Corso di Nefrologia

Corso di laurea

Triennale

FISIOTERAPIA

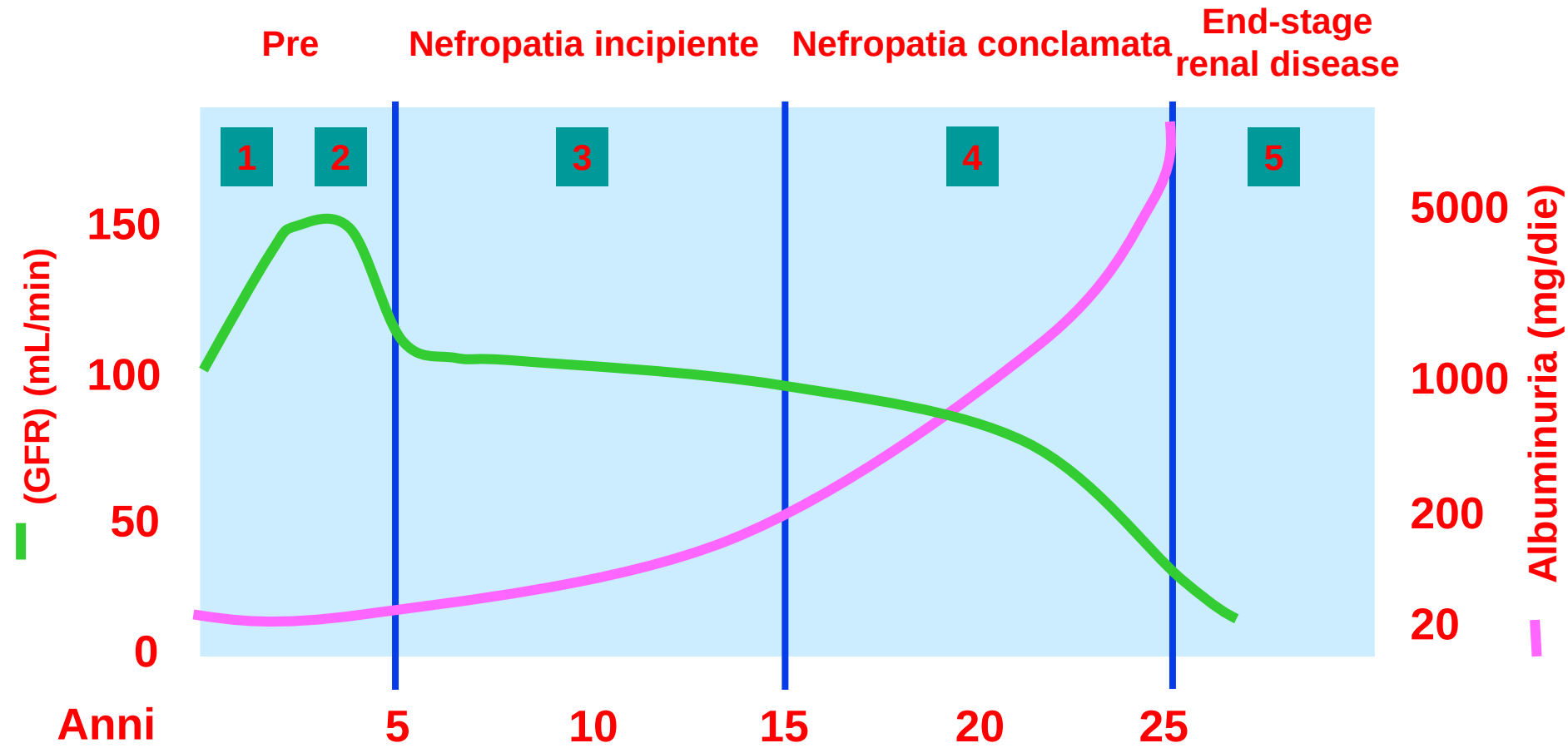
Prof. Carlo Manno

LA NEFROPATIA DIABETICA

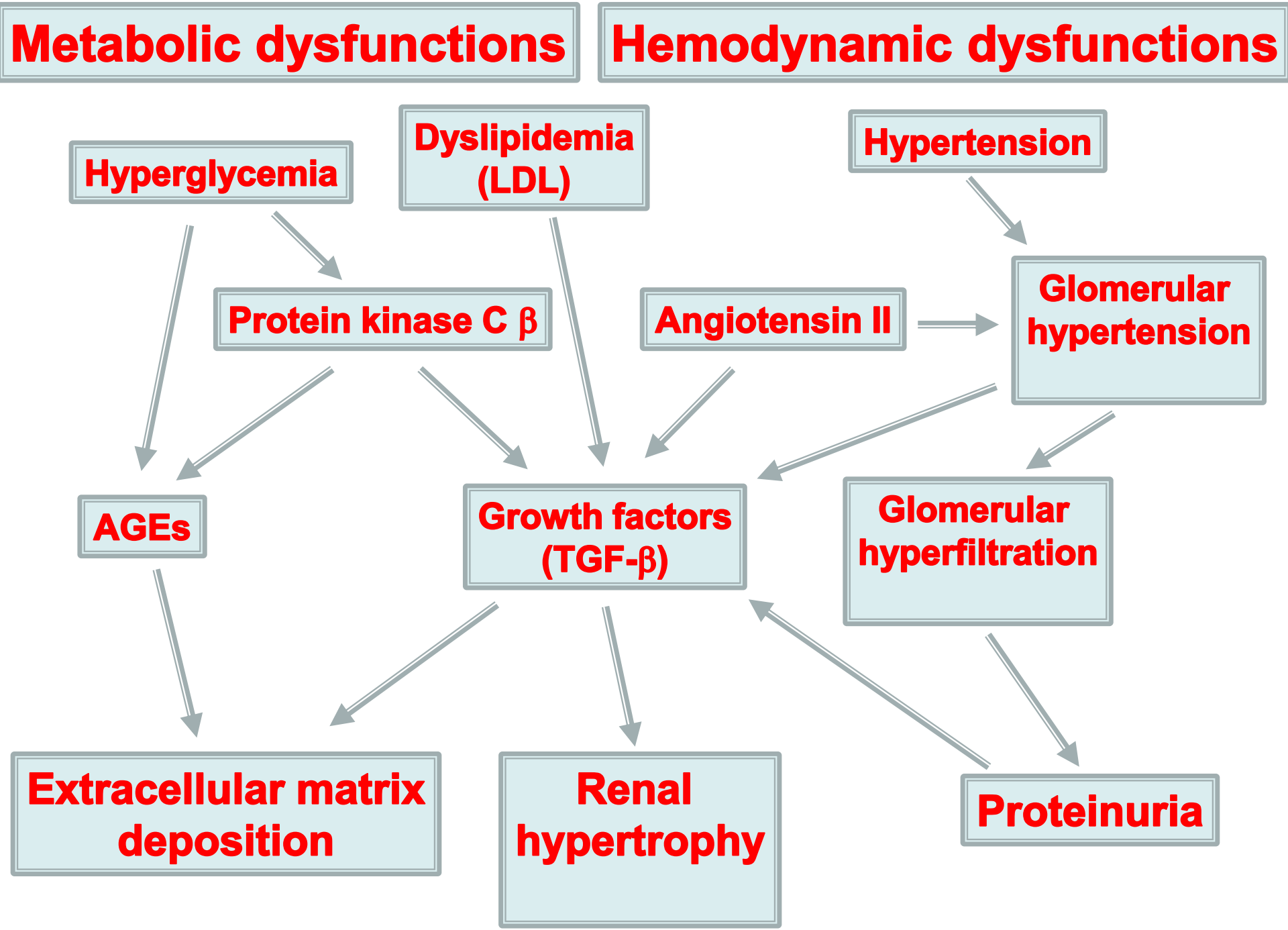
NEFROPATIA DIABETICA

- **Caratterizzata dalla presenza di albuminuria persistente (>300 mg/24h o >200μg/min, valutata in almeno due occasioni a 3-6 mesi di distanza)**
- **Sviluppo di ipertensione, progressivo aumento della proteinuria, declino