KDIGO - Controversies Conference

Chronic Kidney Disease as a Global Public Health Problem: Approaches and Initiatives

12-14 October, 2006

Renaissance Amsterdam, Amsterdam

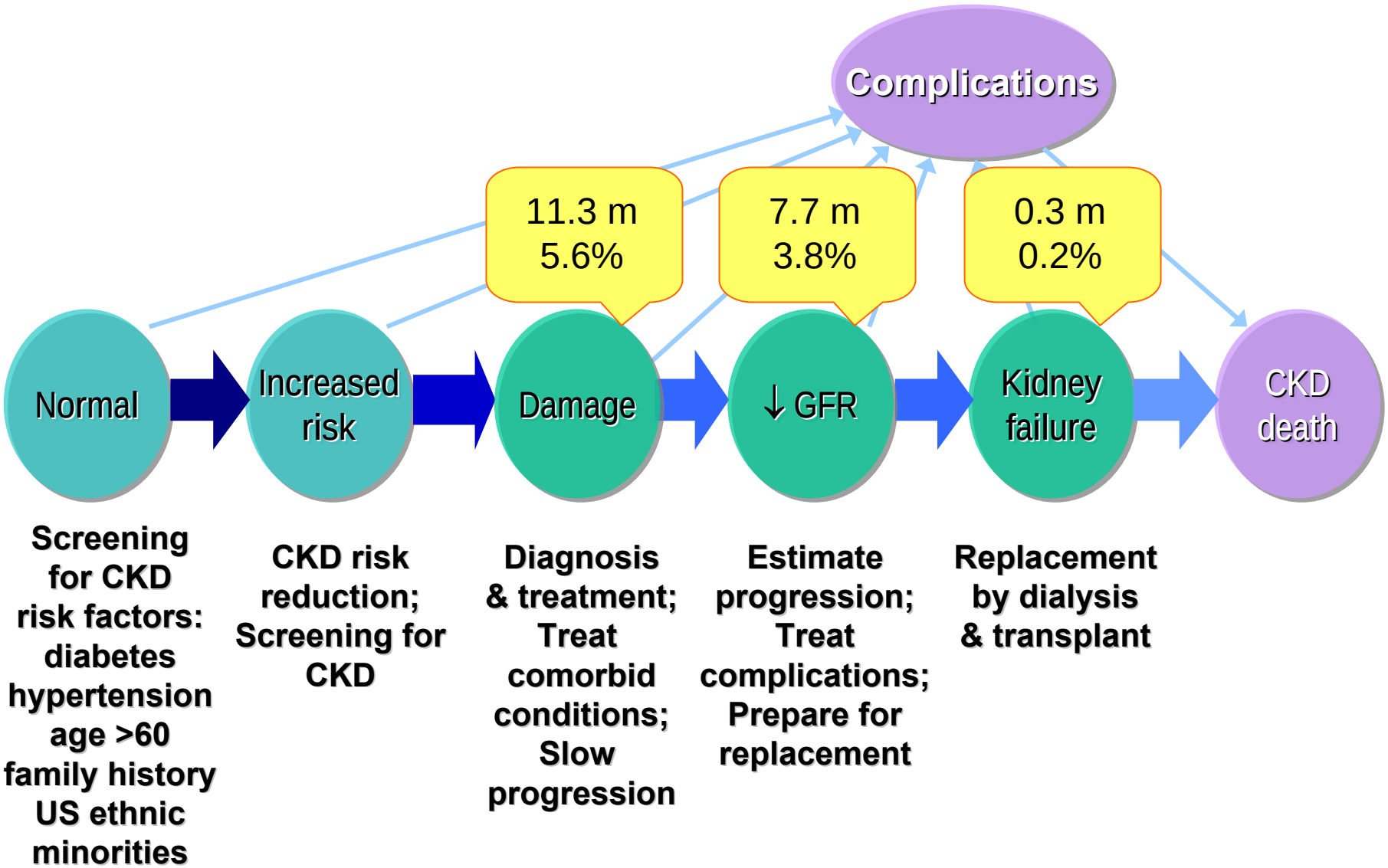
Goals and Objectives

- Simple message
- Conceptual model and definition
- Prevalence
- Testing
- Classification
- Risk factors
- Relationship with other chronic diseases
- Rationale for public health policy

