Understanding the patient voice in hereditary transthyretin-mediated amyloidosis (ATTR amyloidosis)

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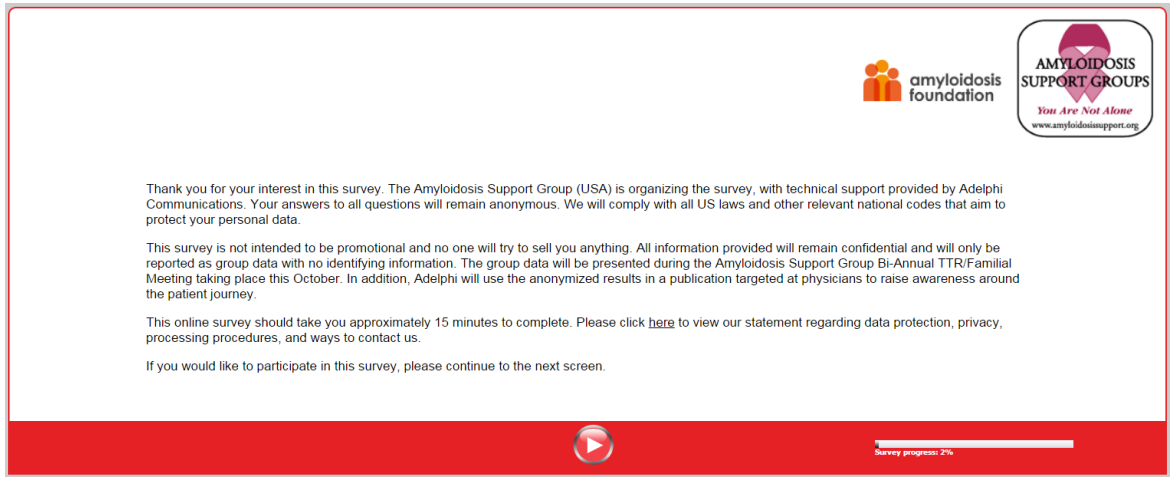
Summary of the patient voice survey



- The survey ran from September 4–30, 2015
- Only patients with hereditary ATTR amyloidosis were eligible to complete the survey
- Patients were classified according to whether the primary involvement was neuropathy, cardiomyopathy, or both
- 64 patients completed the survey
- The survey was supported by the Amyloidosis Foundation and the Amyloidosis Support Groups

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Survey objectives and patient demographics

- The objective of the survey was to collect data to help raise awareness of the patient journey for hereditary ATTR amyloidosis
- The survey was an online, interactive tool, completed by patients or caregivers on behalf of patients

	N=64
Mean age, years	57.9
Male/*female*, n (%)	43 (67)/ *21 (33)*
Patient/*caregiver*, n (%)	60 (94)/ *4 (6)*
Organ involvement, n (%) Neuropathy Cardiomyopathy Both (neuropathy+cardiomyopathy)	 28 (44) 9 (14) 27 (42)
Family history of disease, n (%)	49 (77)
Receiving amyloidosis-specific medication, n (%)	43 (67)

QD2. In which year were you born?
QS1. What type of amyloidosis do you have?
QS10. Do you have a family history of amyloidosis?
QK3. Are you currently receiving any amyloidosis-specific medication?

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Patient journey

Most patients have a family history of disease

- A constellation of symptoms were initially observed, which seriously impacted QoL

- Many specialists were seen, and a delay in diagnosis and/or misdiagnosis were reported
- Family history did not always expedite diagnosis

- Most patients were seeing a specialist
- Yet many patients were not on treatment, or receiving investigational therapies

- Progressive symptoms imparted heavy burden of disease

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QoL, quality of life

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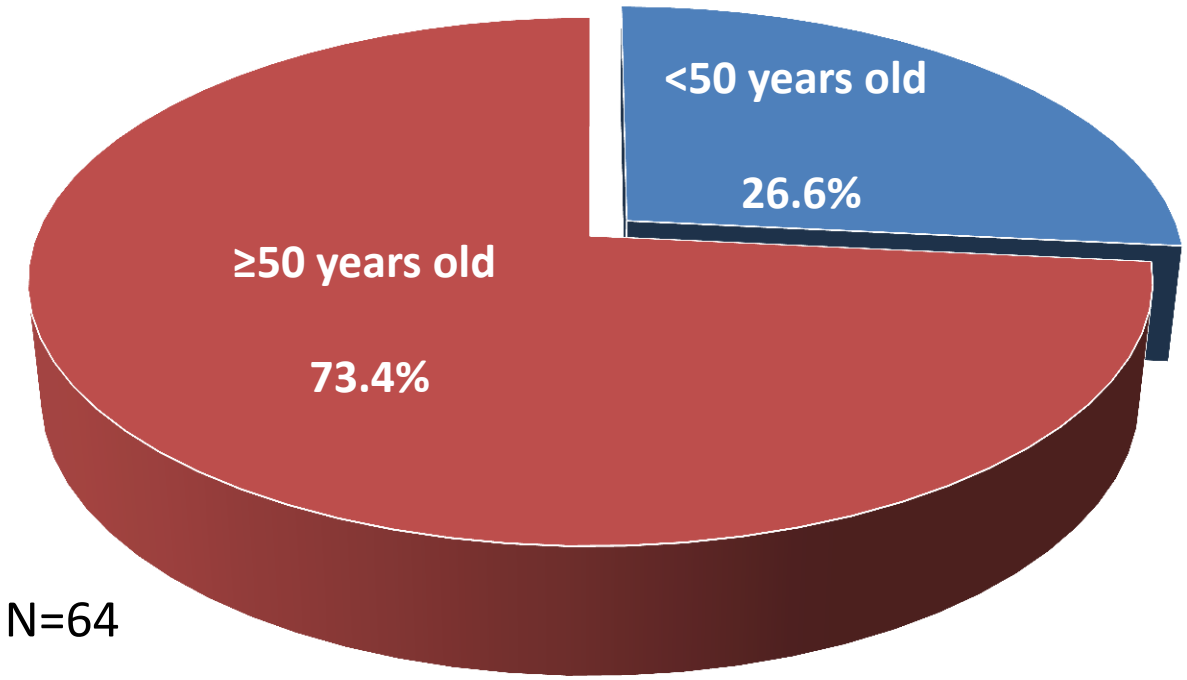
Almost three-quarters of patients were at least 50 years of age

