



MALATTIE RARE NELL'ADULTO

Quali prospettive
nei percorsi di diagnosi e cura

Amiloidosi cardiaca: conoscere per gestire al meglio la patologia



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Amyloidosis Research and Treatment Centre IRCCS Fondazione Policlinico San Matteo, Pavia



Initially based in the Department of Internal Medicine, in 2006 it was moved to a new, dedicated location that was renovated thanks to the generosity of patients



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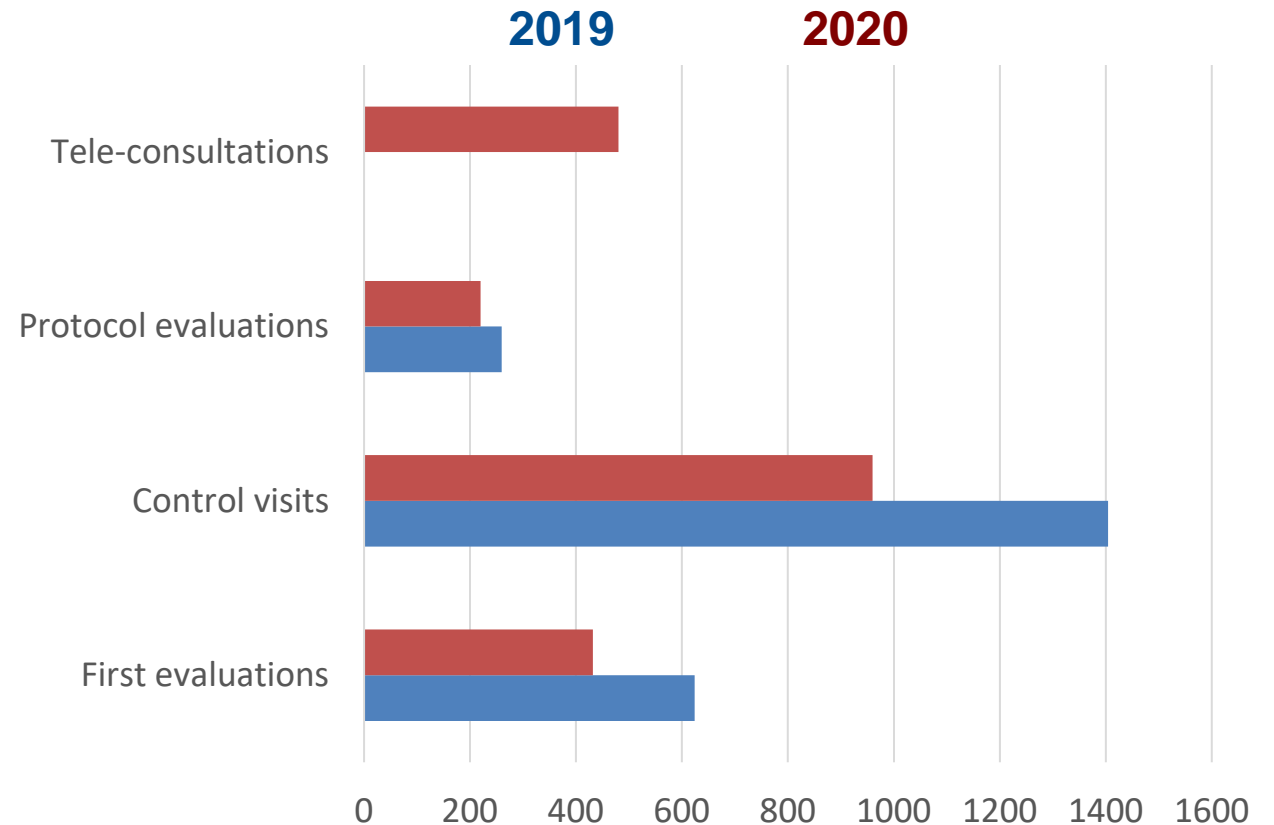


