

# Diabetic kidney disease and bariatric surgery

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Carel le Roux

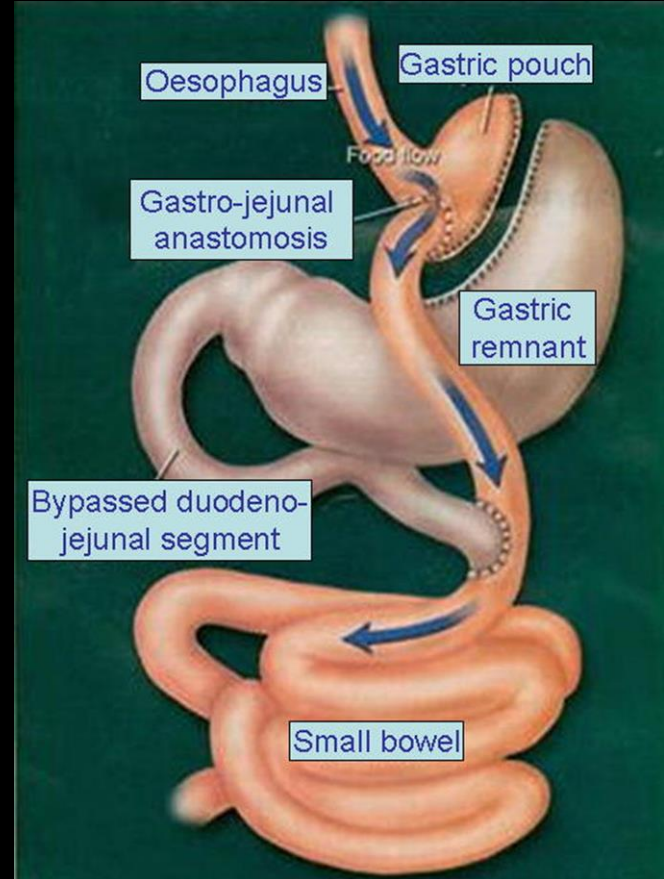
Diabetes Complications  
Research Centre

