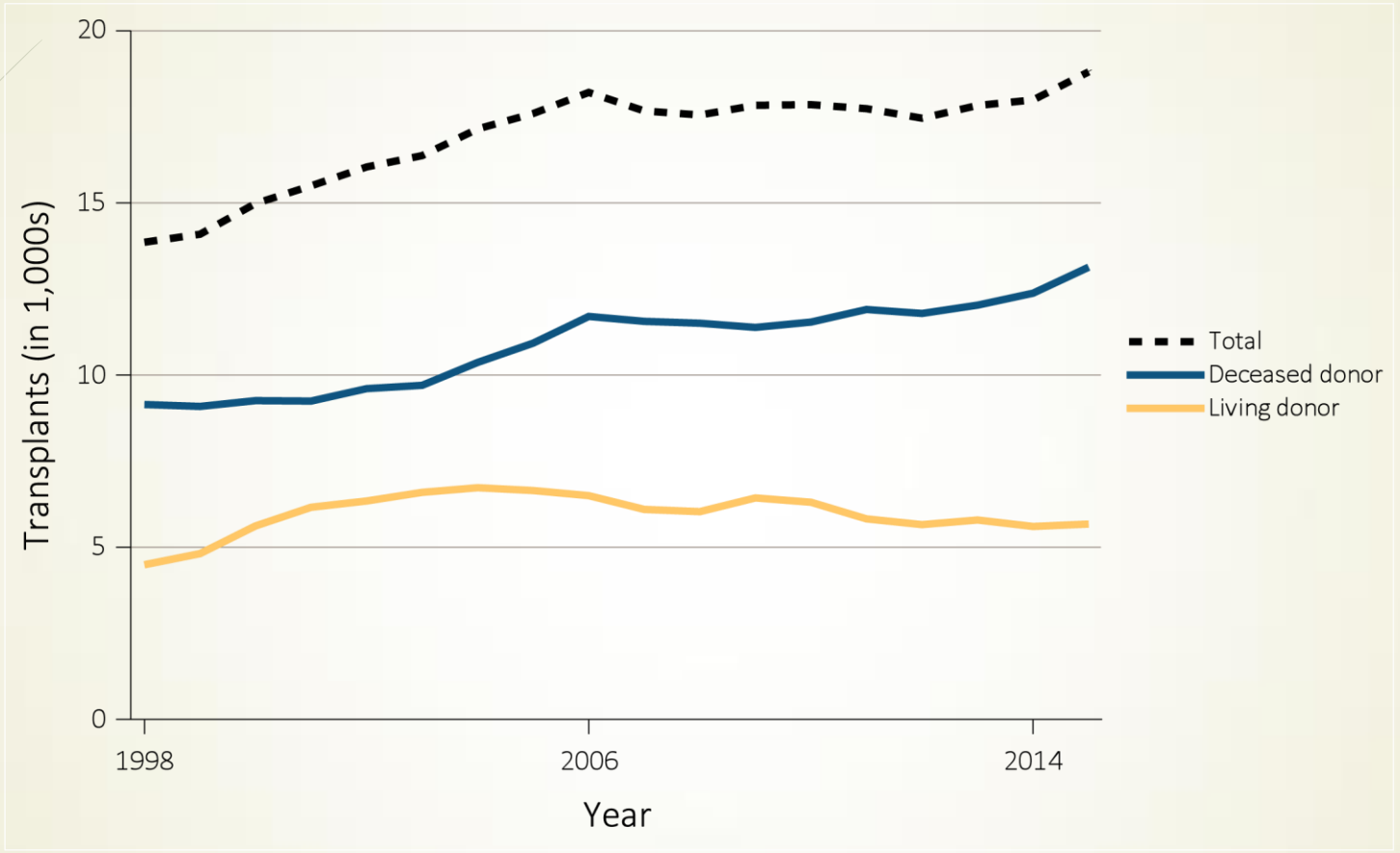
1. EYES/CORNEAS
2. LUNGS
3. HEART/HEART VALVES
4. LIVER
5. PANCREAS
6. BONE
7. VEINS
8. KIDNEYS
9. SMALL INTESTINE
10. FASCIA
11. SKIN
12. CARTILAGE

