

# Epidemiology of Glomerular Disease In Iran and the World

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# Introduction

- Glomerulonephritis (GN) remains among the most commonly recognized causes of end-stage renal disease (ESRD).
- Its overall incidence and prevalence rates and numbers within each specific histologic category remain largely unknown.
- Available data has been derived from regional biopsy series or ESRD registries and has not had a broad-based epidemiological perspective.

- The terminology used for description of GN may not be the same in all studies, neither are the clinical syndromes.
- Pathologic reports are not yet standardized throughout the world, there is inter-pathologic differences in reports.
- The pathologic nomenclature and classifications are changing.

- Its prevalence rate of 20% to 30% of the renal replacement therapy population would put the annual cost of managing ESRD GN patients in the billions.
- Many GNs can be successfully treated, stabilized and sometimes reversed even after renal impairment is present.
- Thus the extremely high numbers and cost of renal replacement may be prevented.

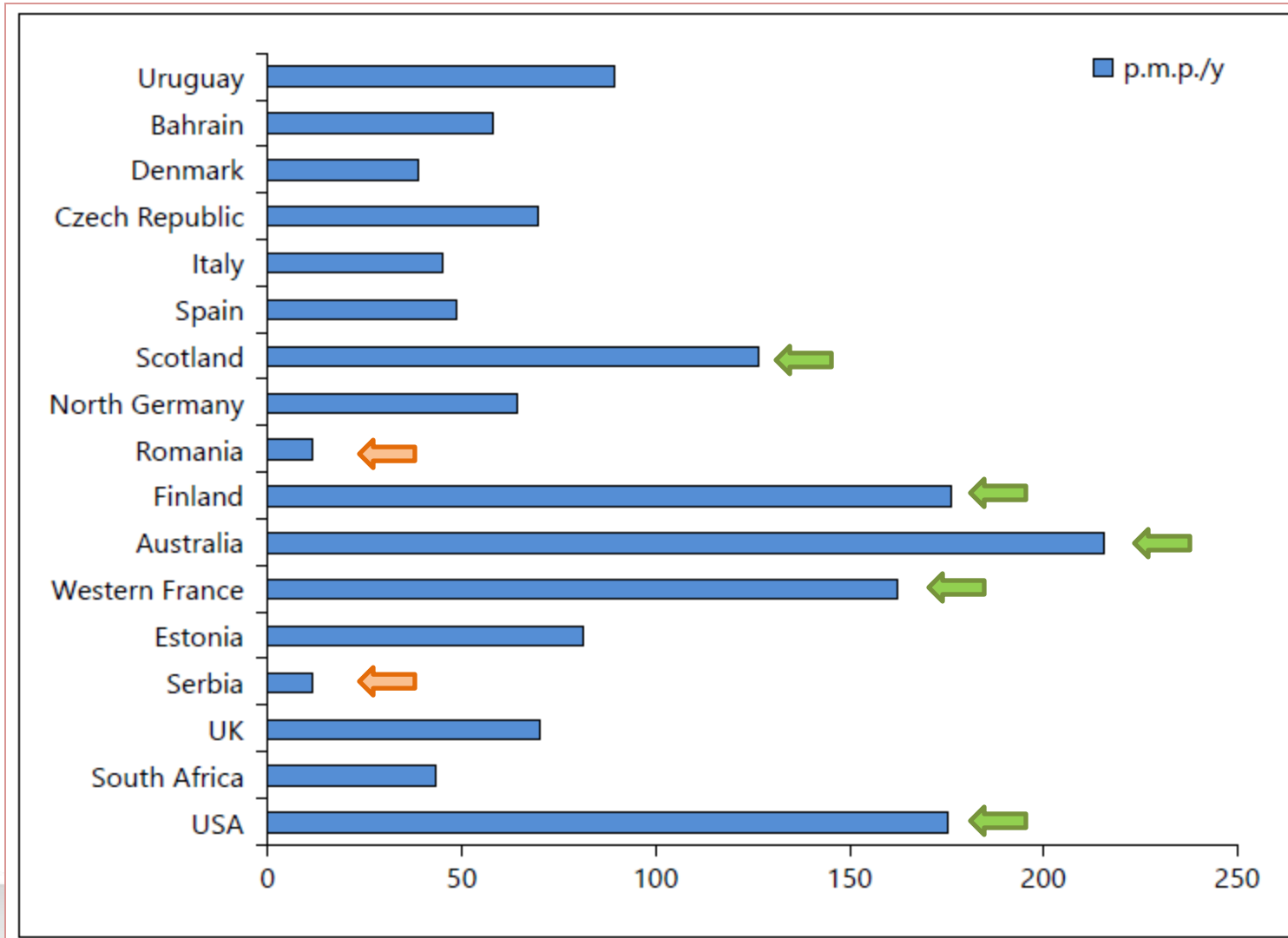
# The incidence of primary glomerulonephritis worldwide: a systematic review

(including 40 studies from Europe, North and South America, Canada, Australia and the Middle East.)

Adult	/100 000/year
MPGN	0.2
Mesangioproliferative	0.2
Minimal change disease	0.6
FSGS	0.8
Membranous nephropathy	1.2
IgAN	2.5
Children	/100 000/year
Overall	0.1
Minimal change disease in Caucasian	2.0
Minimal change disease in Arabian children	9.2
Minimal change disease in Asian Children	6.2-15.6

- Given that GN can exist subclinically, and given differences in access to renal biopsy between different healthcare systems, it is likely that geographical variations found in incidence rates can be explained by differences in diagnosis rather than by genuine difference in disease frequency.

# Annual renal biopsy rate as reported in national and macro-regional registries



# Frequency of renal biopsy

There is large global variation in frequency of renal biopsy – ranging from

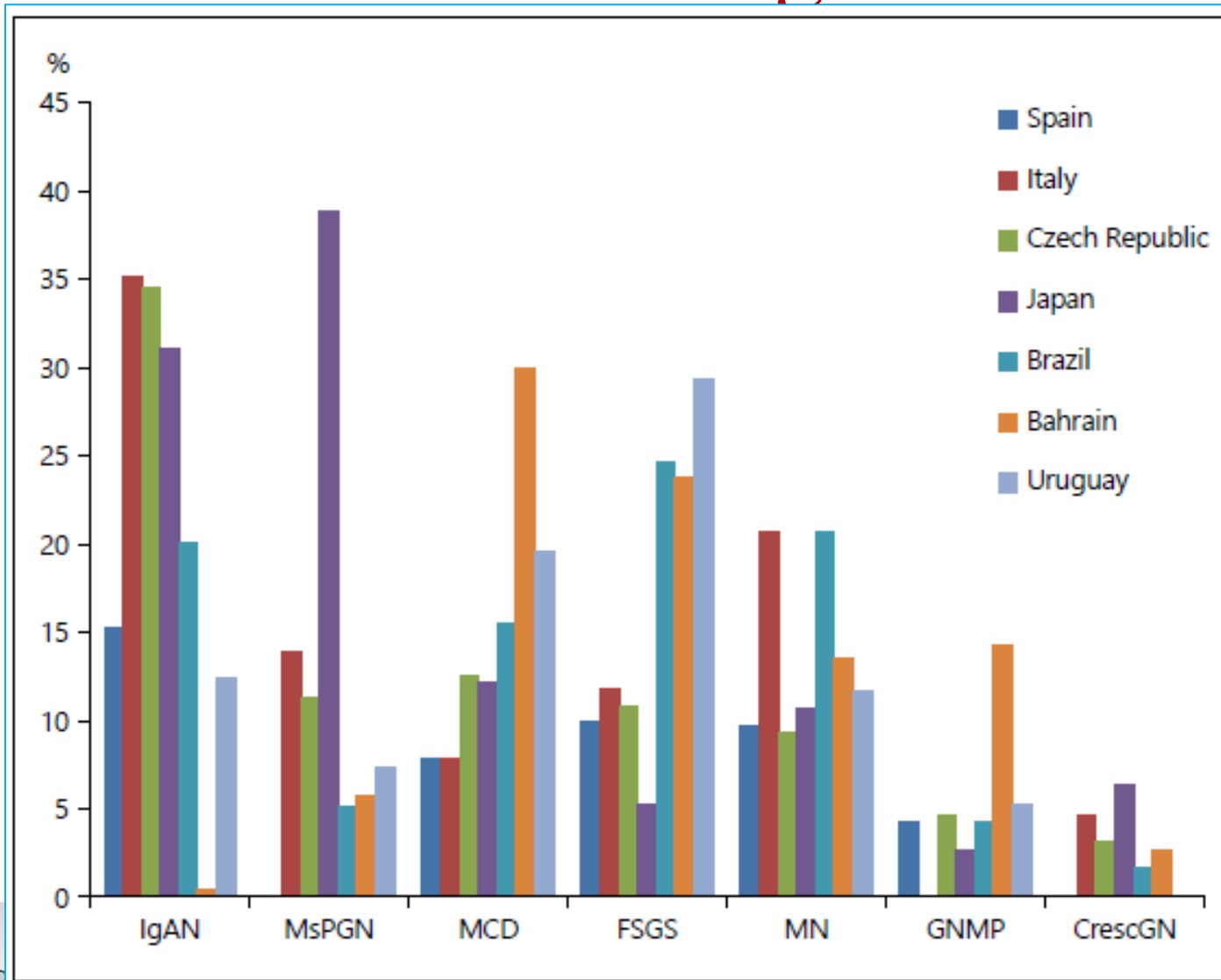
- 1.1 php\*/yr in Serbia,
- 4.8 php/yr in Spain,
- 11.3 php/yr in Romania,
- 16.2 php/yr in France,
- 16.4 php/yr in Japan, ←
- 17.5 php/yr in USA
- 17.6 php/yr in Finland.

