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Natural History of Idiopathic Nephrotic Syndrome: The UK National RaDaR Idiopathic Nephrotic Syndrome Cohort

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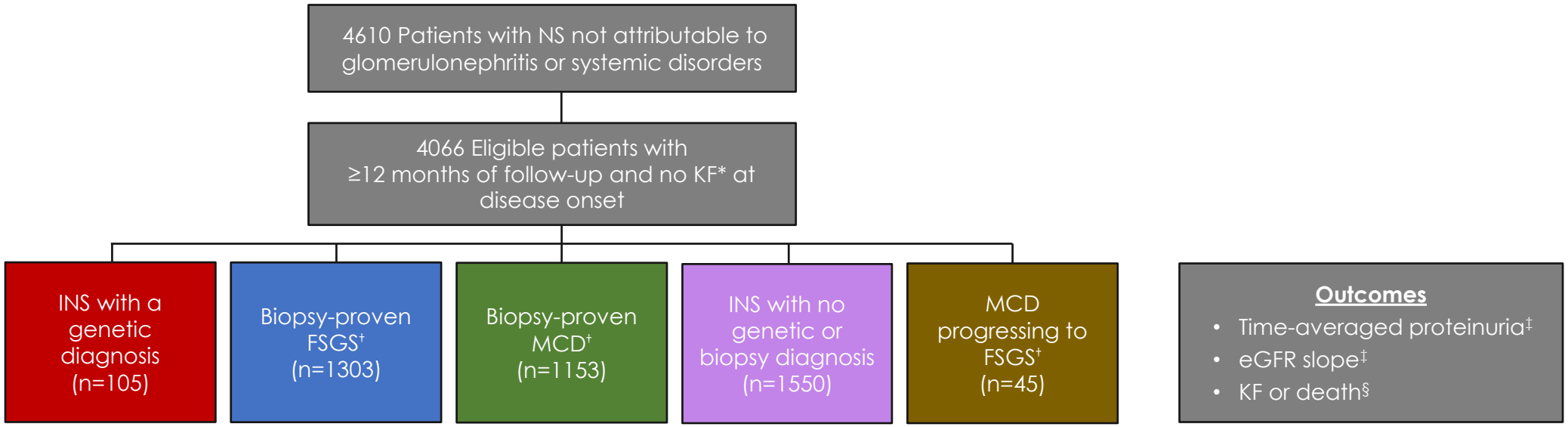
Introduction and Methods

- Idiopathic nephrotic syndrome (INS) is an important class of proteinuric kidney disease leading to kidney failure (KF)
- Here we describe the natural history of INS, including genetic nephrotic syndrome, using the UK National Registry of Rare Kidney Disease (RaDaR) INS Cohort



eGFR, estimated glomerular filtration rate; FSGS, focal segmental glomerulosclerosis; MCD, minimal change disease; NS, nephrotic syndrome.

*KF was defined as stage 5 chronic kidney disease or on renal replacement therapy at or prior to disease onset. † Patients with a biopsy-proven MCD and subsequent biopsy-proven FSGS diagnosis are counted in the biopsy-proven MCD, biopsy-proven FSGS, and MCD progressing to FSGS categories. ‡ Calculated over the full duration of follow-up or until KF. §Calculated from disease onset to KF or death and censored at last follow-up.

Characteristics at Disease Onset

- In total, 4066 patients (including 1599 children [39%]) were included, with a median age at disease onset* of 28 years