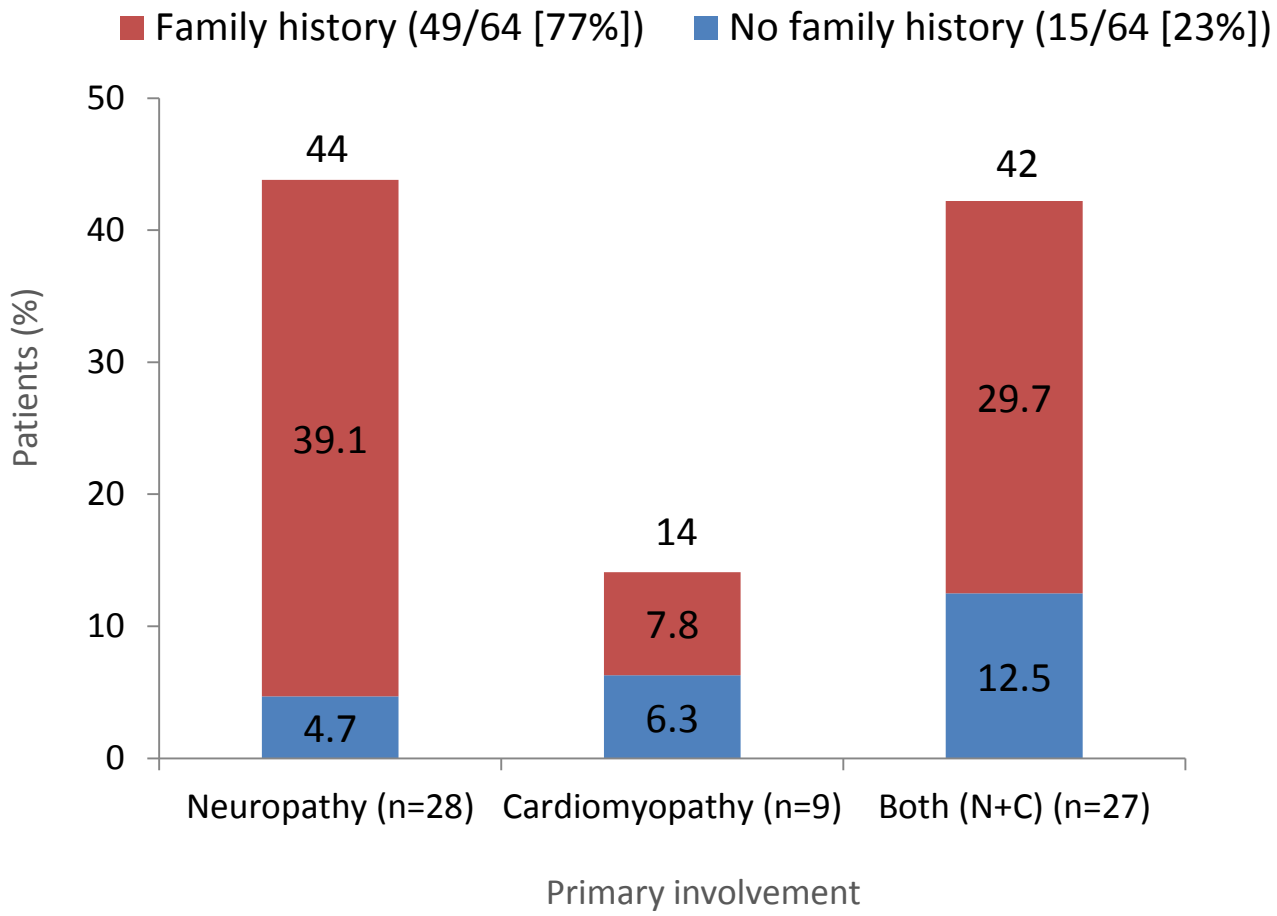


N=64

Mean age = 57.9 (range, 28–77) years

QD2. In which year were you born?

Majority of patients have neuropathy, and 77% have a family history of disease

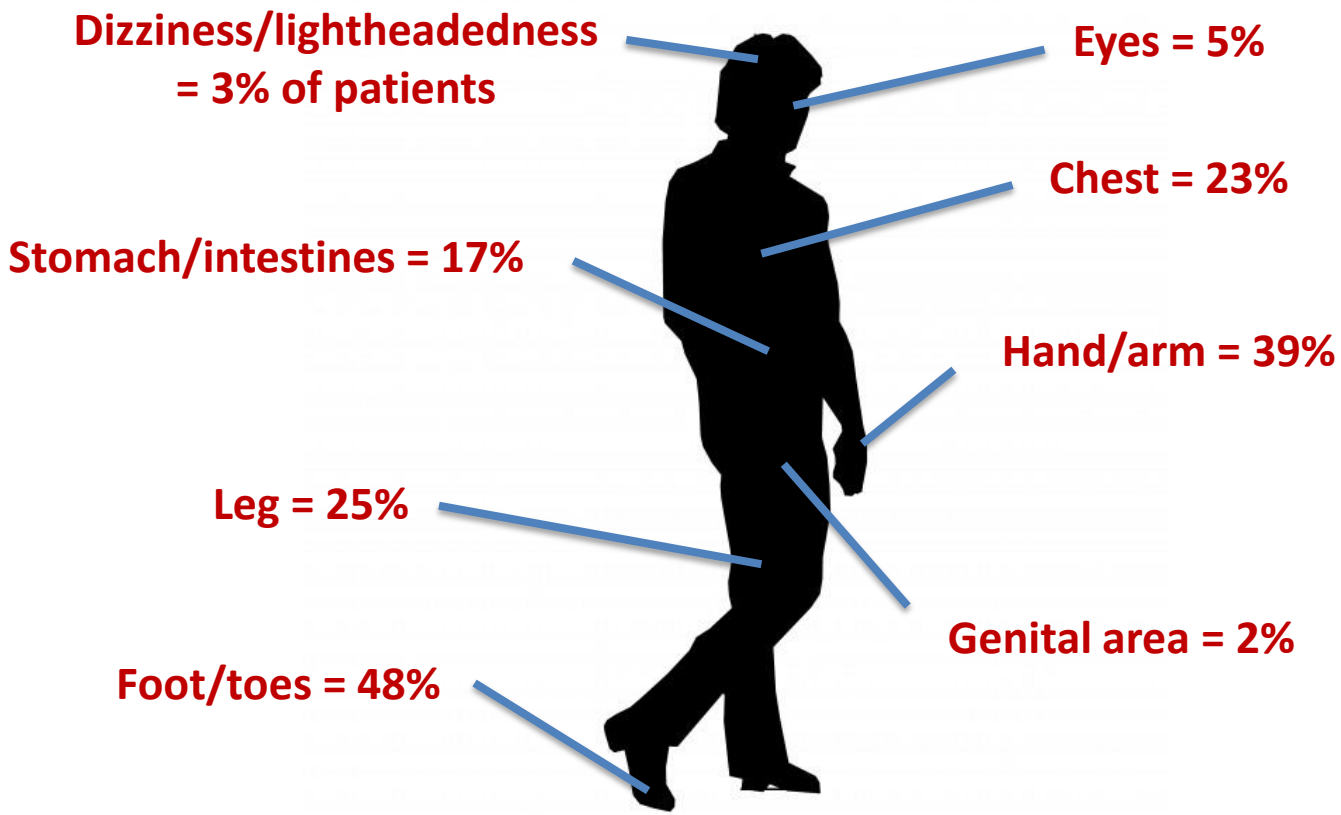


N=64

Cardiomyopathy is present in over half of the patients (56%)

QS1. What type of amyloidosis do you have?
QS10. Do you have a family history of amyloidosis TTR-FAP and/or TTR-FAC?

Initial symptoms of disease were multi-systemic



N=64

Foot/toe symptoms were typically the first symptoms experienced

However, hand/arm symptoms were initially observed in nearly 40% of patients

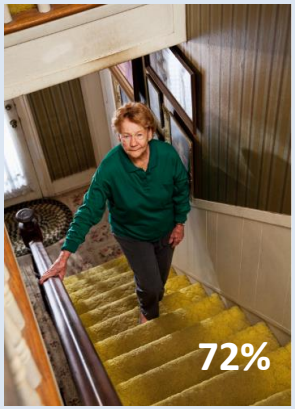
Symptoms impact a number of facets of patient functioning

Patients had at least some difficulty with:

Fine motor skills

Bathroom/self-care

Movement/mobility



Acts of daily living

N=64

QB3. How does amyloidosis affect your daily life?

There was a heavy disease burden for patients and caregivers

At completion of the survey ~1 in 5 patients (11/64) were unable to take care of themselves most of the time/at all

Mental health/outlook on life is affected in 35/64 (55%) of patients

- **Anxiety = 25/35 (71%) patients**
- **Stress = 22/35 (62%)**
- **Depression = 15/35 (43%)**