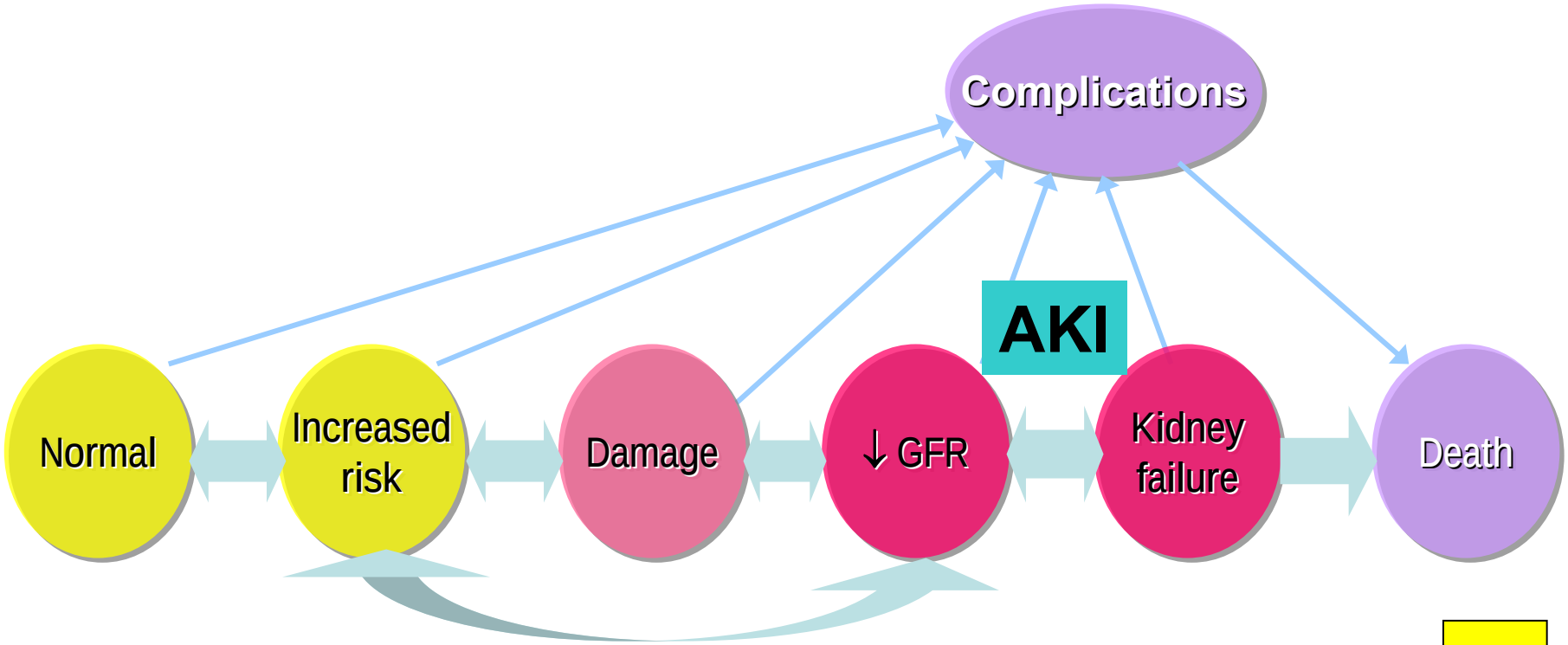
CKD is a Public Health Problem

- CKD is common
- CKD is harmful
- We have treatment

Conceptual Model for CKD



Conceptual Model for AKI



Acute Kidney Injury Network

AKIN Vancouver Conference 2006

NKF-K/DOQI Definition of CKD
KDIGO Modifications (Amsterdam 2004)

Structural or functional abnormalities of the kidneys for ≥3 months, as manifested by either:

