

ICDM

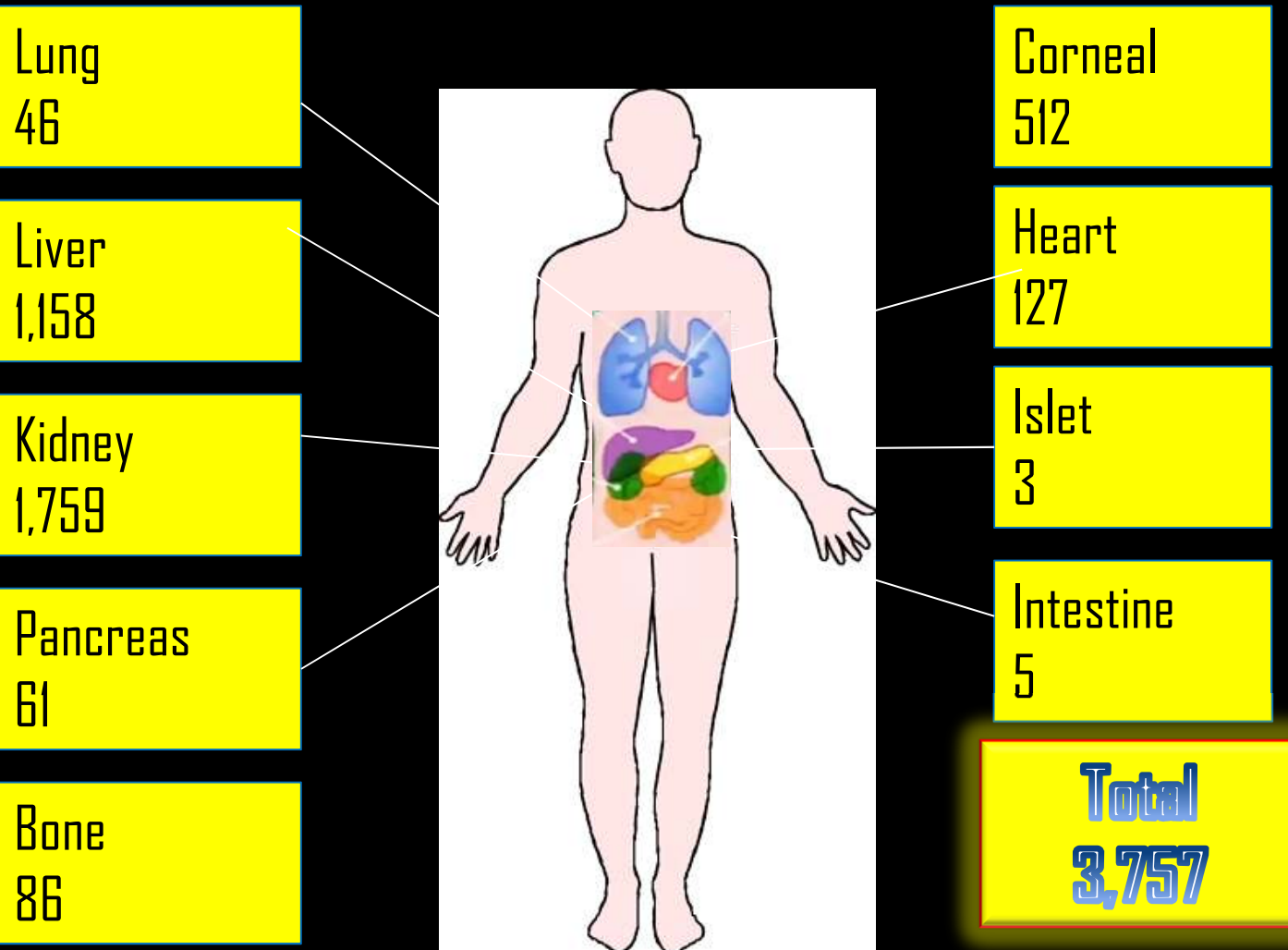
Management of Post-transplantation Diabetes Mellitus(PTDM)

Chosun University Hospital

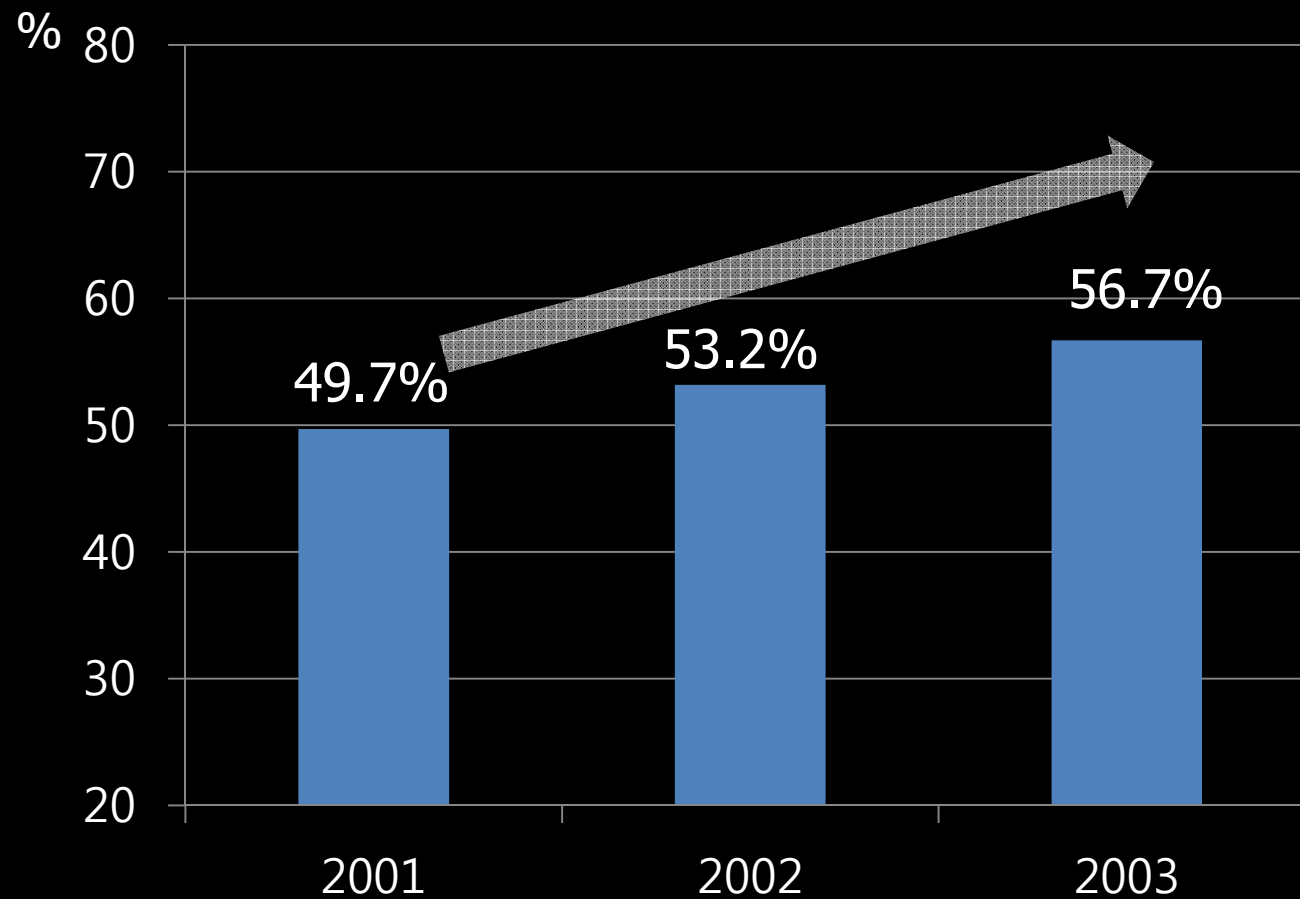
Lee Hae Jeong



Total treatment performed in the Korean to data(2013)

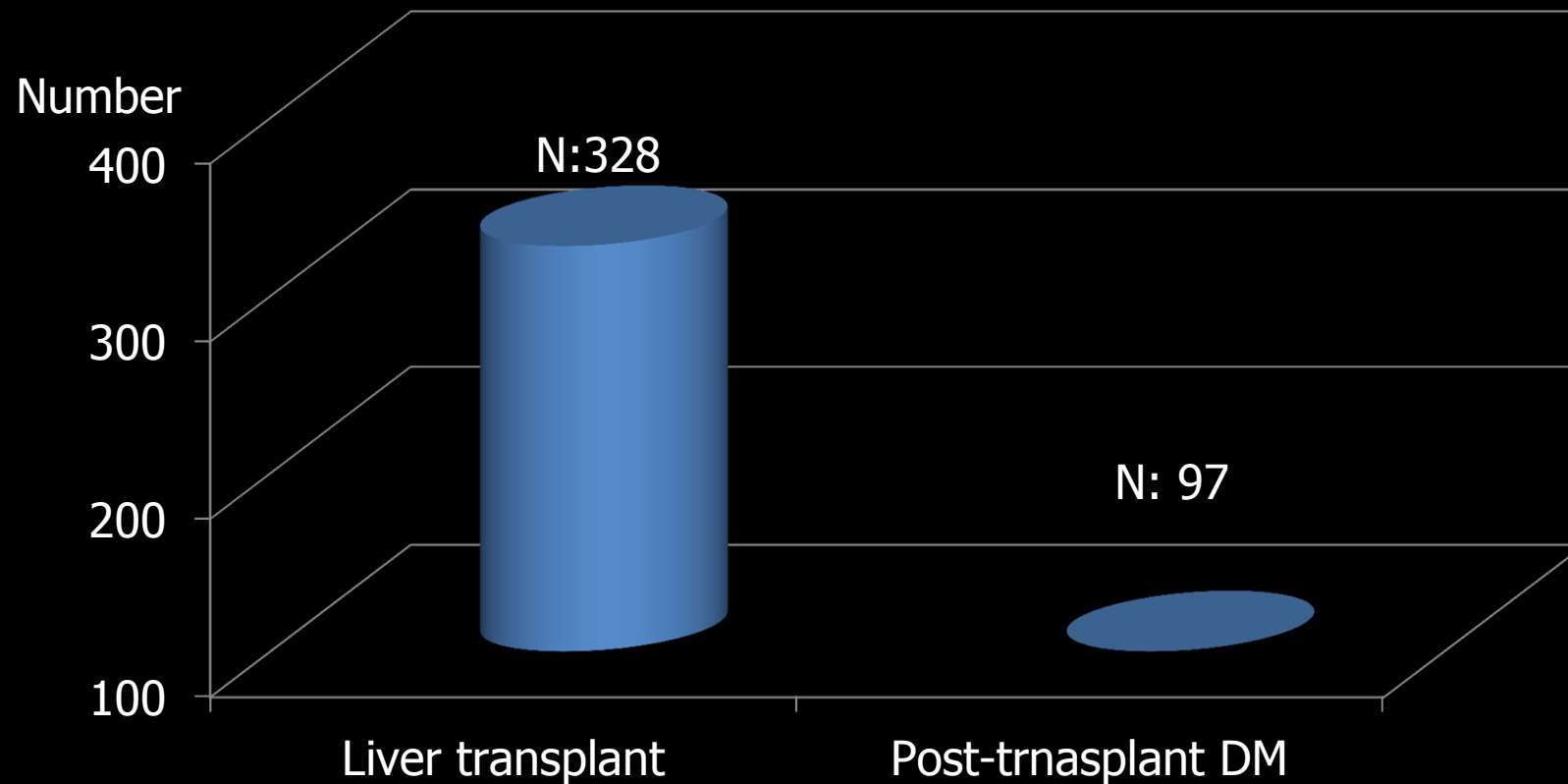


End stage renal disease with diabetes mellitus



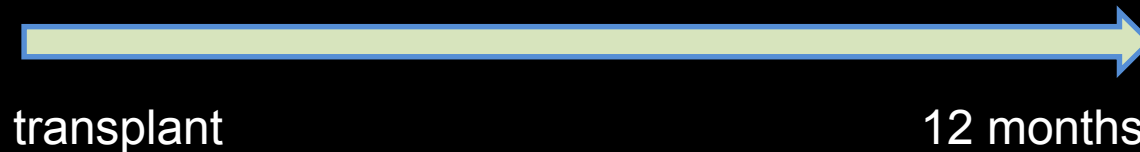
Post-transplant diabetes mellitus following liver transplantation