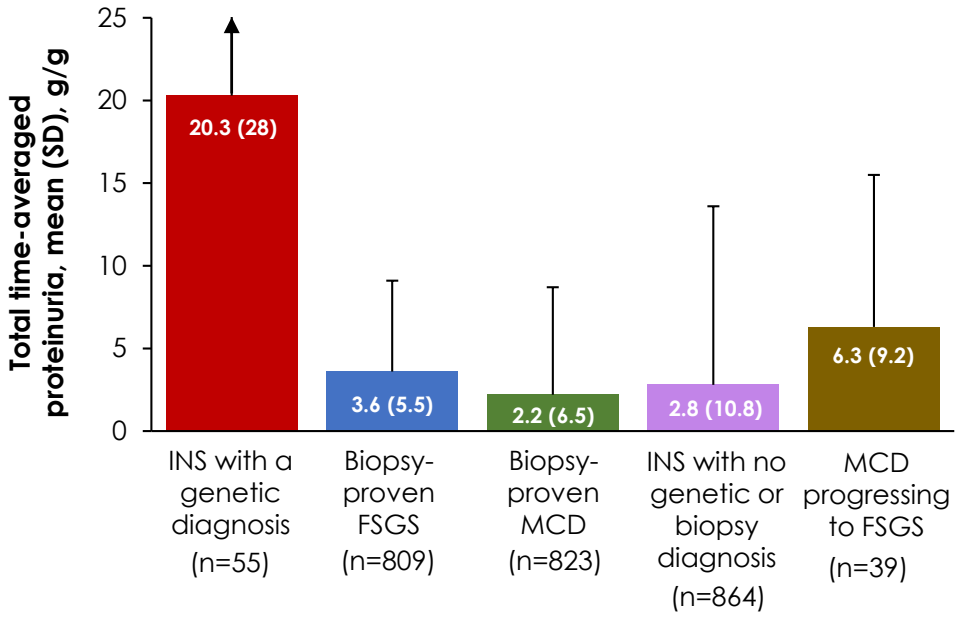
Characteristic	INS with a genetic diagnosis (n=105)	Biopsy-proven FSGS (n=1303)	Biopsy-proven MCD (n=1153)	INS with no genetic or biopsy diagnosis (n=1550)	MCD progressing to FSGS (n=45)
Age at disease onset					
Median (Q1, Q3), years	0.4 (0.1, 7.5)	35.5 (15.3, 53.4)	34.6 (13.3, 54.6)	13.6 (3.8, 45.9)	20.3 (4.9, 37.9)
<18 years at disease onset, n (%)	86 (82)	356 (27)	342 (30)	836 (54)	21 (47)
Female sex, n (%)	53 (50)	552 (42)	519 (45)	639 (41)	19 (42)
Race, n (%)					
Asian	26 (25)	142 (11)	158 (14)	192 (12)	6 (13)
White	59 (56)	920 (71)	812 (70)	888 (57)	14 (74)
Other/missing/not stated	20 (19)	241 (18)	183 (16)	470 (30)	7 (16)
UPCR at disease onset, n†	26	336	323	254	16
Median (Q1, Q3), g/g	28.5 (6.6, 37.8)	5.7 (2.9, 9.5)	6.6 (3.4, 10.3)	6.9 (3.1, 12.7)	5.0 (1.9, 10.5)
Serum albumin at disease onset, n†	52	529	485	478	20
Median (Q1, Q3), g/L	15 (10, 27)	26 (19, 34)	21 (15, 29)	26 (17, 38)	21 (17, 29)
eGFR at disease onset, n†	32	439	375	317	17
Mean (SD), mL/min/1.73 m^2	96 (62)	71 (41)	84 (38)	84 (45)	77 (32)
Length of follow-up					
Median (Q1, Q3), years	4.1 (2.1, 8.6)	7.4 (2.7, 13.1)	9.1 (5.4, 14.6)	8.3 (5.0, 12.6)	9.7 (3.8, 16.7)

eGFR, estimated glomerular filtration rate; FSGS, focal segmental glomerulosclerosis; INS, idiopathic nephrotic syndrome; MCD, minimal change disease; SD, standard deviation; UPCR, urine protein-to-creatinine ratio.

* Disease onset date was defined as the first database occurrence of kidney biopsy, primary diagnosis, or UPCR of ≥1.5 g/g. † Number of patients with available data.