Median waiting time for kidney transplant, 1998-2010



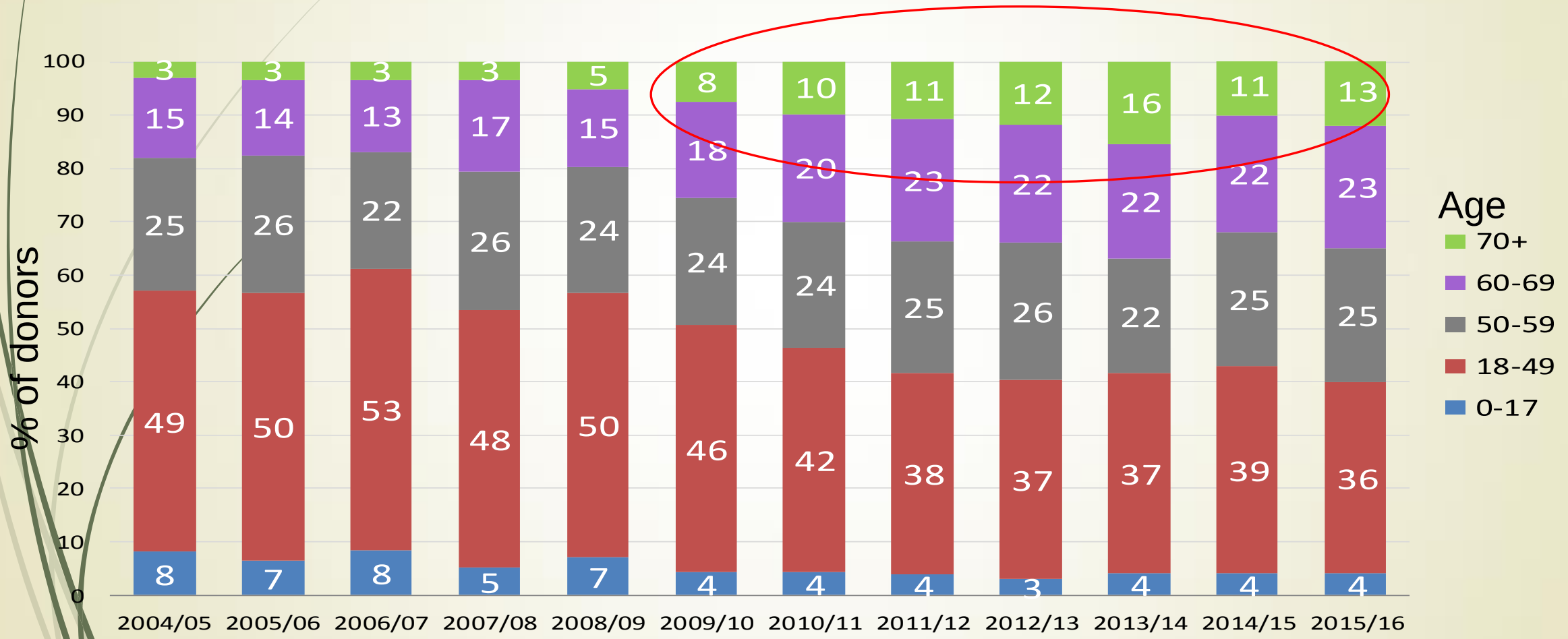
Data Source: Reference Tables E.2. Median waiting time to kidney transplant. Median waiting time is calculated for all candidates enrolled on the waiting list in a given year.

