THAOS®
Transthyretin Amyloidosis Outcomes Survey

THAOS data updates: renal function

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Renal Disease and TTR Amyloidosis

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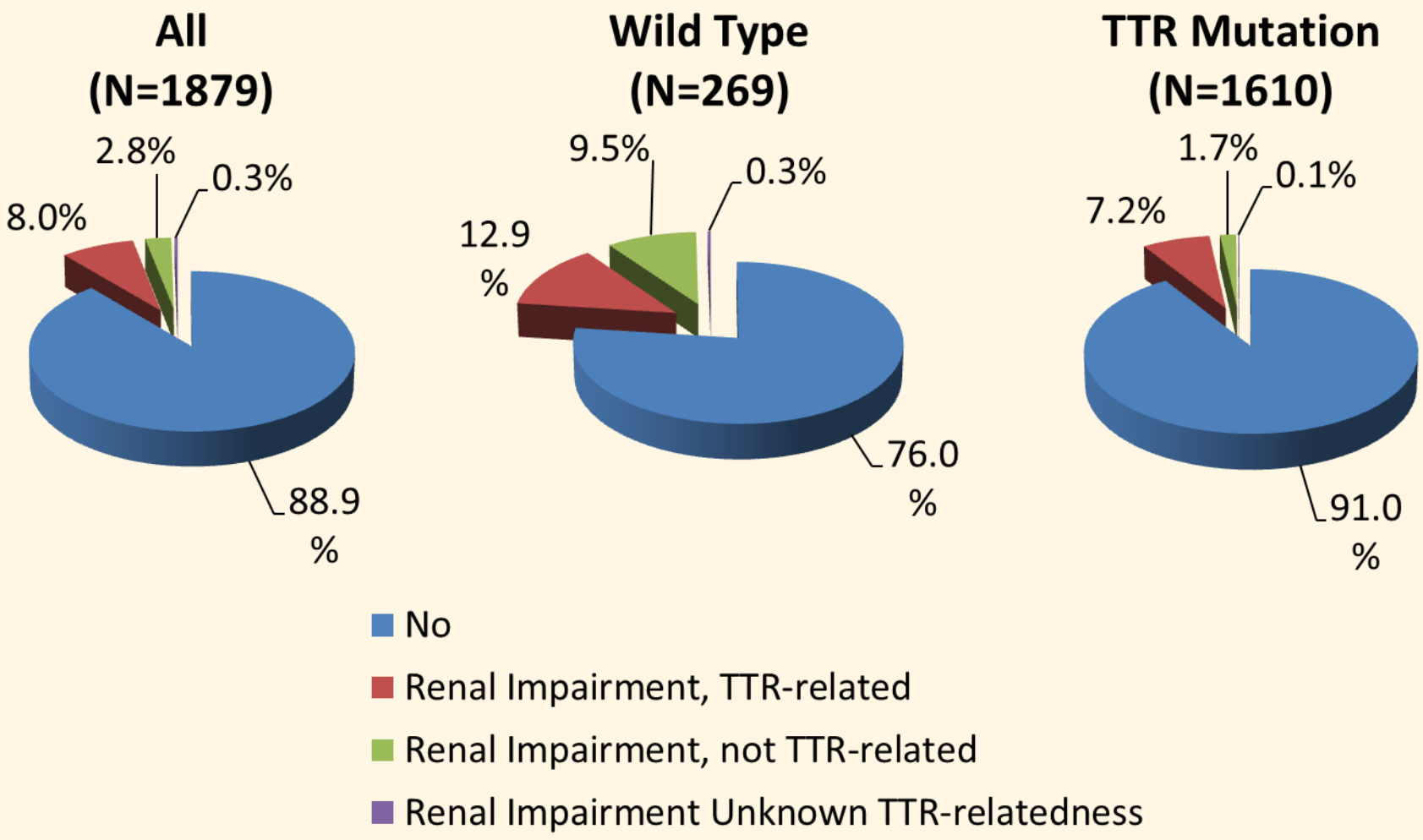
Background

- Little is known about renal disease progression and its interaction with heart disease in TTR amyloidosis
- Small observational studies in TTR:
  - Incidence of renal disease: 13-50% of these patients.
  - First manifestation of renal dysfunction is microalbuminuria
    - Patients with microalbuminuria developed nephropathy within 2 years
    - Among patients with proteinuria 18.8% progressed to ESRD within 5 years
    - In a Portuguese cohort of 403 patients, approximately 1/3 had proteinuria, with 10% progressing to ESRD
  - Mean survival of ATTR (V30M) patients who developed ESRD: 21 months
  - Even though most patients with ATTR have histopathology positive for amyloid not all patients develop renal disease
- We aim to determine the relationship between cardiac ATTR and renal disease progression

