中山大學附属第一医院
The First Affiliated Hospital, Sun Yat-Sen University

Generating a Big Database for Research in Nephrology

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CKD：Major Public Health Problem

Incidence of CKD (eGFR<60 +Albuminuria)： 10.8%

～ 12million CKD Patients

1%～2% progressing to ESRD： ～ 1.3 M

Prevalence of chronic kidney disease in China: a cross-sectional survey

Lancet. 2012; 379: 815-822

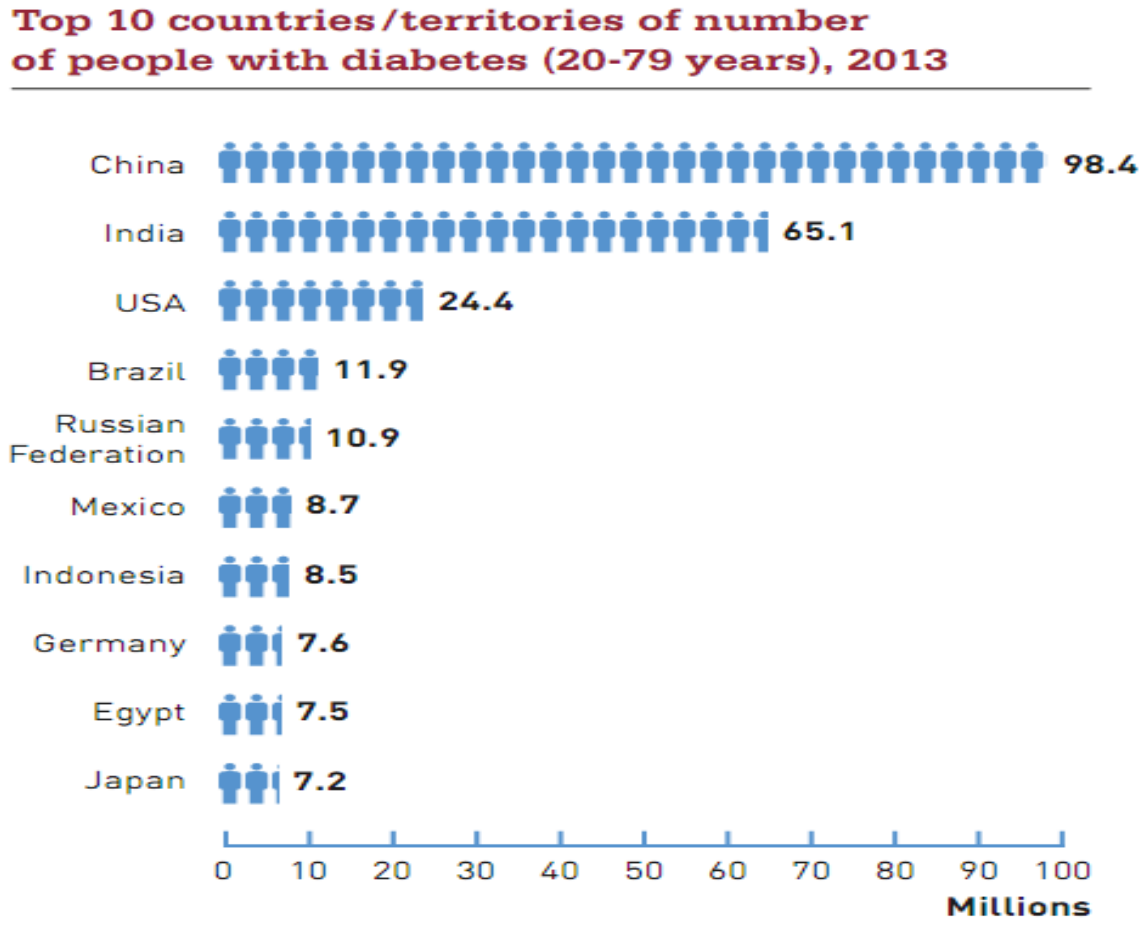
Luxia Zhang, Fang Wang*, Li Wang†, Wenke Wang†, Bicheng Liu†, Jian Liu†, Menghua Chen†, Qiang He†, Yunhua Liao†, Xueqing Yu†, Nan Chen†, Jian-e Zhang, Zhao Hu, Fuyou Liu, Daqing Hong, Lijie Ma, Hong Liu, Xiaoling Zhou, Jianghua Chen, Ling Pan, Wei Chen, Weiming Wang, Xiaomei Li, Haiyan Wang*

CKD Prevalence in Geographic Features

- CKD in South of China 12.1%
- CKD in Rural Area 13.6%
- CKD Periodontal Patients 18.2%
- CKD in High Altitude Area 19.1%
- CKD in First Degree Relatives 29.7%

• Chen W, et al. NDT 2009; 24:1205-12
• Liu Q, et al. PLos One 2012;7:e47100
• Liu K, et al. PLos One. 2013;8:e70767
Chen W, et al. NDT 2011;26:1592-9
Wei X, et al. Nephrology 2012;17:123-30

China: The Biggest Population with Diabetes



International Diabetes Federation 2013

Prevalence of Diabetes and Pre-DM in China

- Prevalence of diabetes: **9.7%**

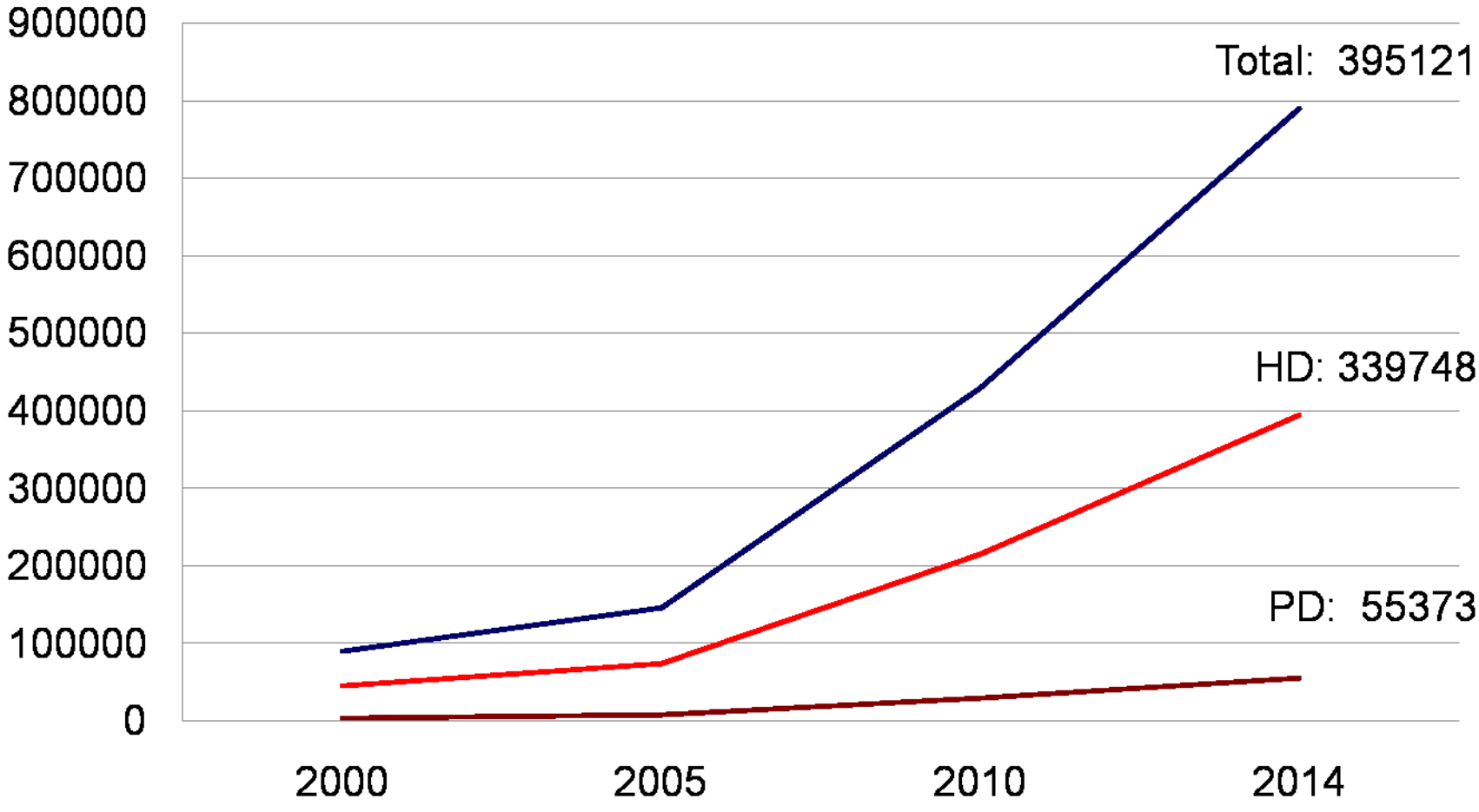
  Total Diabetic Population: 92,400,000

- Prevalence of pre-diabetes: **15.5%**

  Total Pre-diabetes: 148,200,000

Yang WY, et al. N Engl J Med 2010;362:1090-101

HD and PD Population in China



Data for China Dialysis Registration Database 2014

Key Issues of CKD in China

- CKD: prevalence, incidence and risk factors
- ESKD: How to slow down progress to ESKD
- Predictive markers, new target intervention
- Appropriate technology promotion in rural area

Thoughts on future scientific commitment

- Questions or evidences driven research
- Breakthroughs of some scientific issues
- Do something but not everything
- What and How to do? What are we capable of ?

Chronic Kidney Diseases

- Who are subjects to CKD?
- Who are likely to progress to ESRD?
- Traditional risk factors?
- Novel risk factors of CKD?
- Progress mechanism of CKD?

Nephrotic syndrome

Who are likely to have NS?

Who are responsive to therapy?

Who will progress to ESRD?

ESRD - Uremia

- Patient survival
- Technical survival
- Possibility of back to work
- Capability of Labor

Research Mission

- International standard
- High quality
- International recognition
- International sharing

Clinical Research System

- Institutional Review Board
- Ethic Committee
- Department of Bio-statistics
- Clinical Trial Centre

Urine/CSF protein

Biochemistry Analyzer

Microbiology

Emergency

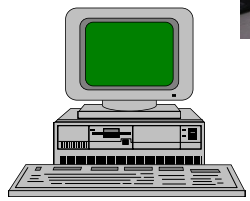
Hematology Analyzer

PCR Instrument

ELISA Analyzer

i2000®

LIS Terminal



IMMUNO Analyzer

Automation\ Versatility \ Standard

Bio-Bank for Kidney Diseasses

Patients Registration System in SYSU

IgA肾病登记系统和队列研究

IgA **N**ephropathy Regi**s**tration **I**nitiative of Hi**gh** Quali**t**y

(INSIGHT)

ClinicalTrials.gov ID：NCT 03001947

http://igan.medidata.cn/

截止2017年9月29日，共纳入 **74** 家单位，录入患者 **15,678** 例

IgA肾病早期预警生物标记物的前瞻性队列研究

IgA Nephropathy Biomarkers Evaluation Study (INTEREST)

ClinicalTrials.gov ID：NCT 02954419

截止2017年9月29日，共纳入**31**家单位，录入患者**1,032**例

肾病综合征登记系统和队列研究

Super **C**hinese Nephrotic Syndrom**e** Regi**s**tration **S**ystem
(SUCCESS)

ClinicalTrials.gov ID：NCT 03001934

http://ns.medidata.cn

截止2019年9月29日，共纳入 **96** 家单位，录入患者 **4,749** 例

腹膜透析登记系统和队列研究

Peritoneal Dialysis Registration (PERSIST)

ClinicalTrials.gov ID：NCT 02989298

http://pd.medidata.cn

截止2017年9月29日，共纳入 **66** 家单位，录入患者 **15,280** 例

血液透析登记系统和队列研究

Wise Practice of Chinese Hemodialysis (WISHES)

ClinicalTrials.gov ID：NCT 03001921

http://hd.medidata.cn

截止2017年9月29日，共纳入 **72** 家单位，录入患者 **29,347** 例

Baseline assessment on risk factors

- Socio-economic status
- Lifestyle (diet, smoking, drinking, exercise…)
- Health history, comorbidities, medications
- Psychology/psychiatry status
  - Depression, anxiety, QOL…
- Genetic susceptibility (family history, SNPs, CNV)
- Physical assessments
  - anthropometrics, BP, …
- Laboratory tests
  - eGFR, albuminuria, glucose, cholesterol, TG…

Cohort studies

(Follow-up for 10 yeas)

Disease	Follow-up	patients anticipated	patients available
IgAN	10Y	10,000	**15,678**
LN	10Y	5,000	**5,502**
NS	10Y	10,000	**4,749**
PD	10Y	10,000	**15,280**
HD	10Y	30,000	**29,347**

Sample and disease cohort: strategic resources

- **Sample collection:**

  Cover **30** provinces, **153** hospitals

  Kidney disease:**68,383** cases

  Normal control: **30,291** cases

- **Disease cohort:**

  Cover **30** provinces, **163** hospitals

  Kidney disease: **78,431** cases

IgA肾病登记系统和队列研究

IgA **N**ephropathy Regi**s**tration **I**nitiative of Hi**gh** Quali**t**y

(INSIGHT)

ClinicalTrials.gov ID：NCT 03001947

http://igan.medidata.cn/

截止2017年9月29日，共纳入 **74** 家单位，录入患者 **15,678** 例

INSIGHT-data Overview

Real-time dynamic statistic analysis

Demographic & clinical characteristics

- Annual registration number
- Patient birthplace distribution
- Sex distribution
- Age distribution
- BMI
- Dyslipidemia
- Hyperuricemia
- Hypertension
- Proteinuria
- CKD stage
- Scr ≥ 1.5mg/dl
- Serum calcium, phosphorus and iPTH
- Clinical manifestation

Pathological characteristics

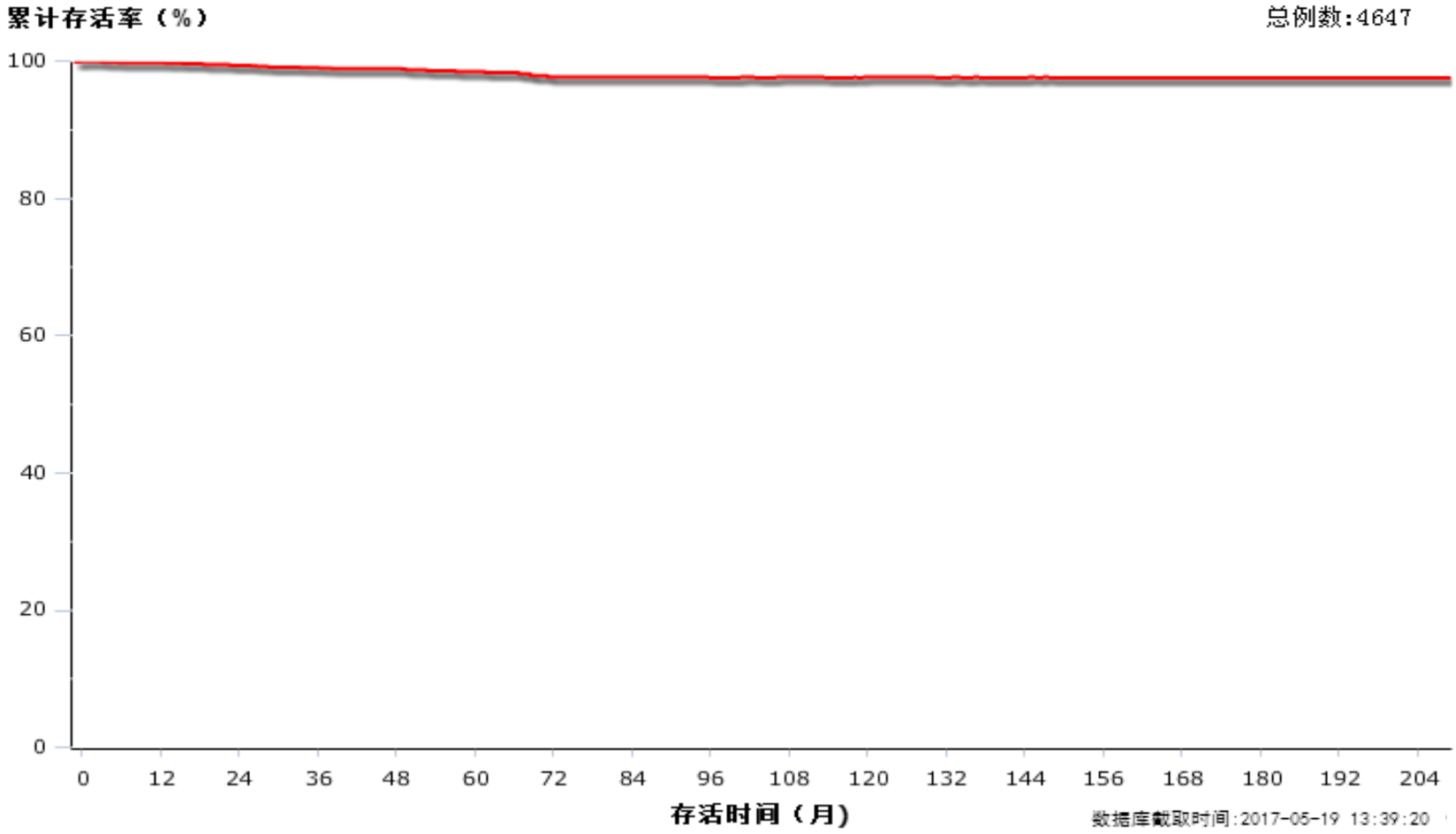
- Lee's classification
- Oxford classification
- Mesangial hypercellularity
- Segmental sclerosis or glomerular adhesion
- Endocapillary hypercellularity
- Crescent
- Segmental glomerular necrosis
- Interstitial fibrosis
- Tubular atrophy
- Arteriolar wall thickness

Outcome

- Patients survival
  - All-cause mortality
  - Different levels of proteinuria
  - Different levels of average MAP
  - Different CKD stage
- Renal survival
  - Overall
  - Different levels of proteinuria
  - Different levels of average MAP
  - Different CKD stage

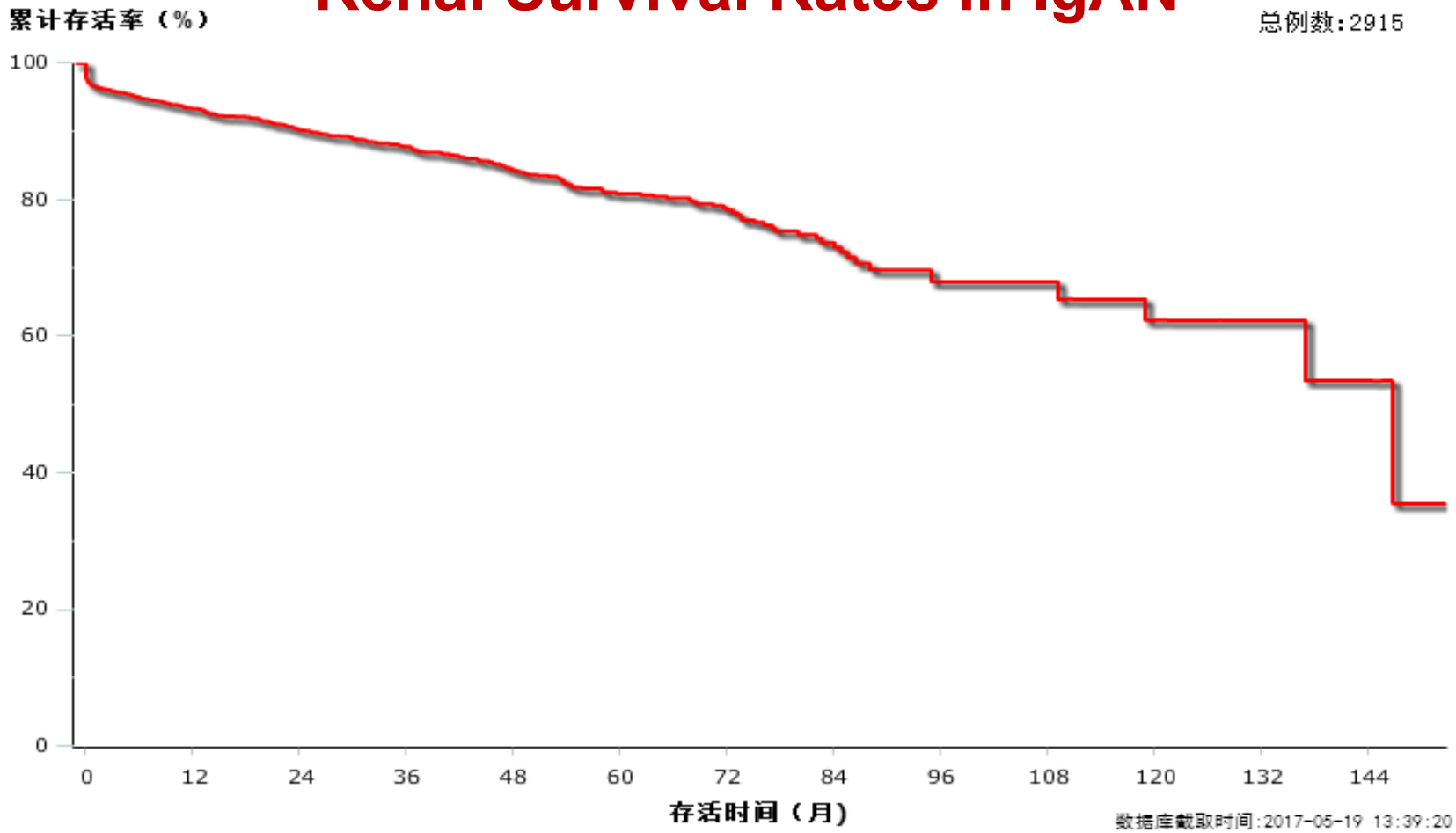
http://igan.medidata.cn/

Patients Survival in IgAN



Patient survival（%）				
patient	Year 1	Year 3	Year 5	Year 10
4647	99.79	99.13	98.65	97.90