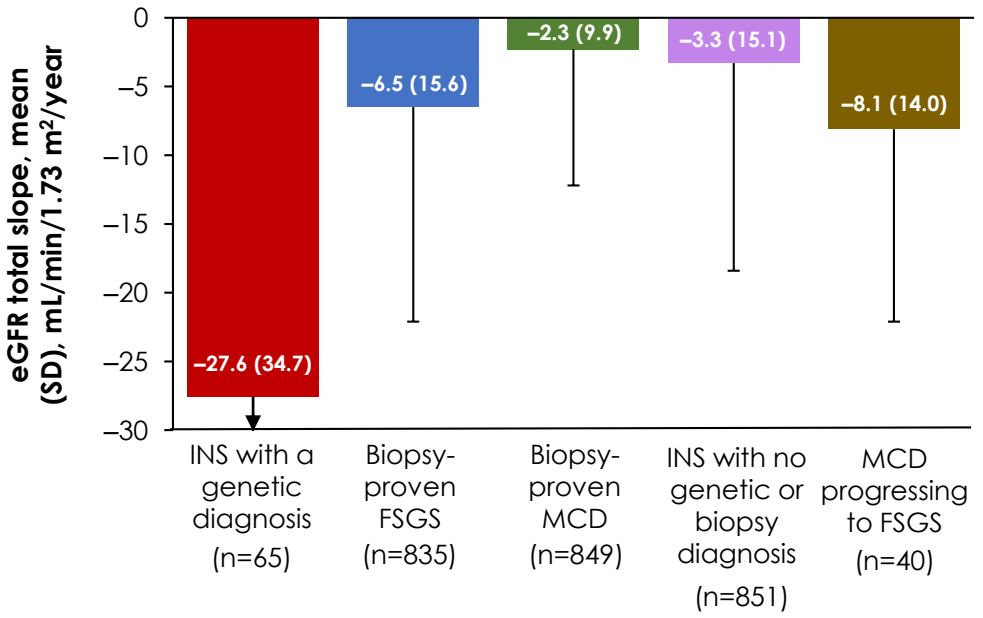
Proteinuria and Annual Rate of eGFR Loss

Time-Averaged Proteinuria (All Ages)



Mean time-averaged proteinuria was greater in children than adults (5.0 vs 1.9 g/g)

Annual Rate of eGFR Loss (All Ages)