Number of kidney transplants by donor type, 1998-2015

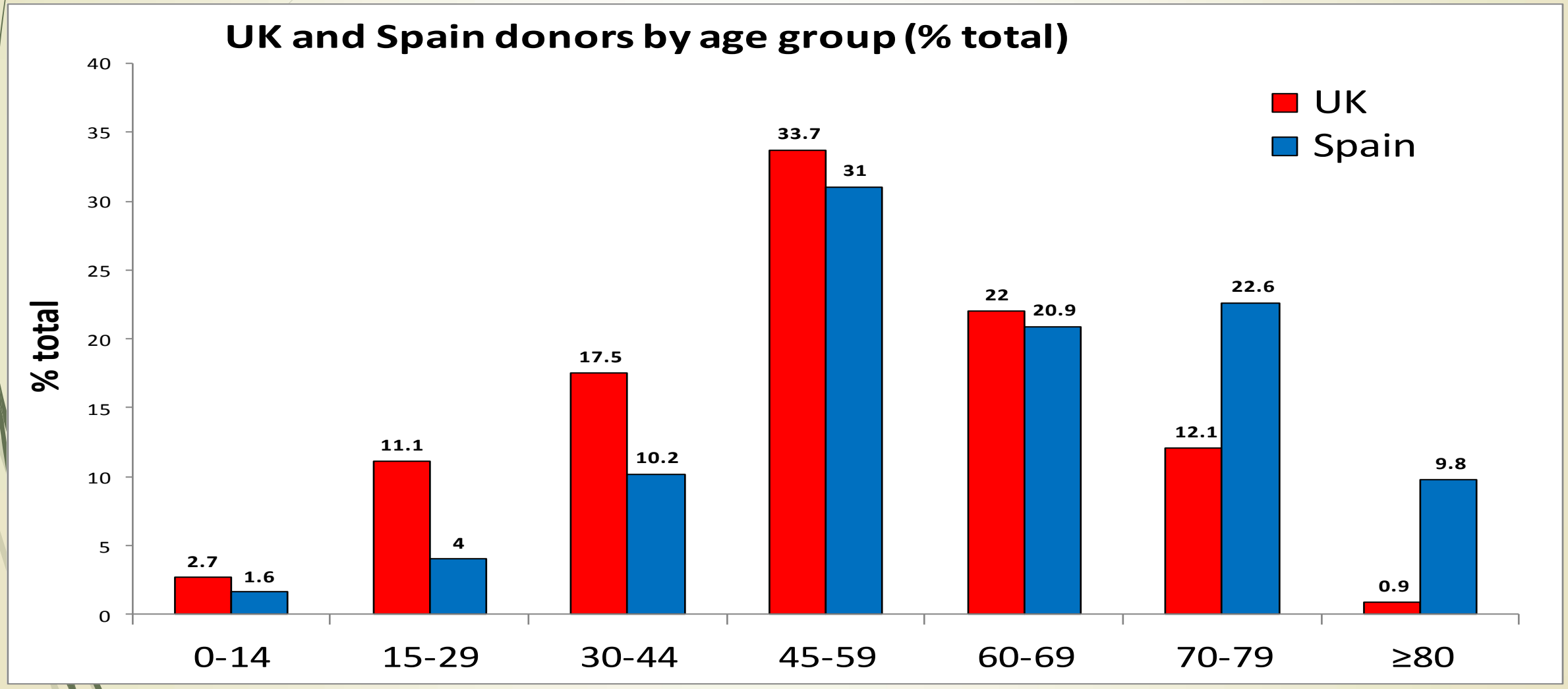


Data Source: Reference Tables E.8, E.8(2), and E.8(3). Number of kidney transplants by donor type. Note that trends may be influenced by changes to the kidney allocation system (KAS) policy that were implemented in December 2014.

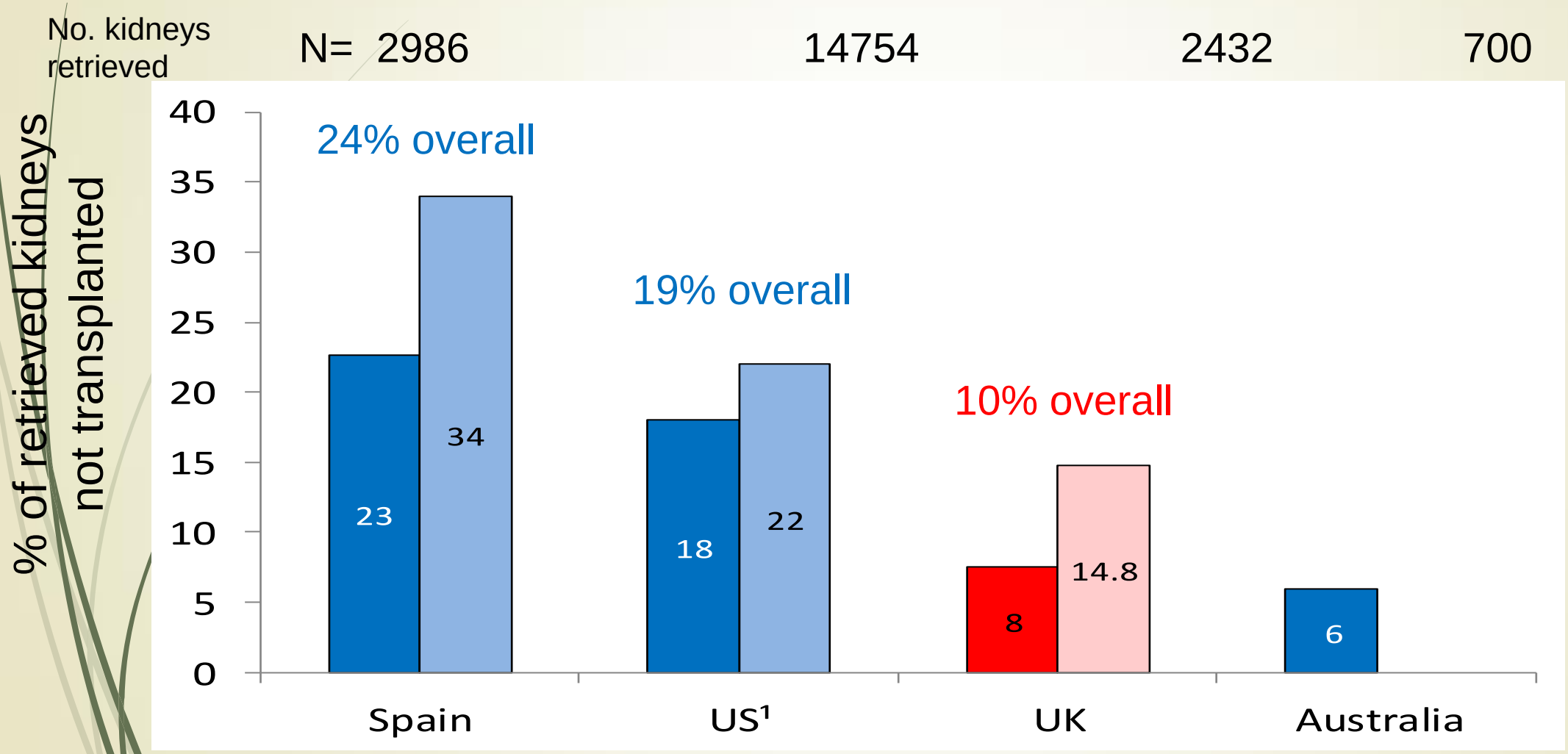
Age of UK deceased donors



Age of deceased donors – UK vs Spain (2015)