Liver transplant from Jan 2004 to May 2007



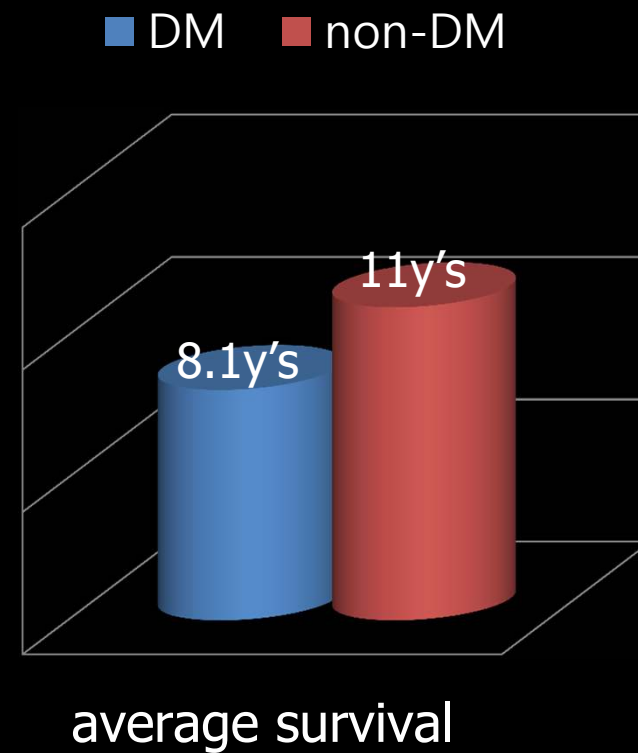
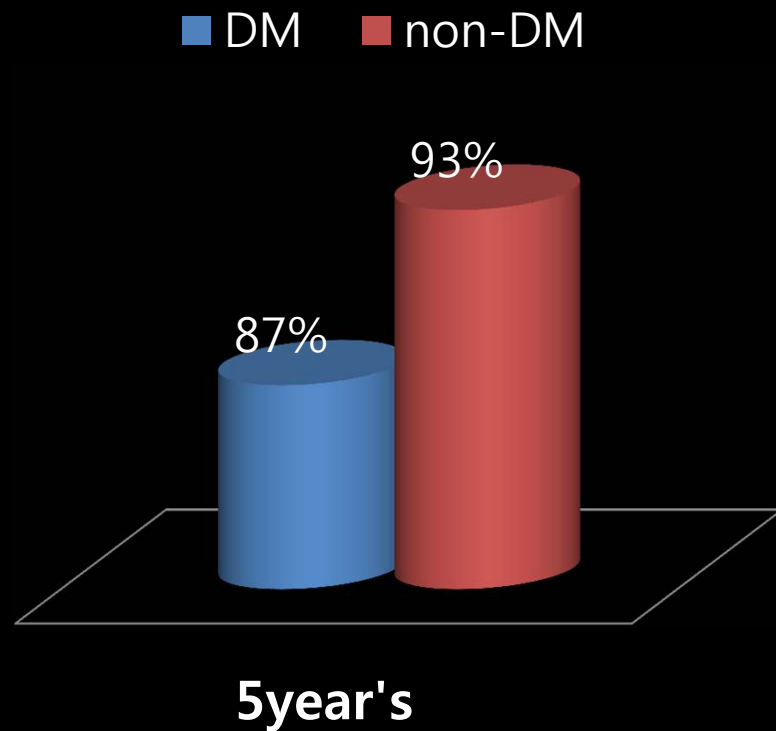
Estimated rate of post-transplant diabetes mellitus

14-74%	Kidney transplants
7-30%	Liver transplants
11-38%	heart transplants
6-45%	lung transplants
15%	Bone marrow transplants

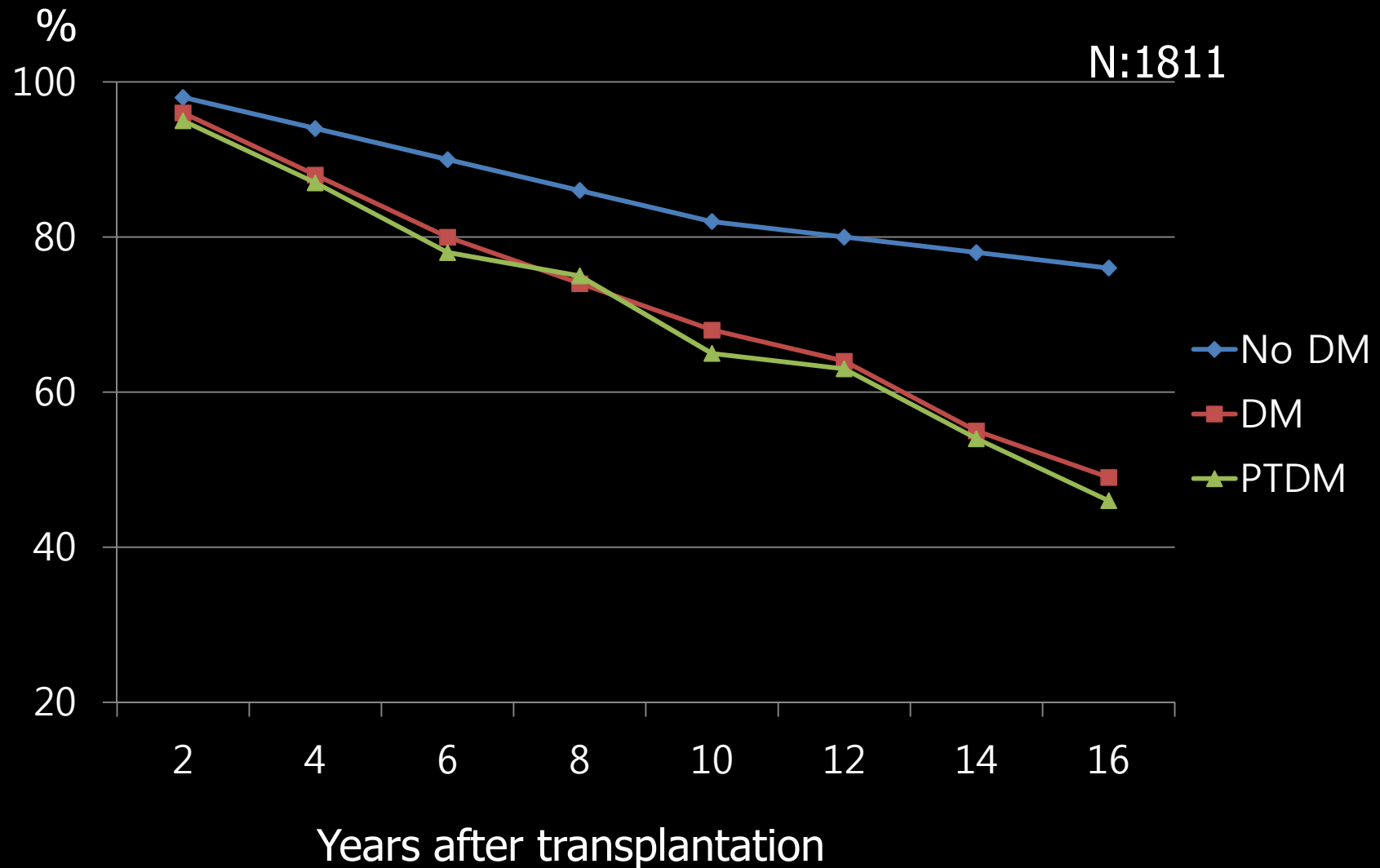


Transplantation 80:945, 2005. Transplantation 88:429, 2009.
Liver transplantation 15. Suppl 2:S79, 2009. Transplantation 89:1526, 2010

