

# Diabetes and Kidney



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# Diabetic Nephropathy

**Diabetic Nephropathy (DN)** is the most common cause of end-stage renal disease (ESRD)

The percentage of patients with ESRD who have Diabetes Mellitus, specially **Type II patients**, have increased over the past decade

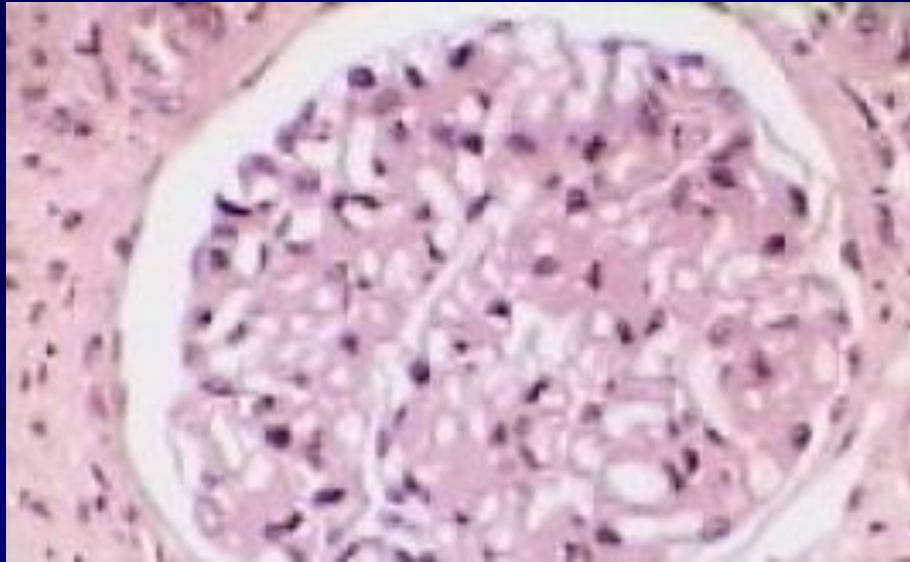
The incidence of Diabetes Mellitus is rising world wide

It is estimated that **20-40%** of all diabetic patients will develop diabetic nephropathy

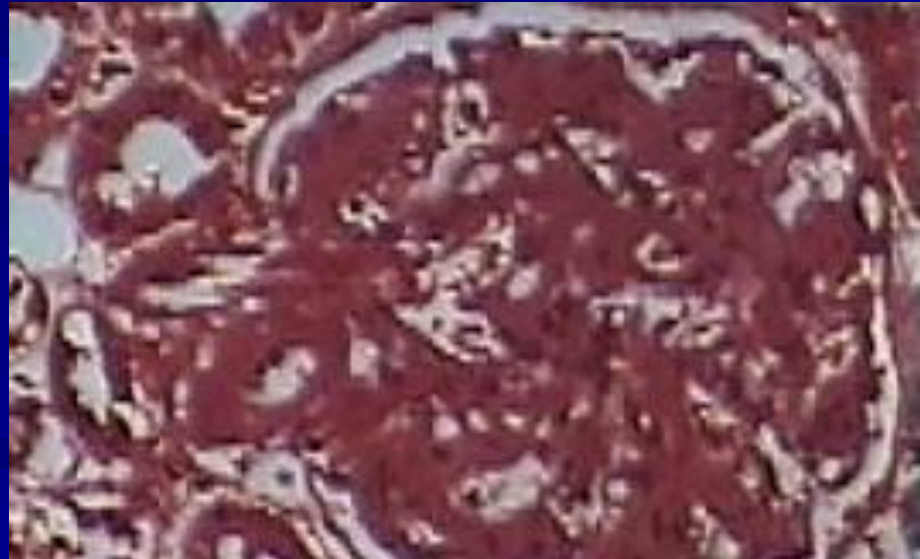
# ...Tiger by the tail







Normal Kidney



Diabetic Kidney

# What is the Diabetic Nephropathy?

Clinical syndrome

- Persistente proteinuria
- Hypertension
- Progressive decline in renal function

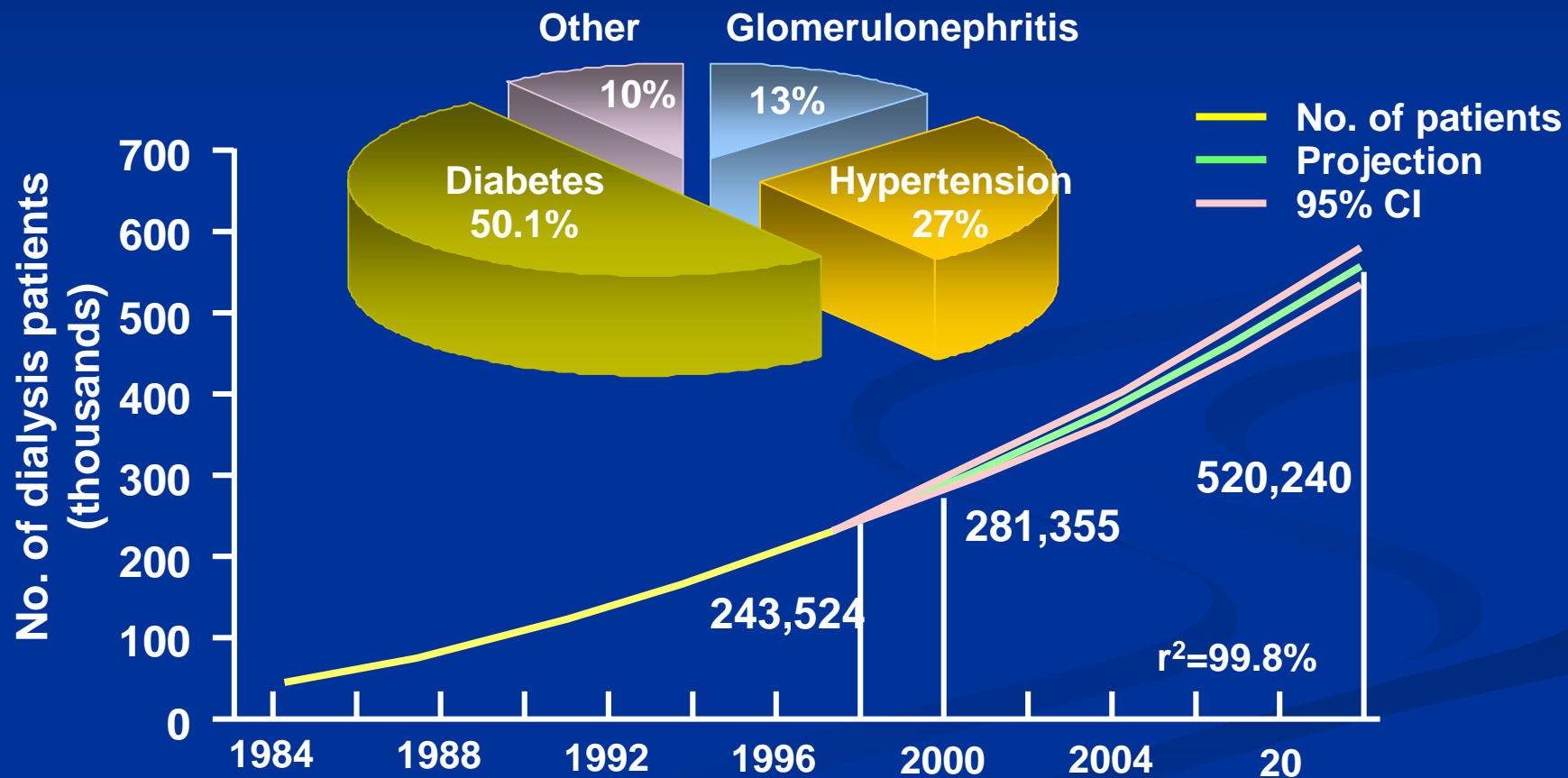
# Introduction

- Increased prevalence of DM
- Diabetic nephropathy – commonest cause of ESRD
- heavy burden on resources