Discard rates for kidneys from deceased donors, 2014

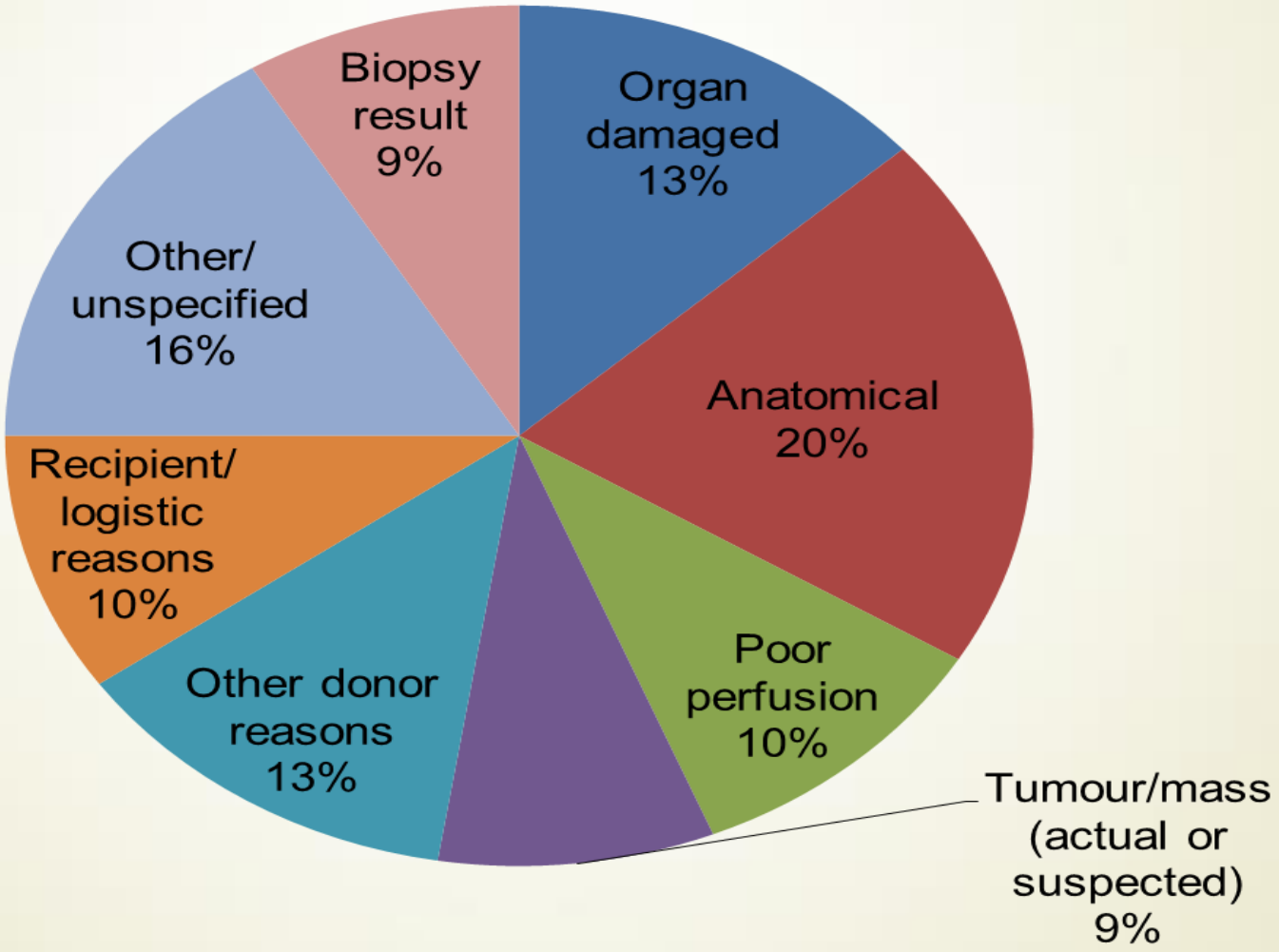


Source: ONT – Spain data, OPTN - US data
ANZ - Australia data, NHSBT - UK data

¹ 2012 data

Reasons for retrieved organs not being transplanted (2015/16)

KIDNEY
N=276



NUMBERS TO REMEMBER

- 52% of adults in the United States are on a donor registry
- 75% of families say yes when offered the option of organ donation
- 35% of families say yes when offered the option of tissue donation

- The World Health Organization (WHO): 80,000 kidney transplants are performed each year in the 112 member states
- Approximately 60% from deceased donors.
- One-year patient and graft survival: 96%.
- Kidney have a five-year survival rate close to 90%.
- Recipient five years survival of 80% is necessary for deceased donor kidney wait-listing.
- Inclusion criteria for being listed for deceased donor kidney transplantation are: End-stage kidney disease on dialysis or GFR <15-20 ml/min/1.73m2

Death Diagnosis

- An individual who has sustained either irreversible cessation of circulatory and respiratory functions, or irreversible cessation of all functions of the entire brain, including the brain stem is dead.
- The concept included an absence of spontaneous respiration.
- As opposed to other organs, the brain cannot be supported or replaced by medical technology.
- So the loss of the function of the heart, and other organs that are replaceable, does not solely constitute death.