Renal Survival Rates in IgAN



Renal survival of IgA patients（%）				
Patient No	**Year 1**	**Year 3**	**Year 5**	**Year 10**
2915	93.07	87.34	80.61	68.85

Risk Factors on IgAN Progression

	Univariable			
	OR	95% CI lower	95% CI upper	P value
Age	1.050	1.033	1.068	<0.001
Male	2.061	1.472	2.887	<0.001
Chronic tonsillitis	4.427	2.377	8.246	<0.001
Drinking history	.580	.124	2.709	.489
Smoking history	1.795	.792	4.067	.161
Family history of hypertension	.876	.091	8.474	.909
Glucose	1.527	.848	2.749	.158
Hyperuricemia	10.350	6.704	15.977	<0.001
Hypoalbuminemia	2.152	1.242	3.728	.006
Chol	2.057	1.431	2.957	<0.001
TG	2.558	1.751	3.737	<0.001
HDL-C＜1.04 mmol/l	2.459	1.681	3.597	<0.001
LDL-C≥3.37 mmol/l	1.477	1.026	2.128	0.036
Hemoglobin (g/l)	.968	.959	.976	<0.001
Proteinuria in 24h (g/24h)	1.001	.999	1.002	.291
Microscopic RBC ≥2+	.833	.570	1.217	.345
Global sclerosis	9.652	4.976	18.720	<0.001

	OR	95% CI lower	95% CI upper	P value
Crescents	1.665	1.191	2.326	0.003
Loops necrosis	.844	.441	1.616	.609
Mesangial hypercellularity (M1)	.960	.687	1.342	.812
Endocapillary proliferation (E1)	.948	.628	1.431	.800
Segmental glomerulosclerosis (S1)	2.487	1.771	3.493	<0.001
Renal tubular atrophy/fibrosis (T1-2)	19.332	12.753	29.303	<0.001
Interstitial inflammatory cell infiltration>25%	10.695	6.961	16.433	<0.001
Small artery wall thickening	5.019	3.519	7.159	<0.001
Angiohyalinosis	2.406	1.657	3.494	<0.001
Fibrinoid necrosis	3.776	1.495	9.536	0.005
Immunofluorescence IgA≥3+	.606	.429	.854	0.004

Logistic Regression of Risk factors for renal survival

	multivariable			
	OR	95% CI lower	95% CI upper	P value
Age	1.100	1.064	1.138	<0.001
Male	3.462	1.668	7.186	0.001
Hyperuricemia	5.017	2.696	9.334	<0.001
HDL-C＜1.04 mmol/l	2.416	1.222	4.776	0.011
Hemoglobin(g/l)	.964	.948	.981	<0.001
global sclerosis	3.055	1.112	8.396	0.030
Renal tubular atrophy/fibrosis (T1-2)	5.242	2.574	10.677	<0.001
Interstitial inflammatory cell infiltration >25% (n, %)	4.441	2.068	9.537	<0.001

狼疮肾炎登记系统和队列研究

High Quality Evidence of Chinese Lupus Nephritis (HELP)

ClinicalTrials.gov ID：NCT 03001973

http://ln.medidata.cn

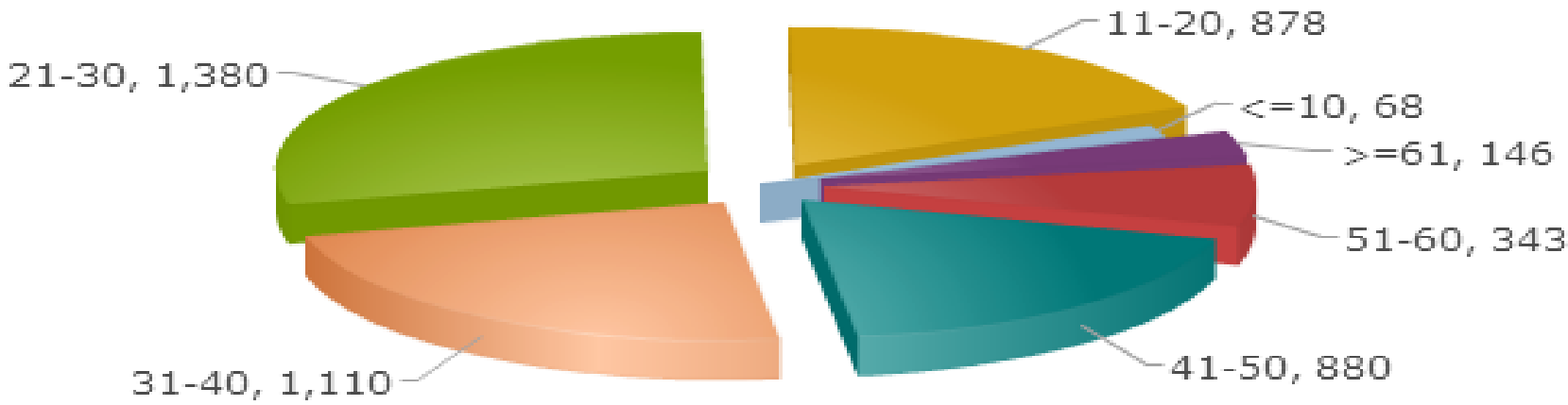
截止2017年9月29日，共纳入 **80** 家单位，录入患者 **5,502** 例

LN Database System-data Overview

Real-time dynamic statistic analysis

Baseline demographic and clinical characteristics	Pathological characteristics	Outcome analysis
• Incident patient distribution • Native place distribution • Gender distribution • Age distribution • BMI • Dyslipidemia • Hyperuricemia • Hypertension • Proteinuria • CKD stage • Autoimmune antibody	• 2003 ISN/PRS classification • Mesangial proliferative • Segmental sclerosis or adhesion • Proliferation of endothelial cells • Crescent • Loop necrosis • Interstitial fibrosis • Tubular atrophy • Vessel wall thickening	• Patient survival • Renal survival • Relapse

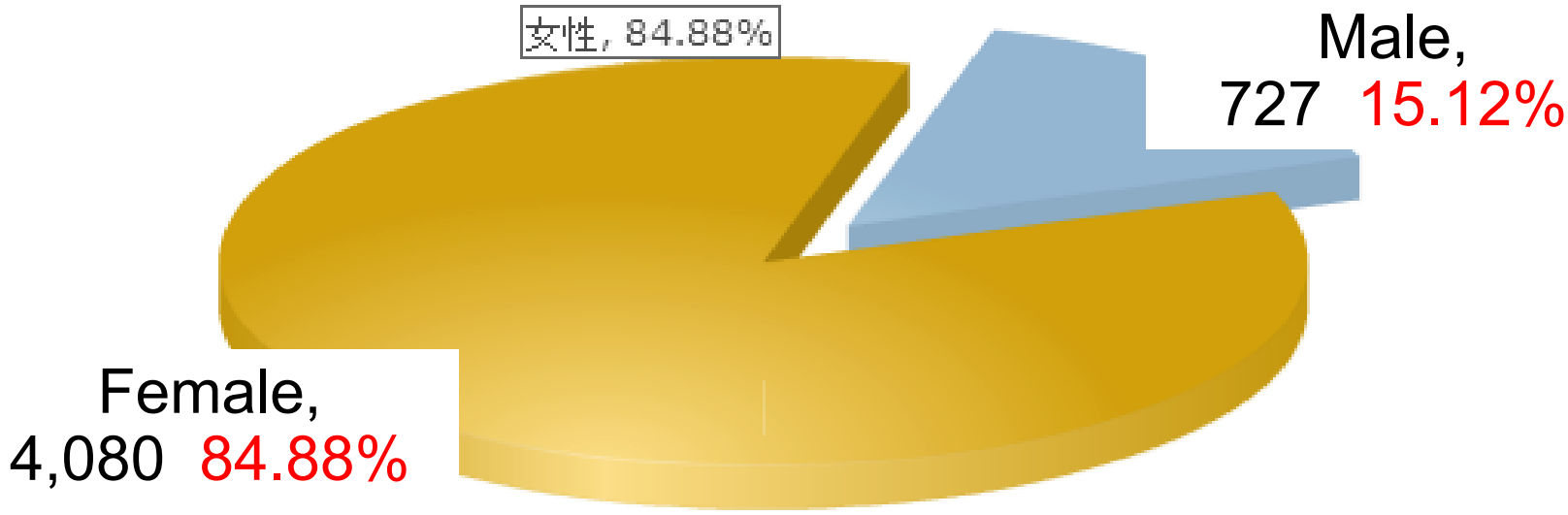
Age distribution– Young patient dominant



Age (yr)	No. of cases	Percentage(%)
<=10	68	1.42
11-20	878	18.27
21-30	1380	28.72
31-40	1110	23.10
41-50	880	18.31
51-60	343	7.14
>=61	146	3.04
合计	4805	100

http://ln.medidata.cn/

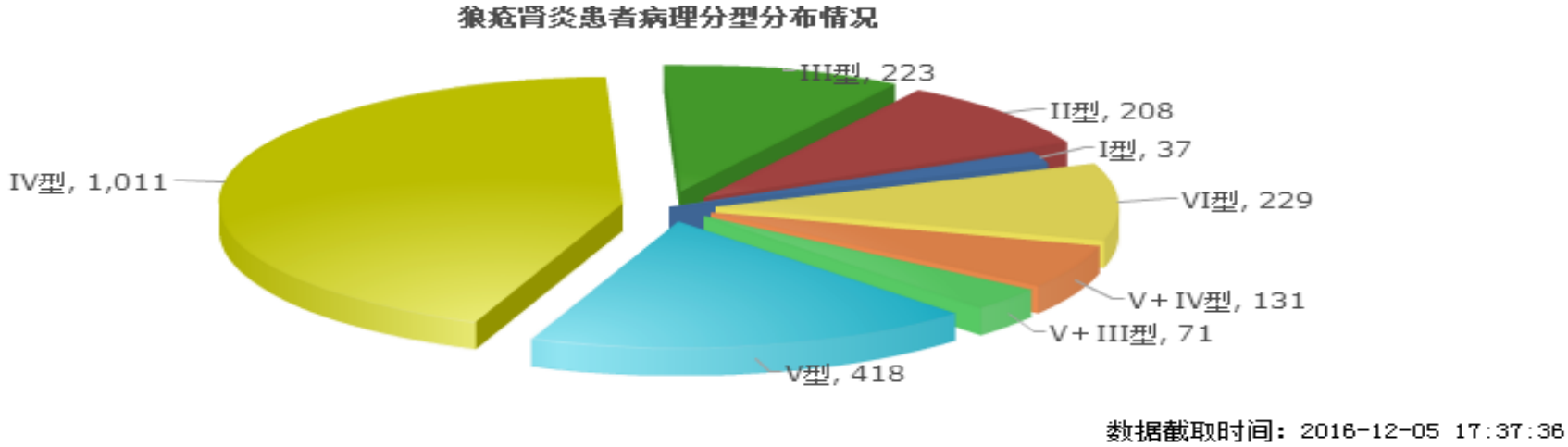
Gender distribution - Female dominant



Sex	No. of cases	Percentage(%)
Male	727	15.12
Female	4080	84.88
All	4807	100

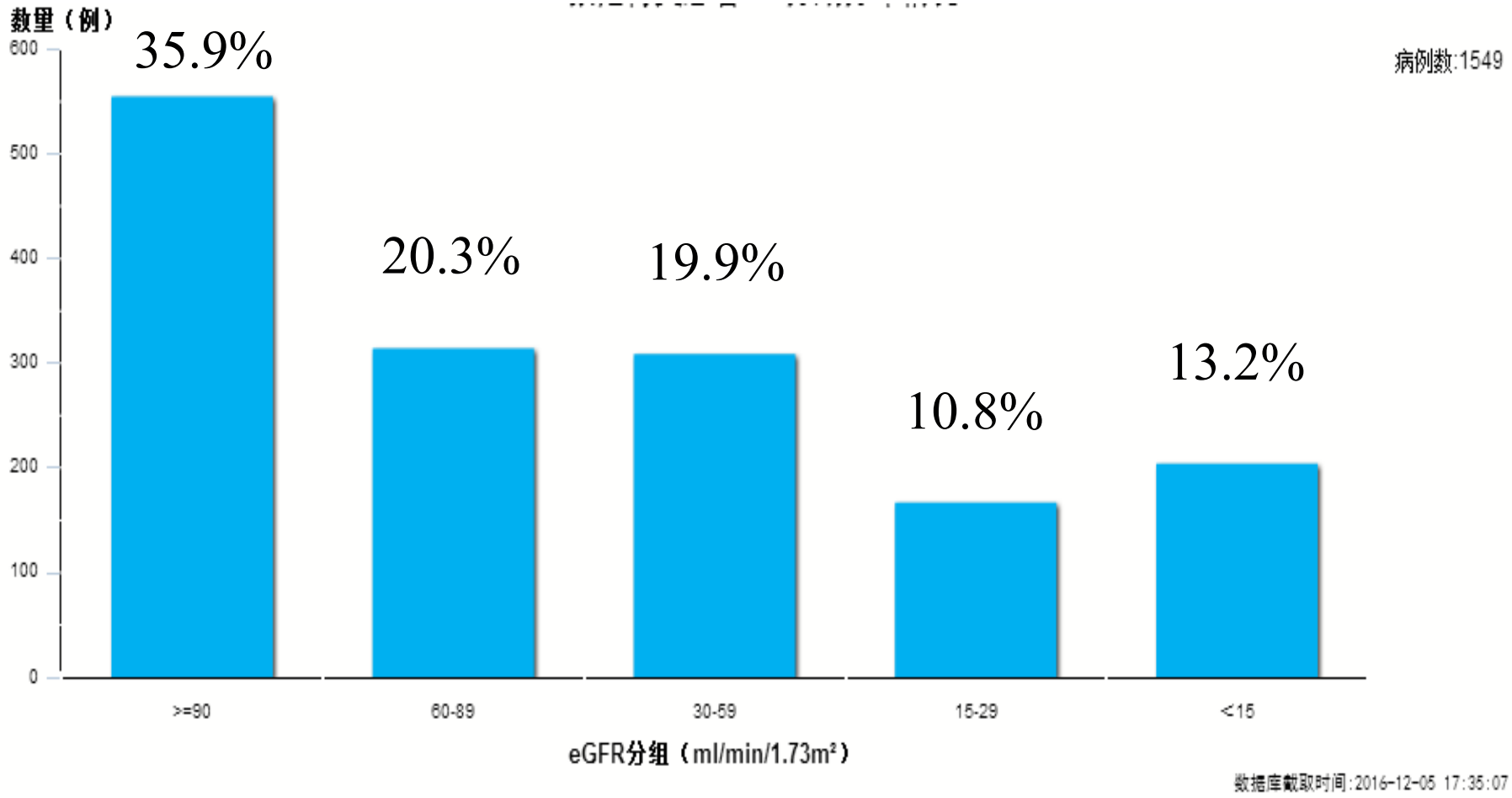
http://ln.medidata.cn/

Distribution of Pathological types- IV, V



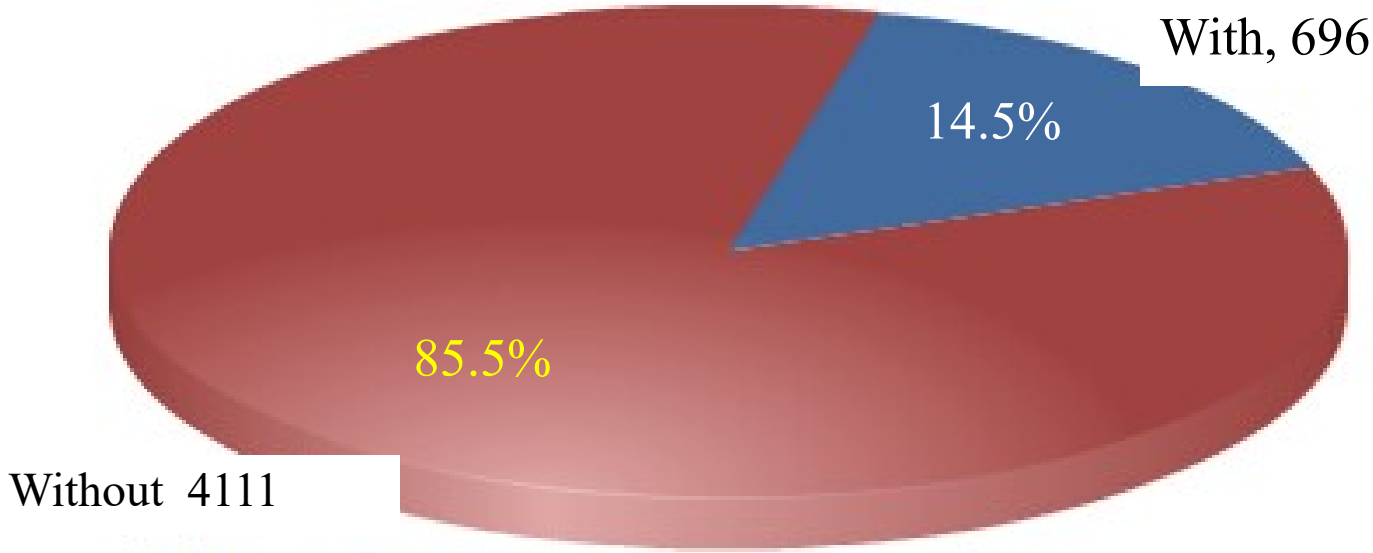
Pathological classification	No. of cases	Percentage (%)
I	37	1.59
II	208	8.93
III	223	9.58
IV	1011	43.43
V	418	17.96
V+III	71	3.05
V+IV	131	5.63
VI	229	9.84
All	2328	100

Distribution of CKD Stages – 1-3 stages



http://ln.medidata.cn/

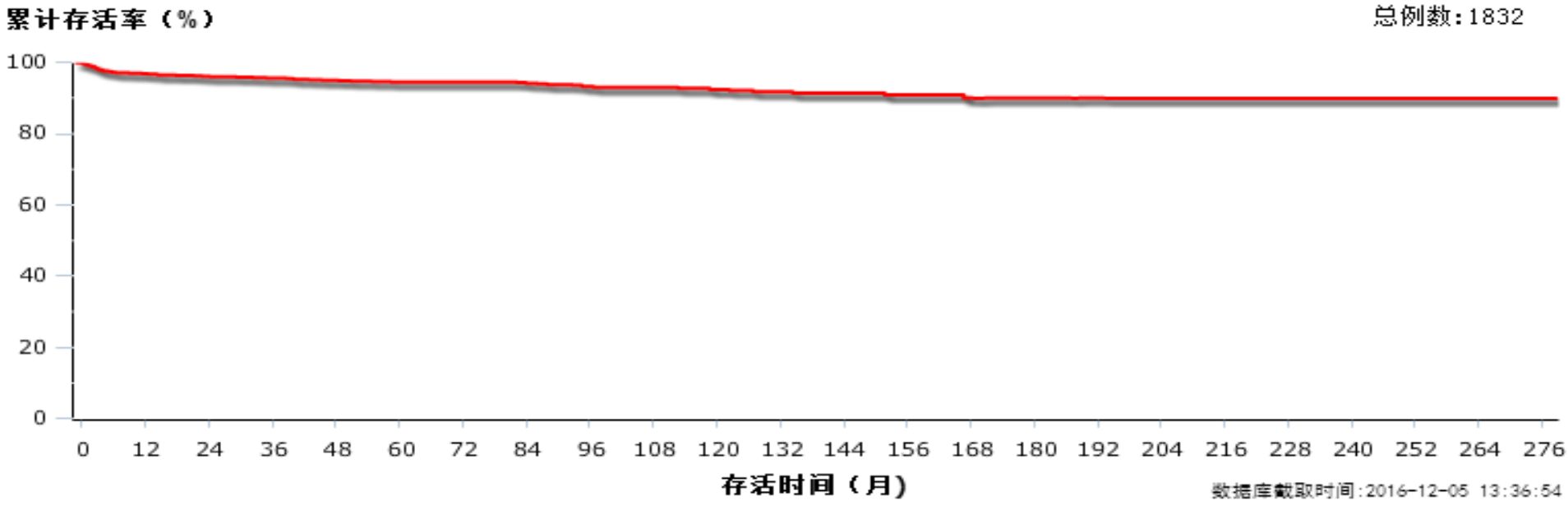
Relapse rate in HELP Cohort



Relapse	No. of cases	Percentage(%)
Yes	696	14.5
No	4111	85.5
All	4807	100

http://ln.medidata.cn/

Patient Survival in HELP Cohort



Cumulative patient survival rate（%）

3 year	5 year	10 year	20 year
95.61	94.59	92.51	90.14

http://ln.medidata.cn/

Risk factors associated with worse patient outcomes

Factors	Univariate analysis		Multivariate analysis	
	HR(95%CI)	P Value	HR(95%CI)	P Value
Age (per ↑ 10 years)	1.114(0.933,1.330)	0.232	**1.087(0.912,1.295)**	**0.350**
Gender (male VS female)	2.167(1.318,3.563)	0.002	**1.832(1.088,3.083)**	**0.023**
SLE prebiopsy duration (per ↑ 1 m)	0.999(0.994,1.005)	0.822		
LN prebiopsy duration (per ↑ 1 m)	1.000(0.997,1.003)	0.984		
ACLA (positive VS negative)	1.158(0.735,1.824)	0.528		
Mean arterial pressure (per ↑ 10mmHg)	1.324(1.154,1.519)	<0.001	**1.227(1.049,1.435)**	**0.011**
Proteinuria (per ↑ 1+)	4.847(1.525,15.406)	0.007	**3.425(1.050,11.174)**	**0.041**
Microhematuria (per ↑ 1+)	1.131(0.965,1.325)	0.130		
Serum creatinine (>177umol/L VS ≤ 177umol/L)	2.896(1.772,4.733)	<0.001	**2.233(1.327,3.755)**	**0.002**
Serum albumin (per ↑ 10 g/L)	0.772(0.556,1.073)	0.124		
SLEDAI (per ↑ 1)	1.041(1.001,1.083)	0.045	**1.038(0.993,1.086)**	**0.097**
Immunsuppresion (yes vs. no)	0.641(0.402,1.023)	0.062	**0.583(0.358,0.949)**	**0.030**

