MAYO CLINIC

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Glomerular Diseases: IgA Nephropathy in Elderly

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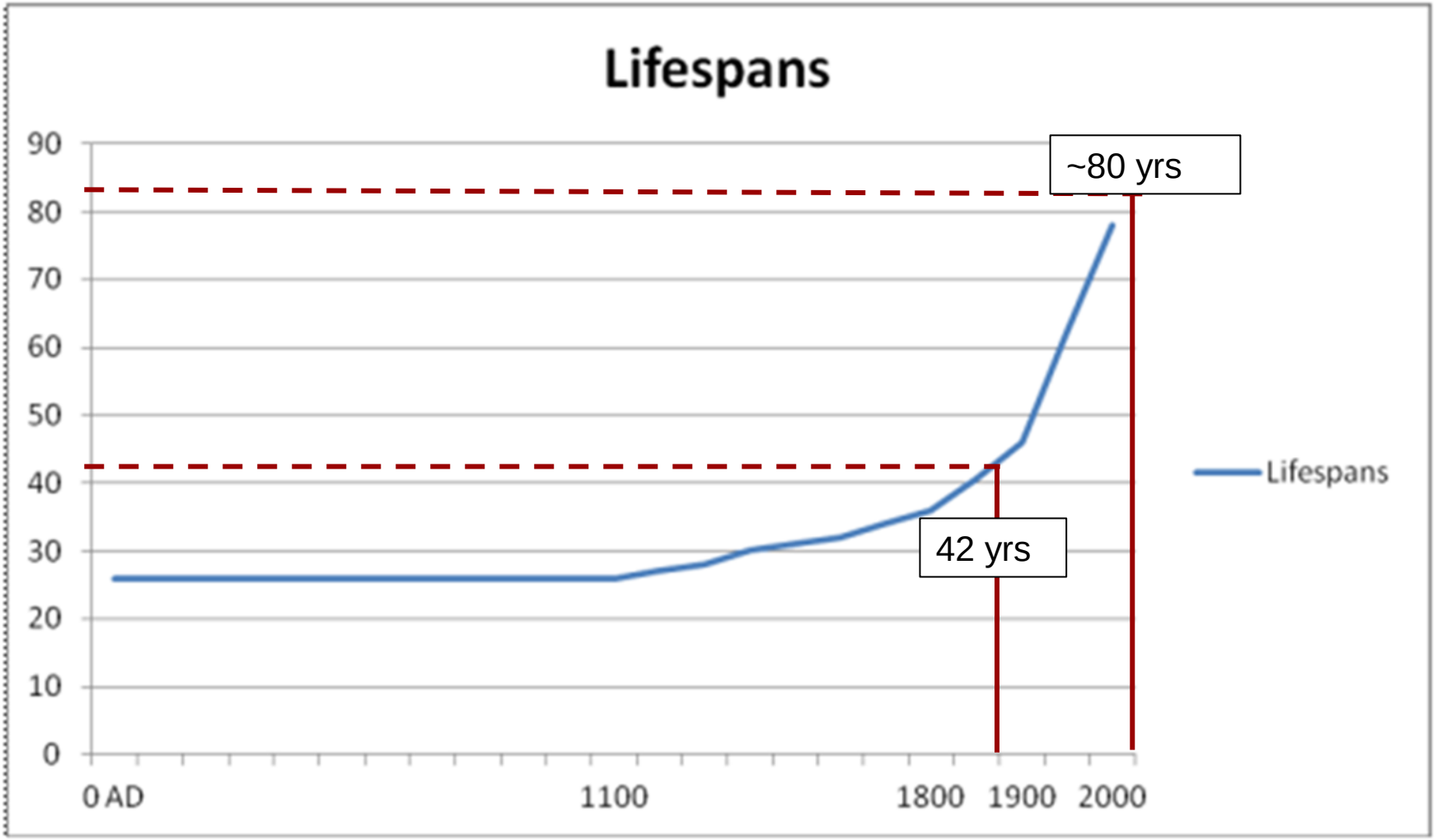
Financial Disclosure:

None

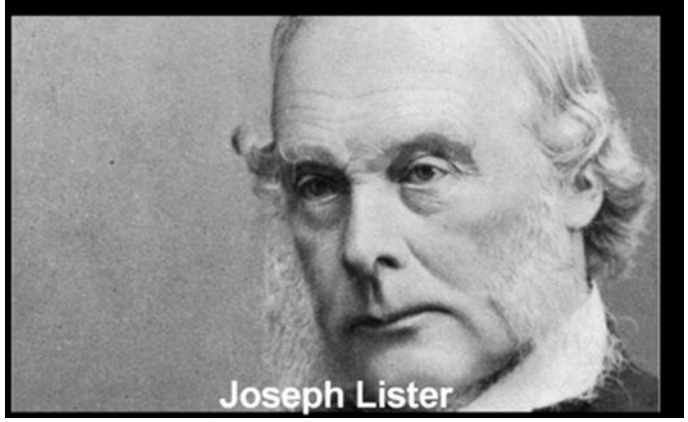
Objectives:

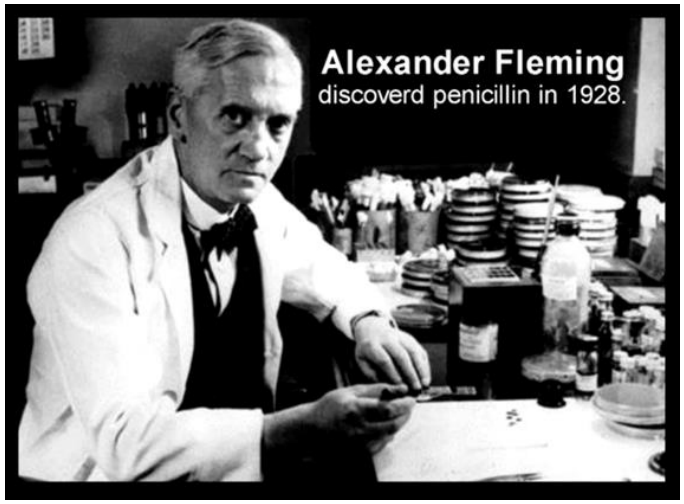
To examine:

1. Changing healthcare landscape: Aging population
2. Elderly glomerular diseases: Overview
3. IgA nephropathy in elderly (Europe/U.S and Asia)

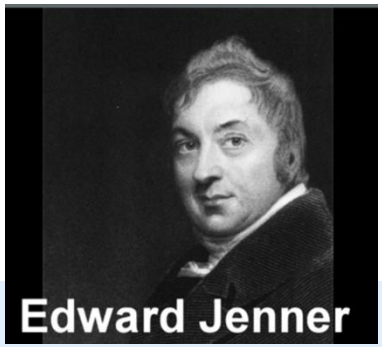


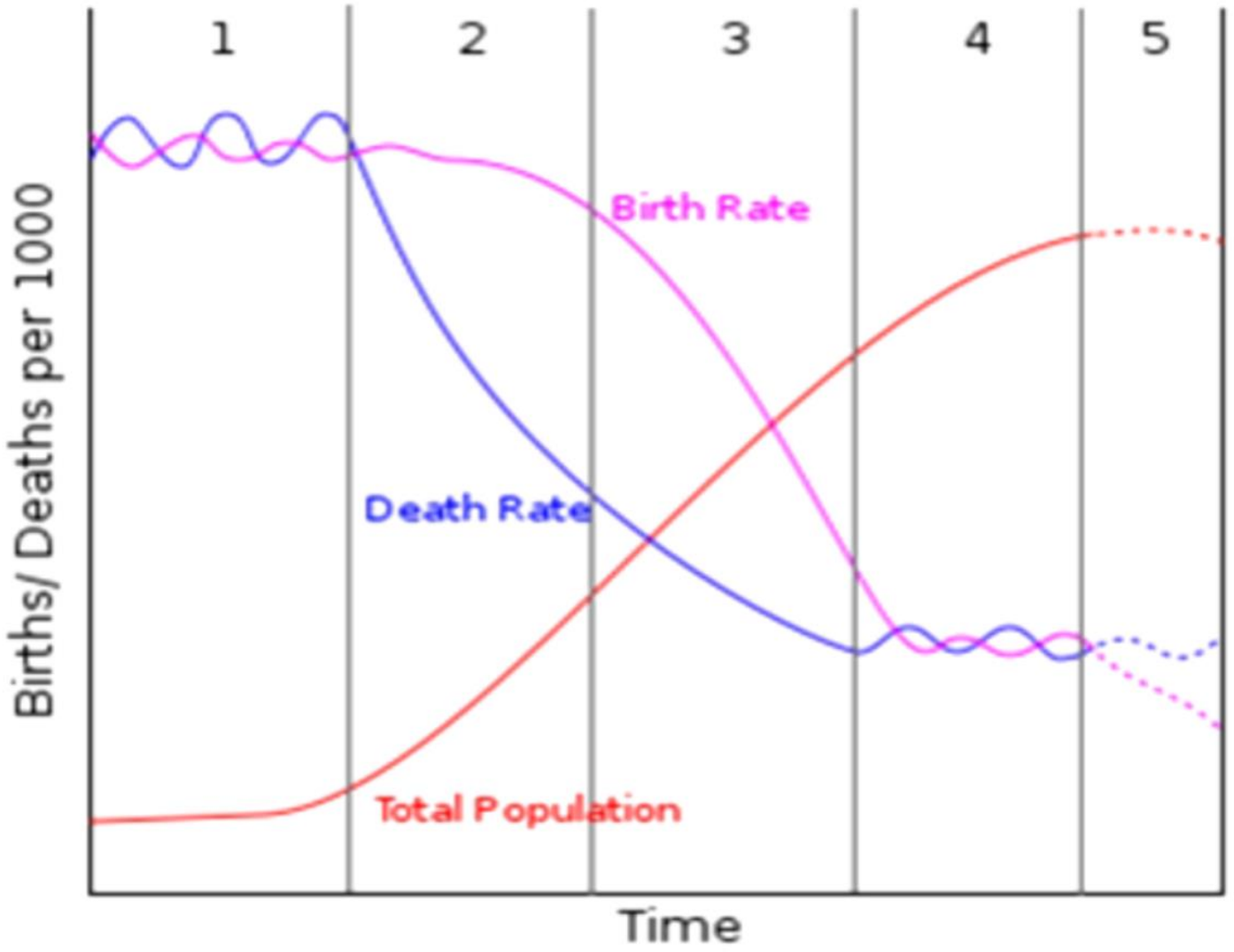
The rise of the nation state, the steam engine, electricity, the advent of the social safety net, the personal computer, the internet (social media), and ---