Renal Status at Enrollment

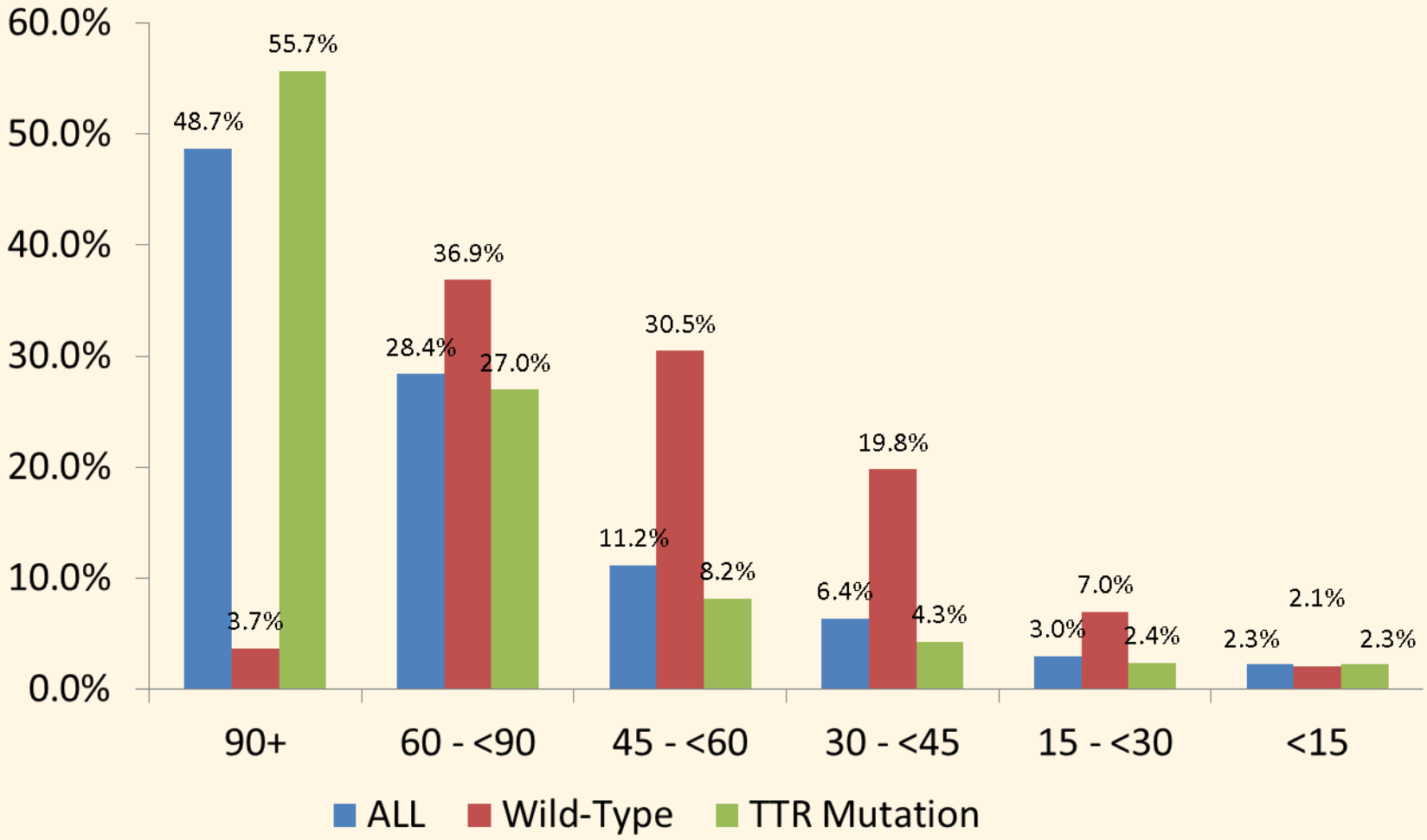


Estimated GFR at Enrollment

Wild Type vs. TTR Mutation

Estimated GFR (mL/min per 1.73m^2)	ALL (N=1389)	Wild-Type (N=187)	TTR Mutation (N=1202)
Availability of data	73.9%	69.5%	74.7%
Mean ± SD	93.39 ± 113.61	55.45 ± 20.92	99.30 ± 120.79
Median	88.50	54.00	95.60
25, 75 Percentile	62.00, 115.70	42.40, 66.30	70.90, 119.40
Mean age at enrollment	52.40±17.42	75.13±6.96	48.87±15
Male, N (%)	864 (60.0%)	185 (94.9%)	679 (54.5%)