Causes of Death in LN

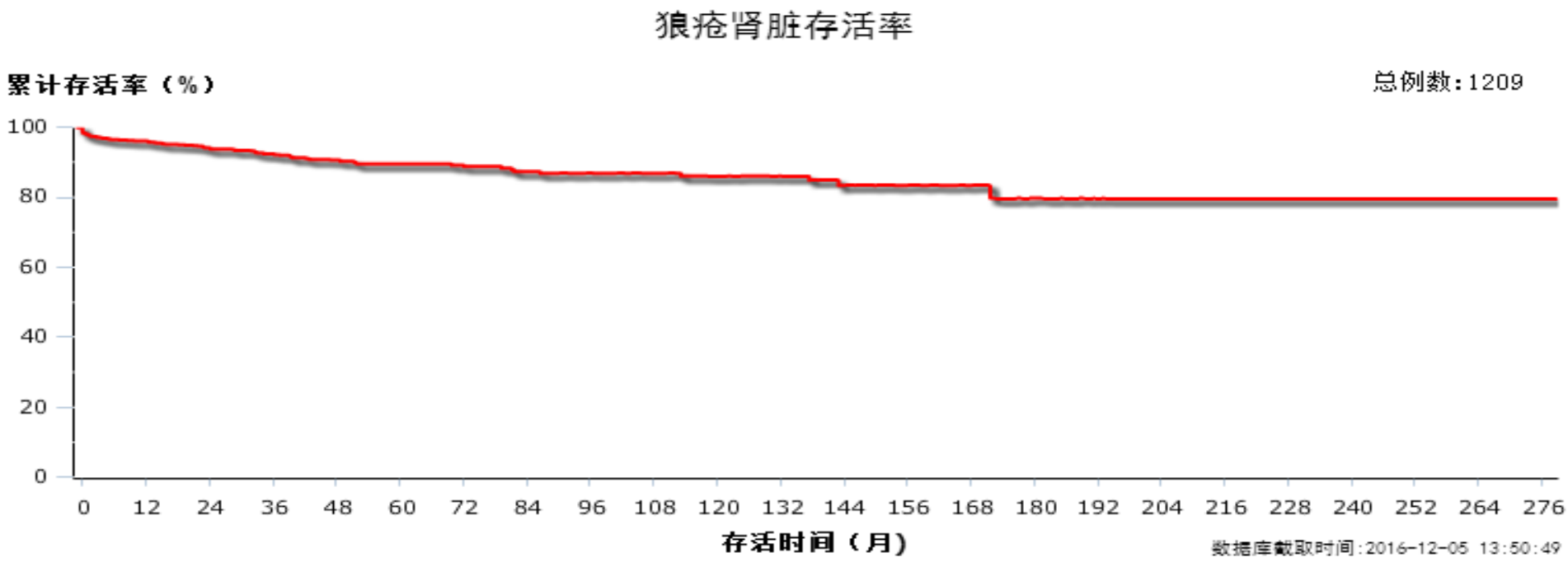
Causes	Patients No	Percentage (%)
Cardiovascular events	**17**	**21.25**
Malignant arhythmia	**2**	11.76
ACS	**1**	5.88
AHF	**10**	58.82
Other CVD events	**4**	29.41
Cerebrovascular events	**3**	**3.75**
Infection	**22**	**27.50**
Unknown	**28**	**35.00**
Other	**10**	**12.50**

Causes of Mortality in Different SLE/LN Cohorts

	Infection	CVD	Tumor
SLE	50%	20.8%	12.5%
LN	37.8%	27%	13.5%
HELP	31.4%	19.8%	-

Nephrol Dial Transplant (2012) 27: 3248–3254
Rheumatology 2015;54:836843
http://ln.medidata.cn/

Renal Survival in HELP Cohort



Cumulative renal survival rate（%）

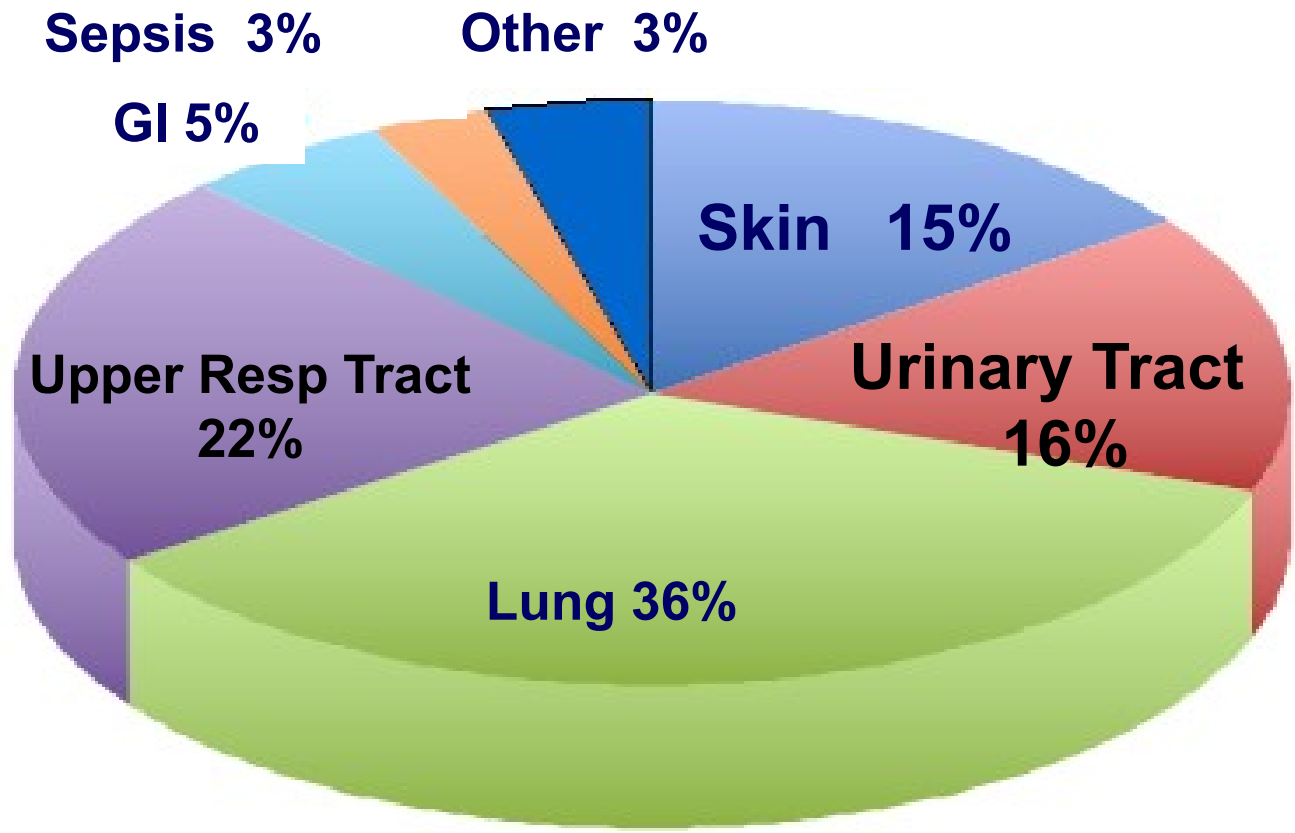
3 year	5 year	10 year	20 year
92.45	89.61	86.12	79.84

http://ln.medidata.cn/

Risk factors associated with worse renal outcomes

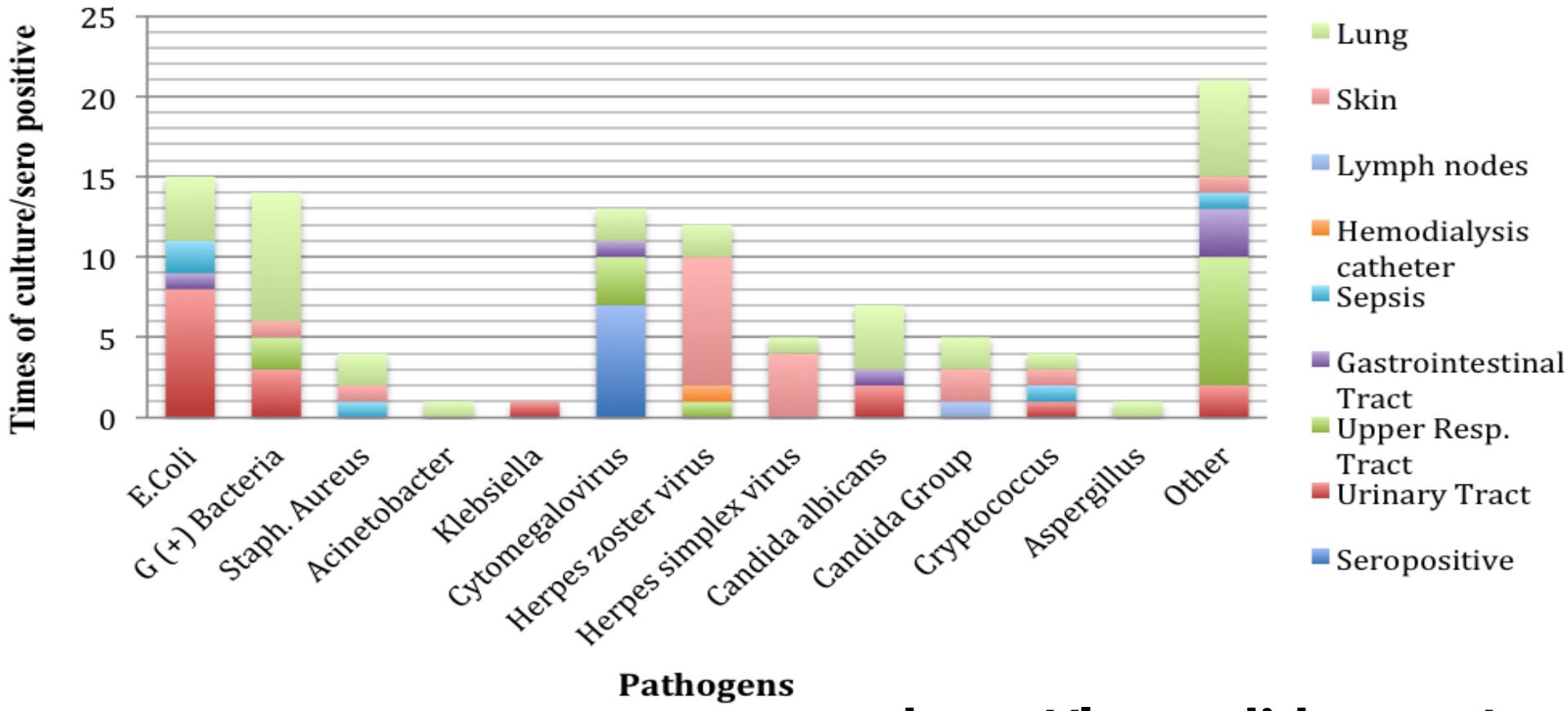
Factors	Univariate analysis		Multivariate analysis	
	HR(95%CI)	P Value	HR(95%CI)	P Value
Age (per ↑ 10 years)	0.996(0.804,1.235)	0.971	0.934(0.742,1.176)	0.561
Gender (male VS female)	0.945(0.465,1.921)	0.876	0.911(0.444,1.870)	0.799
SLE prebiopsy duration (per ↑ 1 m)	1.005(1.000,1.009)	0.040	1.006(1.001,1.011)	0.021
LN prebiopsy duration (per ↑ 1 m)	1.001(0.998,1.003)	0.591		
ACLA (positive VS negative)	1.714(1.024,2.871)	0.040	1.742(1.040,2.919)	0.035
Mean arterial pressure (per ↑ 10mmHg)	1.179(1.004,1.384)	0.045	1.090(0.912,1.303)	0.344
Proteinuria (per ↑ 1+)	1.363(1.064,1.745)	0.014	1.315(1.023,1.690)	0.032
Microhematuria (per ↑ 1+)	0.969(0.815,1.153)	0.724		
Serum creatinine (>177umol/L VS ≤ 177umol/L)	2.109(1.158,3.839)	0.015	1.913(1.037,3.528)	0.038
Uric acid(per ↑ 100 μmol/L)	1.141(0.977,1.333)	0.096		
C3 (per ↑ 1g/L)	1.168(0.466,2.926)	0.740		
C4 (per ↑ 1g/L)	0.755(0.171,3.323)	0.710		
Cholesterol (per ↑ 1 mmol/L)	1.054(0.945,1.175)	0.343		
Triglyceride (per ↑ 1 mmol/L)	0.991(0.843,1.166)	0.916		
Serum albumin (per ↑ 10 g/L)	0.892(0.620,1.284)	0.539		
SLEDAI (per ↑ 1)	1.016(0.971,1.063)	0.498		

Infectious Sites of LN



http://ln.medidata.cn/

Pathogens of Infection in LN



http://ln.medidata.cn/

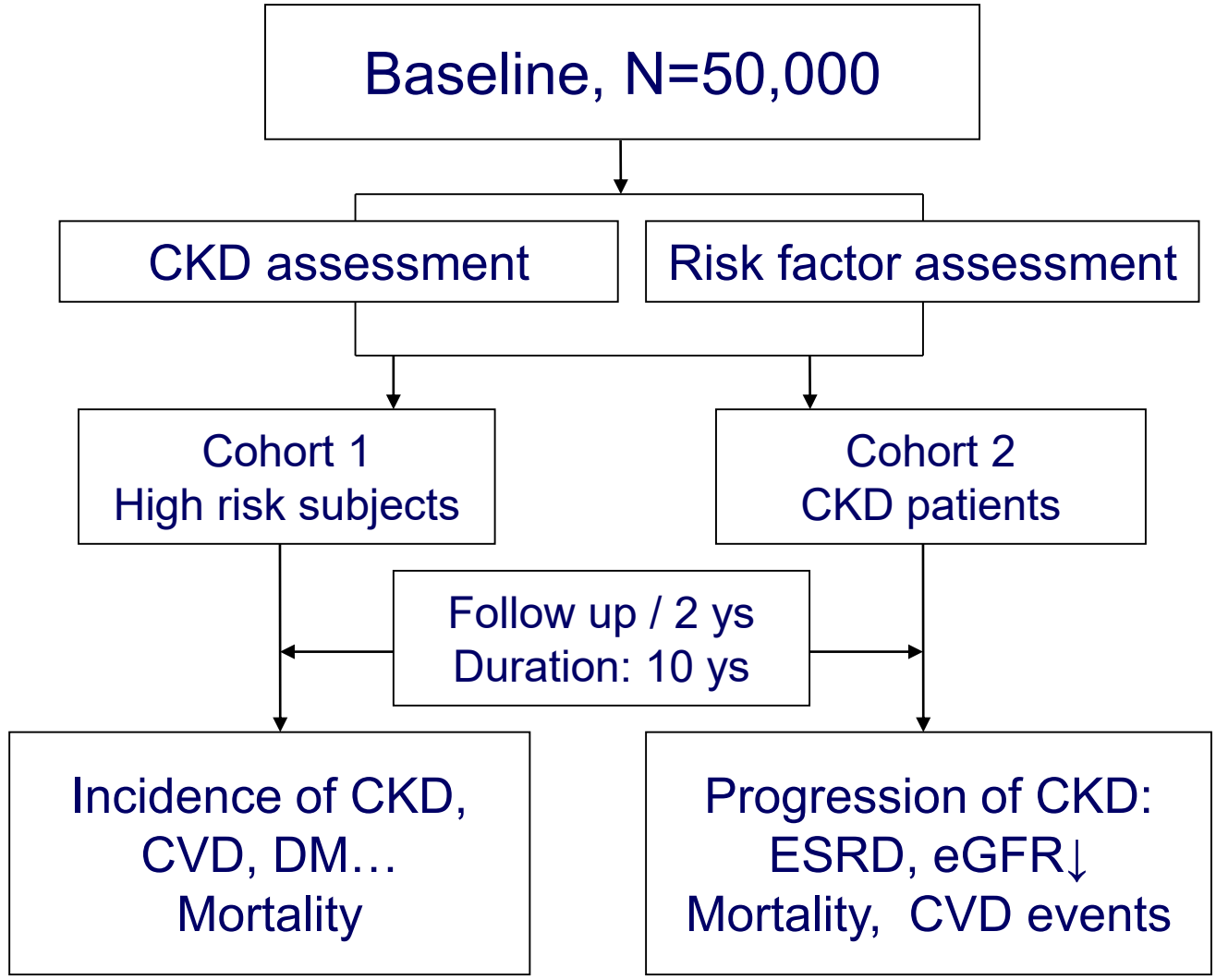
Challenges of CKD Management

- **Clinical patterns**: Microscopic haematuria to massive proteinuria
- **Pathological features:** slightly mesangial proliferative to global sclerosis
- **Response to therapy:** Sensitive, dependent, or resistant to treatment agents
- **Clinical outcomes:** stable renal function for lifetime or progress to ESRD

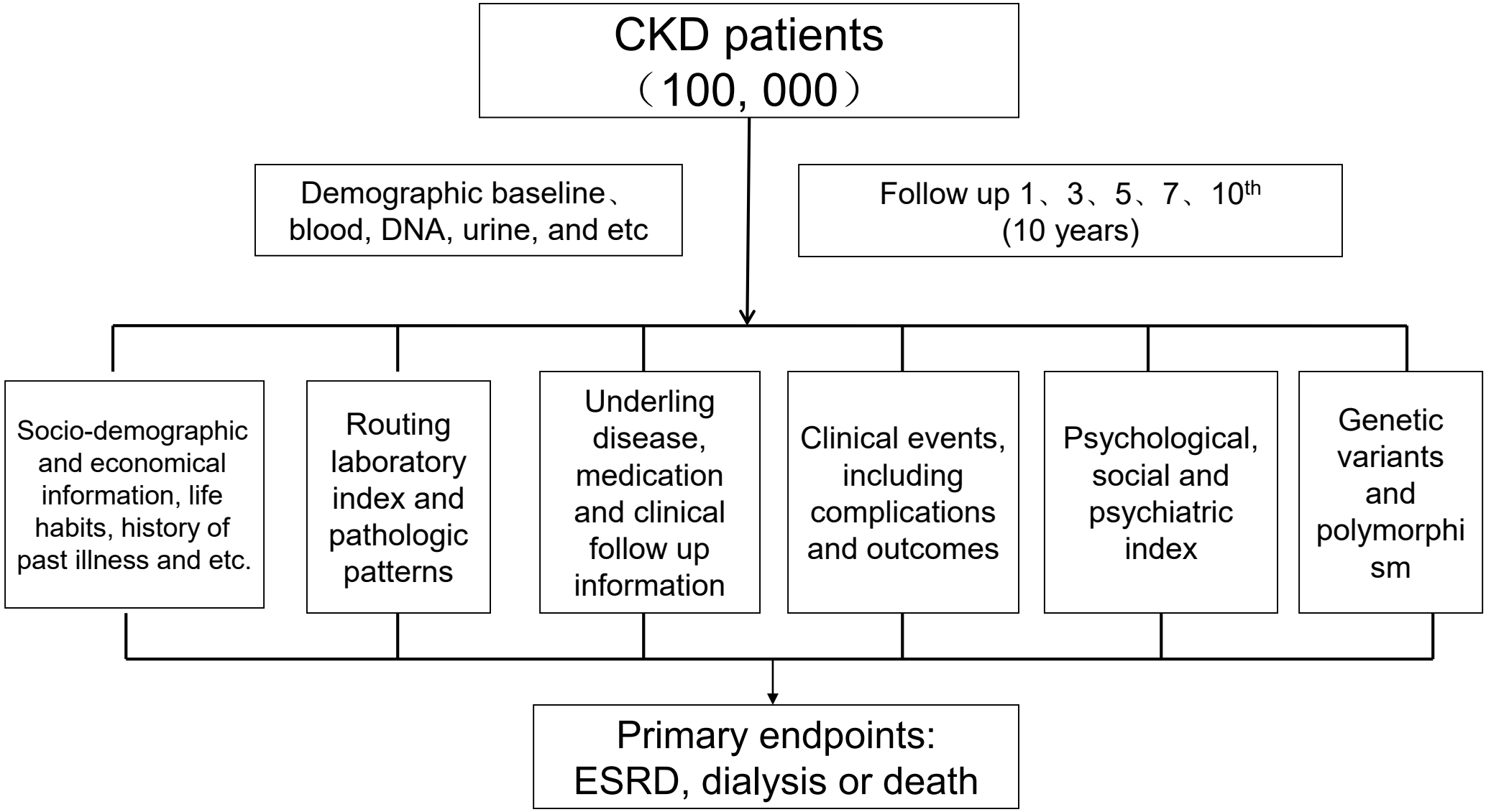
CKD Program in The Future

- Precision Prevention
- Precision Prediction
- Precision Treatment

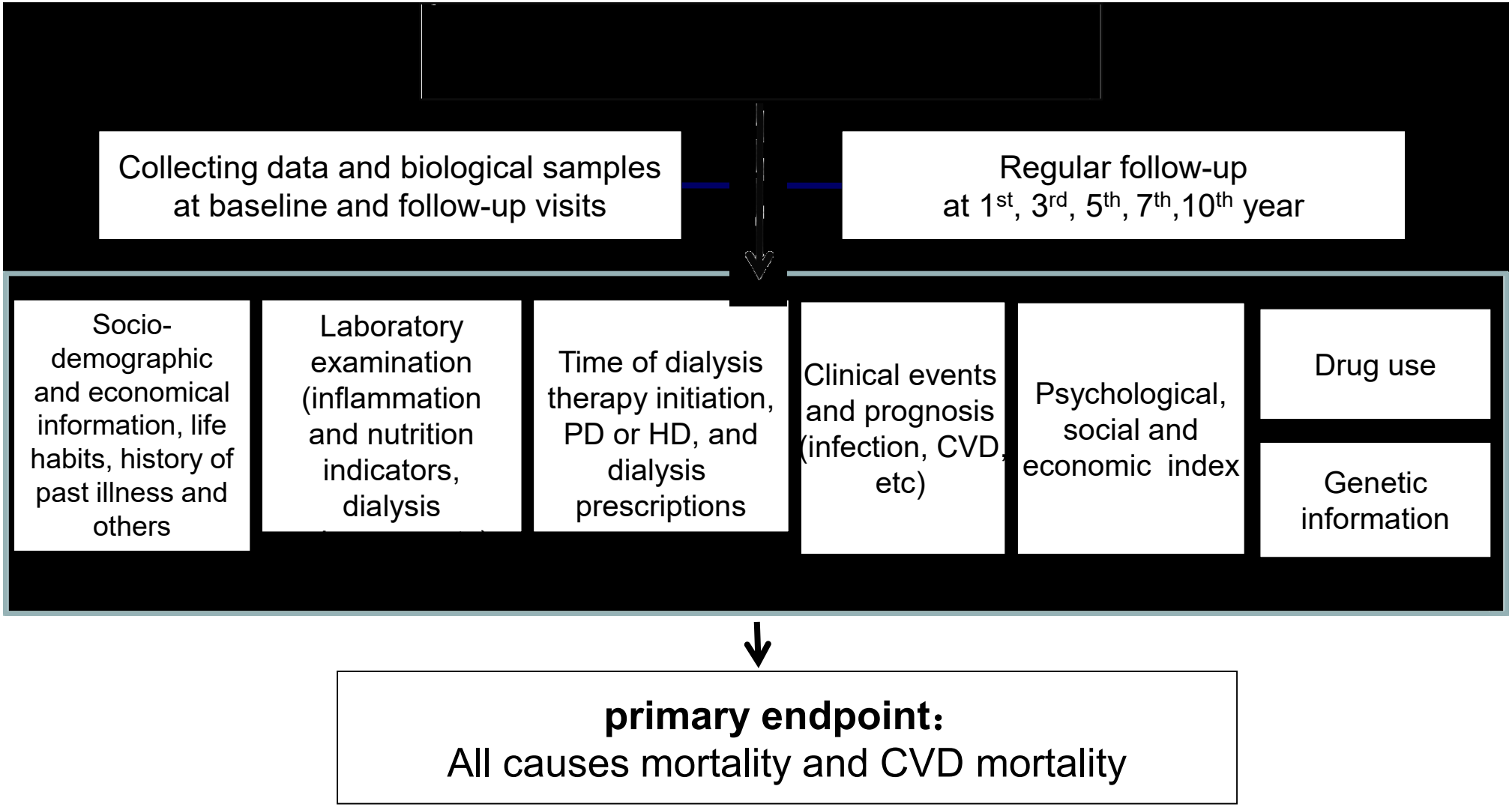
Cohort 1 Risk factors of CKD development