# Diabetes: The Most Common Cause of ESRD

## Primary Diagnosis for Patients Who Start Dialysis



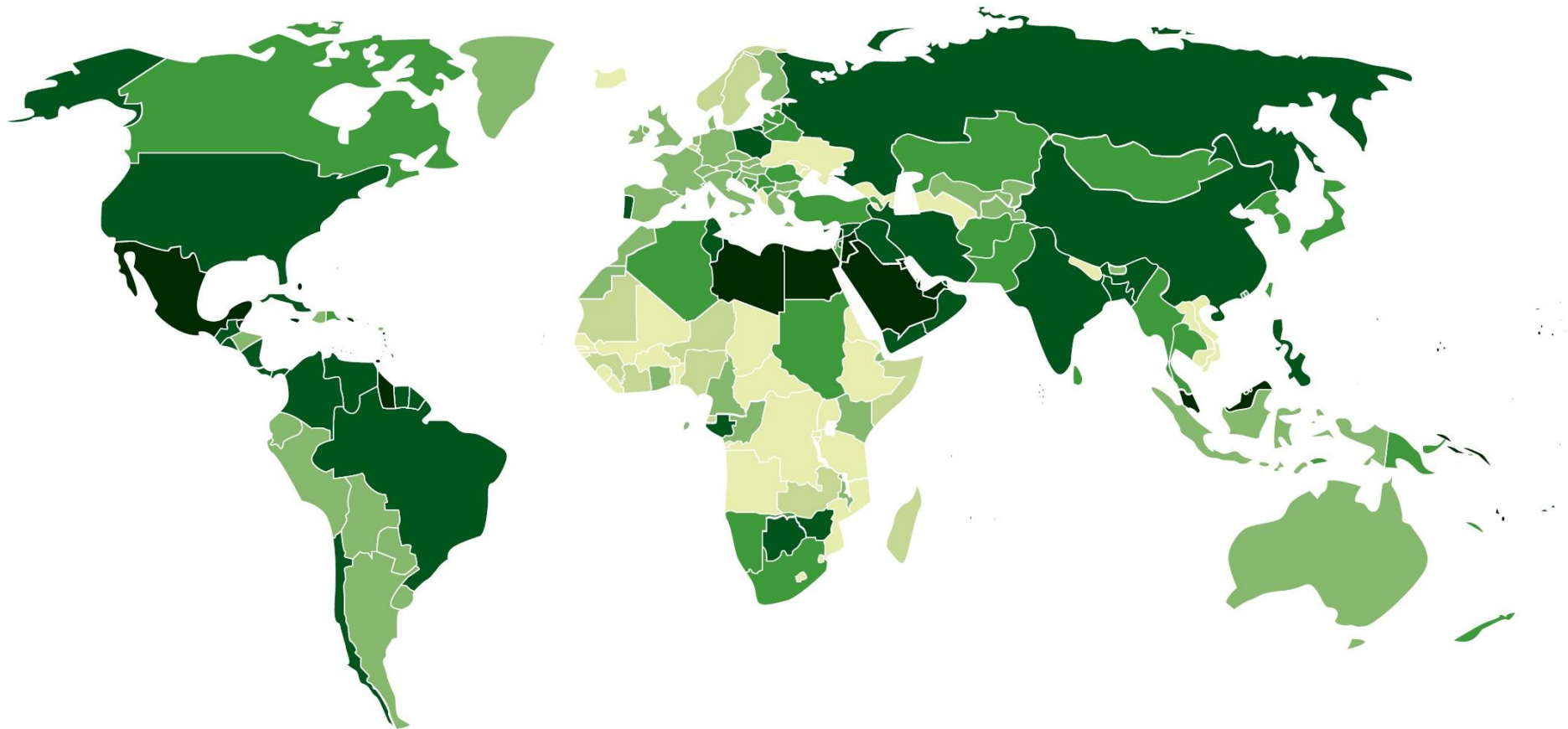
# Diabetes Statistics

310 million diagnosed with Diabetes in  
2015 USA spent \$201 billion of its  
healthcare dollars on diabetes or 43% of  
global healthcare expenditure due to  
diabetes