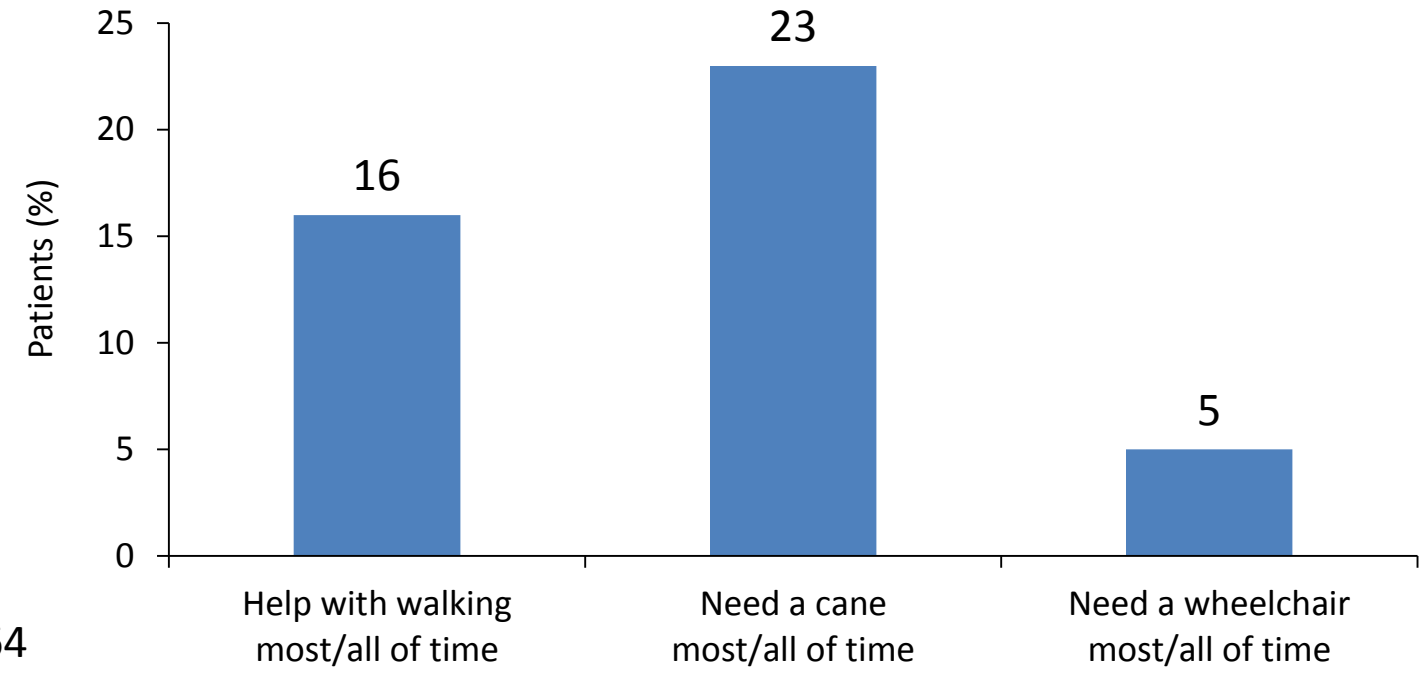
"Preparing myself and children for the inevitable"

"Physical limitations stop me doing things I love"

"Anger, impatience"

QS7. Has your mental health and/or outlook on life been affected by your amyloidosis?
QS7_A. Description of how amyloidosis has impacted on mental health and/or outlook on life
QB1_1. Are you able to take care of yourself?
QB3. How does amyloidosis affect your daily life?

Patient mobility was impacted by the disease



N=64

Almost half of patients (45%) have suffered falls

6% of patients had broken or fractured a bone as a result of an amyloidosis-related fall

QB1_2. Do you need help with walking?
QB1_3. Do you ever need to use a walking stick?
QB_4. Do you ever need to use a wheelchair?
QB1_5. Have you fallen over?
QB1A1_1. Have you ever broken or fractured a bone as a result of an amyloidosis-related fall?

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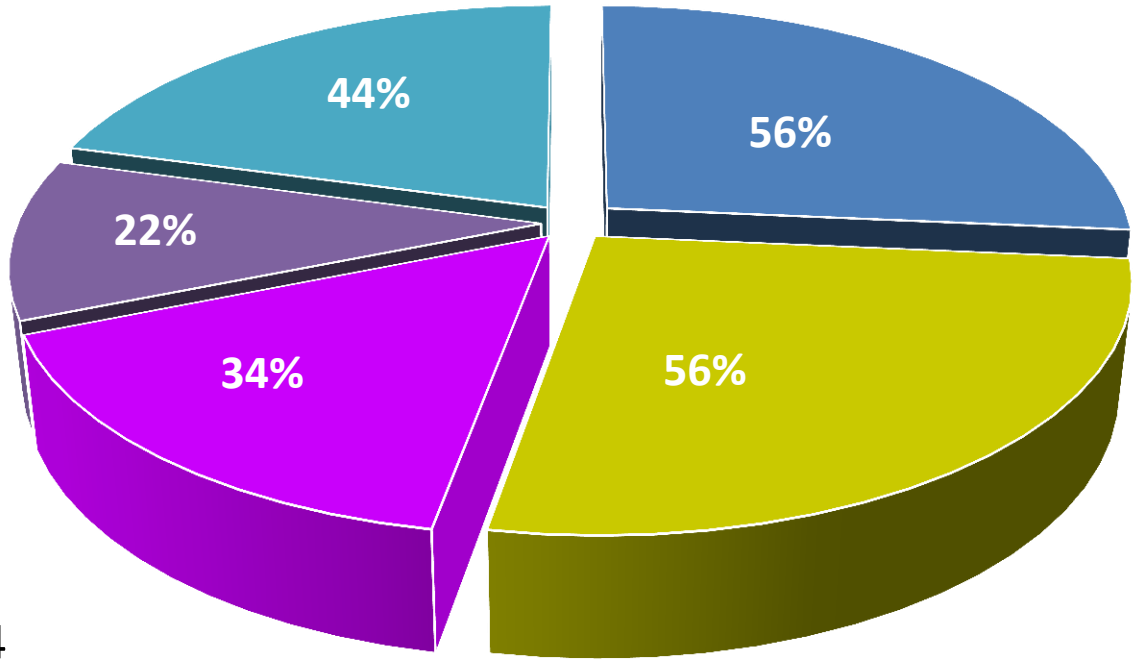
A range of specialists were consulted before patients were correctly diagnosed



*Other specialists seen include: genetic counselor, nephrologist, hematologist, ophthalmologist, rheumatologist, urologist, oncologist, surgeon, pulmonologist

N=64

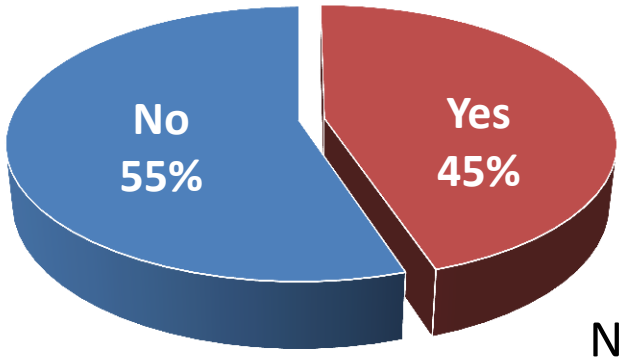
(41 patients [64%] saw >1 type of specialist clinician)

Prior to diagnosis, primary care physicians and neurologists were the most common clinician that provided consultation

QS6. Which specialist(s) did you consult before your amyloidosis was correctly diagnosed?

Disease misdiagnosis was not uncommon

Was your amyloidosis misdiagnosed as another disorder?



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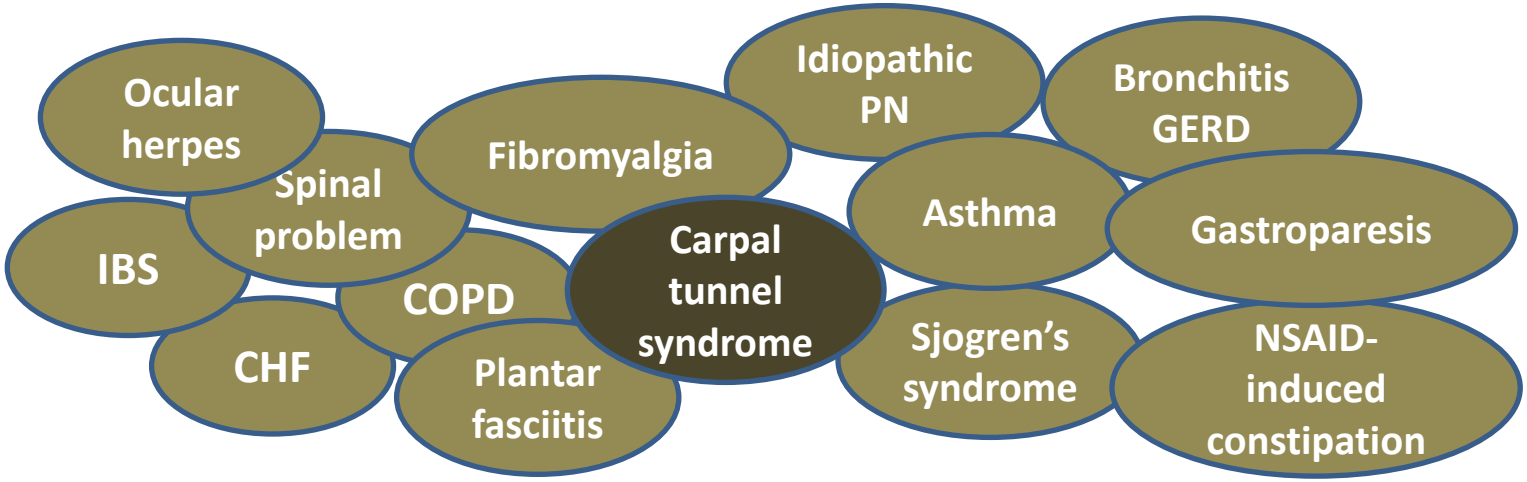
Misdiagnosed conditions:



Carpal tunnel syndrome (6/64) was the most common misdiagnosis

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QS8. Was your amyloidosis misdiagnosed as another disorder?