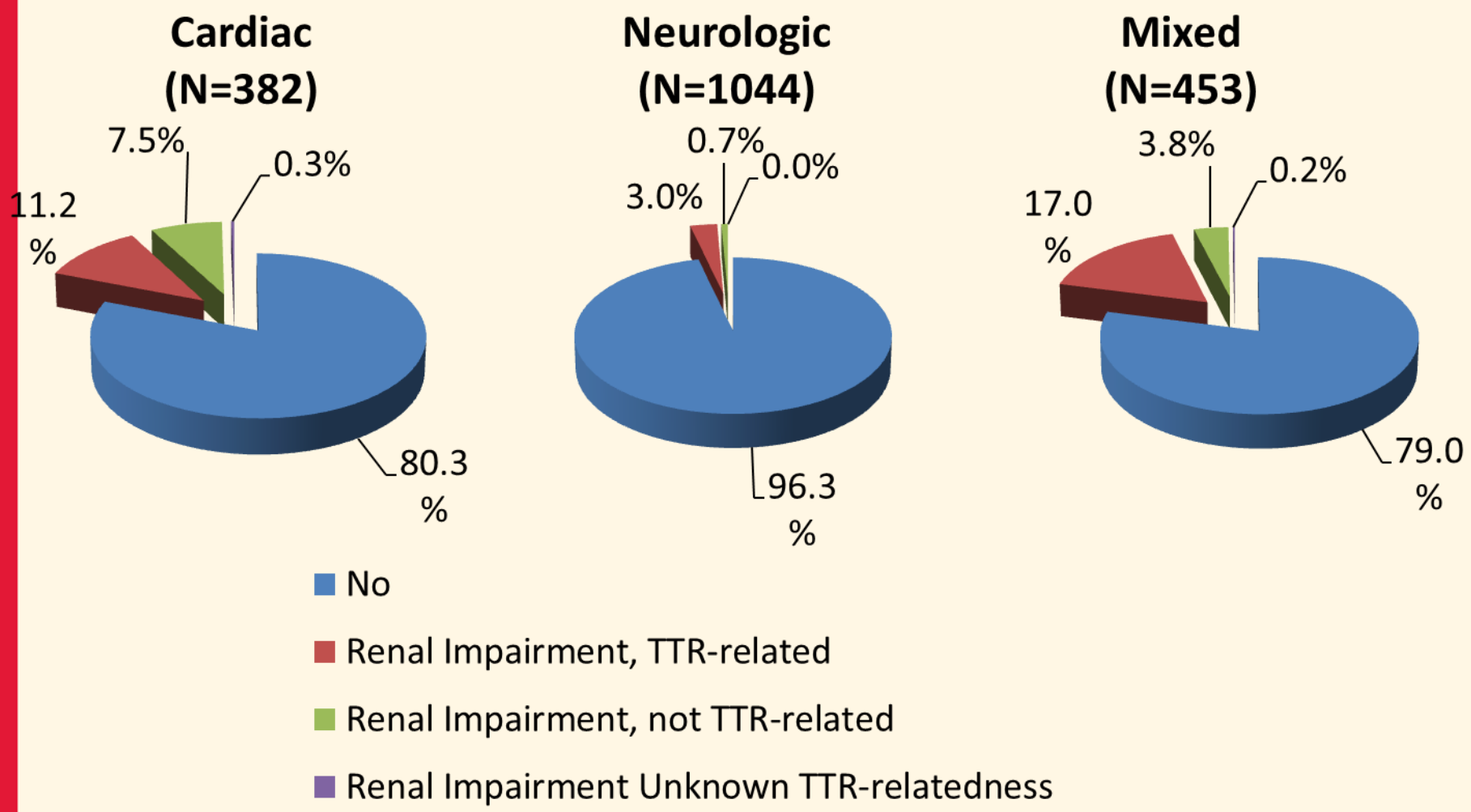
Estimated GFR at Enrollment
Wild Type vs. TTR Mutation



- Wild type vs. ATTR
  - Renal function very different
  - Many potential differences other than organs affected
- How about cardiac vs. neurologic symptoms?