Transplant patient 5-years survival



Patient survival after kidney transplant: effect of diabetes



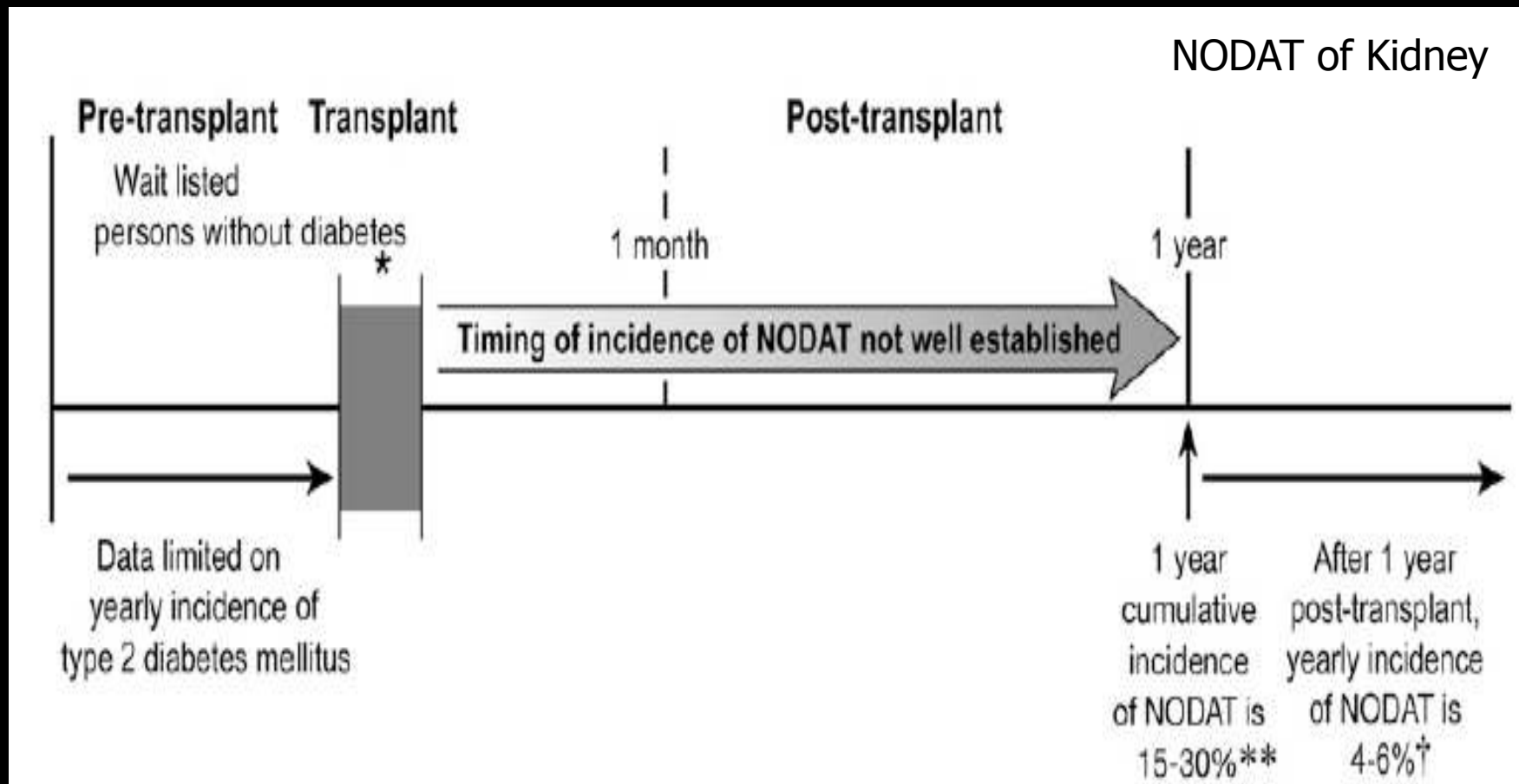
Important to decrease the incidence of PTDM

- Avoid complications of PTDM in each individual transplant recipient
- Protect the social investment already made in the transplant recipient
- Optimize the distribution of a scarce resource

Criteria of Post-transplant diabetes mellitus

	PTDM		PTDM
≥ 126 mg/dL		≥ 200 mg/dL	
< 126 mg/dL	Prediabetes	< 200 mg/dL	
≥ 110 mg/dL		≥ 140 mg/dL	
< 110 mg/dL	Normal	< 140 mg/dL	
Fasting plasma glucose		2 hours plasma glucose	

New onset diabetes after transplant(NODAT)



- Not all diabetes is "new" so may prefer term Post –Transplant Diabetes(PTDM)

Criteria of Post-transplant diabetes mellitus

- **Follows ADA criteria**
- Doesn't distinguish time from transplant
1 month and 10 years considered same
- A1C less reliable so not an established criteria
- NODAT is spontaneous remission
- 50% people;
Improvement in glucose tolerance after the
immunosuppressive agents decrease or taper

Mechanism in the pathogenesis of PTDM

Pre-transplant

Genetic variables

- Older age
- Family history of type 2 diabetes mellitus
- Race
- Hepatitis C
- Obesity
- Inflammation

Post-transplant

- ### Cessation of dialysis
- Improved appetite
 - Relaxed diet/obesity

Immunosuppression

Glucocorticoids

Increased hepatic
Glucose production

Calcineurin
inhibitors
Sirolimus

CMV
infection

Positive energy balance

Increased insulin resistance
or decreased insulin sensitivity

Impaired
 β cell secretory
capacity

Impaired
glucose tolerance

New onset diabetes mellitus after kidney transplantation

Incidence of PTDM among nondiabetes

Type of graft	Incidence estimate
Kidney	14-74%
Liver	7-30%
Heart	11-38%

Incidence varies with patient population and center immunosuppression used, diabetes screening protocol, interval of testing, who is **looking at that data!**

Transplantation 80:945, 2005. Transplantation 88:429, 2009.

Liver transplantation 15. Suppl 2:S79, 2009. Transplantation 89:1526, 2010

Post-Transplant Diabetes Risk Factors

Pre-transplant

Genetic variables

- Older age
- Family history of type 2 diabetes mellitus
- Race
- Hepatitis C
- Obesity
- Inflammation

Post-transplant

- Cessation of dialysis
- Improved appetite
 - Relaxed diet/obesity

Immunosuppression

Glucocorticoids

Increased hepatic Glucose production

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CMV infection

Positive energy balance

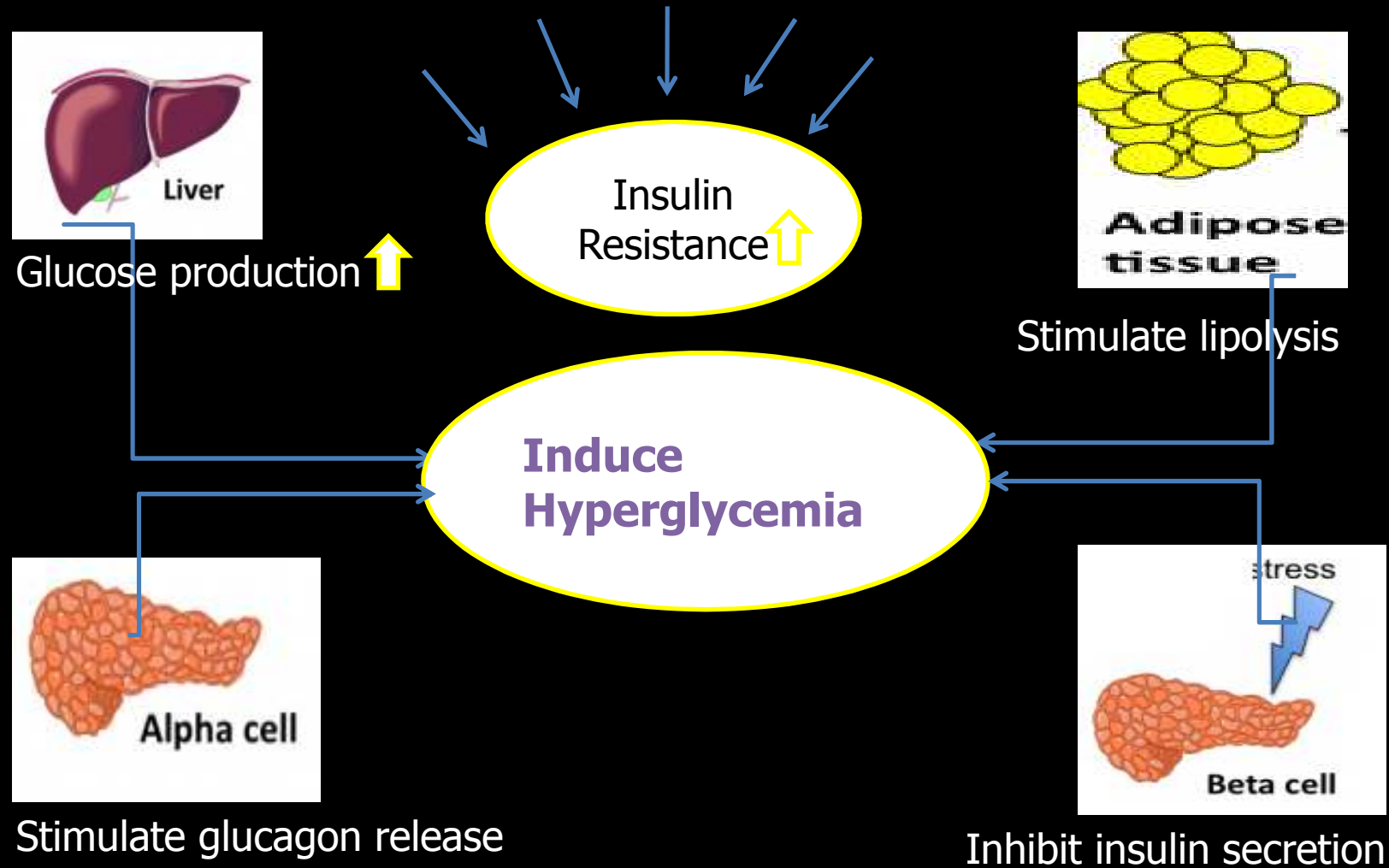
Increased insulin resistance or decreased insulin sensitivity

Impaired β cell secretory capacity

Impaired glucose tolerance

New onset diabetes mellitus after kidney transplantation

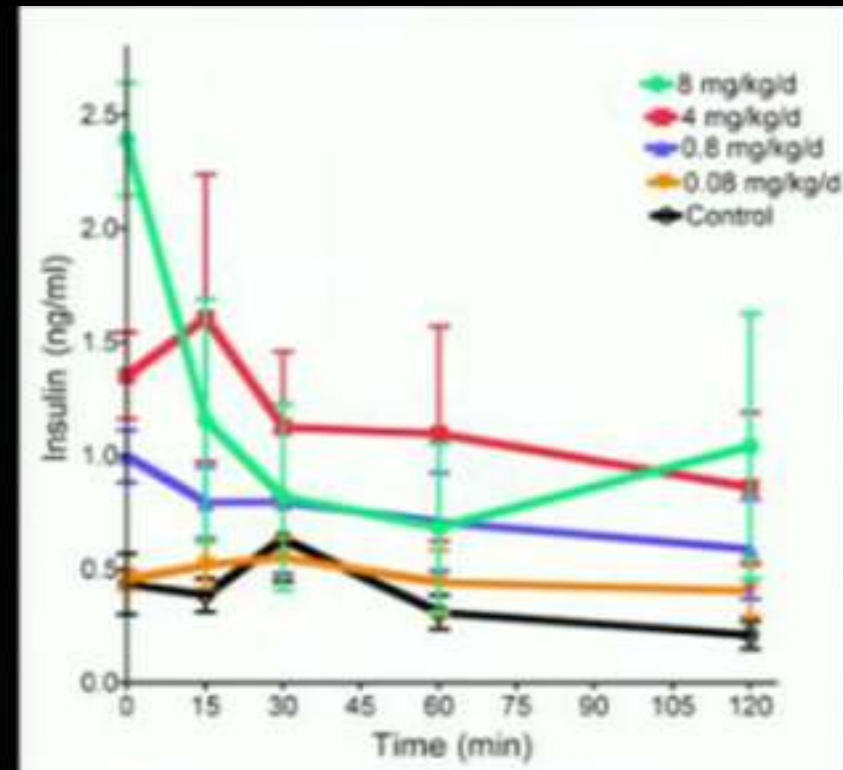
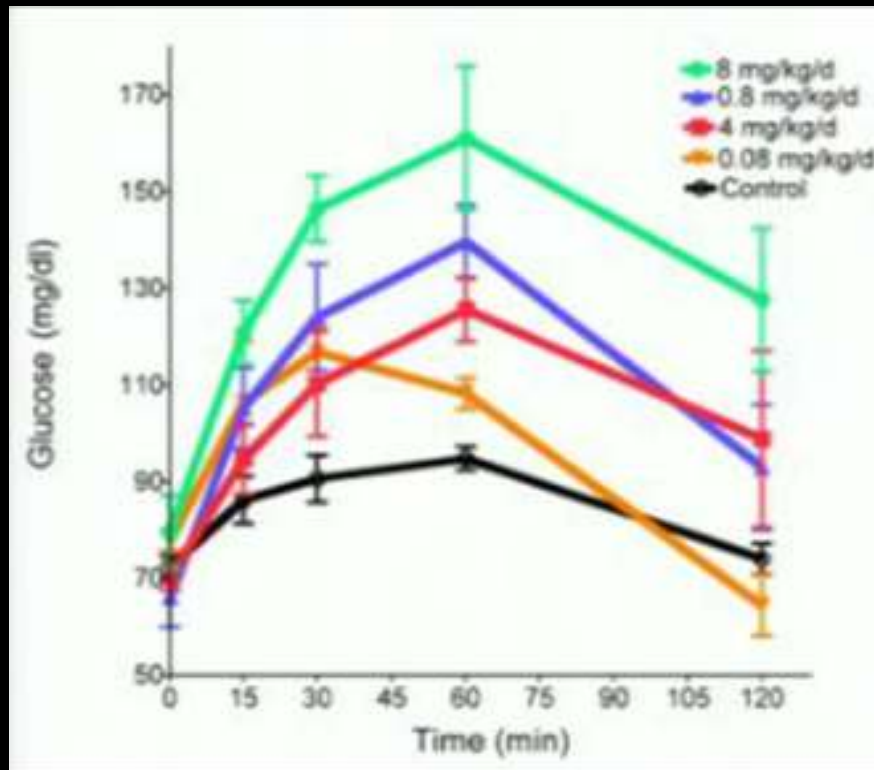
Glucocorticoid steroids is