University College Dublin  
Imperial College London

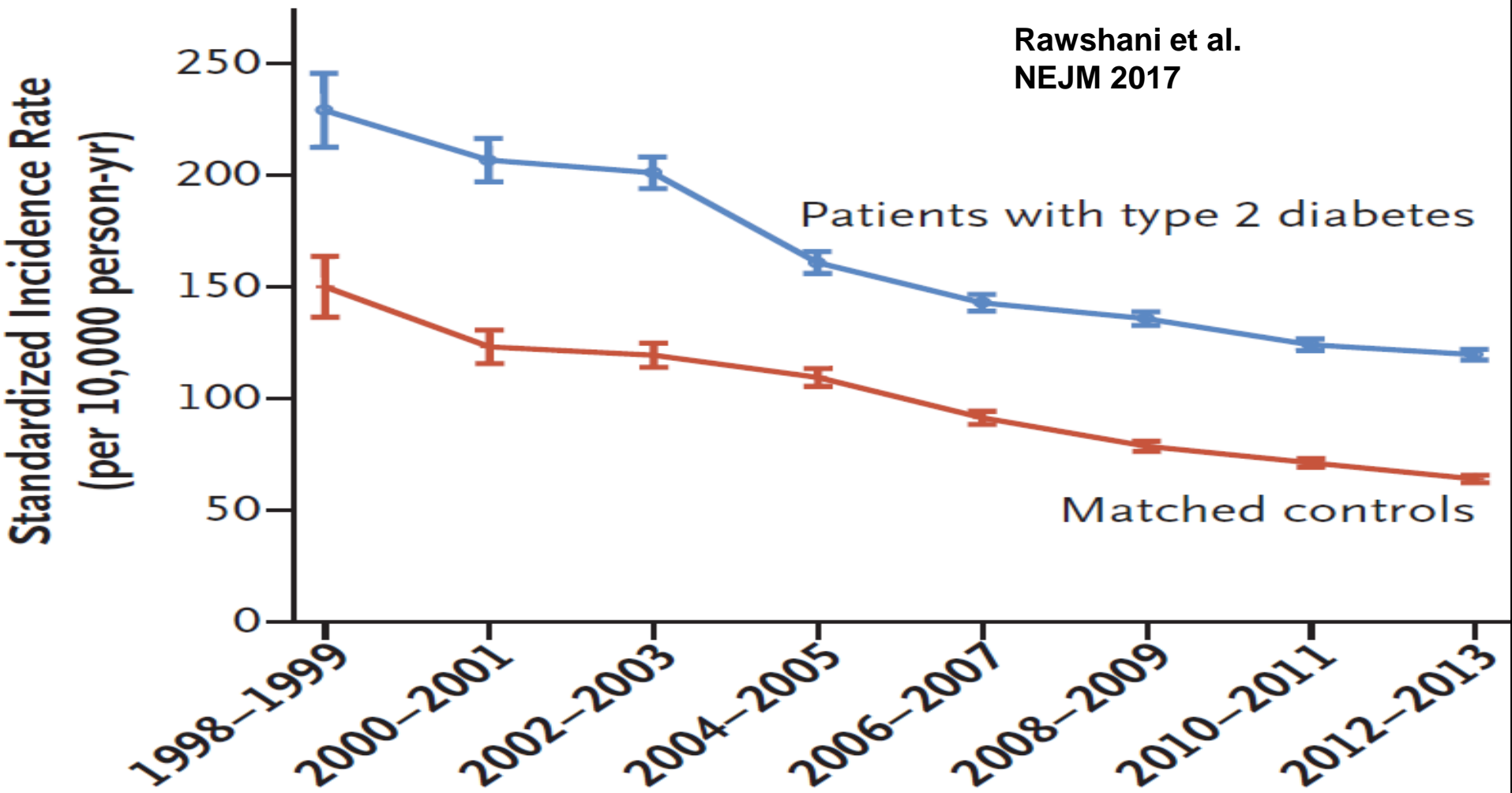


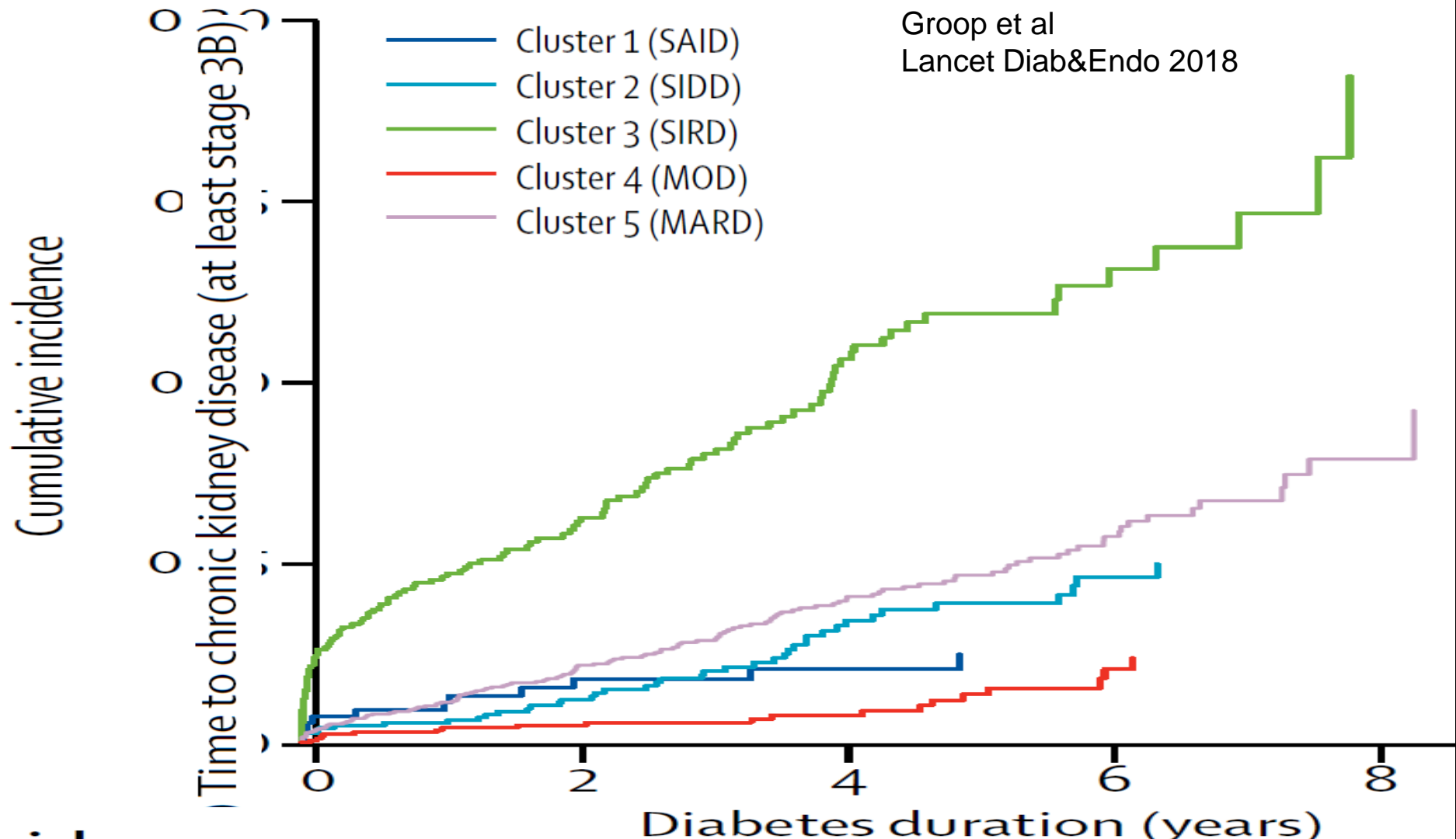
# Conflict of interest

Consilient Health,  
NovoNordisk,  
Johnson & Johnson,  
ONO pharmaceuticals,  
Covidien,  
Fractyl,  
GI Dynamics,  
Roche,  
AstraZeneca  
Lilly  
Boehringer Ingelheim