Renal Status at Enrollment

Symptomatic Subjects, by Phenotype



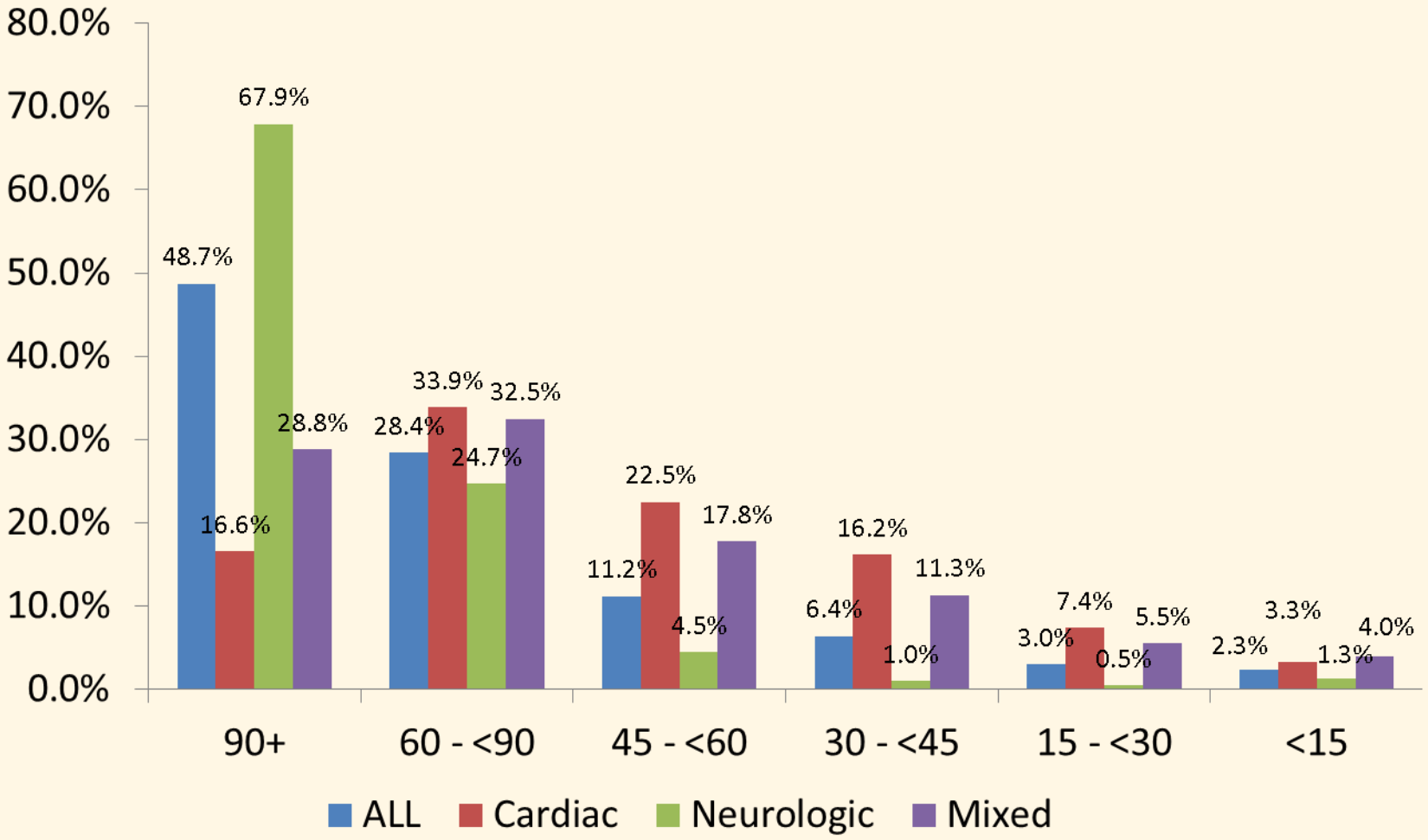
Estimated GFR at Enrollment

Symptomatic Subjects, by Phenotype

Estimated GFR (mL/min per 1.73m^2)	ALL (N=1389)	Cardiac (N=271)	Neurologic (N=792)	Mixed (N=453)
Availability of data	73.9%	70.9%	75.9%	72.0%
Mean ± SD	93.39 ± 113.61	64.51± 32.18	107.05± 37.93	84.21± 222.54
Median	88.50	60.20	104.80	68.35
25, 75 Percentile	62.00, 115.70	42.80, 81.10	83.90, 127.30	49.00, 95.10