\*per hundred thousand people per year

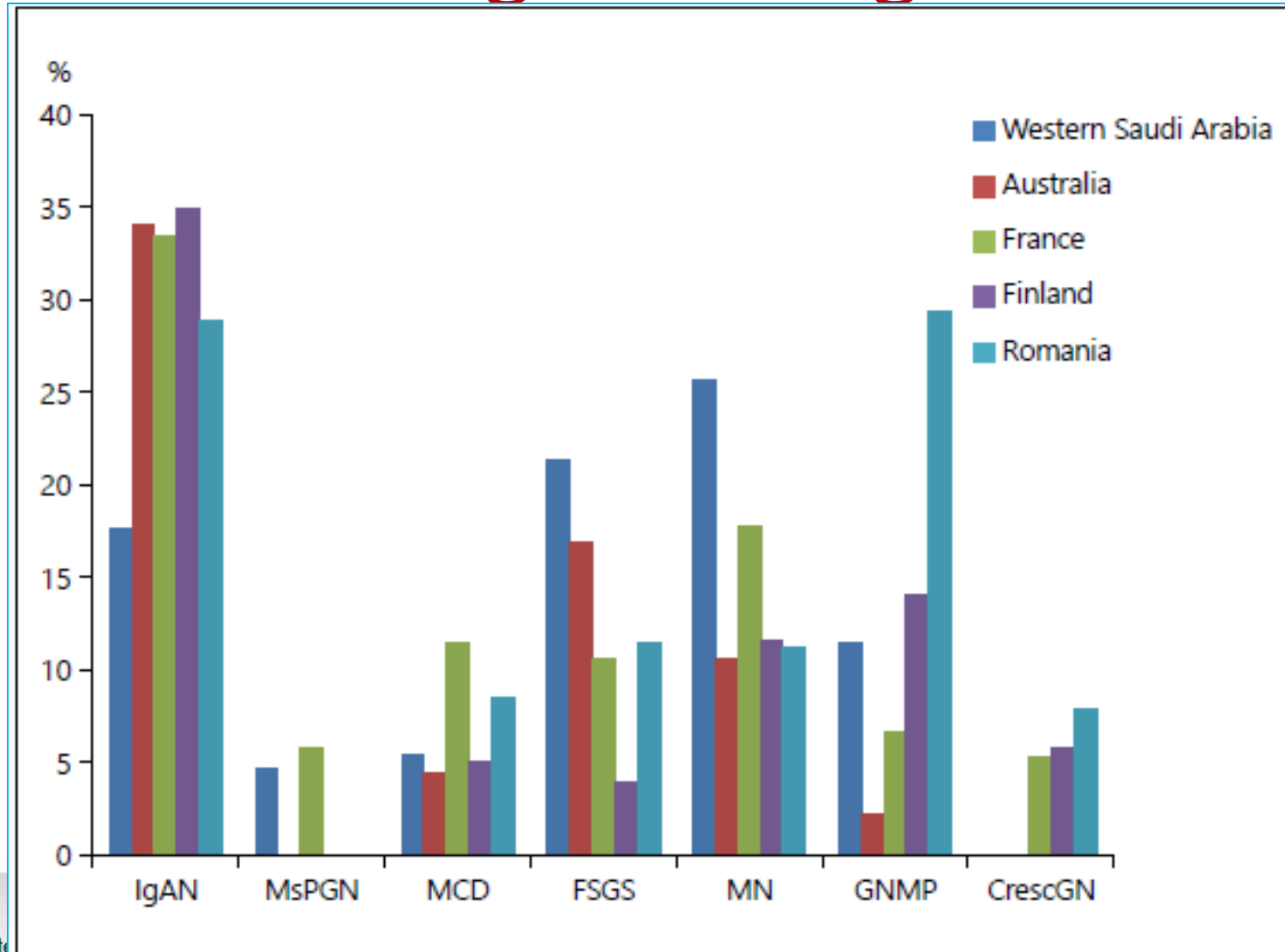


# Comparison of Incidence of GNs between different regions

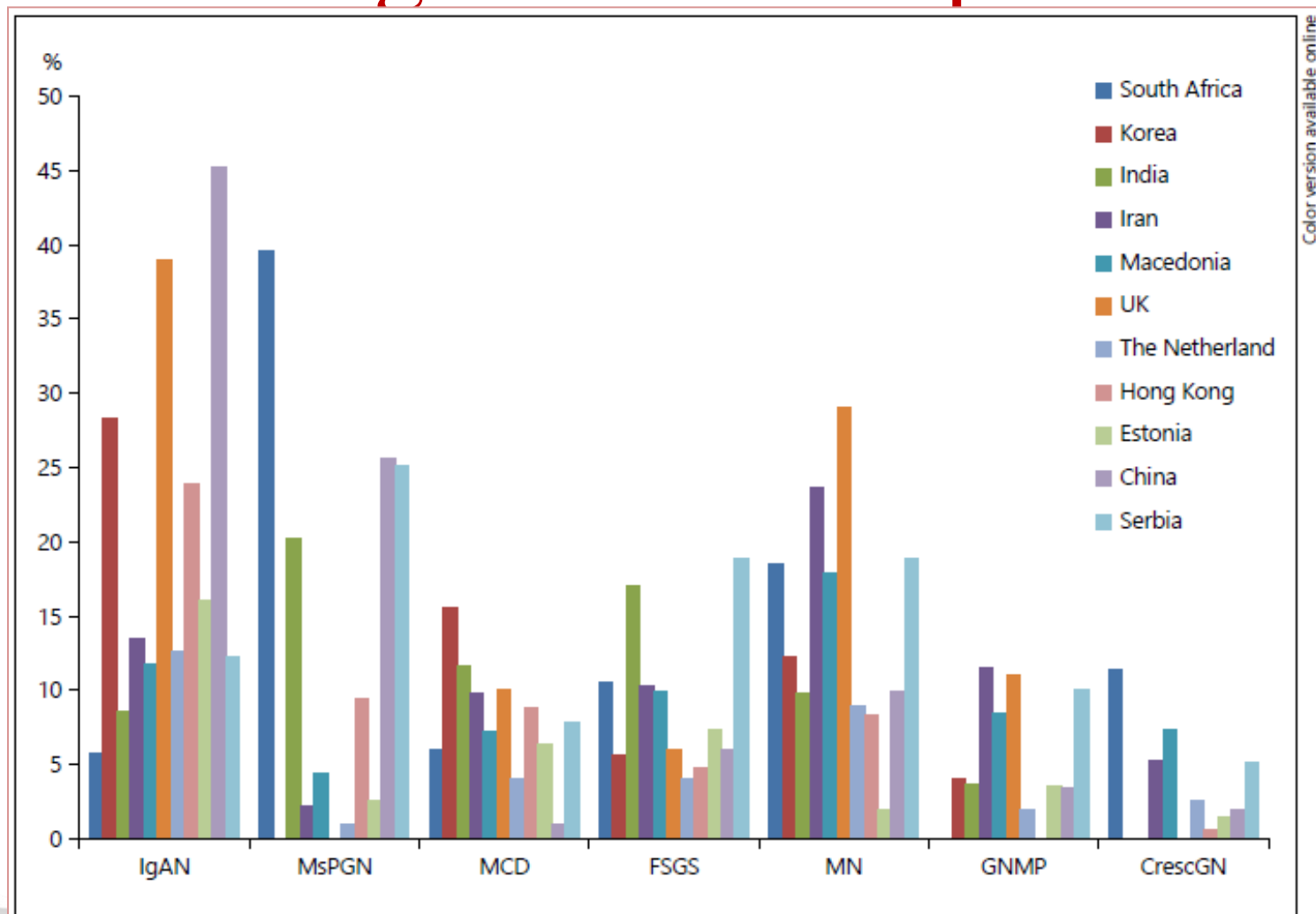
# Different Incidence of Primary GN in National Registries



# Different Incidence of Primary GN in Macroregional Registries



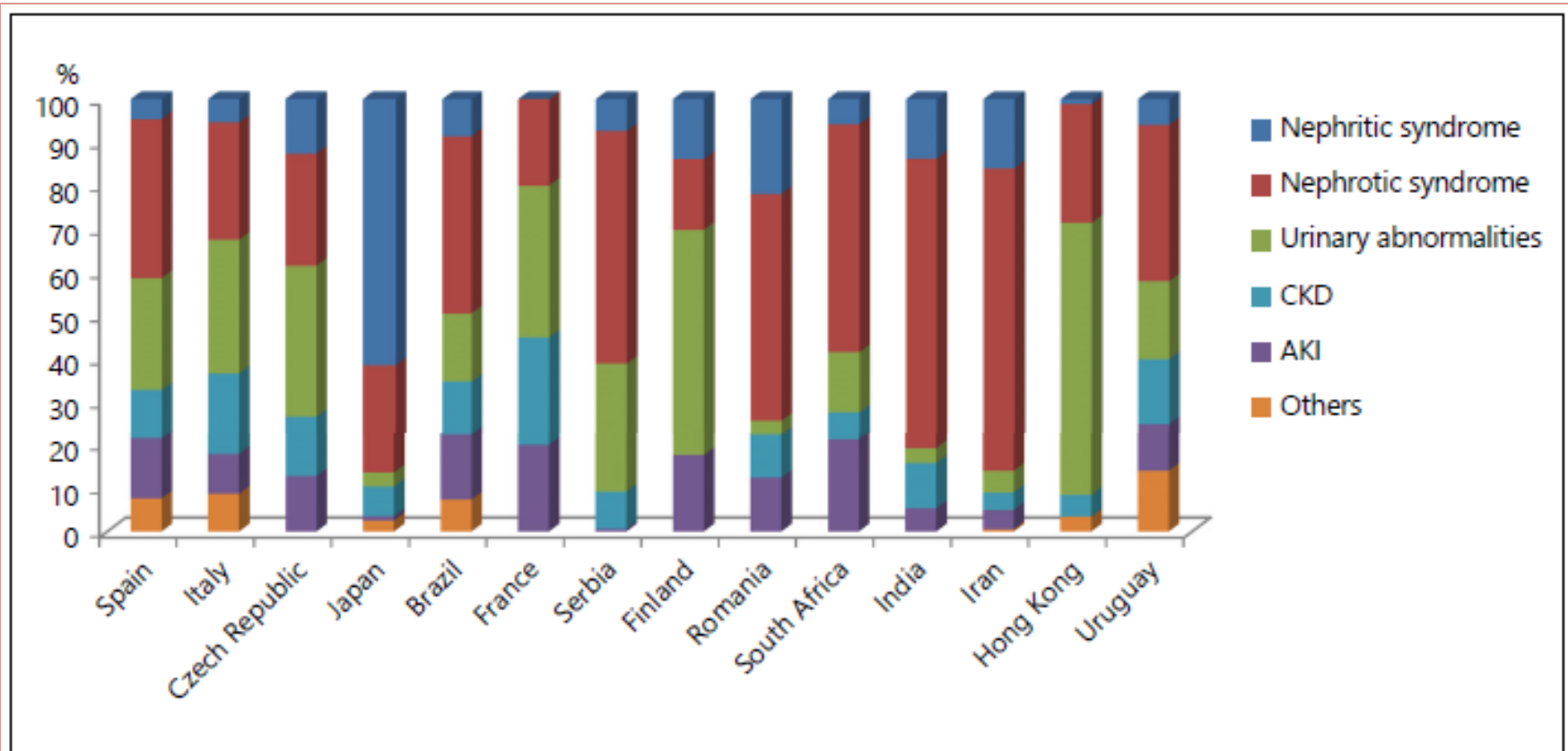
# Different Incidence of Primary GN in Single Center Reports



Color version available online

**Fig. 4.** Different incidence of primary glomerulonephritides in single-center reports (the data are obtained from table 2). MsPGN = Mesangioproliferative GN.

# Main Indications for Renal Biopsies



**Fig. 5.** Main indications for renal biopsy as reported in national and macro-regional registries. Data are obtained from the national and macro-regional registries reported in the text.

- **IgAN** represents the most frequent primary, biopsy-proven GN in 6 out of 8 national registries (Italy, Spain, Czech Republic, Denmark, Scotland, Japan), in 3 macroregional (Western France, Finland, Victoria-Australia) and 7 single-center databases with a percentage of total diagnoses ranging from **12.6%** (Limburg- Belgium) to **45%** (China).

- **FSGS** was the most frequent primary GN in Brazil (24.6%) , in the Uruguayan registry of glomerulopathies (29.3%) and in Bahrain (23.8%).
- **MPGN** appeared to be the most frequent glomerular disease diagnosed in Romania (29.4%).
- **MN** predominated in 2 single- center retrospective reports in Macedonia (17.9%) and Iran (23.6%).

- **Non-IgA mesangioproliferative GN** was the most frequent primary GN in Serbia (25.1%).
- The most frequent secondary GN was **lupus nephritis** in Spain (8.8%), Italy (2.6 p.m.p./year), Brazil (9.8%) , Bahrain (15.7%), Australia (13.9%) , Romania (7.4%), Korea (8.7%), China and Hong Kong (20.5%).
- **Diabetic nephropathy** predominated in Czech Republic (2.6%), Japan (5.3%) and Scotland (7–14 p.m.p./year).
- **AIN** diagnosis was reported in 13 registries, with a percentage ranging across 1.5% to 11% of overall diagnosis.



# Worldwide distribution of Bx-proven GN

Country	Reference	Primary GN (%)	Secondary GN (%)
America			
USA	3	IgAN (22) <sup>a</sup> ←	LN (13) <sup>a</sup>
Brazil	1	FSGS (25) <sup>b</sup>	LN(42) <sup>b</sup>
Europe			
Italy	5	IgAN (37) <sup>b</sup>	LN (26) <sup>b</sup>
Spain	7	IgAN (17) <sup>a</sup>	LN (11) <sup>a</sup>
Czech Republic	8	IgAN (34) <sup>b</sup>	LN (23) <sup>b</sup>
Hungary	10	IgAN (15) <sup>a</sup>	LN (7) <sup>a</sup>
Macedonia	11	MN (13) <sup>b</sup>	
Romania	12	MPGN (29) <sup>b</sup>	LN (29) <sup>b</sup>
Serbia	13	Non-IgA mesangioproliferative (25) <sup>b</sup>	LN (76) <sup>b</sup>
UK	21	IgAN (39) <sup>b</sup>	
Asia			
China	14	IgAN (45) <sup>b</sup>	LN (54) <sup>b</sup>
Korea	16	IgAN (28) <sup>b</sup>	LN (9) <sup>b</sup>
Middle East			
Saudi Arabia	17	FSGS (21) <sup>b</sup> ←	LN (57) <sup>b</sup>
Australia	18	IgAN (34) <sup>a</sup>	LN (14) <sup>a</sup>

<sup>a</sup>Percentage of total glomerular diseases. <sup>b</sup>Percentage of primary or secondary glomerulonephritis.

# British Columbia Glomerulonephritis network and registry

**Table 4 The number of cases of each type of GN in the BC pathology databases from 2000 to 2012**

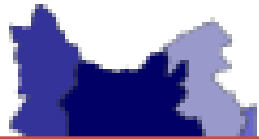
GN type	Number of cases
Minimal Change Disease	263
IgA Nephropathy	827
Focal Segmental Glomerulosclerosis	846
Membranous Nephropathy	418
Lupus Nephritis	738
ANCA Vasculitis	381

The average number of GN cases per year is 267.

Population: 83,104,828 (September 4, 2019)

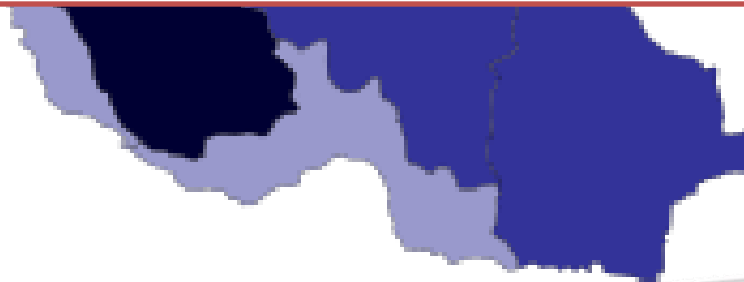
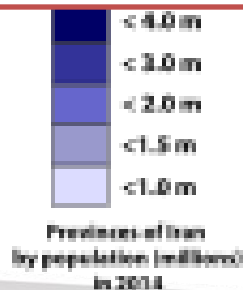
(1.07% of the total world population)

Area: 1.648 millions km<sup>2</sup>



Age adjusted prevalence of CKD, according to eGFR assessed with the CKD-EPI and MDRD the were **8.5%** and **11.3%** (95% confidence interval (CI): 7.9-9.1 and 10.7-12.0), respectively.