1. **Kidney damage**, with or without decreased GFR, as defined by
    - pathologic abnormalities
    - **markers of kidney damage**
        - urinary abnormalities (**proteinuria**)
        - blood abnormalities (renal tubular syndromes)
        - imaging abnormalities
    - **kidney transplantation**
2. **GFR <60 ml/min/1.73 m^2**, with or without kidney damage

An International Symposium, New York, May 16-18, 2004

Role of Albuminuria in Health and Disease: Predicting Targets and Outcomes of Therapy

Guest Editors: De Zeeuw D; Bakris G; Pfeffer M

Kidney International 2004: 66 (Supplement 92): S1-S127

Where we are today:

- Albuminuria is useful for detection, evaluation and management of CKD
- Spot urine albumin-to-creatinine ratio is easier to measure and correlates with timed excretion rate
- Ratio >30 mg/g is a maker of CKD
- Lower level is a risk factor for CVD

Next steps:

- Urine albumin standardization
- Variation by sex, race, ethnicity and age
- Hypothesized relationship to generalized endothelial dysfunction
- Hypothesized surrogate marker for CKD progression

MEDICAL PROGRESS

Assessing Kidney Function — Measured and Estimated Glomerular Filtration Rate

Lesley A. Stevens, M.D., Josef Coresh, M.D., Ph.D., Tom Greene, Ph.D., and Andrew S. Levey, M.D.

N Engl J Med 2006;354:2473-83

Where we are today:

- eGFR is useful for detection, evaluation and management of CKD
- eGFR is more accurate than serum creatinine alone
- eGFR is less accurate at higher vs. lower levels
- eGFR reporting (numeric value only for eGFR <60)

Next steps to improve performance (especially at higher GFR):

- Creatinine standardization
- Race/ethnicity terms
- New equations
  - new filtration markers
    - (cystatin C)
  - additional variables
  - new derivations

Performance of MDRD Study Equation Using Calibrated and Non-Calibrated Creatinine

Study	N	mGFR	Non-Calibrated Creatinine		Calibrated Creatinine	
			%Δ	P30	%Δ	P30
MDRD Study	1085	40	-0.1	90	0.1	90
AASK	1205	57	7.7	85	2.1	86
DCCT	787	124	**14.9**	**81**	**10.1**	**85**
DRDS	126	115	13.5	76	-0.8	79
CSG	266	78	15.6	75	14.6	75
CRIC	446	50	8.0	82	8.7	81
CCF CKD	695	34	2.5	71	0.6	71
CCF Donors	301	106	**8.4**	**86**	**14.4**	**84**
Mayo CKD	221	48	8.0	76	0.4	76
Mayo Donors	372	102	**28.9**	**54**	**13.5**	**87**
Pooled	5504	68	**9.0**	**80**	**5.8**	**83**

Variable	Group	eGFR <60			eGFR ≥60		
		N	%Δ	P30	N	%Δ	P30
Age	<40	596	2.2	83	1468	9.9	83
	40-65	1701	4.6	83	1036	6.8	85
	>65	590	-1.3	82	113	-0.4	87
Female	Y	1218	3.6	82	1179	10.9	82
	N	1669	2.4	83	1438	6.6	86
Black	Y	1090	3.4	83	659	-0.3	87
	N	1797	2.5	82	1958	11.0	83
Diabetes	Y	507	5.9	74	1073	9.6	83
	N	2380	2.3	85	1544	7.7	85
Transplant	Y	178	-1.0	82	73	-9.2	77
	N	2709	3.1	83	2544	9.0	84
BMI	< 25	838	-1.0	80	1022	9.0	82
	25-30	1002	4.3	85	920	9.0	87
	>30	1047	3.5	83	675	6.8	82
Overall		2887	**3.0**	**83**	2617	**8.5**	**84**

Interpretation of CKD Testing

Marker of Kidney Damage	GFR	CKD	What to do?
+	< 60	Y	Action Plan
+	≥ 60	Y	Action Plan
-	< 60	Y	Action Plan*
-	≥ 60	N	

Because of bias in MDRD Study equation in non-CKD populations, some individuals with normal measured GFR may have GFR estimates just below 60. Individual decision-making is required.