Immunosuppressant can cause hyperglycemia

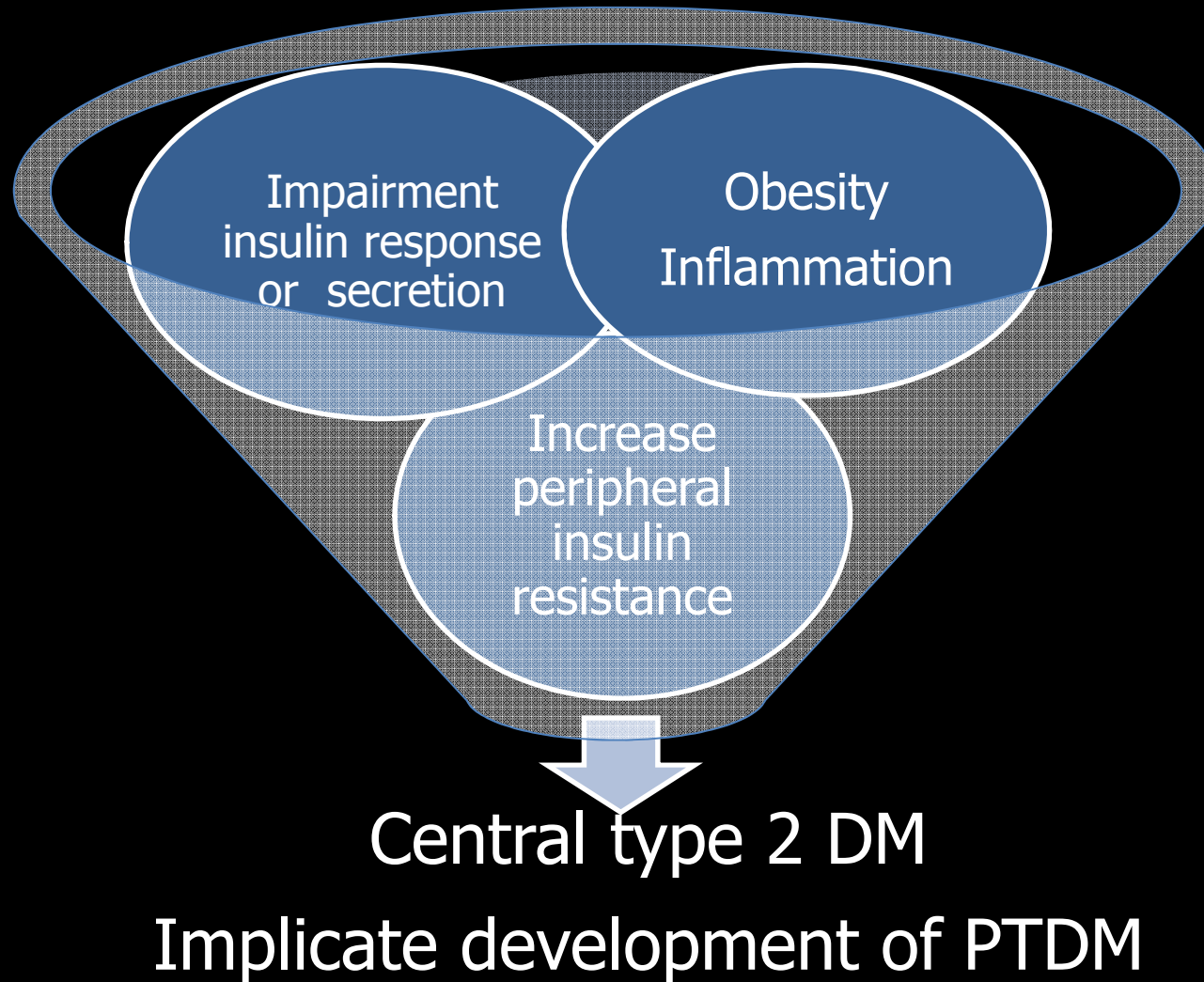
	Cyclosporine A	Tacrolimus	Sirolimus
Glucose intolerance	+ 6%	+++ 8.4%	+ 6.6%
Hypertension	++	+	
Hyperlipidemia	++	-	+++

Calcineurin inhibitors and sirolimus Can cause hyperglycemia

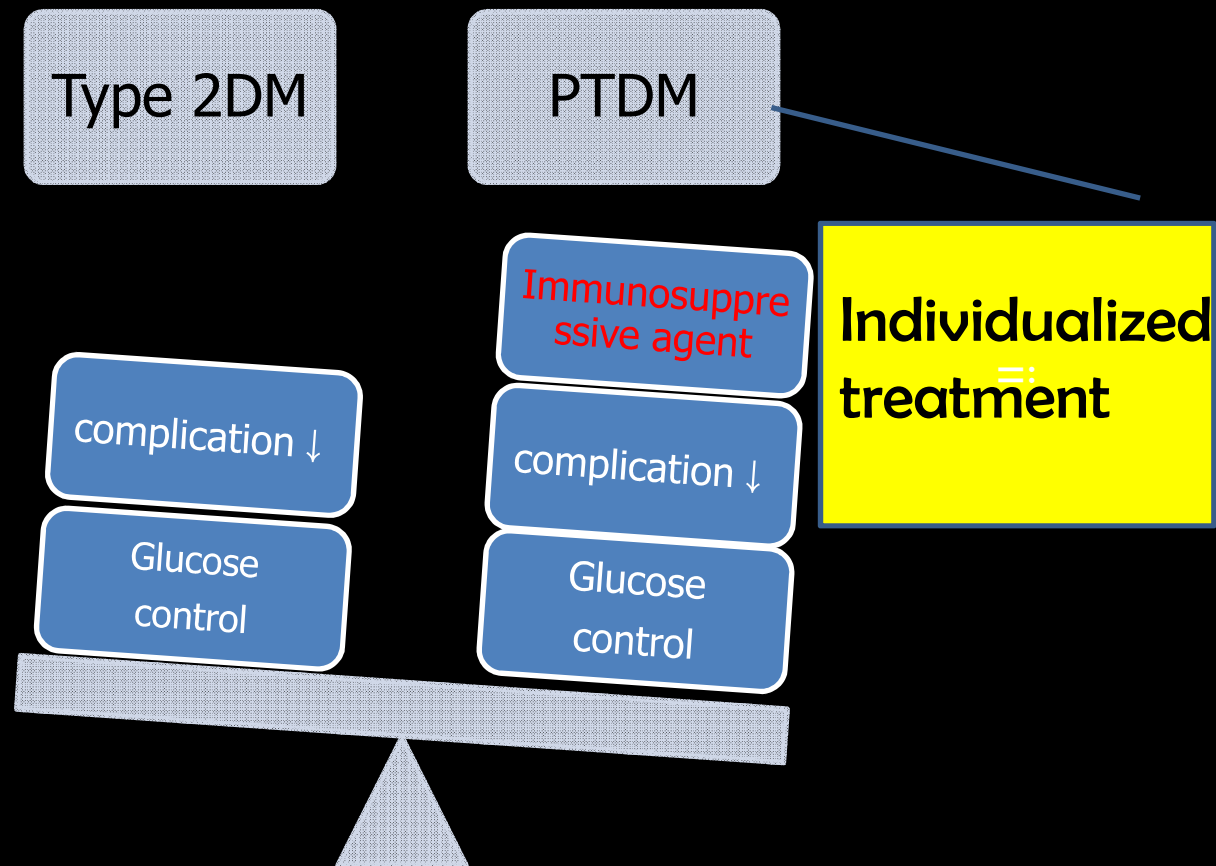


Approach to management of PTDM

Similarities of type 2 DM and PTDM



Management aim of PTDM



Prediction of hyperglycemia and risk of PTDM



Older age



Planned corticosteroid therapy after transplant



Gout medicine



High BMI



Higher fasting glucose



Higher triglycerides



Family history of type 2 DM

Waiting transplant ...