Eftekharzade A. Int J Endocrinol Metab. 2018; 16(4 Suppl)



# Total ESRD Population: 66.899 (836.2 pmp) (2019)

- Total Dialysis Population: **33.775**
  - Maintenance Hemodialysis patients: 32.140 (95.1%)
  - CAPD Patients: 1.637 (4.9%)
- Renal Transplant Patients: **>36.000**
- **Main causes of ESRD:**
  - Diabetes Mellitus, HTN,GN

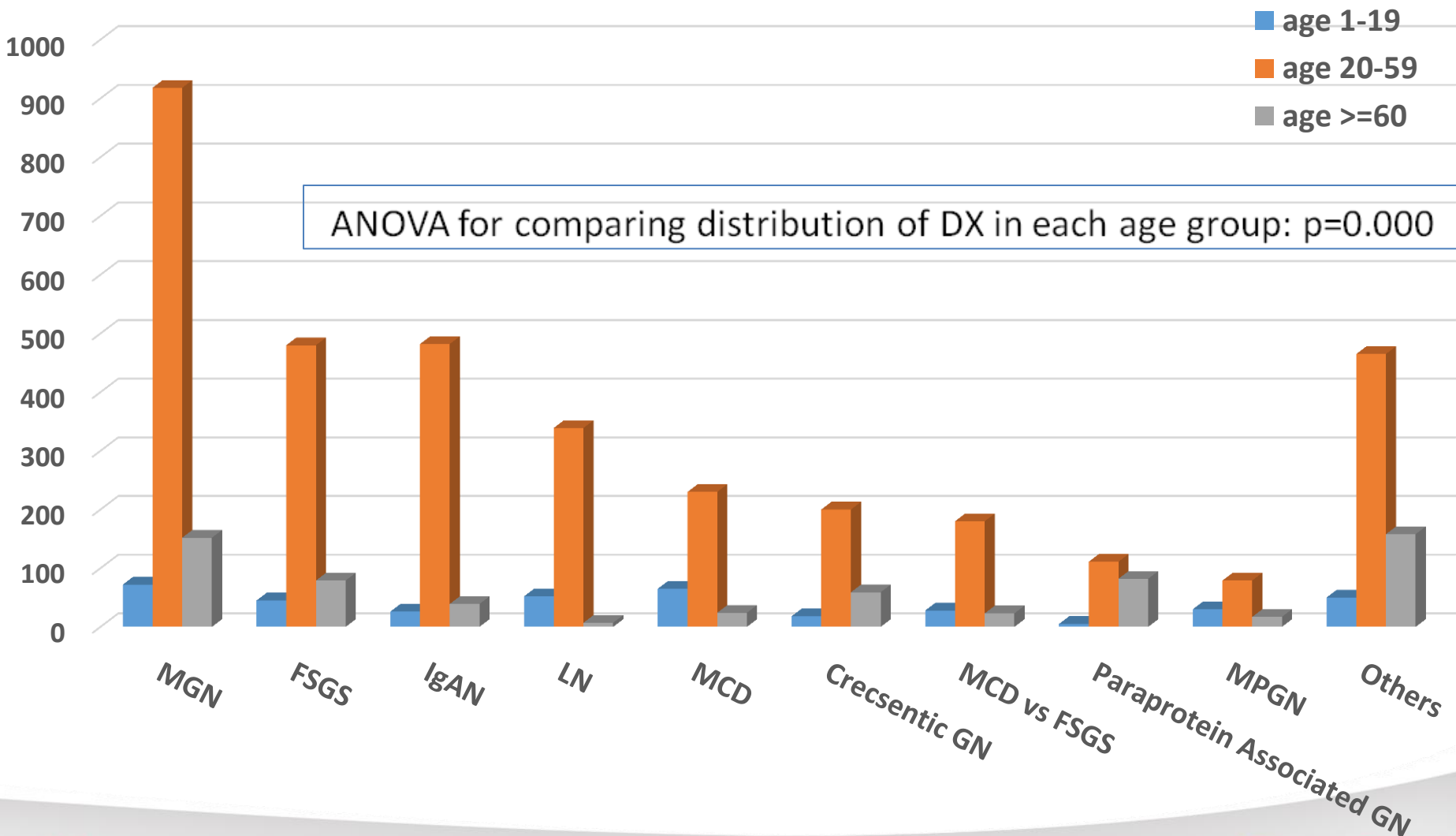
# 4519 Renal Bx Cases in HKC: 1999-2019

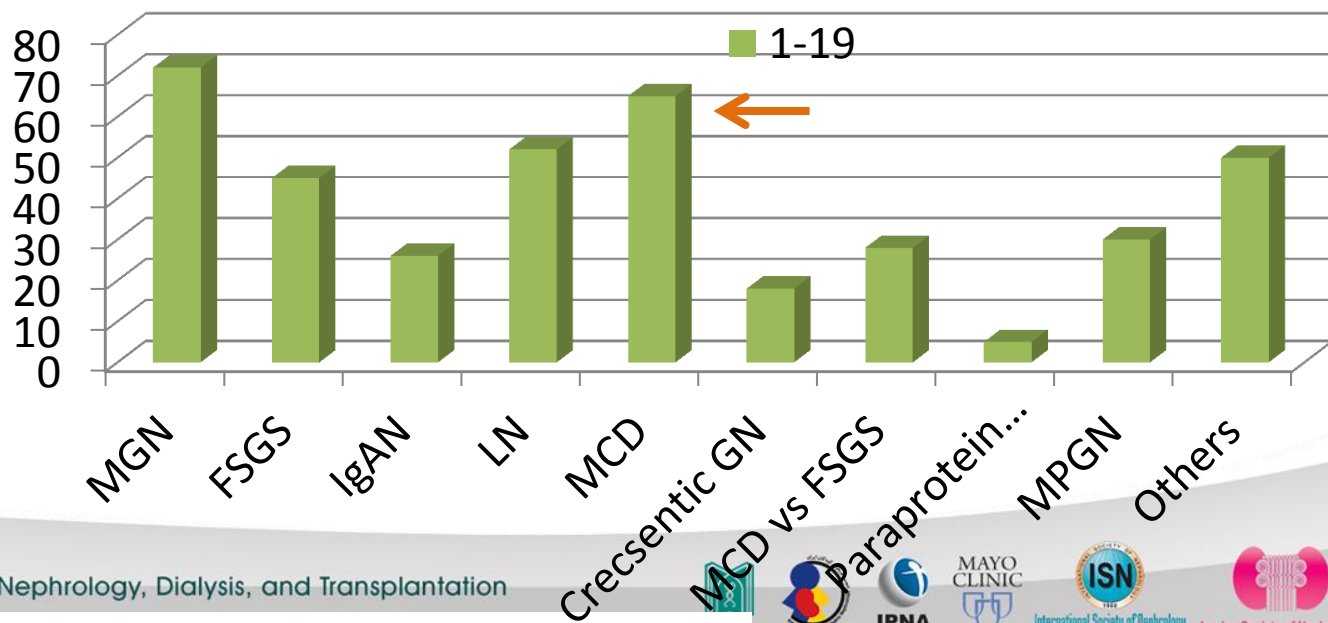
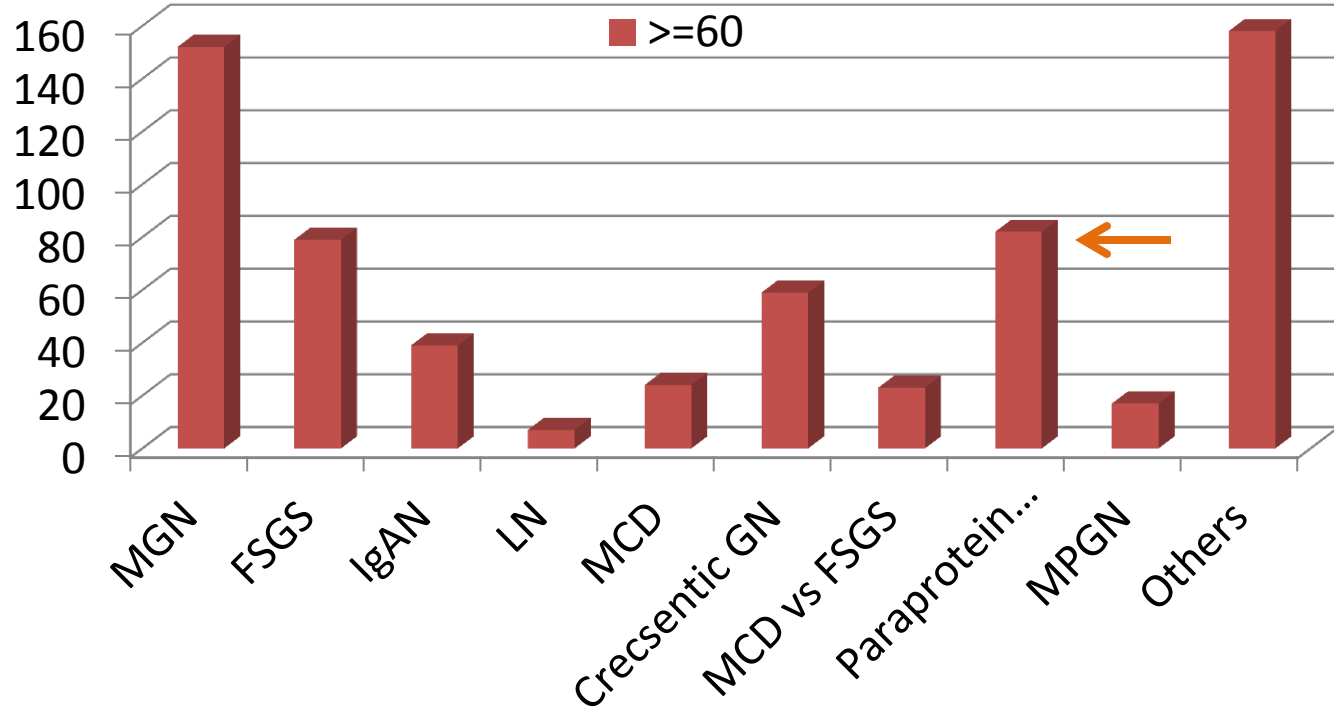
(56.2% male, mean age at biopsy: 39.9±16.1 yrs)

## Demographic & clinical manifestations of the main pathologic Dx

Pathologic Diagnosis	MGN	FSGS	IgAN	LN	MCD	Cresc. GN	MCD vs FSGS	Paraprot Ass. GN	MPGN	Others	Total	p-value
Frequency (%)	1144 (25.3%)	604 (13.4%)	549 (12.1%)	398 (8.8%)	319 (7.1%)	277 (6.1%)	231 (5.1%)	198 (4.4%)	126 (2.8%)	673 (14.9%)	4519 (100%)	
Mean age ±SD	40.8±15.2	39.6±15.8	37.6±12.9	31.3±11.2	33.5±15.2	43.4±17.1	37.5±15	54.6±15.4	34.7±17.6	44.5±17.3	39.9±16	<0.001
M:F	1.3: 1	1.5: 1	2.6: 1	1: 3.7	1.1: 1	1.3: 1	1: 1	1.5: 1	1.5 : 1	1.6: 1	1.3: 1	<0.001
NS (%)	78.6	53.9	46.4	53.6	81.4	49.5	58.1	69.7	75.8	38.6	60.5	<0.001
SCr≥ 1.4 (%)	22.6	54.8	66.7	48.1	27.3	94.2	35.1	71.6	63.5	86.1	52.7	<0.001
HTN (%)	35.2	50.2	51	44.8	24.2	56.6	29.2	35.6	63.9	58.9	44.5	<0.001