Classifications of CKD

- **Severity (stage)**
- **Treatment (HD vs. PD)**
- **Diagnosis (cause)**
- **Prognosis (progression, CVD)**

Stages of CKD, Related ICD 9 Codes and Classification by Treatment

Stage	Description	GFR (mL/min per 1.73 m^2)	ICD 9 Code	Treatment
	At increased risk	>60 (with CKD risk factors)		None
1	Kidney damage with normal or ↑ GFR	≥90	585.1	T if kidney transplant recipient
2	Kidney damage with mild ↓ GFR	60–89	585.2	
3	Moderate ↓ GFR	30–59	585.3	
4	Severe ↓ GFR	15–29	585.4	
5	Kidney failure	<15 (or dialysis)	585.5 585.6 (if ESRD) V codes for dialysis or transplantation	D if dialysis (HD or PD)

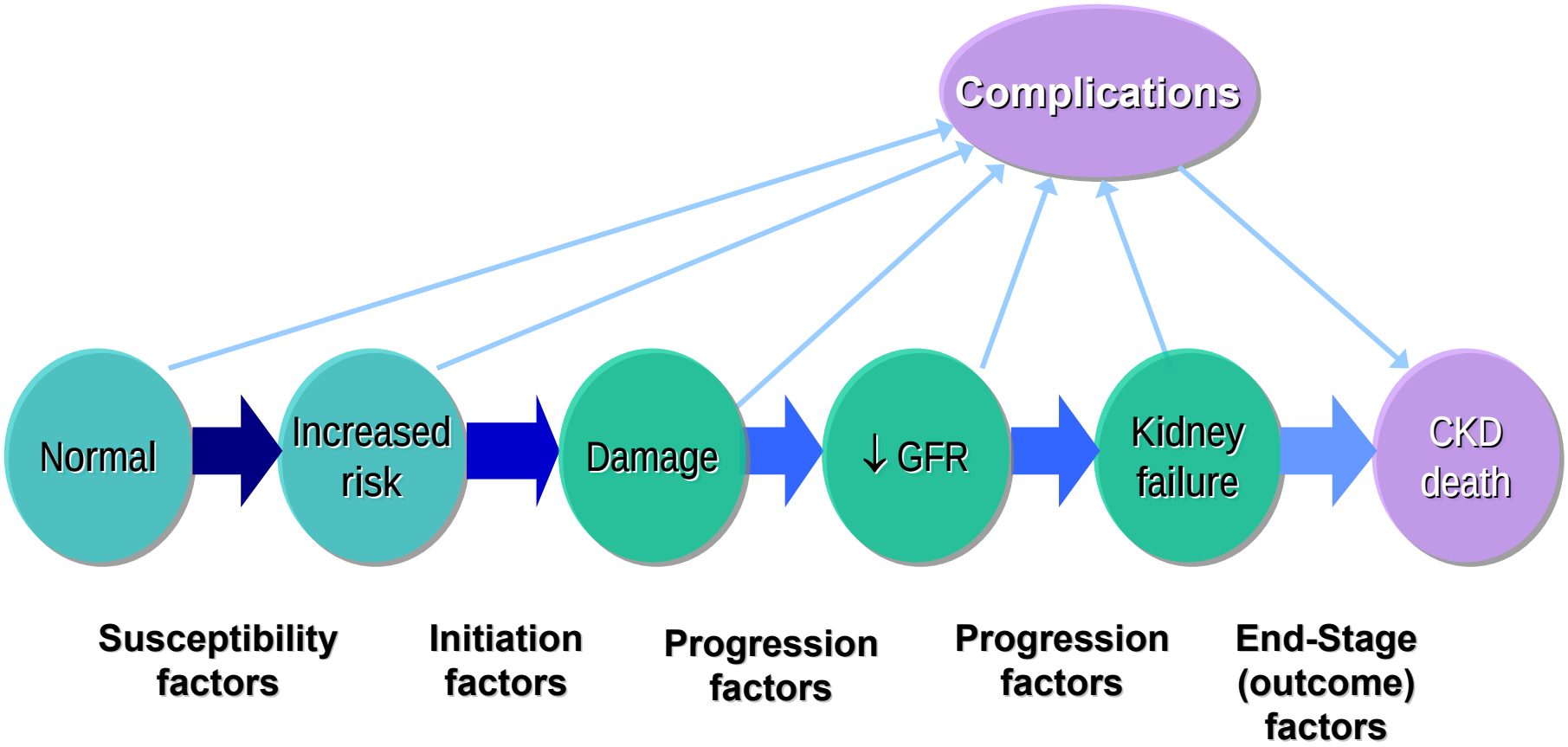
Simplified Classification of CKD by Diagnosis