- Document baseline blood glucose status
- Assess diabetes risk factors
- Identify high-risk subjects
- **Initiate lifestyle intervention**
 - Dietary counseling
 - Exercise counseling

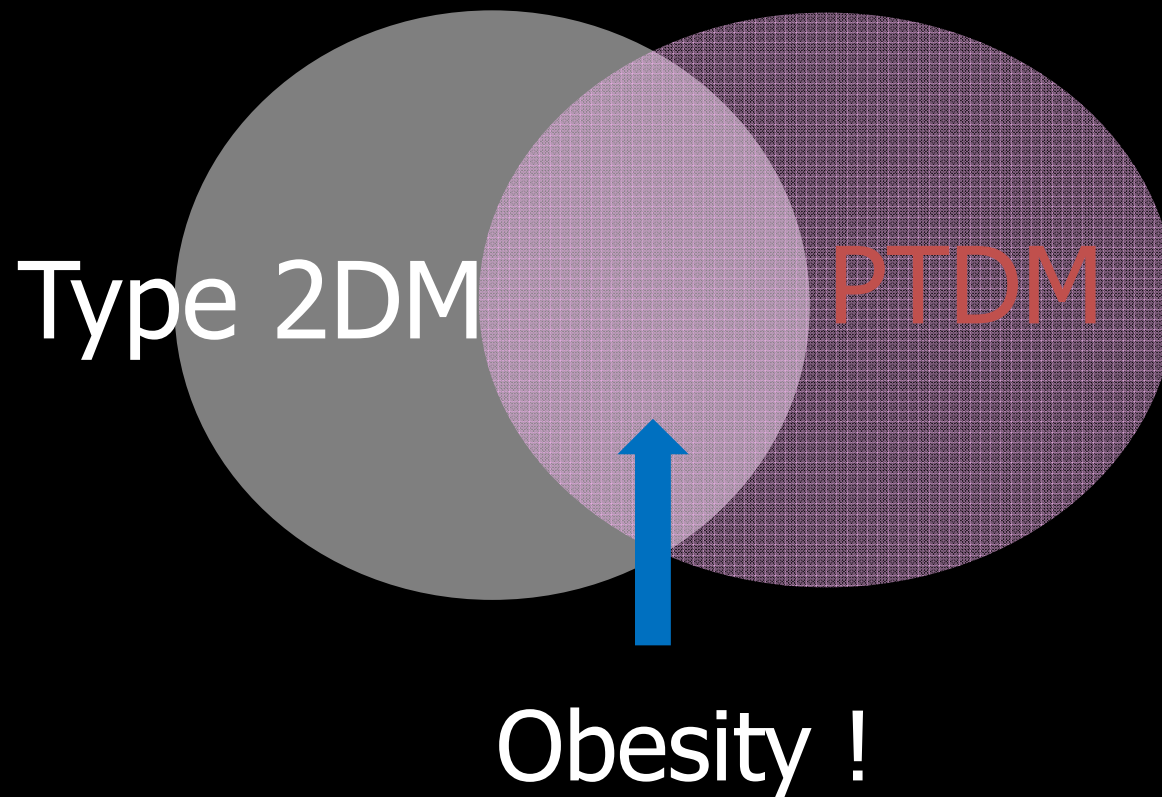
Post-transplant period

- Immunosuppressive regimen
 - Minimize steroid dose
 - Minimize calcineurin inhibitor exposure
- Treat hyperglycemia beginning in the peritransplant period
- Close follow-up of all patients , especially those with prediabetes

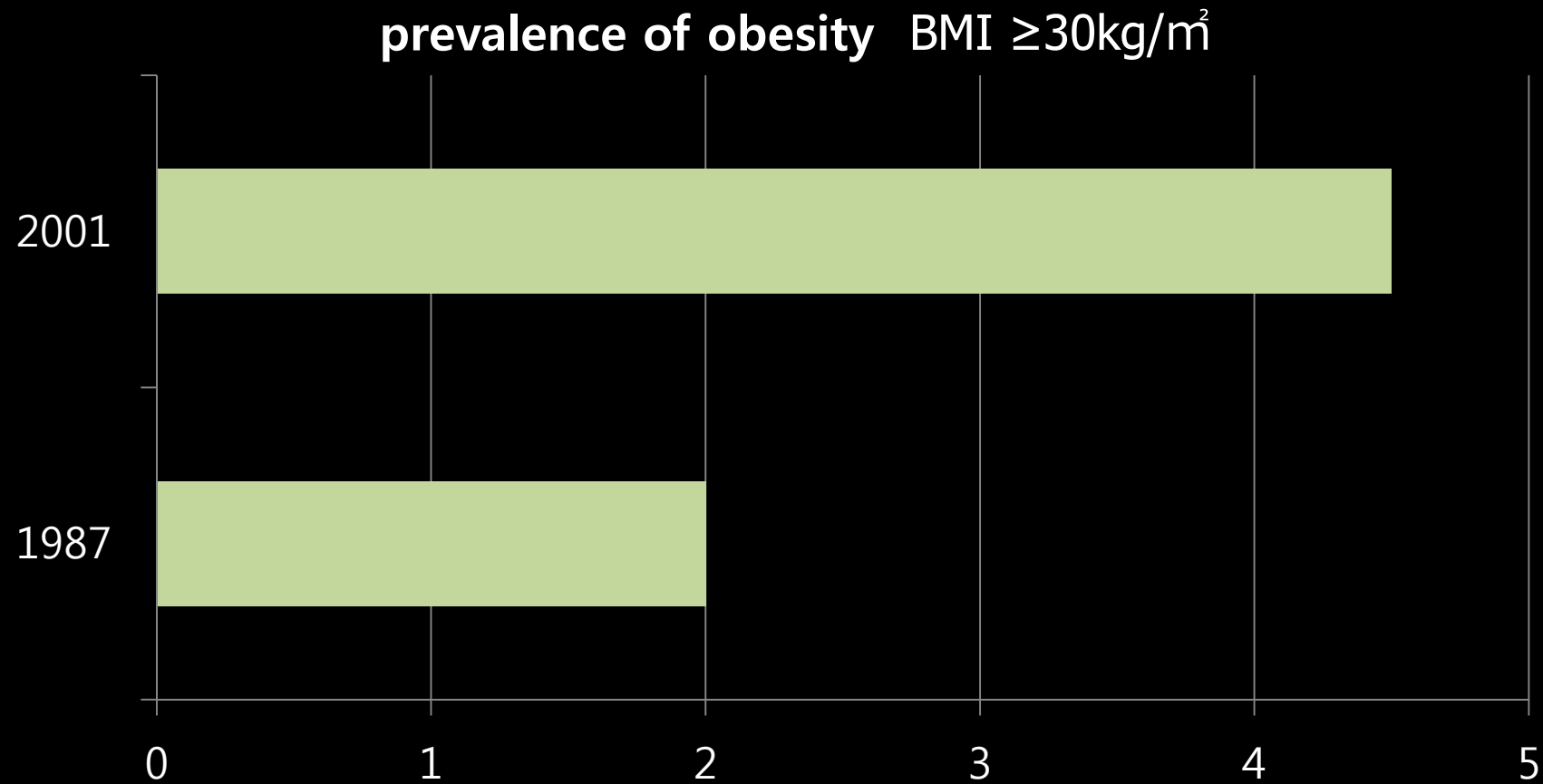
Post-transplant period

- for those develop NODAT
 - diabetes education
 - appropriate medical therapy based of severity of hyperglycemia
- optimize insulin therapy during episodes of high-dose steroid exposure

Can lifestyle modification be adapted for prevention of PTDM?

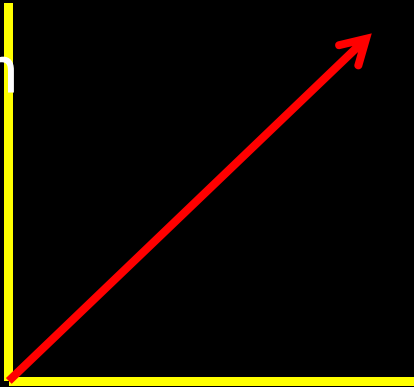


Prevalence of obesity at the time of transplantation among transplant recipients



For the lower the incidence of NODAT

Insulin resistance
After transplantation



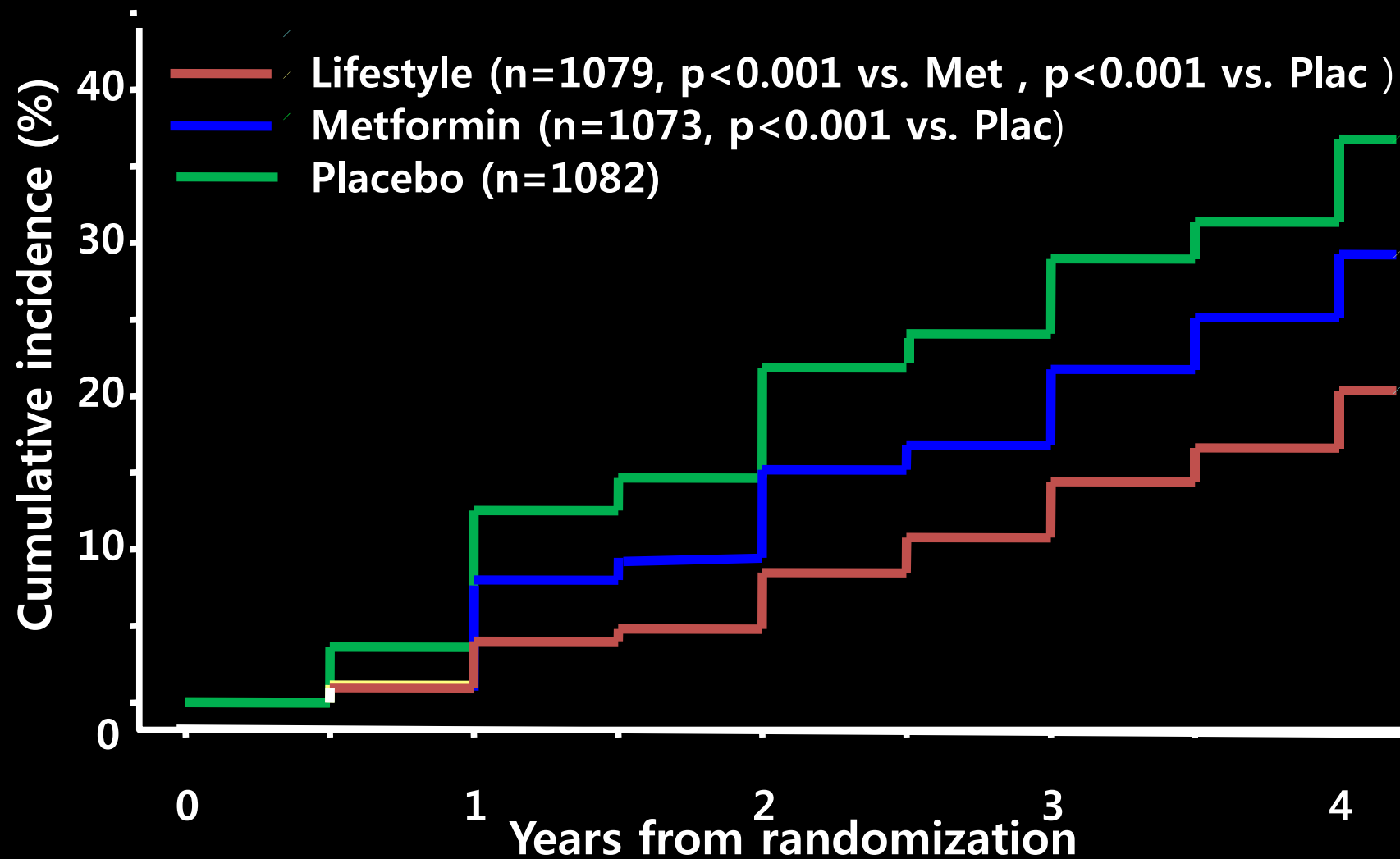
Obesity treatment
seems to reasonable
target for intervention

