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Renal Disease & Transplantation: the Role & Target of Metabolic/Bariatric Surgery

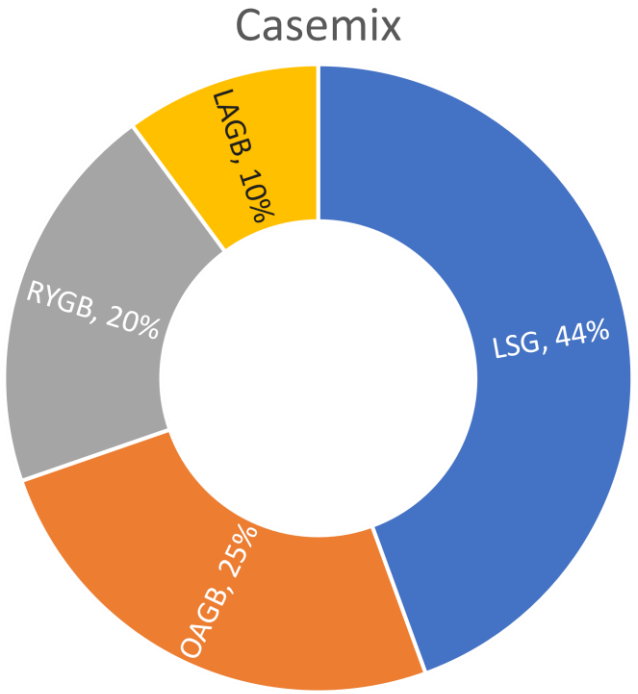
Ian D Michell

I have no potential conflict of interest to report

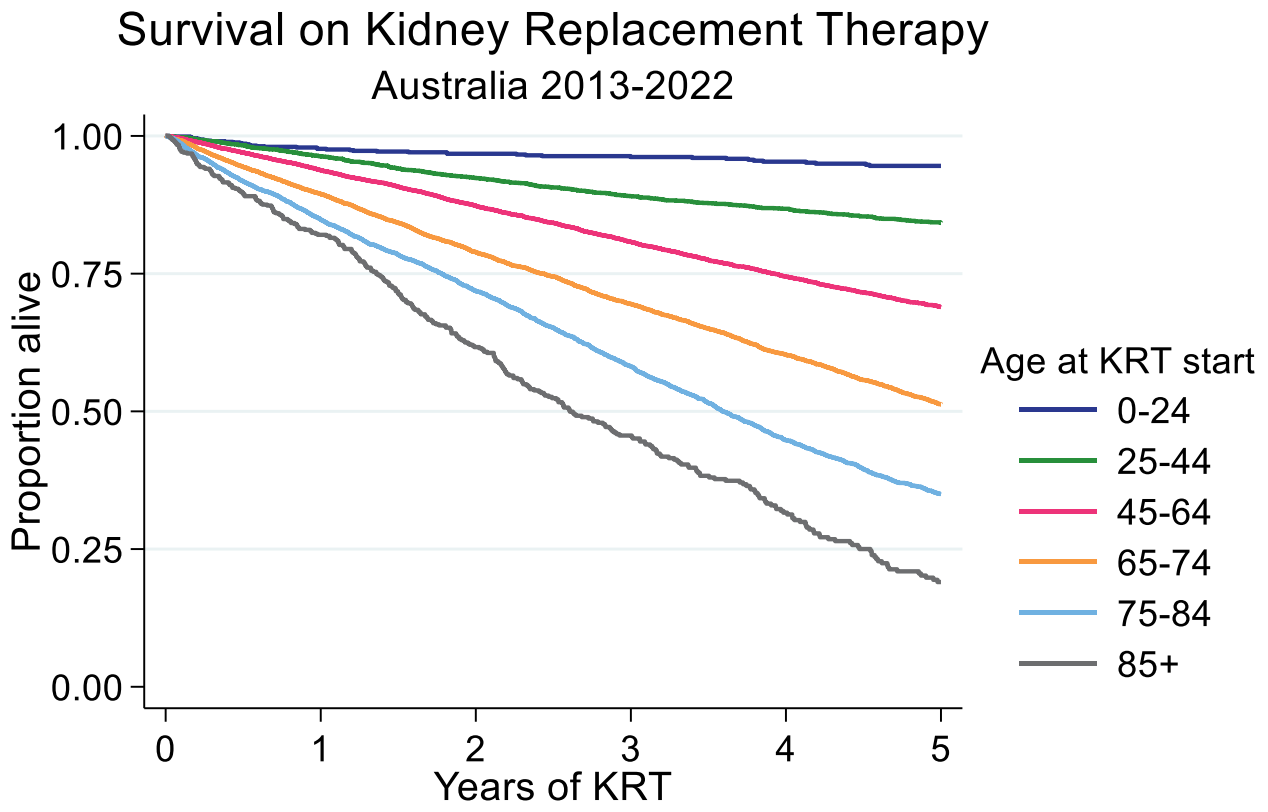
Ian Michell

- Transplant Surgeon, Austin Health
  - Surgical Training Prince Henrys Hospital, Melbourne
  - Transplant training liver and kidneys Birmingham UK
  - Liver Unit Austin Health until 2005
  - Lead Renal Transplant Surgeon until 31/12/2022
- Lead Renal Transplant Surgeon Royal Childrens Hospital (to 2021)

- Bariatric Surgeon in Private Practice.
  - Gastric Banding since 1988, adjustable since 1996
  - RYGBP 1997, laparoscopic from 2000
  - Sleeve Gastrectomy from 2007
  - Mini Gastric Bypass from 2018