del GFR e progressione della malattia renale cronica (MRC)**

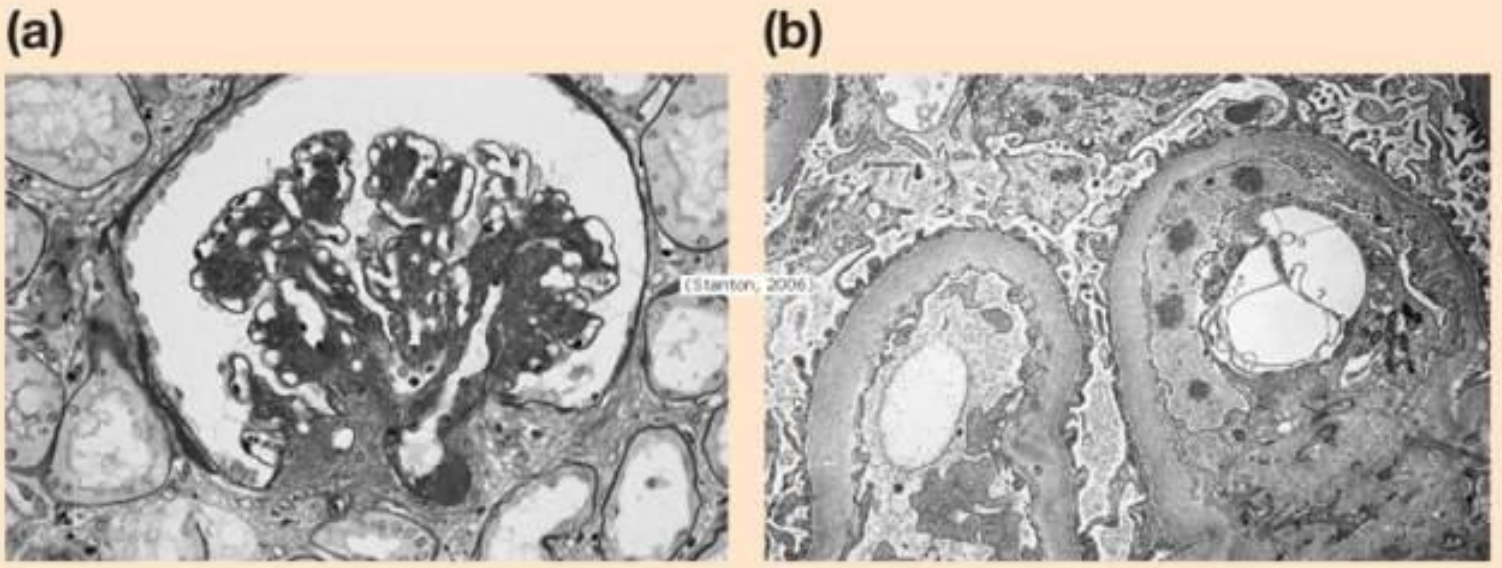
LA STORIA NATURALE DELLA NEFROPATIA DIABETICA



Alterazioni funzionali	GFR ↑	Microalbuminuria, Ipertensione	Macroalbuminuria, sindrome nefrosica, GFR↓
Alterazioni strutturali	Ipertrofia renale	Espansione mesang., Ispessimento GBM, Ialinosi arteriolare	Noduli mesangiali (Kimmesteil-Wilson) Fibrosi tubulo-interstiziale