Outpatient clinic



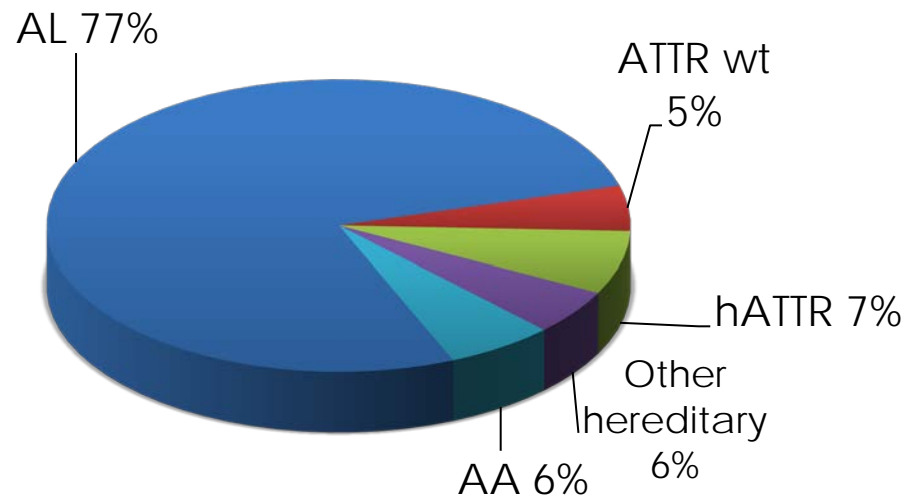
**Diagnostic and research
laboratory**

~400 newly diagnosed patients/year
~2500 clinical evaluations/year
~40,000 patients' samples in the biobank