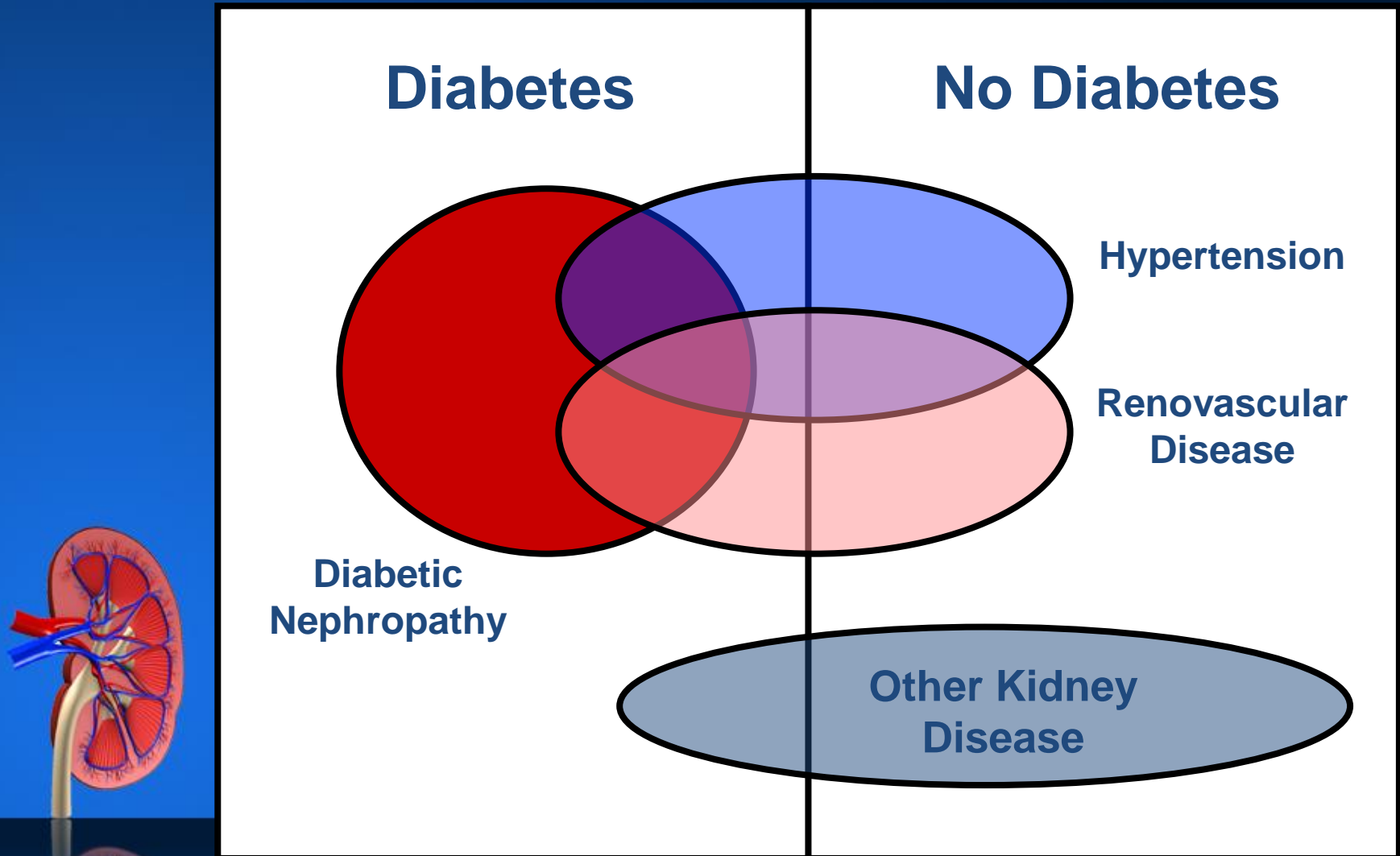


# Worldwide Prevalence of Diabetes



\*comparative prevalence

# The Spectrum of CKD in Patients with Diabetes



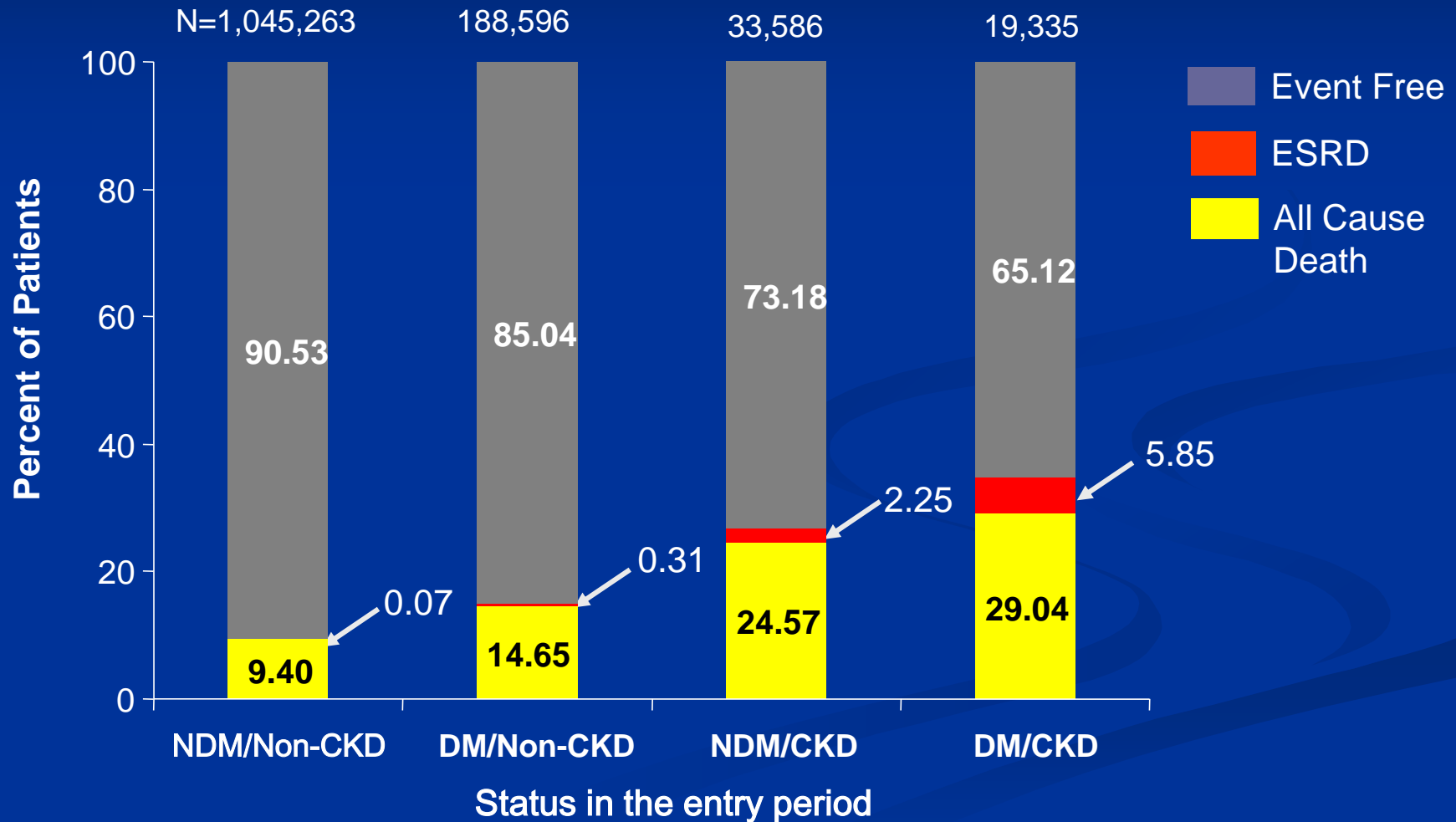
**Diabetes is the most important cause of ESRD but very few diabetics are on renal replacement**



- Diagnosed Diabetes
- Undiagnosed Diabetes
- Diabetics on RRT

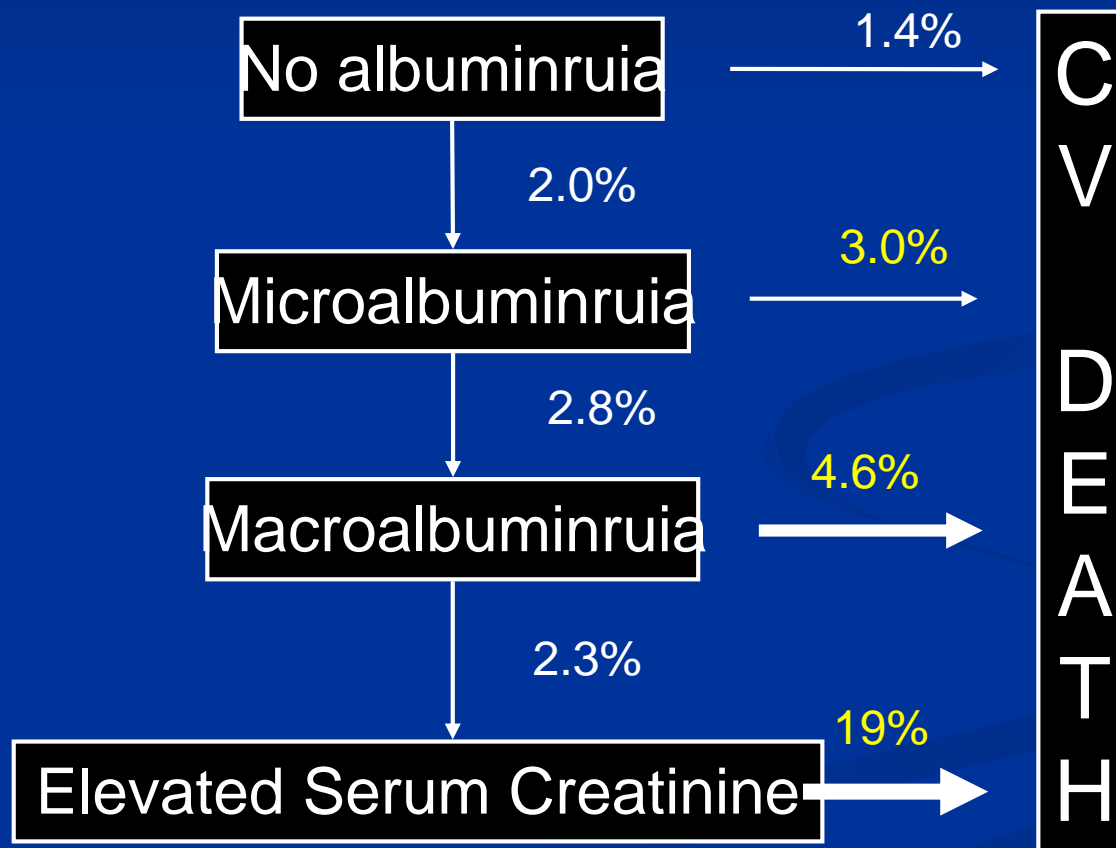
# Diabetics with Nephropathy (DM/CKD) are More Likely to Die than to Progress to ESRD