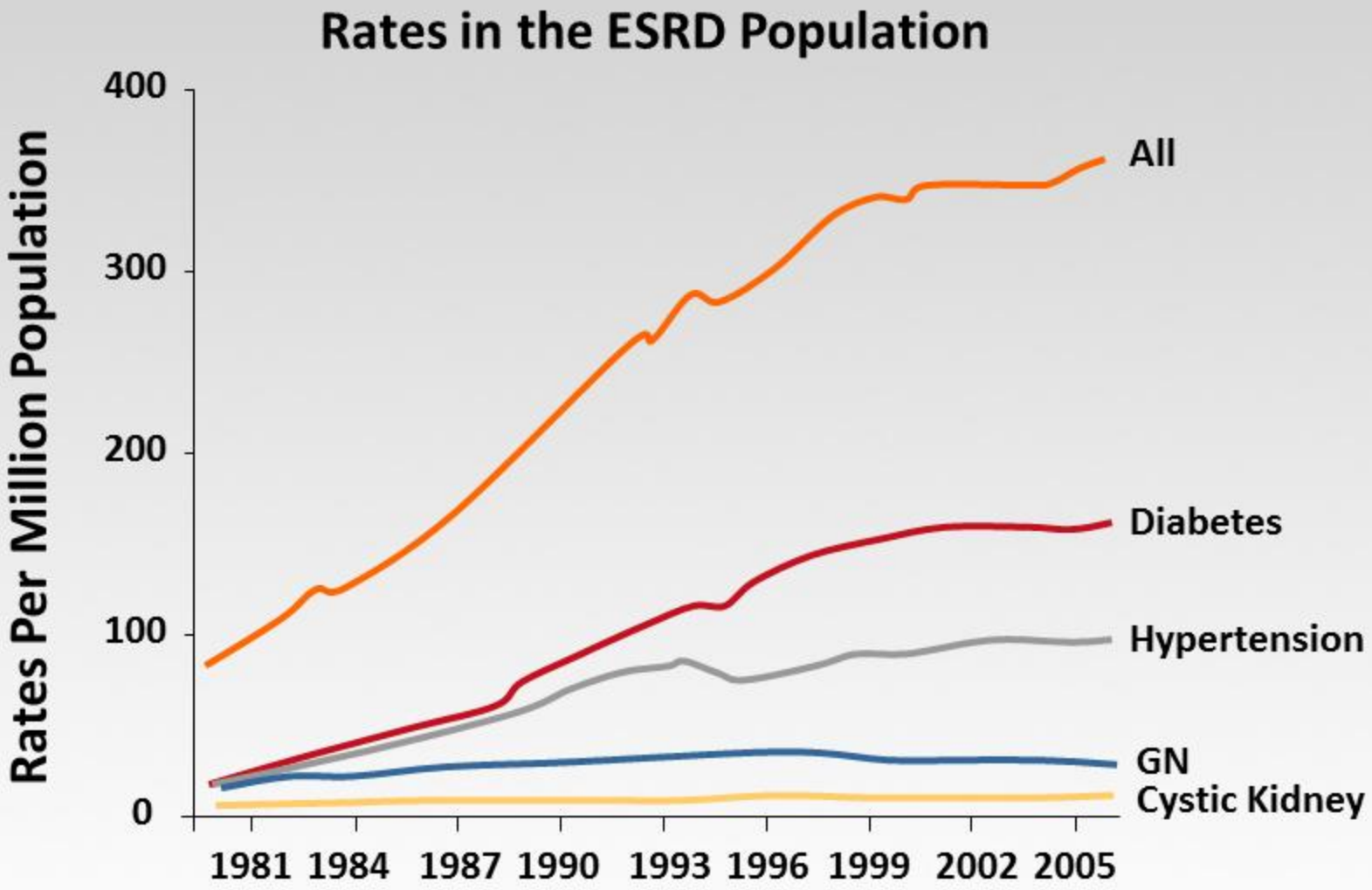

Metabolic dysfunctions
Hemodynamic dysfunctions
Hyperglycemia
Dyslipidemia (LDL)
Hypertension
Protein kinase C β
Angiotensin II
Glomerular hypertension
AGEs
Growth factors (TGF-β)
Glomerular hyperfiltration
Extracellular matrix deposition
Renal hypertrophy
Proteinuria

LESIONI ISTOLOGICHE NELLA NEFROPATIA DIABETICA



From: Stanton RC. *Atlas of Diabetes*. 3rd edn. Skyler J, ed. Current Medicine LLC, Philadelphia, PA; 2006.

Diabetes Is the Major Cause of ESRD



ESRD = end-stage renal disease; GN = glomerular nephritis

http://www.usrds.org/2008/view/esrd_00_intro.asp

UNITED STATES RENAL DATA SYSTEM

INCIDENT AND PREVALENT COUNTS BY QUARTER

October 2011 - Most Current

Incident Counts | Incident Chart | Prevalent Counts | Prevalent Chart

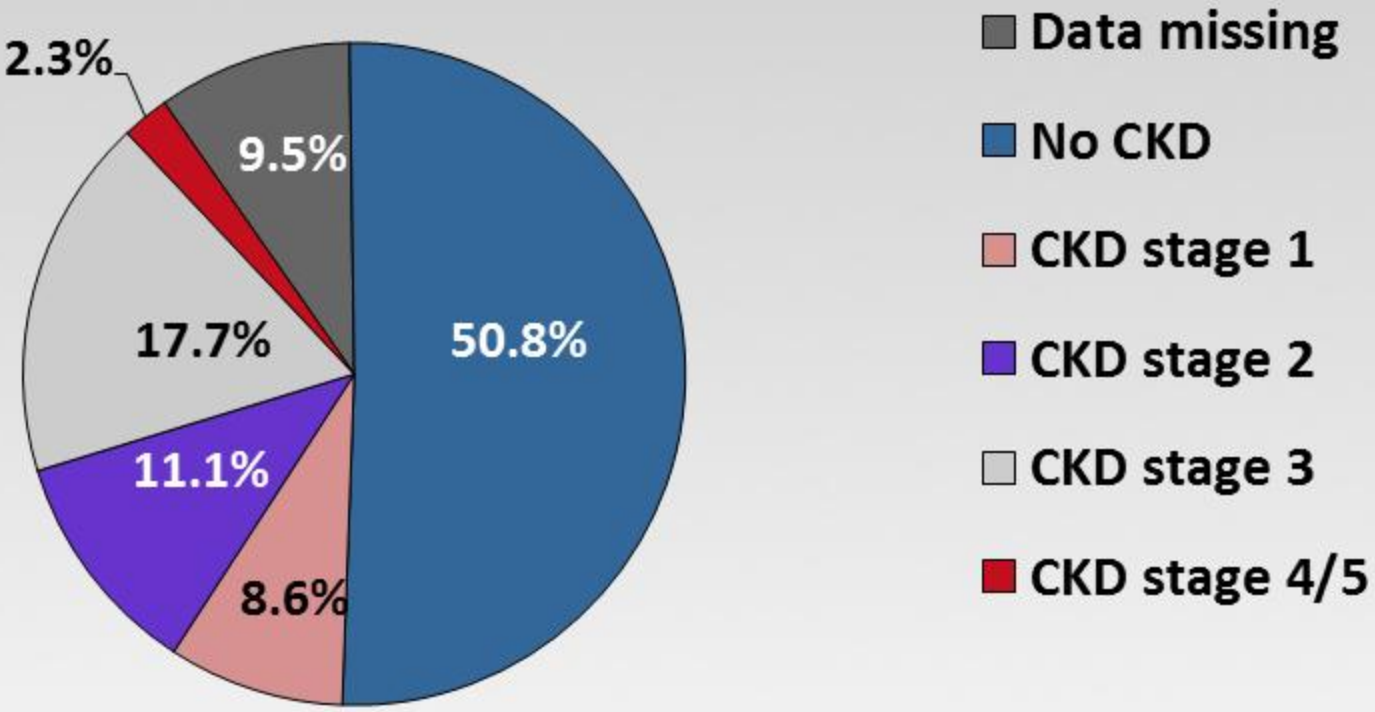
Point prevalent counts of reported ESRD, 2009/4Q - 2011/1Q

	2009^	2010^^				2011^^
	Qtr4	Qtr1	Qtr2	Qtr3	Qtr4	Qtr1
0 - 19	7,738	7,713	7,770	7,774	7,843	7,907
20 - 44	100,031	100,688	101,270	101,453	101,910	102,530
45 - 64	256,803	260,222	263,996	267,081	269,890	273,620
65 - 74	116,607	118,363	120,247	121,866	123,504	125,144
75 +	90,233	91,651	93,162	94,192	95,262	96,171
Missing	*	*	*	*	*	*
Male	323,276	327,752	332,624	336,330	339,804	344,231
Female	248,127	250,873	253,808	256,023	258,589	261,129
Unknown	11	12	13	14	16	16
Diabetes	215,245	218,347	221,277	223,215	225,154	227,490
Hypertension	140,498	142,605	144,652	146,150	147,731	149,623
Glomerulonephritis	84,883	85,342	85,855	86,249	86,604	87,007
Cystic kidney	27,254	27,538	27,790	28,103	28,341	28,576
Other urologic	13,108	13,136	13,185	13,229	13,291	13,285
Other cause	62,315	63,294	64,715	65,921	67,232	68,670
Unknown cause	21,563	21,744	22,067	22,302	22,480	22,633
Missing disease	6,548	6,631	6,904	7,198	7,576	8,092
All	571,414	578,637	586,445	592,367	598,409	605,376

Cause dell'incremento dei diabetici in dialisi

- **Incremento prevalenza del diabete di tipo II nella popolazione generale (invecchiamento della società)**
- **Migliorata sopravvivenza dei diabetici**
- **Limiti meno ristretti all'ammissione al trattamento dialitico cronico**

Renal Dysfunction is Common in US Patients with T2DM



Approximately 40% of patients with T2DM show signs of CKD*

CKD = chronic kidney disease; T2DM = type 2 diabetes mellitus

*Based on US data from 1462 patients aged ≥20 yrs with T2DM who participated in the Fourth National Health and Nutrition Examination Survey (NHANES IV) from 1999 to 2004.