Cohort 2： Risk factors on CKD progression



Cohort 3 Risk factors on mortality of ESRD Pts



Risk Factors of CKD in Chinese

- age
- diabetes
- hypertension
- nephrotoxic drugs
- **hyperuricemia**
- Smoking
- metabolic syndrome
- first-degree relatives
- periodontal disease
- etc, ……

Chen W,……Yu XQ. NDT 2009; 24:1205-12*

Chen W,……Yu XQ. NDT 2011;26:1592-9*

Liu Q, Yu XQ,……Chen W. Plos one 2012;7(10):e47100*

Li Z, ……Yu XQ, Chen W. KBPR. 2012; 36(1):98-106*

Wei X, Li ZJ,…… Yu XQ. Nephrology 2012;17(2):123-30*

Liu KJ, Liu QH,…… Yu XQ. Plos one. 2013; 8(8): e70767*

Hyperuricemia In General Population

- Southern Han Chinese 26.8%
- Southern Han Chinese 25.3%
- The Zang in High Altitude 29.1%

Chen W,…Yu XQ. NDT; 2009,24:1205-12*

Chen W,…Yu XQ. NDT 2011;26:1592-9*

Nan HR, et al. J Rheumatol; 2006,33:1346-50

High Risk Factor of CKD

	eGFR <60 mL/min per 1·73 m²	Albuminuria
Age change by 10 years	1·74 (1·59–1·91)	1·08 (1·02–1·15)
Sex (women *vs* men)	1·66 (1·17–2·37)	1·42 (1·17–1·71)
Nephrotoxic drug use	1·64 (0·94–2·85)	1·31 (0·98–1·75)
History of cardiovascular disease	2·51 (1·24–5·10)	1·40 (0·91–2·14)
Hypertension	1·08 (0·80–1·46)	2·71 (2·31–3·18)
Diabetes	2·00 (1·35–2·97)	1·99 (1·60–2·48)
Hyperuricaemia	9·30 (6·80–12·72)	0·88 (0·68–1·13)
Urban residents (*vs* rural residents)	1·12 (0·86–1·48)	0·97 (0·81–1·16)

Zhang L, Wang F, Wang L, et al. The Lancet, 2012, 379(9818): 815-822.

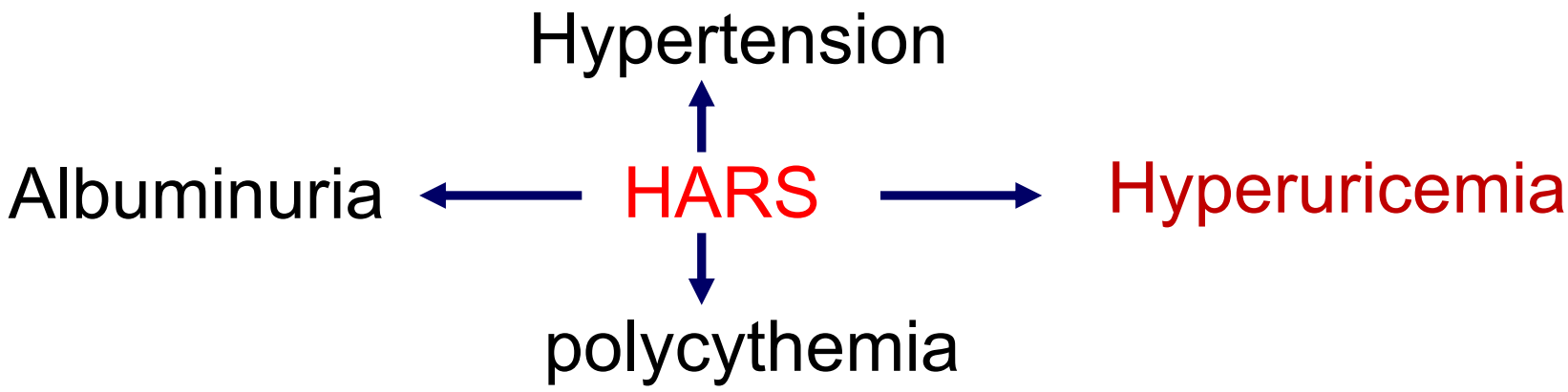
Hyperuricemia: High Altitude Renal Syndrome

SPECIAL ARTICLE www.jasn.org

JASN

High Altitude Renal Syndrome (HARS)

Abdias Hurtado Arestegui,* Richard Fuquay,† Jeffrey Sirota,† Erik R. Swenson,‡ Robert B. Schoene,‡ J. Ashley Jefferson,‡ Wei Chen,§ Xue-qing Yu,§ Jackeline Pando Kelly,‖ Richard J. Johnson,† and Elizabeth Escudero*



Chen W,…Yu XQ. NDT 2011;26:1592-9*
Arestegui AH, . et al. JASN 2011;22:1963- 8.

Hyperuricemia in IgA Patients

- IgA patients: 2566
- Hyperuricemia: 36.6%

CKD stage	n	HU（N）	(%)
1	1282	208	16.2
2	589	220	37.4
3	384	255	66.4
4	171	150	87.7
5	140	107	76.4

Liang M, ….Yu XQ。Chinese Jouranl of Nephrology. 2013;5(29):326-332

Hyperuricemia on Renal Survival Independent on eGFR

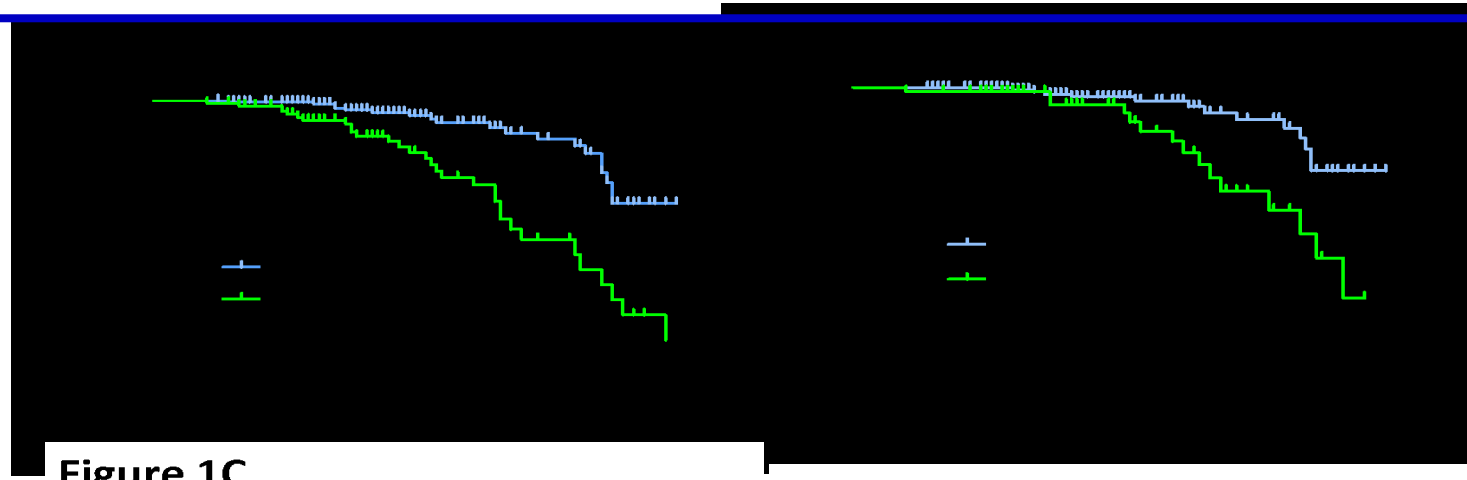


Figure 1C

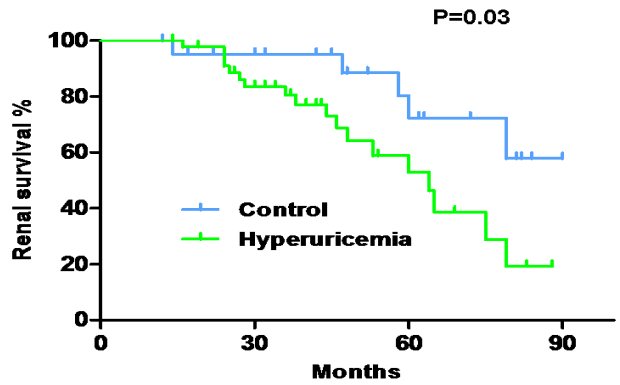


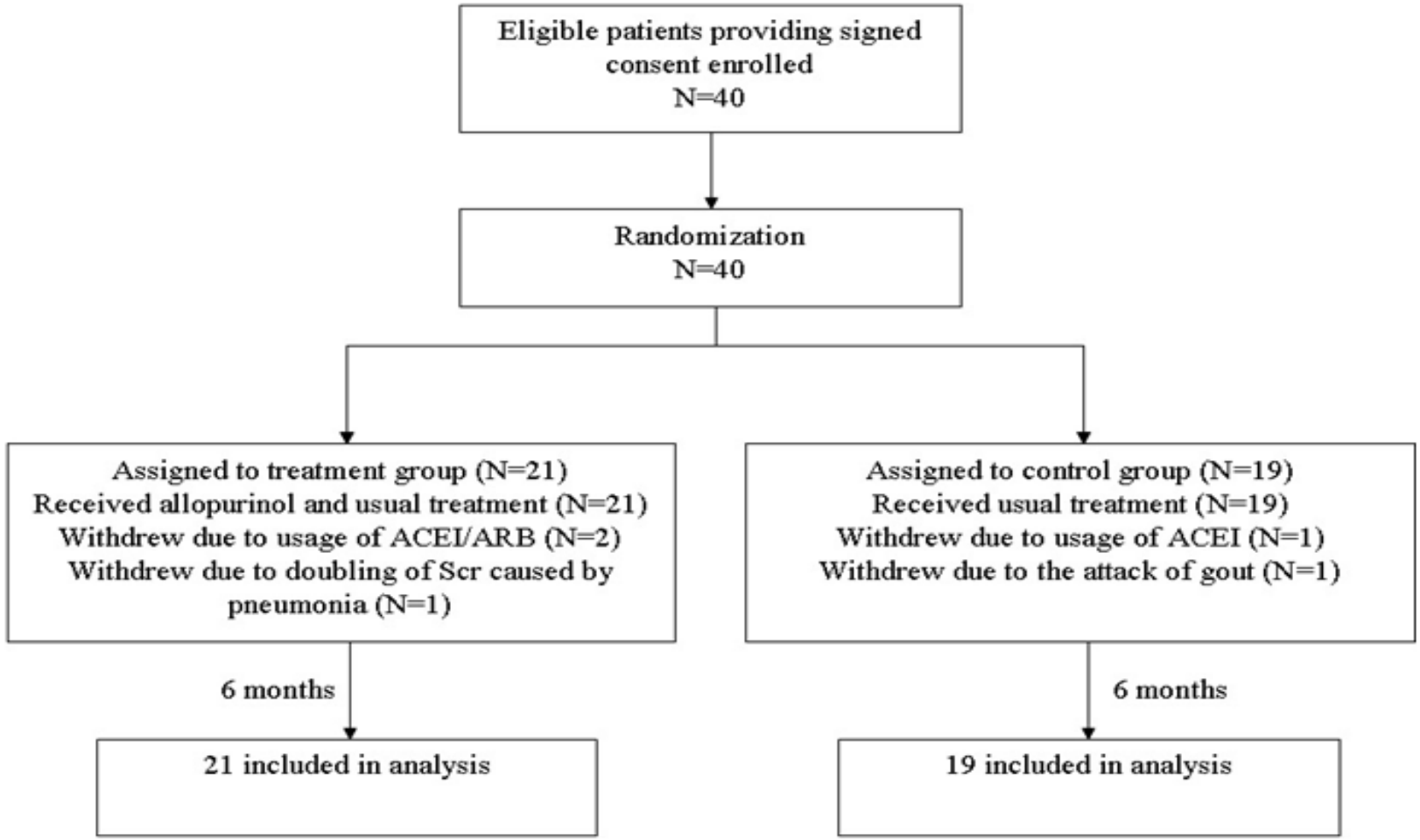
Figure 1D Numbers of patients exposed to risk at the time point

Group	baseline	12mo	36mo	60mo	90mo
CKD1-3					
HUA	112	108	60	22	16
CON	241	231	141	83	52
CKD1-2(eGFR≥60min/ml)					
HUA	64	62	35	12	10
CON	218	209	126	73	44
CKD3 (eGFR< 60min/ml)					
HUA	48	46	25	10	6
CON	23	22	15	10	8

HUA: hyperuricemia; CON: control with normouricemia

Shi Y, Chen W et al. Kidney & Blood Pres Res. 2012;35(3):153-160*

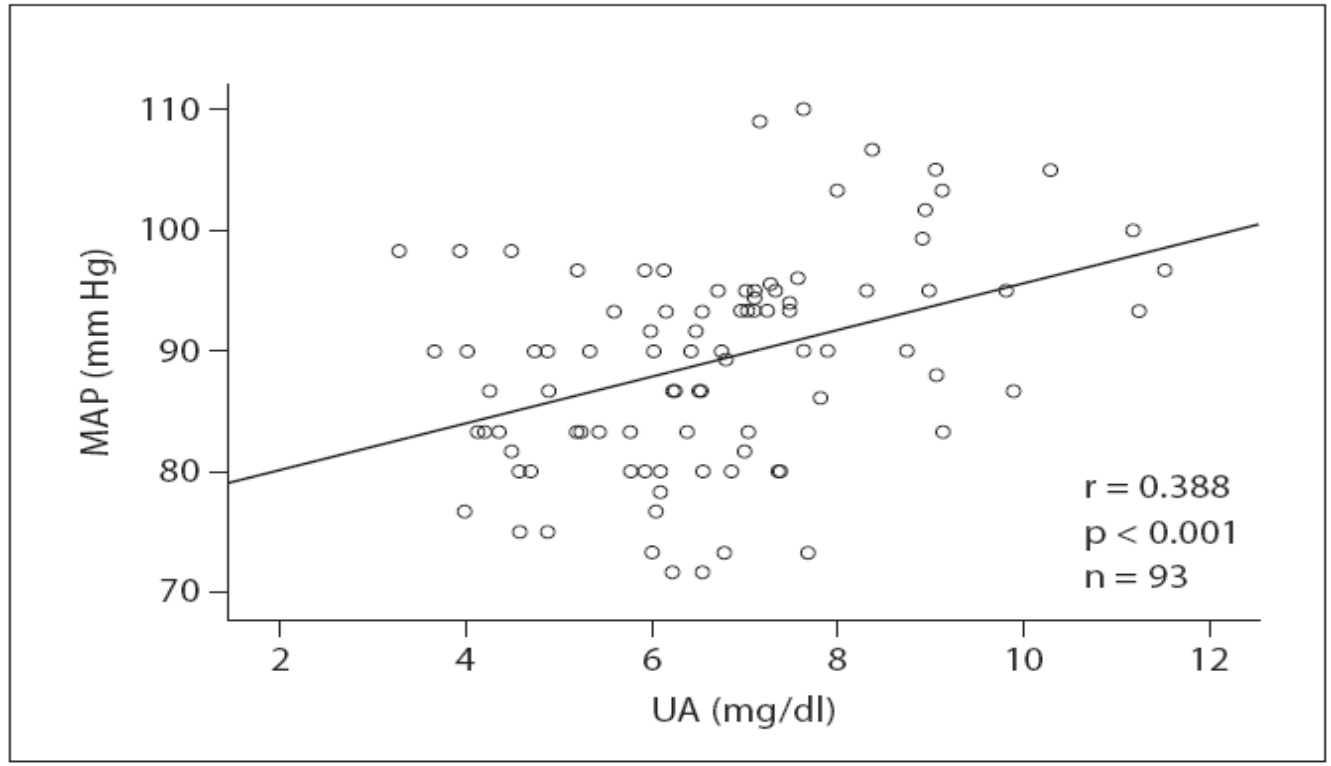
Lowing Uric Acid on Renal Survival: RCT



Shi Y, Chen W et al. Kidney & Blood Pres Res . 2012;35(3):153-160*

Lowing Uric Acid on Renal Survival: RCT

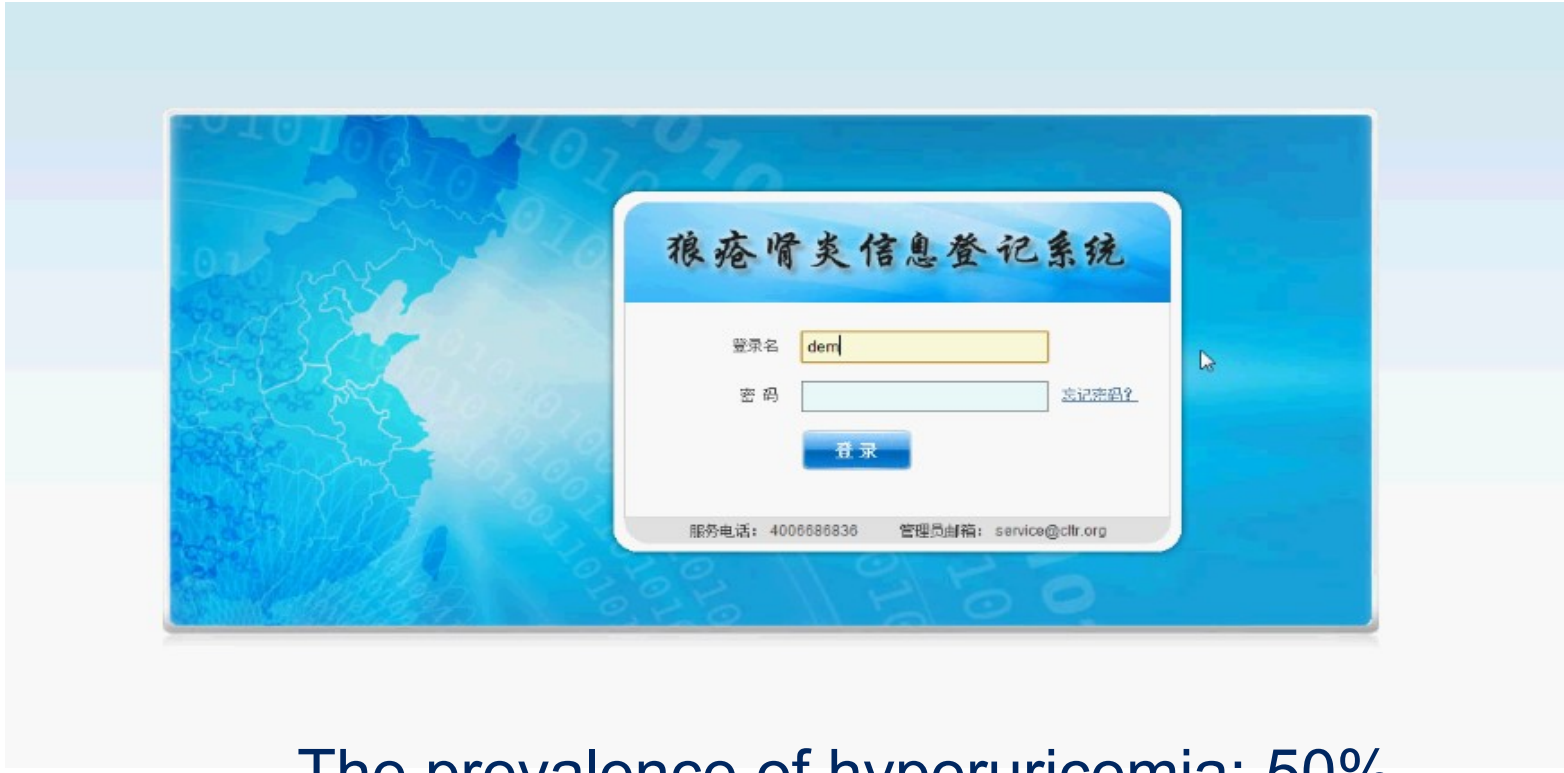
- Blood pressure and uric acid were closely correlated
- Lowing UA is benefit for BP control