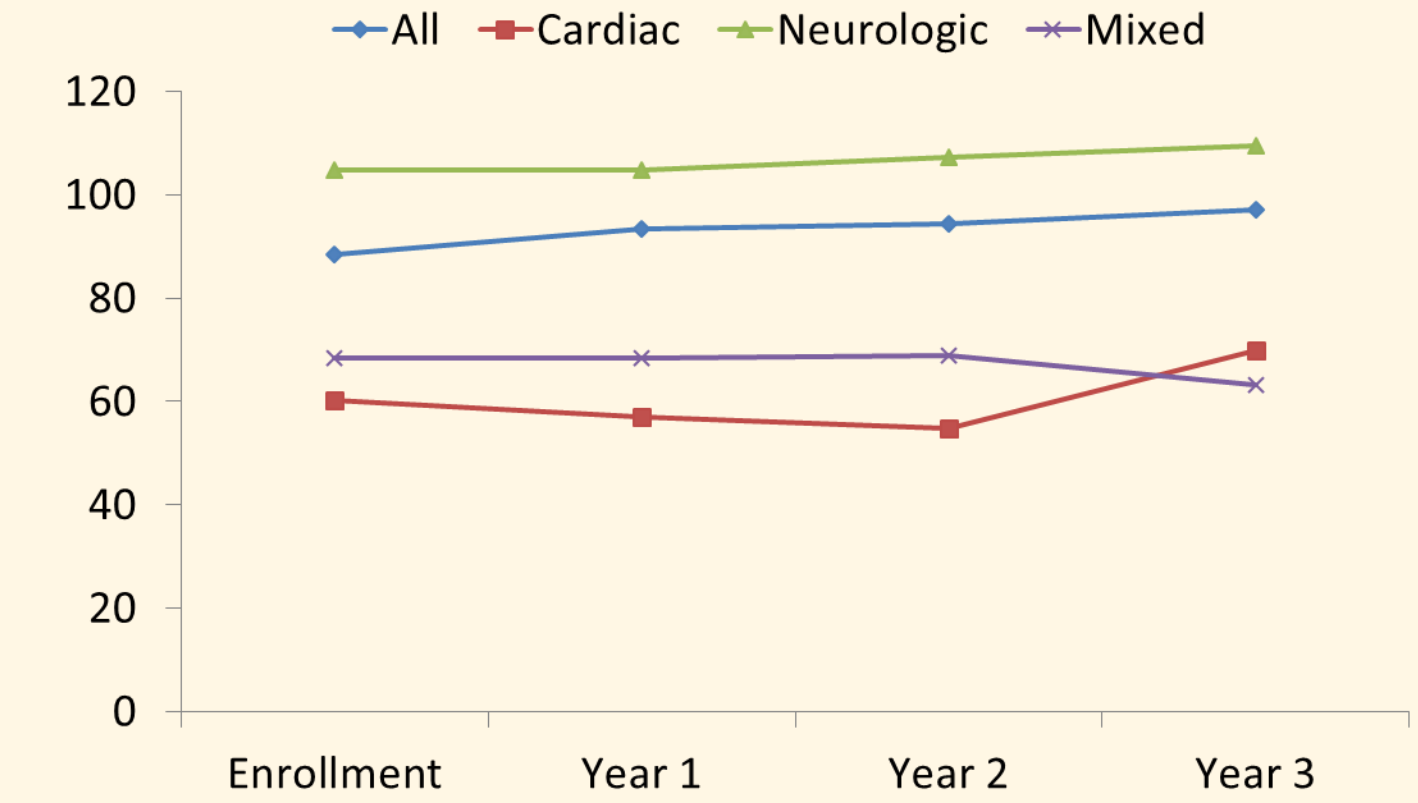
Estimated GFR at Enrollment

Symptomatic Subjects, by Phenotype



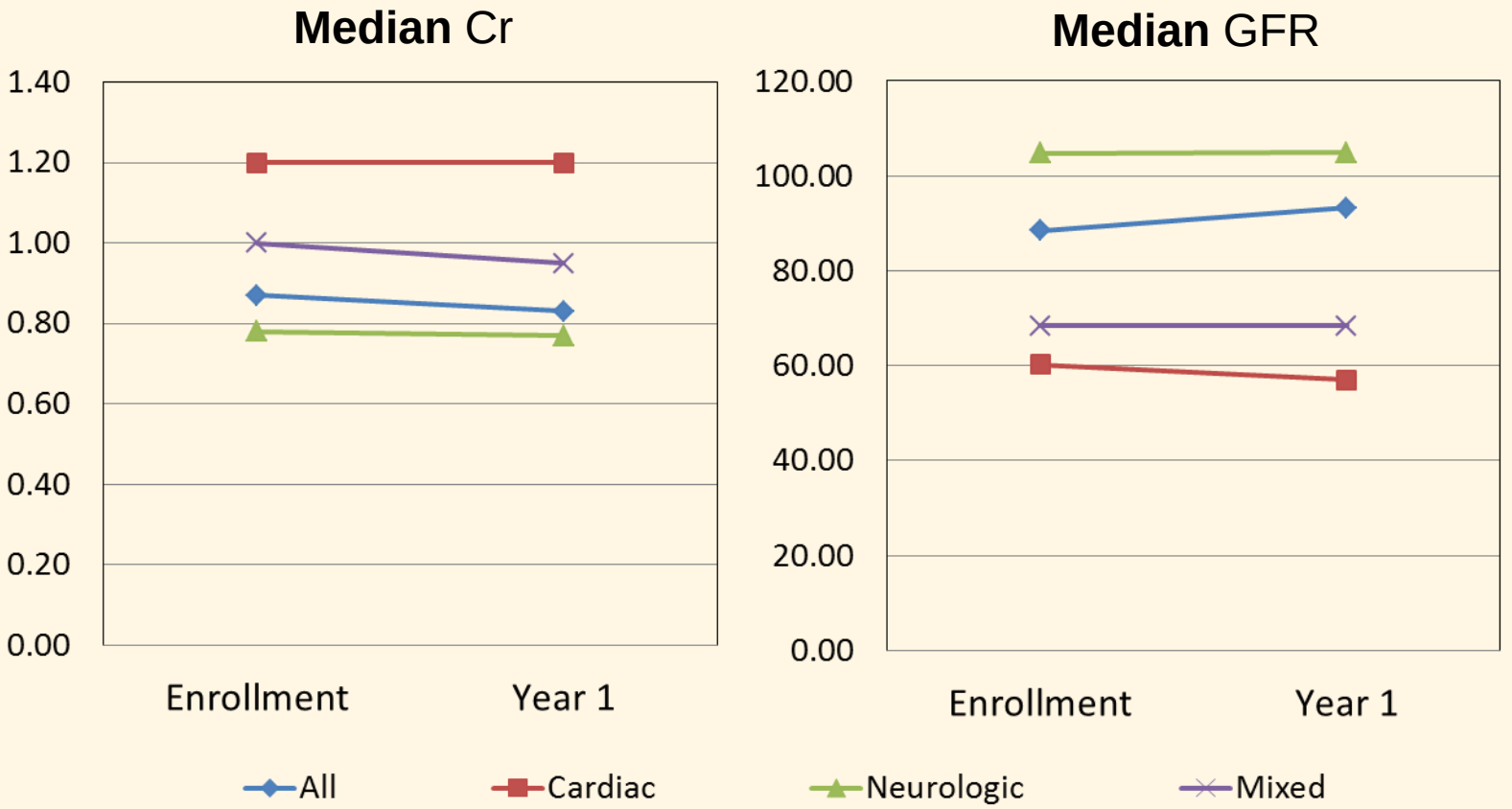
- GFR includes age and sex
  - Will eliminating this limit the differences?
- How much of the difference is because of demographic factors?
  - Looked at creatinine and GFR
- What happens over time?