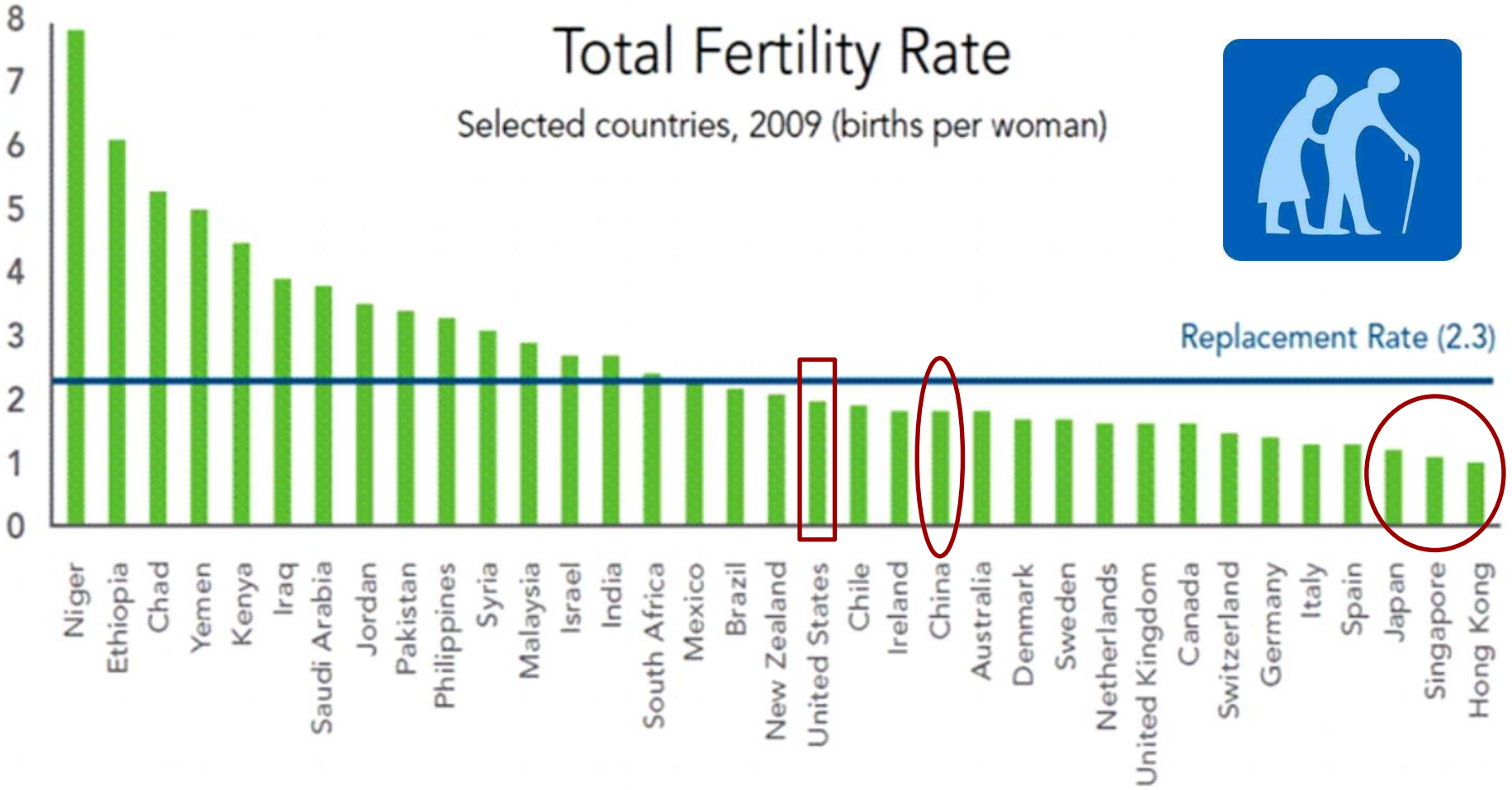


1. Vaccination
2. Nutrition
3. Antiseptics
4. Antibiotics
5. Advances in medicine



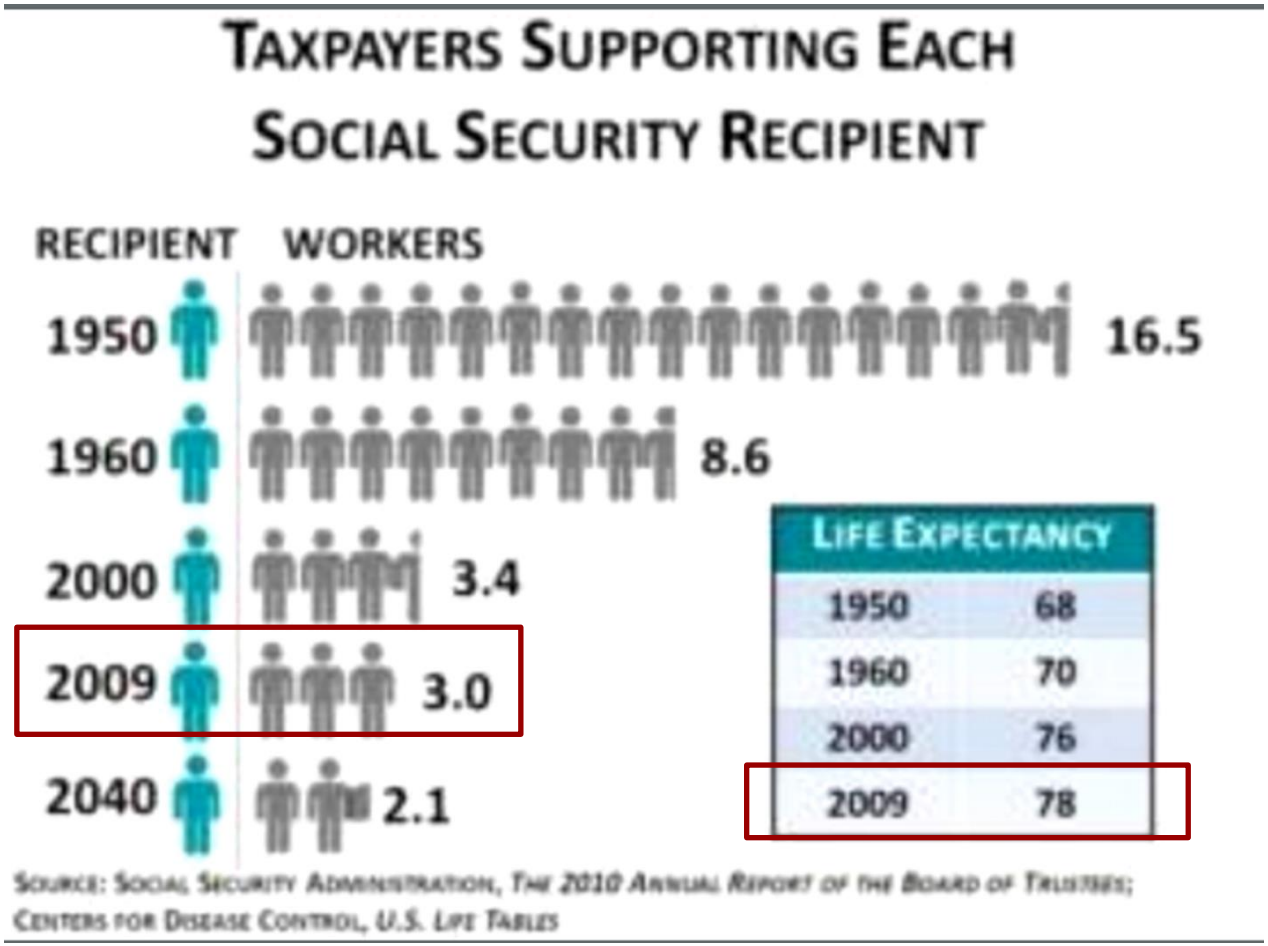


Warren Thompson, 1929



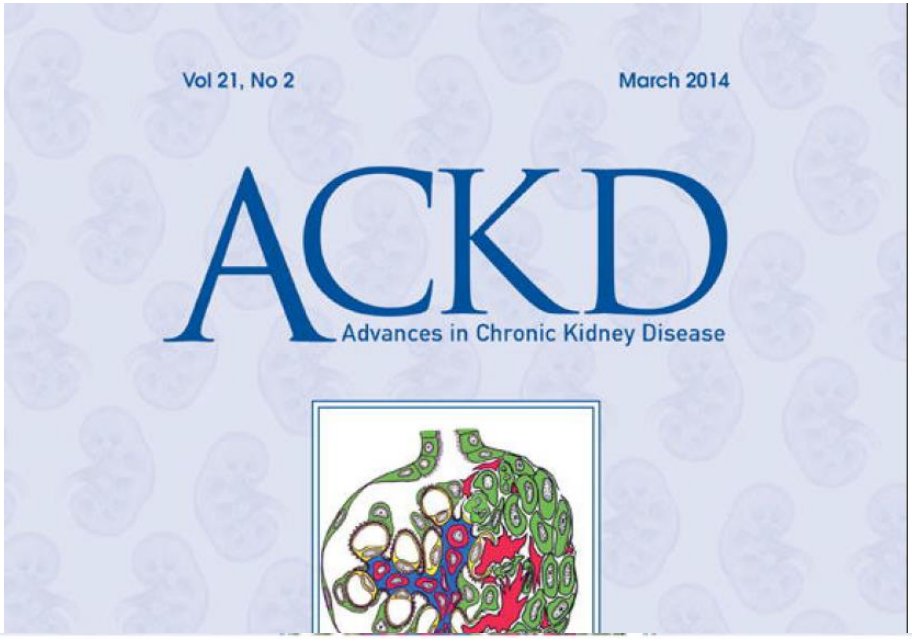
In China: individuals age >65 is expected increase from 8.3% of the population in 2008 to 16.23% by 2030.