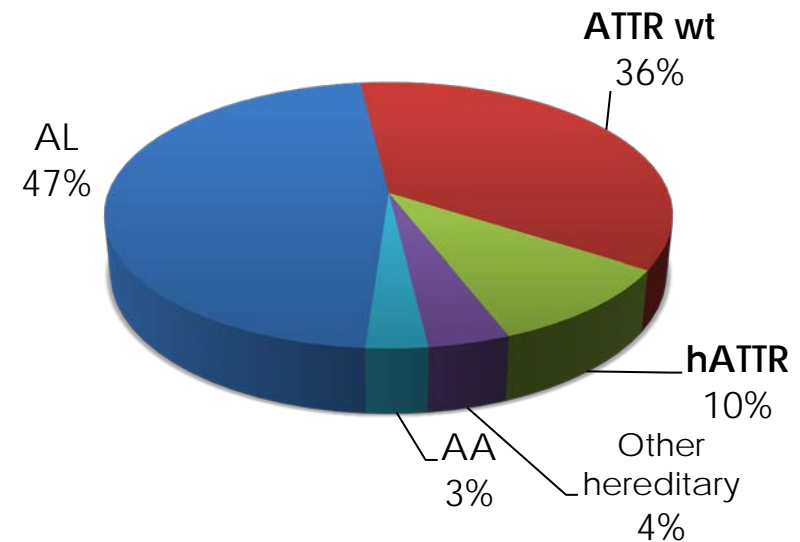


The increasing medical relevance of systemic ATTR amyloidosis

Newly diagnosed patients 2010-2015



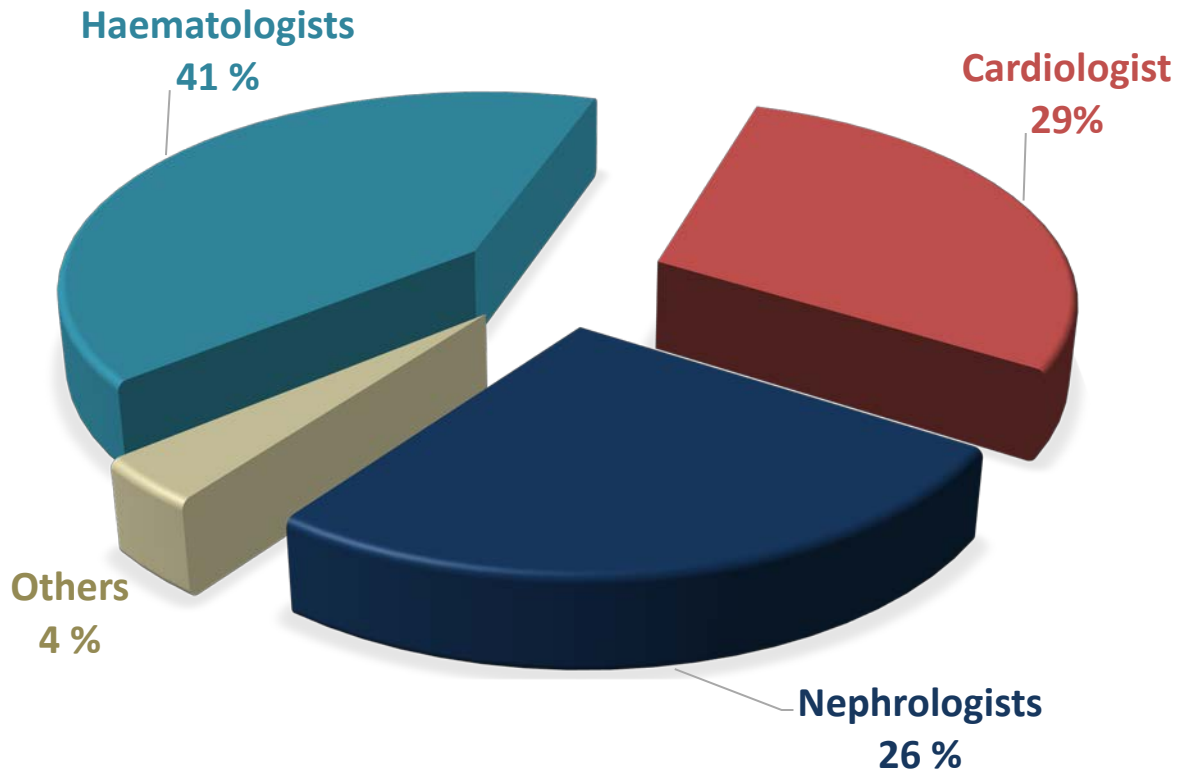
Newly diagnosed patients in 2018-2020