Median Estimated GFR for Symptomatic Subjects, by Phenotype



N	**All**	**1389**	**811**	**566**	**367**
	Cardiac	271	114	64	39
	Neurologic	792	529	393	363
	Mixed	326	168	109	65

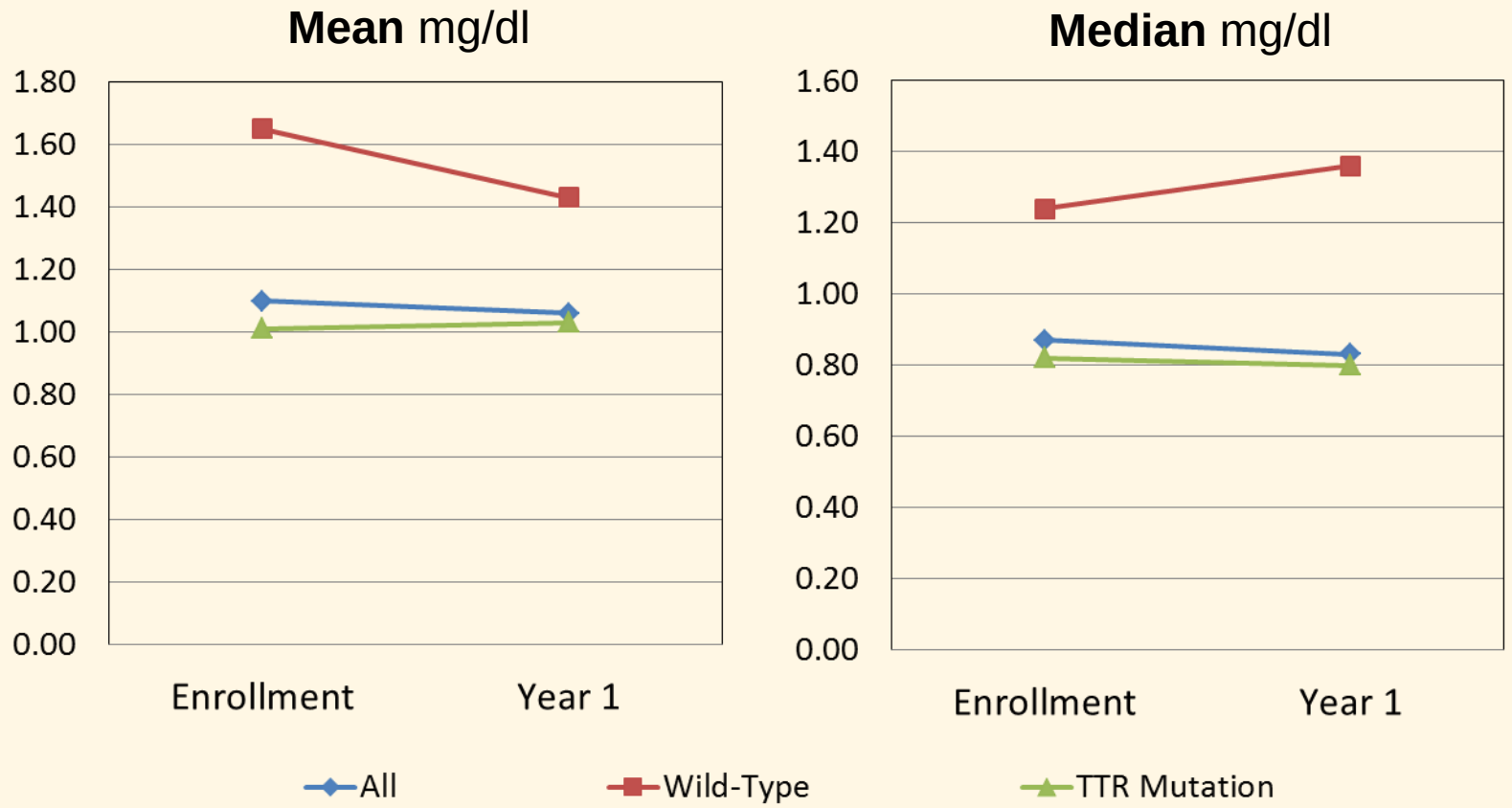