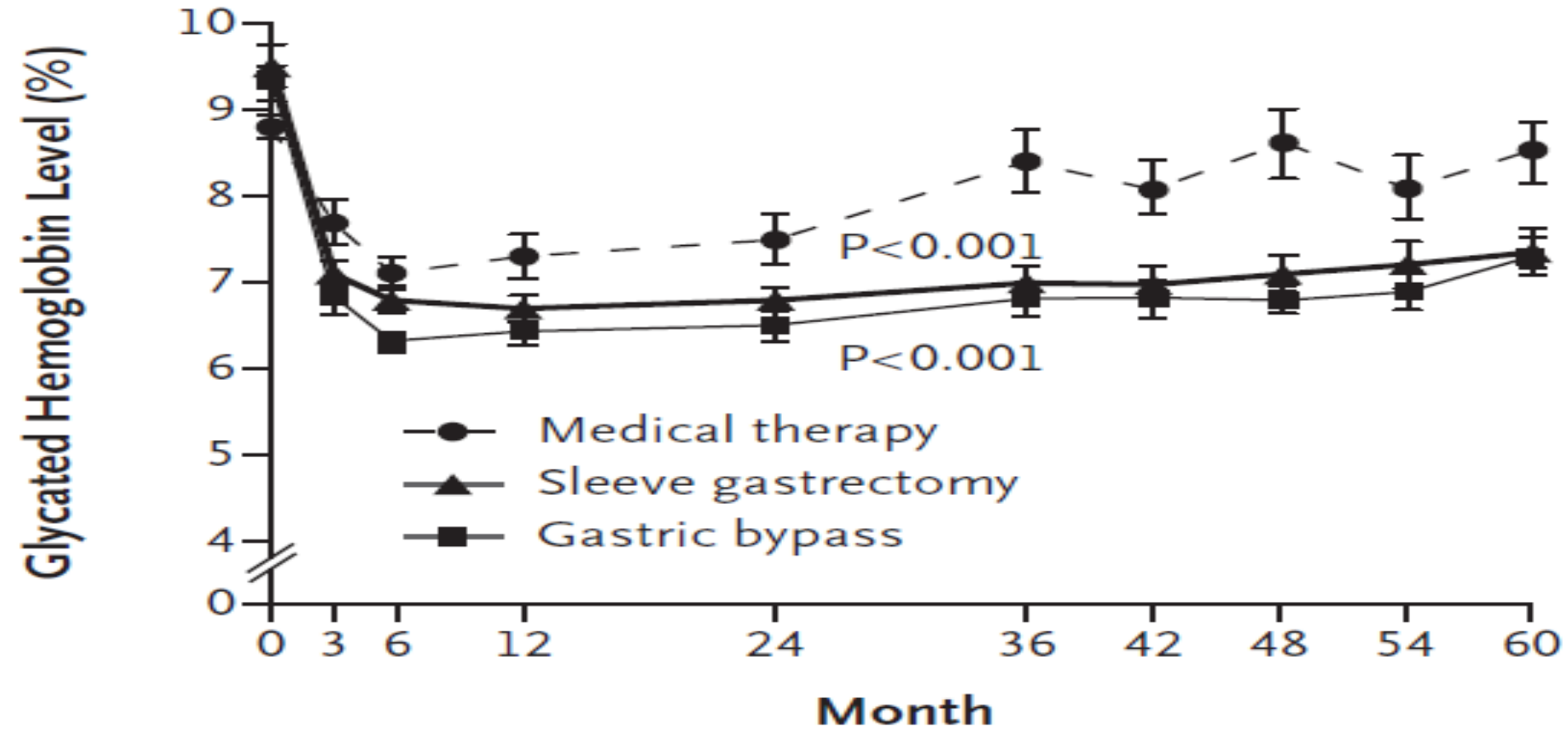


# Death from Cardiovascular Disease



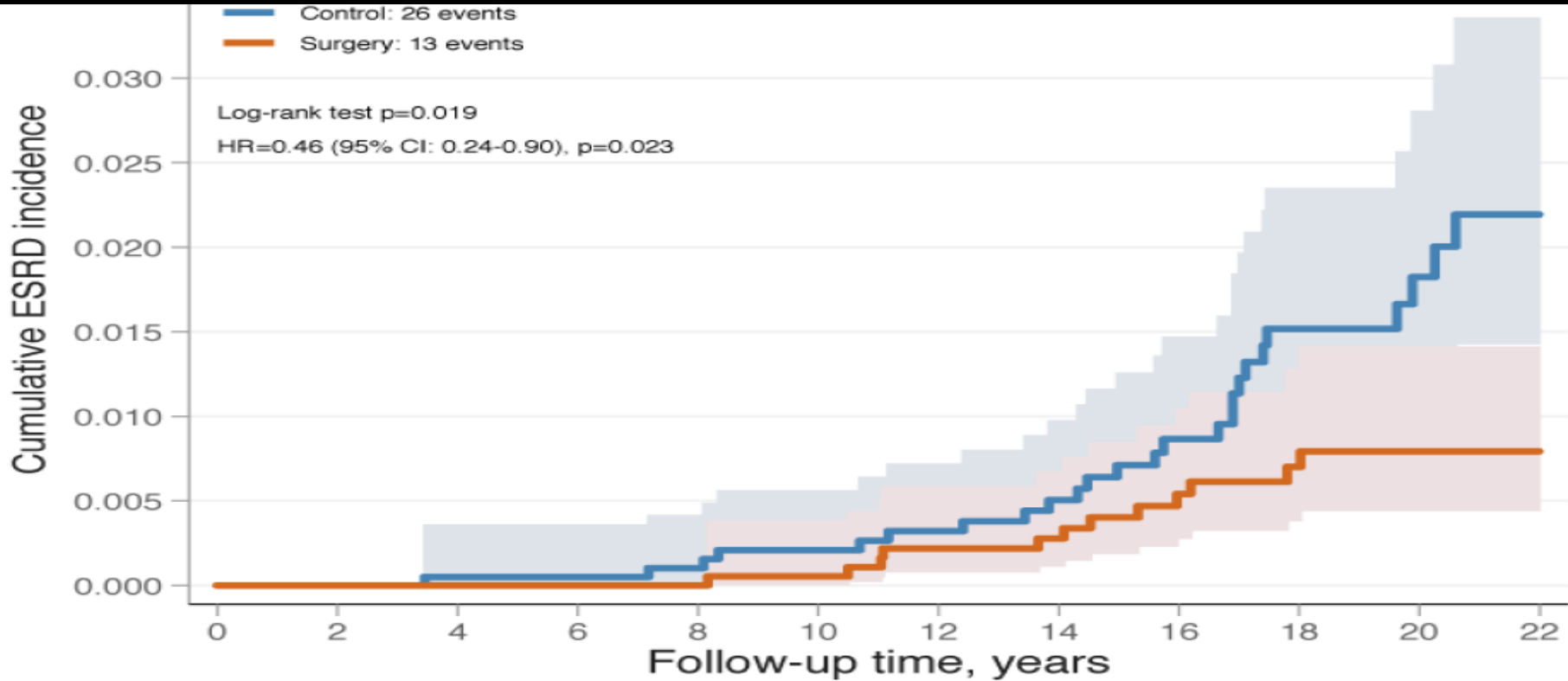


# STAMPEDE Schauer et al NEJM 2017



# Bariatric surgery reduces ESRD

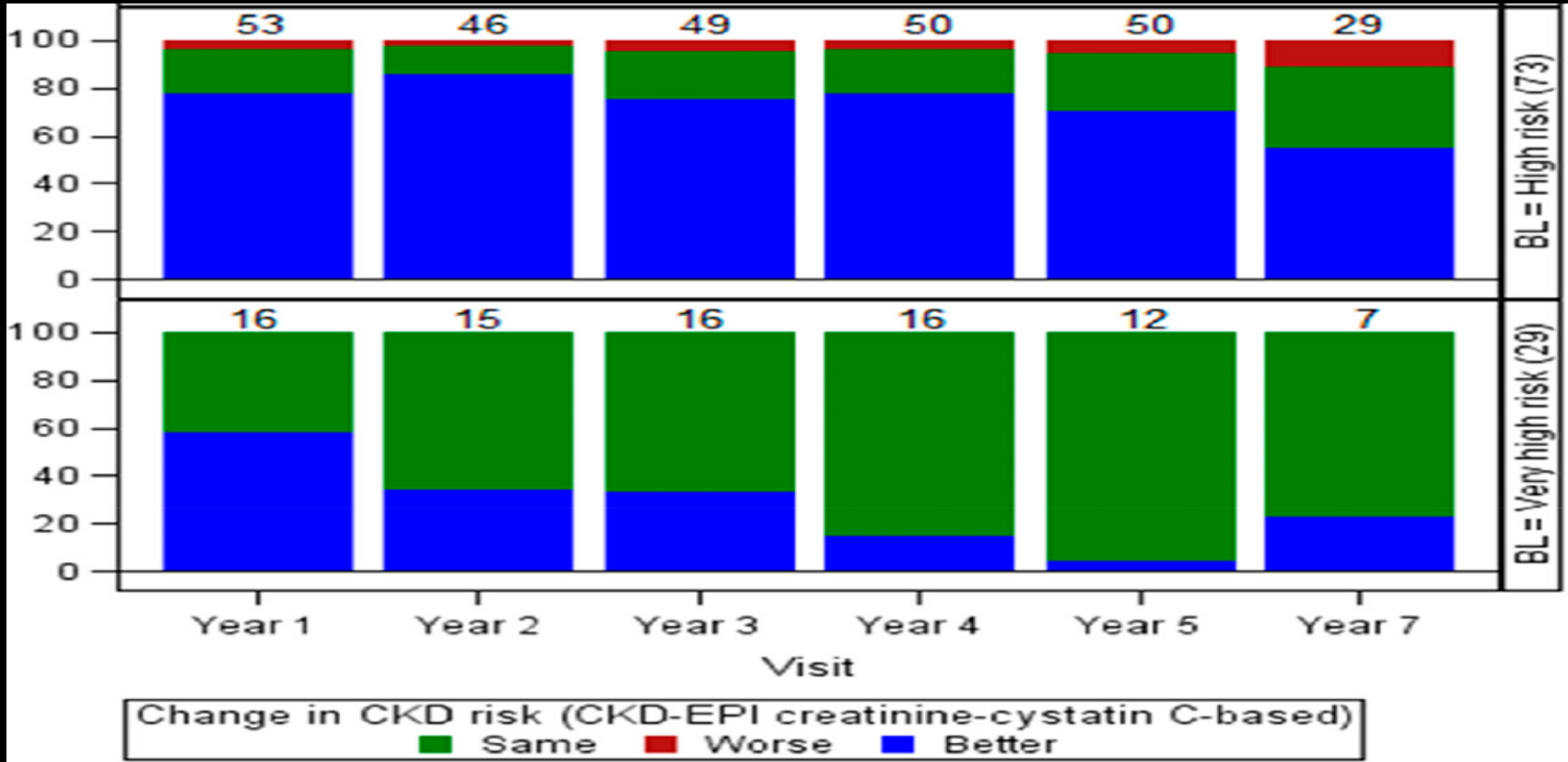
Svensson, le Roux et al Int J Obes 2018



Number at risk

|         | 0    | 2    | 4    | 6    | 8    | 10   | 12   | 14   | 16   | 18   | 20  | 22  |
|---------|------|------|------|------|------|------|------|------|------|------|-----|-----|
| Control | 2040 | 2015 | 1981 | 1934 | 1884 | 1811 | 1732 | 1538 | 1195 | 949  | 592 | 319 |
| Surgery | 2007 | 1966 | 1933 | 1903 | 1871 | 1836 | 1793 | 1645 | 1400 | 1085 | 656 | 344 |