5% Medicare sample , cohort, 2 year follow-up



# Diabetics with Macroalbuminuria are More Likely to Die than Develop ESRD

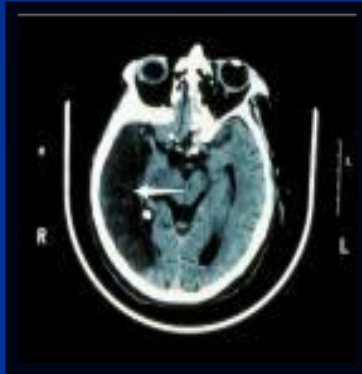
Newly diagnosed, predominantly white, medically treated



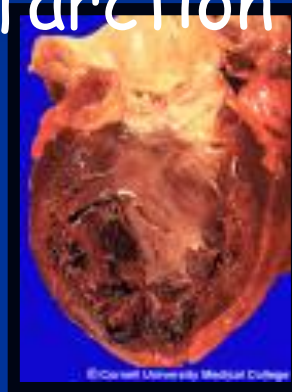


# What are Diabetics with Nephropathy Dying From?

Stroke



Myocardial Infarction



Heart Failure



Sudden Death



# ***Risk factors for developing Diabetic Nephropathy***

- Poor control of blood glucose,
- Long duration of Diabetes,
- Presence of other diabetic complication,
- Ethnicity (Asian, Pima Indians),
- Pre-existing High BP,
- Family h/o of Diabetic Nephropathy,
- Family h/o Hypertension.

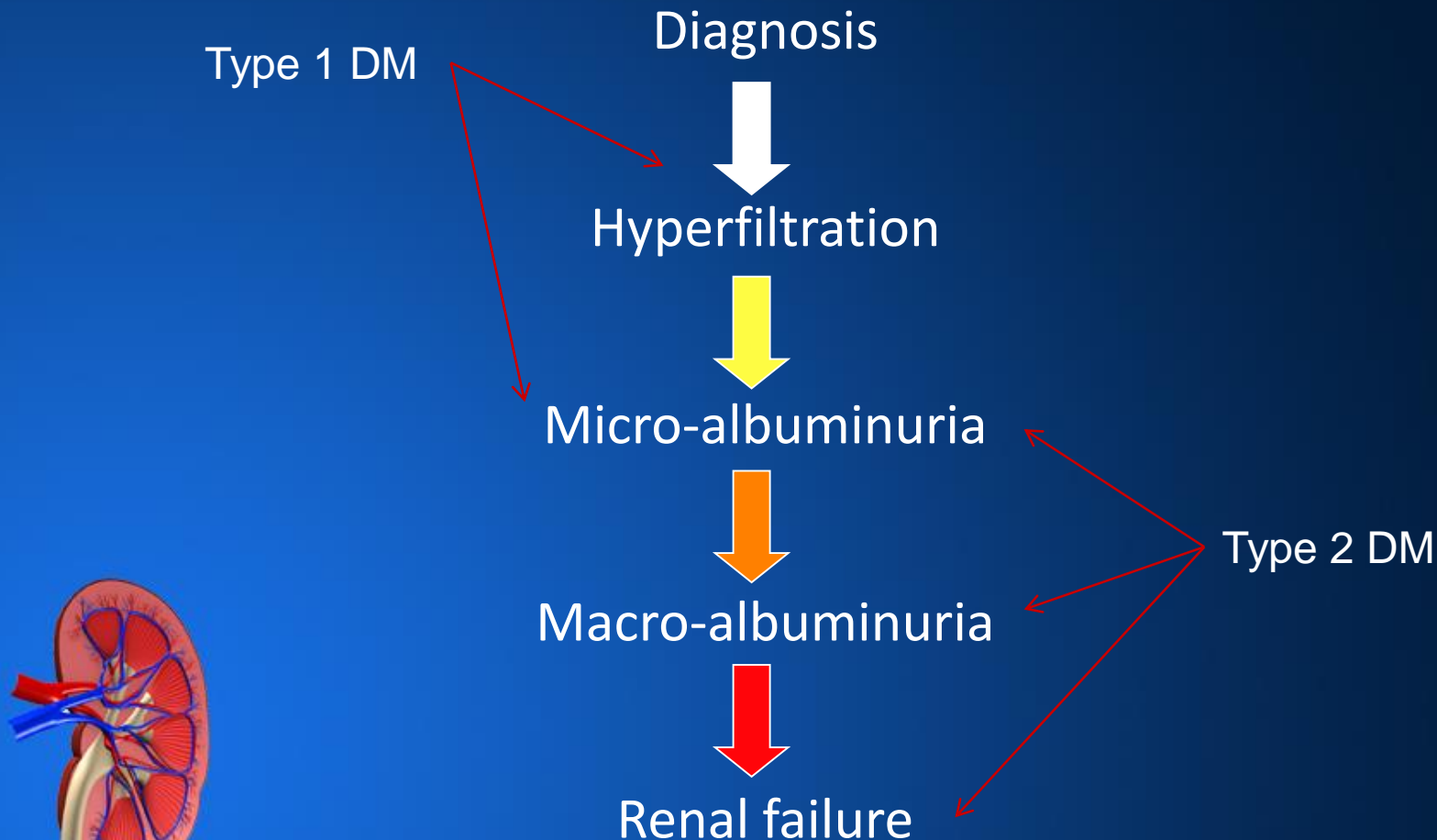
# Definition of Diabetic Nephropathy

- Clinical diagnosis based on Hx, Exam and urine albumin/creatinine ratio in most cases
- Longstanding History of diabetes  $\pm$  retinopathy
- Macroalbuminuria (a.k.a “overt nephropathy”) defined as random urine albumin/creatinine ratio  $\geq 300$  mg/g
- Hypertension ( $> 90\%$ )
- Renal Biopsy confirmation is rare

# Diabetic Nephropathy

- Clinical syndrome consisting of
  - Protein in urine
  - High BP
  - Decline in renal function
- If > 25 years elapse - unlikely to develop nephropathy.