Renal Function by Phenotype



N	**All**	**1400**	**815**
	Cardiac	277	116
	Neurologic	795	530
	Mixed	328	169

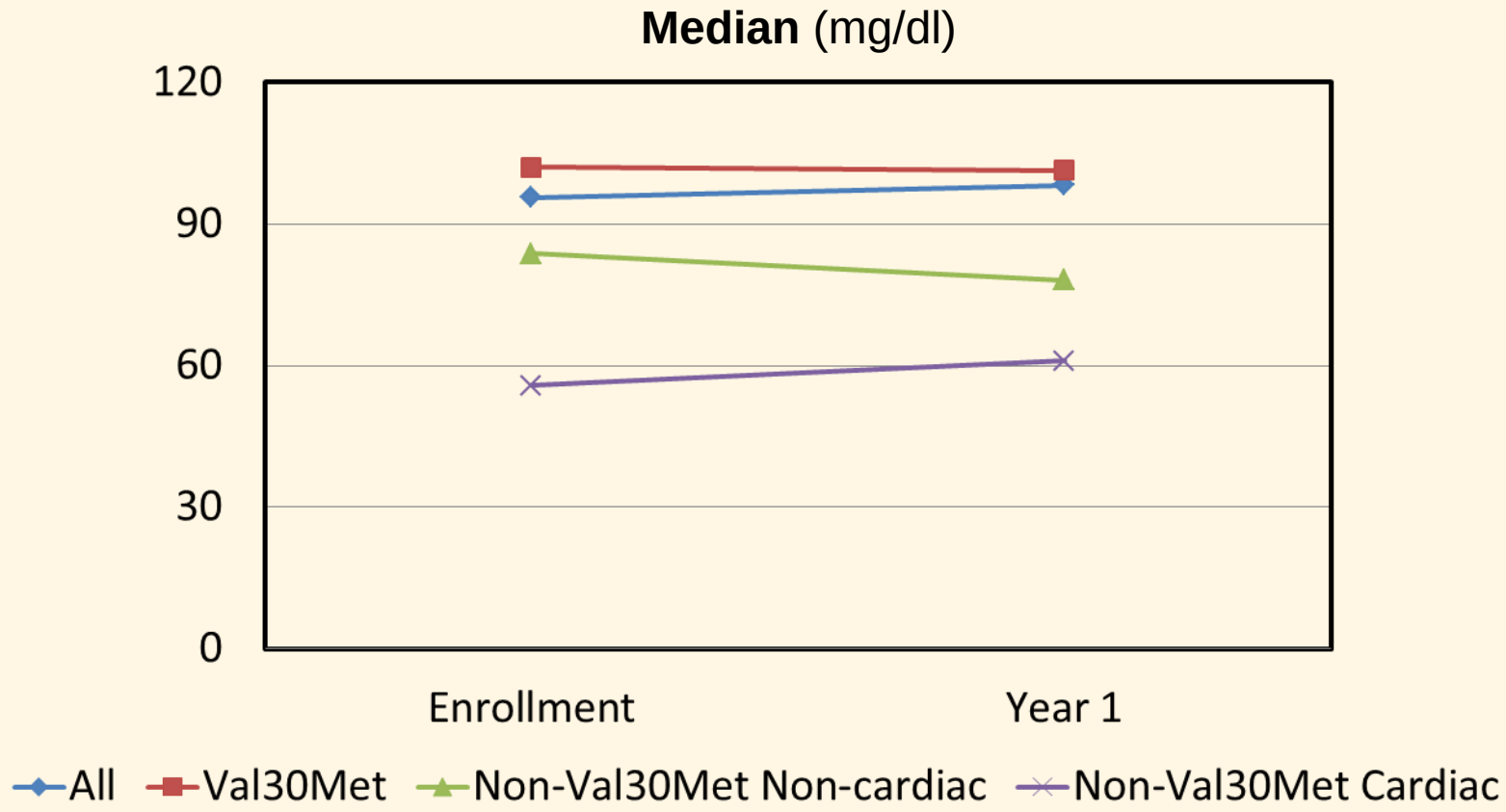
All	**1389**	**811**
Cardiac	271	114
Neurologic	792	529
Mixed	326	168