Survival on Renal Dialysis is Terrible

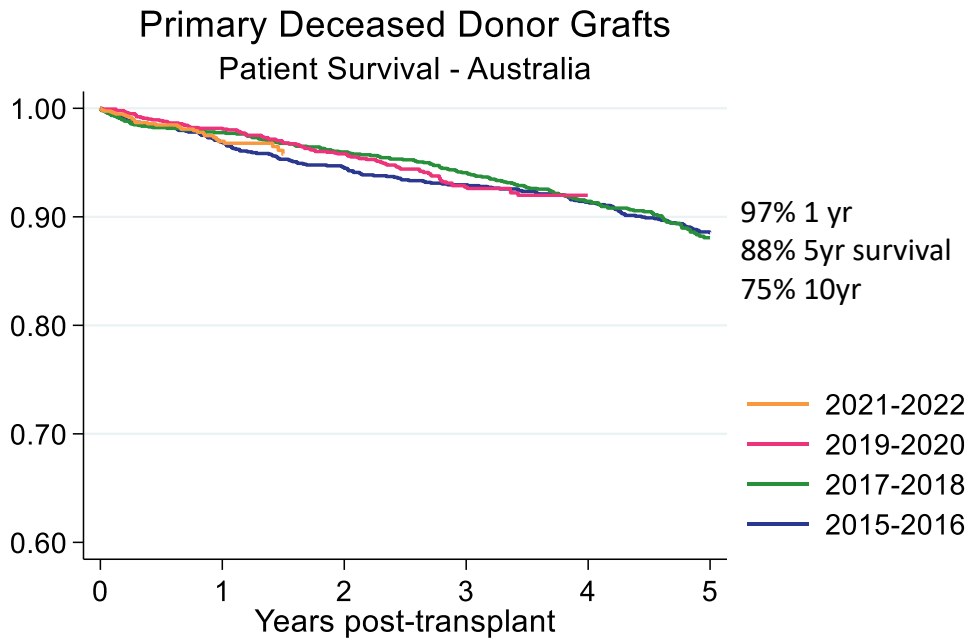


2023 ANZDATA Annual Report, Figure 3.1.1

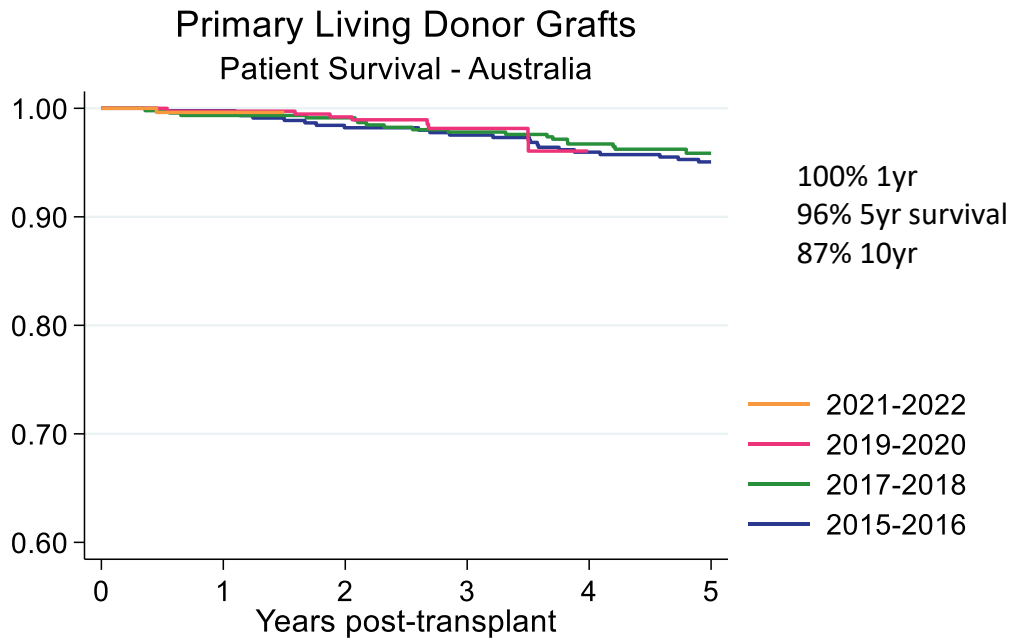
5 yr survival aged 45-64 is 69%

ANZDATA Registry. 46th Report, Australian Transplant Waiting List. Australia and New Zealand Dialysis and Transplant Registry, Adelaide, Australia. 2023.

Renal Transplantation has it all over dialysis (A shock to bariatric surgeons!)