Chinese Population Aging and the Elderly Status of Blue Book. China Society Press, 2010



>90% healthcare cost fells in the last 2 years of life

Elderly glomerular disease: diagnosis and treatment

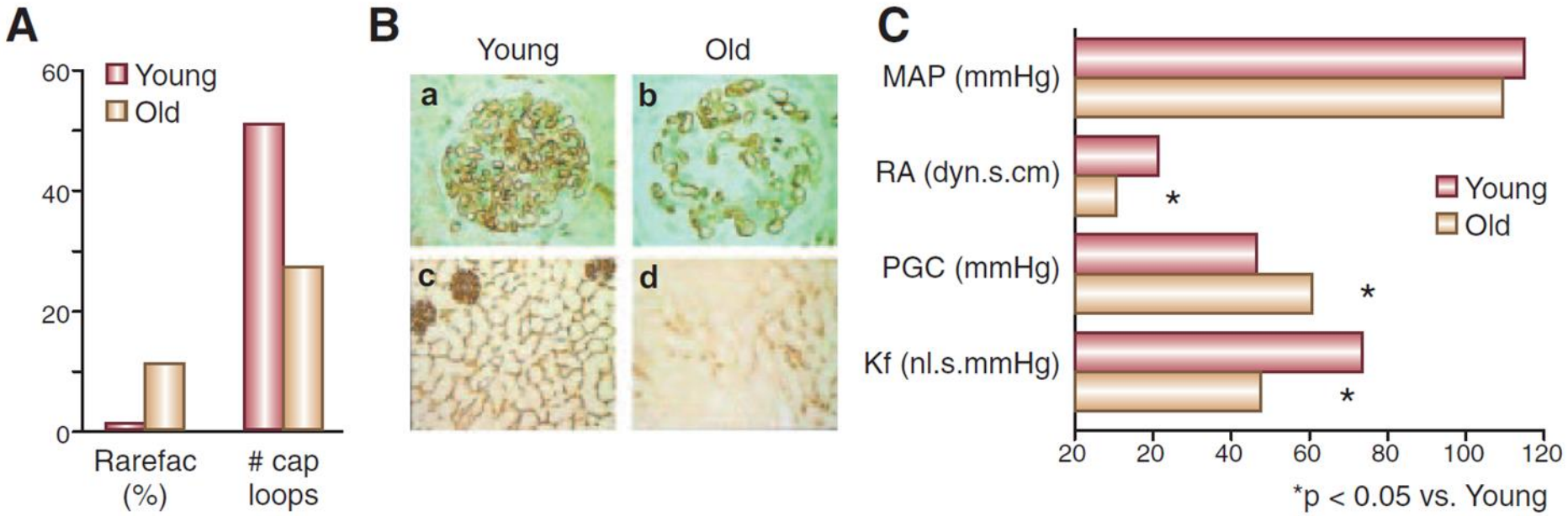


Diagnosis and Treatment of Glomerular Diseases in Elderly Patients

Qi Qian and Samih H. Nasr

Vol 21, No 2 (March), 2014: pp 228-246

- Aging is associated with progressive decline in kidney reserve
- 30% of the glomeruli are sclerotic in healthy individuals by age 75 yrs
- Renal inulin clearance drops by ~ half (from 123 to 65 mL/min/1.73m^2) in healthy adults 20-29 yrs and >80 yrs.



J Am Soc Nephrol 22: 28–38, 2011. doi: 10.1681/ASN.2010090934

What types of glomerular diseases in elderly?

Secondary glomerular dz in majority of the cases:

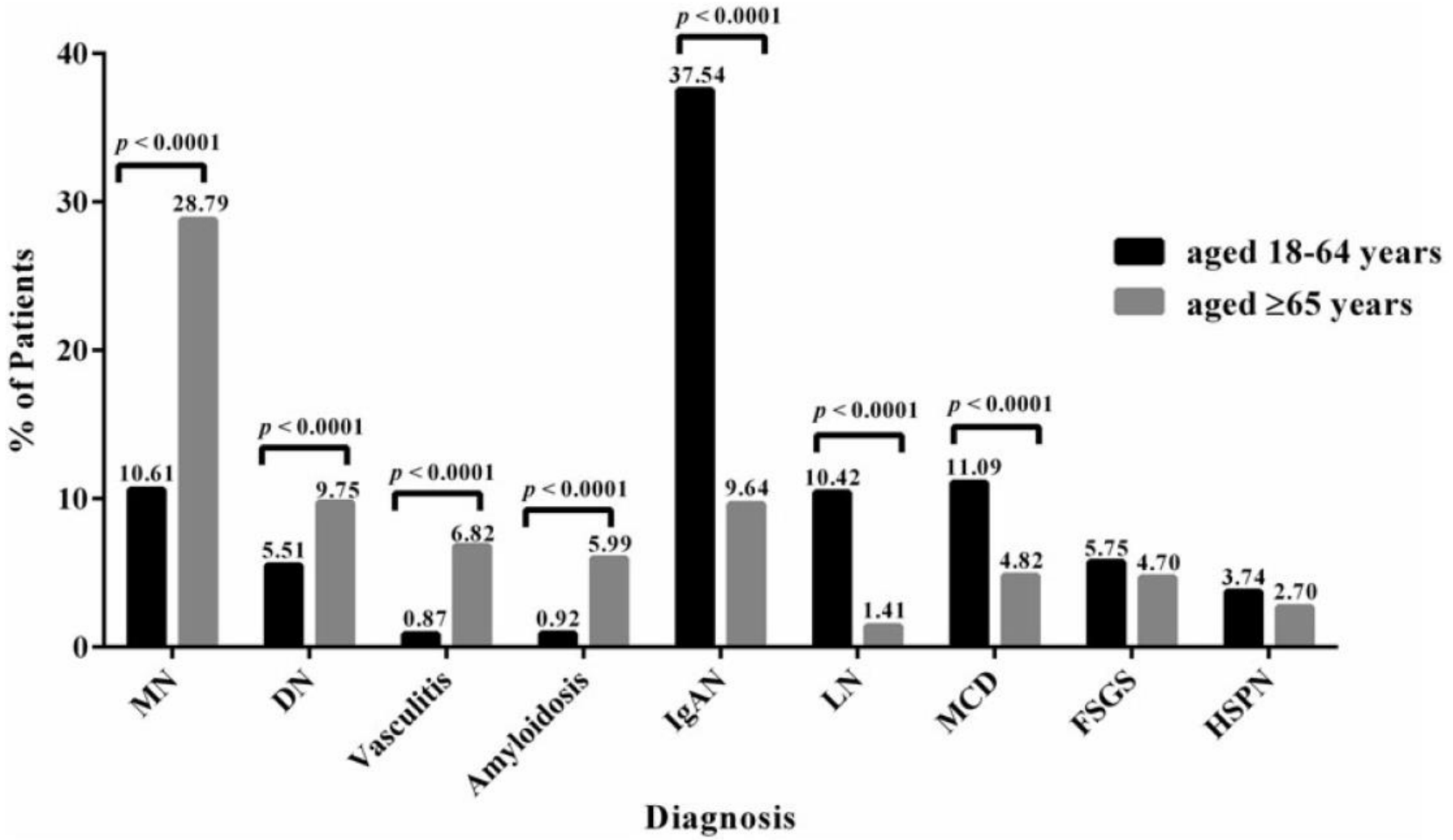
--- chronic HTN, DM and glomerular ischemia

Primary glomerular dz: relatively less.

The spectrum of biopsy-proven kidney diseases in elderly Chinese patients

- N=851 native kidney biopsy, age ≥65 (*3% of all bx*)
- N= 28,574 younger adults, age 18-64
- Single-center (2003-2012)
- Primary GN: 53.9%; 2^{ndary} GN: 36.5%
- MN 28.8%, DN 9.8%, IgAN 9.6%, vasculitis 6.8%
- More MN, DN, vasculitis and amyloidosis than young adults

Nephrol Dial Transplant (2014) 29: 2251–2259
doi: 10.1093/ndt/gfu239
Advance Access publication 17 July 2014



Elderly (≥65 yrs): *3% of all bx*

Nephrol Dial Transplant (2014) 29: 2251–2259
doi: 10.1093/ndt/gfu239
Advance Access publication 17 July 2014

Diagnostic kidney biopsy in elderly?