Koro CE, et al. *Clin Ther.* 2009;31:2608-2617.

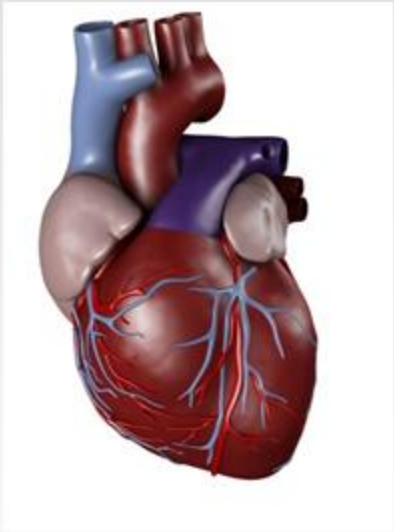
A Close Relationship Exists Between Cardiac and Renal Pathophysiology in T2DM

CKD
Glomerular/Interstitial damage

Cardiorenal risk factors

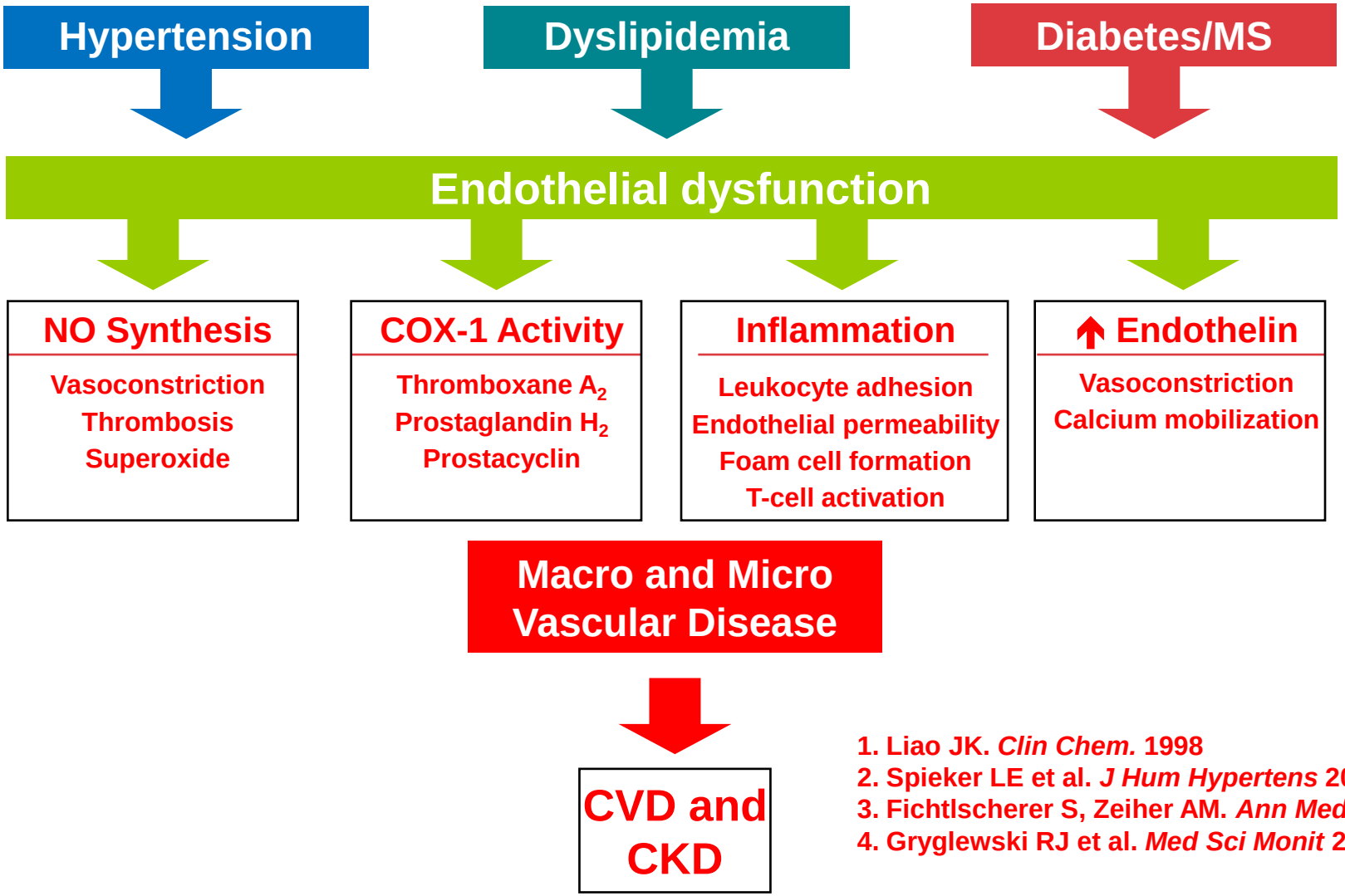
T2DM
Smoking
Obesity
Hypertension
Dyslipidemia
Genetic risk factors
Acquired risk factors

Heart disease
Increased ischemic risk
Left ventricular hypertrophy



Afghahi H, et al. *Nephrol Dial Transplant*. 2011;26:1236-1243;
Ronco C, et al. *J Am Coll Cardiol*. 2008;52:1527-1539.

I fattori di rischio promuovono la malattia cardiovscolare (CVD) e la malattia renale cronica (CKD) mediante la disfunzione endoteliale



1. Liao JK. *Clin Chem.* 1998
2. Spieker LE et al. *J Hum Hypertens* 2000
3. Fichtlscherer S, Zeiher AM. *Ann Med* 2000
4. Gryglewski RJ et al. *Med Sci Monit* 2001

COSA ESPRIME LA MICROALBUMINURIA?