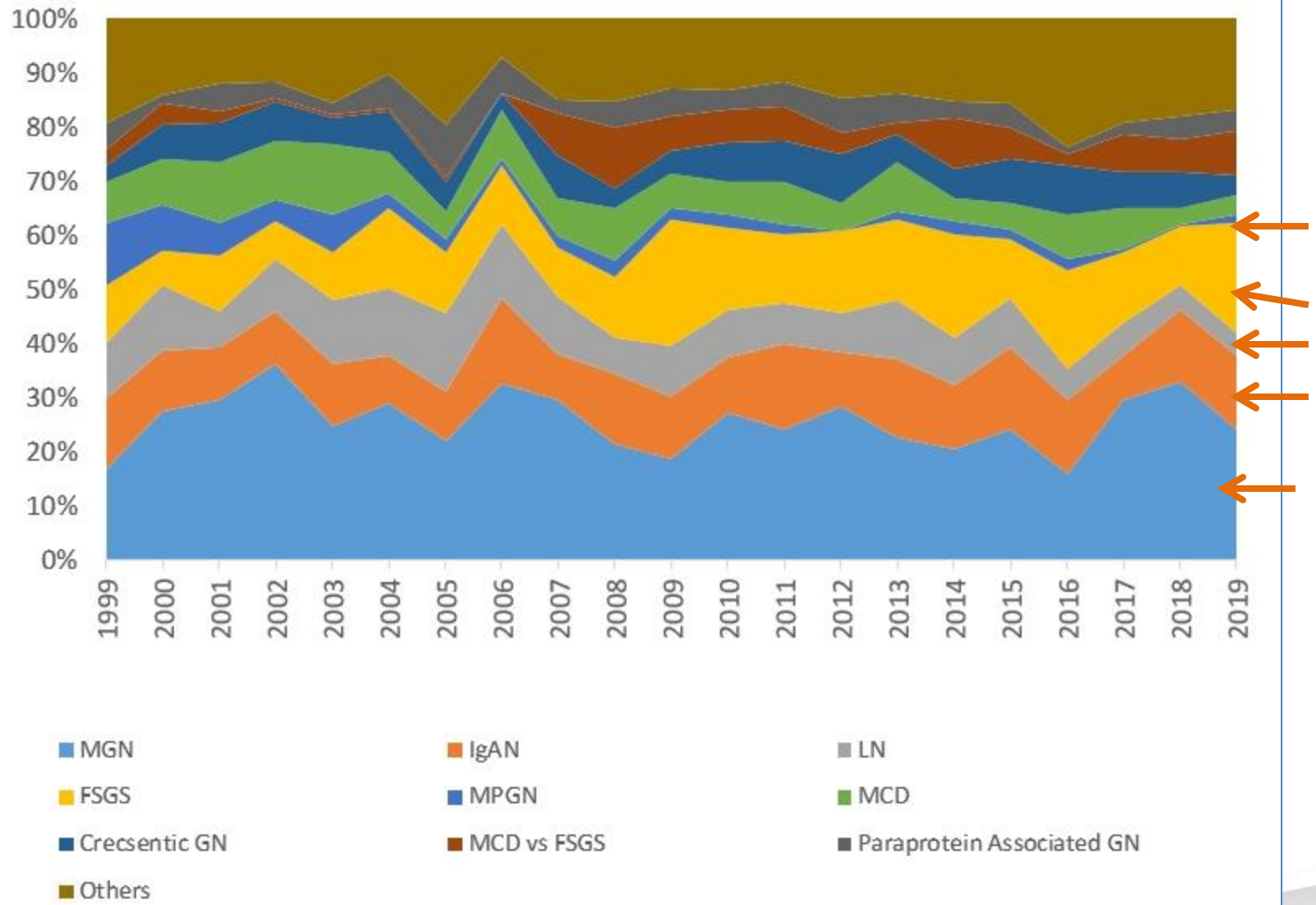
# Age Distribution of Pathologic Dx





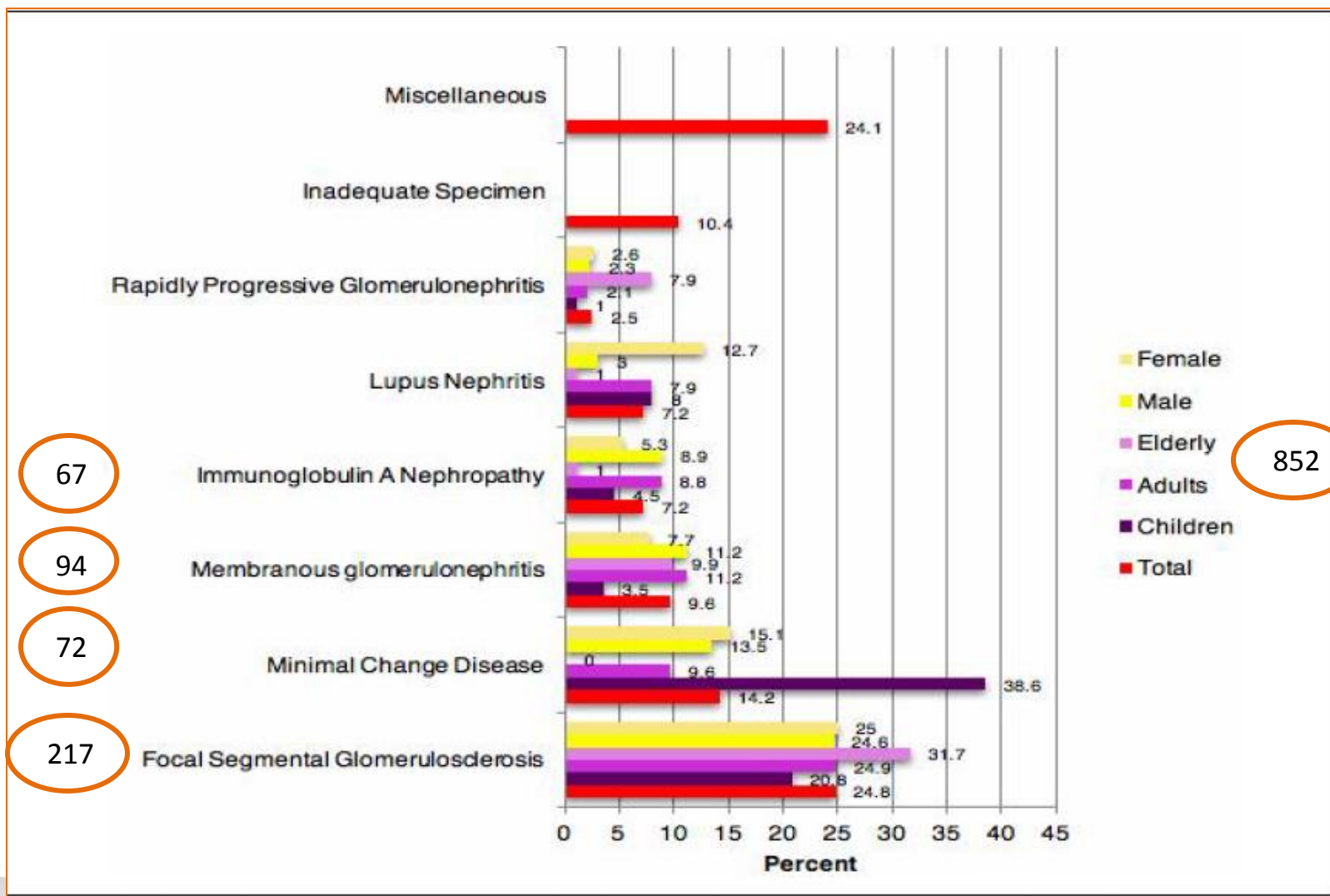


# Pathological DX over time





1054 cases (43.3% female, mean age: 33.1±18.5) yrs



67

94

72

217

852

Figure 1. The overall prevalence (%) of renal biopsy results in all patients and according to age and gender in the study patients.

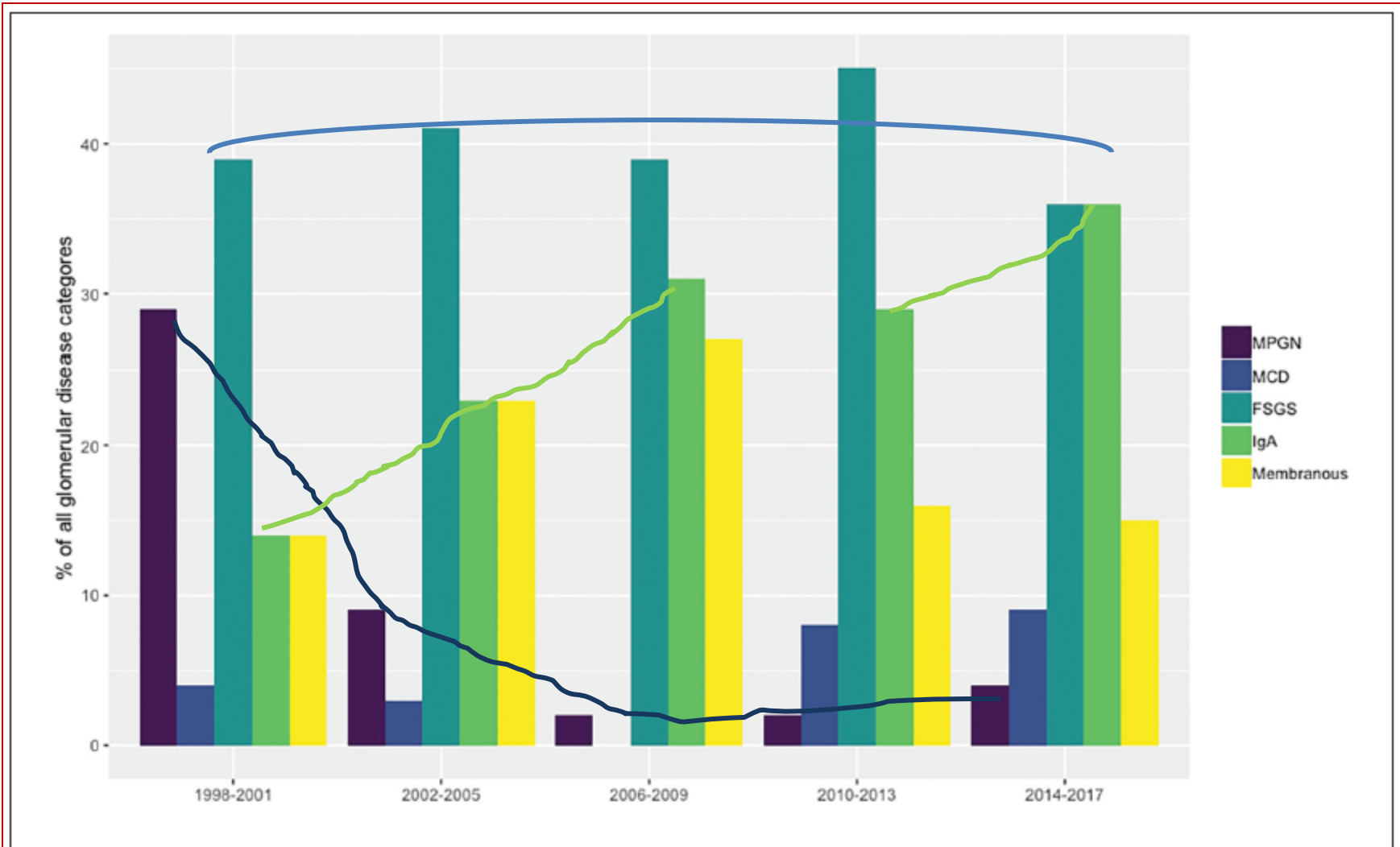
# 2012–2013 Renal Biopsy Diagnoses in Kurdistan Iraq (The annual crude biopsy rate: 7.8/100,000) (381 biopsies/4,900,000 persons)

**Table 5** Kurdistan, Iraq. Age specific and age standardized (total rate) annual incidence per 100,000 population for FSGS, MGN, SLE, and all GN for the years 2012–2013

Age (years)	FSGS	MGN	SLE	IGAN	All GN
0–4	1.4	0.1		0.1	1.8
5–14	0.8	0.1	0.2	0.2	2.0
15–24	1.2	0.5	0.6	0.2	3.2
25–34	1.6	1.2	1.0	0.4	5.7
35–44	2.8	2.6	1.6	0.5	9.5
45–54	2.3	1.9	1.1	0.5	6.9
55–64	2.0	1.5		0.6	5.9
65+	0.6	0.9	0.2	0.2	3.4
Total rate <sup>a</sup>	1.6	1.2	0.7	0.4	5.1

<sup>a</sup>The total rate is adjusted to the 2000 US standard population

# 1070 patients in Saudi Arabia, 18-65 yrs of age; 54.1% female



**Figure 2.** Temporal trends in the relative renal biopsy frequencies of primary glomerular disease subtypes, 1998-2017. Frequencies of the different subtypes shows as proportion of the primary, glomerular disease cohort. , MPGN: membranoproliferative glomerulonephritis, MCD: minimal change disease; FSGS: focal segmental glomerulosclerosis; IgAN: Immunoglobulin A nephropathy.

**Table 5.** The common secondary glomerular disease diagnoses among the 1070 adults who underwent kidney biopsy in Saudi Arabia from 1998 to 2017.

Systemic lupus erythematosus	266 (24.8 )
Diabetic nephropathy	72 (6.7 )
Acute interstitial nephritis	15 (1.4 )
Hypertensive nephrosclerosis	7 (0.6 )
ANCA-associated	15 (1.4 )
Amyloidosis	7 (0.6 )
Anti-GBM	9 (0.8 )
Alport syndrome	6 (0.5 )

Data are number (percentage). ANCA: anti-neutrophil cytoplasmic antibodies, Anti-GBM: anti-glomerular basement membrane. The frequencies of the different subtypes are shown as a proportion of the kidney biopsy cohort.

**Table 6.** Temporal trends in renal biopsy frequencies of common secondary glomerular disease subtypes.

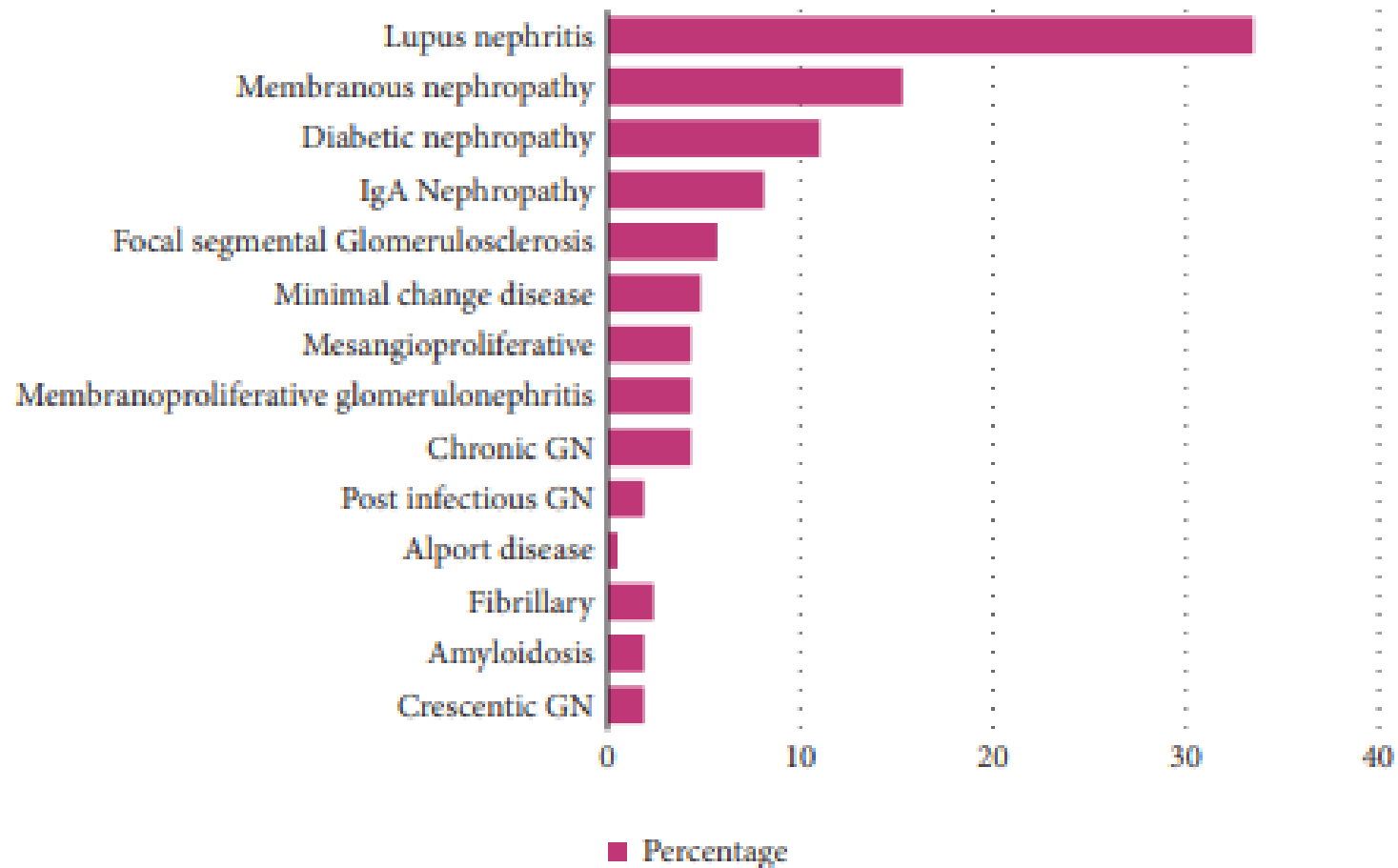
	1998-2002 n=148	2003-2007 n=96	2008-2012 n=253	2013-2017 n=572	P value for the trend <sup>a</sup>
Systemic lupus erythematosus	44 (29.7)	31 (32.2)	68 (26.9)	123 (21.4)	.03
Diabetic nephropathy	1 (1.4)	3 (3.1)	10 (3.9)	59 (10.2)	.001

# Data collected for 209 patients from 2007 to 2018 in Jordan

TABLE 1: Distribution of glomerular diseases based on incidence and patients' sex.