Higher BMI before transplantation

Lifestyle intervention Studies for the Prevention of type 2 DM

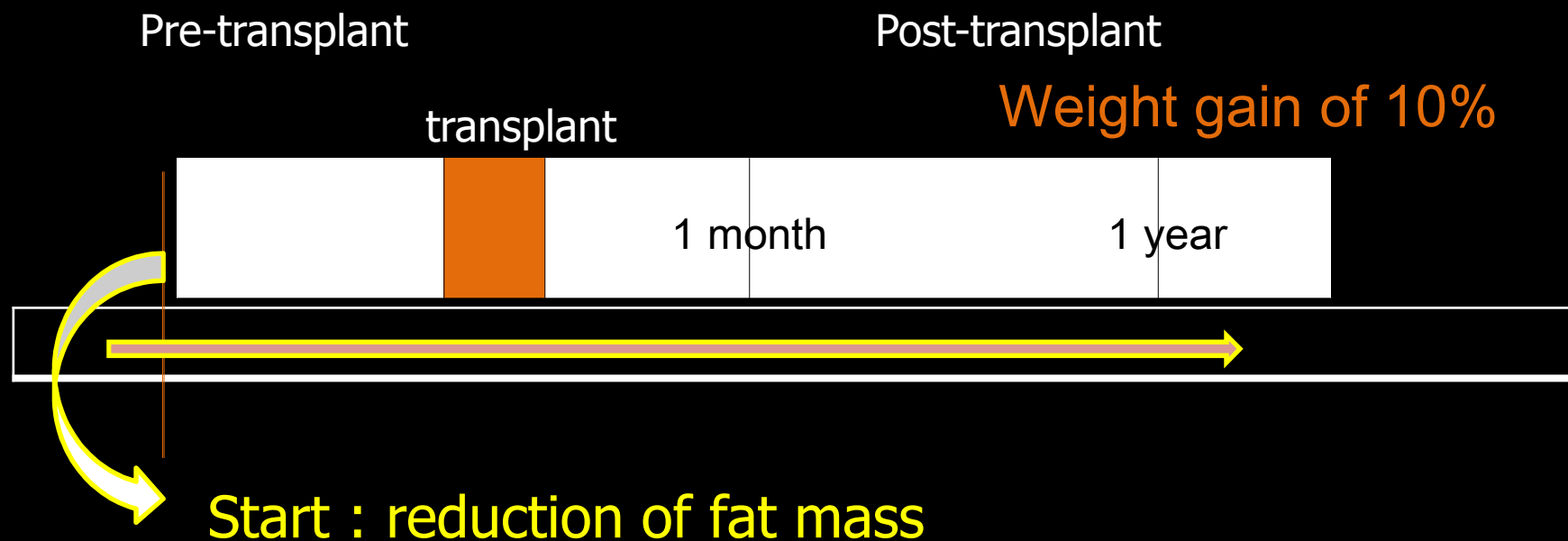
Study	Population	Duration	Conclusions (intervention vs control)
Malmö Feasibility study	181 IGT vs 193 IGT or NGT	5 and 12 y	37% ↓
Da Qing study	577 IGT	6 y	46% vs 67.7%
DPS	522 IGT	3.2 y	11% vs 23%
DPP study	3234 with IGT or IFG	2.8 y	58% ↓
Malmöhus study	267 men with IGT	10 y	13% vs 29%

Percent developing diabetes(DPP study) All participants

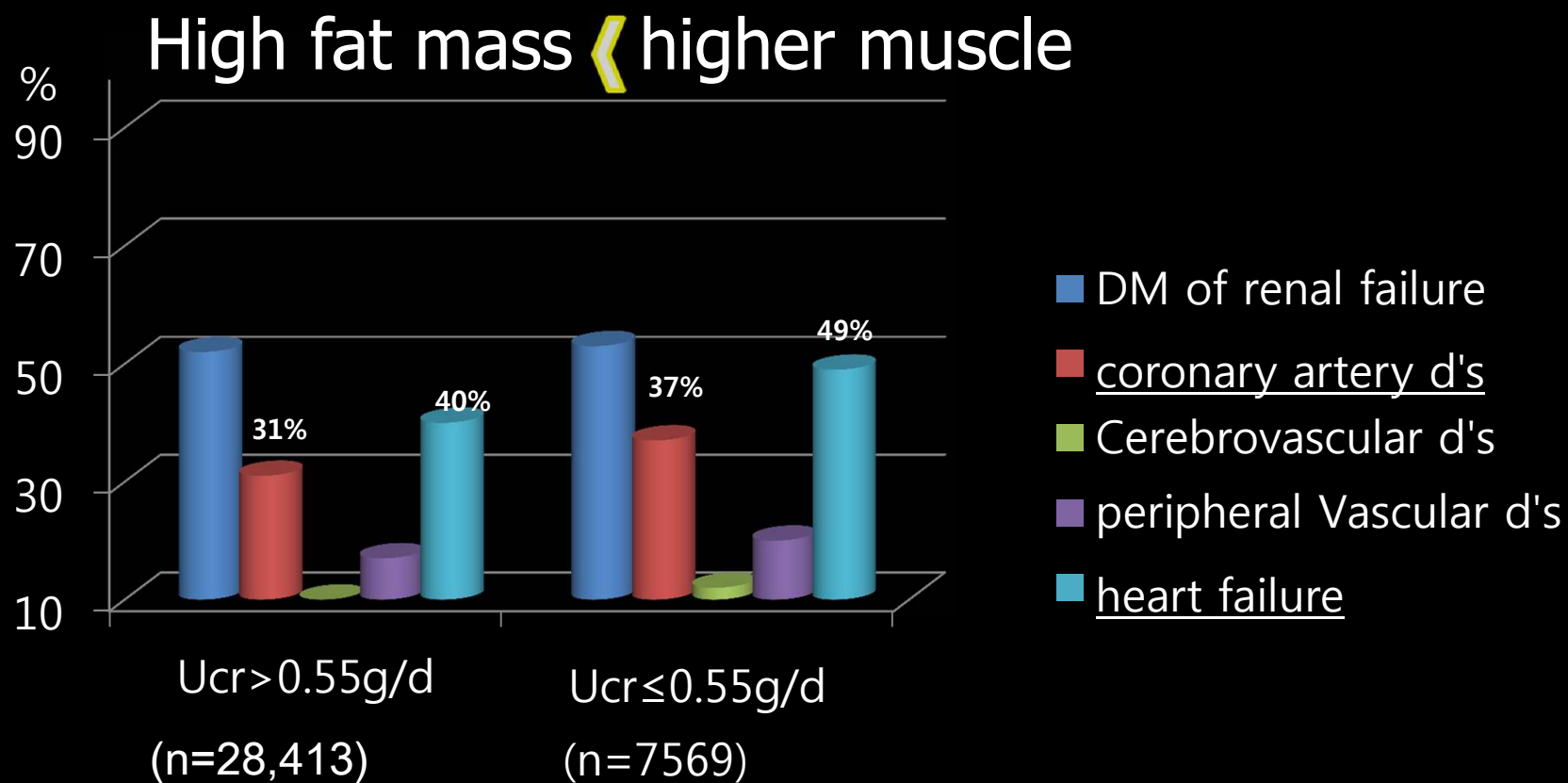


Lifestyle intervention aim

Lowering fat mass may be appropriate
for the prevention of NODAT



Effect of higher muscle on survival in HD patients



High BMI ($\geq 25 \text{Kg/m}^2$) group by muscle mass

Lifestyle intervention similar to the diabetes prevention program



Safely reverse method ?