Shi Y, Chen W et al. Kidney & Blood Pres Res. 2012;35(3):153-160*

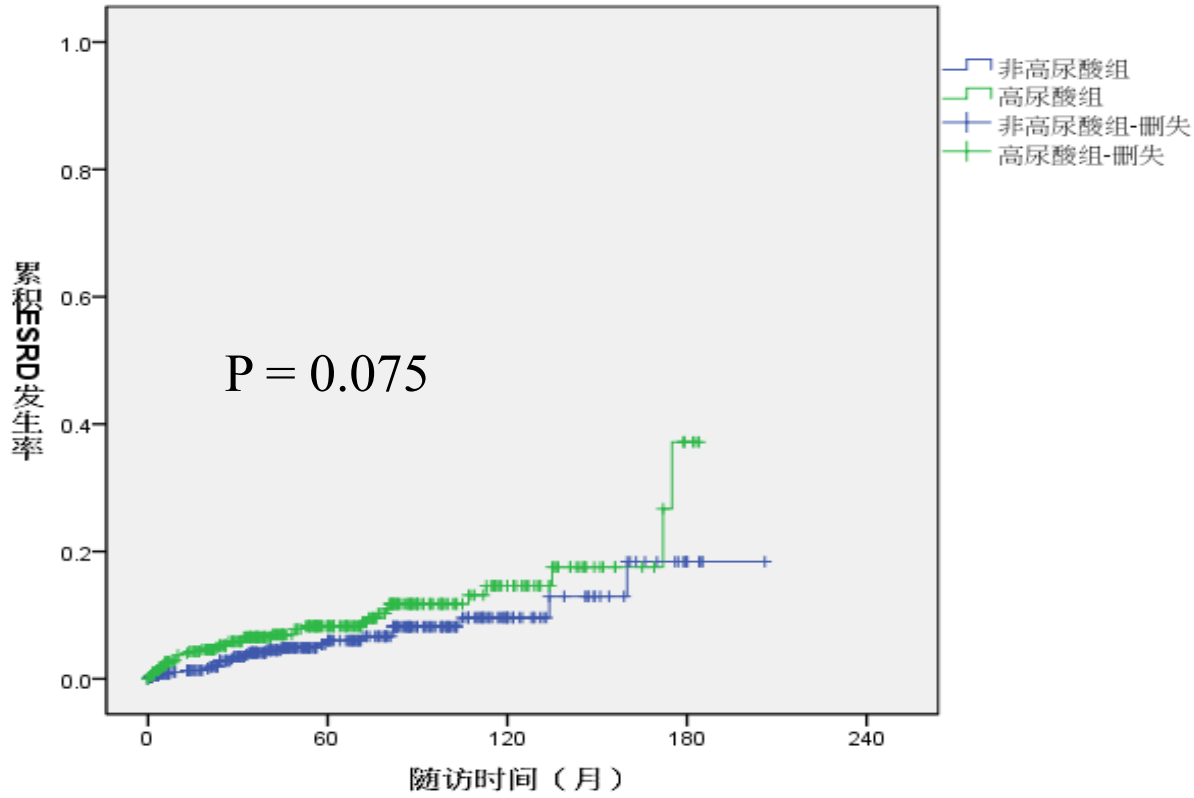
Hyperuricemia in LN Patients

LN: http://ln.medidata.cn/



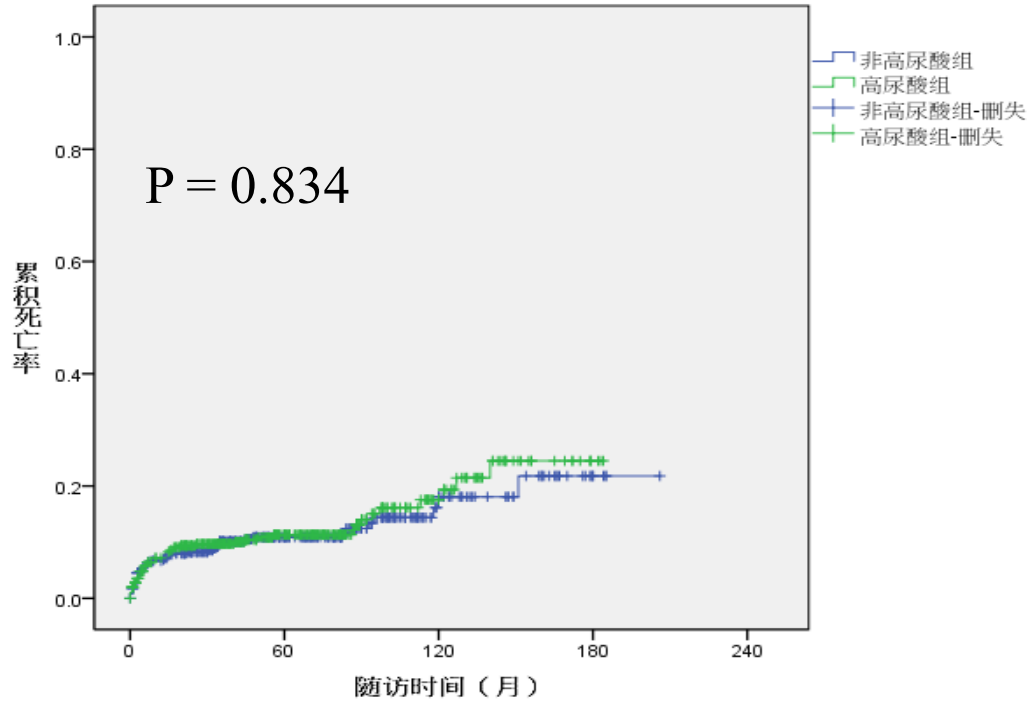
The prevalence of hyperuricemia: 50%

Hyperuricemia: not significant on renal survival



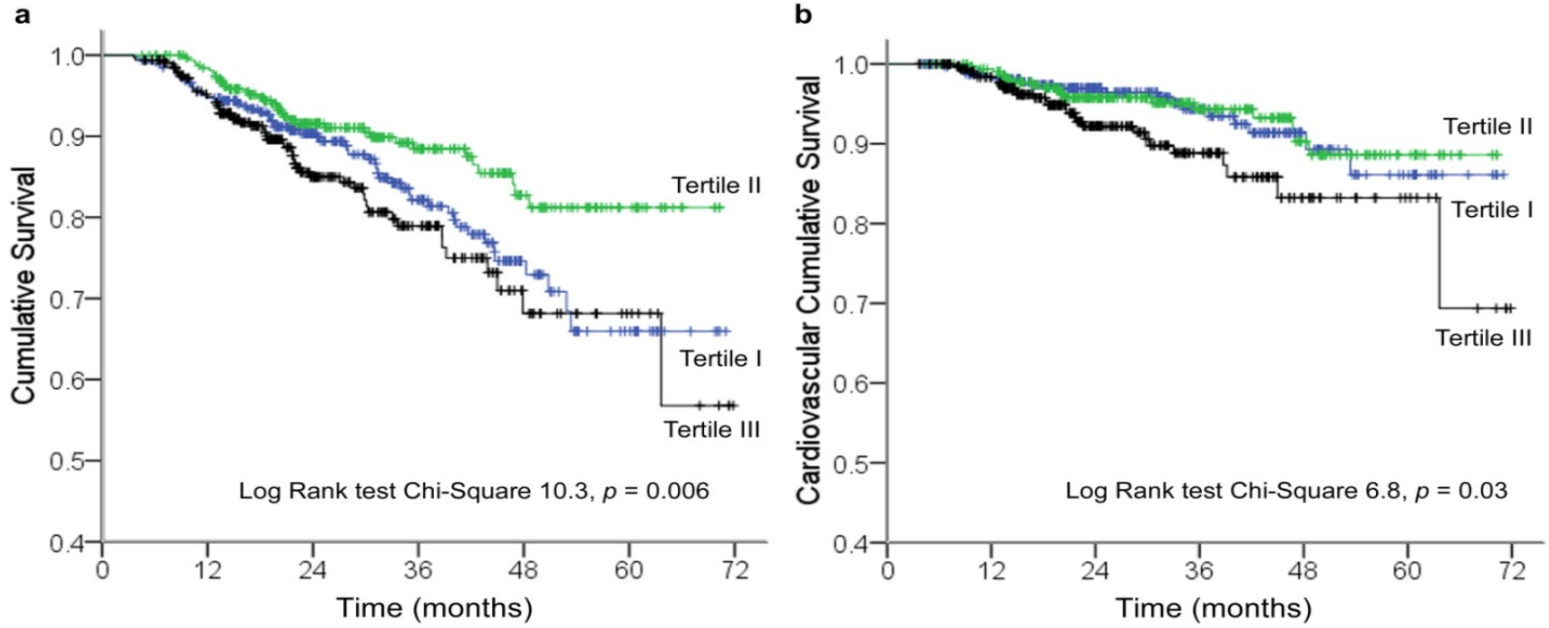
	5Y	10Y	15Y
Normal control (n=398)	5.4 %(n=167)	9.6%(n=41)	18.4%(n=6)
High UA (n=404)	8.3%(n=179)	14.6%(n=49)	37.2%(n=3)

Hyperuricemia: No effect on Patient Survival



	5年	10年	15年
Normal control (n=398)	10.9%(n=171)	16.2%(n=44)	21.8%(n=6)
High UA (n=404)	11.3%(n=181)	17.6%(n=50)	24.5%(n=3)

Risk Factor on All cause and CVD Mortality in PD



Number of patients at risk

	Months of follow-up					
	0	12	24	36	48	60
Tertile I	328	299	195	113	44	18
Tertile II	328	309	192	117	55	20
Tertile III	329	286	150	79	24	10

CAPD n= 985; Follow up (median)= 25 months

Huang F, Xia Q, Yu XQ. Am J Kidney Dis. 2013 Oct 28.*

Much significant in male CAPD patients

		Men		Women		Sex * SUA Interaction	
Group	Mortality Outcome	HR (95% CI)	*P*	HR (95% CI)	*P*	β	*P*
Total cohort[a]	All-cause	1.33 (1.14-1.56)	<0.001	1.03 (0.86-1.24)	0.8	−0.06	0.02
	CV	1.44 (1.17-1.77)	0.001	1.16 (0.97-1.38)	0.1	−0.10	0.02
Excluding patients using allopurinol[a]	All-cause	1.30 (1.10-1.56)	0.002	1.04 (0.87-1.24)	0.7	−0.06	0.04
	CV	1.36 (1.09-1.70)	0.006	1.17 (0.98-1.40)	0.08	−1.04	0.02

Note: $P < 0.05$ for main effect, $P < 0.1$ for interactions.

[a] Adjusted for age, body mass index, Davies score of comorbidities, hemoglobin, serum albumin, serum creatinine, albumin-corrected calcium, serum phosphorus, total triglycerides, low-density lipoprotein cholesterol, residual renal function, log-transformed high-sensitive C-reactive protein, total Kt/V, use of allopurinol, use of loop diuretics, use of angiotensin converting enzyme inhibitor or angiotensin receptor blocker.

Huang F, Xia Q, Yu XQ. Am J Kidney Dis. 2013 Oct 28.*

CKD Program in The Future

- **Precision Prevention**
- **Precision Prediction**
- **Precision Treatment**

High prevalence of Systemic Lupus Erythematosus in Asian

		Lupus Nephritis (LN)		
	Denominator	Cases (% of total)	Prevalence*	95% CI
Total	23,893,092	7,388 (100)	30.92	30.22-31.63
African-American(F)	4,334,630	3,233 (43.8)	74.59	72.06-77.20
African-American(M)	1,589,145	303 (4.1)	19.07	17.04-21.34
Hispanic(F)	2,739,030	1,011 (13.7)	36.91	34.70-39.26
Hispanic(M)	1,027,972	113 (1.5)	10.99	9.14-13.22
White(F)	7,692,686	1,547 (20.9)	20.11	19.13-21.14
White(M)	3,454,024	218 (3.0)	6.31	5.53-7.21
Asian(F)	527,669	426 (5.8)	80.73	73.42-88.77
Asian(M)	301,540	43 (0.6)	14.26	10.58-19.23
Native American(F)	220,836	99 (1.3)	44.83	36.81-54.59
Native American(M)	89,900	14 (0.2)	15.57	9.22-26.29
Other(F)	1,151,105	336 (4.5)	29.19	26.23-32.48
Other(M)	764,555	45 (0.6)	5.89	4.39-7.88

* per 100,000 adults

Feldman,et al.Arthritis Rheum.2013 March;65(3):753–763

Epidemiology of Systemic Lupus Erythematosus

Table 3. Estimated age- and sex-specific prevalence rates of lupus nephritis in the northwest of England (per 100,000 population)*

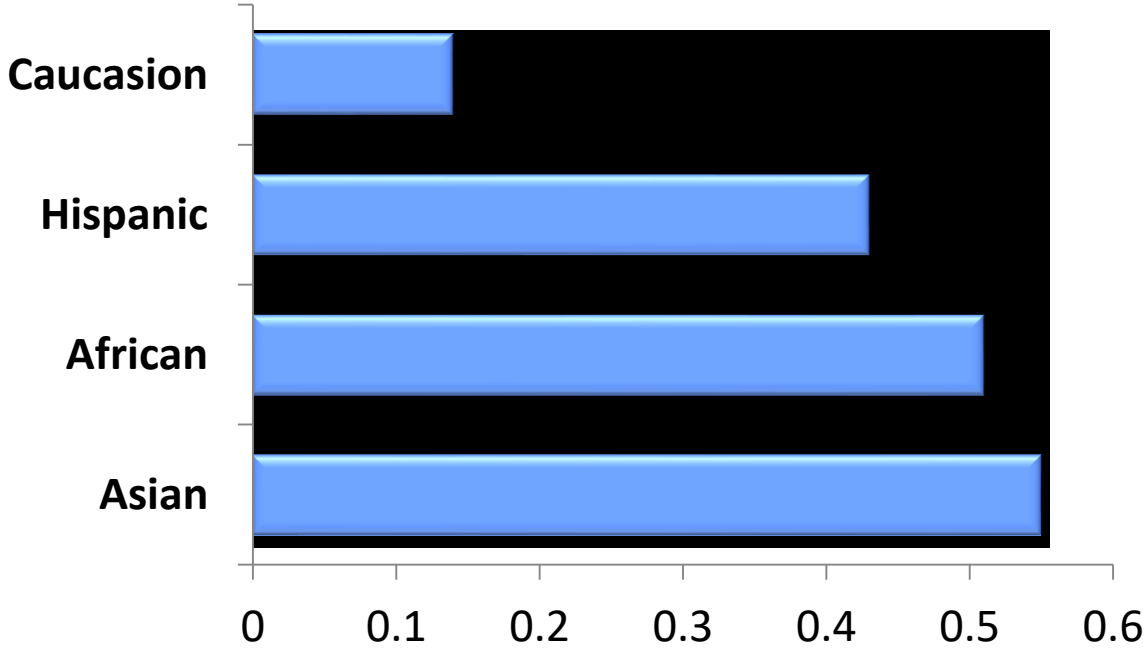
	Women, age group				Men, age group			
Ethnic group	18–39 years	40–59 years	≥60 years	Total, ≥18 years	18–39 years	40–59 years	≥60 years	Total, ≥18 years
White	5.1 (3.7–6.9)	8.3 (6.4–10.6)	3.4 (2.2–5.1)	5.6 (4.7–6.7)	0.6 (0.2–1.4)	0.9 (0.4–1.9)	2.0 (1.0–3.6)	1.1 (0.7–1.6)
Indo-Asian	16.0 (6.4–32.9)	41.0 (17.7–80.8)	–	21.4 (12.0–35.2)	2.3 (0.1–12.7)	5.0 (0.1–27.8)	11.7 (0.3–64.9)	4.1 (0.9–12.1)
Afro-Caribbean	144.1 (74.5–251.8)	47.2 (5.7–170.7)	38.9 (1.0–217.0)	99.2 (55.5–163.6)	11.9 (0.3–66.3)	68.4 (14.1–199.8)	–	24.8 (6.8–63.5)
Chinese	144.0 (62.2–283.8)	94.4 (19.5–275.8)	–	110.3 (55.0–197.3)	36.0 (4.4–130.2)	–	–	20.3 (2.5–73.3)
Total	7.7 (6.0–9.7)	9.6 (7.6–12.0)	3.5 (2.3–5.2)	7.1 (6.1–8.2)	1.0 (0.5–1.9)	1.4 (0.7–2.5)	2.1 (1.1–3.7)	1.4 (1.0–2.0)

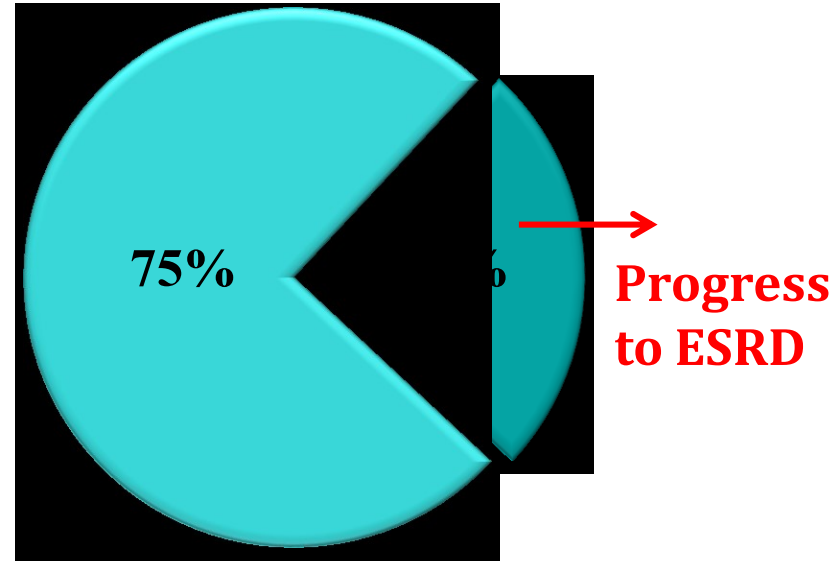
* Values are the mean percentage (95% confidence interval).

Rheumatology.2007;46:1814 –1818

25% LN Patients Progress to ESRD

The prevalence of LN in SLE patients





Autoimmune Dis. 2012;2012:849684

Nephrol Dial Transplant (2007) 22: 2531–2539
doi:10.1093/ndt/gfm245
Advance Access publication 17 May 2007

Original Article

NDT
Nephrology Dialysis Transplantation

The long-term outcome of 93 patients with proliferative lupus nephritis

Gabriella Moroni[1], Silvana Quaglini[2], Beniamina Gallelli[1], Giovanni Banfi[1], Piergiorgio Messa[1] and Claudio Ponticelli[3]

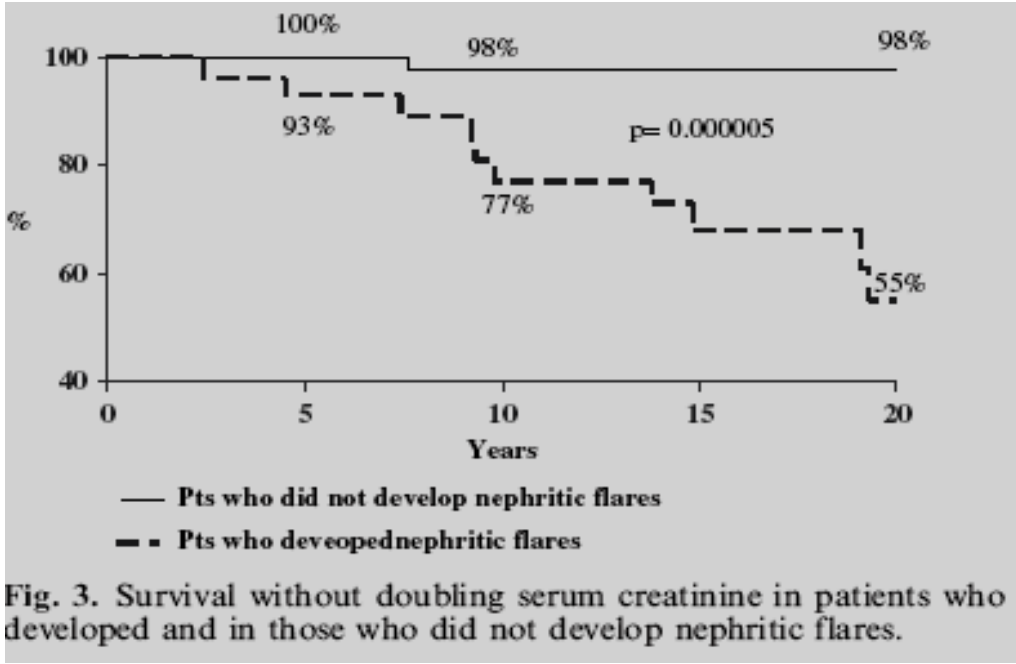


Fig. 3. Survival without doubling serum creatinine in patients who developed and in those who did not develop nephritic flares.