Diagnosis	Number (%)	Male (%)	Female (%)	P value
<b>Primary Glomerulonephritis</b>				
MGN	32 (15.3%)	20 (22.7%)	12 (9.9%)	0.018*
IgAN	17 (8.1%)	9 (10.2%)	8 (6.6%)	0.244
FSGS	12 (5.7%)	8 (9.1%)	4 (3.3%)	0.071
MCD	10 (4.8%)	6 (6.8%)	4 (3.3%)	0.198
MesPGN	9 (4.3%)	5 (5.7%)	4 (3.3%)	0.309
MPGN	9 (4.3%)	2 (2.3%)	7 (5.8%)	0.189
Chronic GN	9 (4.3%)	7 (8.0%)	2 (1.7%)	0.189
Post infectious GN	4 (1.9%)	3 (3.4%)	1 (0.8%)	0.202
Alport disease	1 (0.5%)	1 (1.1%)	0	0
CGN	4 (1.9%)	2 (2.3%)	2 (1.7%)	1
<b>Secondary Glomerulonephritis</b>				
Lupus nephritis	70 (33.5%)	10 (11.4%)	60 (49.6%)	< .001*
Diabetic nephropathy	23 (11.0%)	11 (12.5%)	12 (9.9%)	0.355
Fibrillary	5 (2.4%)	2 (2.3%)	3 (2.5%)	0.647
Renal amyloidosis	4 (1.9%)	3 (3.4%)	1 (0.8%)	0.202
<b>Total</b>	<b>209 (100%)</b>	<b>88 (42.1%)</b>	<b>121 (57.9%)</b>	

\*Statistically significant difference. FSGS: focal and segmental glomerulosclerosis; MGN: membranous glomerulonephritis; IgAN: IgA nephropathy; MPGN: membranoproliferative glomerulonephritis; CGN: crescentic glomerulonephritis; MCD: minimal change disease; MesPGN: mesangioproliferative glomerulonephritis; GN: glomerulonephritis.



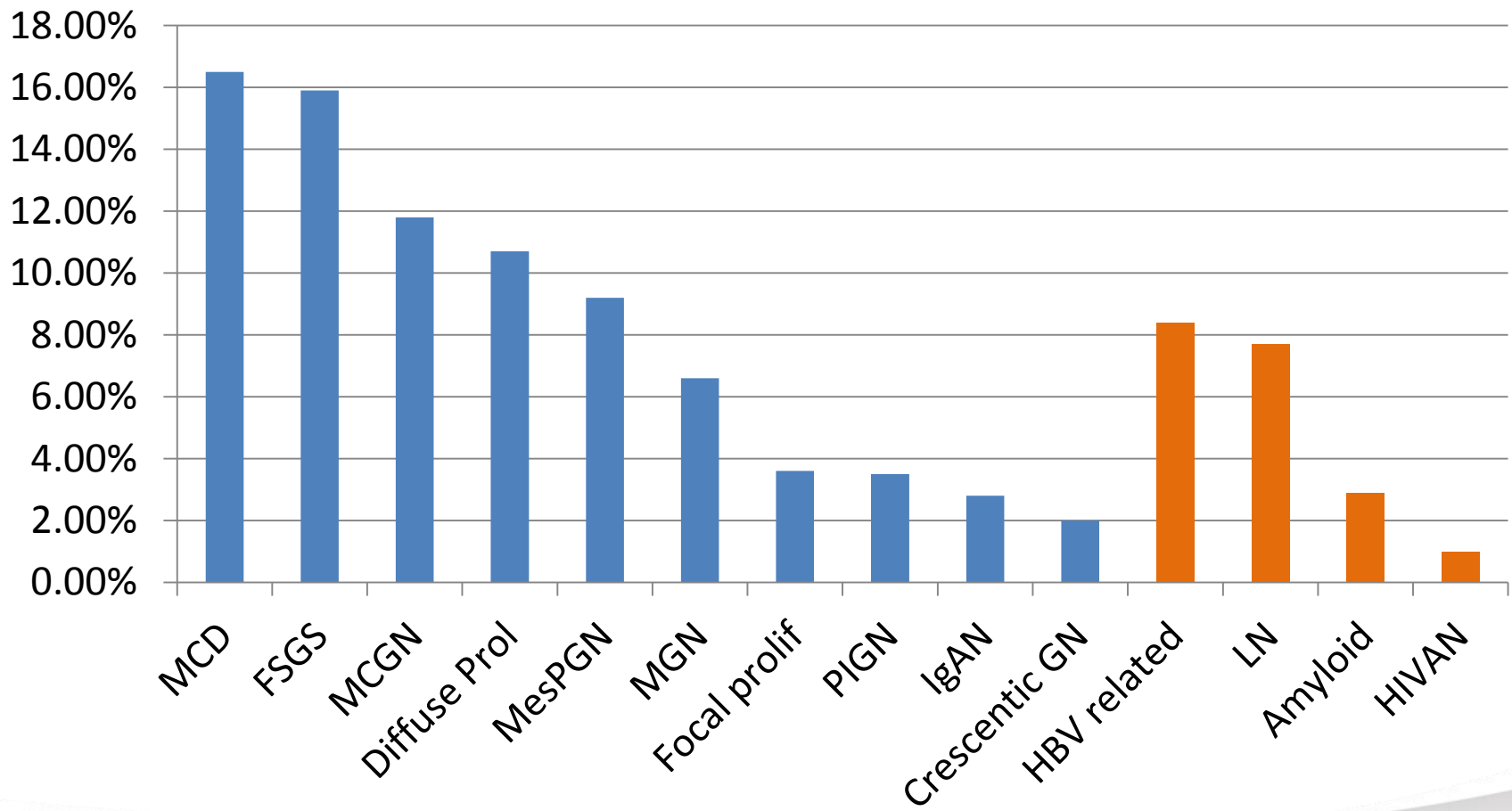
**FIGURE 1:** Incidence of different histopathological patterns of glomerulonephritis in the study population.

# Epidemiology of Histologically Proven Glomerulonephritis in Africa

- Glomerulonephritis is a leading cause of ESRD in Africa.
- 24 studies comprising 12,093 reported biopsies from 13 countries were included in this analysis (1980-2014).
- 70.0% of the data originated from North Africa and the number of performed kidney biopsies varied from 5.2 to 617 biopsies/year.

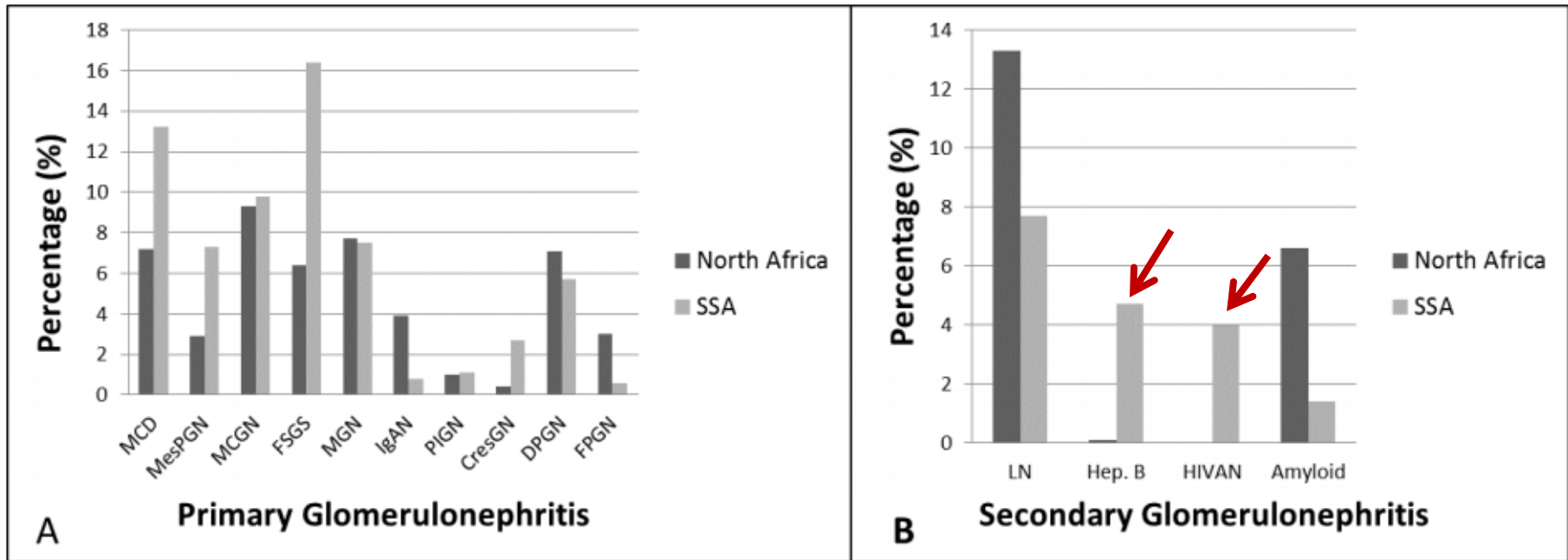


# Only 4 primary disease patterns (MCD, MCGN, FSGS and MGN) were reported from more than 20 of the 24 studies





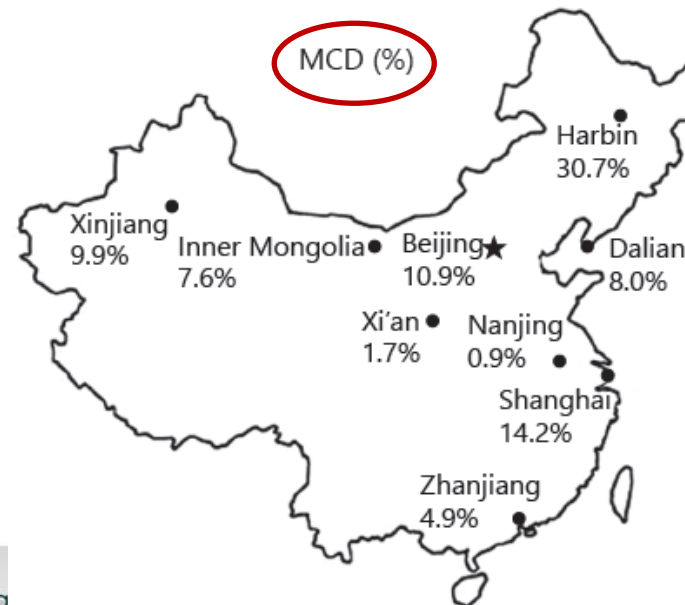
The high frequency of MCD, FSGS and MCGN may be because in 11 of the 24 studies, nephrotic syndrome was the sole indication for performing a renal biopsy.



**Fig 4. Regional differences (North Africa vs sub-Saharan Africa) in the prevalence of GNs.** This figure shows the regional differences in the prevalence of primary GNs (4A) and secondary GNs (4B) for North Africa and sub-Saharan Africa.

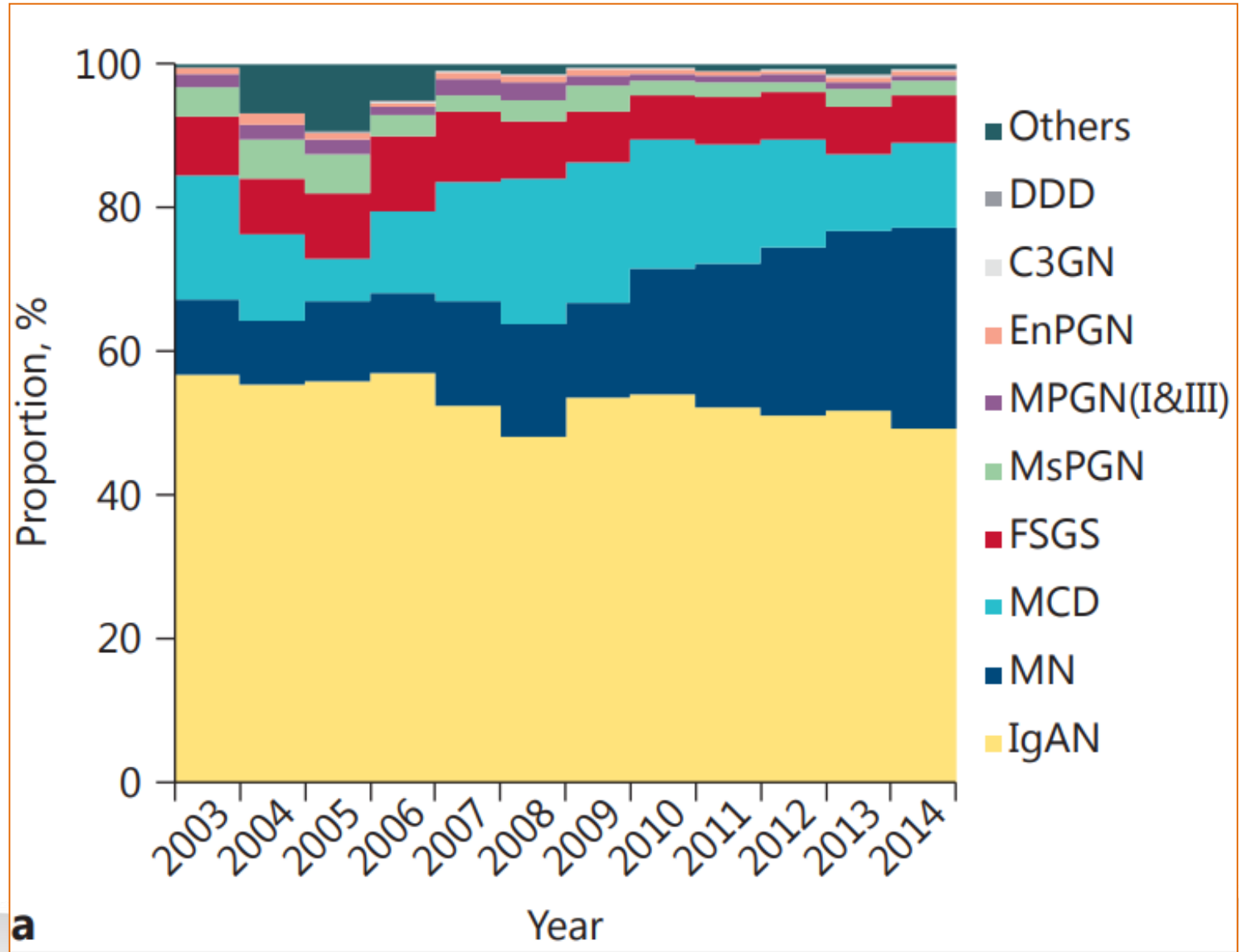
There is a lack of immunofluorescence technology in most of the studies and the absence of uniformity in describing pathologic patterns.