Determining Death by an Absence of Circulation

- Brain function and electrical activity are lost within seconds of the absence of circulation
- Even under normo-thermic conditions, the brain might be able to tolerate as long as 10 to 11 minutes of circulatory arrest without any long-term sequelae.
- The permanent absence of circulation will lead to the irreversible loss of brain function.
- Donation after Circulatory Death (DCD).
- The previous terms: donation after cardiac death or —non–heart-beating donation have been abandoned.

Clinical Evaluation of Brain death

- Coma—patient lacks all evidence of responsiveness
- Absence of brainstem reflexes
- No pupillary response (Fixed Mydriasis)
- No oculocephalic reflex No corneal reflex
- Absence of facial movement to a noxious stimuli
- No tracheobronchial reflex

Clinical Criteria for the Diagnosis of Brain Death

- Establish irreversible and proximate cause of coma
- Exclude the presence of sedating, paralyzing, or toxic drugs
- Exclude apnea in response to acidosis or hypercarbia
- Absence of severe electrolyte, acid–base, or endocrine disturbance
- Achieve normal or near-normal core temperature
- Achieve normal systolic blood pressure >100 mm Hg

The Dead Donor Rule and Organ Donation

- No organ recovery should precede the declaration of death.
- Before the criteria for brain death were accepted in the 1970s, all deceased donor organs were recovered from patients after cardiac and circulatory death.

Maastricht Categories for Non–Heart-Beating Donors Category

- I: dead on arrival Category
- II: unsuccessful resuscitation Category
- III: awaiting cardiac death Category
- IV: cardiac death in a brain-dead donor
- Category I and II DCD donors, also referred to as uncontrolled donors, are pulseless and asystolic after adequate but failed attempts at resuscitation.

Donation after Circulatory Death

- In the United States, DCD is usually category III or —controlled. These donors are comatose, irreversibly brain damaged, and respirator dependent, but are not brain dead by strict definition.
- In these circumstances, the decision to withdraw supportive care is made by the family and primary medical team.
- Ventilator support is discontinued either in the operating room or in an intensive care unit, cardiac function is monitored, and death is pronounced by standard cardiac criteria after a predetermined (usually 5-minute) period of asystole.
- Organ recovery then proceeds expeditiously.
- The organ recovery team plays no part in the diagnosis of death or medical management of the patient before asystole.

When to Notify the Organ Procurement Organization Any Imminent Death

- Severe acute brain injury
- Ventilator dependent
- In an intensive care unit or emergency room
- Glasgow Coma Scale (GCS) < 5 Or

SUITABLE BRAIN DEAD ORGAN DONOR

- Donor declared brain dead by ICU team
- Family informed of donor registry status or approached for authorization for donation
- Donor discharged and readmitted to LifeGift

MULTI-DISCIPLINARY TRANSPLANT TEAM

- Nephrologist
  - Primary nephrologist
  - Transplant nephrologist
- Surgeon/Nurse Practitioner
- Specialty physicians
  - Cardiology
  - Pulmonology
  - Infectious Disease
  - Hematology
  - Additional specialty physicians (endocrinology, urology, neurology, etc)
- Pharmacist
- Dietitian
- Transplant Administrator
- Assistant Clinical Manager
- Transplant Clinic Coordinator
- Transplant Assistant
- Transplant coordinator
  - Pre-transplant Recipient
  - Waitlist
  - Donor
  - National Kidney Registry (NKR)
  - Desensitization
- Social Work (SW)
  - Pre-transplant recipient
  - Waitlist
  - Donor
  - Independent Living Donor Advocate
- Financial Coordinator (FC)
- Quality Coordinator
- Data Coordinator
- Research staff

DONOR SELECTION AND ASSOCIATED RISKS

Deceased donor evaluation and screening consists of:

1. **Attempt to obtain the deceased donor's medical and behavioral history from one or more individuals familiar with the donor**
2. **Deceased Donor Medical and Behavioral History, to screen for medical conditions that may affect the decision to use the donated organ**
3. **Review the deceased donor's medical record**
4. **Complete a physical exam of the deceased donor, including the donor's vital signs**
5. **Transmissible disease transmission screening**

Donor selection …

- Serologic evaluation of organ donors includes screening for hepatitis C (HCV), HIV, hepatitis B virus (HBV), cytomegalovirus (CMV), Epstein–Barr virus (EBV), and syphilis.
- Use of organs from donors who test positive for HIV is contraindicated for HIV-negative recipients owing to the risk of transmission.
- HCV-seropositive donor kidneys may be selected for use in HCV seropositive patients

Organ Donor Contraindication

- Aplastic anemia, agranulocytosis
- Current malignant neoplasms, except non-melanoma skin cancers such as basal cell and squamous cell cancer and primary CNS tumors without evident metastatic disease
- Previous malignant neoplasms with current evident metastatic disease
- A history of melanoma
- Hematologic malignancies: leukemia, Hodgkin's disease, lymphoma, multiple myeloma
- Active fungal, parasitic, viral, or bacterial meningitis or encephalitis
- No discernible cause of death

Management of the Deceased Organ Donor

- The management of the donors is complex and is designed to maximize the function, not only of the kidneys, but of organs both above and below the diaphragm.
- Obviating or minimizing ischemia-reperfusion injury is a major goal made more difficult by the massive release of cytokine at the time of death
- Deceased donors: impaired hormone physiology, tissue hypoxia, increased systemic inflammatory response.
- Large doses of corticosteroids to deplete circulating donor lymphocytes and attenuate brain death–induced inflammatory pathways.