# Longitudinal Assessment Bariatric Surgery (LABS): changes in risk of chronic kidney disease (CKD) Friedman, le Roux, Wolfe et al. JASN 2018



# Changes in microvascular damage after RYGB

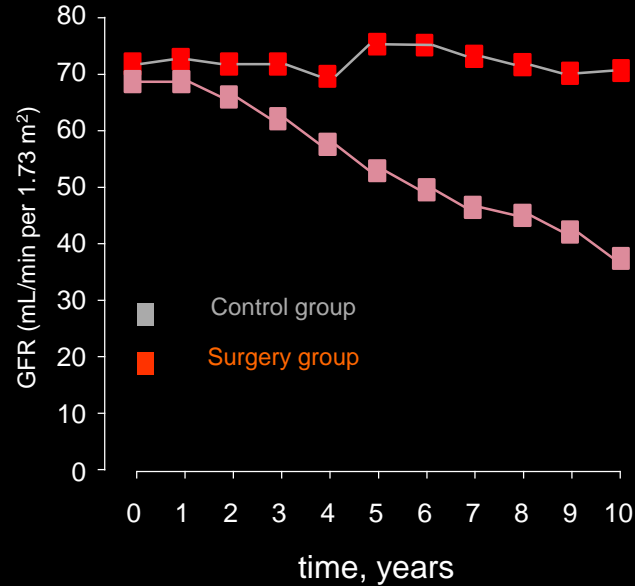
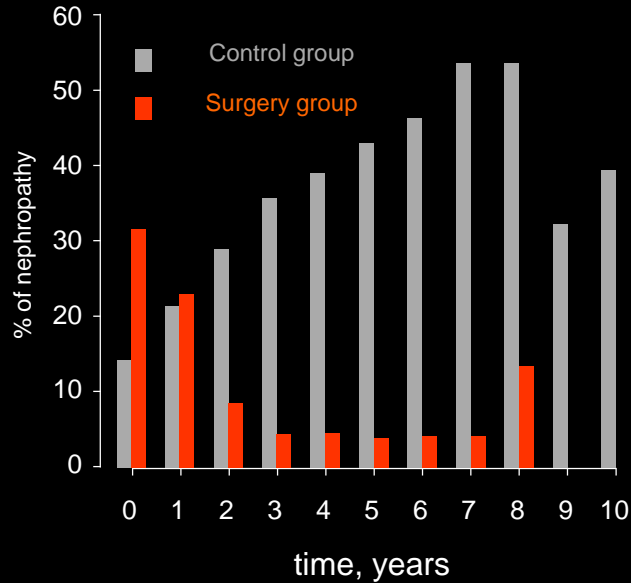
Chauh, Miras, le Roux et al. Diabetologica 2015

|                                | <b>RYGB Surgical group n=70</b> |             |                |
|--------------------------------|---------------------------------|-------------|----------------|
|                                | <b>Pre</b>                      | <b>Post</b> | <b>P value</b> |
| <b>Duration (years)</b>        | 10.0 ± 3                        | -           | -              |
| <b>BMI (kg/m<sup>2</sup>)</b>  | 43.6 ± 5                        | 32.9 ± 3    | <0.001         |
| <b>Systolic BP (mmHg)</b>      | 143 ± 2                         | 130 ± 3     | <0.001         |
| <b>Diastolic BP (mmHg)</b>     | 84 ± 1                          | 80 ± 1      | 0.08           |
| <b>HbA1c (mmol/mol)</b>        | 81 ± 3                          | 45 ± 2      | 0.03           |
| <b>(%)</b>                     | 9.6 ± 0.3                       | 6.3 ± 0.4   |                |
| <b>Urine ACR (mg/mmol)</b>     | 3.6 ± 0.3                       | 1.7 ± 0.1   | 0.02           |
| <b>Superior radial CV(m/s)</b> | 62.0 ± 3                        | 61.3 ± 0.4  | 0.14           |



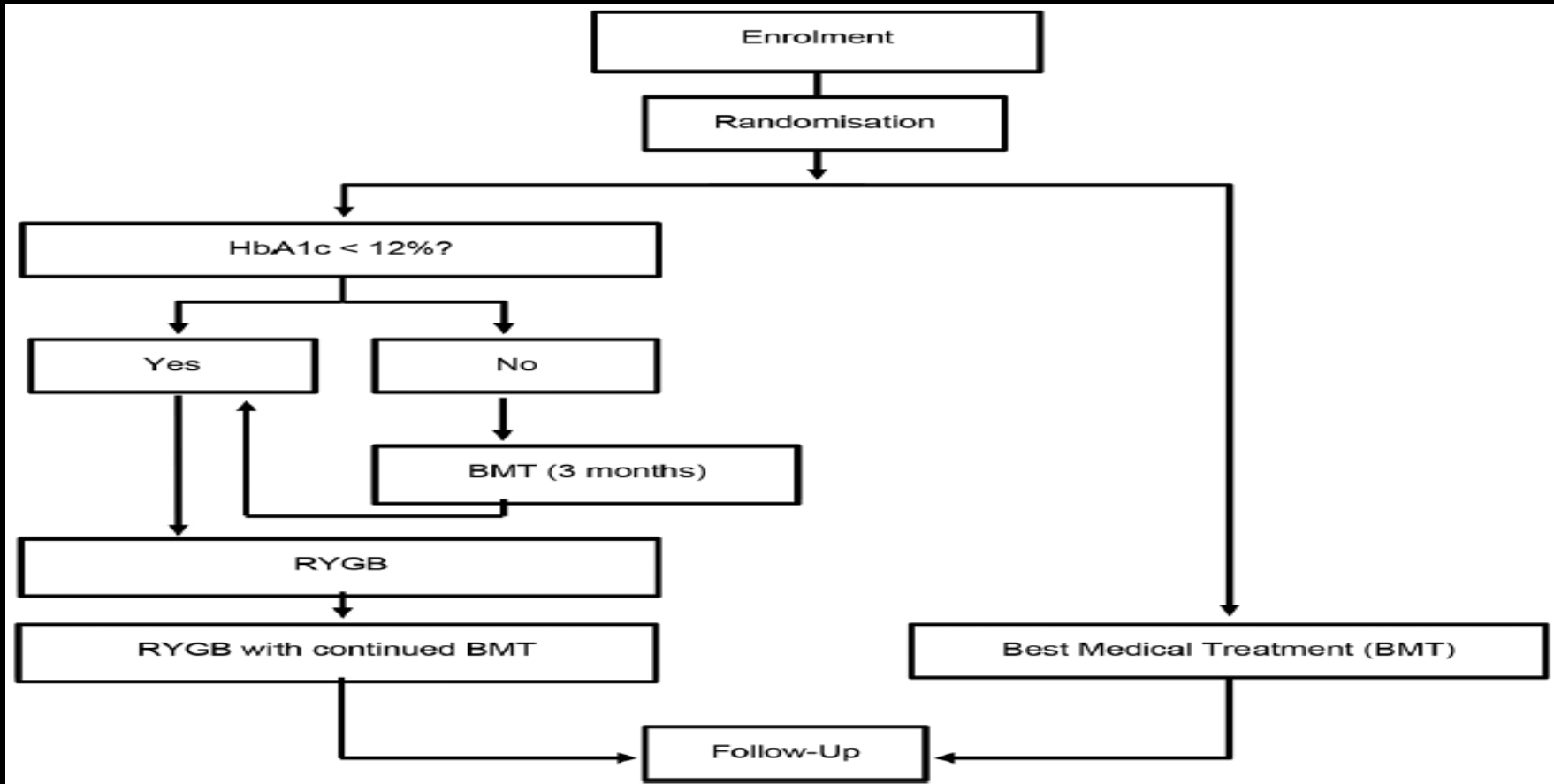
# Damage and function in DKD after surgery