CHF, chronic heart failure; COPD, chronic obstructive pulmonary disease; GERD, gastroesophageal reflux disease; IBS, irritable bowel syndrome; NSAID, non-steroid al anti-inflammatory drug; PN, polyneuropathy

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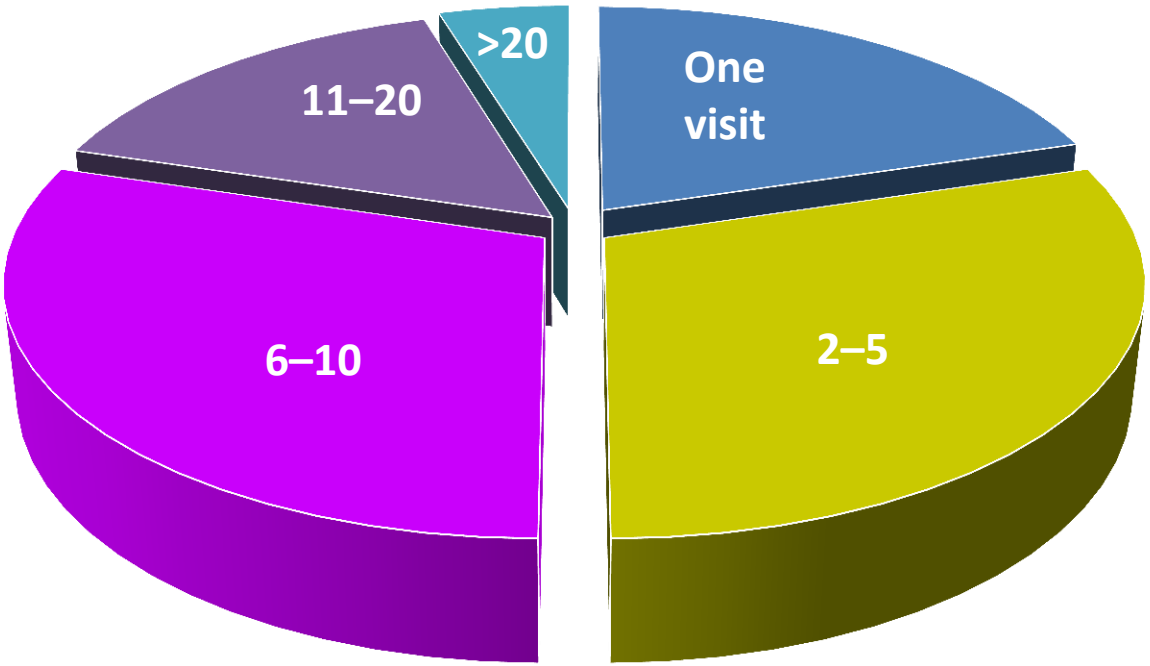
The majority of patients required numerous specialist visits before correct diagnosis



N=64

(Specialty/specialist may have been visited more than once)

For 1 in 5 patients, 1 visit to see a doctor was sufficient, but a large proportion required up to 10 doctors' visits before diagnosis

Some patients even required >20 doctors' visits prior to diagnosis

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QS6_2. Estimate the total number of visits you had with any specialist about your amyloidosis before you were diagnosed.

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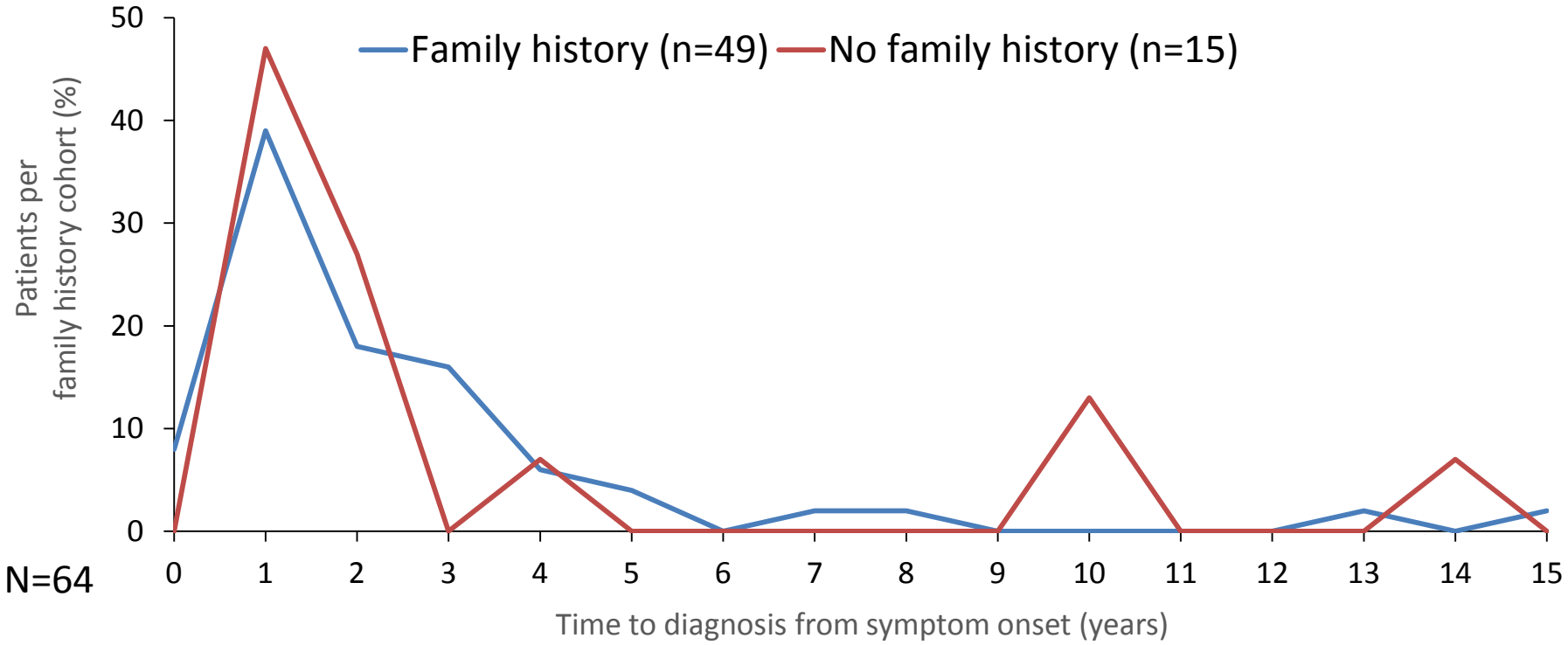
Time to diagnosis was similar irrespective of family history of disease



With or without family history, the majority of patients were diagnosed within 2–3 years of symptom onset

However, delayed diagnosis (>10 years after symptom onset) was observed in patients with a family history of disease

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QS5. What was the duration of time between you first experiencing symptoms of amyloidosis and your confirmed diagnosis of amyloidosis?