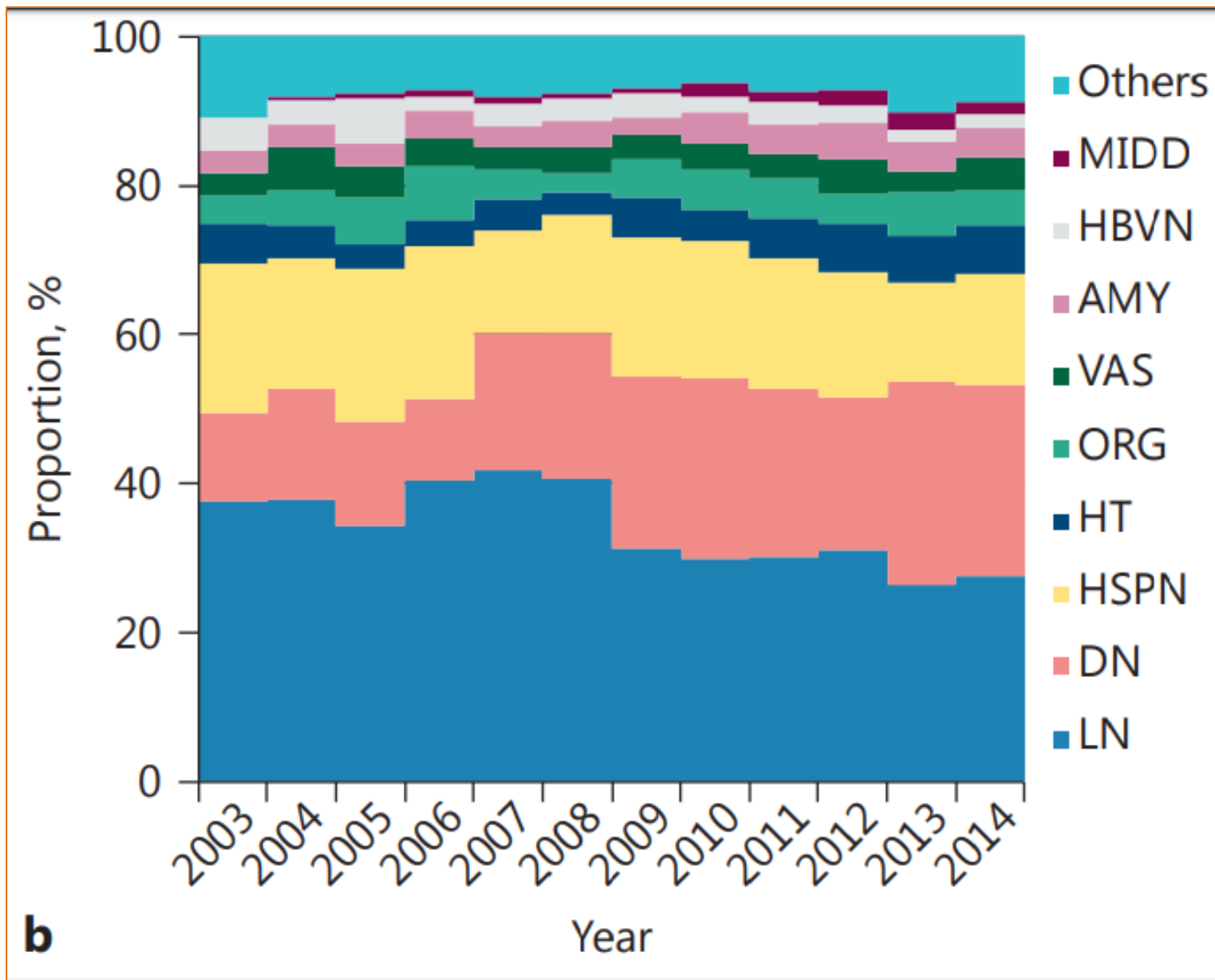
# Primary Glomerulonephritis in Mainland China



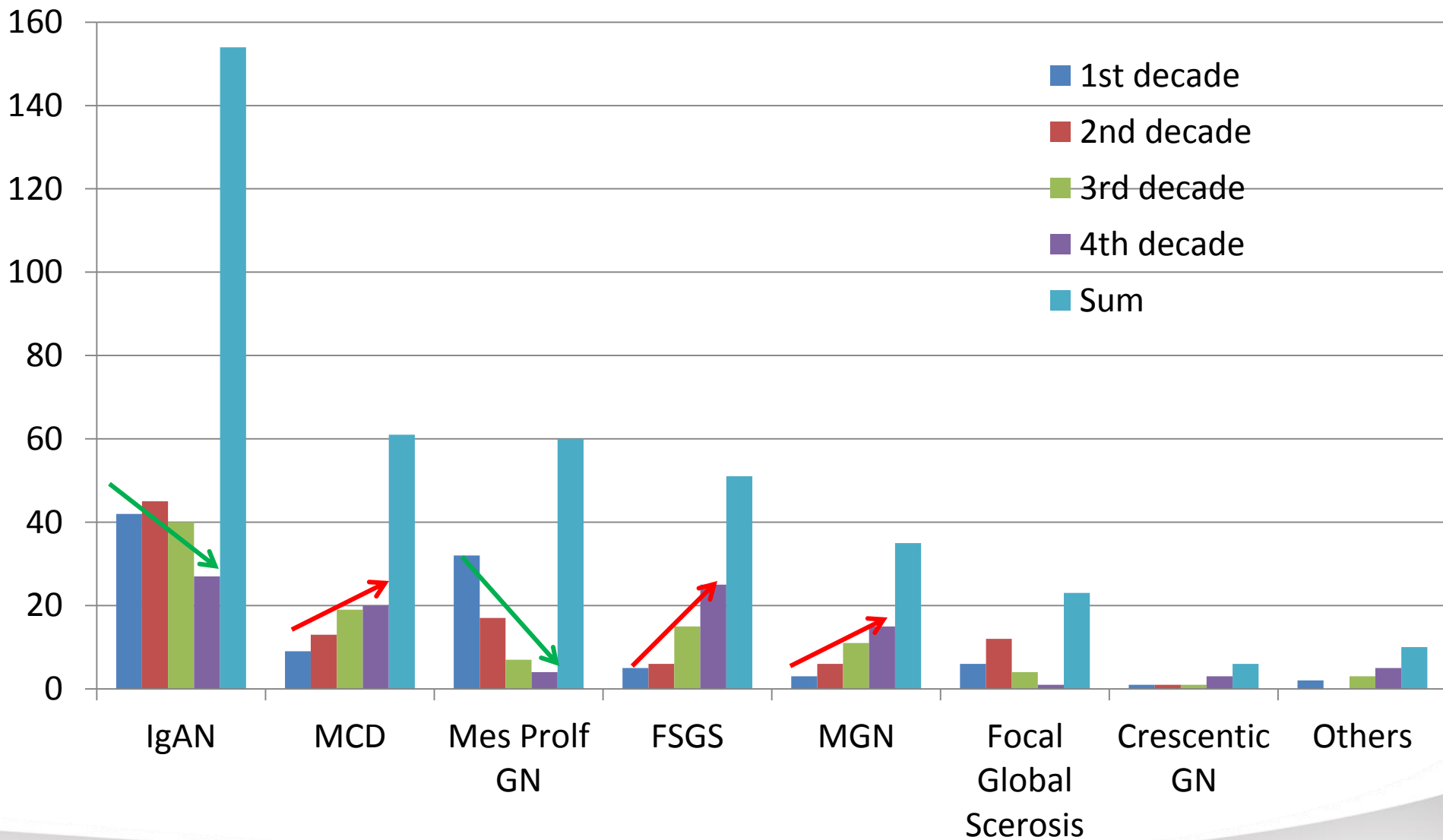
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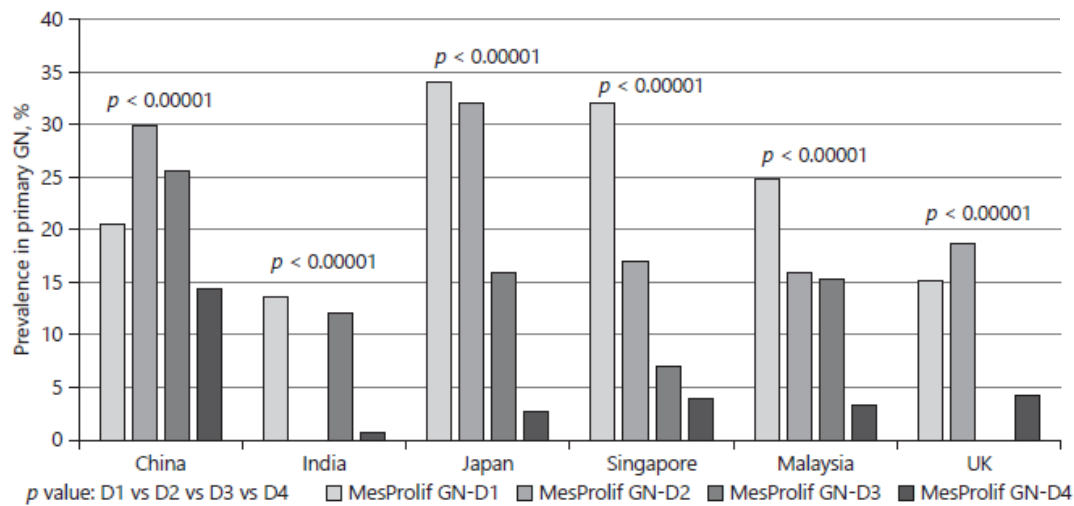
# A total of 40,759 cases of renal biopsy (916 repeat Biopsies)