Iaconelli A, et al. Diabetes Care 2011;34:561–7.



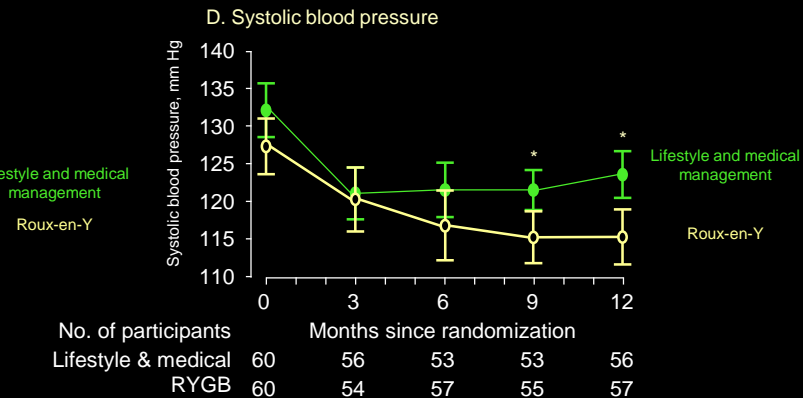
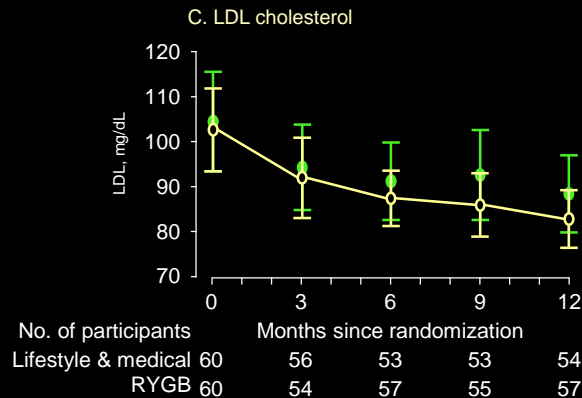
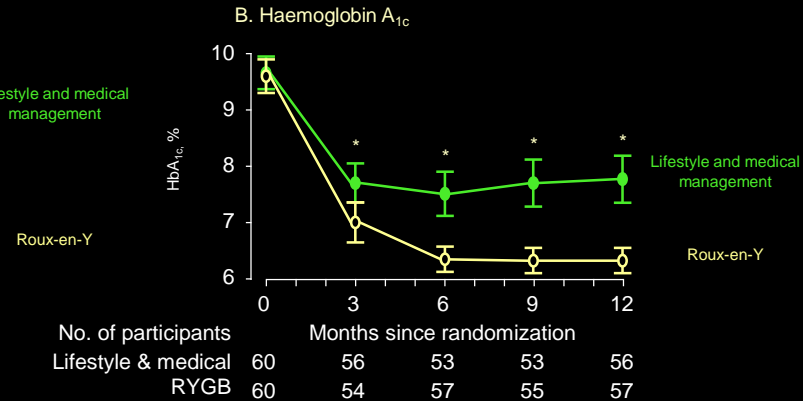
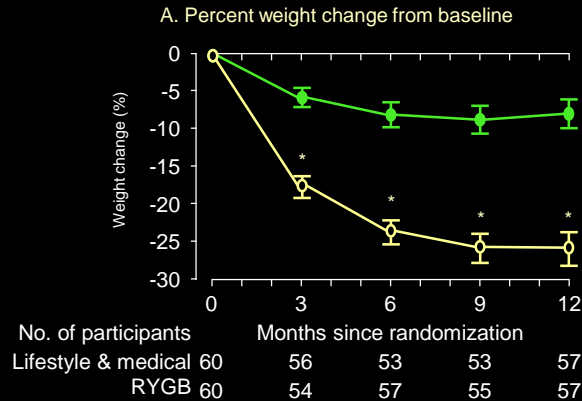
# Microvascular outcomes after Metabolic Surgery (MOMS)

Cohen, le Roux et al BMJ Open 2017



# Changes in metabolic milieu after gastric bypass

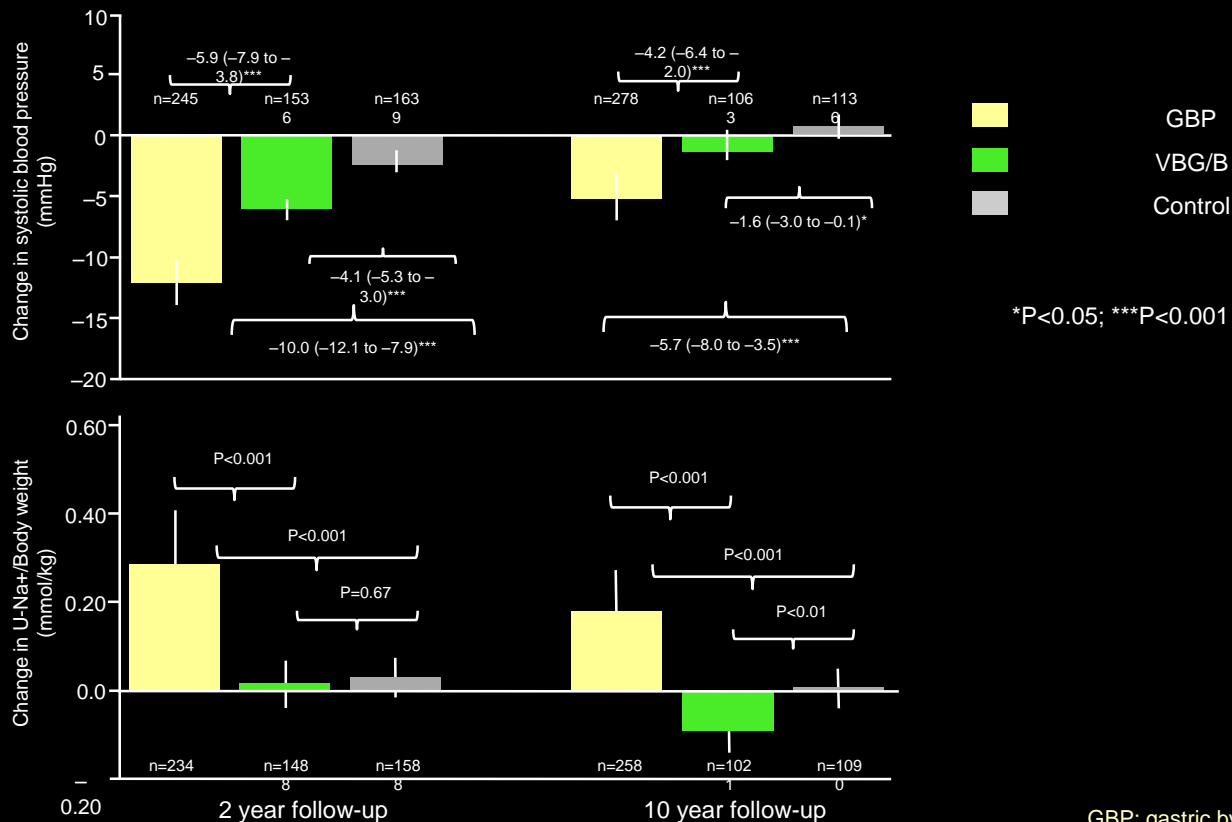
Ikramuddin S, et al. JAMA 2013; 309:2240–9.