A bias toward limited diagnostic investigations (biopsy) based on age alone -

Pathologically, in addition to features of specific glomerular diseases, kidney biopsy from elderly patients often shows aging-related features including varying degrees of background glomerulosclerosis, tubular atrophy, interstitial fibrosis, arterial sclerosis, and arteriolar hyalinosis. Distinguishing a newly developed glomerulopathy from underlying age-associated kidney senescence can, at times, be challenging.

Renal biopsy in patients aged 80 years and older: a single-center experience in Japan.

N=73 patients aged ≥80 years
N=128 patients aged 70 - 79 years.
N=172 patients aged 60 - 69 years

RESULTS:
Biopsy indications: NS > proteinuria without NS and/or hematuria and AKI

Histological diagnoses modified treatment in 57 cases (78.1%).

There were No biopsy-related serious complications.
There were statistically significant differences in the disease spectrum between the very elderly and control groups (ages: 60-79 yrs).

CONCLUSIONS: Histological observations are useful aids in estimating the prognosis and therapy in the very elderly.

Renal biopsy in the very elderly (USA).
N=235 in patients aged ≥80 yr.
N=264 patients aged 60 to 69 yr.

RESULTS:
Biopsy indications: AKI 46.4%, progressive kidney injury 23.8%, NS 13.2%, NS with AKI 9.4%, and isolated proteinuria 5.5%.

Pauci-immune GN was the most frequent diagnosis (19%), FSGS due to HTN (7.6%), hypertensive nephrosclerosis (7.1%), IgAN (7.1%) and MN (7.1%).

In ≥80 yr, pauci-immune GN to be more frequent (P<0.001), DN (P<0.001) and MN (P<0.05) less frequent in the very elderly.

No increase in Bx complications
Diagnostic information modified treatment in 67% of elderly.

CONCLUSIONS: Renal biopsy in very elderly patients is a valuable diagnostic tool that should be offered in clinical settings with maximal potential benefit.

CJASN4(6):1073-82. 2009

JNEPHROL 2010; 23 (S15): S55-S60
www.sin-italy.org/jnonline – www.jnephrol.com

Kidney biopsy in the elderly

Italian study: 2005-2009

DEMOGRAPHIC AND CLINICAL DATA FOR PATIENTS

	Age ≤60 years N=387	Age >60 years N=109	p value
Age mean ± 2SD	38 ± 27	68 ± 11	0.000
Range	(4-60)	(61-86)	
Sex (M/F)	232/156	70/40	ns

POSTBIOPSY COMPLICATIONS IN YOUNG AND ELDERLY PATIENTS

	Age ≤60 years		Age >60 years	
	Number (n=388)	%	Number (n=110)	%
Perinephric hematoma	39	10.1	10	9.1
Arteriovenous fistula	5	1.3	0	0.0
Gross hematuria	0	0.0	1	0.9
Muscular hematoma	2	0.5	0	0.0
Total	46	11.9	11	10.0

Hypertension	35.8%	66.7%	0.000
Neoplasm	1.6%	4.8%	0.003

Kidney biopsy is safe in elderly

Histology is important

- to characterize the glomerular diseases
- to direct the best therapeutic strategies

Nair R, Bell JM, Walker PD: Renal biopsy in patients aged 80 years and older. *Am J Kidney Dis* 44: 618–626, 2004

Parrish AE: Complications of percutaneous renal biopsy: A review of 37 years' experience. *Clin Nephrol* 38: 135–141, 1992

Renal biopsy-related complications in the elderly are shown in Table 5. Of these 48 cases, minor bleeding complications occurred in 43 cases (5.05%). Major complications occurred in five patients (0.59%), who required a blood transfusion; no other invasive intervention procedures were required, and no patients died because of the renal biopsies. The incidence of major complications in 3948 patients aged 18–64 years was 0.2% (8 of 3498), including six cases of gross hematuria and two cases of hematoma. In these eight patients, blood transfusion was needed in seven cases, and radiologic embolization

Table 5. Renal biopsy-related bleeding complications in the elderly ($n = 851$)

Biopsy-related complications	Minor		Major		Total	
	n	%	*n*	%	*n*	%
Hematoma	6	0.71	3	0.35	10	1.18
Gross hematuria	36	4.23	2	0.24	38	4.47
Both	1	0.12	0	0.00	1	0.12
Total	43	5.05	5	0.59	48	5.64

The percentages represent the incidence of complications in all 851 elderly patients.

Nephrol Dial Transplant (2014) 29: 2251–2259
doi: 10.1093/ndt/gfu239
Advance Access publication 17 July 2014

What about treatment for elderly?

- Age-related decline in the capacity of drug metabolism and excretion

- Ongoing loss in muscle mass, deconditioning and increase in frailty = a seemingly near normal s. Cr. In reality, moderate-to-severe loss of kidney function. Always get eGFR or GFR

- Age alone should not be used against initiation of treatment.