Pharmacologic Adjuncts

- Additional hormone treatments including vasopressin and T3 or T4 are routinely administered,
- For adults, 25 g of mannitol is typically given to ensure diuresis and possibly to minimize ischemic injury.
- Dopamine: may lower rates of delayed graft function.
- Heparin at the time of cannula placement with doses of 10,000 to 30,000 units.
- Hypothermia: significantly reduced the rate of delayed graft function among recipients.

Warm Ischemia time

- **Warm ischemia time** refers to the period between circulatory arrest and commencement of cold storage.
- With modern in situ perfusion techniques, the warm ischemia time is essentially zero in brain-dead donors, although there is warm ischemia if hemodynamic deterioration or cardiac arrest occurs before harvest.
- A kidney may function after 60 minutes of warm ischemia, and 90 minutes in a young donor; however,
- Rates of DGF and non-function increase markedly after 20 minutes.

Cold Ischemia Time

- **Cold ischemia time** refers to the period of cold storage or machine perfusion.
- Less than 12 hours is regarded as ideal, and less than 24 hours as acceptable.
- Most centers don't used kidneys with cold storage longer than 40 hours
- **Rewarm time** is the period from removal of the kidney from cold storage to reperfusion.
- This can essentially be eliminated by wrapping the kidney in ice until completion of the vascular anastomosis.

Cold Ischemia Time…

- The two dominant methods of preserving renal allografts for transplantation are cold storage and pulsatile preservation.
- Both methods employ hypothermia for maintenance of cellular viability and minimization of ex vivo ischemic injury.
- Cold-storage solutions include University of Wisconsin (UW) solution and histidine–tryptophan–ketoglutarate (HTK) solution, among others.
- Kidneys preserved in this manner are flushed in situ through the arterial blood supply with the preservation solution of choice, cooled to about 4°C, explanted, separated, and then packaged.

Cold Ischemia Time…

- Hypothermic pulsatile preservation (machine): Dynamic flow of cold perfusate to the allograft during preservation
- Serial evaluation of perfusion data: decision to transplant or discard kidneys and may also predict outcomes.
- Flow rates of 100 to 150 mL/min or higher, and vascular resistance of 0.20 to 0.40, are considered optimal.
- Allografts with persistently low flow (<75 mL/min) and high resistance (>0.40) are usually declined.

Allocation of Deceased Donor Kidneys

- Organ Procurement and Transplantation Network (OPTN)
- The OPTN, through United network for Organ Sharing (UNOS), works to balance the ethical principles of
- justice(عدالت),
- utility (امکانات),
- respect for persons(احترام به افراد) ,
- autonomy(استقلال),

Allocation of Deceased Donor …

- transparency(شفافیت), which requires that data on all organ transplants be available to the general public through a governmental organization.
- traceability(ردیابی), identification of the source of the donor organs

UNOS Point System for Allocation of Kidneys from Deceased Donors in Place from 2009 to December 2014

Factor	Point	Condition
Time waiting	1 for each year of waiting time	
Quality of HLA match 0-A, B, DR mismatch	2 1	Zero DR mismatches One DR mismatch
Panel-reactive antibody (PRA)	4	>80% PRA and negative crossmatch
Pediatric recipient priority for donors younger than 35 years	4	
Organ donor	4	Expanded criteria donor longest waiting patient

POINT SYSTEM FOR DECEASED DONOR KIDNEY ALLOCATION

- A candidate of kidney transplant must fulfill certain listing criteria.
- Renal transplant recipients must either be receiving chronic dialysis or have a GFR ≤ 20 mL/min or less.
- Waiting patients are ranked by a central computer that is located in the UNOS offices.
- The ultimate decision: responsible physician or surgeon
- A reason or refusal code must be provided to UNOS about the rejection of the offer.

POINT SYSTEM FOR DECEASED DONOR KIDNEY ALLOCATION

- Thus, kidney allocation rules were, at first, based on matching and waiting time.
- About17% of kidney transplant patients can receive a zero-mismatched kidney.
- Patients with better antigen matching to their donors were prioritized over others with similar waiting time but poorer matches(utility).

POINT SYSTEM …

- Remove of HLA-B priority points, resulted in a 37% improvement in the likelihood of African Americans receiving a transplant (justice).
- The pediatric priority: While increasing utility by providing pediatric patients access to kidneys from deceased donors under the age of 35 with longer expected graft survival (justice).