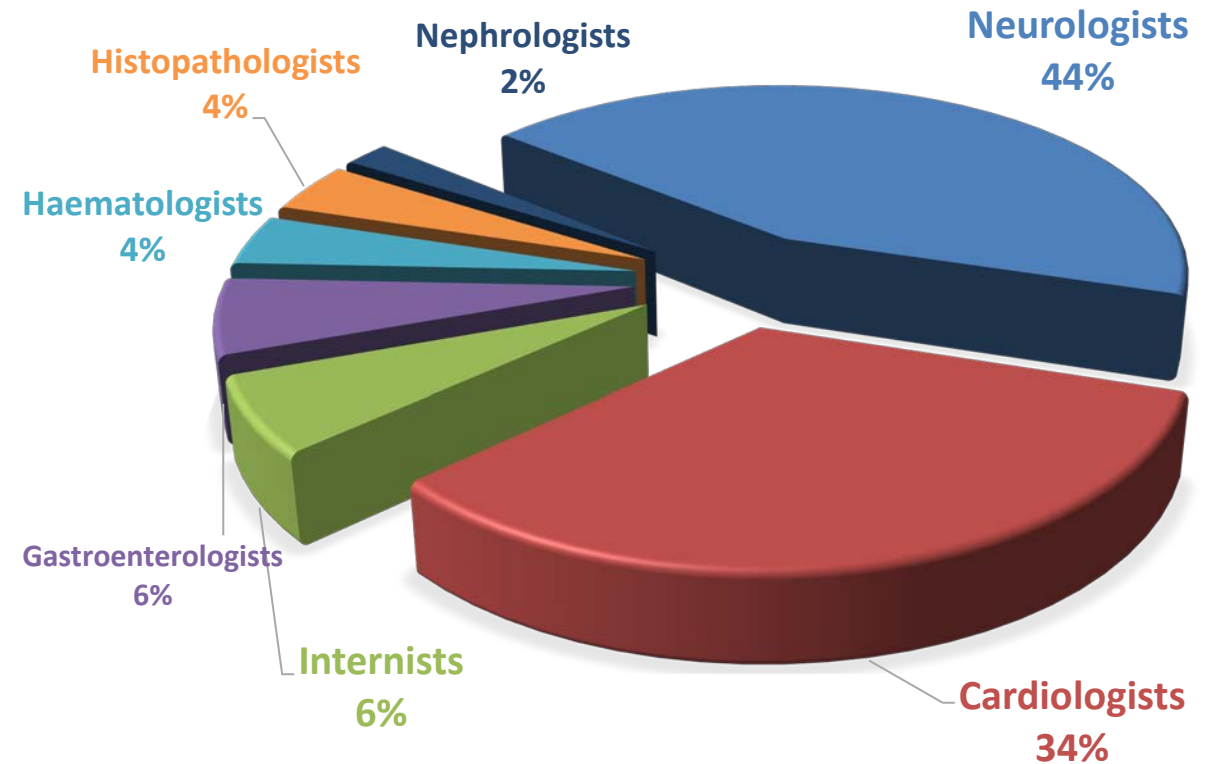
Amyloid type	Organ involvement					
	Heart	Kidney	Liver	PNS	ANS	GI
AL amyloidosis	++	++	+	+	+	+
hATTR amyloidosis	++	+	-	++	++	++
ATTRwt amyloidosis	++	-	-	±	-	-
AA amyloidosis	±	++	++	-	+	+
AApoA-I amyloidosis	+	++	++	±	-	-