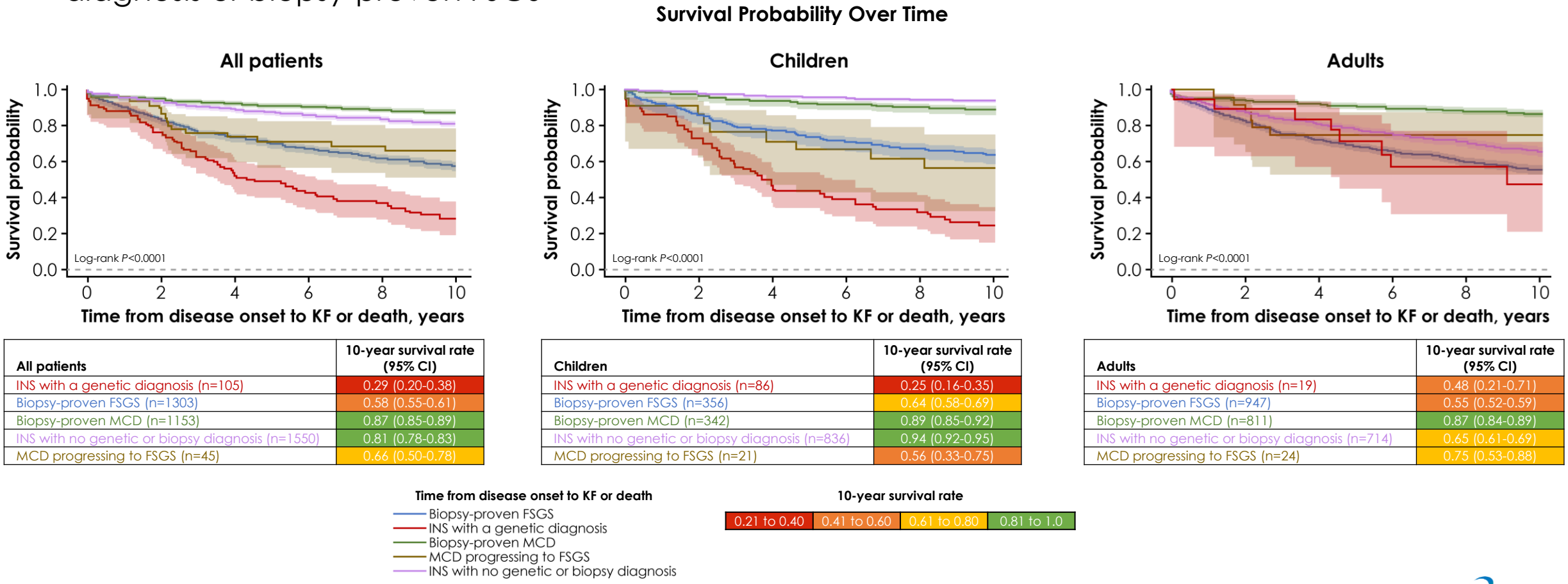


The annual rate of eGFR loss was greater in children than adults (–7.4 vs – 3.1 mL/min/1.73 m^2/year) and varied by underlying cause or histological pattern

eGFR, estimated glomerular filtration rate; FSGS, focal segmental glomerulosclerosis; INS, idiopathic nephrotic syndrome; MCD, minimal change disease; SD, standard deviation.

Time to Kidney Failure or Death

- Over a median follow-up duration of 8.2 years, KF or death occurred in 30% of patients
- Survival probability was generally poor for patients with INS, particularly those with a genetic diagnosis or biopsy-proven FSGS



All patients	10-year survival rate (95% CI)
INS with a genetic diagnosis (n=105)	0.29 (0.20-0.38)
Biopsy-proven FSGS (n=1303)	0.58 (0.55-0.61)
Biopsy-proven MCD (n=1153)	0.87 (0.85-0.89)
INS with no genetic or biopsy diagnosis (n=1550)	0.81 (0.78-0.83)
MCD progressing to FSGS (n=45)	0.66 (0.50-0.78)

Children	10-year survival rate (95% CI)
INS with a genetic diagnosis (n=86)	0.25 (0.16-0.35)
Biopsy-proven FSGS (n=356)	0.64 (0.58-0.69)
Biopsy-proven MCD (n=342)	0.89 (0.85-0.92)
INS with no genetic or biopsy diagnosis (n=836)	0.94 (0.92-0.95)
MCD progressing to FSGS (n=21)	0.56 (0.33-0.75)

Adults	10-year survival rate (95% CI)
INS with a genetic diagnosis (n=19)	0.48 (0.21-0.71)
Biopsy-proven FSGS (n=947)	0.55 (0.52-0.59)
Biopsy-proven MCD (n=811)	0.87 (0.84-0.89)
INS with no genetic or biopsy diagnosis (n=714)	0.65 (0.61-0.69)
MCD progressing to FSGS (n=24)	0.75 (0.53-0.88)

CI, confidence interval; FSGS, focal segmental glomerulosclerosis; INS, idiopathic nephrotic syndrome; KF, kidney failure; MCD, minimal change disease.

Conclusion

- In a large cohort of patients with INS, 10-year kidney survival/death rates ranged from 29% for genetic INS to 58% for biopsy-proven FSGS and 87% for MCD
- The disease burden in these populations highlight an unmet need for effective treatments for patients with nephrotic syndrome and FSGS

Acknowledgments

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Disclosure

DP has nothing to disclose.

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FSGS, focal segmental glomerulosclerosis; INS, idiopathic nephrotic syndrome; MCD, minimal change disease.