\*P-value for difference is <0.01

# Blood pressure and urinary sodium excretion

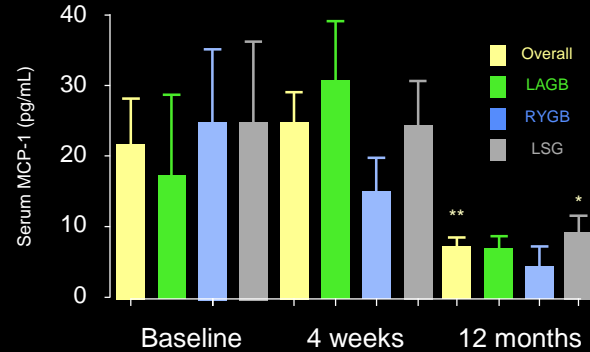
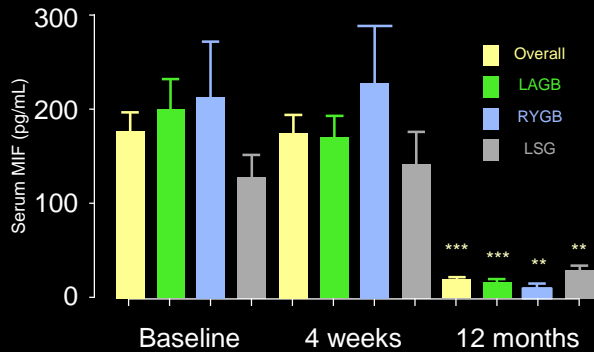
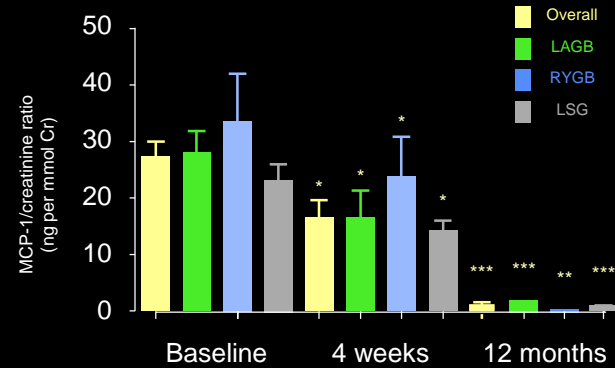
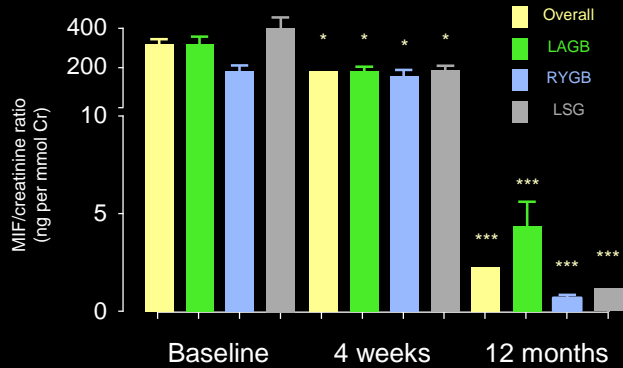
Hallersund P, et al. PLoS One 2012; 7:e49696.



GBP: gastric bypass  
VBG/B: vertical banded gastroplasty or gastric banding

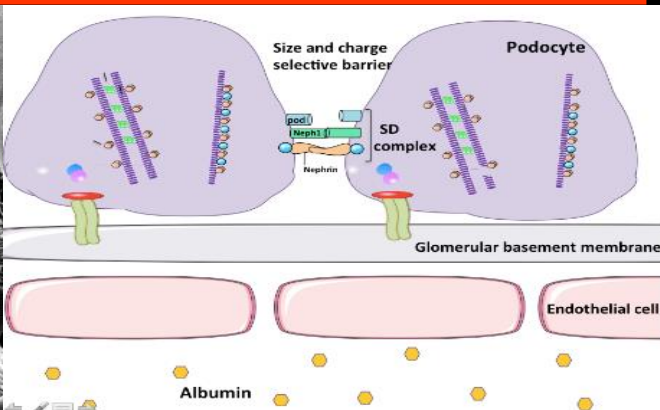
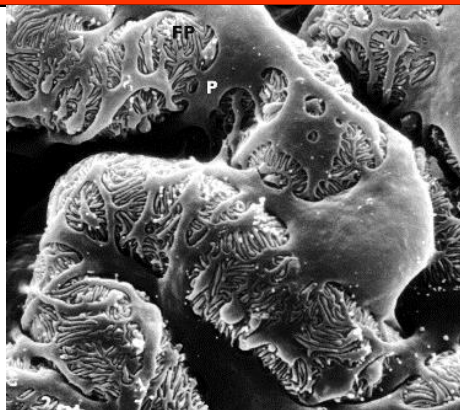
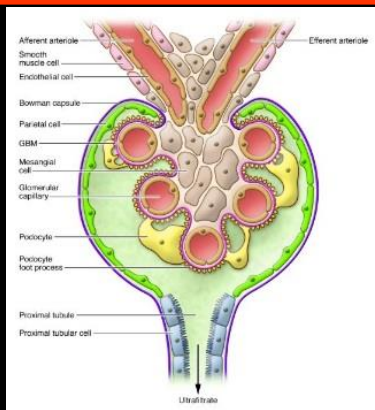
# Urine markers of renal inflammation

Fenske WK, le Roux CW et al. Surg Obes Relat Dis 2013;9:559–68.