Three times/week
For 3-4h's treatment

Inactivity

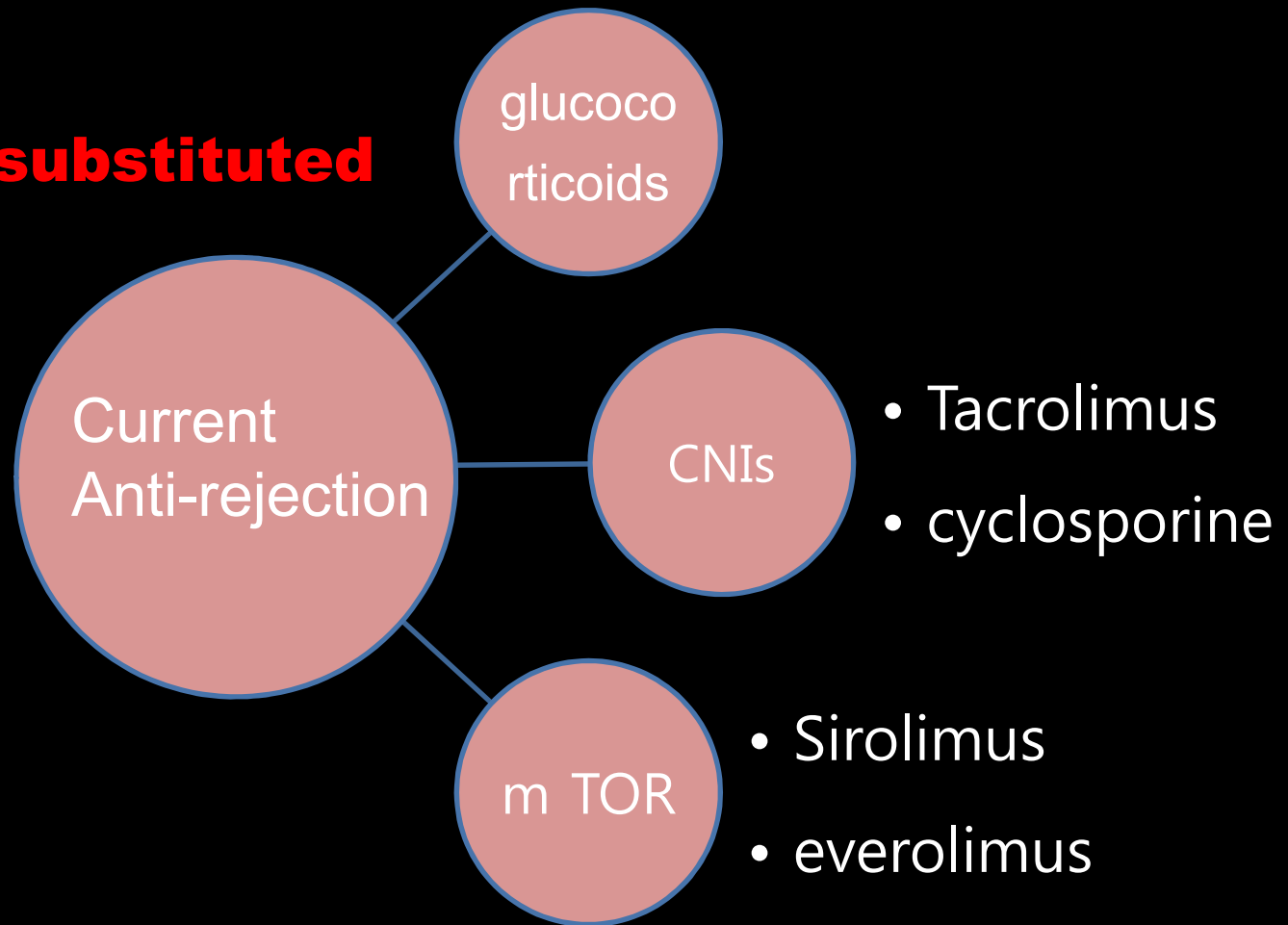
anemia

hypervolemia

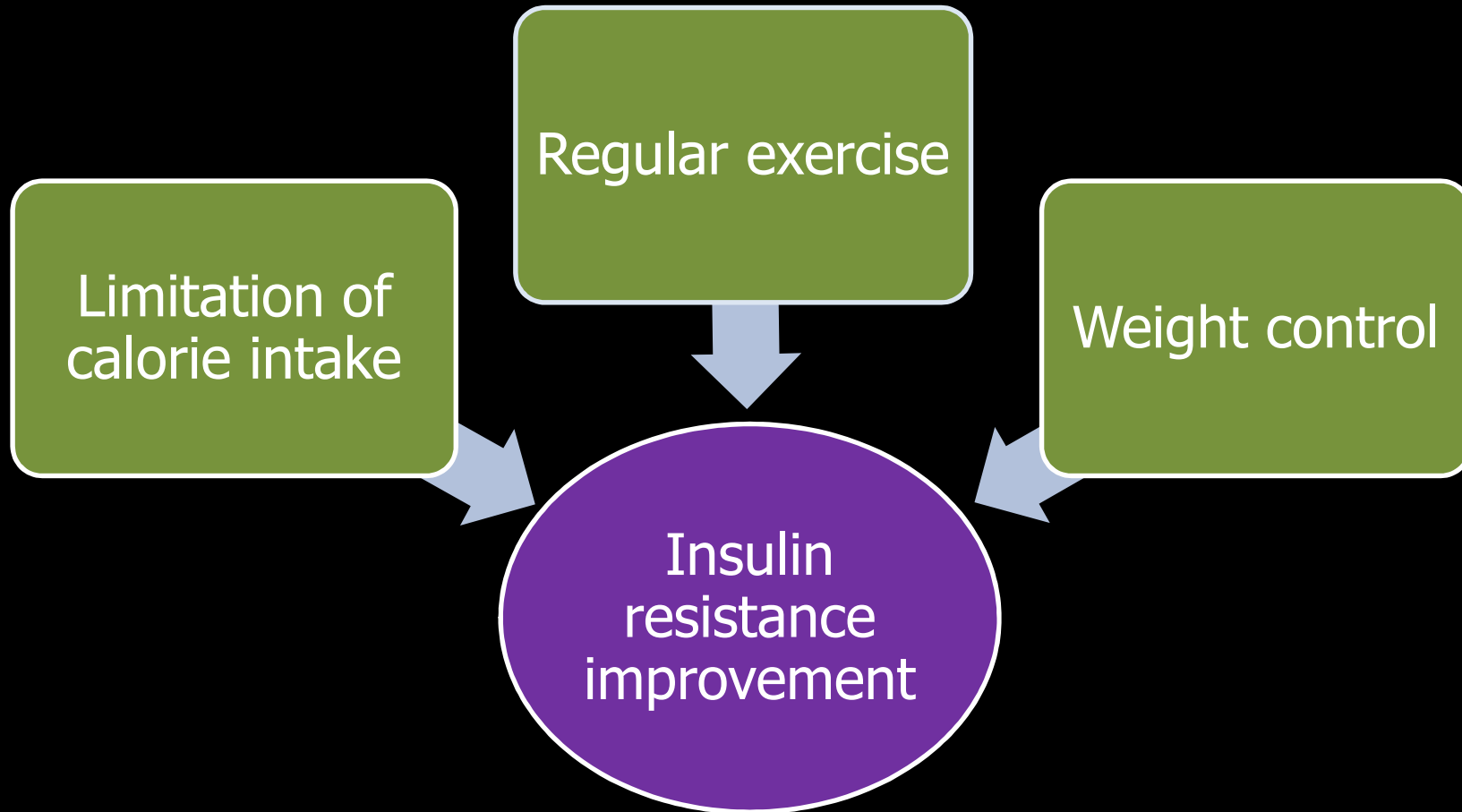
Uremic
cachexia

Potential effectiveness of lifestyle intervention importance

Yet not easily substituted



Direction of lifestyle modification



Treatment guideline for Post-transplantation diabetes mellitus

Index	
HbA1c	<7.0%
Blood pressure	
Systolic	<130mm
Diastolic	<80mm
Lipid profile	
LDL-chol	<100mg
HDL-chol	>40mg
Triglyceride	<150mg/dL

immunosuppression used

Self monitoring blood glucose

Maximization of
curative effect

HbA1c <7.0%

OHA Therapy
Insulin therapy
Lifestyle modification

interval: 3months
Especially attention
: Renal failure
: anemia

Glucose control: should goals be different?

ADA guidelines	
ICU	140-180mg/dl
Non- ICU	Pre-meal < 140mg/dl Random < 180mg/dl

Diabetes care 36 Suppl 1;S11-66, 2013

Value of tighter control?

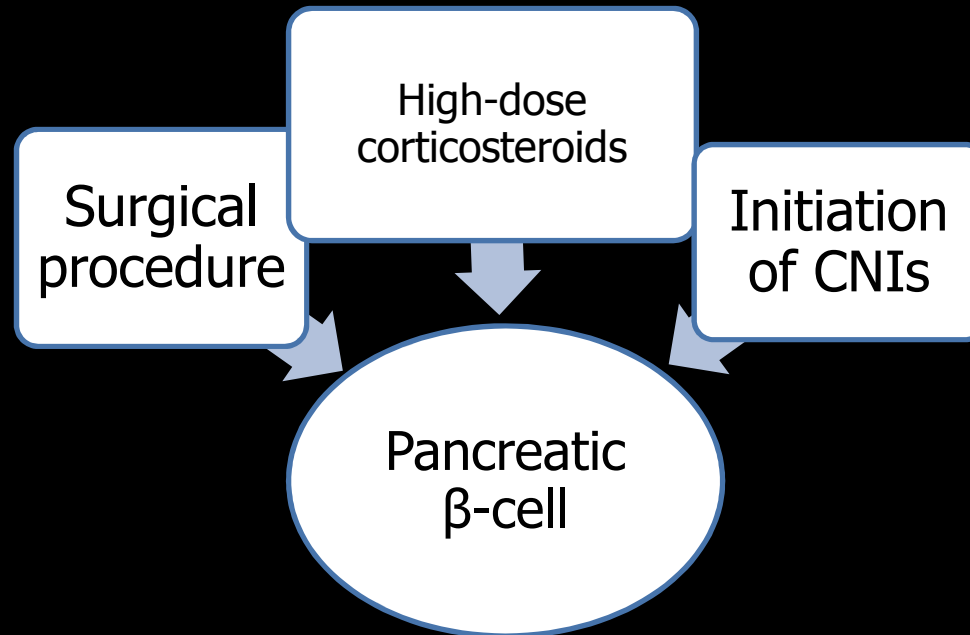
Kidney Transplant RCT: 70-100 vs <180mg/dl

More hypoglycemia, rejections => no benefit

JCEM 97; 4399, 2012

Insulin therapy

Several stressors after trans-plants surgery



Thus

Treatment goals

Resting the β -cell with Basal insulin and β -cell

Protection with near-normo-glycemic control

:reduce IGT and NODAT

Insulin therapy

Used widely

Basal insulin, split-mix,
basal-bolus

Flexibility and
creativity

Oral agents post-transplant

Oral /SQ agent	Effective Post-TX?	Potential limitations
Sulfonylureas & repaglinide	Yes	Drug-drug interactions with cyclosporine, risk of hypoglycemia with GFR ↓, less with repaglinide
Metformin	Yes	Contraindicated in hospital with GFR ↓, LFTs ↑, CHF, infection
Exenatide	Not studied	
DPP-IV inhibitors	Yes	Reduce dose for most with GFR ↓
TZDs	Yes	Risk of LFTs ↑, CHF, weight gain
Acarbose	Yes	Avoid with GFR ↓, ineffective as single agent

Hypoglycemia can

- Induce seizure and arrhythmia
- Triggers adrenergic discharge
- Expression of pro-inflammatory cytokines



Adverse outcomes in high-risk patients

Dyslipidemia

- Calcineurin inhibitors:
 - increase cholesterol level
 - Preferentially pravastatin, fluvastatin
- Sirolimus and glucocorticoids:
 - increase hypertriglyceridemia
 - Be used fibrate, fish oil

Hypertension

- Premorbid hypertension
- Recommends BP: 130/80 mmHg ↓
- β -blockers, calcium channel blockers to be effective
- ACE inhibitors, ARB are associated decreases in GFR and hyperkalemia

Transition to home: always tricky

- Diet
- Exercise
- Sick day management
- Self-blood glucose monitoring
- Insulin injection method



Check list
Sticker

Diary of
diet
/exercise
SMBG

Make sure
Feed back!!

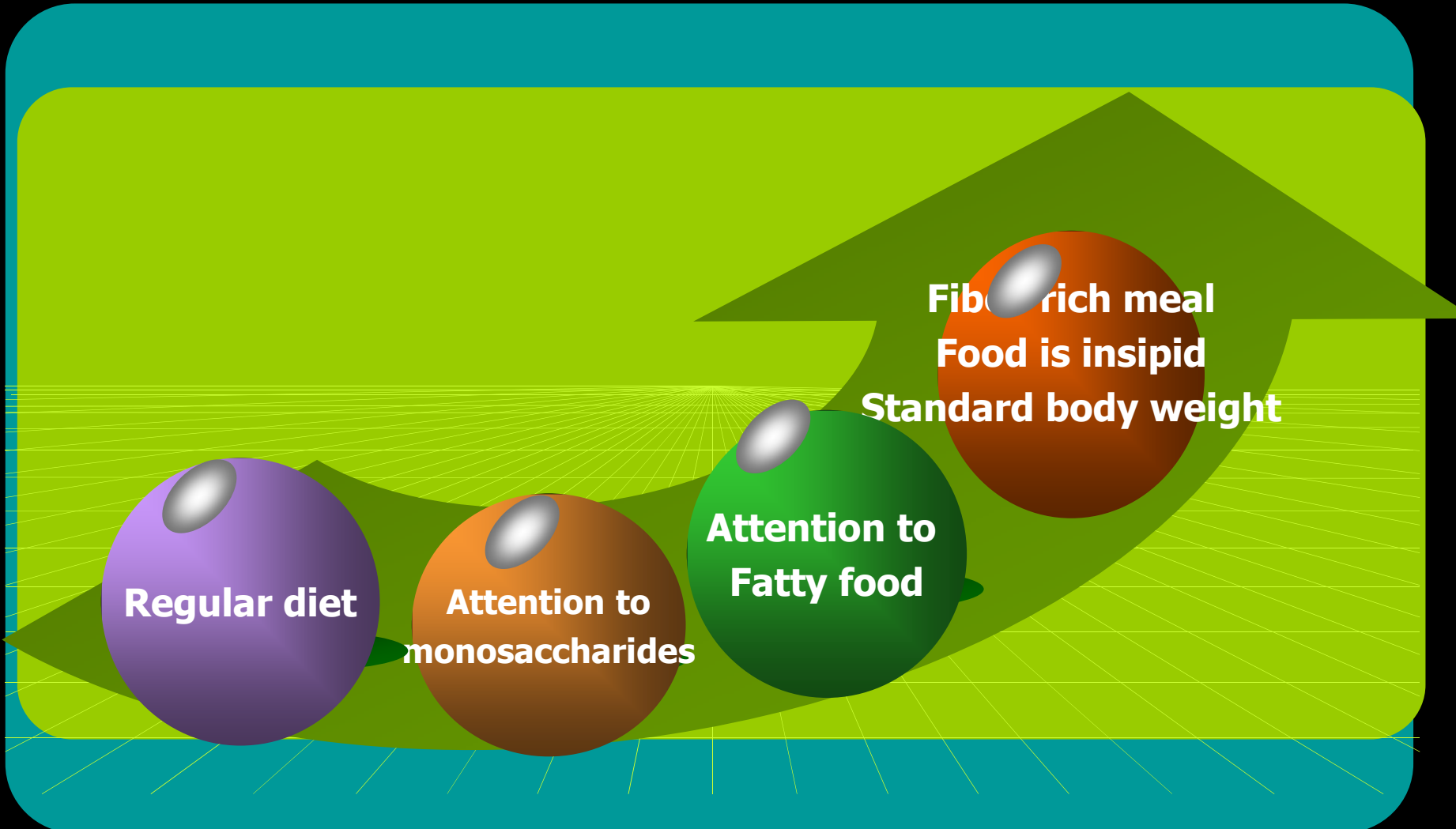
You are what you eat!