Disease	Major Types (Examples)
Diabetic kidney disease	*Type 1 and type 2 diabetes*
Nondiabetic kidney diseases	*Glomerular diseases* *(autoimmune diseases, systemic infections, drugs, neoplasia)*
	Vascular diseases (renal artery disease, hypertension, microangiopathy)
	Tubulointerstitial diseases (urinary tract infection, stones, obstruction, drug toxicity)
	Cystic diseases (polycystic kidney disease)
Diseases in the transplant	Acute rejection
	Allograft nephropathy (chronic rejection, calcineurin toxicity, *glomerulopathy*)
	Recurrent diseases (glomerular diseases)

Proposed Classification using ICD Codes

Disease		CKD Classification		
		Stage and Treat-ment	Marker of Kidney Damage	Disease (ICD Code)
Diabetic Kidney Disease	Type 1	585.X (585.6 For ESRD) With V codes for D or T	Proteinuria	
	Type 2		Proteinuria	
Non-Diabetic Kidney Disease	Glomerular diseases		Hematuria ±Proteinuria	
	Vascular diseases		±Proteinuria	
	Tubulointersitial diseases		±Pyuria, ±Proteinuria, ±Imaging studies	
	Cystic diseases		Cysts	
	Non-diabetic kidney disease not otherwise specified		±Proteinuria	
Transplant			±Proteinuria	