Serum Creatinine for Symptomatic Subjects, Wild-Type vs. TTR Mutation



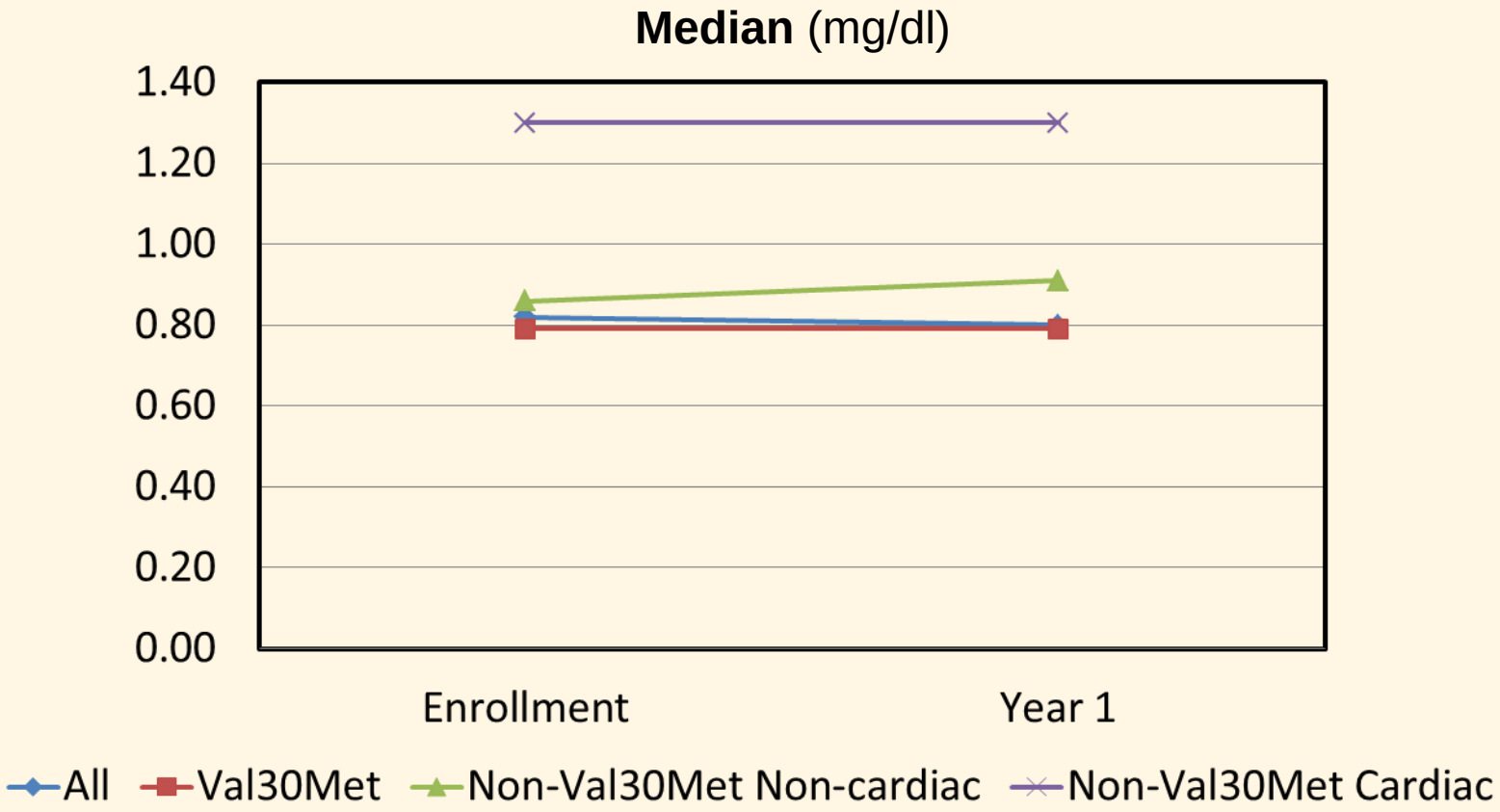
N	**All**	**1400**	**815**
	Wild-type	191	80
	TTR mutation	1209	735

Estimated GFR for Symptomatic Subjects, by Genotype



N	**All**	**1389**	**811**
	Val30Met	271	114
	Non-Val30Met Non-Cardiac	792	529
	Non-Val30Met Cardiac	326	168

Serum Creatinine for Symptomatic Subjects, by Genotype



N	**All**	**1209**	**735**
	Val30Met	925	624
	Non-Val30Met Non-Cardiac	180	70
	Non-Val30Met Cardiac	104	41

Problems / Proposals

- Patients vary by many characteristics
- GFR affected by age, sex
  - What's the appropriate way to control?
  - What's the appropriate comparison group?
- Median vs mean?
- Look at progression of renal dysfunction
  - Need more complete follow-up
- Look at protenuria
- Impact of cardiorenal effect