# When does Nephrology get involved?





# What's happening in the Nephron?

## Earliest change:

- Glomerular enlargement
- GBM widening

## Early lesions:

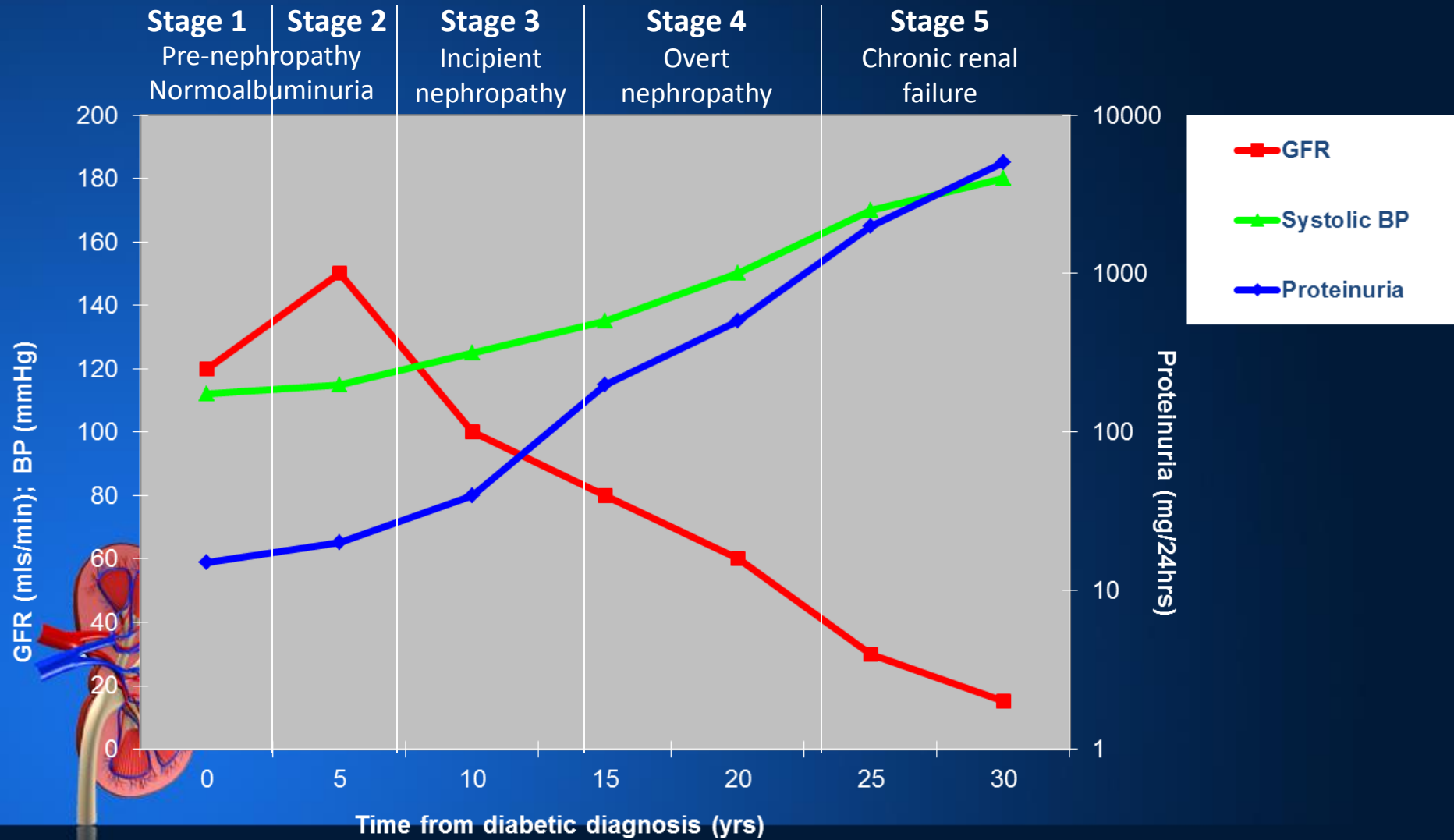
- Mesangial expansion
- Mesangiolysis

## Established lesions

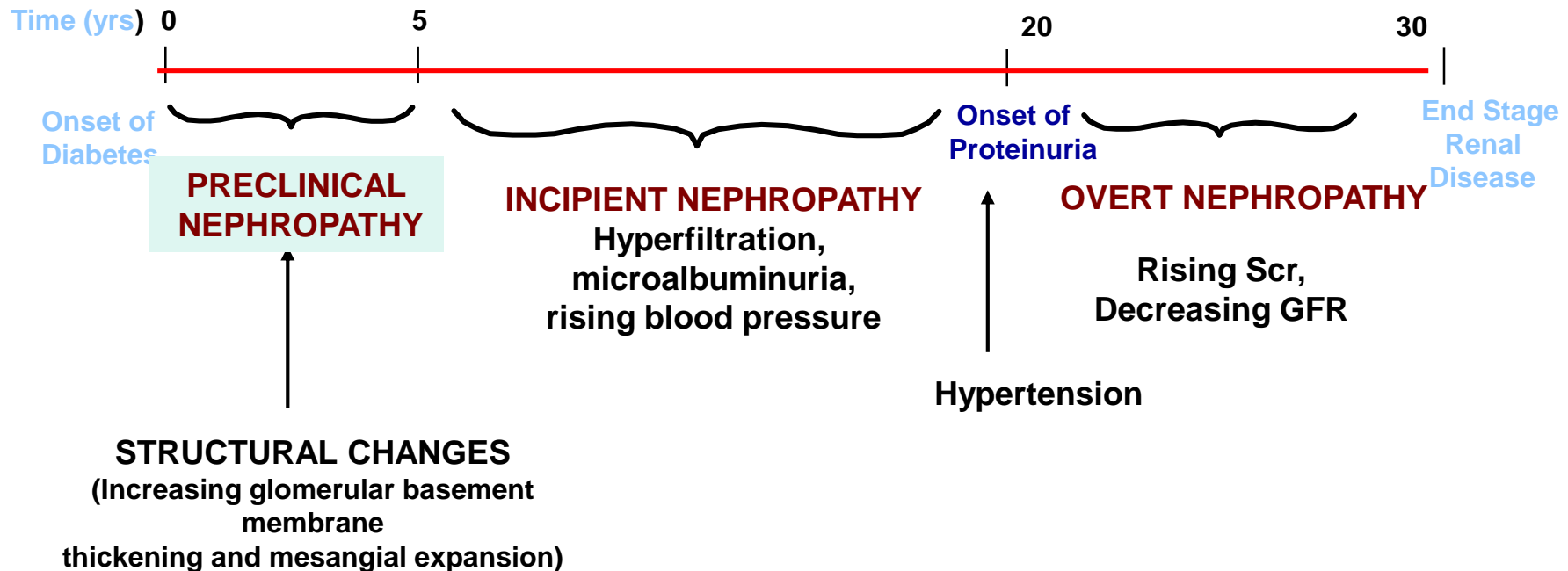
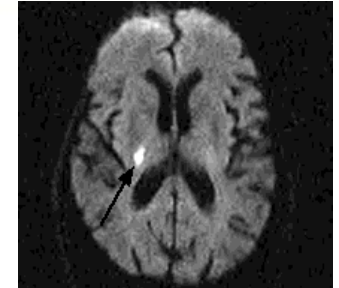
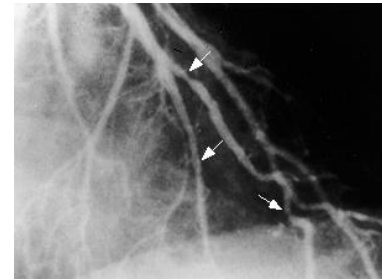
- Nodular sclerosis
- Marked mesangial expansion
- Afferent, efferent arteriolar hyaline
- Microaneurysms



# Natural history of diabetic nephropathy



# Course of Diabetic Nephropathy



# Diabetic Nephropathy

## Microalbuminuria :

- ✗ first sign of nephropathy
- ✗ a strong and independent predictor of cardiovascular disease