2023 ANZDATA Annual Report, Figure 7.15



2023 ANZDATA Annual Report, Figure 7.25

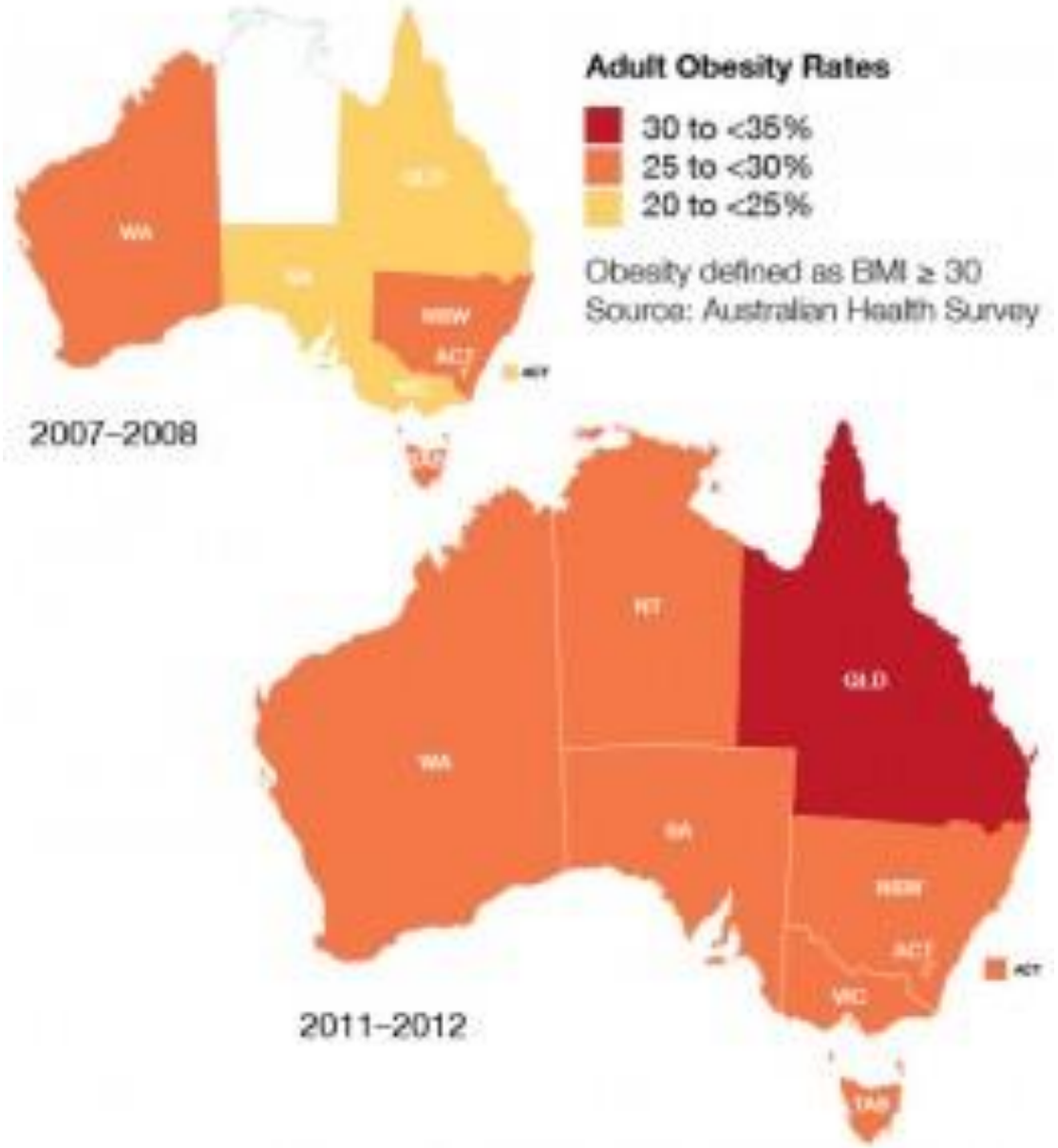
ANZDATA Registry. 46th Report, Australian Transplant Waiting List. Australia and New Zealand Dialysis and Transplant Registry, Adelaide, Australia. 2023.

Obesity and Kidney Transplantation

- Inferior Outcomes of KT
  - Increased Risk of Delayed graft function
  - Increased risk of acute rejection
  - Reduced graft survival
    - Gore, J. L., et al. (2006). "Obesity and outcome following renal transplantation." Am J Transplant **6**(2): 357-363.
    - BUT- Registry data (27377 UNOS recipients)
      - Stratified into underweight (<18.5)
      - Normal 18.5-24.9
      - Overwt 25-29.9
      - Obese 30-34.9
      - Severe Obese >35
    - Only the very best of the obese patients would have been selected for transplantation
    - Only 1 categorisation of Severe obesity
    -