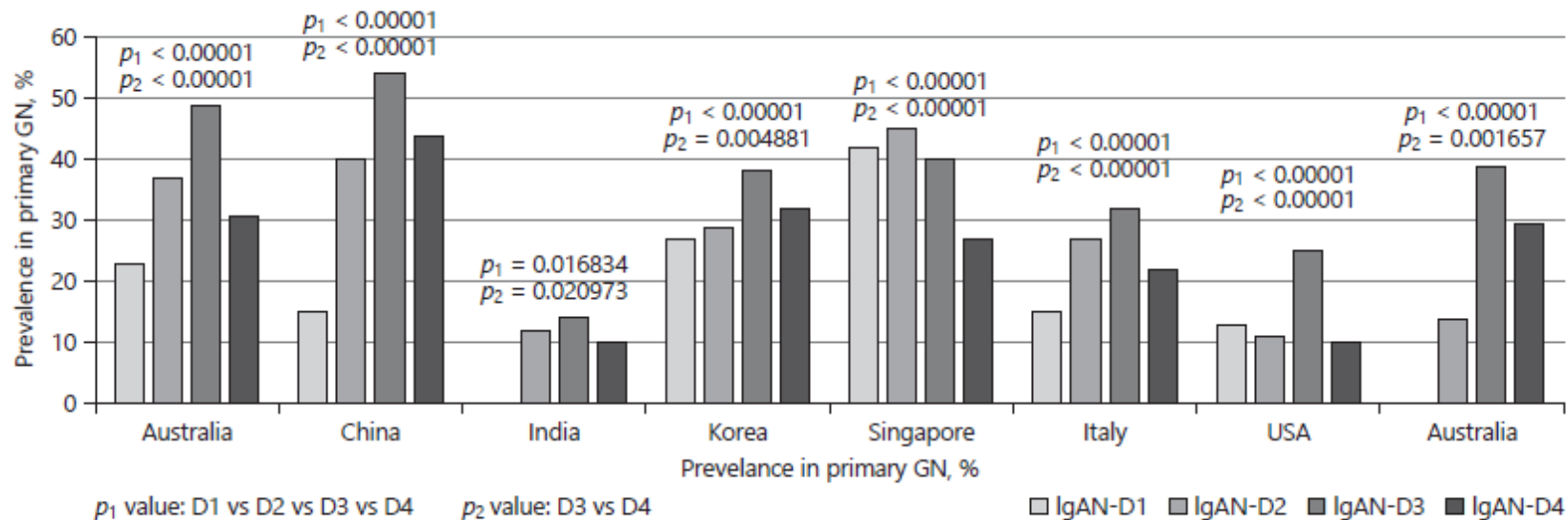


# Histologic Presentation Over 4 decades in Singapore

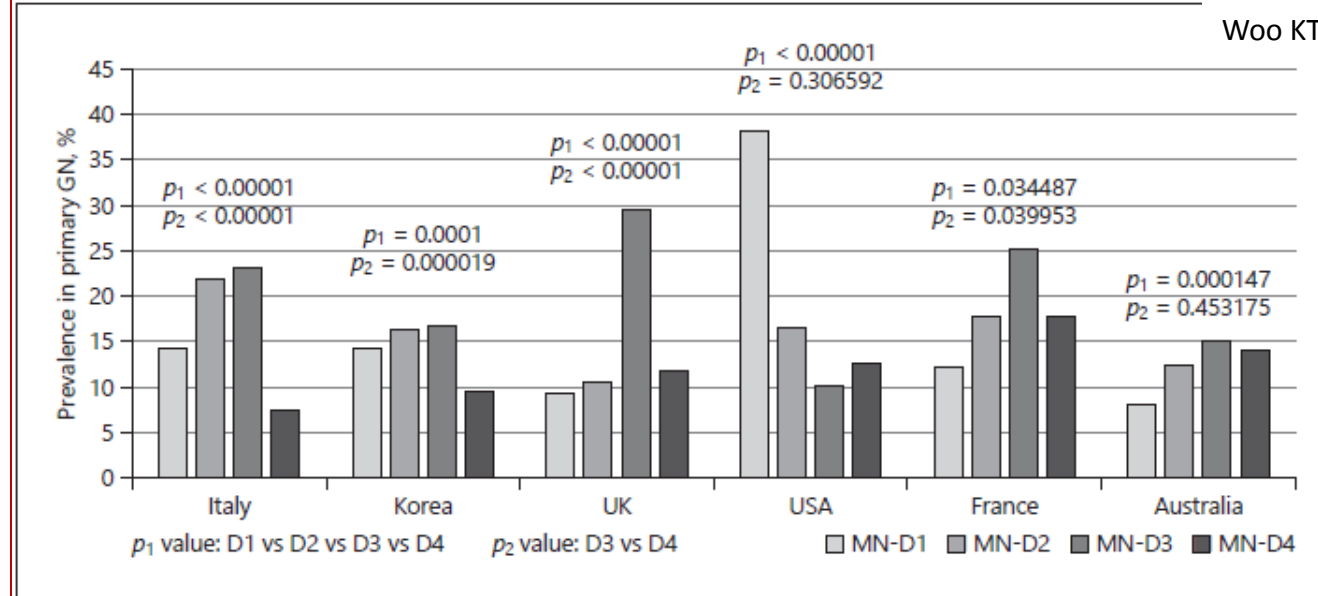




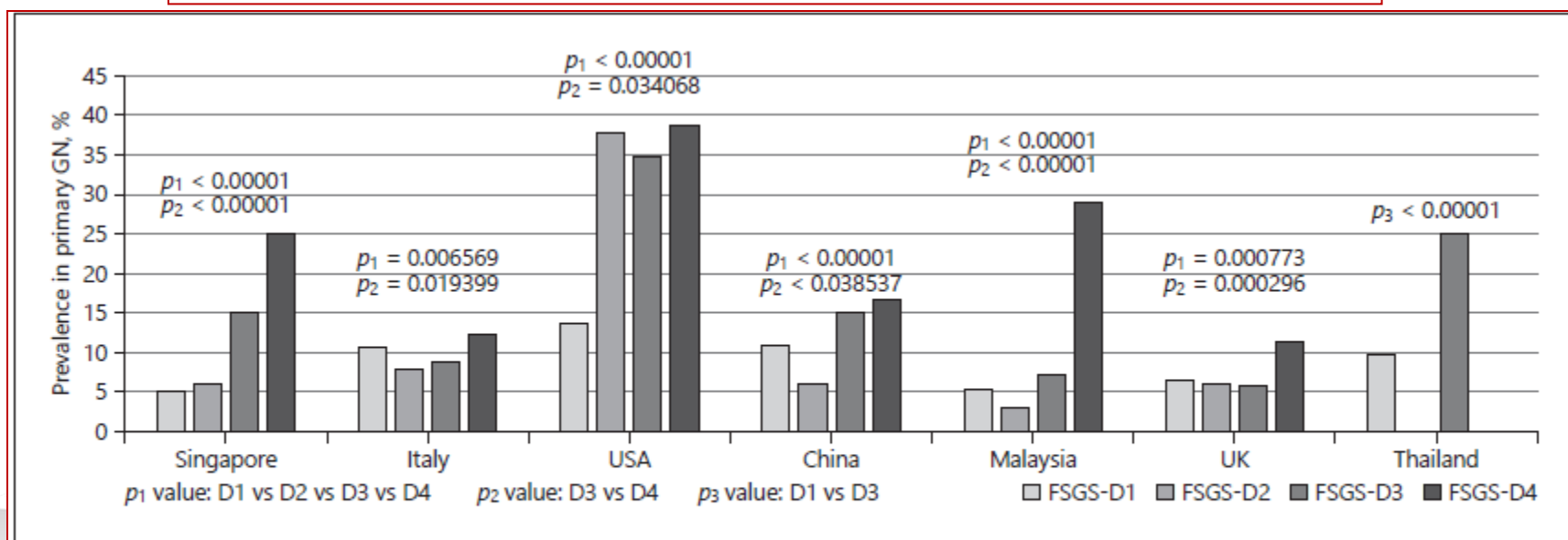
**Fig. 1.** Countries with decreasing trends for mesangial proliferative GN (Non-IgAN) over the past 4 decades. Most countries show a progressive decrease. GN, glomerulonephritis.



**Fig. 2.** Countries with decreasing trends for IgA Nx over the past 4 decades. In the first 3 decades, there was a progressive increase, but in the 4th decade, this had decreased. IgA Nx, IgA nephritis; GN, glomerulonephritis.



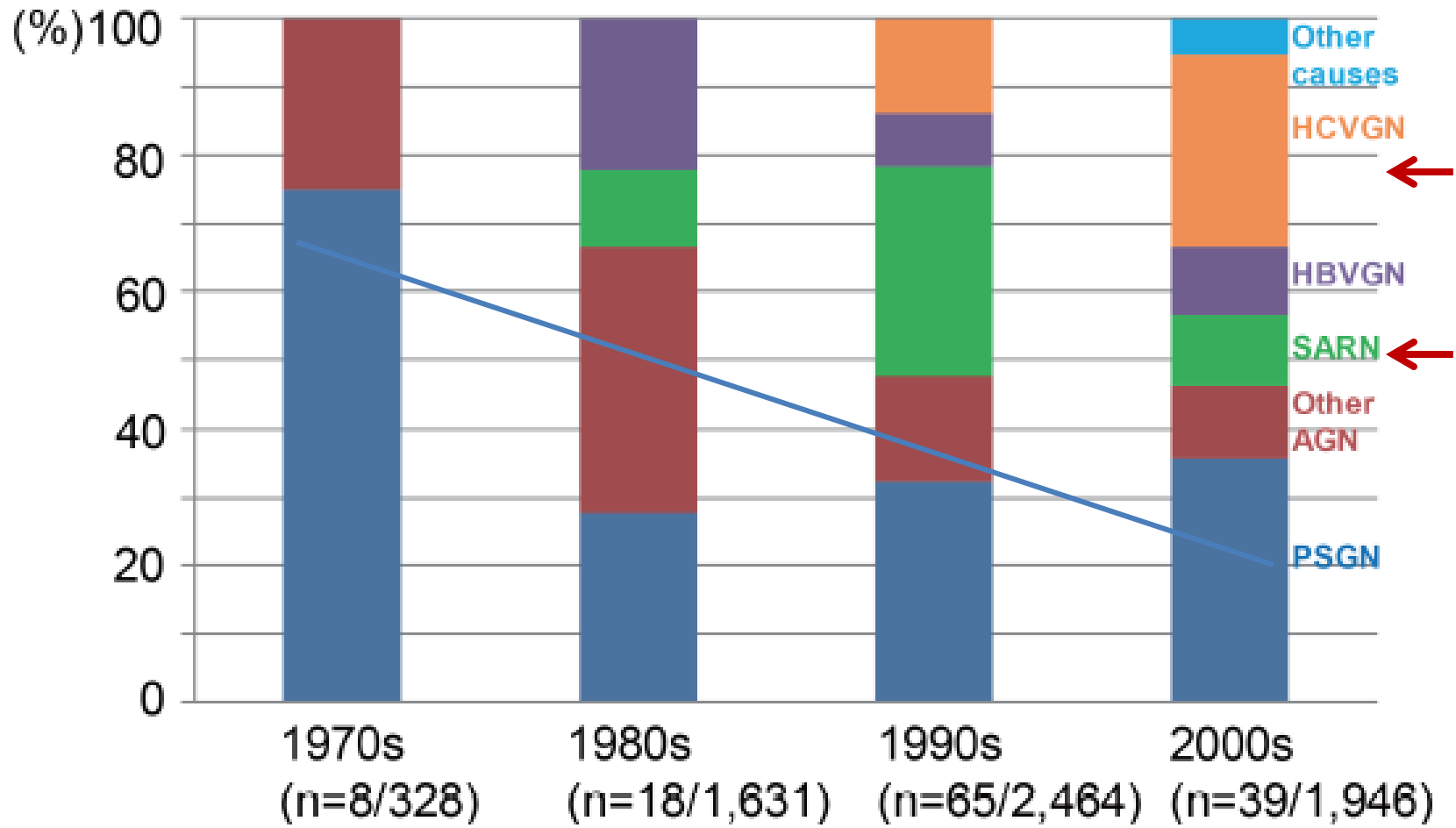
**Fig. 3.** Countries with decreasing trends for membranous nephropathy over the past 4 decades. For most countries, there was a progressive increasing trend, but in the 4<sup>th</sup> decade, this has declined. GN, glomerulonephritis.



**Fig. 4.** Countries with increasing trends for focal segmental glomerulosclerosis over the past 4 decades. There is a progressive increase in all the countries. FSGS, focal sclerosing glomerulosclerosis; GN, glomerulonephritis.



With some exceptions, the incidence of PSGN has fallen in most developed countries.





- PSGN remains much more common in regions such as Africa, the Caribbean, India, Pakistan, Malaysia, Papua New Guinea, and South America.

<https://www.medscape.com/answers/239278-168231/what-is-the-global-prevalence-of-acute-glomerulonephritis-gn>

# The Spectrum of Renal Diseases Observed in Native Renal Biopsies in a Single North Indian Tertiary Care Center

Table 4. Comparison of our study with other studies across India.

Parameters	Present study	Jaipur <sup>11</sup>	Kolkata <sup>12</sup>	Hyderabad <sup>13</sup>	Chandigarh <sup>9</sup>
Study period	2007–2016	2008–2013	2010–2012	1990–2008	2002–2007
Sample size	343	588	653	1587	364
Average age	32.4	30.3	28	32.3	31.5
Primary GN	297, 86.6%	496, 84.4%	514, 78.7%	1250, 78%	324, 89.0%
FSGS	84, 28.3%	65, 13.1%	119, 23.2%	195, 15.6%	99, 30.6%
MCD	61, 20.5%	131, 26.4%	134, 26.1%	279, 22.3%	48, 14.8%
MN	45, 15.2%	93, 18.8%	76, 14.8%	129, 10.3%	79, 24.4%
Crescentic GN	29, 9.8%	16, 3.3%	41, 8.0%	83, 6.6%	13, 4.0%
MPGN	28, 9.4%	60, 12.1%	33, 6.4%	73, 5.8%	58, 17.9%
IgAN	24, 8.1%	46, 9.3%	54, 10.5%	81, 6.5%	6, 1.8%
DPGN/PIGN	12, 4.0%	33, 6.7%	33, 6.4%	190, 15.2%	9, 2.8%
MesPGN	8, 2.7%	40, 8.1%	4, 0.8%	96, 7.7%	-
CGN	2, 0.7%	12, 2.4%	20, 3.9%	124, 9.9%	12, 3.7%
Secondary GN	46, 13.4%	92, 15.6%	139	337	40
Lupus nephritis	33, 71.7%	47, 51.1%	102, 73.4%	270, 80.1%	25, 62.5%

GN: Glomerulonephritis, FSGS: Focal segmental glomerulosclerosis, MCD: Minimal change disease, MN: Membranous nephropathy, MPGN: Membranoproliferative GN, IgAN: IgA nephropathy, DPGN: Diffuse proliferative GN, PIGN: Postinfectious GN, MesPGN: Mesangioproliferative GN, CGN: Chronic GN.

# Schistozoma Glomerulopathies

- Schistozoma Glomerulopathies have been mainly reported in Africa, Latin America and China.
- Brazil, Puerto Rico, Tanzani, Egypt, Sudan, Somalia, Nigeria, Madagascar, Arabia, Malaysia and others.