Referral pathway to Pavia centre

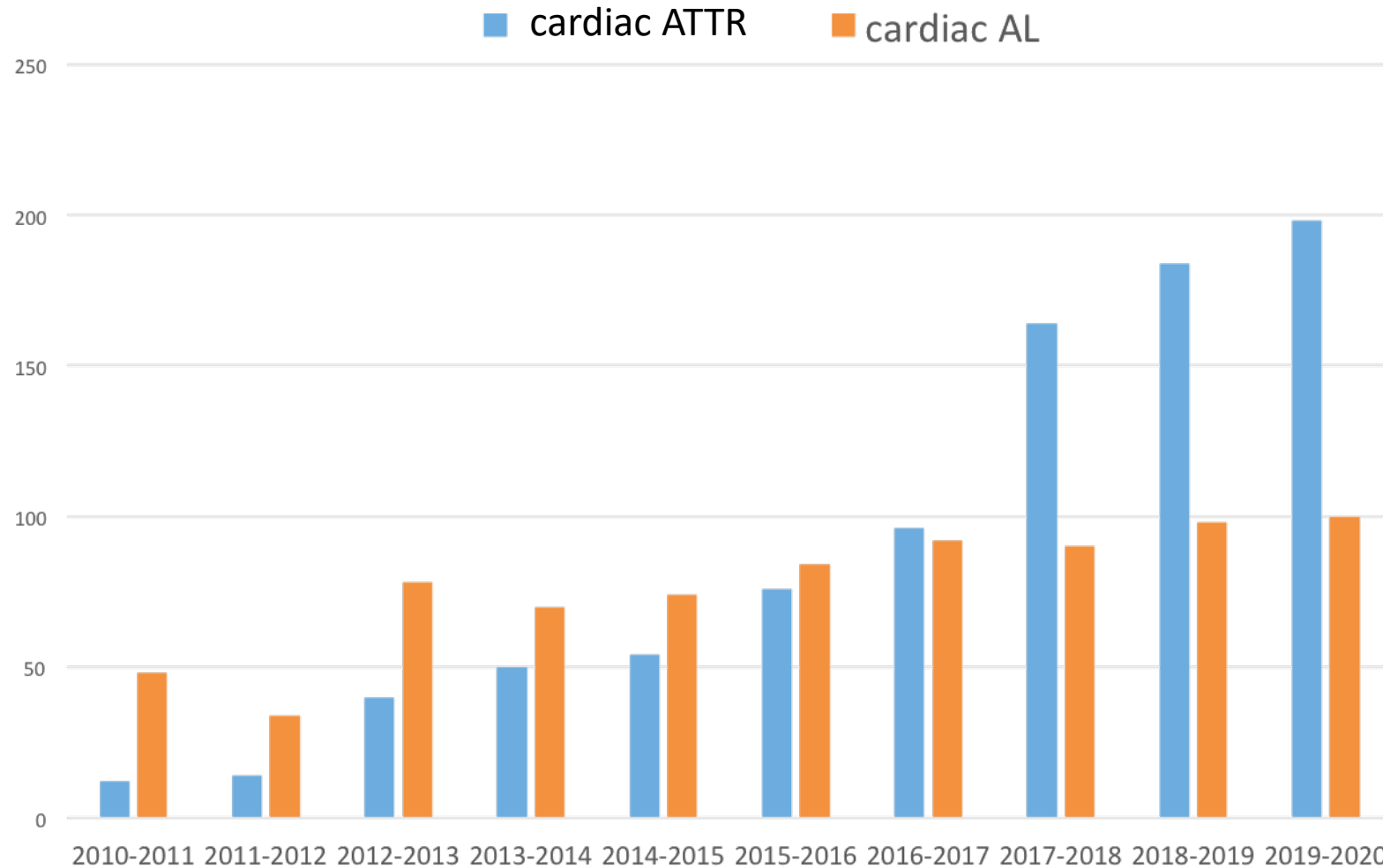
AL amyloidosis



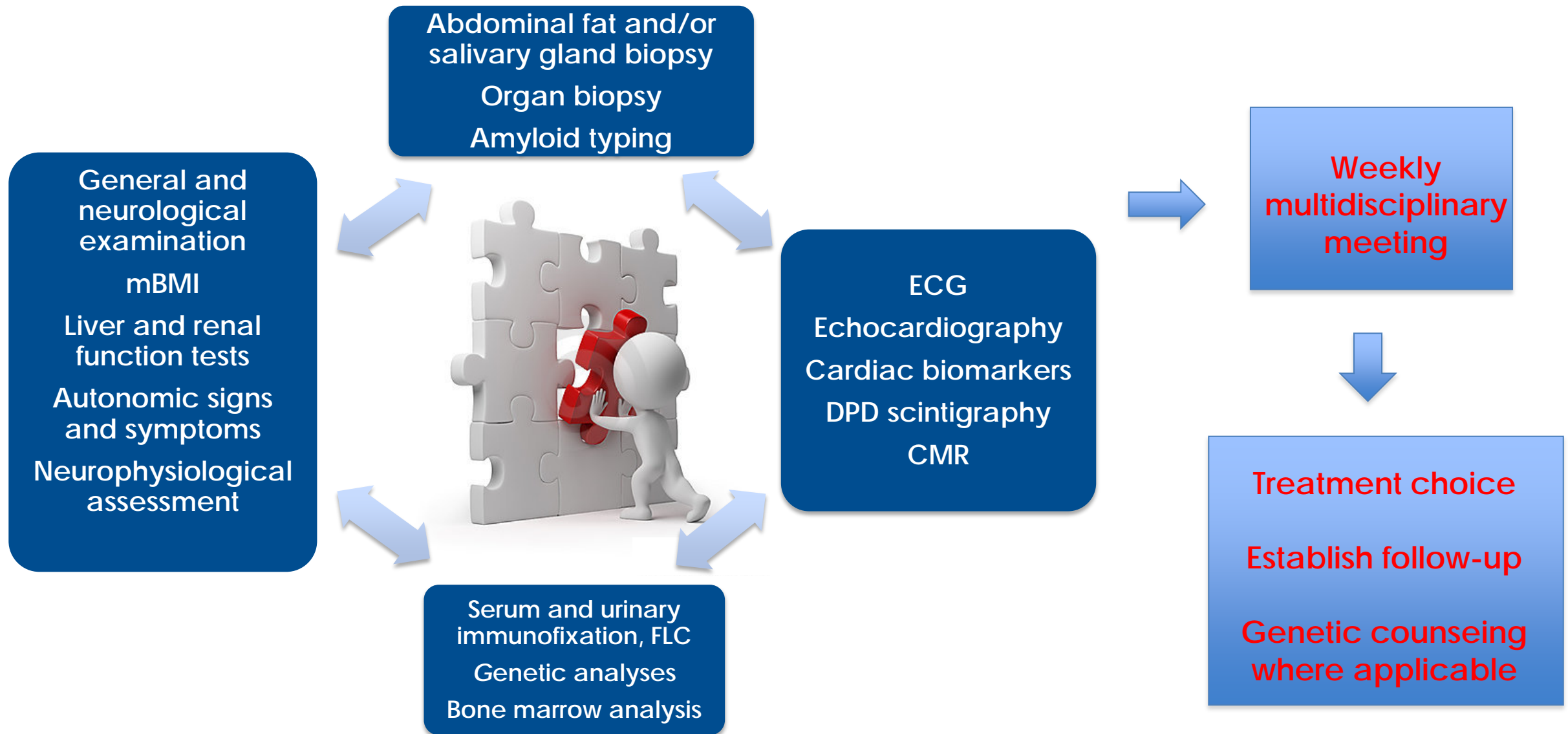