Regular diet

**Attention to
monosaccharides**

**Attention to
Fatty food**

**Fiber rich meal
Food is insipid
Standard body weight**



What about foods high in carbohydrates?

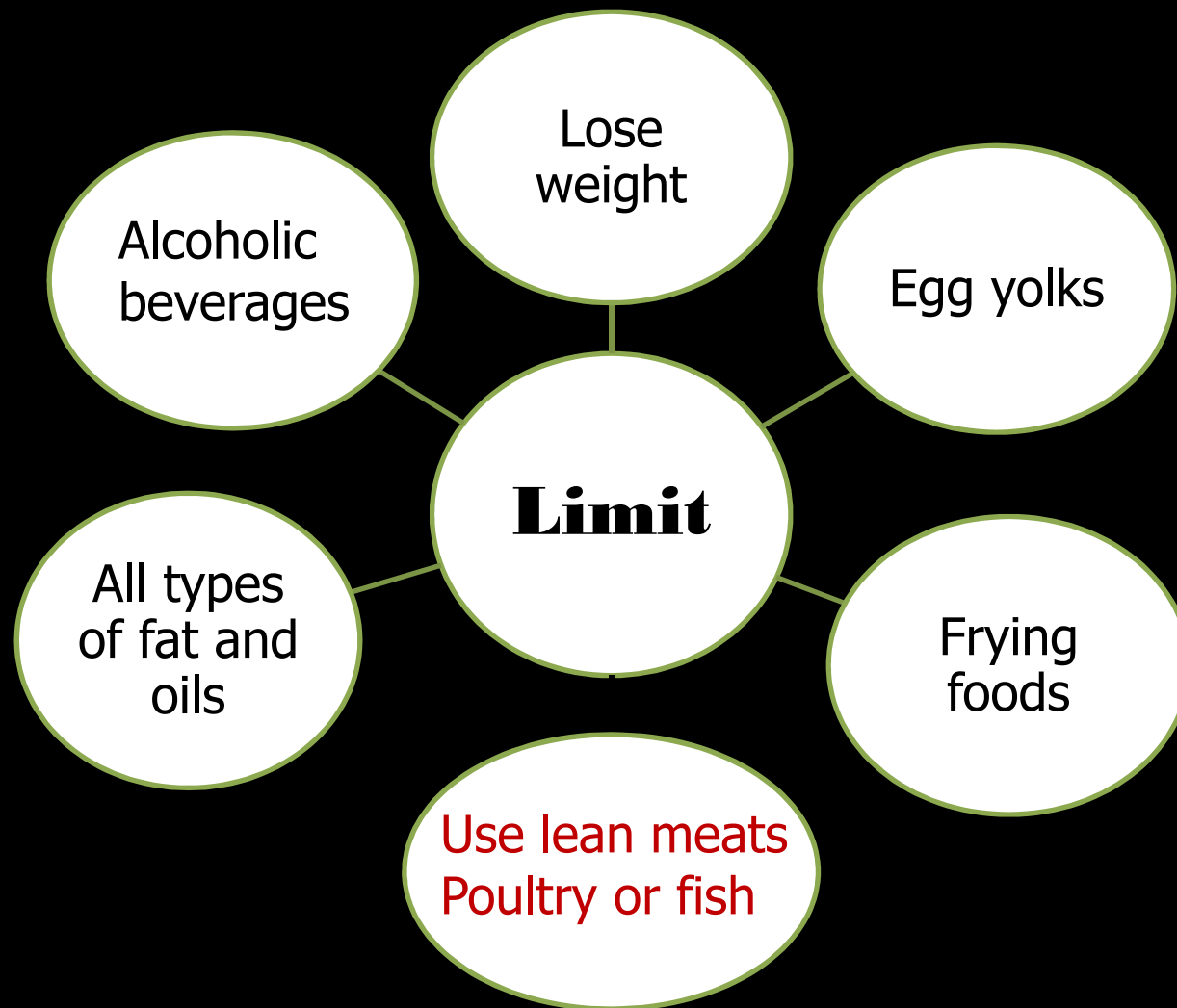
- Come from sugars and starches
- provide fuel and energy
- Take steroid medication, it's difficult for your body to use extra carbohydrates

For these reasons

Fewer "simple"
carbohydrates

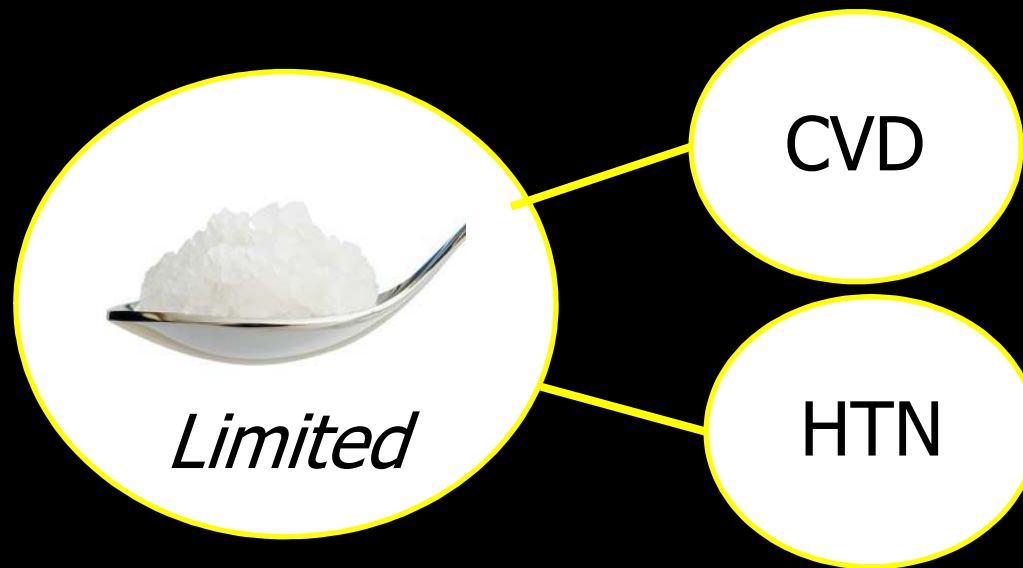
Moderately "complex"
carbohydrates

What about cholesterol and triglyceride levels?



Still need to follow a low-salt diet?

- Transplant medications, Steroids may cause to retain fluid
- Salt makes this problem worse, increasing fluid retention and raising blood pressure



When cooking...



What about protein?

- Especially...
- It builds and repairs muscles and tissues
- It helps you heal after surgery
- 1.0g~1.2g/Kg (15~20%/ day)



Take care of the meal

- Calcium-rich foods
 - Food rich dietary fiber
- } **suitable**

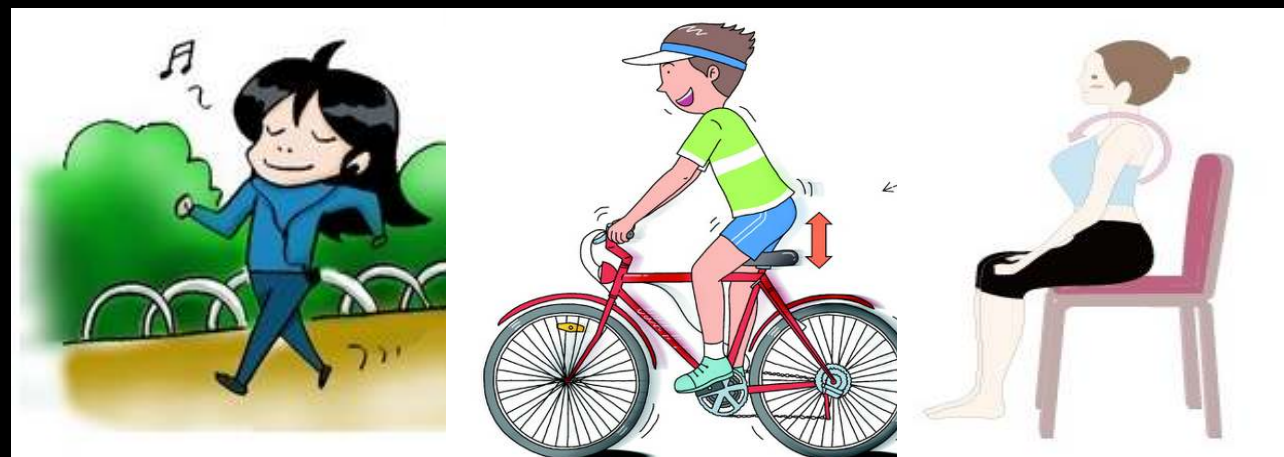


- Not eat the health supplements food



Will gain weight?

- Many people have a better appetite after they get a transplant, and gain unwanted weight.
- Avoid high-calorie foods, fatty foods, sweets, pastries, sugar
- Important to controlling weight
Help to: exercise and regular physical activity plan



Legacy effect

*Knowing is not enough;
We must apply.*

*Willing is not enough;
We must do.*

-Goethe-

I should...

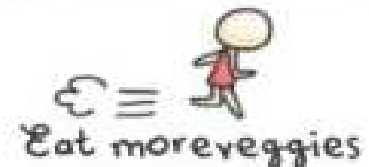
Get more sleep



Drink more water



Get more exercise



chibird.tumblr.com

Thank you for your attention