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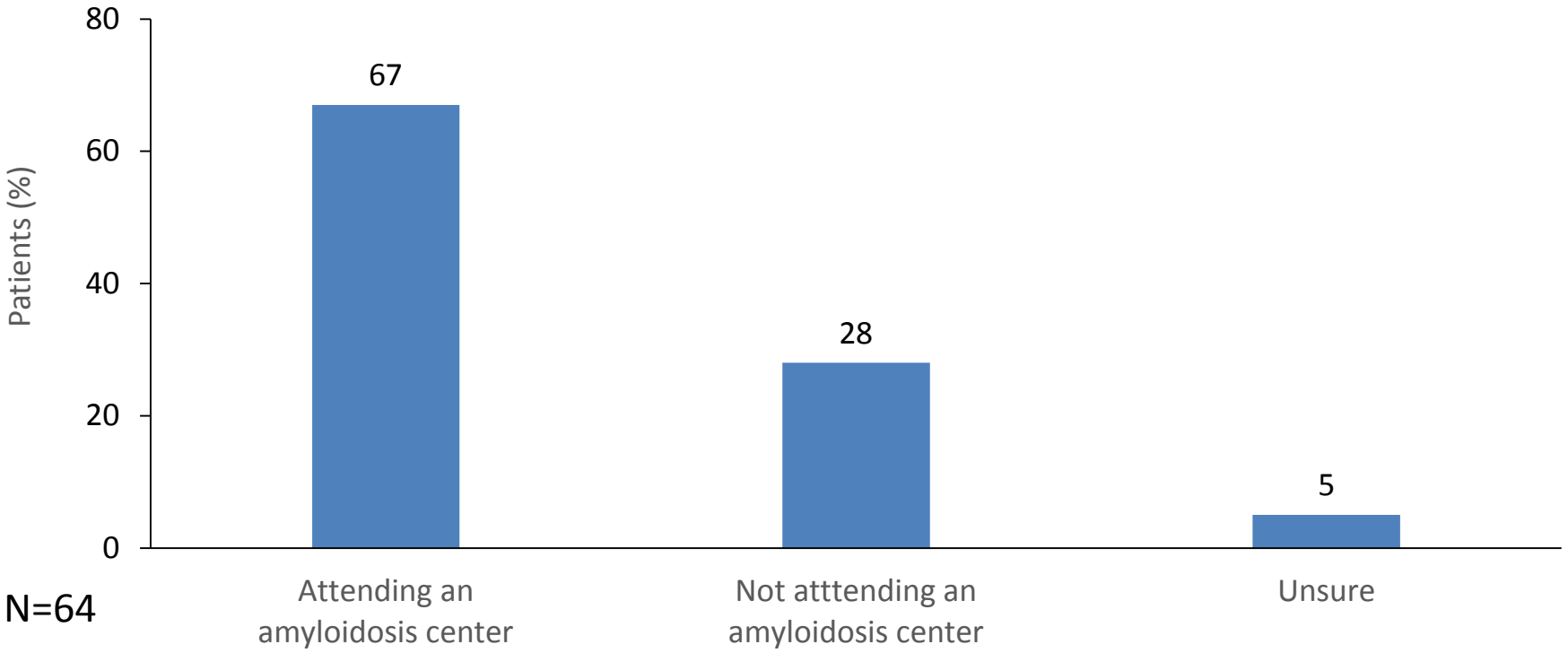
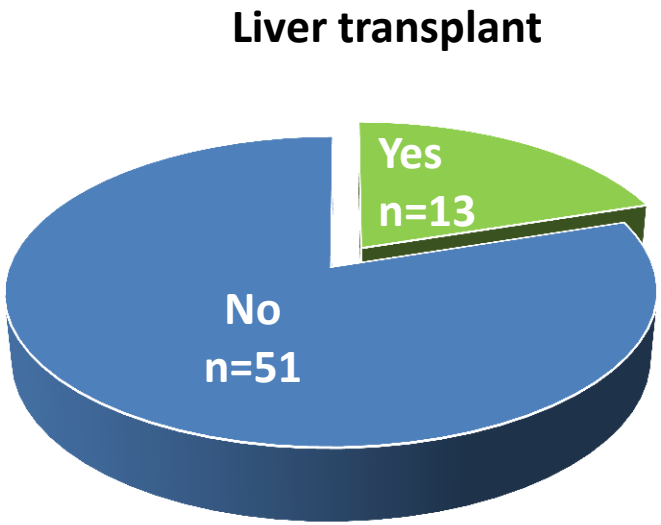
The majority of patients were seen at an amyloidosis center



A little over one-quarter of patients have not been to an amyloidosis center

QK1. Are you currently seeing a doctor at an amyloidosis specialist center?

1 in 5 patients have had a liver transplant



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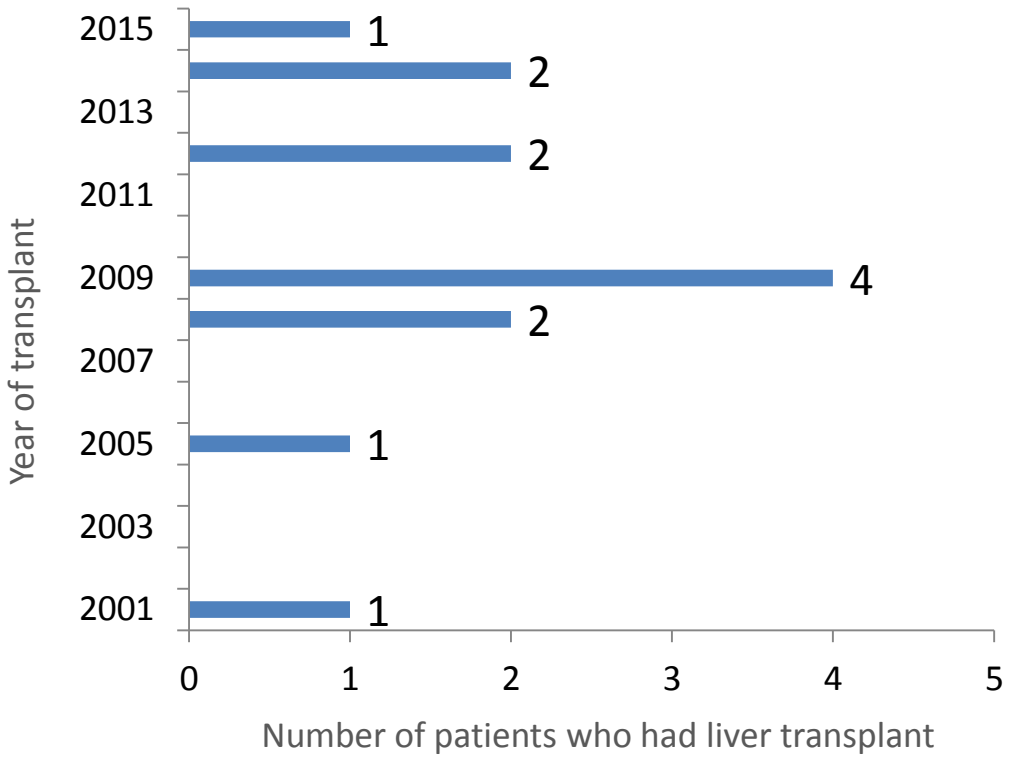

Following liver transplant , 4/13 patients (31%) reported no improvement in symptoms; Slowing/halt of symptom progression post-transplant was not measured

2/13 patients have received amyloidosis-specific medication after liver transplant

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QK3. Are you currently receiving any amyloidosis-specific medication?
QK4. What medication are you currently receiving?