# **Guidelines 1:**

## **Screening for proteinuria**

**Screening for proteinuria should be performed yearly in the following patients\*:**

**(a) Type 1 DM : 5 years after diagnosis of diabetes, or earlier in the presence of other CV risk factors**

**(b) Type 2 DM: at the time of diagnosis of diabetes**

**Grade C**

*\*Other factors affecting urinary albumin excretion should be excluded when screening for microalbuminuria and proteinuria*





## **Guidelines 2:**

### **Method of screening for proteinuria**

**Urine should be screened for proteinuria with conventional dipstick on an EMU specimen\***

**Grade C**

*\*Other factors affecting urinary albumin excretion should be excluded when screening for microalbuminuria and proteinuria*



# *Microalbuminuria*

- Called micro... because it is not detectable by normal urine dip stick
- Urinary albumin (30 - 300 mg/day)
- Becomes irreversible when reaches 300
- Detected by newer generation dipstix (micral)

## **Guidelines 3:**

### **Screening for microalbuminuria**

- (a) If urine dipstick for proteinuria is -ve, screening for MA should be performed on an EMU specimen**
- (b) Urine dipstick for MA is an acceptable screening test**
- (c) If MA is detected, confirmation should be made with 2 further tests within a 3 to 6 month period**

Grade C

*\*Other factors affecting urinary albumin excretion should be excluded when screening for microalbuminuria and proteinuria*



# SPECIMEN COLLECTION

- - 
  - 
  - 
  -
- ★ Collect freshly voided urine in a clean, dry container
  - ★ Preservatives should be avoided
  - ★ Samples which cannot be tested within 3 days of collection should be refrigerated
  - ★ Samples should not be frozen
  - ★ The test should be free from significant interference from glucosuria, pH, ketonuria or bacterial contamination

# ADVANTAGES AND DISADVANTAGES

## *METHODS OF MICROALBUMINURIA ANALYSIS*

Random  
spot collection

Easy to perform  
Generally provides accurate information

First void  
or morning  
collection

Preferred due to diurnal variation in albumin excretion

Timed  
collection

Gold standard  
Notoriously labour and time intensive    Patients co-operation difficult



# SCREENING FOR MICROALBUMINURIA

## Three methods

- Albumin to creatinine ratio in random spot collection
- 24 - h urine collection with creatinine
- Timed collection (4-h or overnight)

# Screening methods

## Microalbuminuria testing



# Factors affecting urinary albumin excretion

Increases AER	Decreases AER
<ul style="list-style-type: none"><li>■ Strenuous exercise</li><li>■ Poorly controlled DM</li><li>■ Heart failure</li><li>■ UTI</li><li>■ Acute febrile illness</li><li>■ Uncontrolled HPT</li><li>■ Haematuria</li><li>■ Menstruation</li><li>■ Pregnancy</li></ul>	<ul style="list-style-type: none"><li>■ NSAIDs</li><li>■ ACE inhibitors</li></ul>



# DEFINITION OF MICROALBUMINURIA

Stage	24h collection	Timed collection	Spot collection
Normoalbuminuria	< 30 mg/24h	<20 $\mu$ g/min	<30 $\mu$ g/mg creat
Microalbuminuria	30-300 mg/24h	20-200 $\mu$ g/min	30-300 $\mu$ g/mg creat
Clinical albuminuria	>300 mg/24h	>200 $\mu$ g/min	>300 $\mu$ g/mg creat



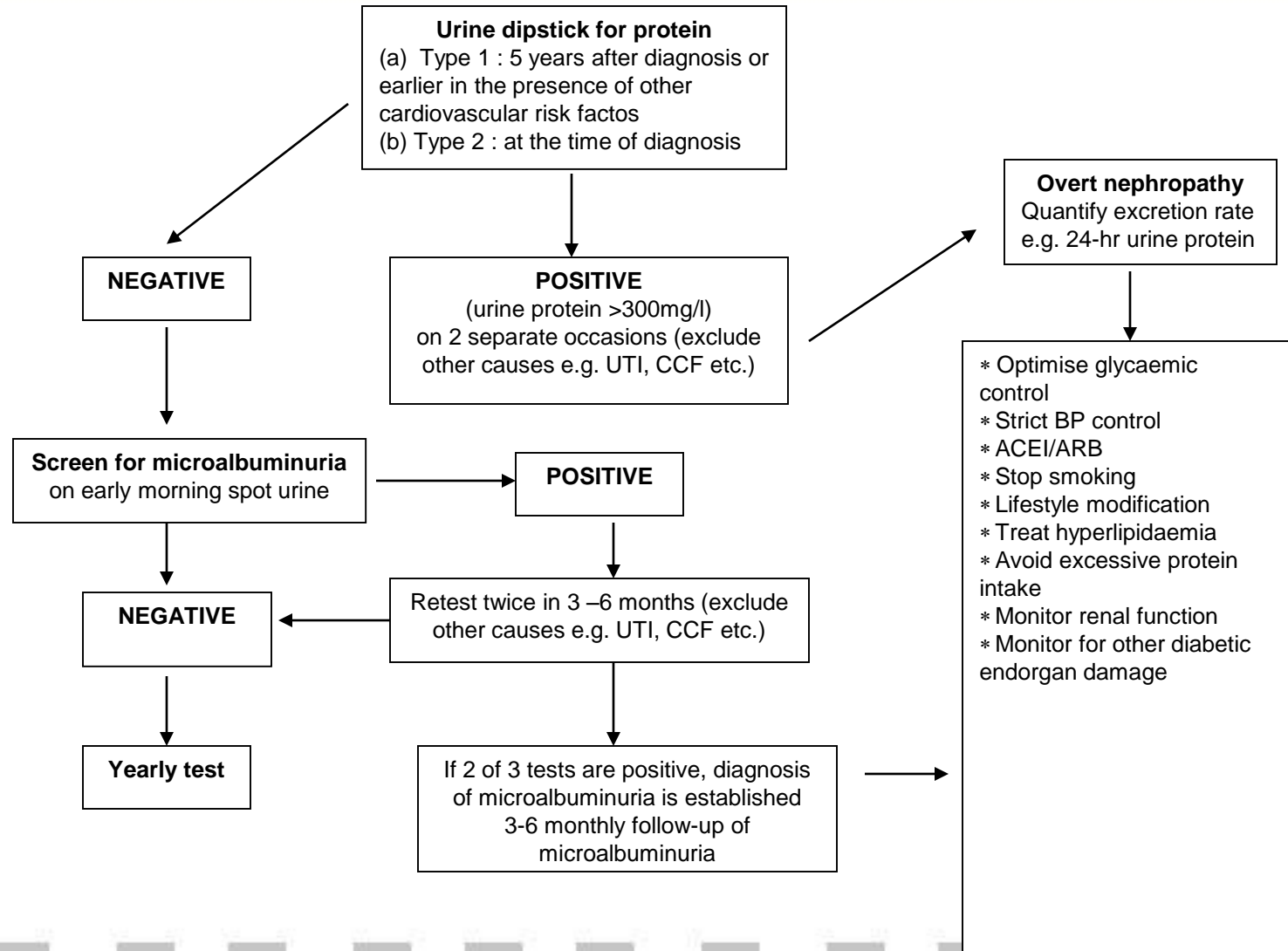
## SPECIFICITY AND SENSITIVITY FOR MICROALBUMINURIA

*Timed urine collection - gold standard*

	Sensitivity (%)	Specificity (%)
Random spot specimen	89	85
First morning void	70	93