1) **Microalbuminuria come espressione di iperfiltrazione glomerulare**
2) **Microalbuminuria come espressione di danno endoteliale sistemico**

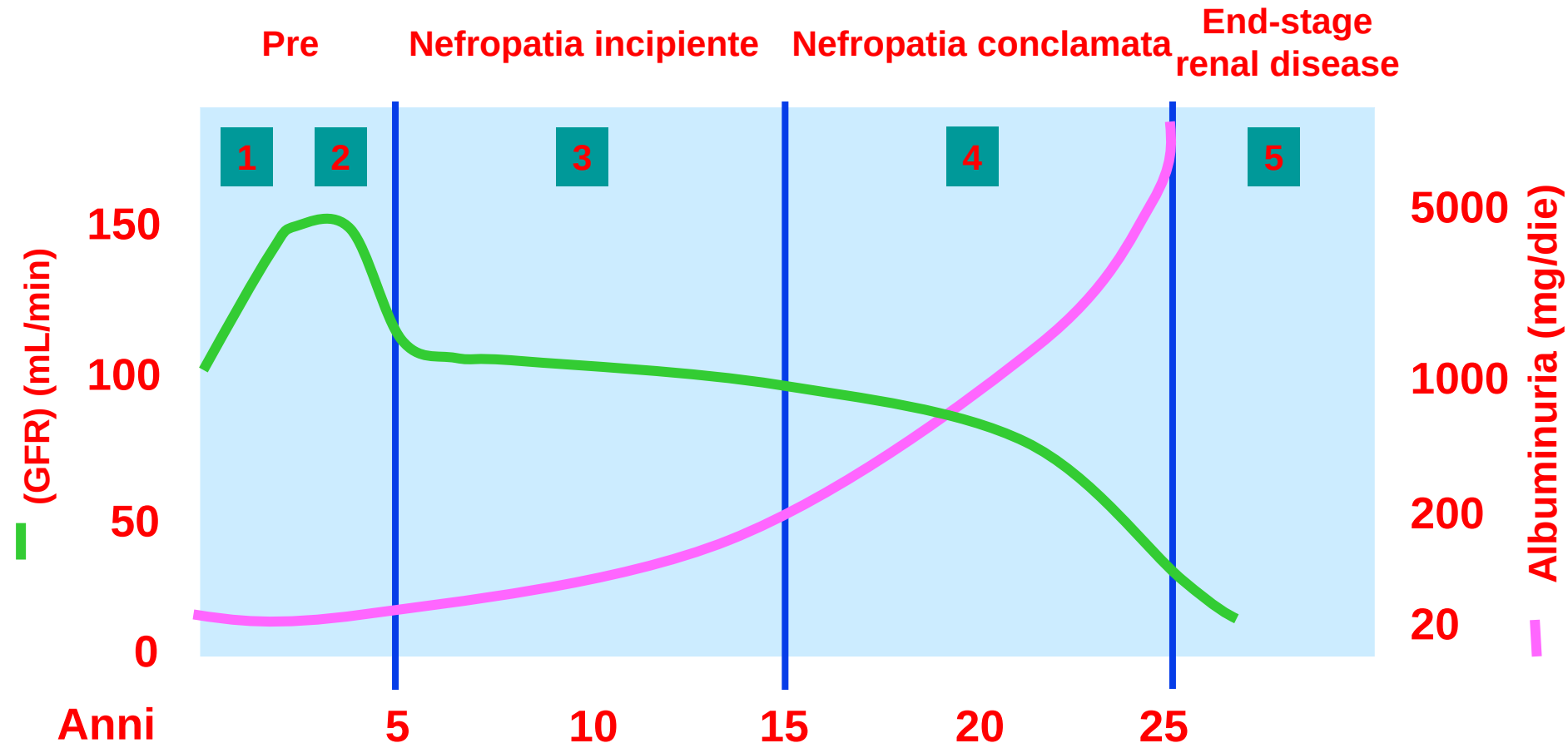
TABLE 1. **Definitions of Abnormalities in Albumin Excretion**

Category	Spot collection (mg/g creatinine)	24-h collection (mg/24 h)	Timed collection (μg/min)
Normal	<30	<30	<20
Microalbuminuria (low-level albuminuria)	30-299	30-299	20-199
Albuminuria	≥300	≥300	≥200

From *Diabetes Care*,[2] with permission from the American Diabetes Association.

PREVENZIONE E TRATTAMENTO CONSERVATIVO

LA STORIA NATURALE DELLA NEFROPATIA DIABETICA



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Prevenzione della Nefropatia Diabetica

- **Primaria: prevenzione della microalbuminuria**
- **Secondaria: bloccare/ridurre la progressione dalla micro- alla macro-albuminuria**
- **Terziaria: rallentare la progressione dell'in-sufficienza renale**

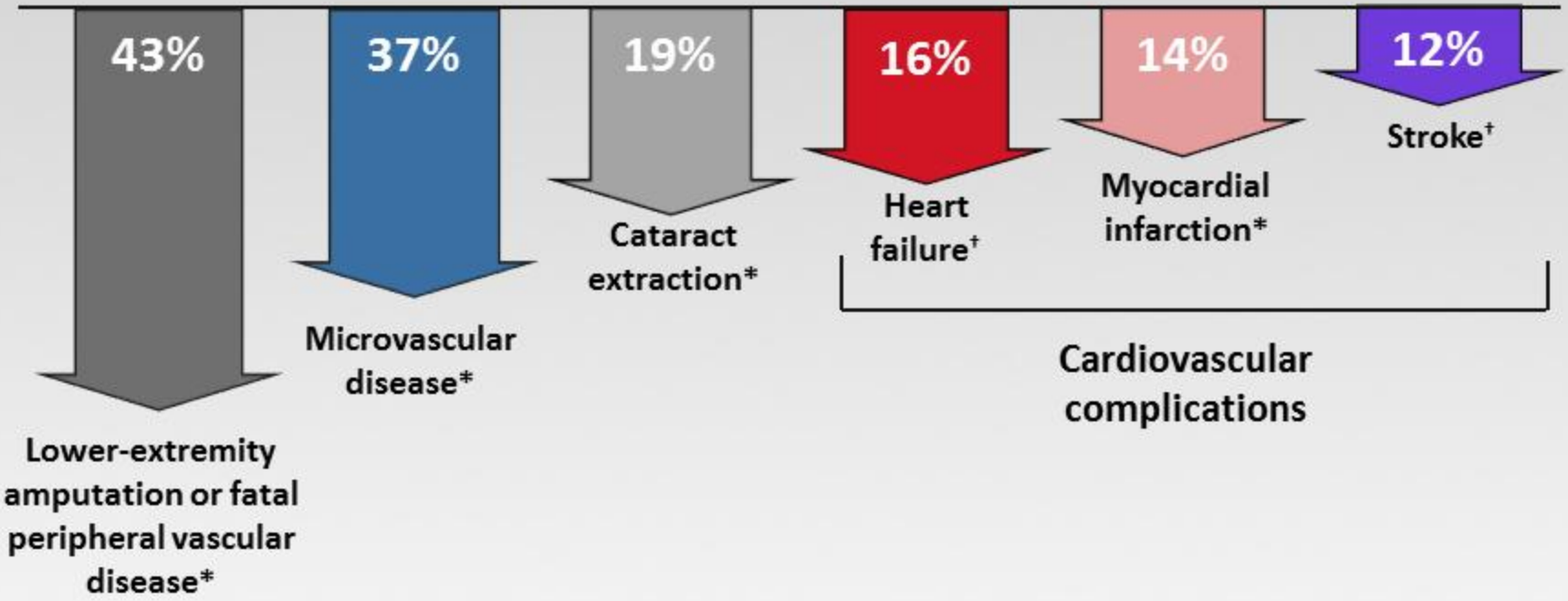
Recognition, Pathogenesis, and Treatment of Different Stages of Nephropathy in Patients With Type 2 Diabetes Mellitus