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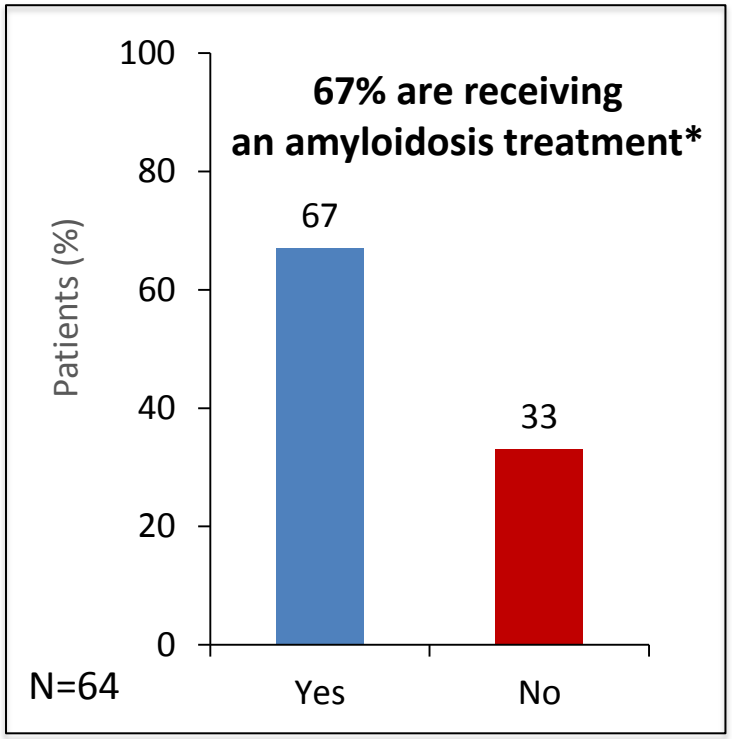
The majority of patients are receiving amyloidosis-specific or investigational drug



*Patients may have received medication during participation in a clinical trial

Therapy, n (%)	(n=43)
Diflunisal	19 (44)
ISIS-TTR$_{Rx}$	15 (35)
Patisiran	5 (12)
Doxy/TUDCA	3 (7)
Revusiran	3 (7)
Doxy only	2 (5)
Tafamidis	1 (2)

(5 patients are taking >1 medication)

Approximately half of the patients (47%) prescribed amyloidosis-specific therapy are taking a TTR stabilizer

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QK3. Are you currently receiving any amyloidosis-specific medication?
QK4. What medication are you currently receiving?

Doxy, doxycycline;
TUDCA, tauroursodeoxycholic acid

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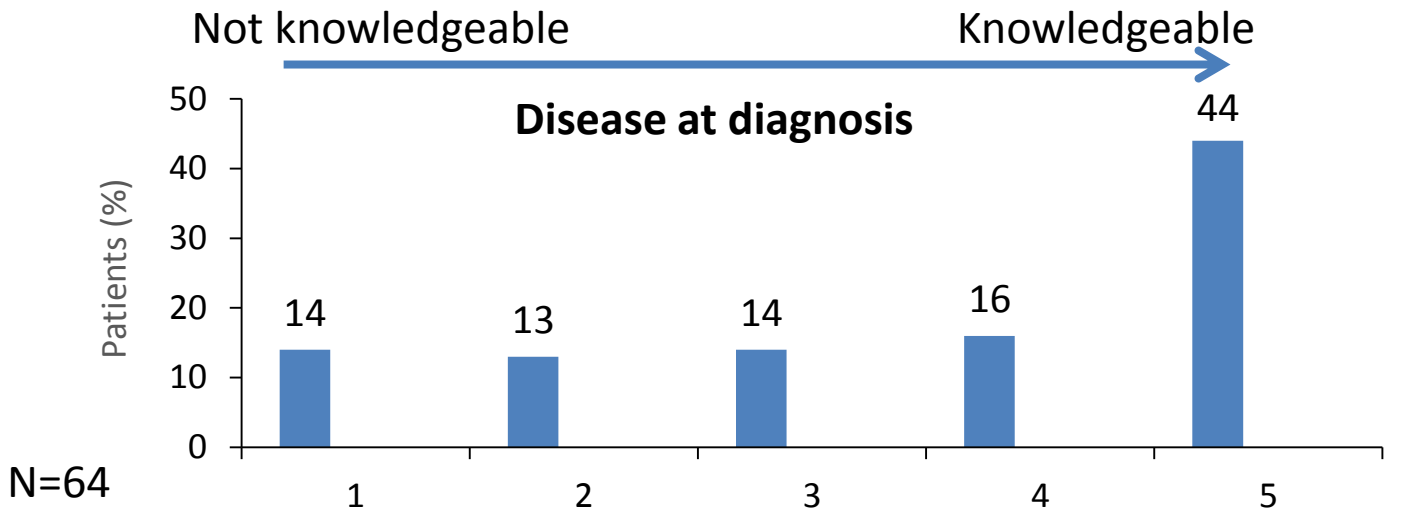
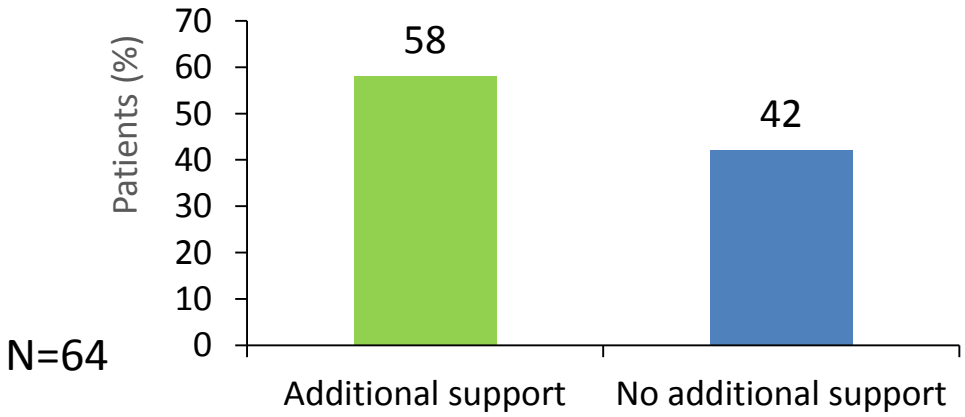
Patient education and support



58% of patients requested additional support/information



Further support requested included:
More disease information (11/64)
More information on trials (11/64)
Emotional support (5/64)

QK5. Do you think you were given enough information about amyloidosis when you were first diagnosed?
QS6.2.. Do you feel knowledgeable about clinical trials in amyloidosis?

Summary

- The pathway to diagnosis can be complex, involving many specialists, and can be prolonged if disease is not recognized early after symptom onset
  - Family history does not always reduce delay in diagnosis
- Fine motor skills are commonly affected by the disease, difficulty is also observed in performing more common tasks (e.g., walking up stairs)
  - Disease also creates a burden for caregivers
- Mobility is impacted by the disease, with >25% of patients dependent on a cane or wheelchair most/all of the time
- Approximately 2 in 3 patients (67%) are taking an amyloidosis directed treatment or investigational therapy
  - The most common medication taken is diflunisal (19/64), although a variety of investigational agents are being used
  - Liver transplantation was performed in 20% of patients

Acknowledgments

Thank you to all patients and caregivers who have completed this survey. Your answers have provided genuine insight into the burden of ATTR amyloidosis

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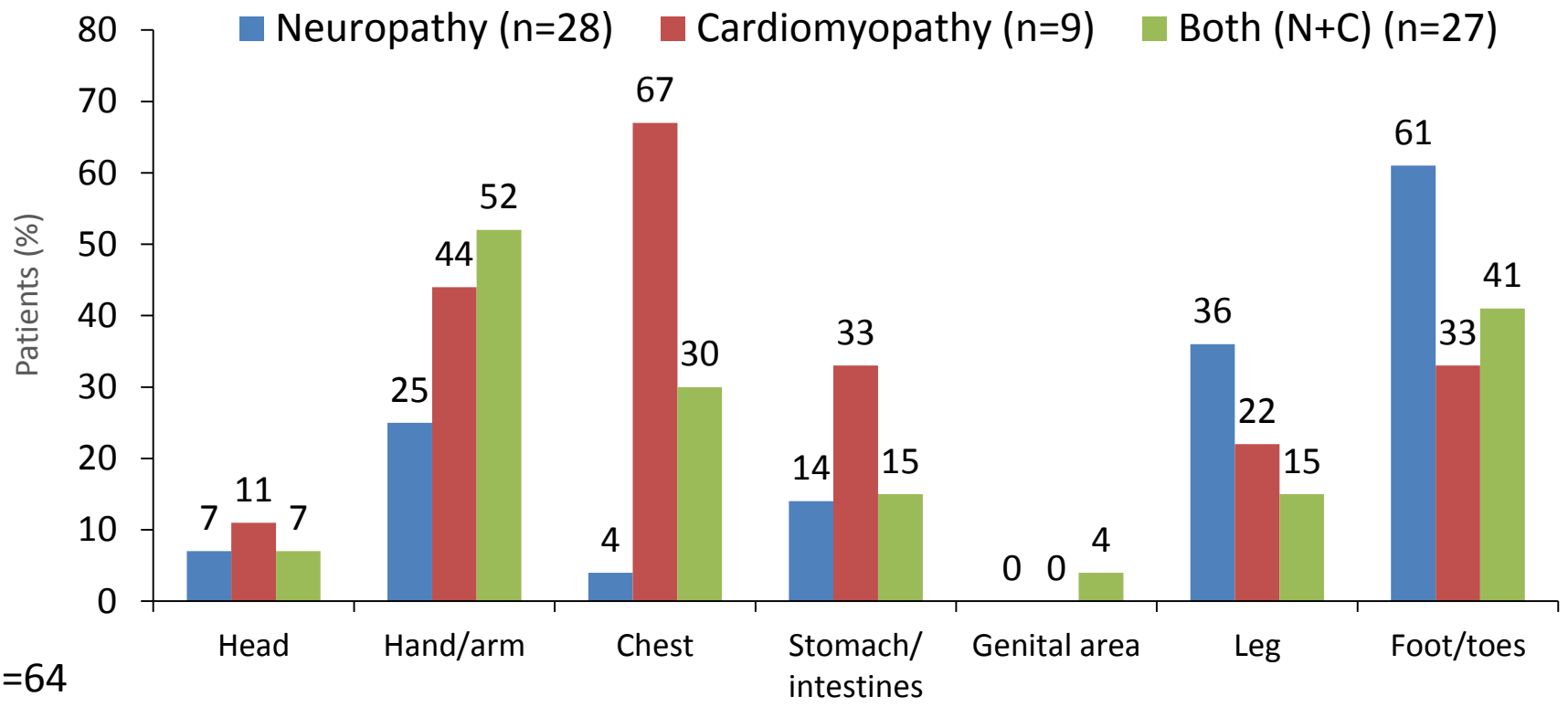
Appendix