Conceptual Model for CKD

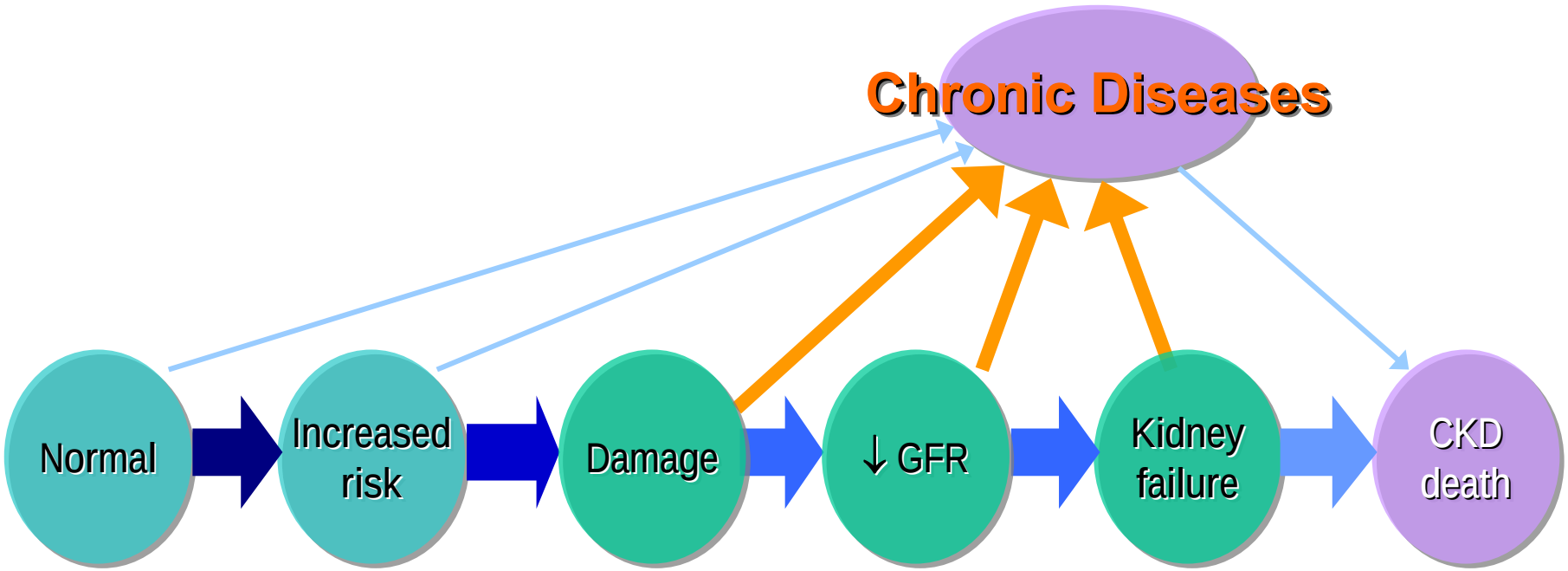


CKD Risk Factors

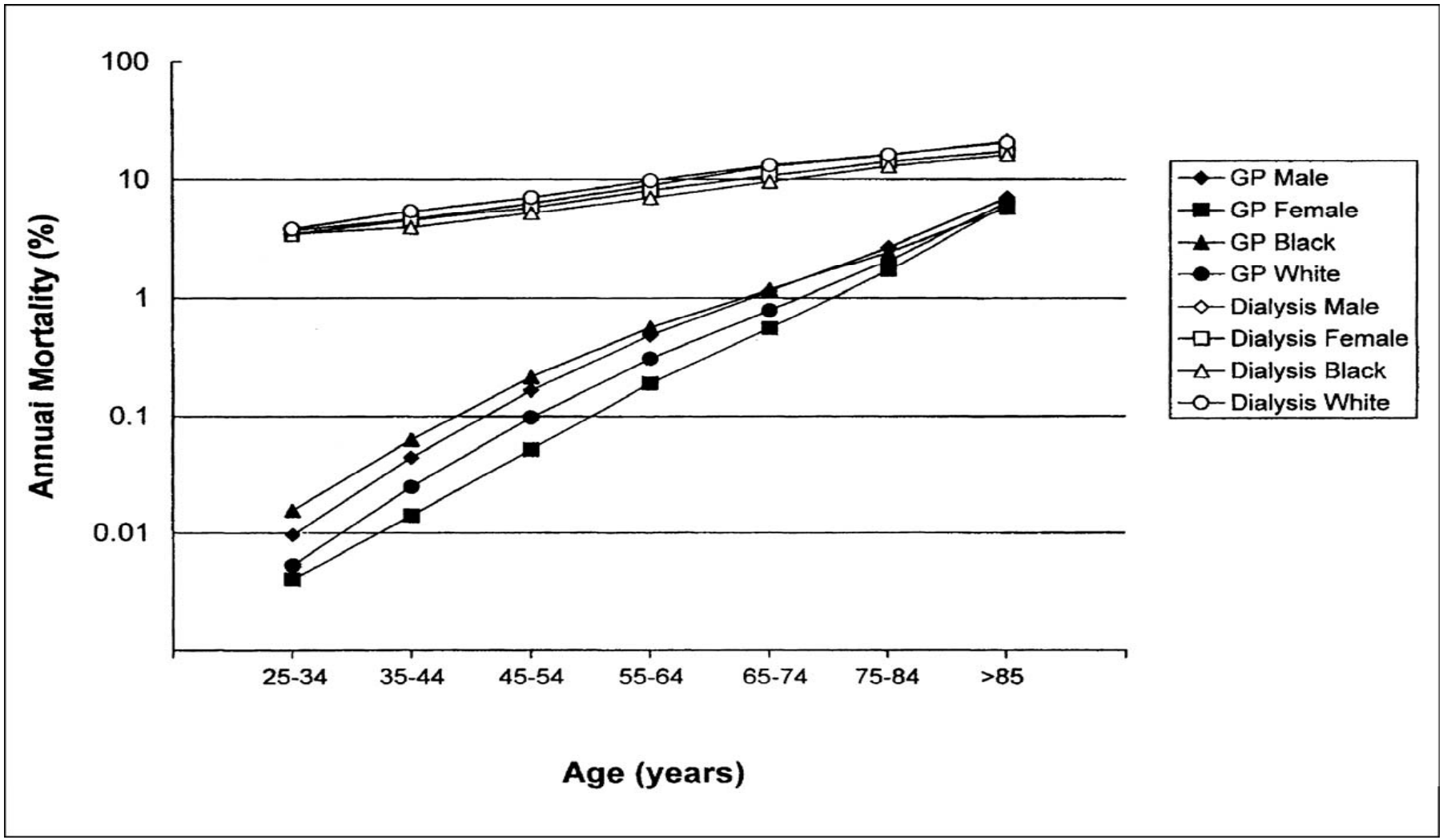
Risk Factor	Definition	Examples
Susceptibility factors	Increase susceptibility to kidney damage	Older age, family history of CKD, U.S. racial or ethnic minority status, reduced kidney mass, hyperfiltration states
Initiation factors	Directly initiate kidney damage	Diabetes, high blood pressure, obesity, dyslipidemia, autoimmune diseases, infections, stones, obstruction
Progression factors	Cause worsening kidney damage and faster GFR decline	Higher level of proteinuria
End-stage (outcome) factors	Increase morbidity and mortality in kidney failure	Lower dialysis dose (Kt/V), temporary vascular access, anemia, low serum albumin level, late referral