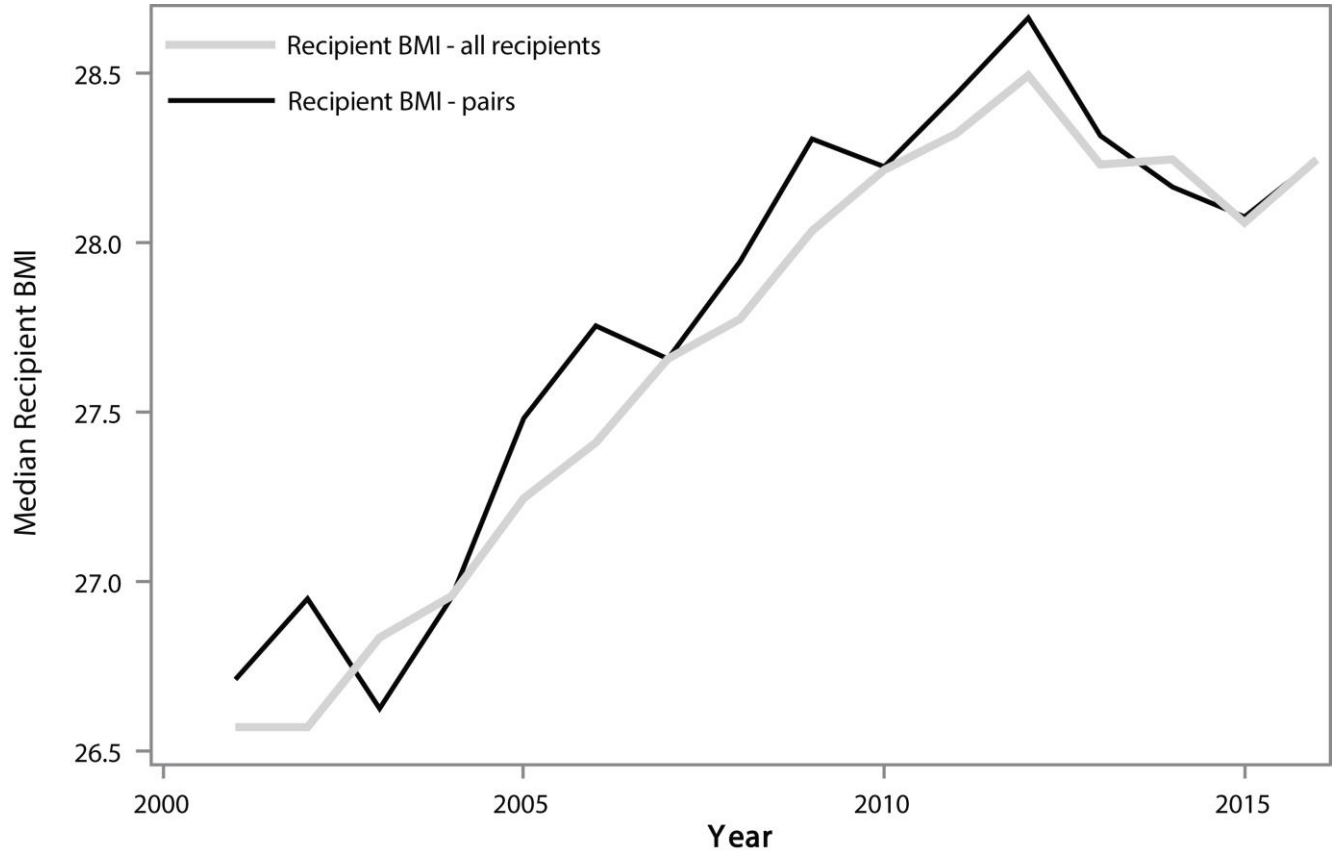
- Mate-Kidney Analysis UNOS database
  - 2001-2016
  - Looked at the outcomes of the other kidney compared with the obese recipient
  - BMI 18-25 12446
  - 25-30 15477
  - 30-35 11144
  - >35 5493 - reference group
  - Normals had less DGF (HR 0.4)
  - Less death censored graft loss (HR 0.66)
  - Sureshkumar, K. K., et al. (2021). "Recipient Obesity and Kidney Transplant Outcomes: A Mate-Kidney Analysis." Am J Kidney Dis **78**(4): 501-510 e501.

Obesity Epidemic in Australia



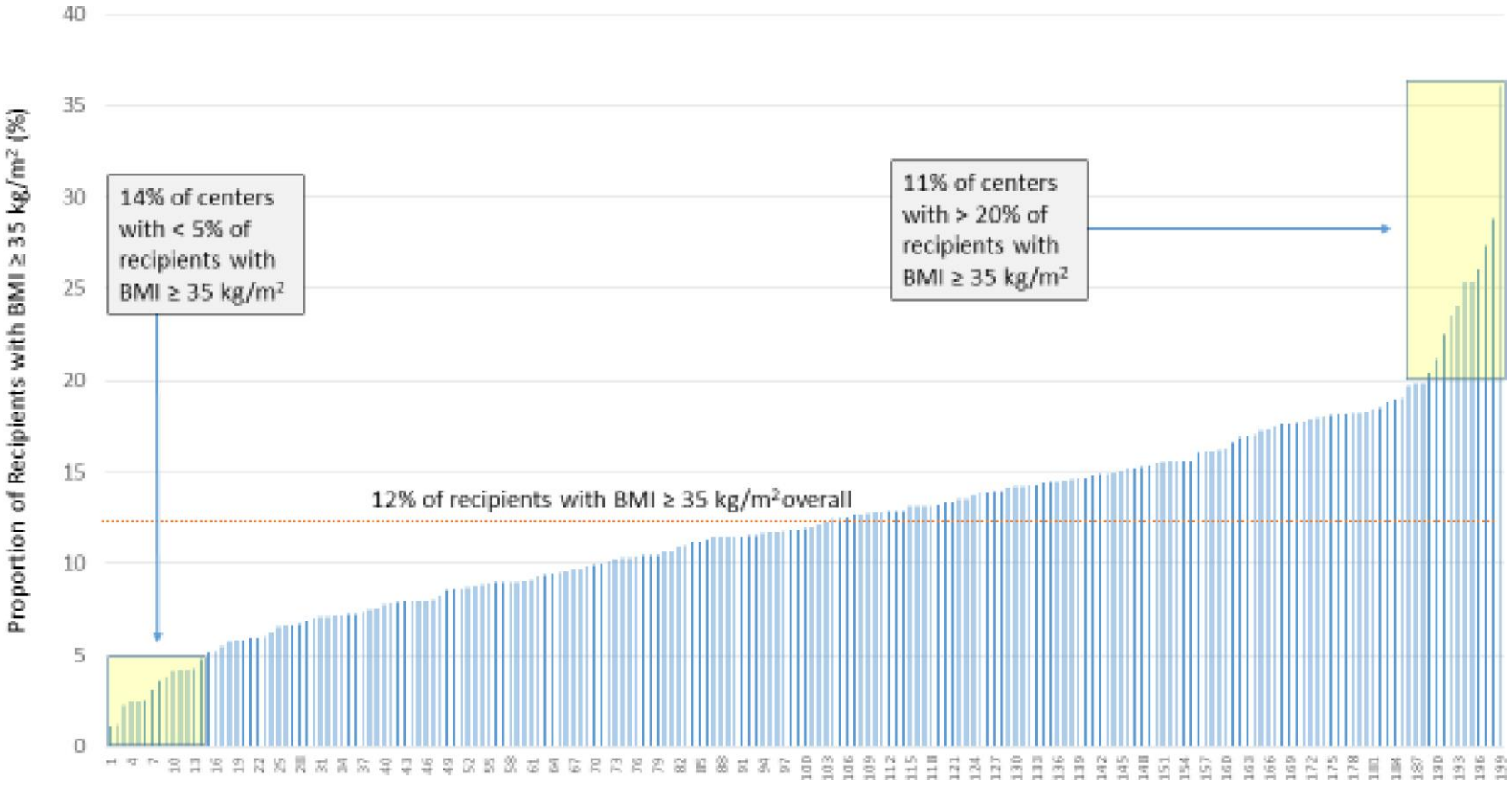
Global, regional, and national prevalence of overweight and obesity in children and adults during 1980—2013: a systematic analysis for the Global Burden of Disease Study 2013.
The Lancet, 384:9945, 766 – 781, 30 August 2014.