Expanded Criteria Donors

- SCD (Standard Criteria Donor)
- ECD (marginal kidney):
- Donor older than 60 years or
- Aged 50 to 59 years with two additional risk factors, including a history of hypertension, death as a result of cerebrovascular accident (DCD), or an elevated terminal serum creatinine.
- ECD kidneys:15% of deceased donor kidneys, 70% increased risk for failing within 2 years,
- SCD kidney has a 2-year graft survival of 88%,
- ECD kidney has a survival at 2 years of 80%).

Expanded Criteria Donors …

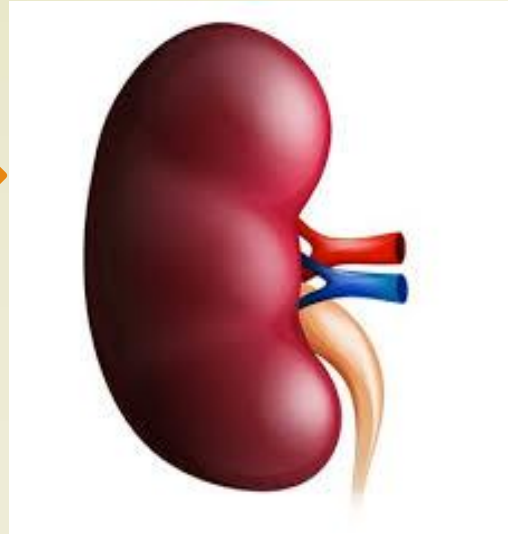
- ECD kidneys were offered only to those patients who were informed of the risk, and who understood that these kidneys were more likely to fail.
- ECD kidneys were allocated according to waiting time alone.

Kidney Allocation System (KAS), Since 2014

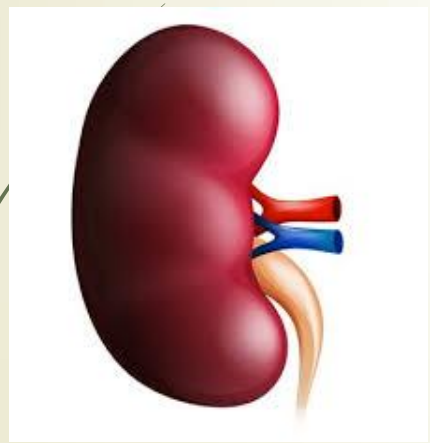
- A Kidney Donor Profile Index (KDPI) score of 20% means that the kidney is likely to function longer than 80% of other available kidneys.
- A person with an Expected Post Transplant Survival (EPTS) score of 20% is likely to need a kidney longer— live longer—than 80% of other candidates.
- KAS: Allocating kidneys with a lower KDPI score (longer estimated function) to recipients with low EPTS scores (better post-transplant survival).
- Age is a critical component of both the KDPI and the EPTS, it is accompanied by other variables.

Kidney Allocation System (KAS)…

- KDPI score of 20% or less will first be offered to patients those with an EPTS of 20% or less.
- Kidneys with a KDPI score of 20% to 85% are allocated according to waiting time
- waiting time: dialysis start date, for pre-dialysis patients, when their eGFR is <20 mL/min.
- KDPI scores ≥ 85% are similar to ECD kidneys viable for transplant in the appropriate recipients