Advances in Chronic Kidney Disease, Vol 21, No 2 (March), 2014: pp 228-246

Nephrol Dial Transplant (2014) 0: 1–8
doi: 10.1093/ndt/gfu070

ndt
Nephrology Dialysis Transplantation

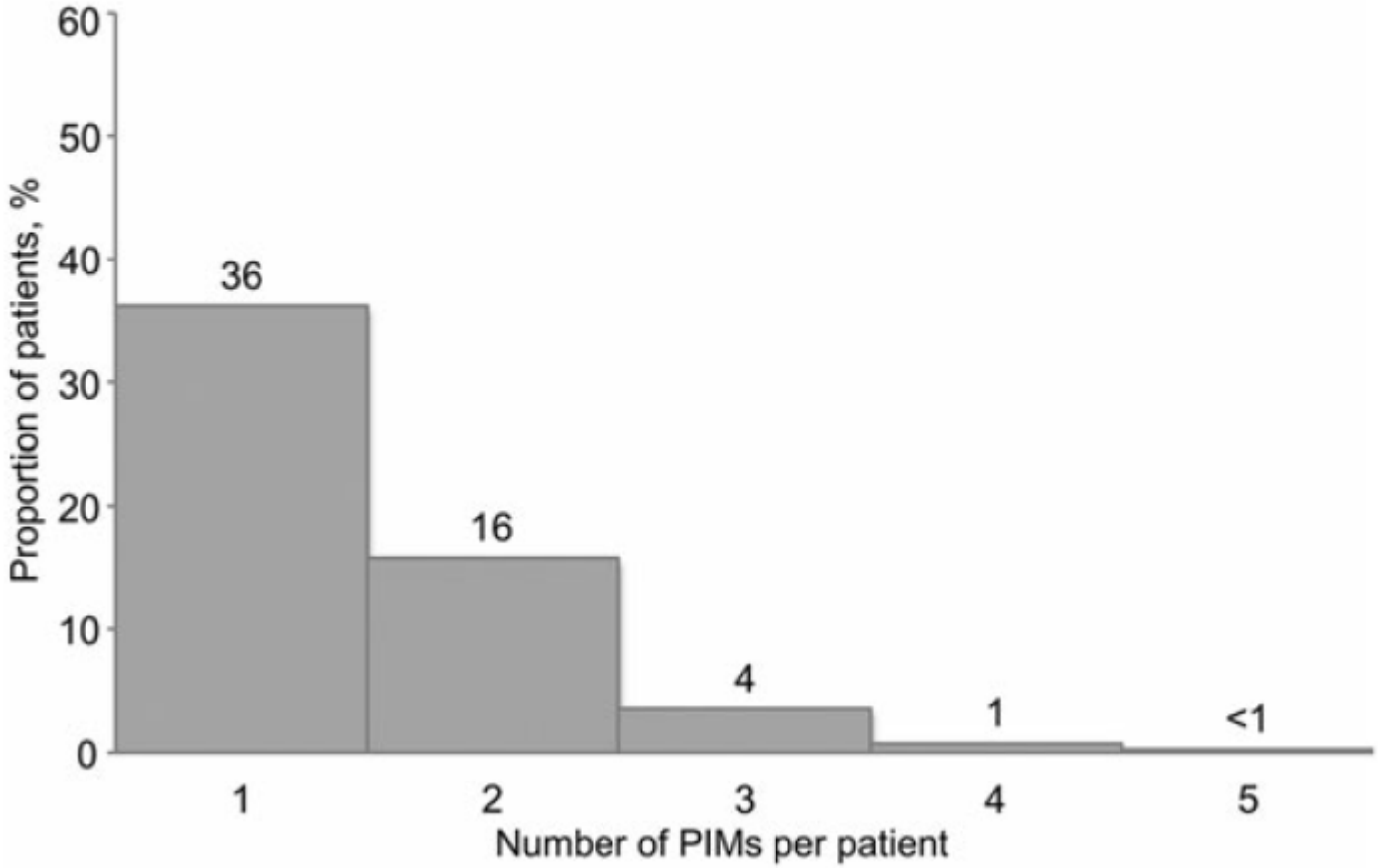
Original Article

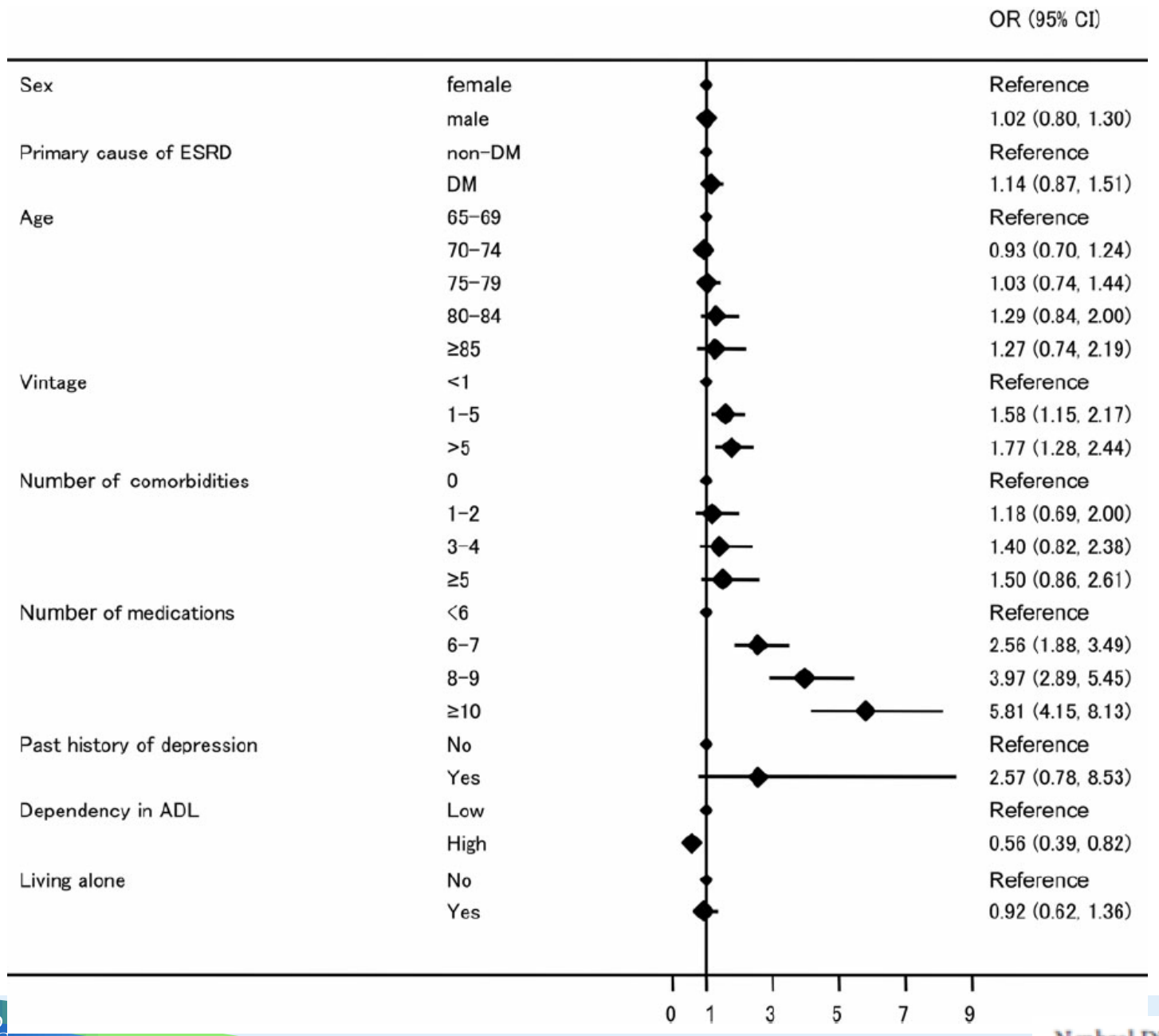
Prescription of potentially inappropriate medications to elderly hemodialysis patients: prevalence and predictors

Naoya Kondo[1], Fumiaki Nakamura[2], Shin Yamazaki[1], Yosuke Yamamoto[1], Tadao Akizawa[3], Takashi Akiba[4], Akira Saito[5], Kiyoshi Kurokawa[6] and Shunichi Fukuhara[1,7,8]

[1]Departmen… …, Kyoto, Japan, [2]Department of Public Healt… …y, Department of Medicine, Showa University S… …dney Center, Tokyo Women's Medical Uni… …i University School of Medicine, Kanagawa, J… …arch in Clinical Evaluative Science, Fukushima … …on Research, Tokyo, Japan

- HD patients
- N=1,367, age ≥65
- 2002-2008, cross sectional study
- 57% had one potentially inappropriate medication


60
50
40
30
20
10
0
Proportion of patients, %
36
16
4
1
<1
1
2
3
4
5
Number of PIMs per patient


OR (95% CI)
Sex
female
Reference
male
1.02 (0.80, 1.30)
Primary cause of ESRD
non-DM
Reference
DM
1.14 (0.87, 1.51)
Age
65–69
Reference
70–74
0.93 (0.70, 1.24)
75–79
1.03 (0.74, 1.44)
80–84
1.29 (0.84, 2.00)
≥85
1.27 (0.74, 2.19)
Vintage
<1
Reference
1–5
1.58 (1.15, 2.17)
>5
1.77 (1.28, 2.44)
Number of comorbidities
0
Reference
1–2
1.18 (0.69, 2.00)
3–4
1.40 (0.82, 2.38)
≥5
1.50 (0.86, 2.61)
Number of medications
<6
Reference
6–7
2.56 (1.88, 3.49)
8–9
3.97 (2.89, 5.45)
≥10
5.81 (4.15, 8.13)
Past history of depression
No
Reference
Yes
2.57 (0.78, 8.53)
Dependency in ADL
Low
Reference
High
0.56 (0.39, 0.82)
Living alone
No
Reference
Yes
0.92 (0.62, 1.36)
0
1
3
5
7
9

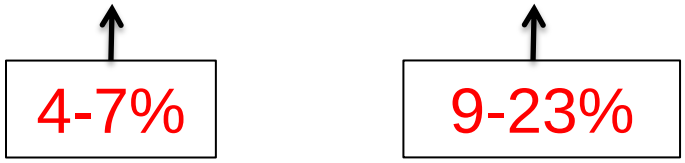
Key Points

1. Glomerular diseases are common in the elderly.
2. Kidney biopsy for elderly is safe and can be clinically informative.
3. Therapeutic recommendations for elderly are mostly extrapolated from younger adults --- need more studies.
4. Treatment for elderly with glomerular diseases should be individualized. ---- *General health, cognitive function, competing comorbidities, life expectancy and patient's preference* should all be taken into consideration.

Objectives:

To examine:

1. Changing healthcare landscape: Aging population
2. Elderly glomerular diseases: Overview
3. IgA nephropathy in elderly (Europe/U.S. and Asia)



Clin Exp Nephrol (2012) 16:903–920
Nephrol Dial Transplant (2014) 29: 2251–2259

In-Depth Topic Review

American Journal of Nephrology

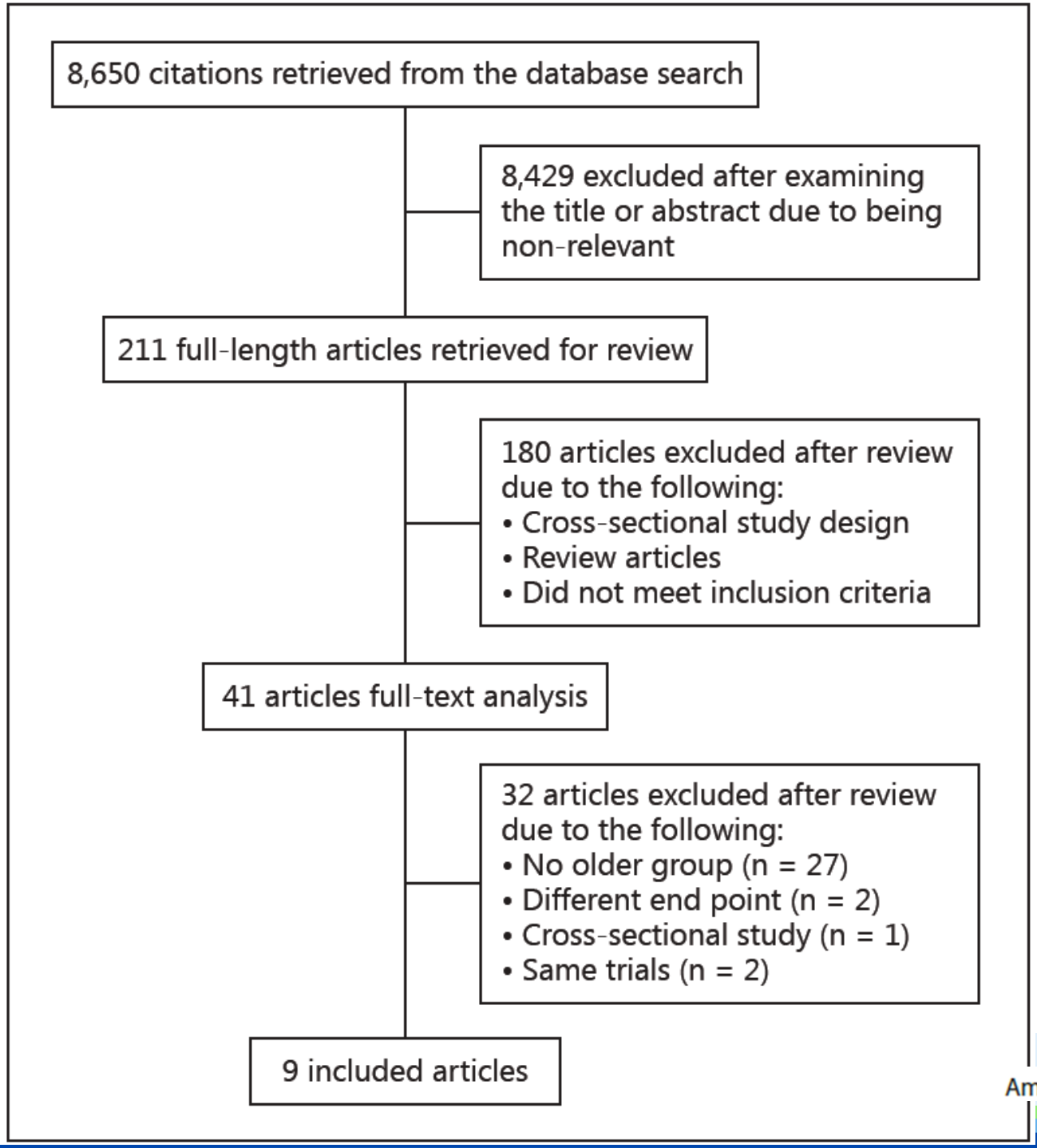
Am J Nephrol 2013;38:241–252
DOI: 10.1159/000354646