How our Data is Changing



Sureshkumar, K. K., et al. (2021). "Recipient Obesity and Kidney Transplant Outcomes: A Mate-Kidney Analysis." Am J Kidney Dis **78**(4): 501-510 e501.

By 2015 – the Landscape is quite different



Proportion of Morbidly Obese Adult Recipients by Kidney Transplant Center in the United States Source: unpublished SRTR data from 1/1/2015–12/1/2020 among adult kidney transplant centers

TSANZ Guidelines

- Renal Transplantation – No specific reference to obesity
  - Criteria that are considered relative or absolute contraindications for deceased donor kidney transplantation wait-listing include:
    - In Australia, if the perioperative and post-transplant risks outweigh the likelihood of deriving significant benefit from transplantation, and in New Zealand if there is a lower than 80% likelihood of surviving at least five years following transplantation.
    - Comorbidities that might have a significant impact on the life expectancy of a kidney transplant recipient include cardiac disease, vascular disease, diabetes mellitus, infection risk and malignancies.

Surgical exclusions including complex vascular anatomy and heightened risks associated with significant obesity.

Ghanem et 2024
Collaboration of ASTS and SAGES

- Obesity is a Risk Factor for ESRF
- Transplant results worse than non obese
  - But still survival advantage
- Weight gain occurs post transplant
  - Concomitant increase in morbidity
- Physicians reluctant to refer for MBS
- There are case series pre Tx, Simultaneous and Post Tx, all with good weight loss results

- Concern about immunosuppression absorption after RYGBP is theoretical
  - Sleeve Gastrectomy showed no changes different from regular monitoring levels
  - RYGBP TAC levels declined slightly

Ghanem, O. M.*, et al.* "Obesity, Organ Failure, and Transplantation: A Review of the Role of Metabolic and Bariatric Surgery in Transplant Candidates and Recipients." *Am J Transplant* (May 15 2024)

Systematic Review

- Metanalysis Comparison of bariatric surgery outcomes in patients with (128 – 2852) and without ESRF (113k - 718K)
- Comparison of RYGB and SG in patients with ESRD
- 6 studies, all retrospective, 3 had case control matching
  - Mostly with data from 2006
- 5 studies (128 patients) reported listing and transplantation after MBS.
  - 73.5% listed, 33% transplanted, 41% still waiting, 25% not listed
  - Major post op complications in ESRF (6.3% vs 2.3%)
  - 3 studies reported leaks – 0.54% vs 0.27% - Odds Ratio 1.72 not significant
  - 4 studies reported deaths – 0.39% vs 0.1% - Odds Ratio 40.04 P=.0007
  - 2 studies compared SG (144)and RYGB (239) in ESRF – 2 deaths in each group, similar weight loss results at 2 years.

Khajeh, Elias*, et al.* "Bariatric Surgery in Patients with Obesity and End-Stage Renal Disease." *Surgery for Obesity and Related Diseases* 19, no. 8 : 858-71.