TABLE 4. **Multifactorial Approach to Treatment in Patients with Diabetic Nephropathy**[a]

Lifestyle modifications
Avoidance or cessation of smoking
Weight reduction (maintain normal body weight [BMI, 18.5-24.9])
Physical activity (engage in regular aerobic physical activity, such as brisk walking for ≥30 minutes per day, most days of the week)
Low protein diet (limit protein intake to 0.8-1.0 g/kg body weight per day in early-stage CKD and to ≤0.8 g/kg per day in late-stage CKD)
Adopt DASH eating plan (consume a diet rich in fruits, vegetables, and low-fat dairy products, with a reduced content of saturated and total fat)
Dietary sodium reduction (reduce dietary sodium intake to ≤100 mmol/d (2.4 g of sodium or 6 g of sodium chloride)
Moderate alcohol intake (limit consumption to ≤2 drinks per day for most men or 1 drink/day for women and lighter-weight individuals)
Achieve glycemic control (<7% HbA_{1c})[b]
Achieve blood pressure <130/80 mm Hg, using an ACE inhibitor or ARB as first-line treatment
Achieve LDL-C <100 mg/dL (<70 mg/dL is an alternative therapeutic option for very high-risk patients), using statins as first-line treatment
Prevent anemia with erythropoietin
Antiplatelet therapy: low-dose aspirin 75-162 mg/d in selected individuals according to clinical judgment

[a] ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; BMI = body mass index; CKD = chronic kidney disease; DASH = Dietary Approaches to Stop Hypertension; HbA_{1c} = hemoglobin A_{1c}; LDL-C = low-density lipoprotein cholesterol.
[b] The American Association of Clinical Endocrinologists guidelines recommend a glycemic goal of <6.5%.
Data from *Endocr Pract*.[25]

Benefits of Glucose Control: Lowering A1c Reduces Microvascular and Macrovascular Complications

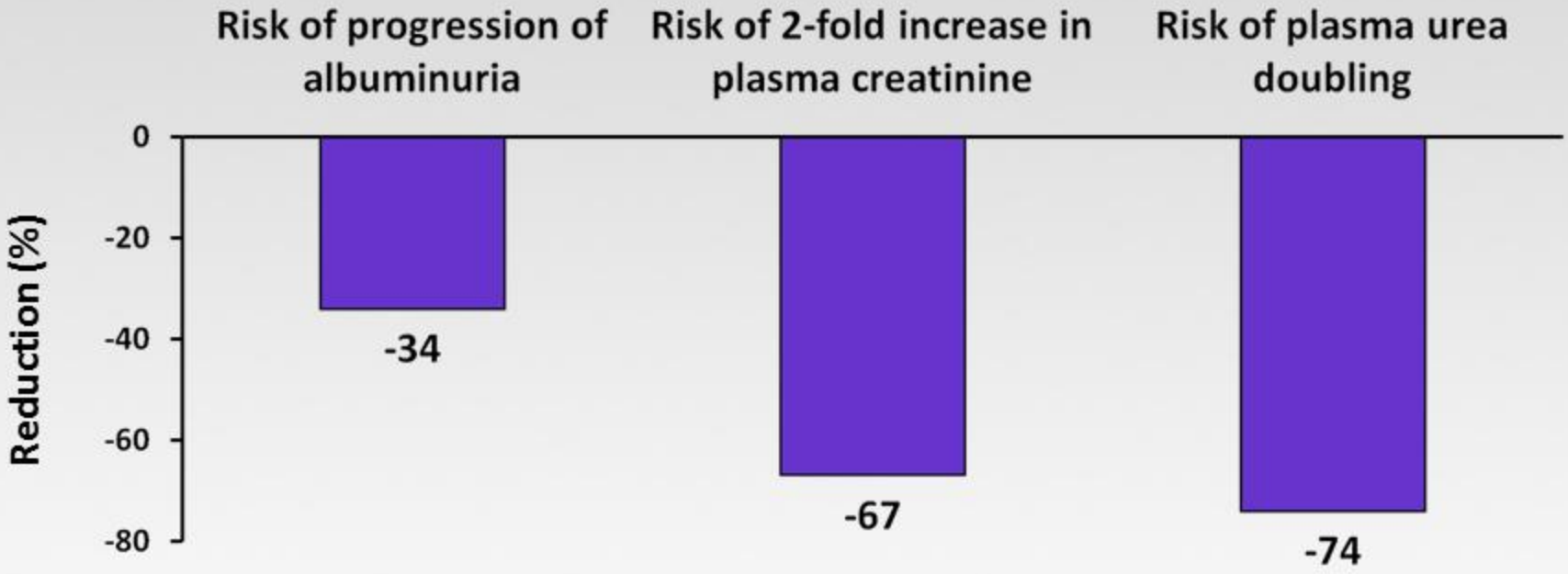


From United Kingdom Prospective Diabetes Study (UKPDS) 35.
*$P < .0001$; †$P < .05$.

Stratton IM, et al. *BMJ.* 2000;321:405-412.