Initial symptoms differed according to disease type



N=64

Initial foot/toe and leg symptoms were more common in patients with neuropathy only

As expected, chest symptoms were frequently observed first in patients with cardiomyopathy only

Initial hand/arm symptoms occurred more frequently in patients with both cardiomyopathy and neuropathy vs neuropathy alone

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QS2. First experienced symptoms of amyloidosis

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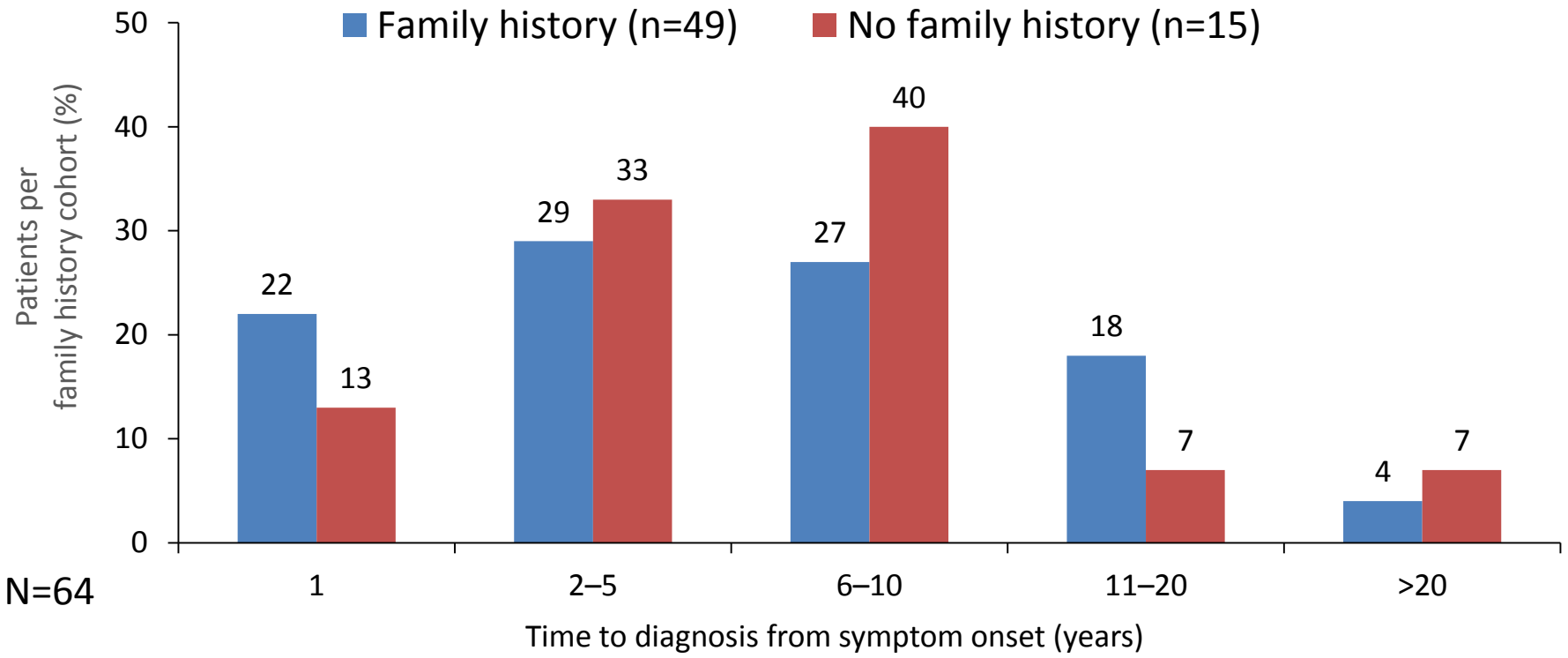
The number of visits before diagnosis was similar regardless of family history of disease



A slightly higher proportion of patients with family history were diagnosed on the first visit to a doctor

However, even with a family history, >20 visits were required before diagnosis for some patients

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QS6. What type of specialist diagnosed your amyloidosis?
QS6.2.. Please estimate the total number of visits you had with any specialist about your amyloidosis before you were diagnosed

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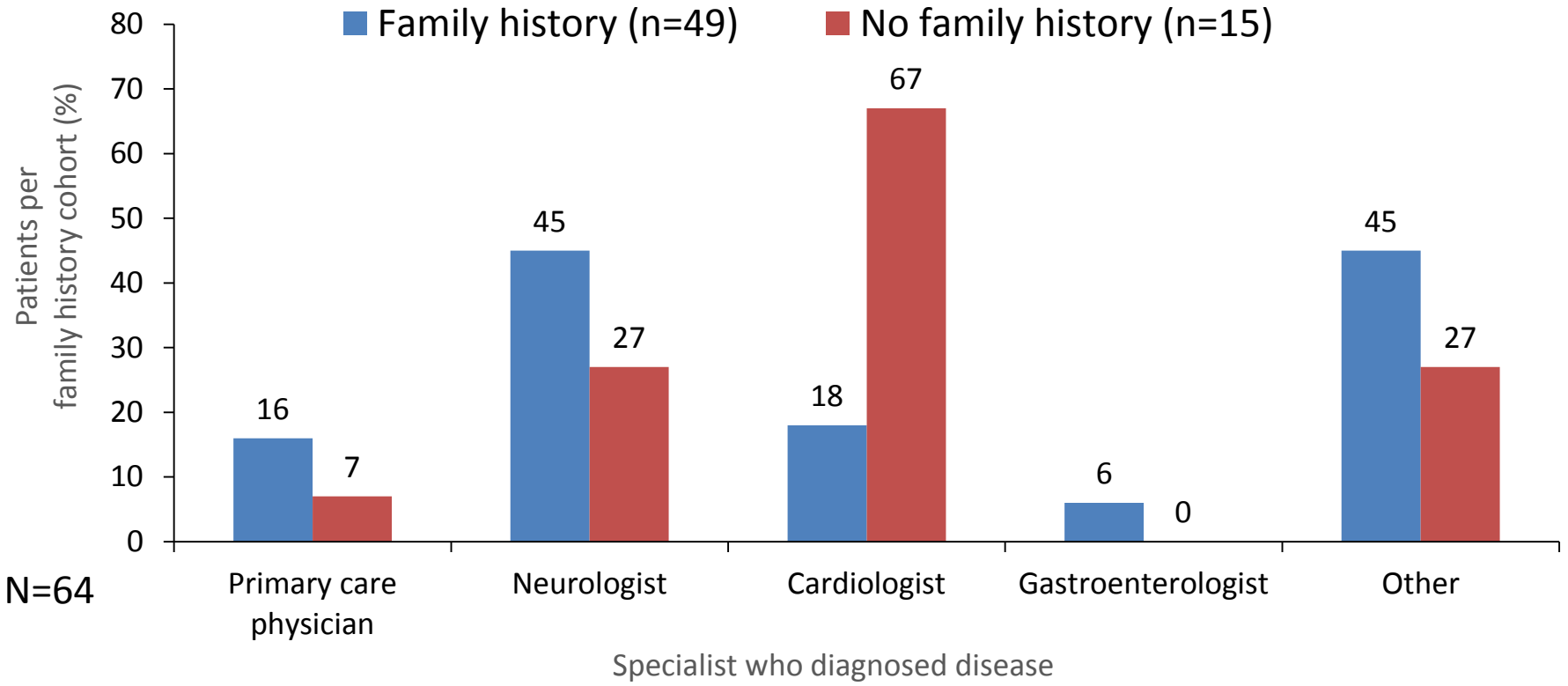
Patients with a family history were most frequently diagnosed by a neurologist