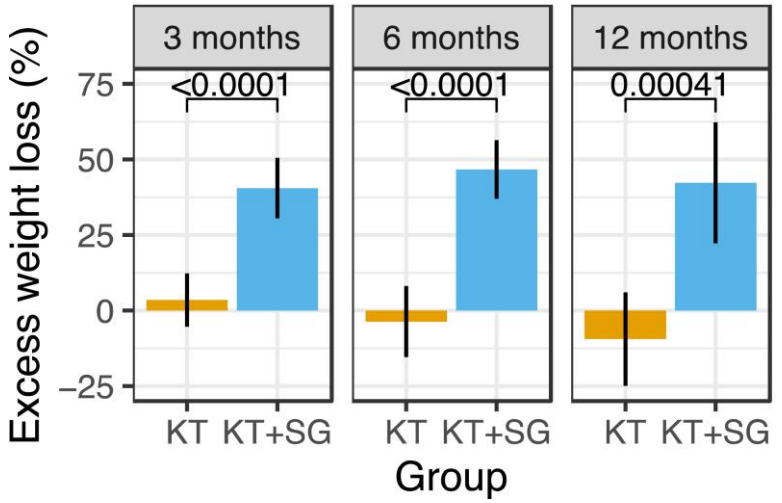
Systematic Review

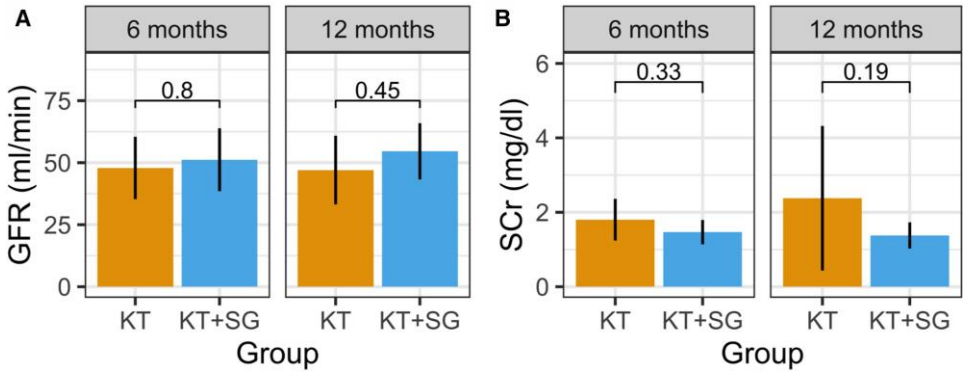
- Fernando et al 28 studies
  - MBS prior to listing 1903 change in BMI -11.3
  - MBS after listing 196 -11.2
  - Combined SG/robotic KT 1
  - Post Tx MBS 198 -11
- Mean change in BMI -11.3
- Combined Mortality Rate (Both procedures) 4%
- But some of this data is from the 1990's!

Fernando, S., J. Varma, F. Dengu, V. Menon, S. Malik, and J. O'Callaghan. "Bariatric Surgery Improves Access to Renal Transplantation and Is Safe in Renal Failure as Well as after Transplantation: A Systematic Review and Meta-Analysis." *Transplant Rev (Orlando)* 37, no. 3 (Jul 2023): 100777.

Simultaneous Robotic SG and KT

- 11 patients combined SG/KT
- 9 controls KT only
- Expected weight loss result.
- No graft loss at 1 yr
- Similar GFR at 1 yr (no power)





Spaggiari, Mario, Pierpaolo Di Cocco, et al. "Simultaneous Robotic Kidney Transplantation and Bariatric Surgery for Morbidly Obese Patients with End-Stage Renal Failure. " *American Journal of Transplantation* 21, no. 4 (2021/04/01/ 2021): 1525-34.

Bariatric Surgery Prior to Transplantation - US Renal Data System - Ku et al

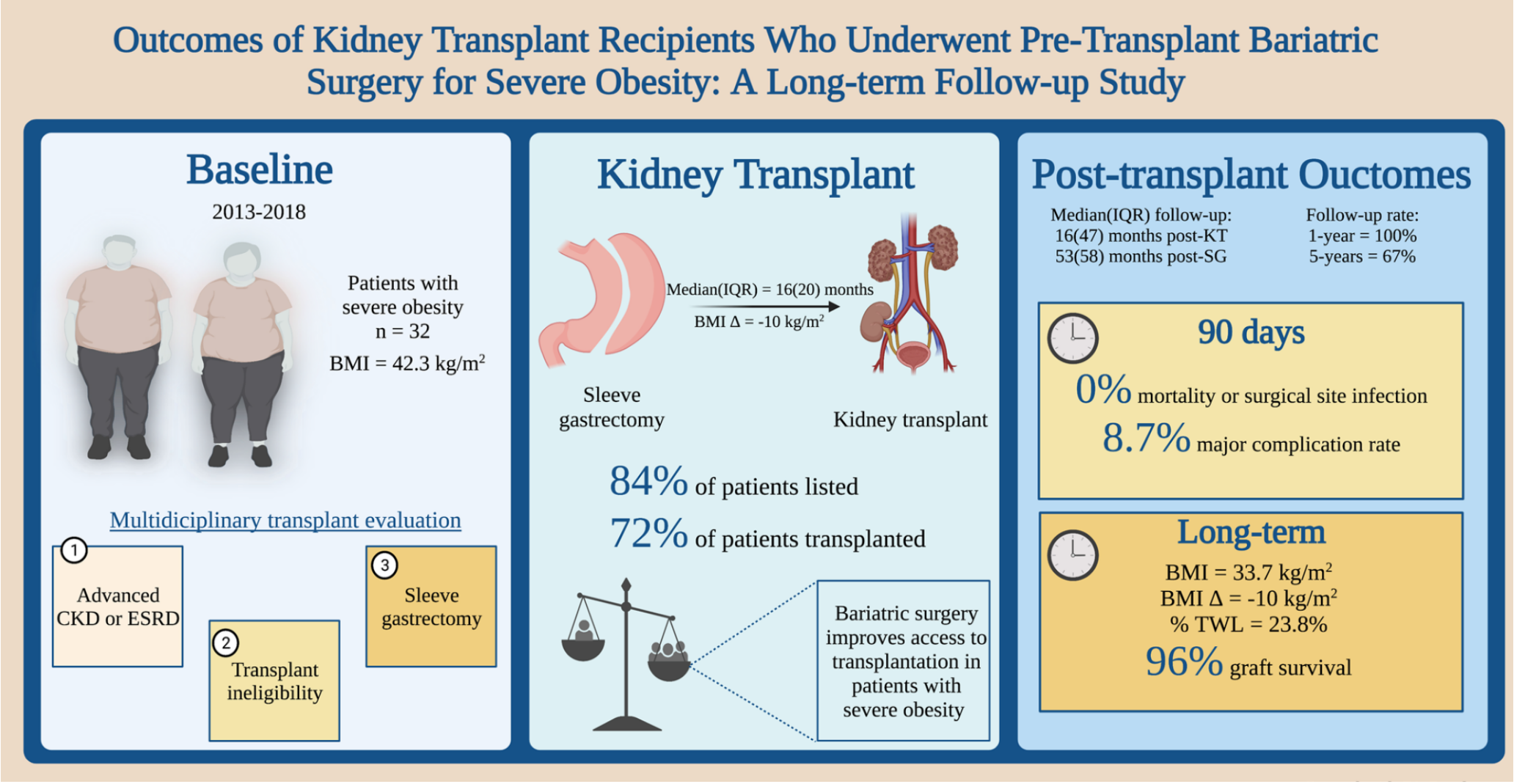
- Used US Medicare data to follow claims made –
- 417032 claims for bariatric surgery 1/1/2003 to 31/12/2016
- 14363 had claim for subsequent kidney Tx
- 12573 had enough data to calculate graft failure and death outcomes
- 10784 had data allowing calculation of rehospitalisations
- ESRF patients who went on to transplant, 503 had bariatric surgery after onset of renal replacement therapy
- The operations were Gastric banding, Sleeve gastrectomy, RYGBP (2 duodenal switches excluded)