KDPI=20% >>>>>> EPTS=15%



KDPI=85%>>>>>> EPTS=80%

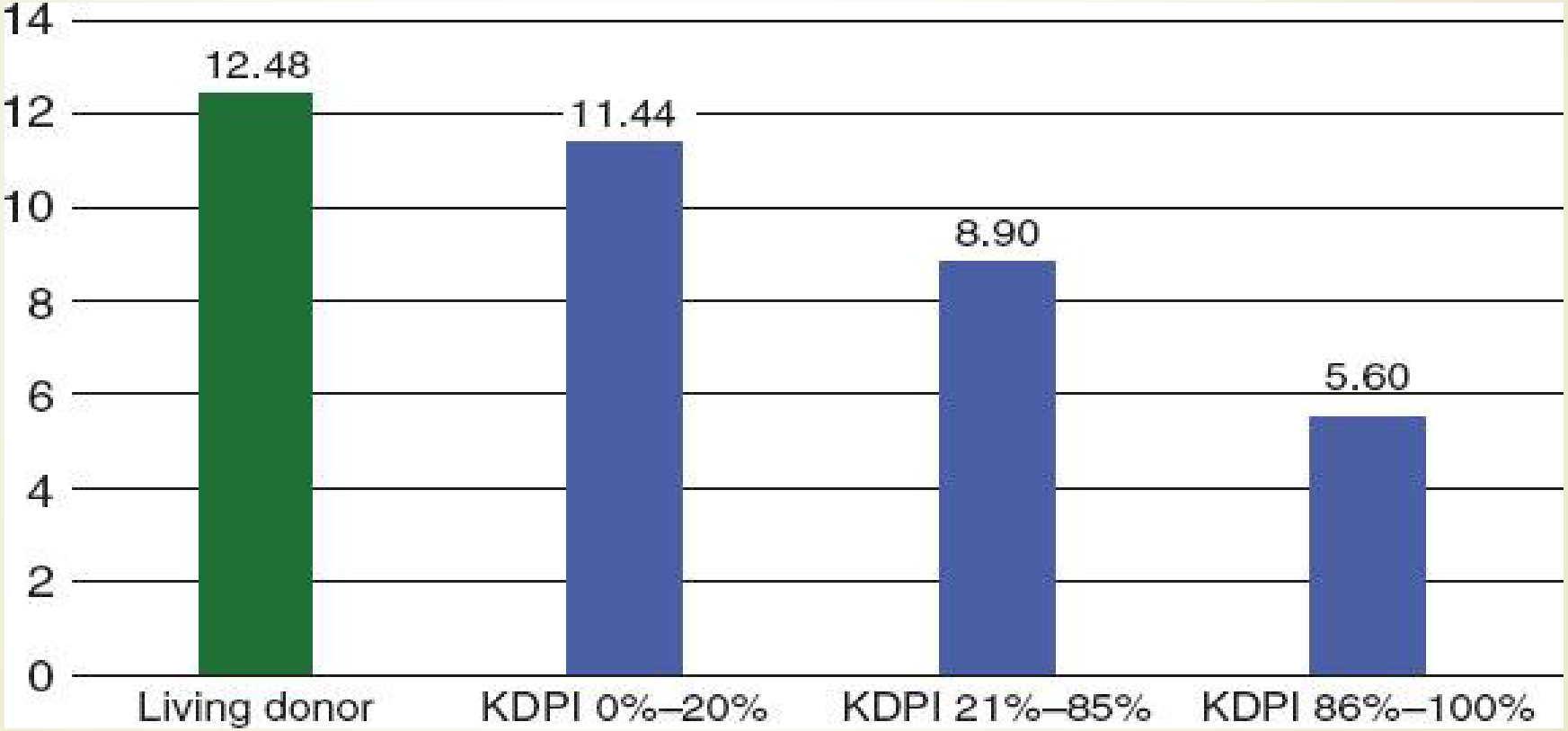
Kidney Allocation System (KAS) …

- Use of KDPI and EPTS would produce a significant rise in the average projected median lifespan after transplantation, as well as the time with a functional allograft.
- KAS; Blood type B can accept a kidney from an A2 or A2B blood type donor.
- In the new system, pediatric priority is based on KDPI less than 35%, instead of donors age less than 35 years.

Factors Determining the Kidney Donor Profile Index (KDPI) and Expected Post Transplant Survival (EPTS)

KDPI	EPTS
Age	Age
Height and weight	Current diabetes status
Ethnicity/Race	Number of previous transplants
History of hypertension	Receiving chronic dialysis
History of diabetes	
Cause of death	
Serum creatinine	
HCV status	
Donor meets DCD criteria	

Estimated graft half-life of kidneys from deceased donors with varying KDPI scores and from living donors



Allocation of Kidney by blood group

ORGANIZATION	ALLOCATION RULE
United network for Organ Sharing (UNOS), US	O >>> O, B >>> B
UK Transplant (UKT)	O >>> O or B
Australia	O >>> O, B >>> B
Eurotransplant (ET)	If no HLA mismatches: O>>>O or B If 1 or more mistmathes: O>>>O
EFG (France)	ABO identical
Scandiatransplant (ST)	O >>> O, B >>> B

Relative Importance of HLA Matching

ORGANIZATION	HLA LOCI
United network for Organ Sharing (UNOS), US	Only DR since 2003
UK Transplant (UKT)	DR > A or B
Australia	DR > A or B
Eurotransplant (ET)	DR=A=B
EFG (France)	DR > B > A
Scandiatransplant (ST)	DR=A=B

ABSOLUTE CONTRAINDICATIONS TO RECEIVING A KIDNEY TRANSPLANT

- ✓ Non-compliance/non-adherence with prescribed medical therapy, including dialysis and medications
- ✓ Unstable cardiac disease
- ✓ Severe pulmonary disease, including uncontrolled/untreated pulmonary hypertension
- ✓ Currently smoking and/or using smokeless tobacco/vaporizers/e-cigs, etc.
- ✓ Active abuse of drugs, alcohol, or other substances
- ✓ Severe vascular disease

ABSOLUTE CONTRAINDICATIONS TO RECEIVING A KIDNEY TRANSPLANT

- ✓ Active infections
- ✓ Age equal to or greater than 80
- ✓ Recent diagnosis or on-going treatment for cancer

  Exception: non-melanoma skin cancers
- ✓ Uncontrolled psychiatric disorders
- ✓ Lack of adequate insurance coverage or an inability to cover the expenses involved with a kidney transplant and subsequent care

RELATIVE CONTRAINDICATIONS TO RECEIVING A KIDNEY TRANSPLANT

- ✓ Acute or chronic liver disease
- ✓ Obesity
  - ✓ BMI > 35
- ✓ Age with associated co-morbidities
- ✓ Financial or insurance concerns
- ✓ Untreated or inadequate treatment for mental illness
- ✓ History of cancer (other than non-melanoma skin cancers)
- ✓ Inadequate social support

Thank you for your attention