# Algorithm : Screening for Proteinuria



## **Guidelines 4: Glycaemic control**

**Glycaemic control should be optimised, with:**

**$\text{FBS} \leq 6 \text{ mmol/l}$  and/or**

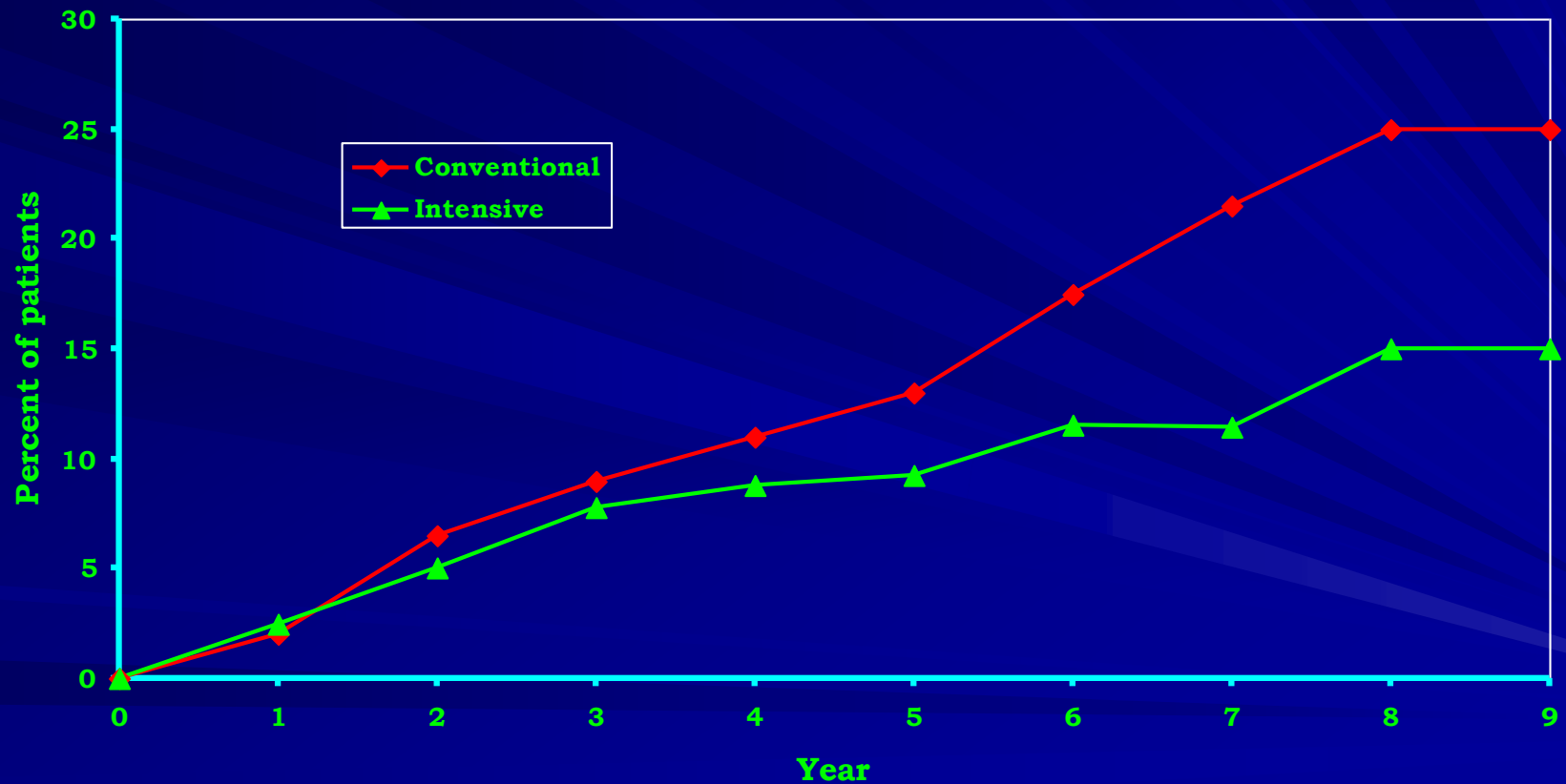
**$\text{HbA1c} \leq 7\%$**

**Grade A**





# *Strict glycemic control prevents microalbuminuria in type 1*



## **Guidelines 5:**

### **Target blood pressure**

**Target blood pressure in diabetics should be less than 130/80**

Grade B



## **Guidelines 7:**

### **Target BP in overt nephropathy**

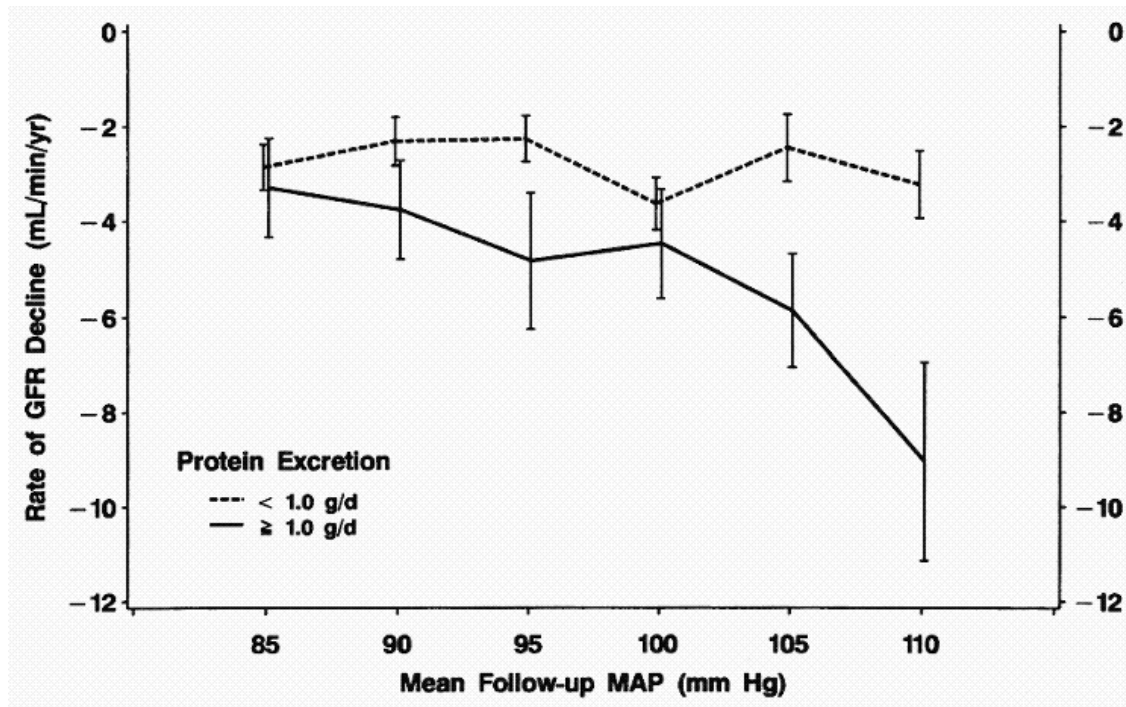
**In patients with proteinuria > 1 g/day, target blood pressure should be lowered to < 125/75**