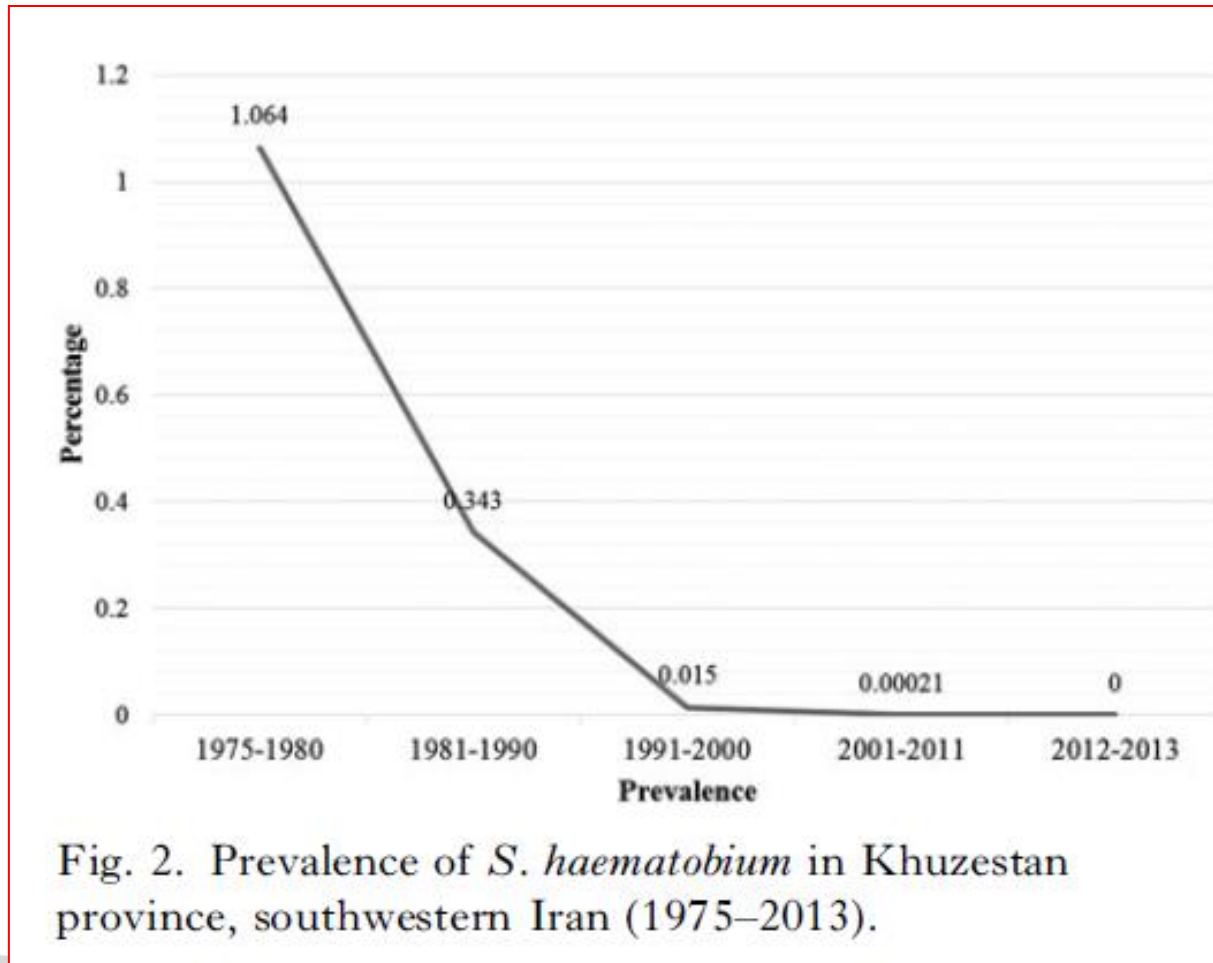
Several patterns of glomerular pathology have been described with schistosomiasis, (mesangioproliferative, exudative, MPGN, sclerosing and amyloid). Transformation in between these types has been reported in several studies. These patterns may reflect certain geographical factors and some pathogenetic differences.

**Table 1.** Principal clinicopathological features of schistosomal glomerulopathy

Class	Histopathological pattern	Glomerular deposits detected by immunofluorescence	Commonly associated infections	Hepatic fibrosis	Features of renal involvement				Response to treatment
					Asymp-tomatic proteinuria	Nephrotic syndrome	Hyper-tension	Progression to ESRD	
I	Mesangioproliferative a) "Minimal lesion" b) Focal c) Diffuse	Mesangial: IgM, C <sub>3</sub> , Schistosomal gut antigens	-	±	+++	+	±	?	± (?)
II	Exudative	Endocapillary: C <sub>3</sub> , Salmonella antigens	Salmonellosis	+	-	+++	-	?	+++
III	A. Mesangiocapillary (type I)	Mesangial: IgG, C <sub>3</sub> , Schistosomal gut antigens (early), IgA (late)	-	+++	+	++	++	++	-
	B. Mesangiocapillary (type III)	Mesangial & subepithelial: IgG, C <sub>3</sub> , Schistosomal gut antigens (early), IgA (late)	Hepatitis B	+++	+	+++	+	++	-
IV	Focal & segmental glomerulosclerosis	Mesangial: IgG, IgM, IgA	-	+++	+	+++	+++	+++	-
V	Amyloidosis	Mesangial: IgG	?Salmonellosis ?E.coli UTI	±	+	+++	±	+++	-

# Elimination of urogenital schistosomiasis in Iran: past history and the current situation.

## Khuzestan province



- Actions:
  - Selective population chemotherapy,
  - snail control,
  - population education,
  - environmental improvement,
- Iran can be a successful model for countries suffering from this disease. (78 developing countries with 800.000.000 inhabitants and 240.000.000 persons are infected in rural and semiurban regions).

# *Factors Influencing the Pattern of GN*

- In the past 20–30 years, the spectrum of primary GN has changed substantially.
- With improved living standards, better public health care and the early and effective antibiotic treatment of pharyngeal infections, the prevalence of PSGN has declined sharply in most countries.

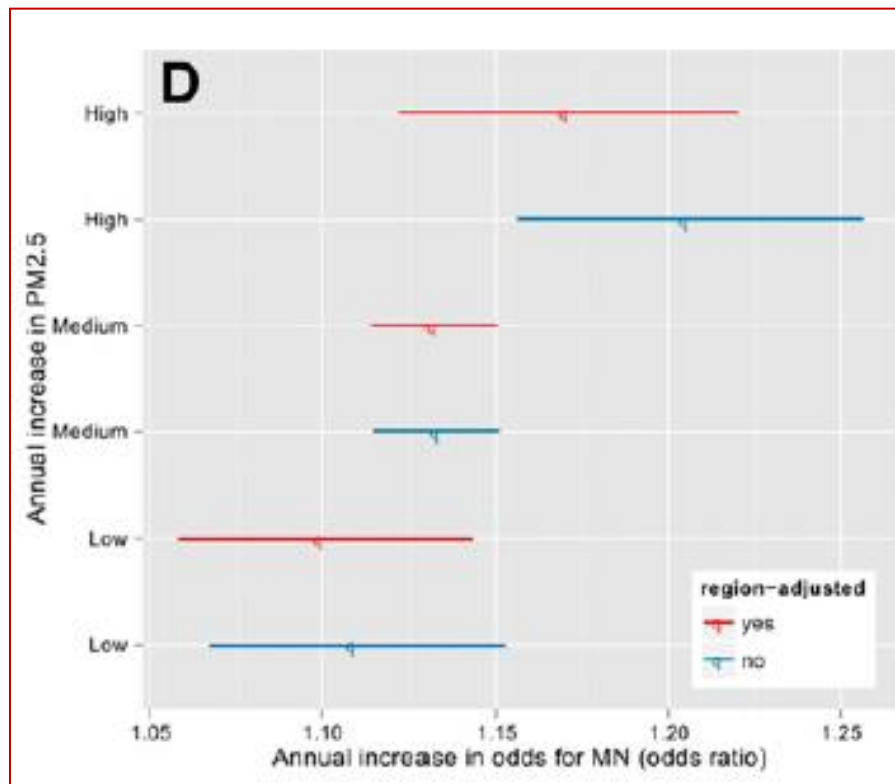
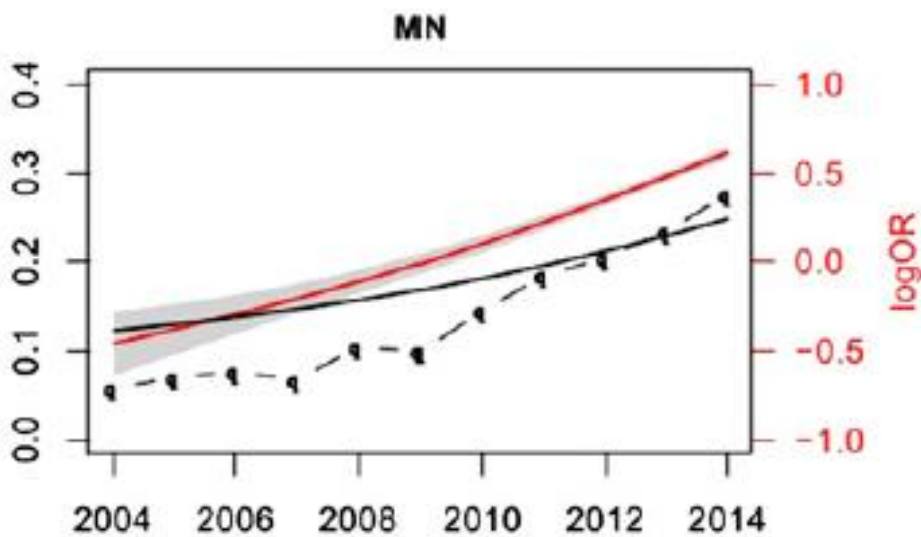


- The infective pathogenesis involved larger immune complexes with deposition in the mesangium giving rise to mesangial proliferative GN and MPGN.
- MGN represents infective pathogenesis with smaller immune complexes deposition in the GBM maybe be from viral or pollution origin (industrial allergens, heavy metals and organic solvents).



The profile of and temporal change in glomerular diseases was estimated in an 11-year renal biopsy series including 71,151 native biopsies at 938 hospitals spanning 282 cities in China from 2004 to 2014, and the association of long-term exposure to fine particulate matter of 2.5 mm (PM2.5) with glomerulopathy was examined.

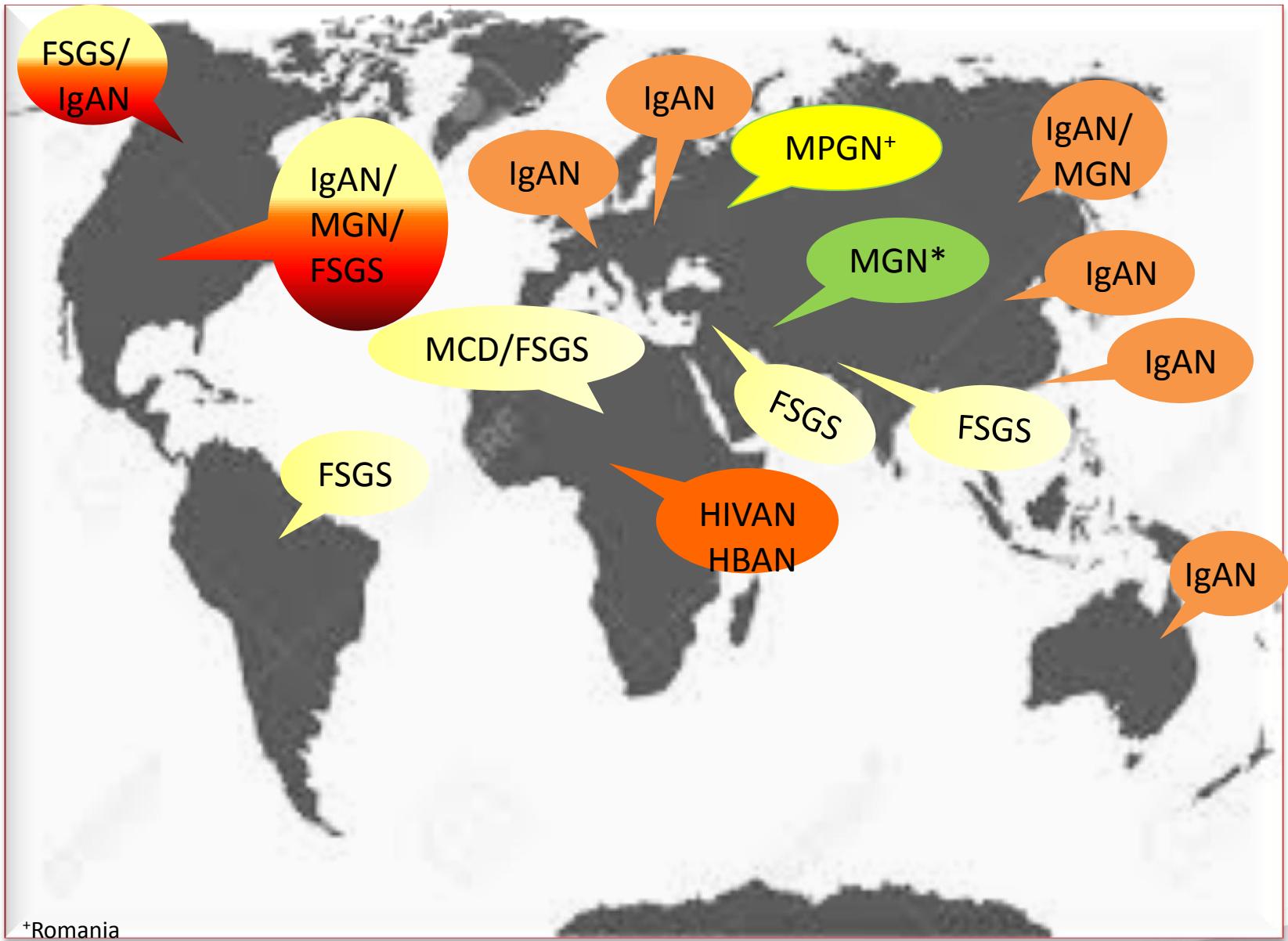
The risk for MN increased 13% annually



- In a regression analysis with adjustments for the confounders, including age and clinical characteristics:
  - Each increase of  $10 \mu\text{g}/\text{m}^3$  was associated with 14% higher odds for MGN (OR, 1.14; 95% CI, 1.10 to 1.18) in regions with  $\text{PM}_{2.5}$  concentrations above  $70 \mu\text{g}/\text{m}$ .
- Projected from this trend, MN would soon pass IgAN to become the leading type of nephropathy in China.

- IgA nephritis is on the decline in many countries, though it still remains the commonest GN overall the world.
- MGN that used to be more frequently present in western countries has also declined though it continues to be on the top of the list in a large series in Iran and has rising trend in Singapore and China.
- Worldwide, the frequency of FSGS continues to increase in many countries.

- Many of the developed countries have gone past the phase of increasing membranous GN and together with the decline in IgAN and membranous GN, they are now faced with the dilemma of ever increasing FSGS, which may a disease reflecting the changing era of the digital age.



+Romania

\*Iran and Macedonia





Thanks for your attention