# Podocyte Stress: A Central Mechanism in DKD

Nair, le Roux et al. Curr Opin Endocrinol Diabetes Obes. 2016

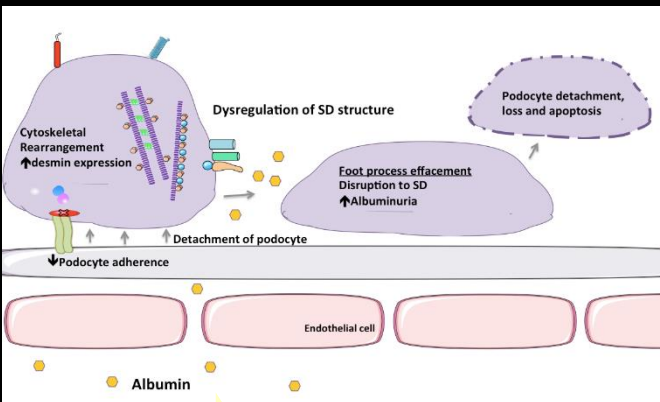
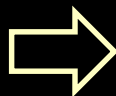


## Diabetic Glomerulus

Afferent vasodilatation hyperglycaemia)

Efferent vasoconstriction  
(RAS and lipid mediators)

Pro-inflammatory, glucotoxic & lipotoxic



Podocyte dysfunction & dropout



Proteinuria & DKD Progression

# Zucker Diabetic Fatty Rat (ZDF)

Neff, Docherty, le Roux et al. Surg Obes Relat Dis. 2017 Jan;13(1):21-27

GENETICS



DIET

Homozygous truncated LepR (fa/fa)

- Hyperphagia
- Hyperleptinemia
- 16.7% Kcal from lipid

Visceral obesity



Triglyceridaemia



Hyperinsulinaemia



HYPERTENSION  
HYPERGLYCEMIA  
SYSTEMIC INFLAMMATION

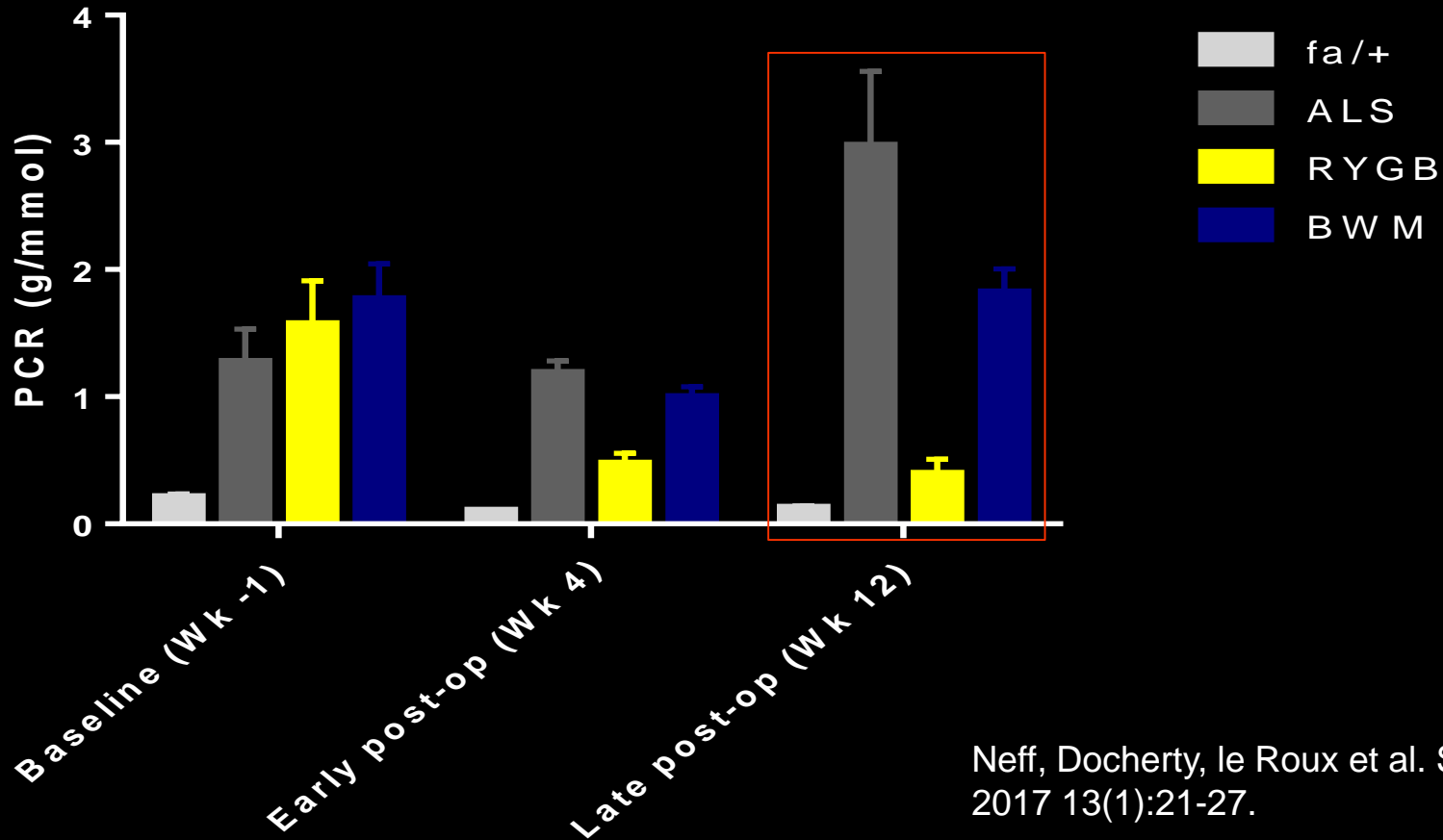


PROGRESS  
T2DM

7 week-----12 weeks

- Onset of proteinuria from 10 weeks
- Glomerular lesions prominent by 20 weeks

# Urinary Protein Excretion in ZDF RYGB versus Matched Weight Loss





# “Medical bypass” in ZDF

Miras, le Roux. Cell Metab. 2017 May 2;25(5):985-987.