Grade B



# Target BP in Overt Nephropathy MDRD

Mean GFR decline and achieved follow-up BP according to baseline proteinuria



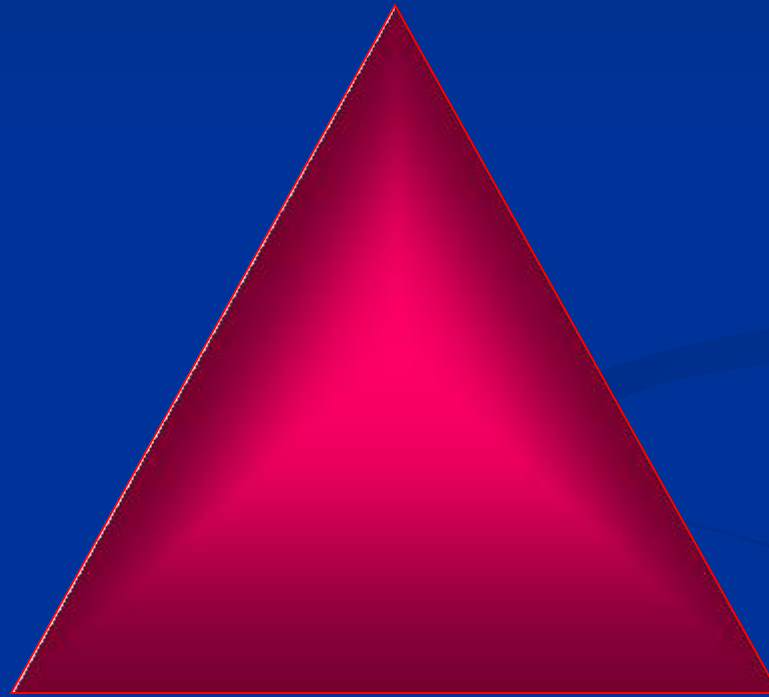
What is the Proper Therapy  
of Kidney Disease in patients  
with Diabetes?

# The Renal Injury Triad

Angiotensin II

Hypertension

Proteinuria



## **Guideline 6:**

### **Treatment of microalbuminuria**

**ACEIs or ARBs should be initiated for reduction of microalbuminuria unless contraindicated**

ACEIs in type 1 & type 2 diabetics : Grade A

ARBs in type 2 diabetics : Grade A





**Evidence for use of  
ARB  
in  
type 1 and type II  
Diabetes mellitus with  
microalbuminuria**



**Are ARBs  
superior to  
ACE inhibitors  
in DM with  
microalbuminuria?**



**Is Combination Therapy With  
An ACE Inhibitor And An ARB  
Safe And Effective For Patients  
With Diabetic Renal Disease?**

## **Guideline 7:**

### **Treatment of overt nephropathy**

- **In Type 1 diabetics with overt proteinuria, ACEIs should be initiated unless contraindicated**

Grade A

- **In Type 2 diabetics with overt proteinuria, ARBs or ACEIs should be initiated unless contraindicated**

ARBs : Grade A

ACEIs : Grade B



## *Diet*

- Calories - 35 K cal / kg
- Proteins of high quality - 0.8 gm / kg
- Salt - 4 - 5 gm / day
- Potassium - 50 - 60 meq/day
- Lipids 30 % of calorie intake.

## *Others*

- Lipid lowering - diet, statins
- Low dose aspirin
- Avoid nephrotoxic drugs & contrast procedures
- Prevent & treat infections energetically
- Hepatitis B immunization
  - Early immunization ideal
  - if Cr. > 3 double & more frequent dosing

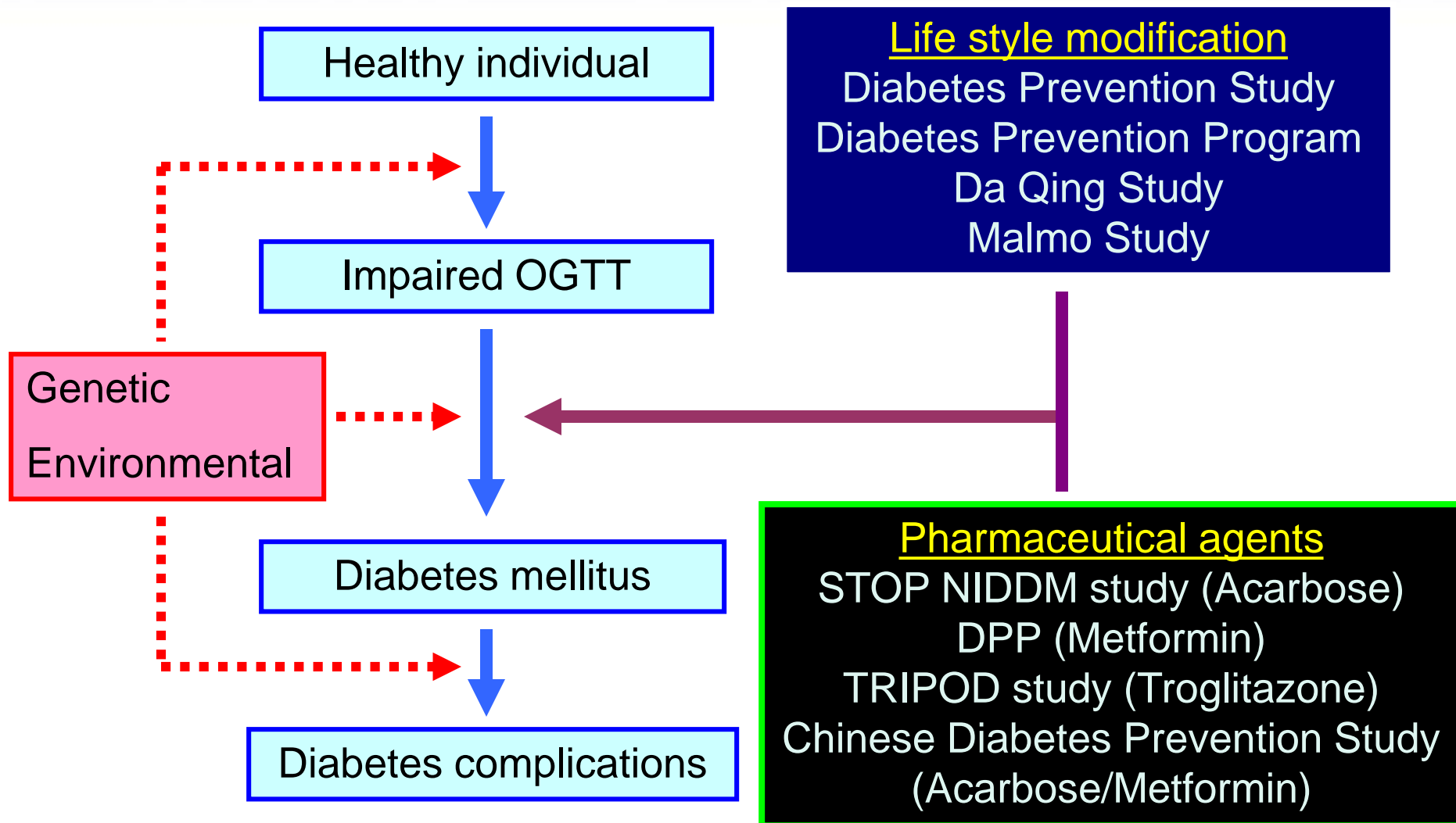
# Referral to nephrologist

## Earlier referral to a nephrologist may be indicated if:

- ✗ the diagnosis of diabetic nephropathy is in doubt
- ✗ nephrotic syndrome or unexplained haematuria occurs
- ✗ a sudden worsening of renal function occurs
- ✗ blood pressure is difficult to control
- ✗ hyperkalaemia arises
- ✗ renal artery stenosis is suspected



# Prevention of Diabetes





# Prevention of Diabetes