Received: May 7, 2013
Accepted: July 19, 2013
Published online: September 10, 2013

Aging Promotes Progression of IgA Nephropathy: A Systematic Review and Meta-Analysis

Zhi-Yu Duan Guang-Yan Cai Yi-Zhi Chen Shuang Liang Shu-Wen Liu
Jie Wu Qiang Qiu Shu-Peng Lin Xue-Guang Zhang Xiang-Mei Chen

Department of Nephrology, State Key Laboratory of Kidney Diseases, Chinese PLA General Hospital, Beijing, PR China



Am J Nephrol 2013;38:241–252

Table 1. Main characteristics of the included studies

Study	Design	Sample size	Nation-ality	Males, %	Age, years	Exposure definition[1], years of age	Outcome definition	Events	Follow-up
Goto [7]	cohort study	2,283	Japanese	48.7	31.2	≥60	ESRD: beginning of chronic hemodialysis	252	87 months
Kuhara [18]	cohort study	291	Japanese	45.4	54.6±2.8	≥50	CRF	24	older group: 4.9±2.9 years
Takeda [20]	cohort study	117	Japanese	57.3	NS	≥50	CRF	16	3.8 years
Frimat [13]	cohort study	129	French	81.4	38.4	≥50	ESRD, required dialysis or kidney transplantation	22	41 months
Soleymanian [12]	cohort study	70	Iranian	35.7	39±12.1	≥50	ESRD, need for renal replacement	10	23.5 months
Yang [21]	cohort study	152	Chinese	56.6	older group: 65.2±4.7 control group: 34.2±9.4	≥60	ESRD	5	34.6±33.3 months
Ferro [22]	cohort study	392	Italian	58.2	53	≥65	CRF	10	NS
Rivera [23]	cohort study	total: 9,378	Spanish	60.4	NS	≥65	CRF	148	NS
Yokoyama [24]	cohort study	total: 3,109	Japanese	50.1	NS	≥65	CKD stage 5	48	NS

CKD = Chronic kidney disease; CRF = chronic renal failure; NS = without giving specific figure.
[1] Old age designated as older than 50 years.

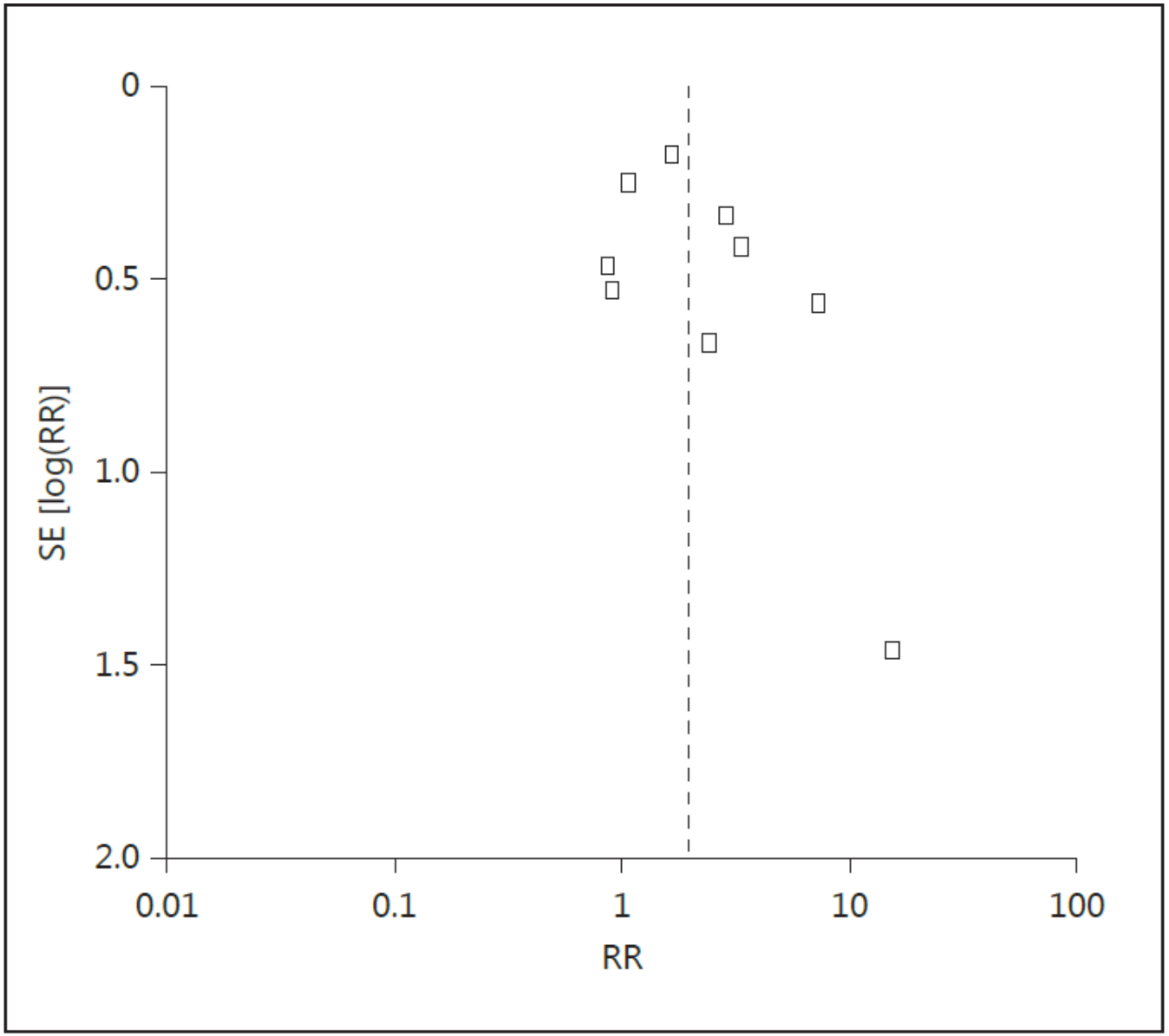


Fig. 9. Funnel plot of 9 trials on the effect of aging on the progression of IgAN to ESRD.

Frimat et al.

- N= 33 patients with age ≥50 and
- N= 96 younger adults with ages 15-64.
- Multi-center.
- A higher blood pressure and proteinuria in the elderly patients (no specific treatment information was provided)
- Did not use the Oxford classification of IgAN.
- Only 16 patients had histological information.
- Vasculopathy was the single histological difference between the two groups
- No outcome difference in terms of end-stage renal failure

Nephrol. Dial. Transplant. 1996; 11: 1043–7.

Mayo Study (1994-2013):

This single-centre cohort study was designed to compare elderly and younger adults with IgAN. It involved 45 elderly (age ≥65 years) and 162 younger adults (age 18–64 years) with a median follow-up of 36 ± 42.3 and 55.4 ± 46.4 months, respectively, which constitutes the largest study in a Western country and the only study from the United States.

Nephrology. 2015 Jun;20(6):419-25.

Table 1 Clinical features between elderly and adult patients with IgA nephropathy at the time of kidney biopsy

Clinical features	Elderly (n = 45)	Adult (n = 162)	P-value
Age, year	71 ± 5	42 ± 13	
Male gender	31 (69%)	112 (69%)	0.97
Race, White	38 (84%)	127 (78%)	0.37
BMI, kg/m^2	30.1 ± 5.7	30.1 ± 15.3	0.98
Charlson Comobidity Index score	5.5 ± 2.6	1.8 ± 2.4	<0.001
Onset of the disease (elevation of serum creatinine haematuria or proteinuria), month	0.7 ± 0.5	0.4 ± 0.2	0.08
Chronic hypertension	28 (62%)	44 (27%)	<0.001
Hypertension at diagnosis	19 (42%)	47 (29%)	0.09
SBP, mmHg	138 ± 22	130 ± 21	0.06
DBP, mmHg	73 ± 14	89 ± 12	0.03
Pulse pressure, mmHg	65 ± 17	51 ± 15	<0.001
Number of patients on antihypertensive	36 (80%)	138 (85%)	0.40
Serum creatinine, mg/dL	2.6 ± 1.3	2.2 ± 1.5	0.07
GFR, mL/min per 1.73 m^2	29 ± 17	51 ± 30	<0.001
GFR at diagnosis (mL/min per 1.73 m^2)			0.003
≥90	4 (9)	24 (15)	
60–89	1 (2)	36 (22)	
30–59	15 (33)	55 (33)	
15–29	18 (40)	32 (20)	
<15	7 (16)	16 (10)	
Haemoglobin, g/dL	11.1 ± 2.3	12.7 ± 2.1	<0.001
Serum albumin, mg/dL	3.6 ± 0.6	3.8 ± 0.7	0.08
24 h urine protein, mg	2428 ± 3221	2862 ± 3823	0.46
24 h urine protein level			0.54
<1000 mg	21/41 (51%)	67/161 (42%)	
1000–3500 mg	11/41 (27%)	51/161 (32%)	
>3500 mg	9/41 (22%)	43/161 (27%)	
Total cholesterol, mg/dL	197 ± 66	204 ± 70	0.62
Coexist positive ANCA	3 (6%)	8 (5%)	0.65
Total MEST score	2.0 ± 1.1	1.9 ± 1.0	0.34
Total MEST score ≥ 2	28 (62%)	98 (60%)	0.83
Absolute renal risk score (ARR)†			0.68
ARR = 0	9 (20)	32 (20)	
ARR = 1	14 (31)	45 (28)	
ARR = 2	13 (29)	61 (38)	
ARR = 3	9 (20)	24 (15)	

Elderly at the time of biopsy:

- More comorbidities
- More HTN
- Lower eGFR
- Lower HGB

Nephrology. 2015 Jun;20(6):419-25.