- Results:
  - History of bariatric surgery was NOT associated with graft failure (HR 1.02)
  - Sleeve gastrectomy had lower risk of graft failure (HR 0.39, CI 0.16- 0.95)
    - RYGB – HR 1.04, LAGB hazard ratio 1.31 – not significant
  - Bariatric surgery not associated with increased rate of acute rejection

Ku, E., et al. (2021). "Bariatric surgery prior to transplantation and risk of early hospital re-admission, graft failure, or death following kidney transplantation." Am J Transplant **21**(11): 3750-3757.

Case Series:

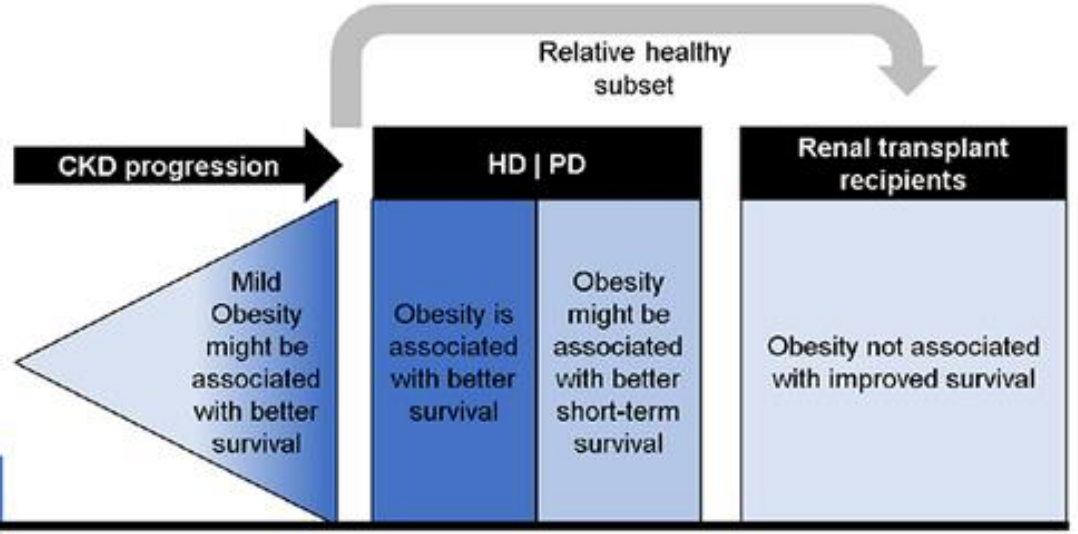
Zaminpeyma, R., et al. (2023).
"Outcomes of kidney transplant recipients who underwent pre-transplant bariatric surgery for severe obesity: a long-term follow-up study." Surg Endosc **37**(1): 494-502.



Which Operation

- Low risk – there is minimal literature regarding procedures other than SG, RYGB (and LAGB)
- Renal Patients seem to do better with sleeve gastrectomy
  - Fewer Complications
  - Better Graft Survival
  - Theoretically less alteration of pharmacodynamics
  - Less risk of oxalosis
  - No data yet on reflux /conversion to RYGB

The Obesity Paradox and ESRF



Legend:

☐ Less pronounced

■ More pronounced

Factor	Potential modification by obesity	
Restricted Nutrition/ Diet contribute to cachexia and PEW	Obese patients may be more resistant to the impact of cachexia and PEW	More restriction
Higher level of inflammation	Adipose tissue may sequester inflammatory cytokines	Higher chronic inflammation
Intradialytic hemodynamics	Less intradialytic hypotension in obese patients	Only HD
Browning of white AT	Obese patients may be more resistant to this effect	Browning of AT more likely
Body fat distribution	Less inclined to develop cachexia	Not modifiable, racial/ethnic & individual differences
Genetics	More likely to have underlying mechanisms preventing inefficient energy use	Not modifiable, racial/ethnic & individual differences

Naderi, N., et al. (2018). "Obesity Paradox in Advanced Kidney Disease: From Bedside to the Bench." Prog Cardiovasc Dis **61**(2): 168-181.