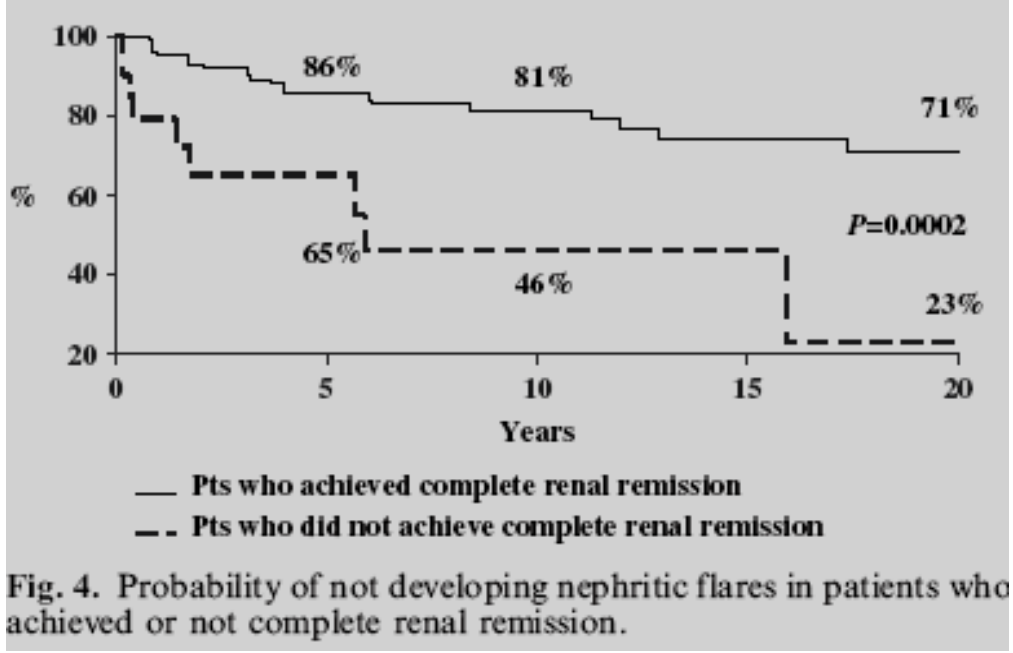
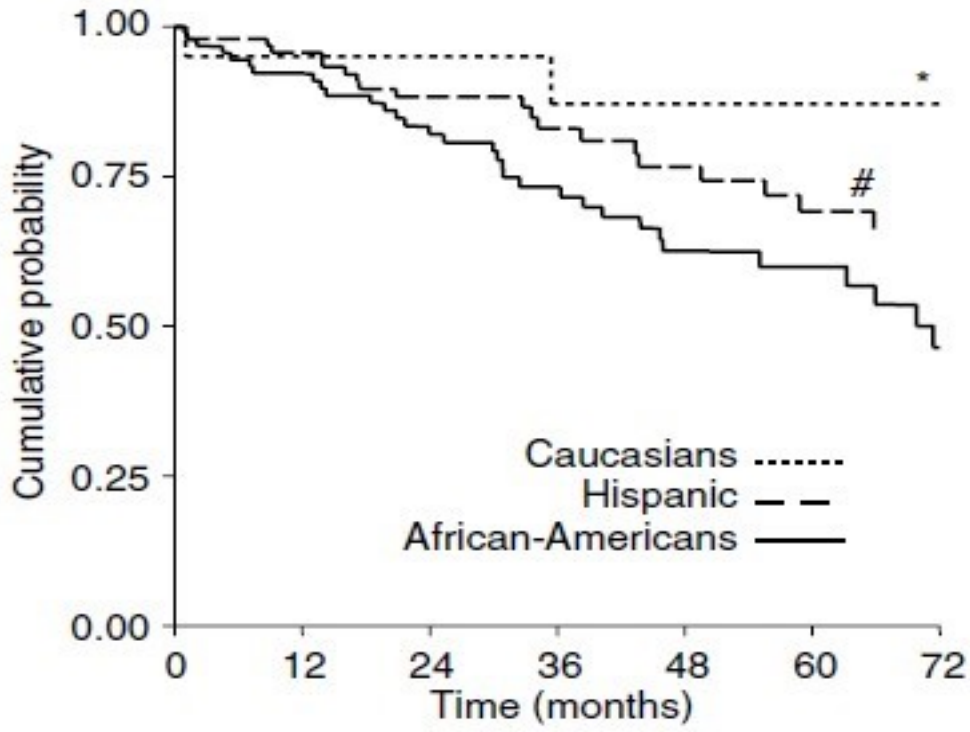


Fig. 4. Probability of not developing nephritic flares in patients who achieved or not complete renal remission.

Poor Clinical Outcome in African American



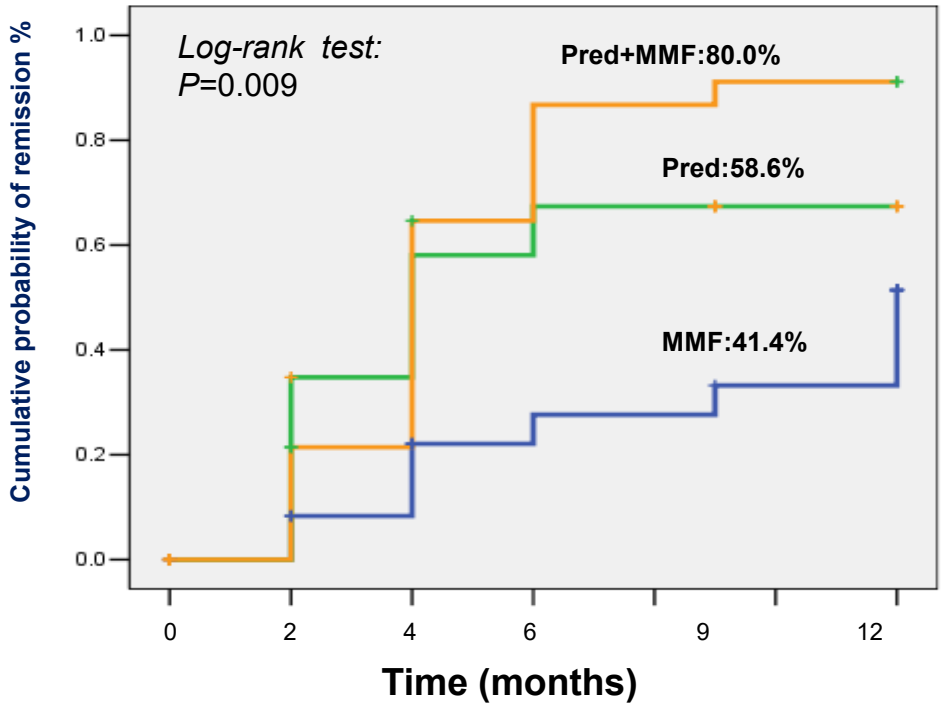
P=0.04

P=0.05

G Contreras,et al. Kidney Int.2006;69:1846–1851

Study	Patient selection	Protocols and grouping	Follow-up	Outcome
Maes BD et al. 2004 (n=34)	20<Ccr<70ml/min/, Upro>1g/d, Grade II to IV by Churg and Sobin SBP≥140 or DBP≥90	MMF (2.0/d)/Placebo(21/13)	CCr, Upro, 3ys Follow up	No benefit
Frisch G et al. 2005 (n=32)	20<Ccr<80ml/min/ Upro>1g/d, Glomerulosclerosis or tubulointerstitial atrophy and fibrosis ≥25% BP≥150/90 mmHg	MMF (2.0/d, n=17)/Placebo(17/15)(n=15) for 1yr	Scr,Upro, 3ys Follow up	No benefit
Chen et al 2002 (n=62)	Scr<4mg/dl, Upro≥2g/d, Grade IV-V by Lee No mention BP	OP(n=31, OP 0.8/kg.d) ; MMF(n=31, 1.5~2.0/d) 6 mons	Upro, Follow up 18 mon	reduction Upro
Tang S et al	Scr<3.4mg/dl, Upro>1g/d, Haas Grade II-IV <125/85 treated with ACEI/ARB	Control (n=20), ACEI or ARB; MMF(1.5-2.0/d,n=20),ACEI or ARB, 72 weeks	Upro follow up for 72 wks	reduction Upro

Low dose steroid and MMF in IgA nephropathy treatment in China

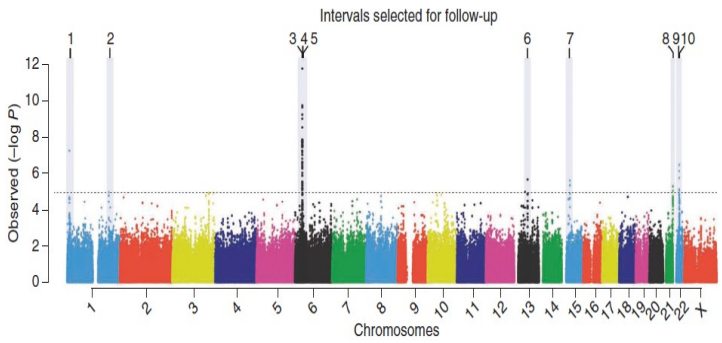


Response rate:

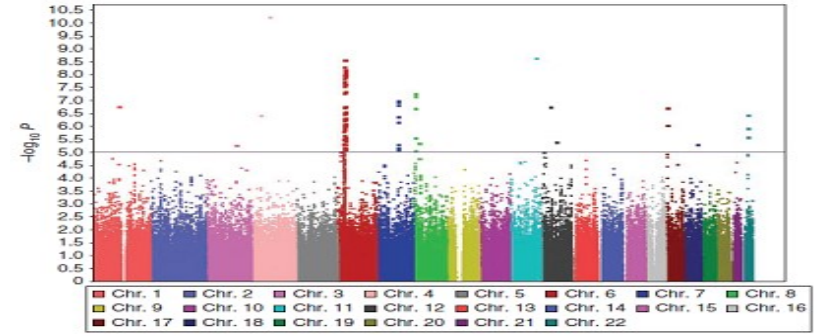
- **Pred+MMF: 80.0%**
- **Pred: 58.6%**
- **MMF: 41.4%**

GWAS study of IgAN

Susceptible loci	MHC	1q32	22q12	Others
IgAN study in Columbia, USA	√	√	√	
IgAN study in SYSU, China	√	not confirmed	√	two new loci (17p13,8p23)

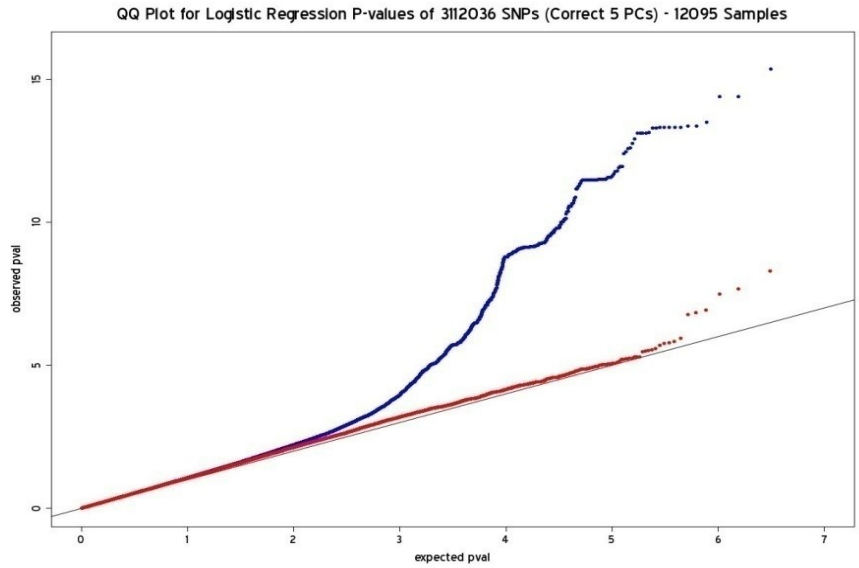


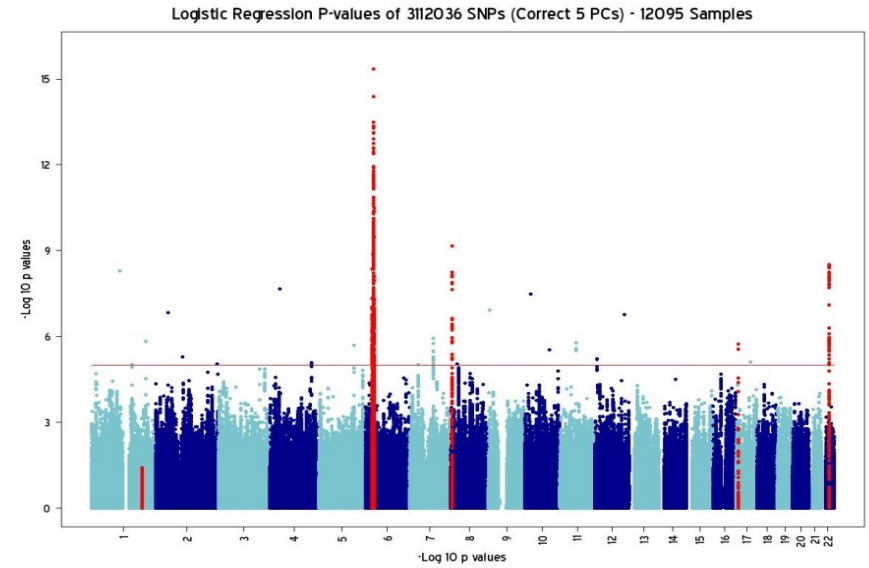
Gharavi AG, et al. Nat Genet 2011;43:321-7



Yu XQ, et al. Nat Genet 2012;44:178-82

Phase II GWAS: imputation study



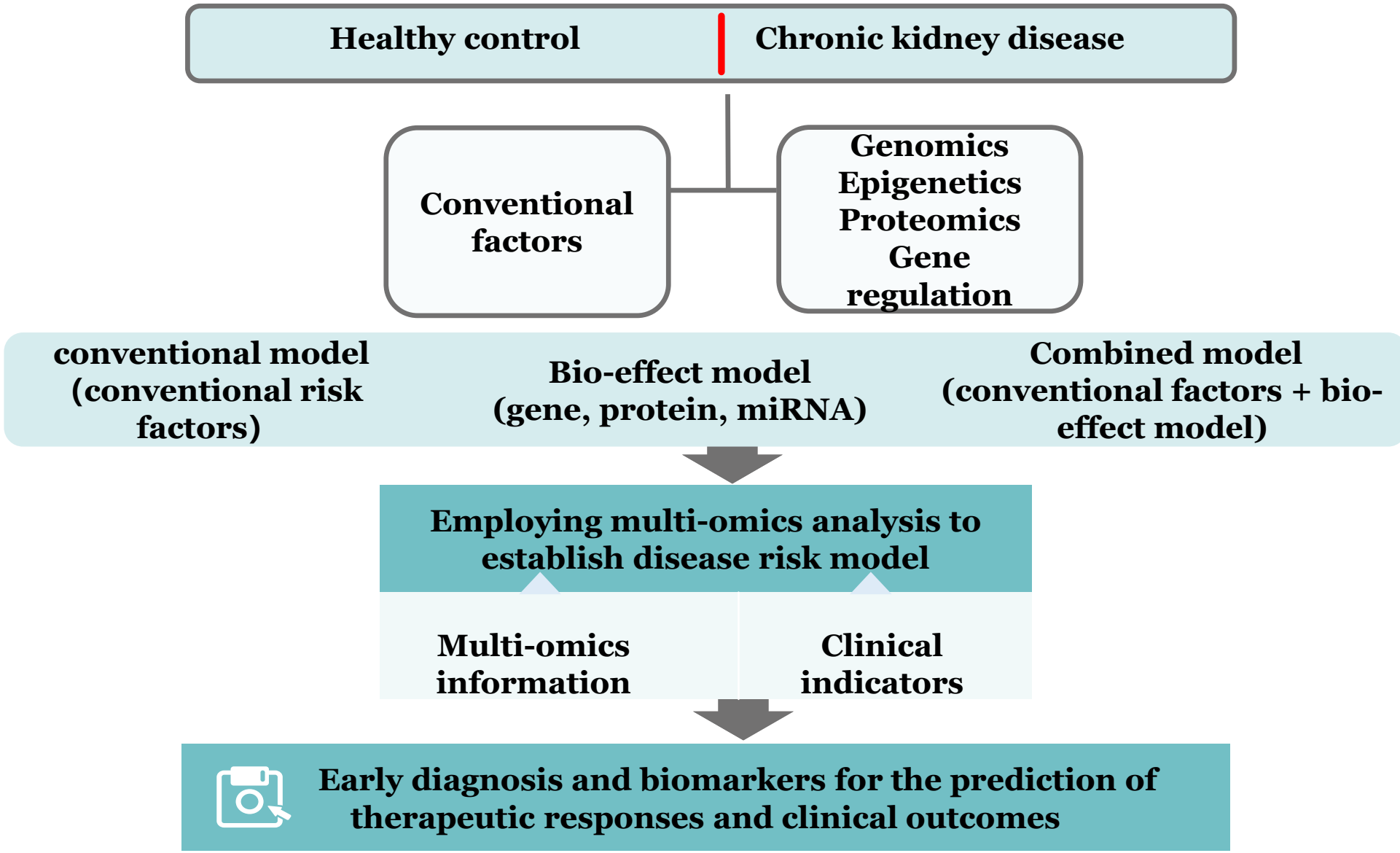


(a) Study 2: 12,095 Samples, $\lambda_{GC} = 1.089$ (3,112,036 SNPs); $\lambda_{GC} = 1.081$ (3,082,471 SNPs, removed 5 IgAN loci)

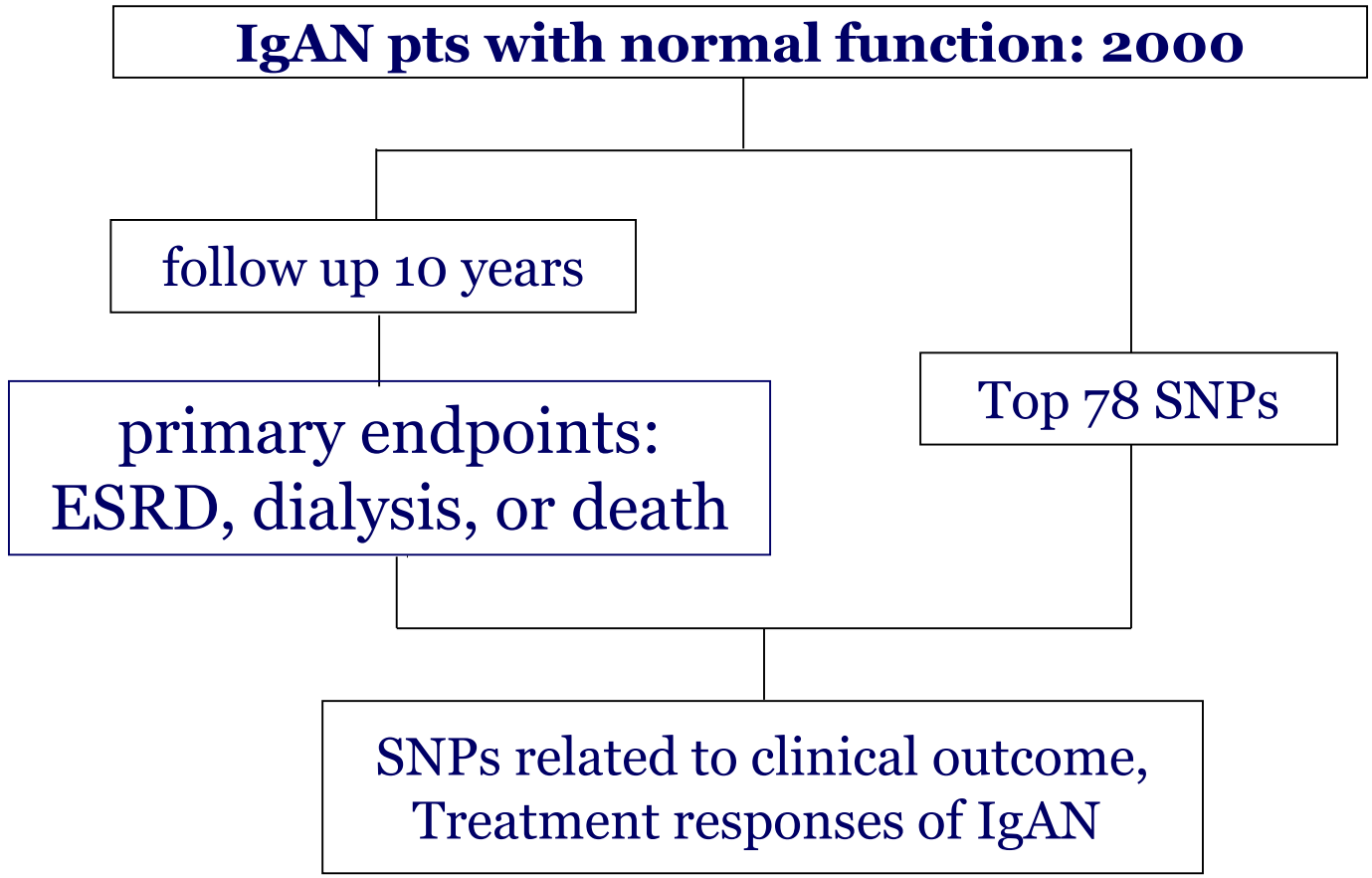
(5 new loci were discovered and validated)