Reduced Risk of Progressive Kidney Damage with Intensive Glycemic Control

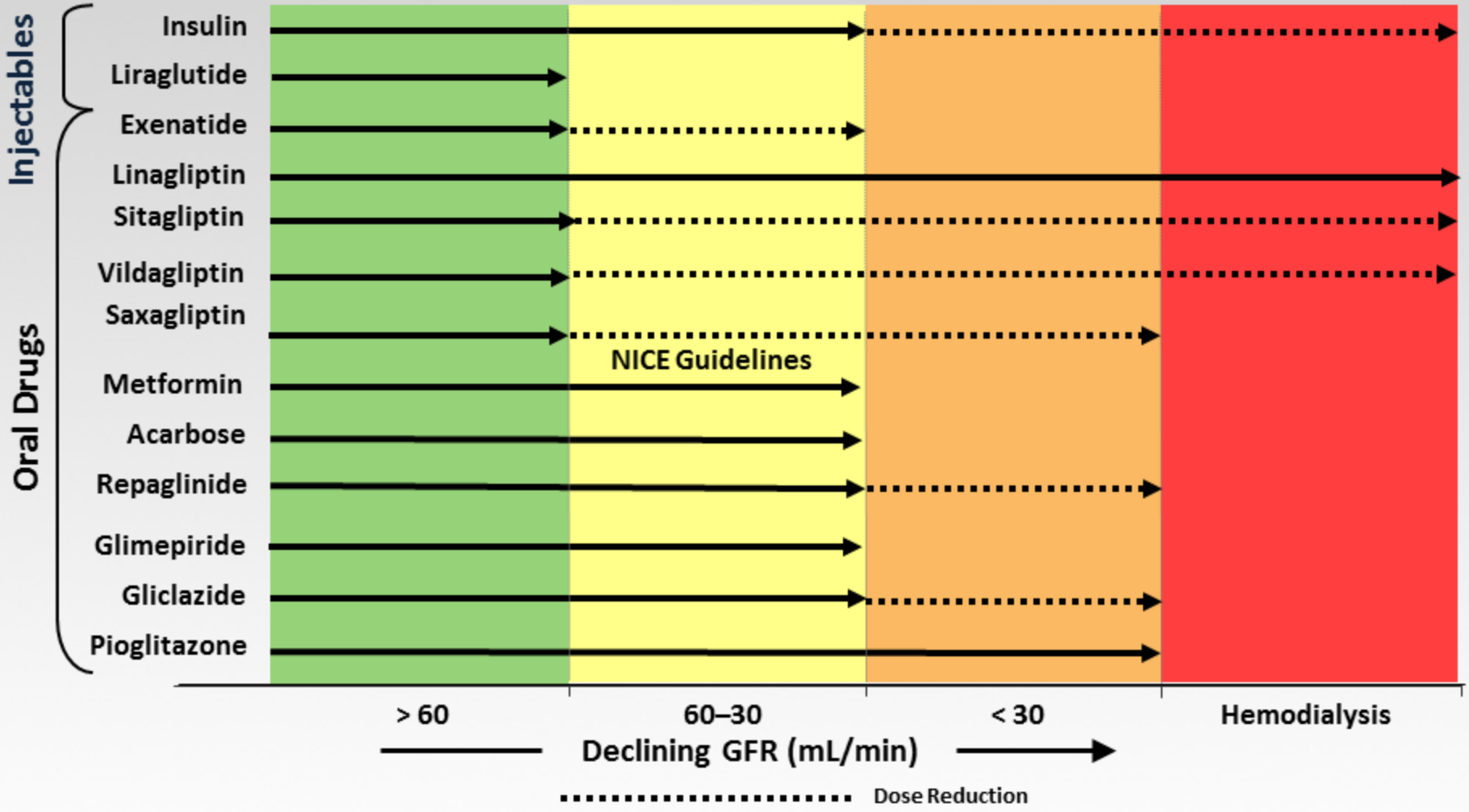
UKPDS 33: 10-year risk reduction



Intensive glycemic control by either sulphonylureas (SU) or insulin to fasting plasma glucose < 6 mmol/L.

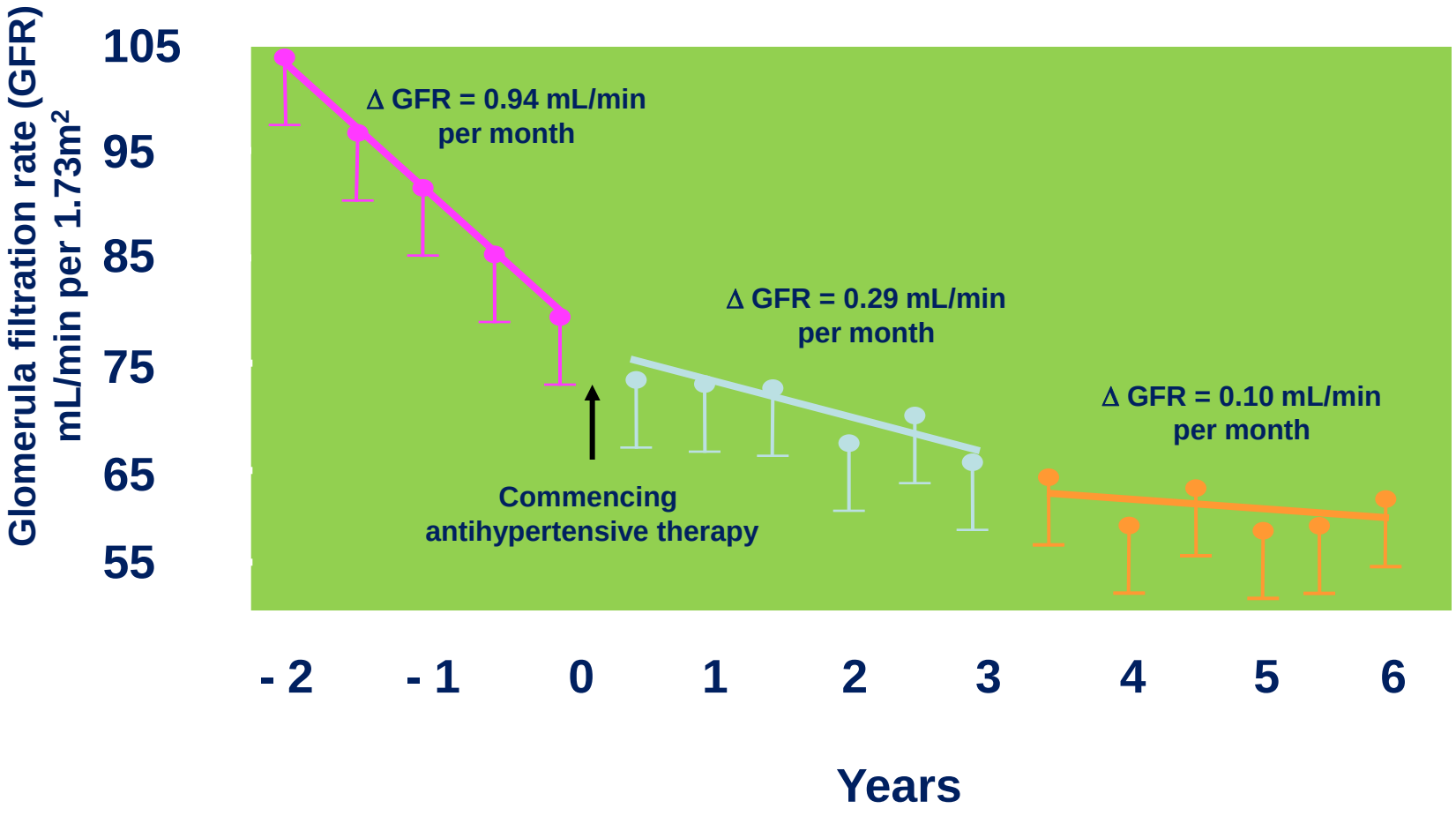
UKPDS Group 33. *Lancet*. 1998;352:837-853.