Table 2 Pathological features between elderly and adults patients with IgA nephropathy

Histological findings	Elderly (n = 45)	Adult (n = 162)	P-value
Mesengial hypercellurity (M1)	41/43 (95%)	141/162 (87%)	0.17
Endocapillary proliferation (E1)	7/43 (16%)	18/162 (11%)	0.36
Segmental glomerulorosclerosis (S1)	19/43 (44%)	88/162 (54%)	0.25
Tubular atrophy/interstitial fibrosis	24/44 (55%)	119/161 (74%)	0.04
T0	16/44 (36%)	31/161 (19%)	
T1	4/44 (9%)	11/161 (7%)	
T2	2.0 ± 1.1	1.9 ± 1.0	
Total MEST score			0.34
MEST score			0.51
MEST = 0	2 (4)	11 (7)	
MEST = 1	15 (33)	53 (33)	
MEST = 2	11 (24)	56 (35)	
MEST = 3	14 (31)	33 (20)	
MEST = 4	3 (7)	9 (6)	
MEST = 5	0 (0)	0 (0)	
Global sclerosis	35/43 (81%)	124/162 (77%)	0.49
% global sclerosis	27 ± 24	25 ± 25	0.68
% segmental sclerosis	8.6 ± 13.6	8.7 ± 11.3	0.97
Cellular/fibrocellular crescents	6/42 (14%)	31/162 (19%)	0.47
% cellular/fibrocellular crescents	3.2 ± 11	3 ± 9	0.83
Fibrinoid necrosis	2/42 (5%)	12/162 (7%)	0.54
% fibrinoid necrosis	1.8 ± 10.1	0.7 ± 2.8	0.47
Arterial and/or arteriolar sclerosis			<0.001
Mild	14/44 (32%)	55/162 (34%)	
Moderate	11/44 (25%)	34/162 (21%)	
Severe	6/44 (14%)	0/162 (0%)	
Arterial hyalinosis			0.40
Mild	11/44 (25%)	25/162 (15%)	
Moderate	4/44 (9%)	15/162 (9%)	
Severe	2/44 (5%)	4/162 (2%)	
Coexist diabetes nephropathy	3/45 (7%)	4/162 (2%)	0.17
Coexist acute tubular necrosis	3/45 (7%)	6/162 (4%)	0.41

Pathological features:

More
- interstitial fibrosis
- tubular atrophy
- vascular changes

Nephrology. 2015 Jun;20(6):419-25.

Table 3 Treatment and treatment response between elderly and adult with IgA nephropathy at 6 months

	Elderly (n = 45)	Adult (n = 162)	P-value
Treatment			
ACEI or ARB	15 (33%)	70 (43%)	0.23
Immunosuppression	14(31%)	54(28%)	0.66
Steroid	14 (31%)	40 (25%)	0.39
Immunosupression other than steroid	4 (9)	22 (14)	0.21
Cyclophosphamide	3 (7%)	4 (2%)	0.17
Azathioprine	0 (0%)	2 (1%)	0.45
Cyclosporine	0 (0%)	4 (2%)	0.29
Mycophenolate mofetil	1 (2%)	12 (7%)	0.20
Fish oil	8 (18%)	52 (32%)	0.06
Treatment response at 6 months			
SBP, mmHg	159 ± 25	149 ± 26	0.06
DBP, mmHg	84 ± 9	90 ± 16	0.02
Pulse pressure, mmHg	75 ± 21	59 ± 17	0.001
Number of patients on antihypertensive meds	35 (78%)	106 (65%)	0.12
Serum creatinine, mg/dL	2.3 ± 2.2	2.1 ± 1.5	0.60
GFR, mL/min per 1.73 m^2	38 ± 19	54 ± 31	0.023

Nephrology. 2015 Jun;20(6):419-25.

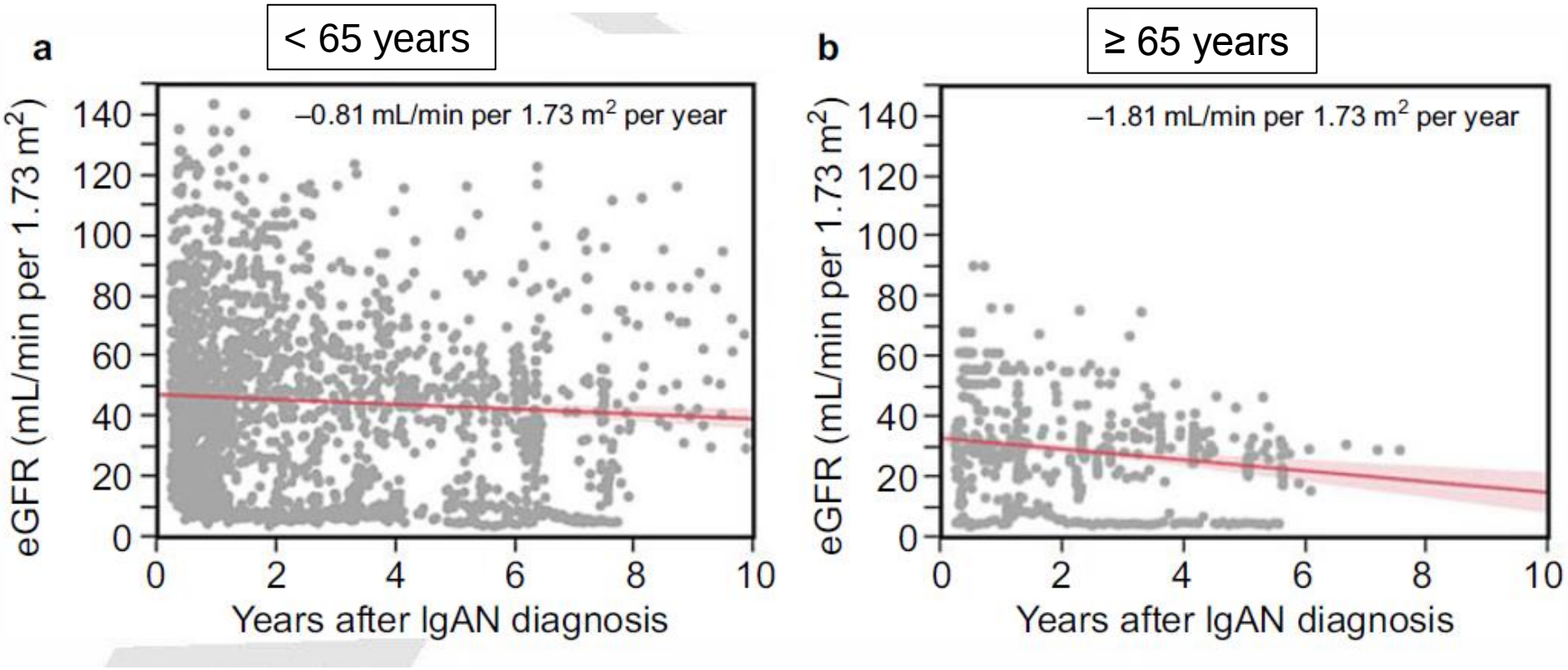
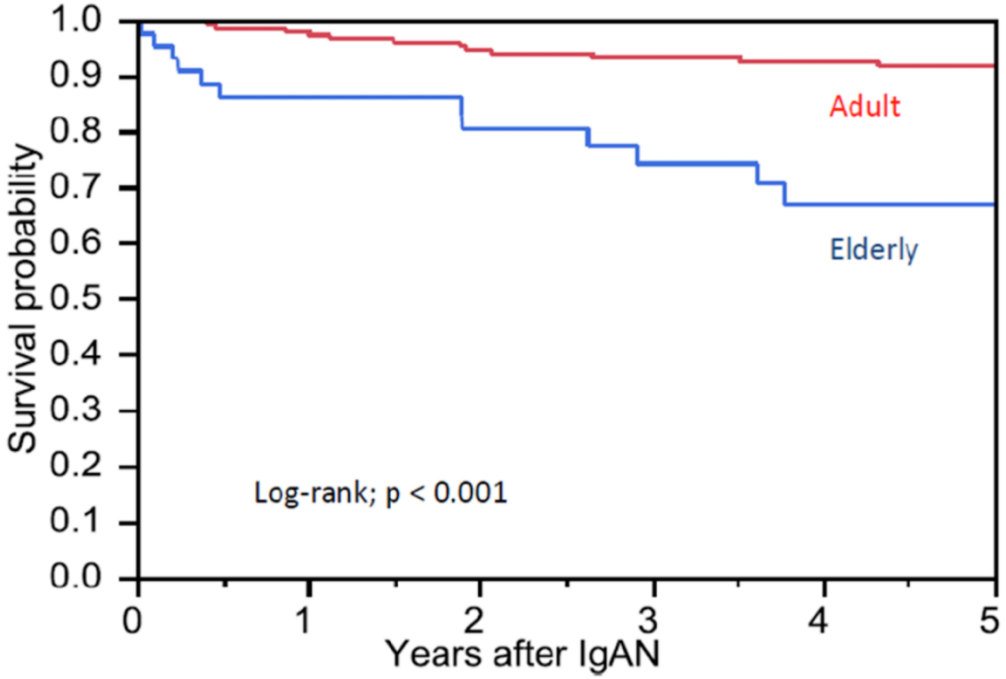


Fig. 1 The eGFR (CKD-EPI) decline after IgAN diagnosis was faster in younger (a) than in elderly adults (b) ($P = 0.04$). eGFR, estimated glomerular filtration rate; IgAN, IgA nephropathy.