Li Ming, et al. Nature Communications 2015

Biomarkers for precision predication



Predictive Biomarkers in IgAN Patients



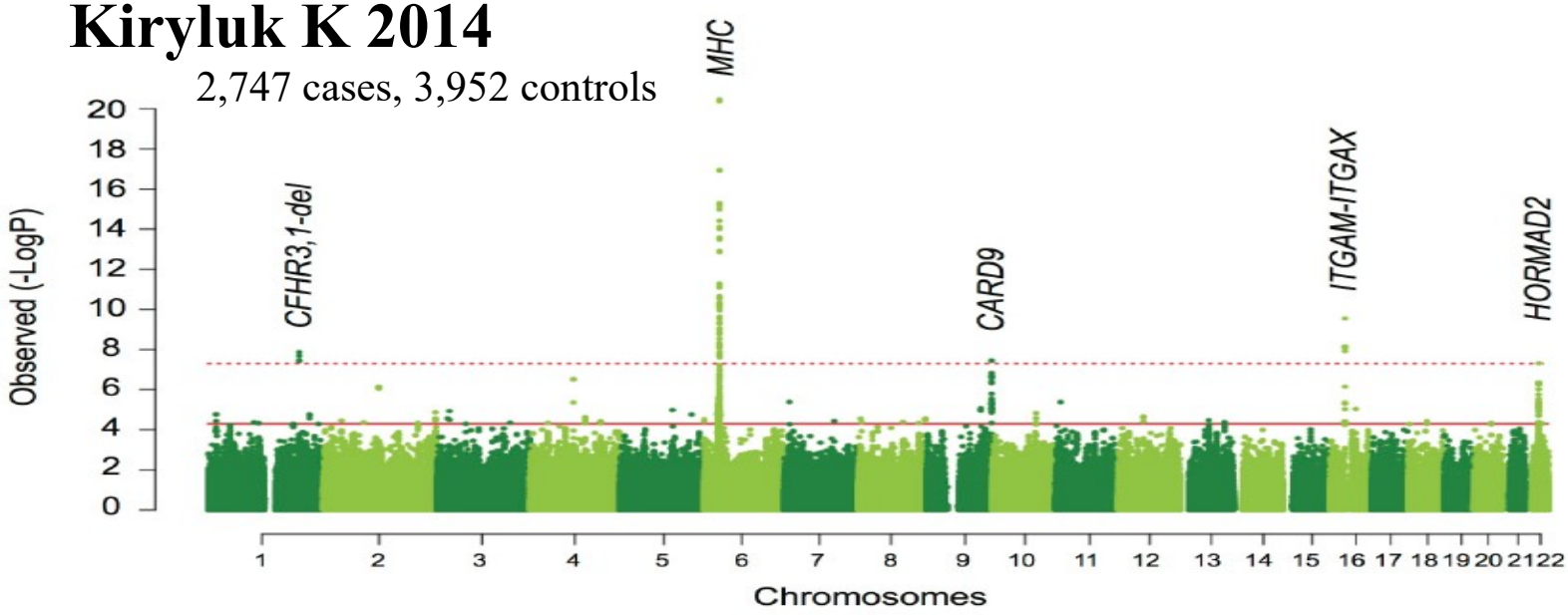
CKD Program in The Future

- Precision Prevention
- Precision Prediction
- Precision Treatment

Multiple susceptible loci from GWAS

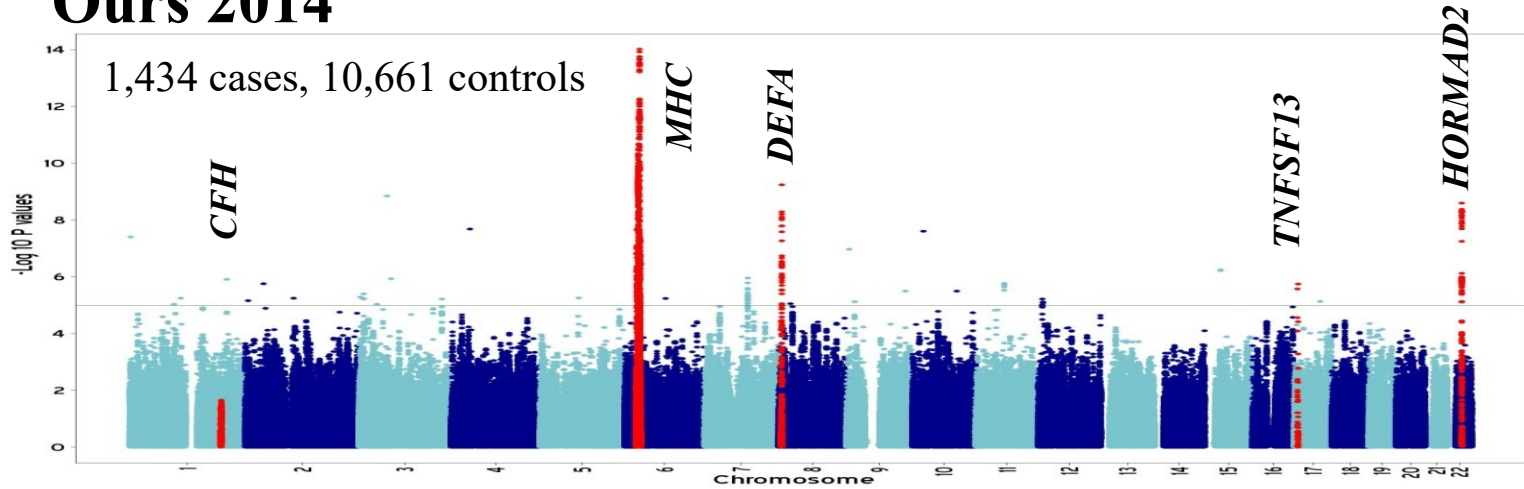
Kiryluk K 2014

2,747 cases, 3,952 controls

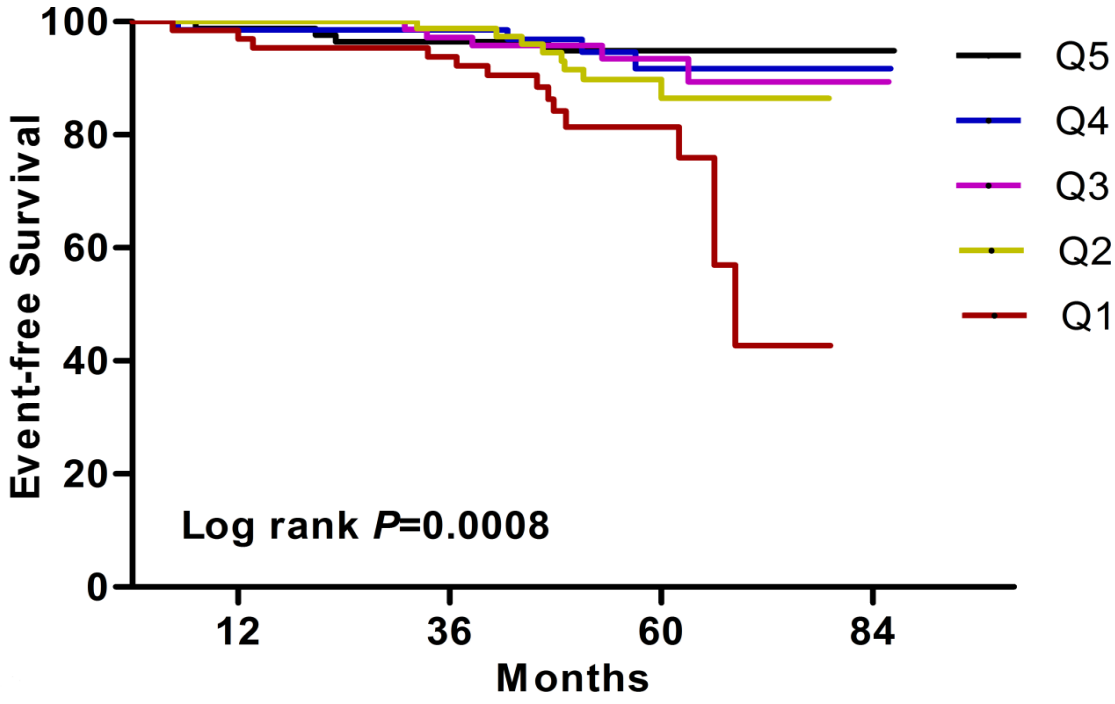


Ours 2014

1,434 cases, 10,661 controls



Genetic scores of *DEFA* CNPs associated with renal outcomes



Q5: average GS=9.57;

Q4: average GS=7.22;

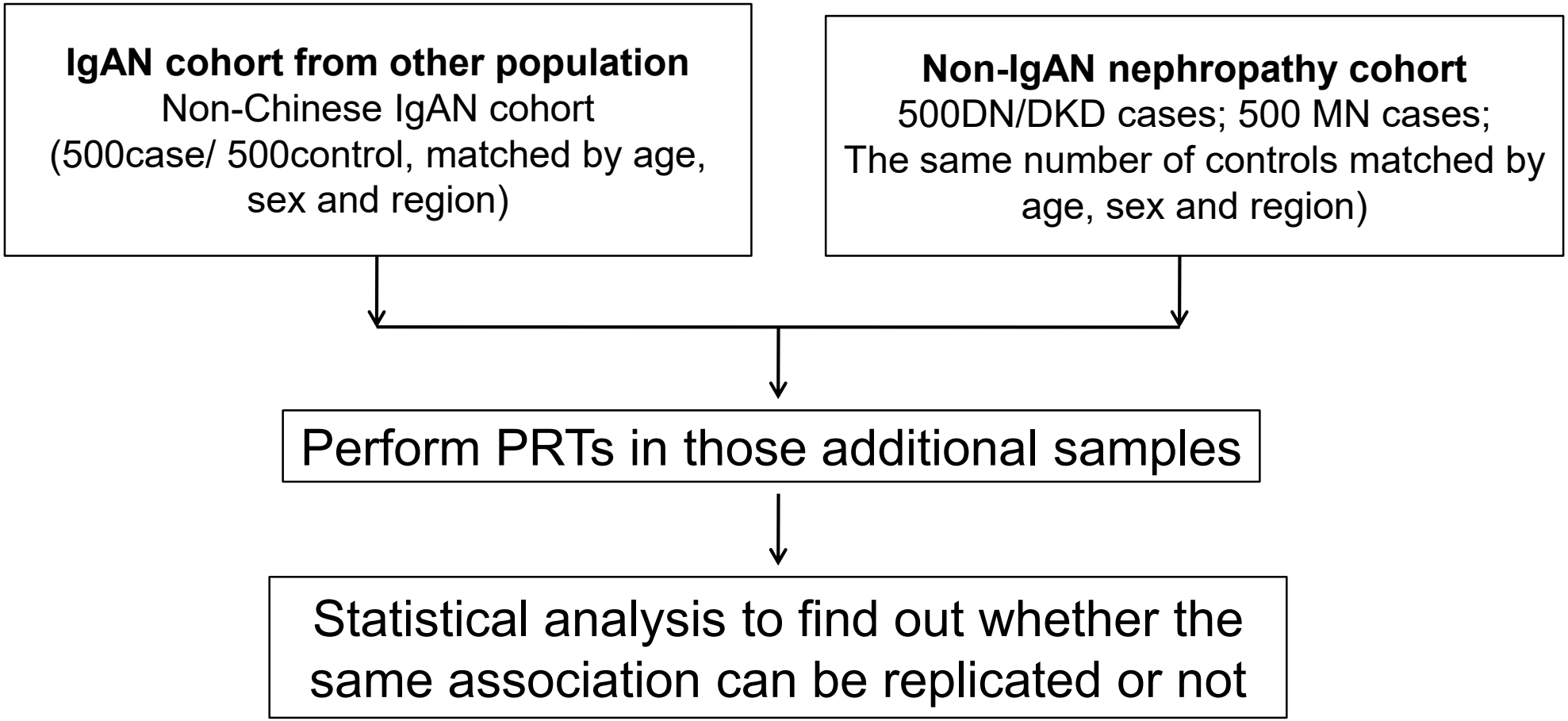
Q3: average GS=5.95;

Q2: average GS=4.52;

Q1: average GS=3.06.

DEFA CNV is IgAN Specific or Not?

Validation in other kidney disease population non-IgAN nephropathy cohort



DEFA CNV in DN/DKD cohort

Origin	Cases			Controls		
	Sample size	Mean age	M/F (%)	Sample size	Mean age	M/F (%)
Southern Chinese	331	57.83	67.2/32.8	329	57.51	68.7/31.3
Singaporean Chinese	475	60.53	58.7/41.3	457	58.06	58.4/41.6
Total	806	59.43	62.2/37.8	786	57.83	62.7/37.3

CN Distributions in DKD cases and controls

Gene/ alleles	**Cases** (n=806)		**Control** (n=786)		*P* value
	Median	Interquartile range	Mean	Interquartile range	
DEFA1A3	7.00	(6.00,8.00)	7.00	(6.00,8.00)	0.952
DEFA1	6.00	(4.00,7.00)	6.00	(4.00,7.00)	0.690
DEFA3	1.00	(1.00,2.00)	2.00	(1.00,2.00)	0.991
215bp	6.00	(5.00,7.00)	6.00	(5.00,7.00)	0.612
211bp	1.00	(0.00,2.00)	1.00	(0.00,2.00)	0.222

Association analysis in DKD adjusted by age and sex

Variants	DKD cohort (806 cases/786 controls)	
	P	OR[a](95%CI)
DEFA1A3	0.448	0.98(0.94,1.03)
DEFA1	0.487	0.99(0.94,1.03)
DEFA3	0.778	0.99(0.89,1.09)
215bp	0.884	1.00(0.96,1.05)
211bp	0.158	0.94(0.87,1.02)

DEFA CNV in MN cohort

Origin	Cases			Controls		
	Sample size	Mean age	M/F(%)	Sample size	Mean age	M/F(%)
Southern Chinese	493	45.97	53.3/46.7	500	45.67	53.2/46.8

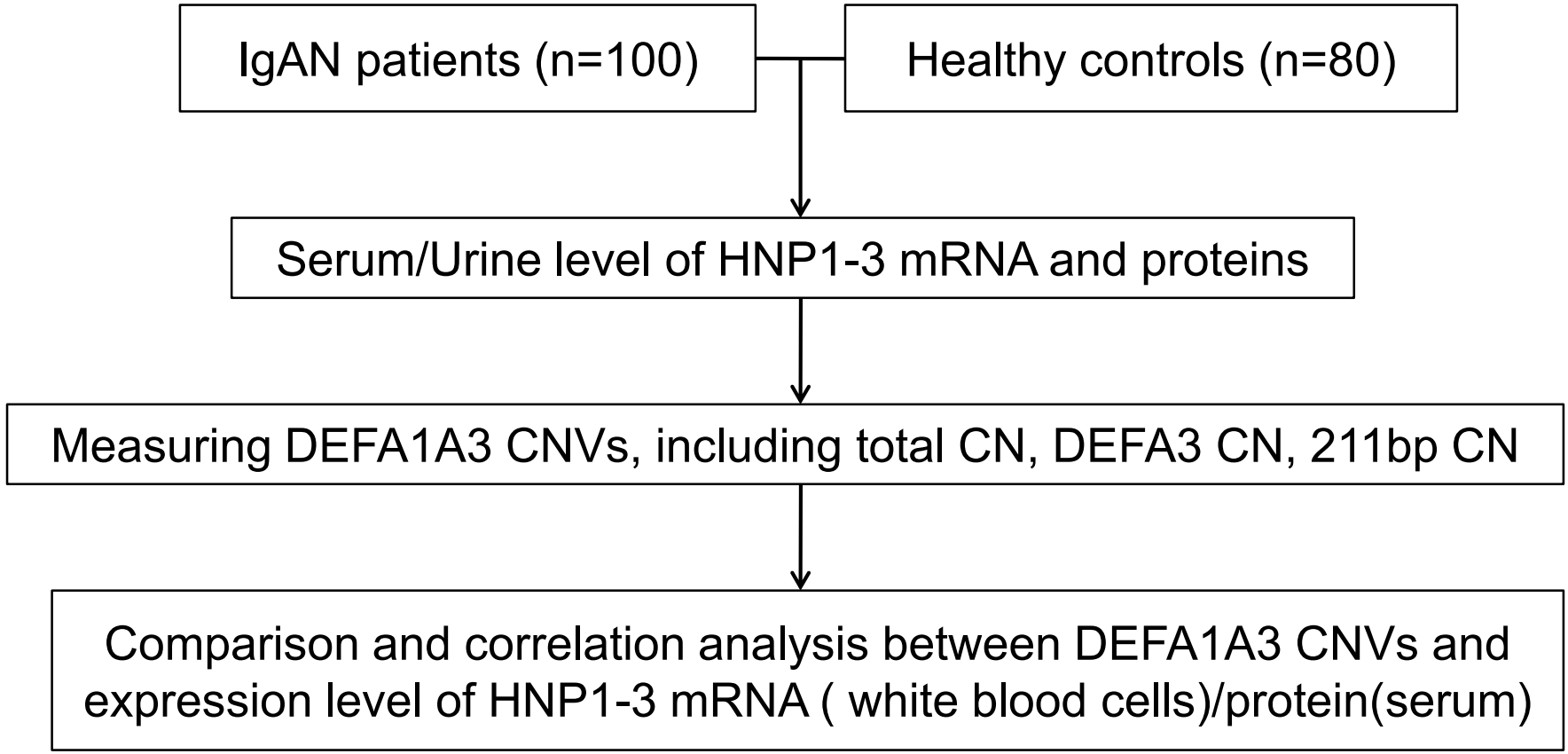
CN Distribution in MN cases and controls

Gene/ alleles	**Cases**		**Control**		*P* value
	Mean	Interquartile range	Mean	Interquartile range	
DEFA1A3	7.00	(6.00,8.00)	7.00	(6.00,8.00)	3.41×10^{-1}
DEFA1	5.00	(4.00,7.00)	5.00	(4.00,7.00)	6.09×10^{-1}
DEFA3	2.00	(1.00,2.00)	1.00	(1.00,2.00)	1.00×10^{-2}
215bp	6.00	(5.00,7.00)	5.00	(4.00,6.00)	1.03×10^{-5}
211bp	1.00	(0.00,2.00)	2.00	(1.00,2.00)	2.82×10^{-7}

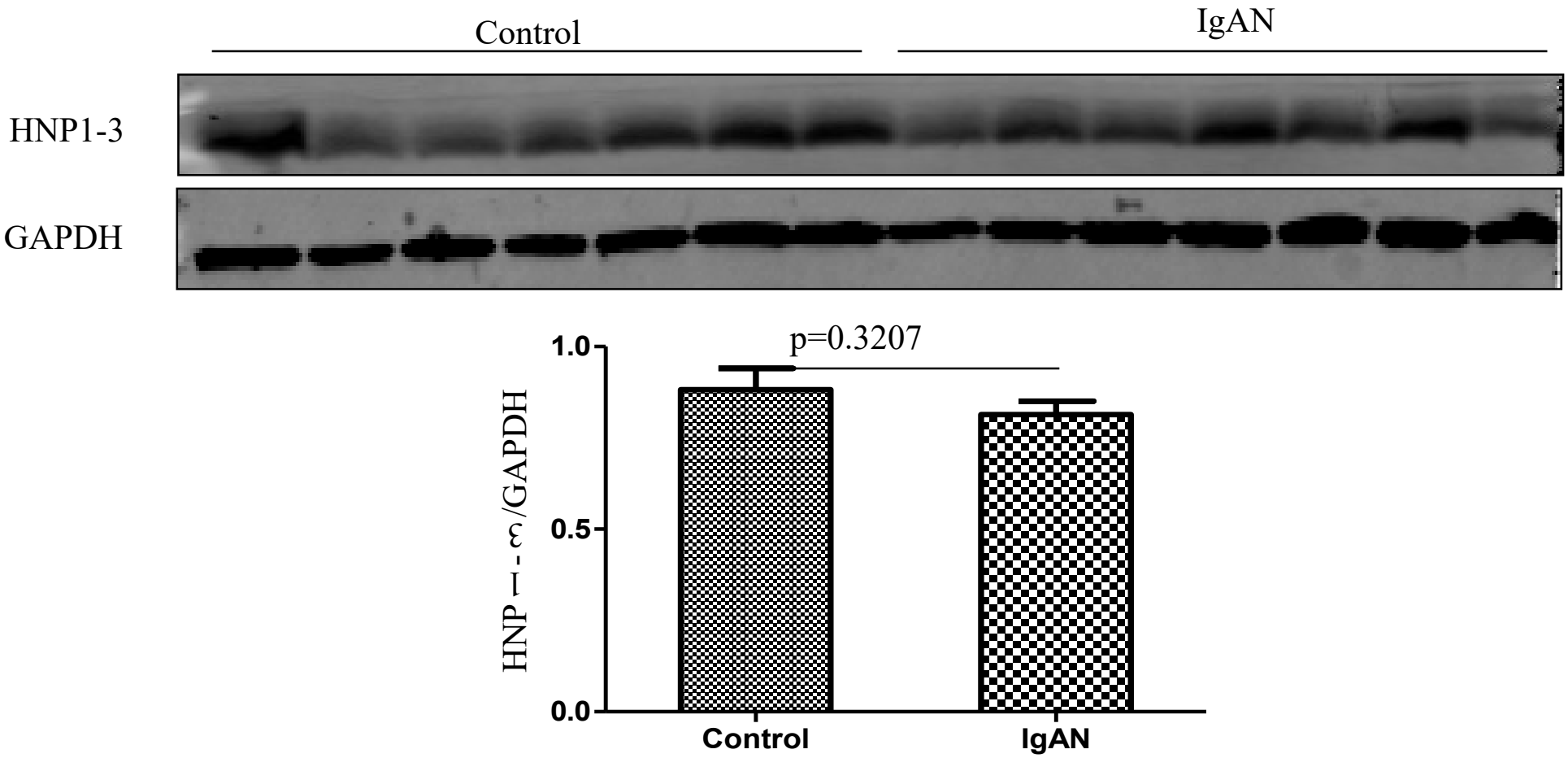
Association analysis in MN adjusted by age and sex

Variants	MN cohort (493 cases/ 500 controls)	
	P	OR[a](95%CI)
DEFA1A3	8.76×10^{-1}	1.00(0.94,1.07)
DEFA1	5.93×10^{-1}	0.98(0.93,1.04)
DEFA3	6.50×10^{-2}	1.16(0.99,1.35)
215bp	6.63×10^{-4}	1.12(1.05,1.20)
211bp	1.11×10^{-7}	0.74(0.67,0.83)