65% (32/49) of patients with family history of disease saw >1 type of specialist ahead of correct diagnosis vs 80% (12/15) without family history

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QS6. Which specialist(s) did you consult before your amyloidosis was correctly diagnosed?
QS6. What type of specialist diagnosed your amyloidosis?

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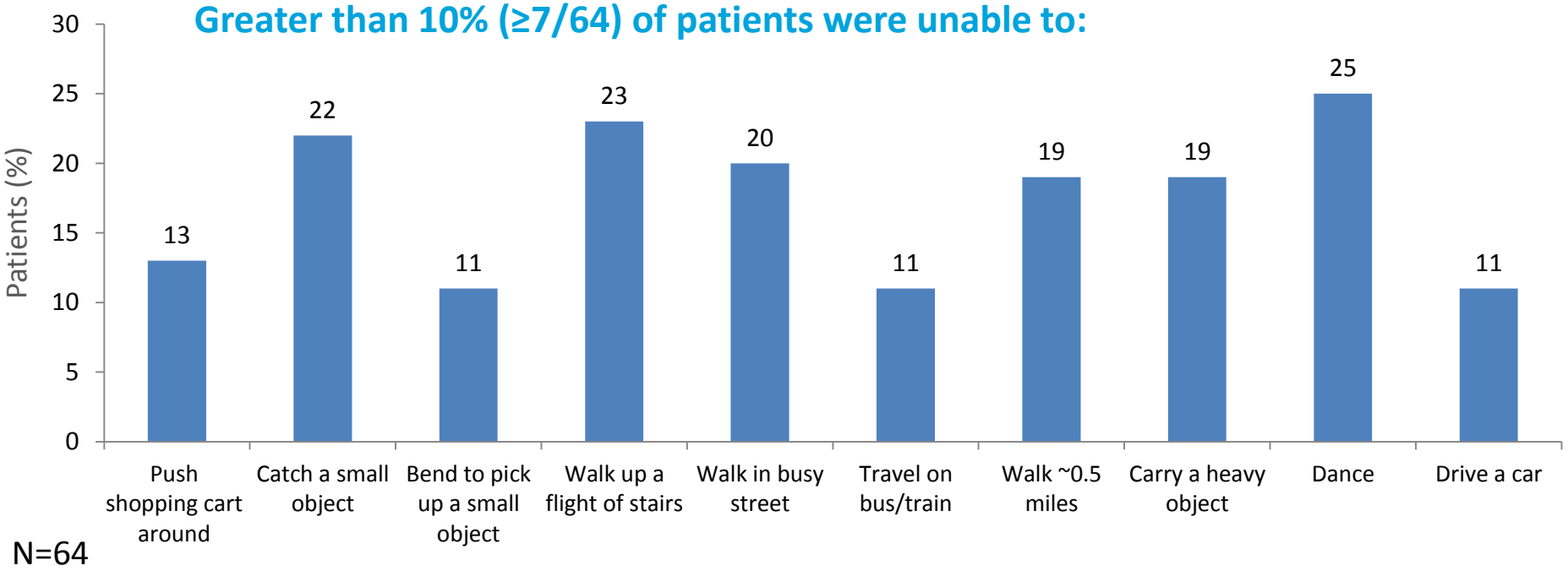
There was a heavy disease burden for patients and caregivers

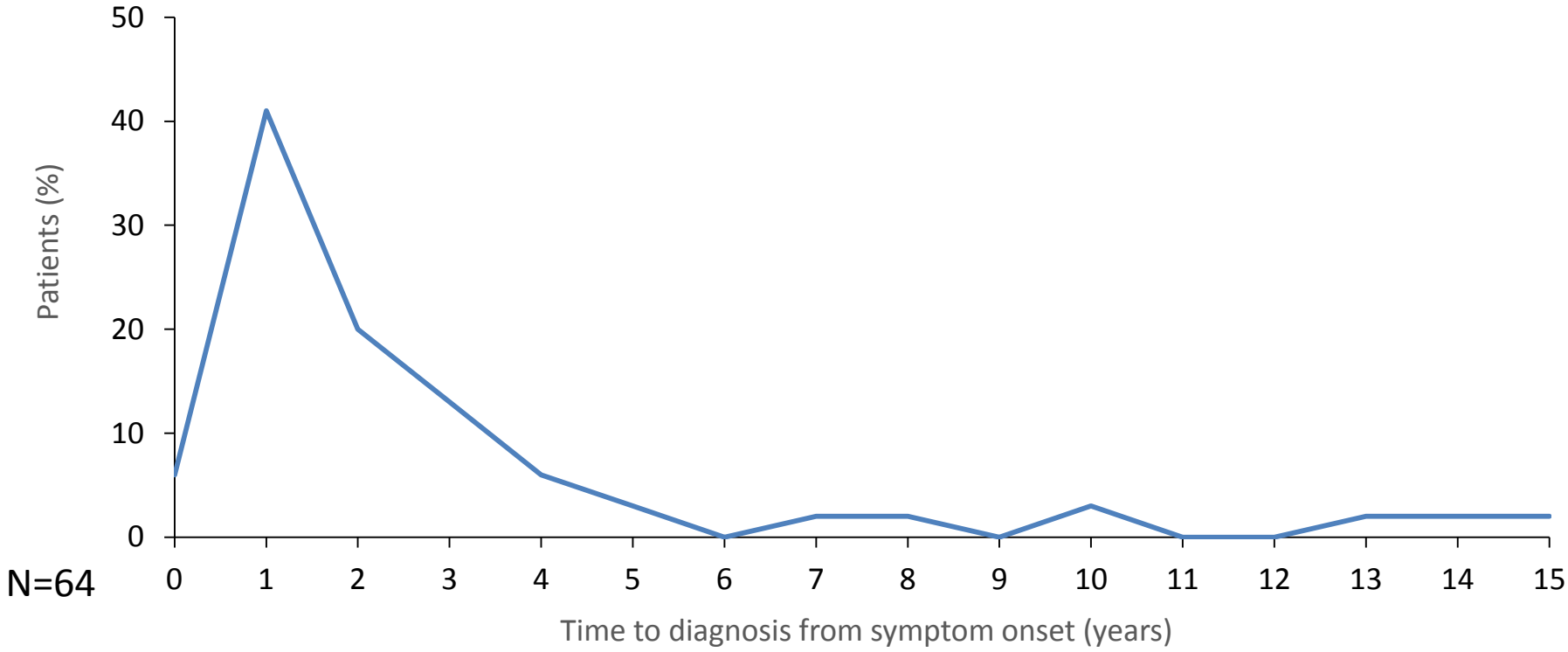
At completion of the survey ~1 in 5 patients (11/64) were unable to take care of themselves most of the time/at all



N=64

QB1_1. Are you able to take care of yourself?
QB3. How does amyloidosis affect your daily life?

Time to diagnosis of hereditary ATTR amyloidosis



Many patients are diagnosed shortly after symptom onset, but those who are not may wait a number of years before correct diagnosis

For ~1 in 10 patients, diagnosis took >6 years after onset of symptoms

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QS5. What was the duration of time between you first experiencing symptoms of amyloidosis and your confirmed diagnosis of amyloidosis?

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