Nephrology. 2015 Jun;20(6):419-25.

Kaplan-Meier curve for survival analysis



Number at risk

elderly	45	35	28	25	19	16
adult	162	157	143	125	108	97

Nephrology. 2015 Jun;20(6):419-25.

Beijing Da Xue Xue Bao. 2008 Aug 18;40(4):401-4.

[Clinicopathologic characteristics and outcomes of IgA nephropathy in elder patients].

[Article in Chinese]

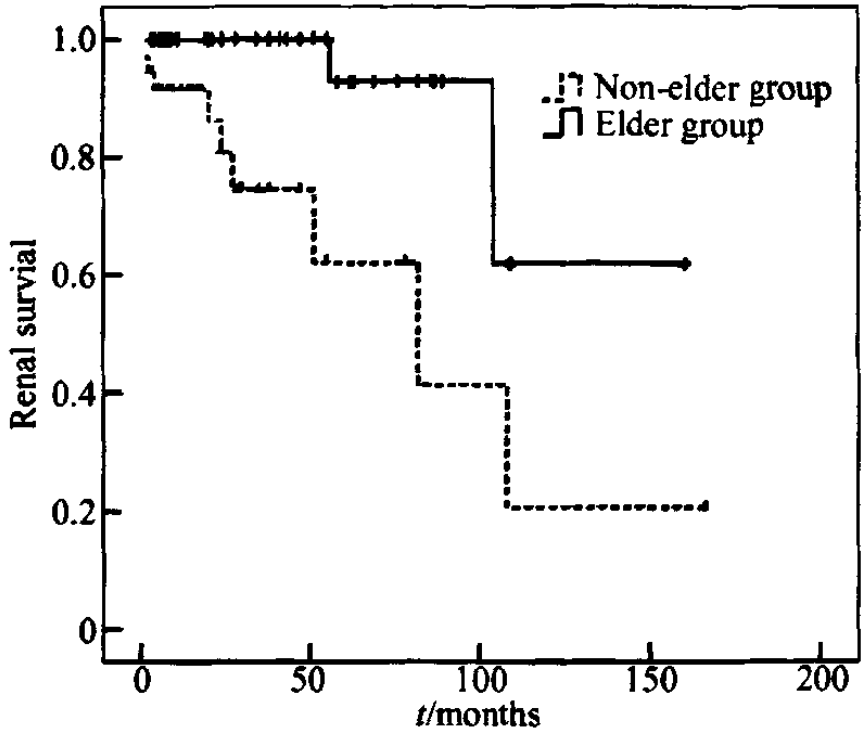
Yang YR1, Lv JC, Jiang L, Zhang YM, Song YH, Li RS, Zhang H.
1Department of Nephrology, Peking University First Hospital, Beijing, China.

Single center, retrospective (1993-2007)
N=70 age>60
N=82 age <60

RESULTS:

Elder group patients had

- higher BP, sCr, cholesterol, 24 hr urinary protein, CKD progression.
- Renal pathology: chronic lesions: glomerular sclerosis, renal tubule atrophy/interstitial fibrosis and arteriolosclerosis.
- the 3-year and the 5-year renal survival rates for elder group were 74.6% and 62.2%, respectively, which were lower than those of non-elder group (100% and 92.9%, P=0.002).



1 老年组和非老年组 IgAN 患者预后的 Kaplan-Meier 生存分析

Figure 1 Kaplan-Meier renal survival curves of patients with IgAN in elder and non-elder group

CONCLUSION: Elder patients with IgA nephropathy were more likely to have HTN, hyperlipidemia, renal insufficiency and chronic pathologic lesions --- the risk factors for the patient's unfavorable prognosis.

Characteristics of IgA nephropathy in advanced-age patients

Yasuko Oshima · Takahito Moriyama ·
Mitsuyo Itabashi · Takashi Takei · Kosaku Nitta

600 IgAN cases 1992-2011

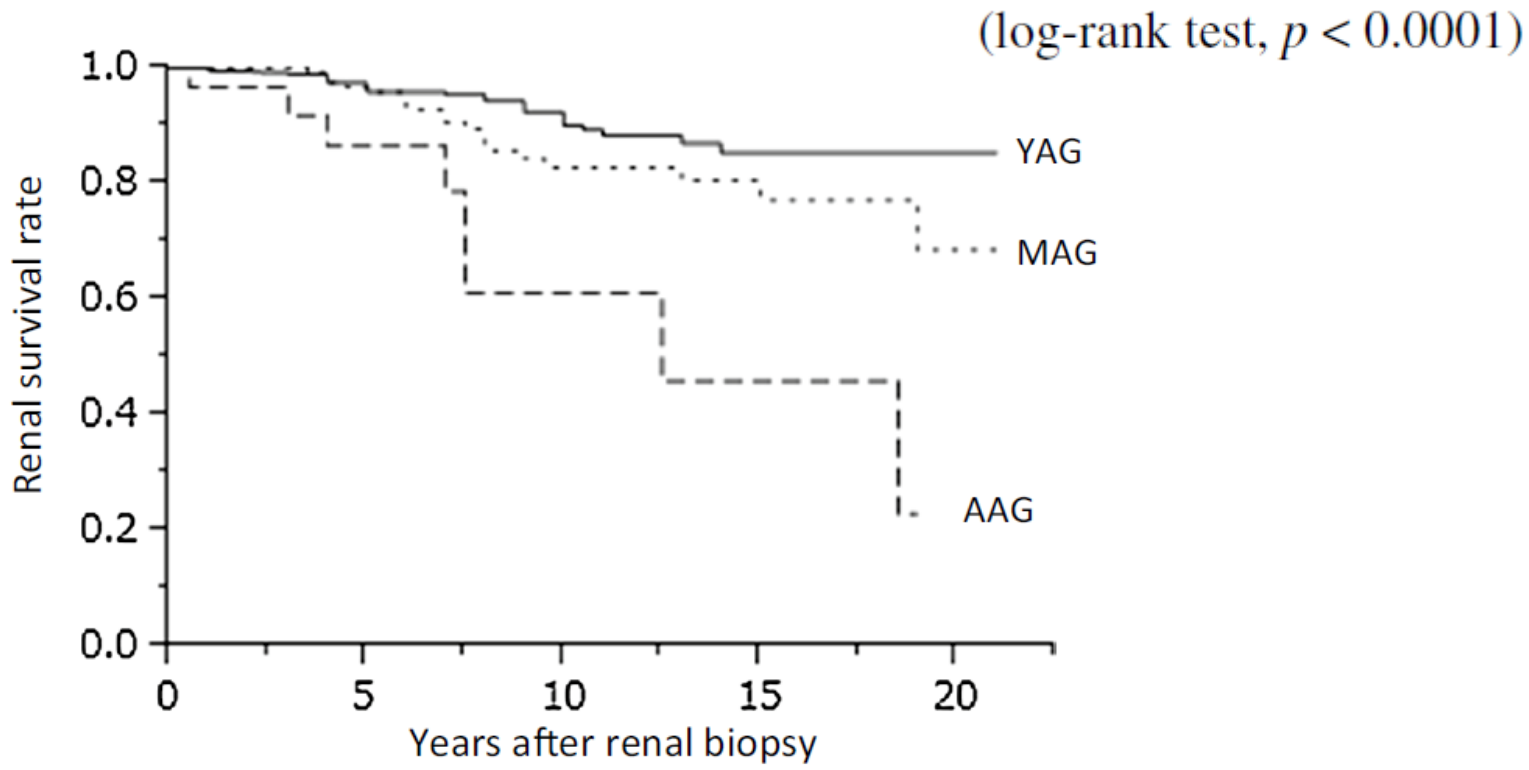
N=31, Advanced-age group (AAG) ≥60 years (5.2%)
N=162, middle-age group (MAG) 40 - 59 years.
N=407, young-age group (YAG) 20-39 years

RESULTS: in AAG

- MAP higher
- s.albumin, eGFR lower
- Interstitial fibrosis/tubular atrophy higher
- More ACEi/ARB tx
- Renal survival lower

MAP and proteinuria – predicted ESRD

Int Urol Nephrol 2014
DOI 10.1007/s11255-014-0872-1



YAG	407	246	121	44
MAG	162	107	54	24
AAG	31	14	6	4

CONCLUSIONS: AAG had lower renal function, high levels of proteinuria, severe interstitial change, and arteriolosclerosis. concomitant diseases, such as hypertension, dyslipidemia, and hyperuricemia.

Prognosis was poor, and >70 % developed ESRD within 20 years.

Conclusion:

Compare to younger adults, elderly IgAN patients show

(1) a higher level of pre-existing comorbidity,
(2) biopsy: more tubulointerstitial fibrosis and vasculopathy
(3) progression: faster to renal failure
(4) reduced patient survival – despite similar treatment for IgAN.

Summary:

1. Changing healthcare landscape: aging burden

2. Elderly glomerular diseases: diagnosis and treatment
   Diagnosis should be timely. Kidney biopsy is safe.
   Tx should be individualized

3. Elderly IgAN in the Western countries and Asia

- more common in Asia (2-3 fold more)
- A higher degree of comorbidity at the biopsy,
- Biopsy: higher degrees of interstitial fibrosis/tubular atrophy and vascular diseases
- faster renal disease progression
- IgAN in elderly is an independent risk factor for the decline in renal function and patient survival.

Thank You!