Function study of DEFA1A3 CNVs

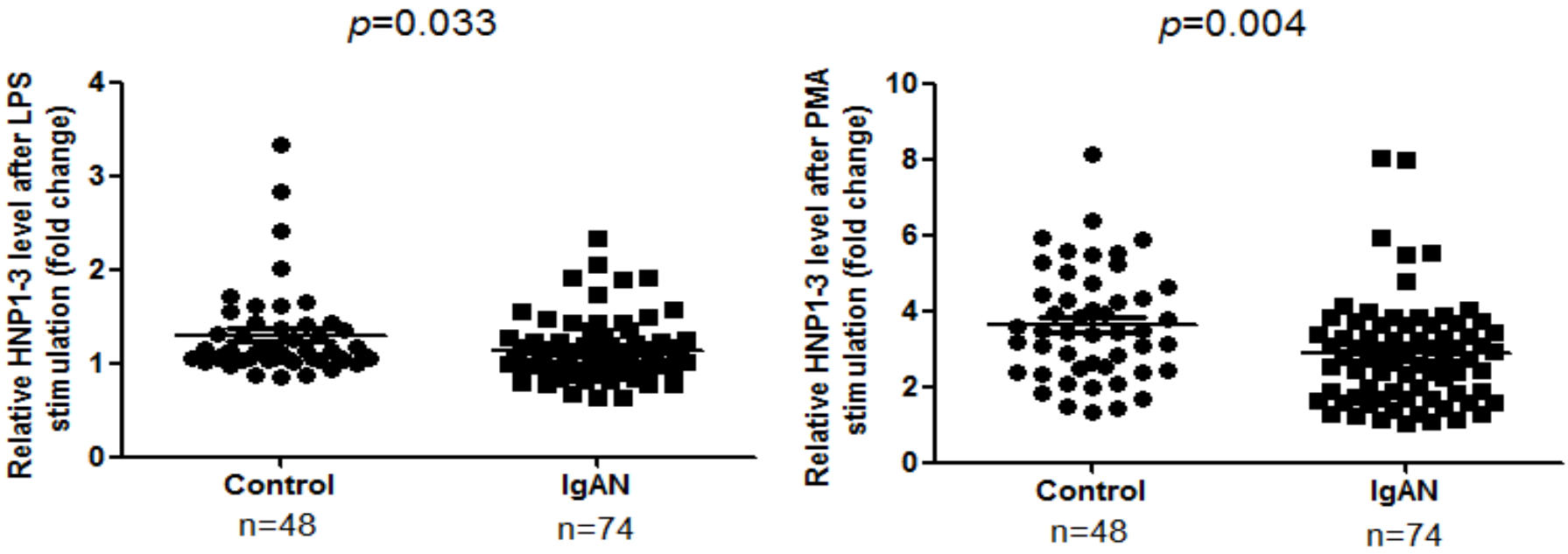


HNP1-3 expression level in neutrophils isolated from IgAN patients and controls



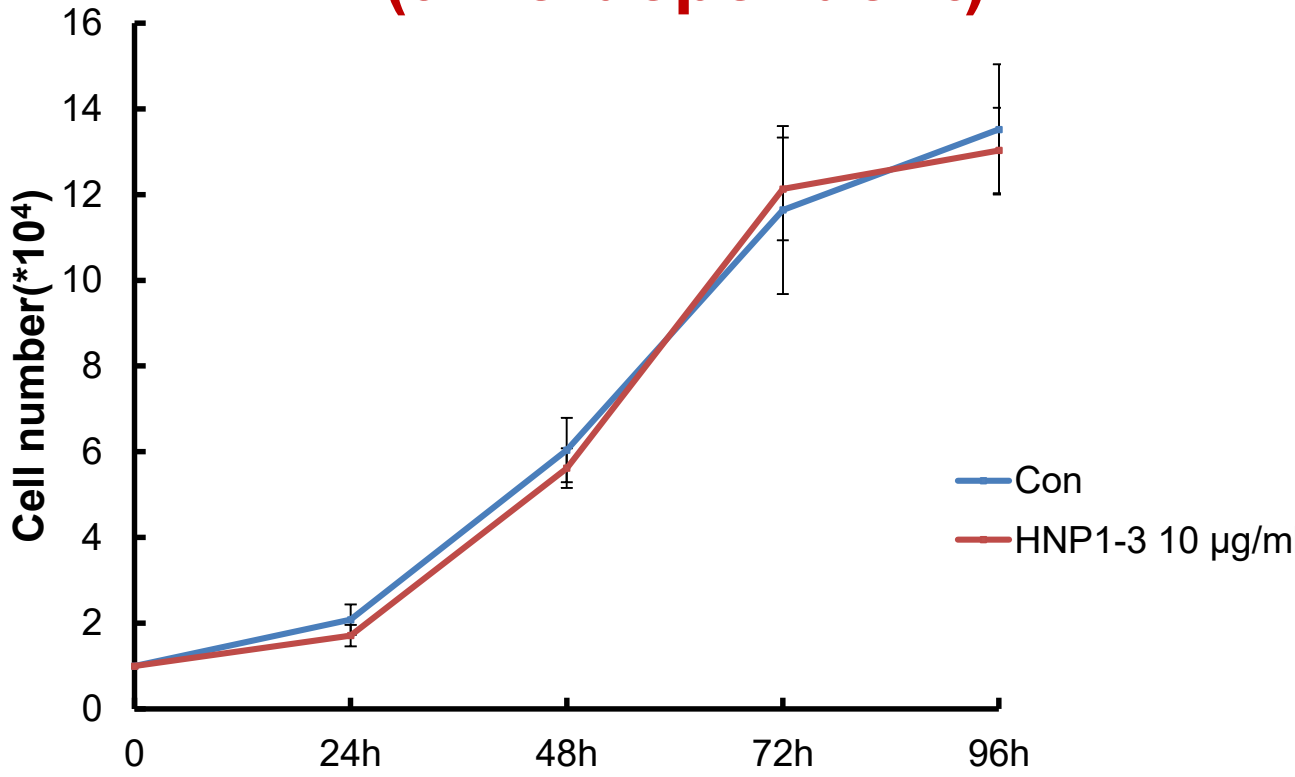
Western Blot: Total HNP1-3 expression showed no difference in neutrophils isolated from IgAN patients and controls.

HNP1-3 secretion by neutrophils after stimulated by LPS or PMA



ELISA: After stimulation of LPS (100ng/ml, 6h) or PMA (20ng/ml, 6h), the extracellular HNP1-3 levels are significantly lower in neurophils isolated from IgAN patients than controls.

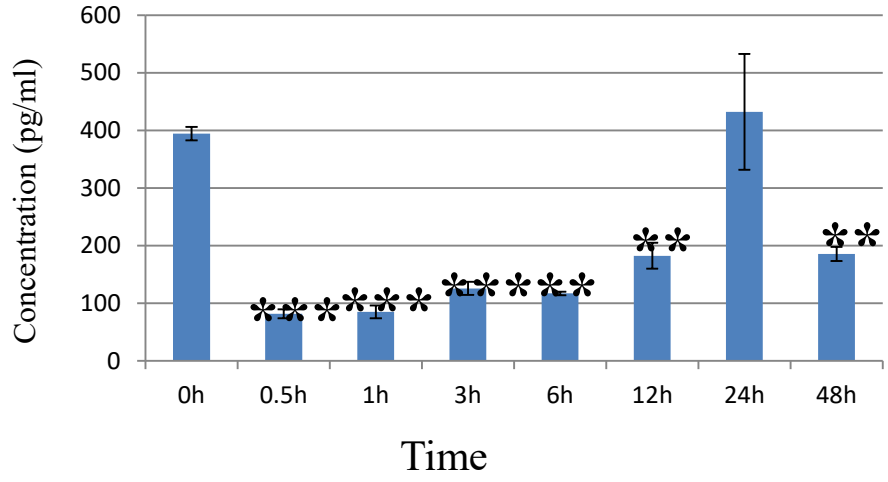
The Effect of HNPs on Cell Proliferation (time-dependent)



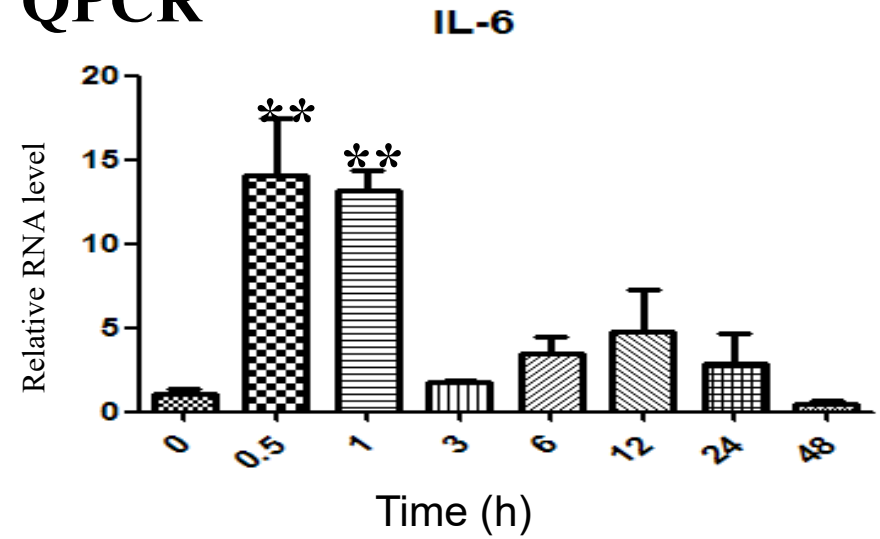
HNP1-3 10 μg/mL treated HMC for 0,24,48h,72h,96h in 48-well plates.
No significant differences.

Elisa

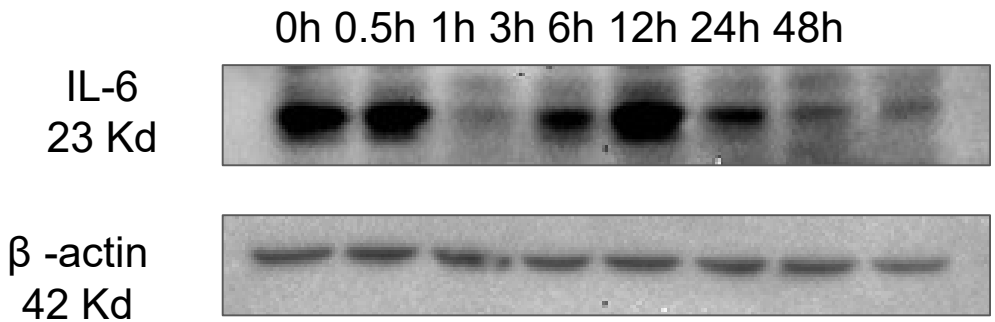
IL-6 (cell supernatant)

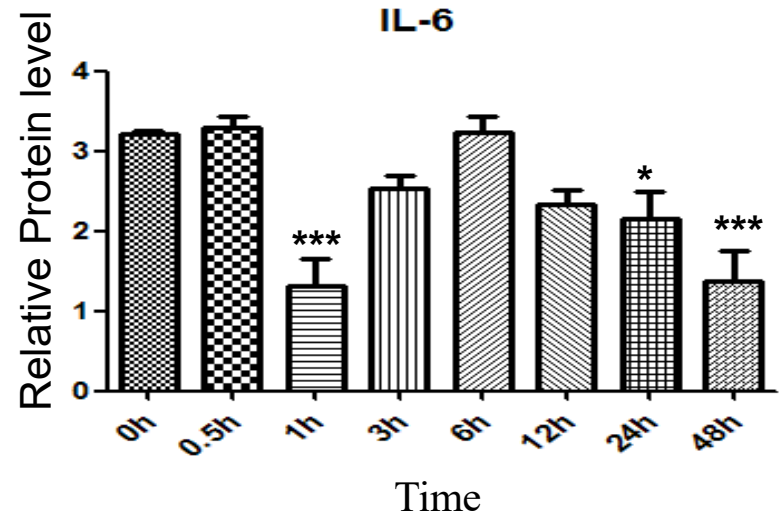


QPCR



Whole cell lyses

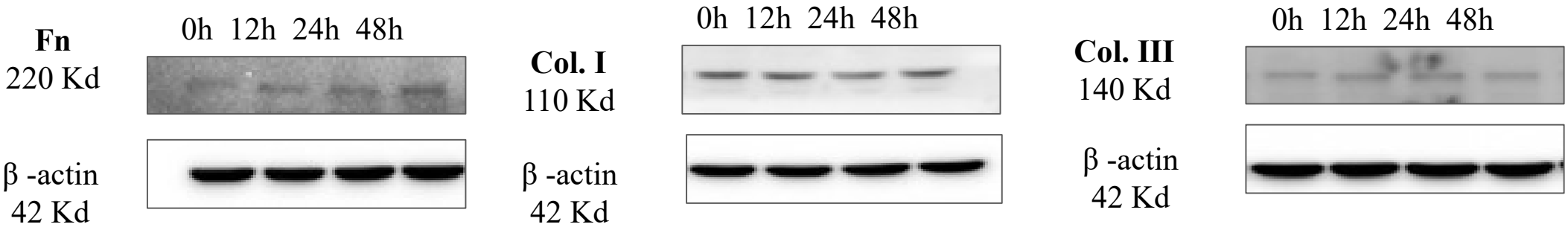


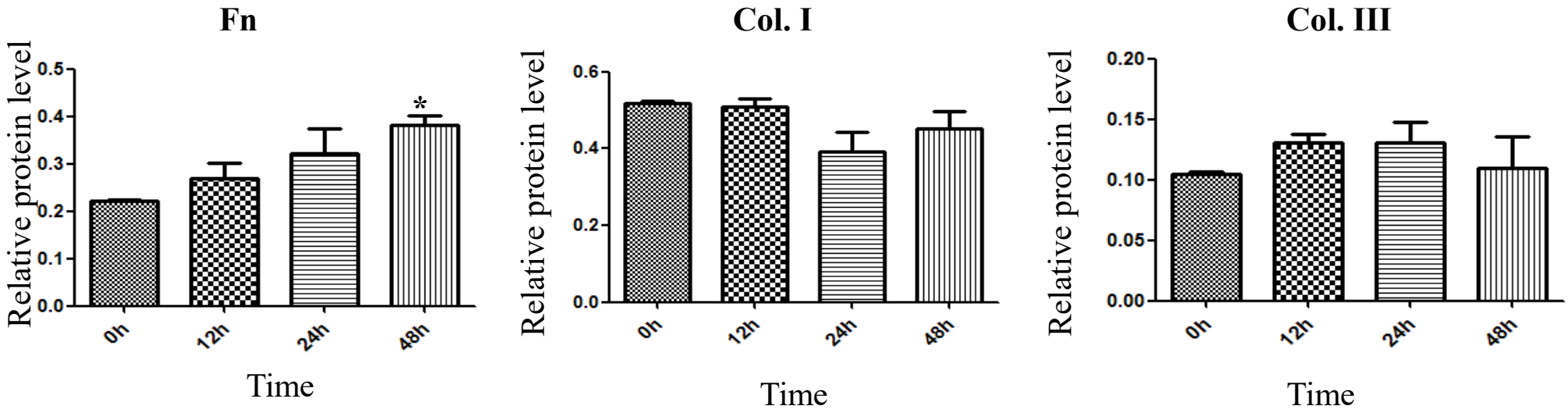


HNP1-3 treated HMC for 0,0.5,1,3,6,12,24,48h. *p<0.05, ***p<0.001 vs 0h

The Effect of HNP1-3 on ECM Accumulation

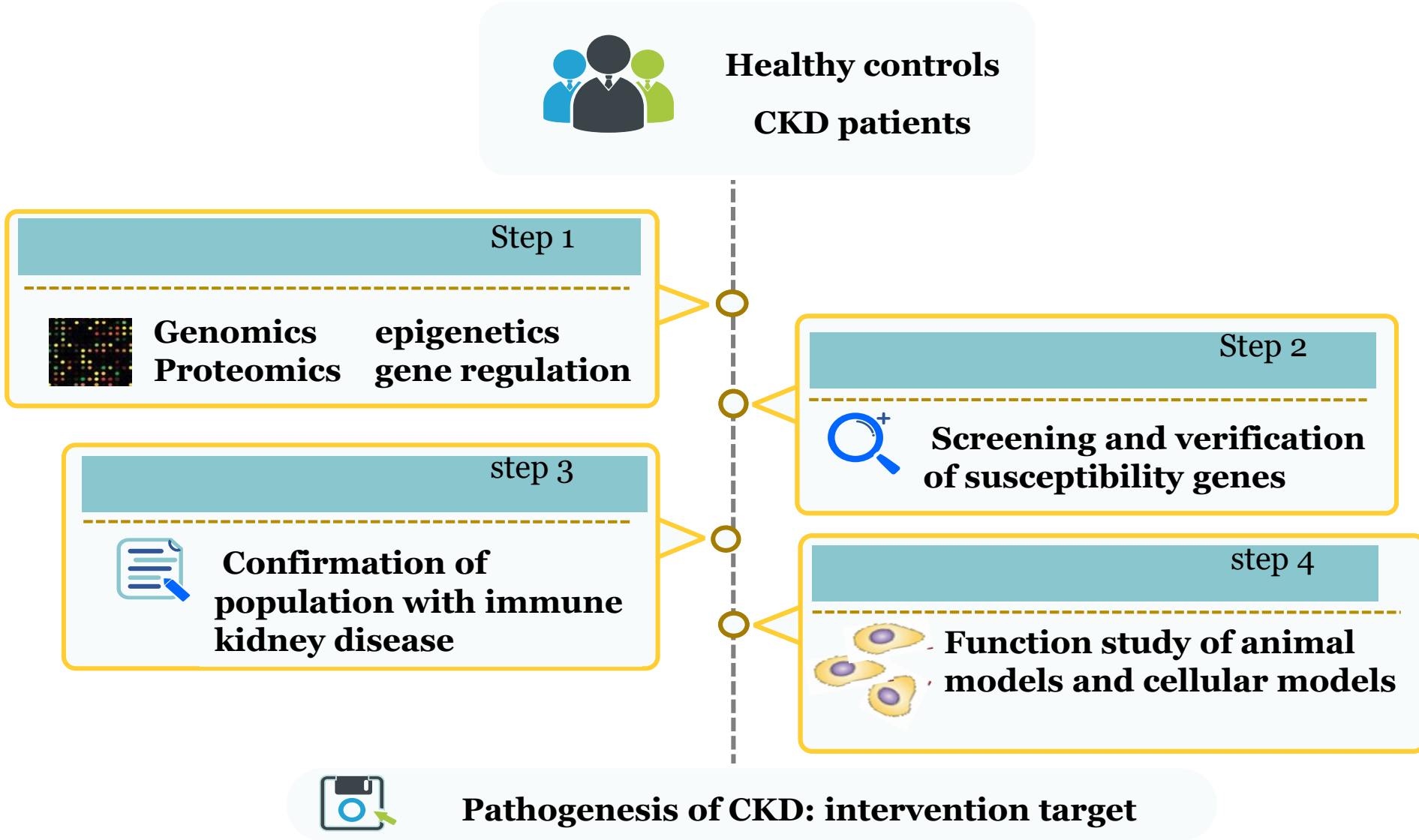
WB



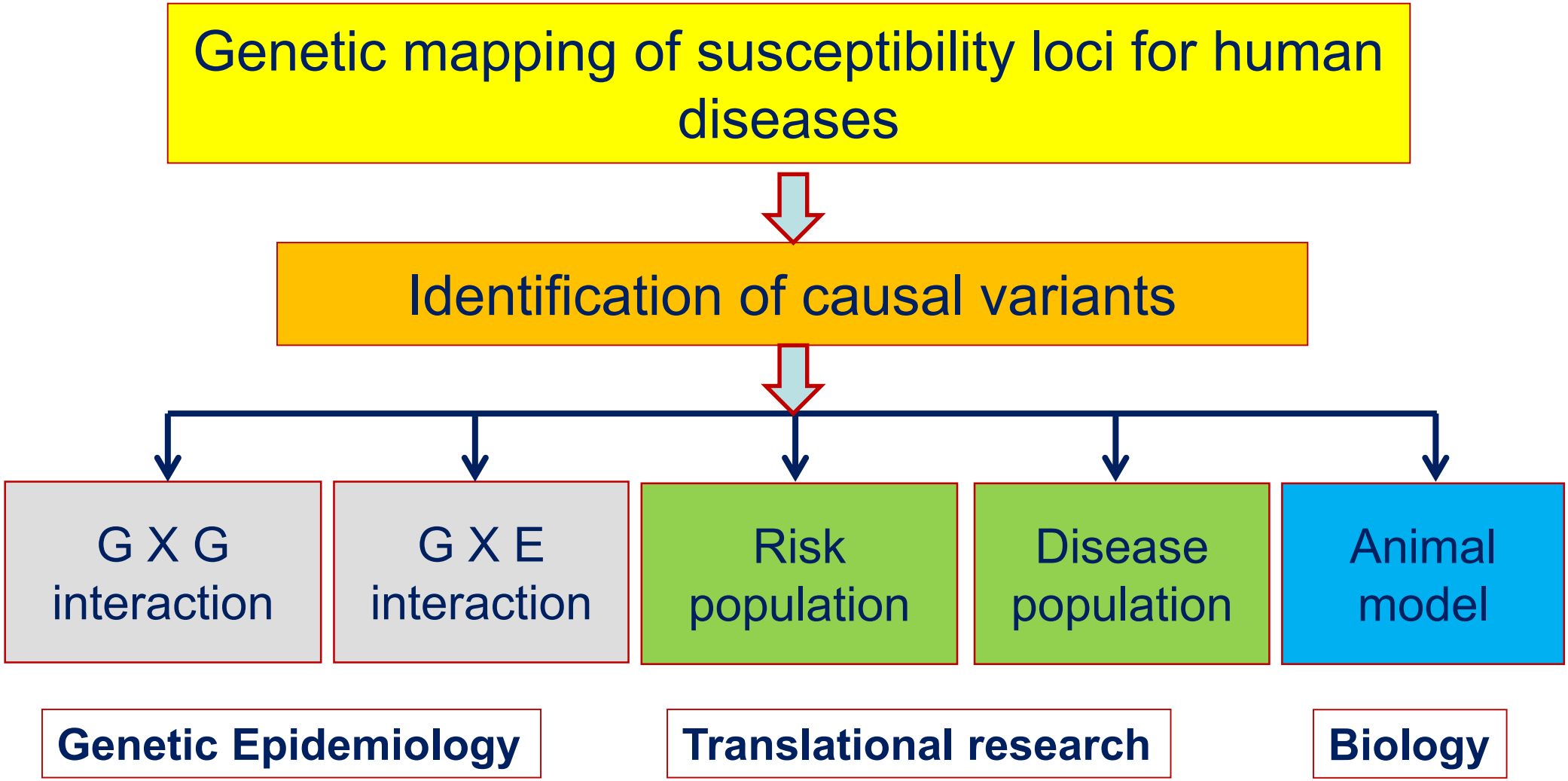


HNP1-3 10 μg/mL treated HMC for 0,12,24,48h, *p<0.05, vs 0 h

Precision treatment: novel intervention target



Beyond GWAS: Translational Research



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CHINA CKD ALLIANCE

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Welcome to
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Thank you !