Cadaveric Renal Transplant Candidates Need Effective and **Durable** Weight Control

Waiting time on the
Australian Kidney Transplant Waiting List
according to Blood Group, 2022

Group	Median	75%
A	2.3	3.3yr
B	2.6	4.0yr
AB	1.8	3.1yr
O	2.7	4.1yr

- The weight loss intervention needs to be enough to allow listing
- The relevant weight is the one at transplantation – 4-5 years after listing

ANZDATA Registry. 46th Report, Chapter 6: Australian Transplant Waiting List. Australia and New Zealand Dialysis and Transplant Registry, Adelaide, Australia. 2023.

Organ Donation in Australia and Aotearoa New Zealand

- Deceased Donation
  - No Codified Guidelines for acceptance prior to retrieval
    - Attention paid to presence of diabetes and cardiovascular disease.
  - Cardiothoracic Organs are size matched
  - Liver Transplant concerns about NASH
- Live Donation – Australian and New Zealand Paired Kidney Exchange Programme
  - The unit who assesses the donor and performs the donor nephrectomy is responsible for ensuring the suitability, safety and the well-being of the donor.
  - Risk Calculators include BMI noting link between high BMI and ESRF
  - Exclusion of donor diabetes in PKE programmes.
    - Concern about metabolic syndrome
    - Concern with BMI >30

Obese Live Renal Donors

- Higher long term risk of developing ESRF
- Higher risk of Post donation diabetes, hypertension, dyslipidaemia
  - They are screened out for these conditions predonation
- These are special people who require careful follow up
- Live Kidney Donation scenarios frequently have emotional element
- Evidence - Only Case Series:

Managing the Obese Organ Donor

- Bielopolski, D, *et al*.

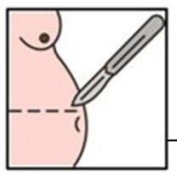
"Bariatric Surgery in Severely Obese Kidney Donors before Kidney Transplantation: A Retrospective Study." *Transplantation* 107, no. 9 (Sep 1 2023): 2018-27.

- Case series 23 donors underwent MBS prior to donation.
- 72 matched non obese kidney donors
- 42 matched MBS patients

Bariatric surgery in Severely Obese Kidney Donors Prior to Kidney Transplantation, a Retrospective Study

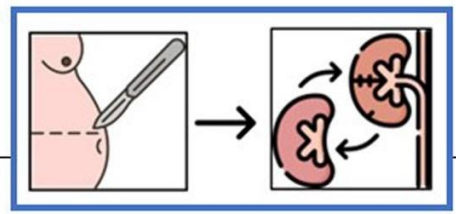
Introduction: the obesity epidemic limits the donor pool, as more than 52% of potential donors have a BMI > 35

Control: bariatric surgery only (n = 46)



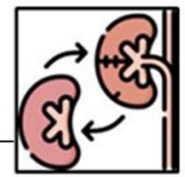
VS

Study group: bariatric surgery followed by kidney donation (n = 23)



VS

Control: non-obese, kidney donation (n = 63)



Results: (at end of follow up)

- Similar weight loss
- Study group had worse lipid profile

- Similar eGFR and proteinuria
- Absolute GFR reflected both weight loss and nephron loss.

Conclusion: Bariatric surgery prior to live kidney donation is a safe procedure that could increase the donor pool and improve their health in the long run. Donors should be encouraged to maintain their weight, avoid adverse lipid profile & hyperfiltration.

Bielopolski et al. *Transplantation*. March 2023

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Transplantation

TRANSPLANTATION

Experience of MBS prior to Live Kidney Donation

- 7 studies – 2 case reports, 25 patients overall
- 7 band, 10 RYGBP, 7 sleeve, 1 BPD.
- All underwent successful laparoscopic nephrectomy
  - No complications
- No long term follow up data
  - Durable weight control would appear supremely important for these individuals.

Paoletti, F., et al. "Bariatric Surgery in Prospective Obese Living Kidney Donors: Scoping Review and Management Decision Algorithm."
[In eng]. *Minerva Surg* 79, no. 2 (Apr 2024)

Where are we Now?

- Transplantation saves lives compared with dialysis
- We have established that bariatric surgery enables renal transplantation in candidates who otherwise would be unsuitable
  - The risk of bariatric surgery is small compared to the transplant operation
  - But the level of evidence of effectiveness still remains low

The Next Era in Managing Obesity in ESRF

- Choose those patients who would be suitable candidates for transplant with appropriate weight loss.
  - Weight loss can be harmful in the non transplant patient
- Be aware of the weight loss required for listing and the median results for intervention;
  - Semaglutide 20% tbwl may not be sufficient to achieve listing
- Mindful of the timeframe of weight loss for acceptability
  - Cadaveric listing requires durable weight loss.
  - Bariatric surgery might delay Live Donor Surgery
- Awareness of the relative advantages of bariatric procedures
  - Esp Sleeve vs RYGBP
  - What about the OAGB?
- More Registry Data, RCT's?
  - What about sleeve revisions?
  - How soon after bariatric surgery can we transplant?

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