Hereditary ATTR amyloidosis



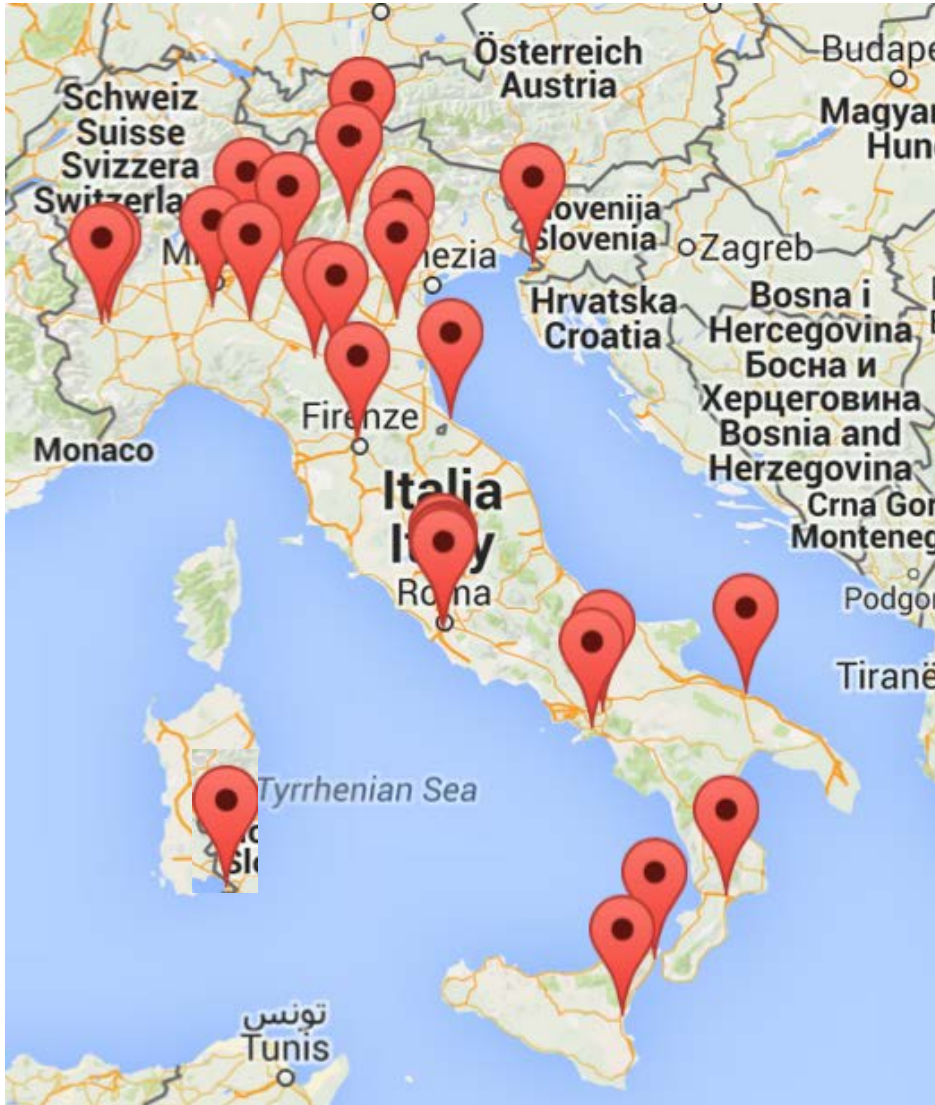
The increasing medical relevance of systemic ATTR amyloidosis