**Weight loss:** 20% by diet restriction

**Glycaemic control:** Metformin, Liraglutide, Insulin

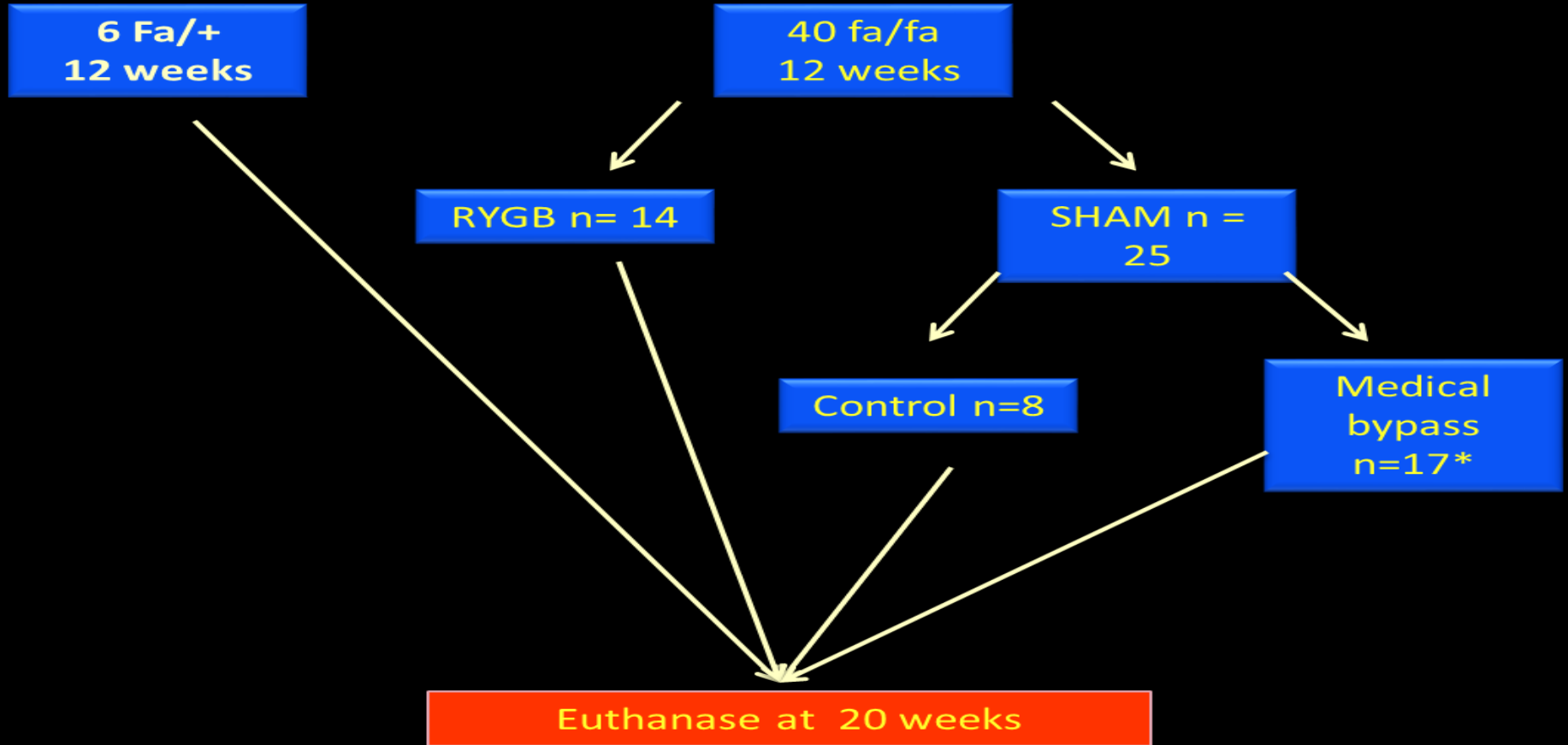
**Blood pressure control:** Ramipril

**Lipid control:** Rosuvastatin, Fenofibrate



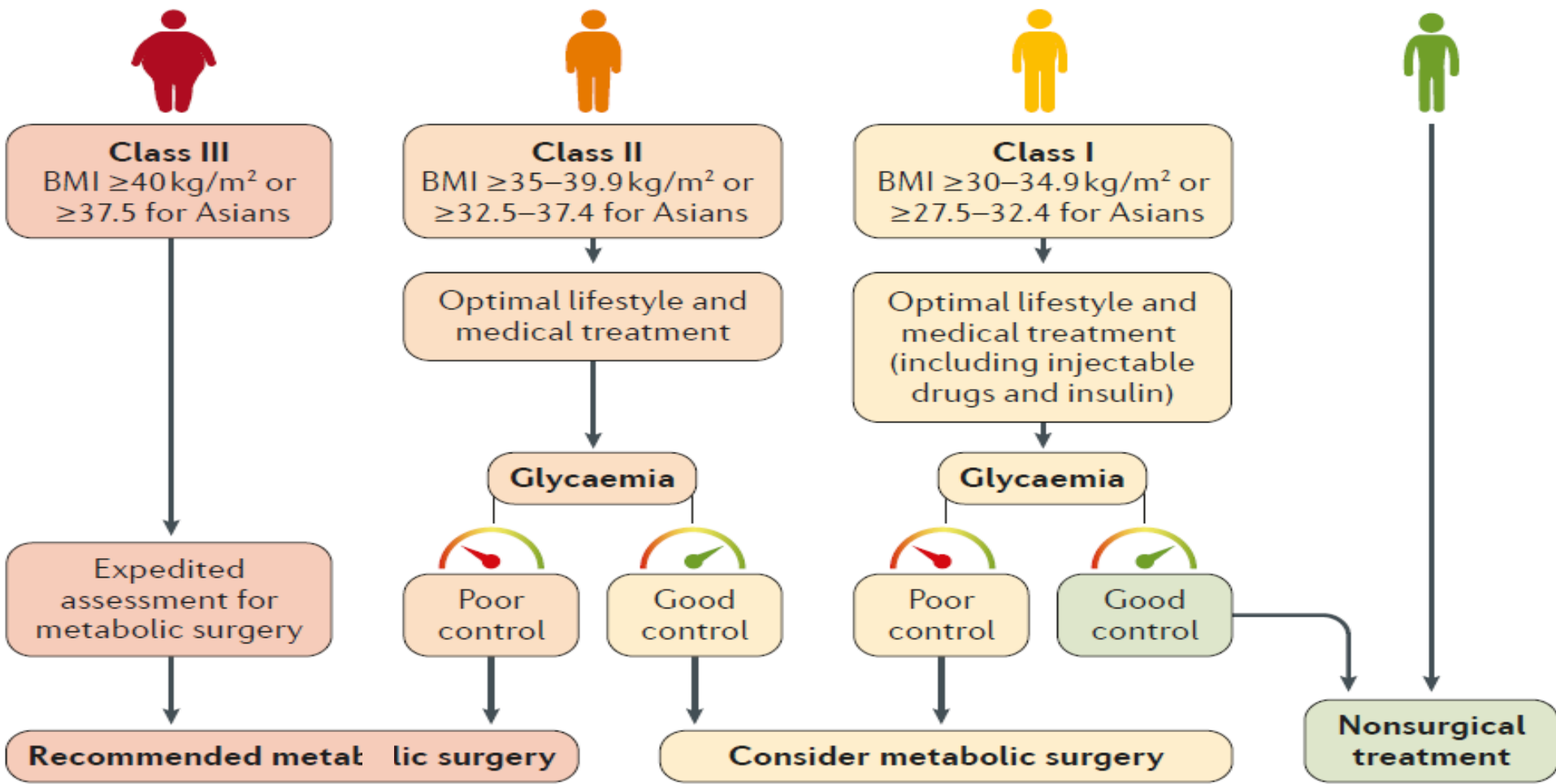
# Study Design

Nair M et al. unpublished.



**Obese**  
BMI  $\geq 30 \text{ kg/m}^2$  or  $\geq 27.5$  for Asians

**Non-obese**  
BMI  $< 30 \text{ kg/m}^2$  or  
 $< 27.5$  for Asians



# Conclusions

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- Metabolic surgery improves the metabolic micro milieu
- Structural improvements in the glomerulus after RYGB
- Combination surgery + medicine may be even more beneficial



**METABOLIC  
MEDICINE**

**HEROES**

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