Factors that are implicated at different stages in the development and progression of CKD are listed in the initial category in which they could potentially appear.

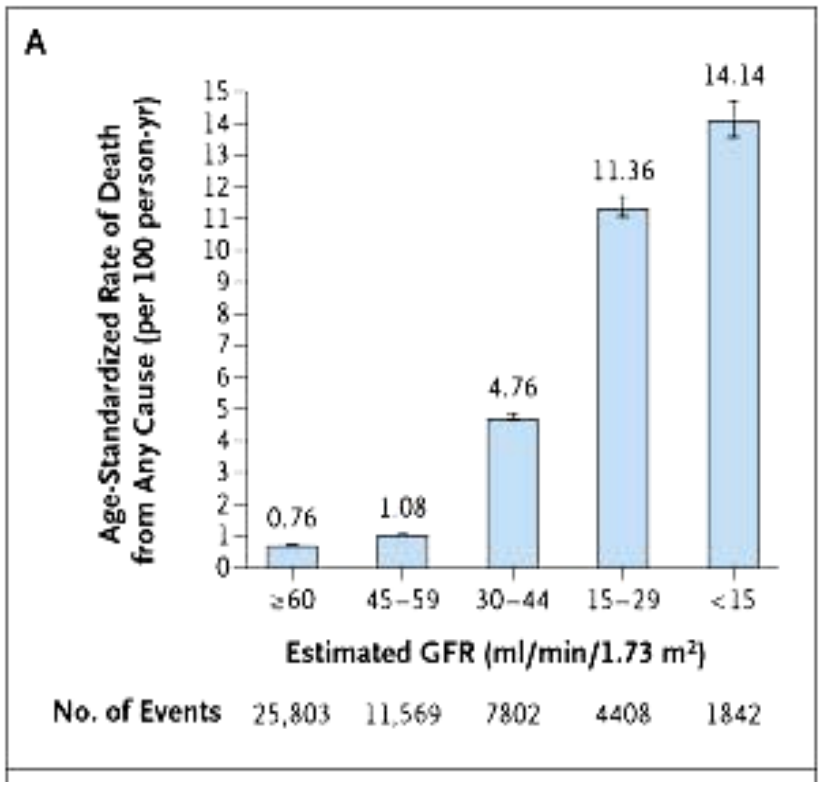
Conceptual Model for CKD

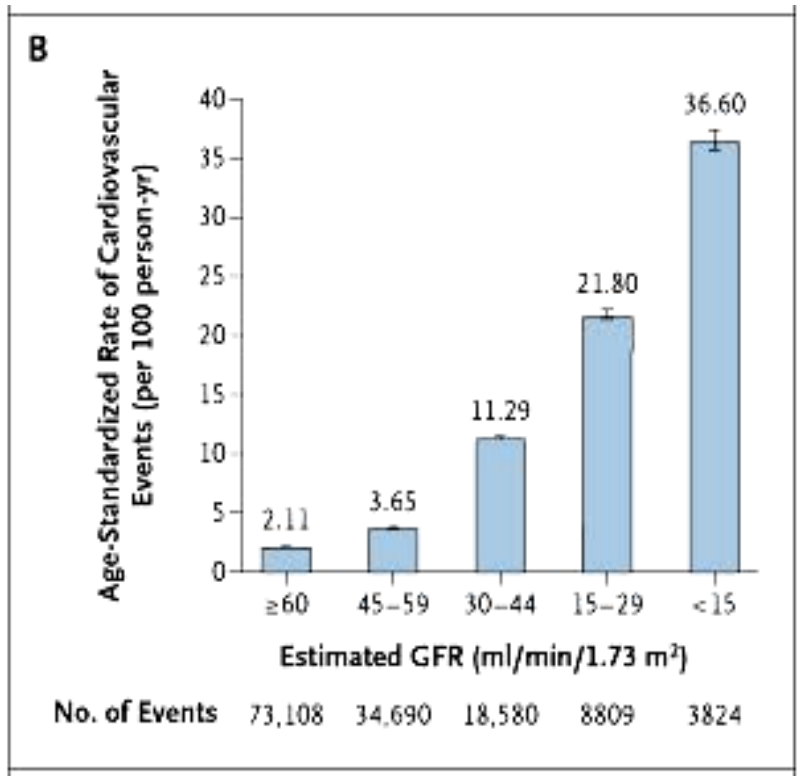


CVD Mortality in GP (NCHS) and in Dialysis Patients (USRDS)



Rates of Death from Any Cause and from CVD by Estimated GFR





Go *et al* NEJM 2004

CKD as a Risk Factor for CVD in CVD Risk Factor Conditions

CVD Risk Factor	CKD prevalence	CKD as a risk factor for CVD morbidity	CKD as a risk factor for CVD mortality
Hypertension	↑	↑	↑
Diabetes	↑	↑	↑
Dyslipidemia	↑	↑	↑

Rationale for Public Health Policy

- CVD is most common cause of death in developed nations
- CKD is common in people with CVD risk factors
  - Hypertension, diabetes, dyslipidemia
- CKD multiplies risk for CVD
- Patients with CVD risk factors and CKD are more ill compared to those without CKD
  - Risk factor levels are higher
  - Risk factor control is more difficult
  - CVD outcomes are worse
  - Costs of care are higher
- CVD risk factor management differs in patients with CKD compared to those without CKD
- Treatments are available and effective NOW
  - To reduce CVD risk
  - To manage complications of CKD
  - To slow kidney disease progression

Chronic Kidney Disease is a Public Health Problem

- CKD is common
  - 11% of US adults
  - Higher prevalence in patients with CVD risk factors
- CKD is harmful
  - Increased risk for CVD
  - Complications of decreased kidney function
  - Progression to kidney failure
- We have treatment

Recommendations

- CKD testing for all patients with CVD risk factor conditions
- CKD Action Plan for all patients found to have CKD

CKD as a Risk Factor for Adverse Outcomes of Infectious Diseases

Infectious Disease	CKD prevalence	CKD as a risk factor for ID morbidity	CKD as a risk factor for ID mortality
HCV			
HBV			
HIV			
TB			
Malaria			

CKD as a Risk Factor for Adverse Outcomes of Cancer

Cancer	CKD prevalence	CKD as a risk factor for cancer morbidity	CKD as a risk factor for cancer mortality
Kidney and urinary tract tumors			
Other solid tumors			
Hematologic malignancies			

CKD Concepts	Where We Are Now	Where We Need to Go
Conceptual Model	Well developed	Link to AKI and AKD
Definition	Inclusive	Markers of damage
Testing	Spot urine albumin-to-creatinine ratio >30 mg/g; eGFR <60 ml/min/1.73 m^2	Standardization Race/ethnicity terms Optimal use
Prevalence	US	World
Classification	Severity (ICD9) Treatment	Link to ICD I0-11 Diagnosis, Prognosis
Risk Factors	Framework	Focus on CVD risk factors
Outcomes	CVD	ID, cancer
Public Policy		Simple messages Coordinate with other chronic diseases

CKD as a Global Public Health Problem