Current Treatments for T2DM Have Limitations When Renal Function Declines

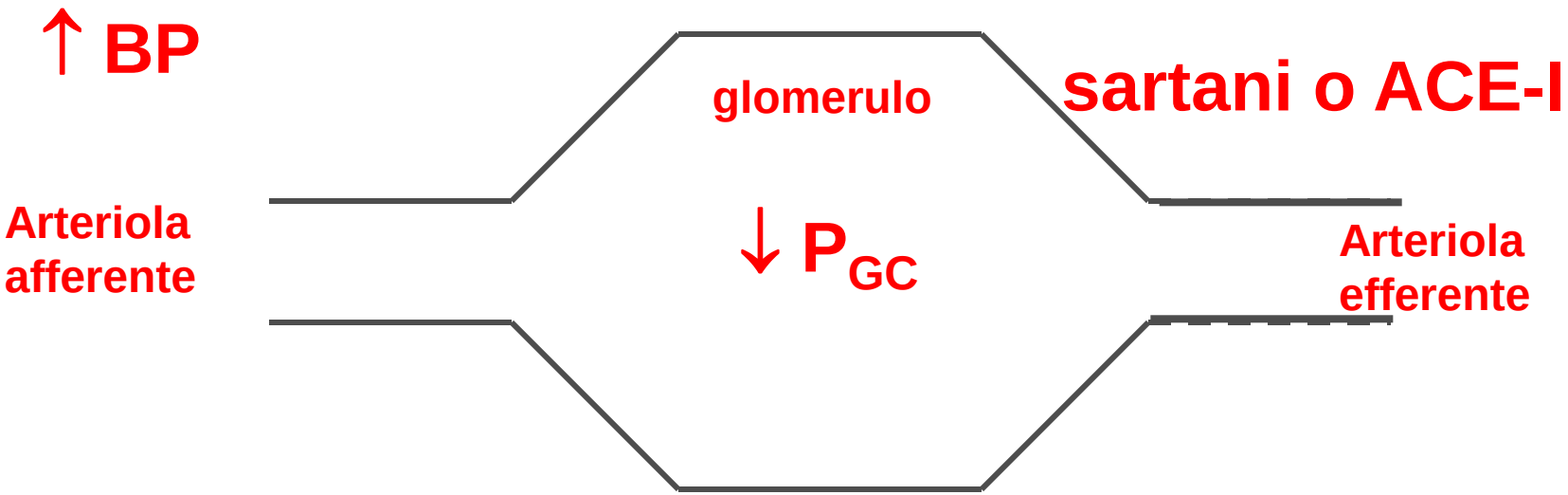


lapted from Schernthaner G. *Nephrol Dial Transplant*. 2011;26(2):454-457.
ww.nice.org.uk/nicemedia/live/11983/40803/40803.pdf

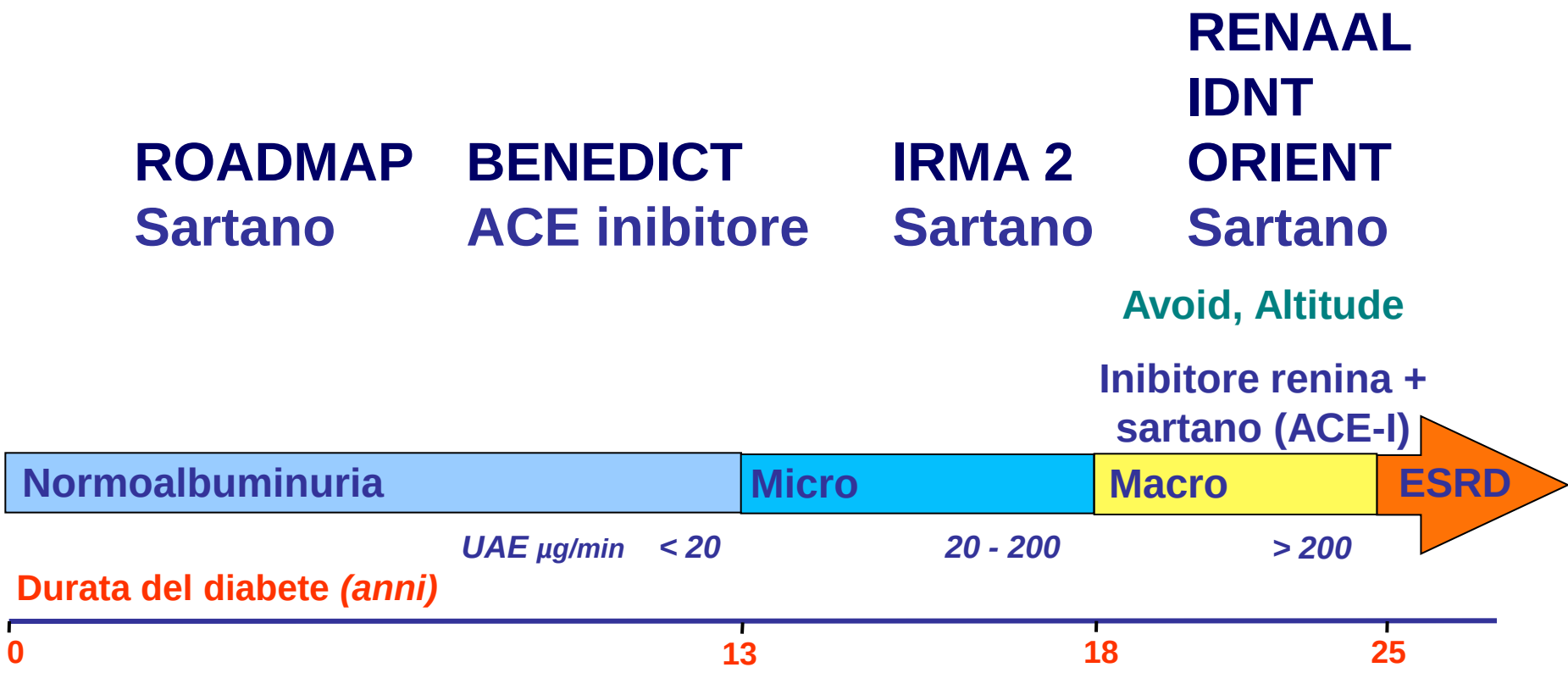
Control of blood pressure retards progression of type 1 diabetic nephropathy



Modificazioni del tono dell'arteriola efferente a seguito dell'impiego di ACE-I o di bloccanti del recettore dell'angiotensina II



Gli inibitori del sistema renina angiotensina impiegati nelle varie fasi della nefropatia diabetica



Terapia sostitutiva

PREPARAZIONE AL TRATTAMENTO SOSTITUTIVO DEL PAZIENTE DIABETICO

- **Mantenimento di un buon controllo glicemico**
- **Accurato controllo della pressione arteriosa**
- **Buono stato nutrizionale**
- **Preparazione precoce dell'accesso vascolare e/o inserimento catetere peritoneale**
- **Assenza di sintomatologia uremica**

Diabete in Terapia Sostitutiva

- **Ottimizzare le prestazioni**
  - **-Trapianto (prima scelta)**
  - **-Aumentare l'efficienza dialitica**

- **Ottimizzare l'assistenza generale**
  - **-ipertensione**
  - **-Iperglicemia**
  - **-iperlipemia**
  - **-malnutrizione (ipoalbuminemia!)**
  - **-dosaggio Epo**
  - **-complicanze**

Take home messages

La nefropatia diabetica è una malattia con una prevalenza molto elevata ed in continuo aumento

La malattia è evolutiva ed è un fattore di rischio indipendente per malattie cardiovascolari e per mortalità per tutte le cause

La malattia è spesso diagnosticata in fase avanzata ("late referral")

La diagnosi precoce è possibile e permette di intervenire efficacemente sul rischio di progressione e sulle complicanze cardiovascolari

I costi socio-economici sono elevati e vanno necessariamente controllati

La gestione ideale è multidisciplinare, a partenza dal medico di medicina generale e del patologo clinico e con il coinvolgimento successivo del nefrologo e di altri specialisti