Diagnostic pathway at Pavia Amyloid Centre



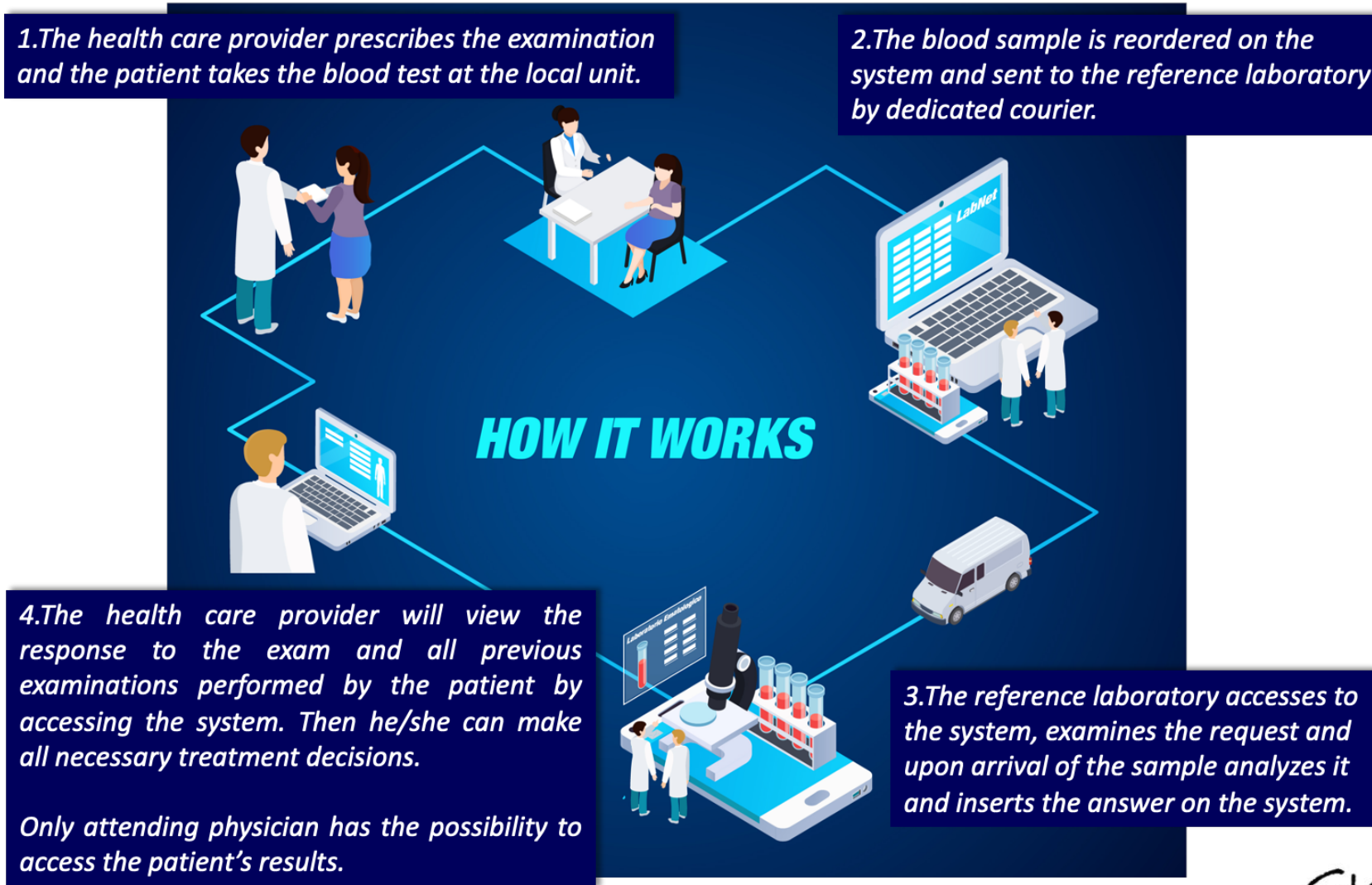
Italian Amyloidosis Study Group



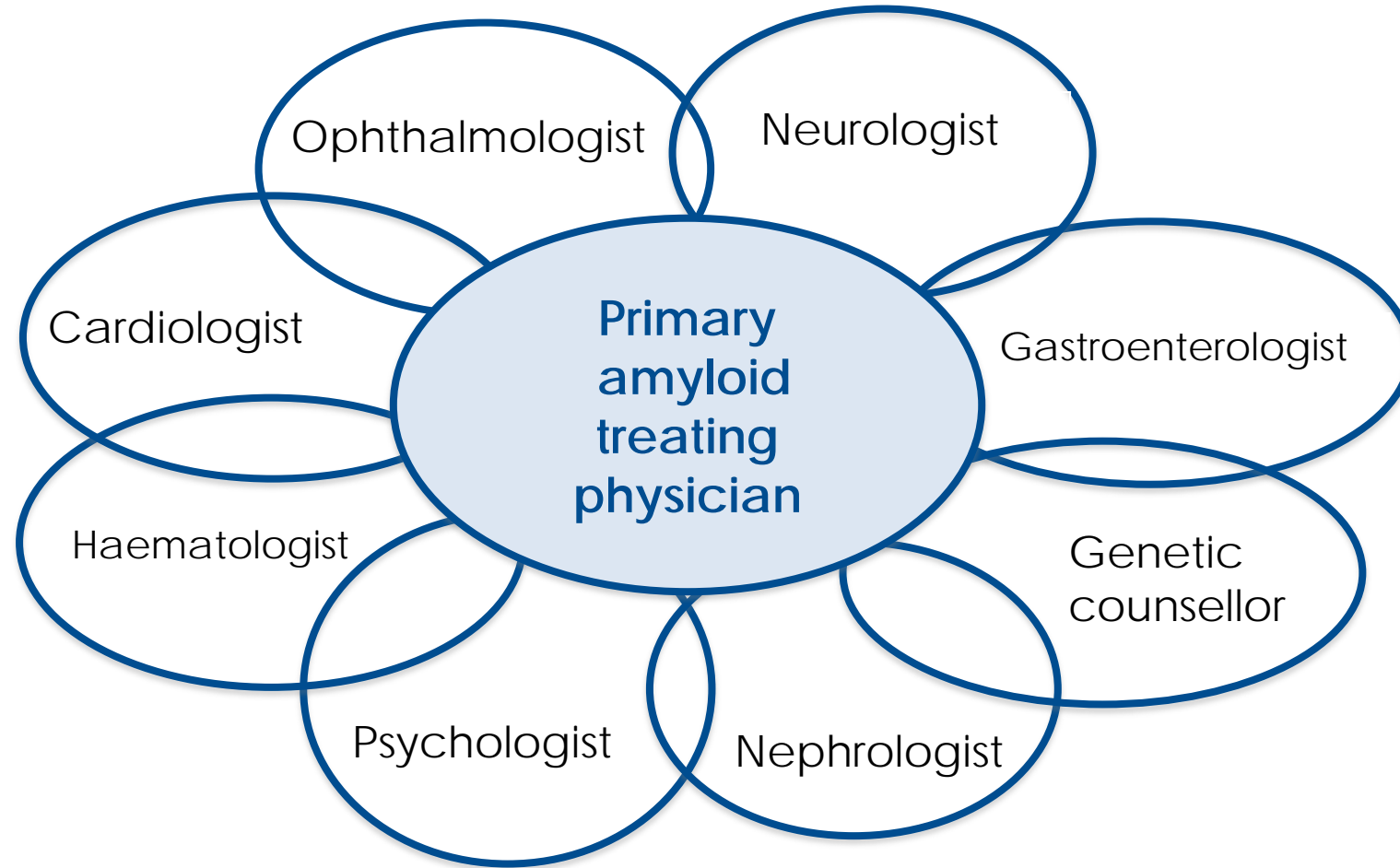
A network of > 60 clinical institutions throughout the country collaborate within the framework of the Italian Society for Amyloidosis

- Sharing common, annually updated diagnostic and therapeutic protocols
 - Making qualified care readily accessible to patients
 - Facilitating enrollment in clinical trials
-
- Participation to other Regional/National/International networks (i.e Telethon registry, ERN-RITA, ERN-EuroBloodNet)
 - Development of international clinical guidelines
 - Development of regional clinical recommendations (PDTA)
 - Collaboration with Patients' Advocacy Groups

The Italian Transthyretin Amyloidosis Web-Network (ITA-WebNet)



A multidisciplinary approach to patients and families



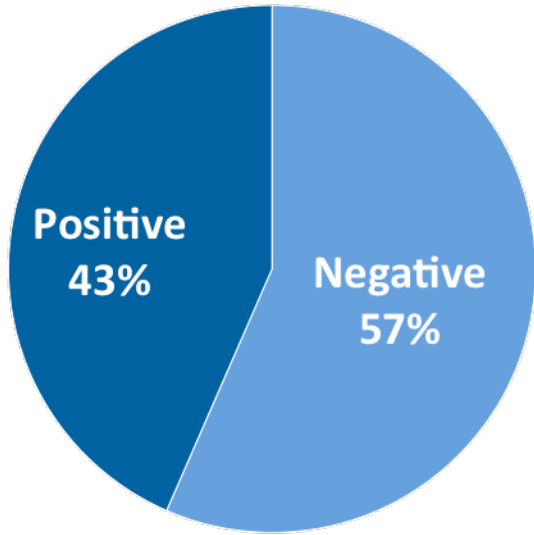
Helps patient and family intake and promotes a long-term relationship
Improves adherence to treatment and motivates follow-up in asymptomatic carriers
Increases staff skills and experience

Taking care of people with systemic amyloidosis

“Look out the other’s window. Try to see the world as your patient sees it.”
— Irvin D. Yalom, *The Gift of Therapy*



TTR pre-symptomatic testing: Pavia experience



290 presymptomatic tests performed

- 76 (27%) siblings
- 214 (73%) offspring

Median age at PST was **47 years** (range 19–86)

81/126 carriers periodically followed-up with at least one contact in the past 12 months

Once asymptomatic mutation carriers are identified, a structured follow-up will help to identify the earliest signs of the disease, allowing for prompt treatment initiation

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Giovanni Palladini
Giampaolo Merlini

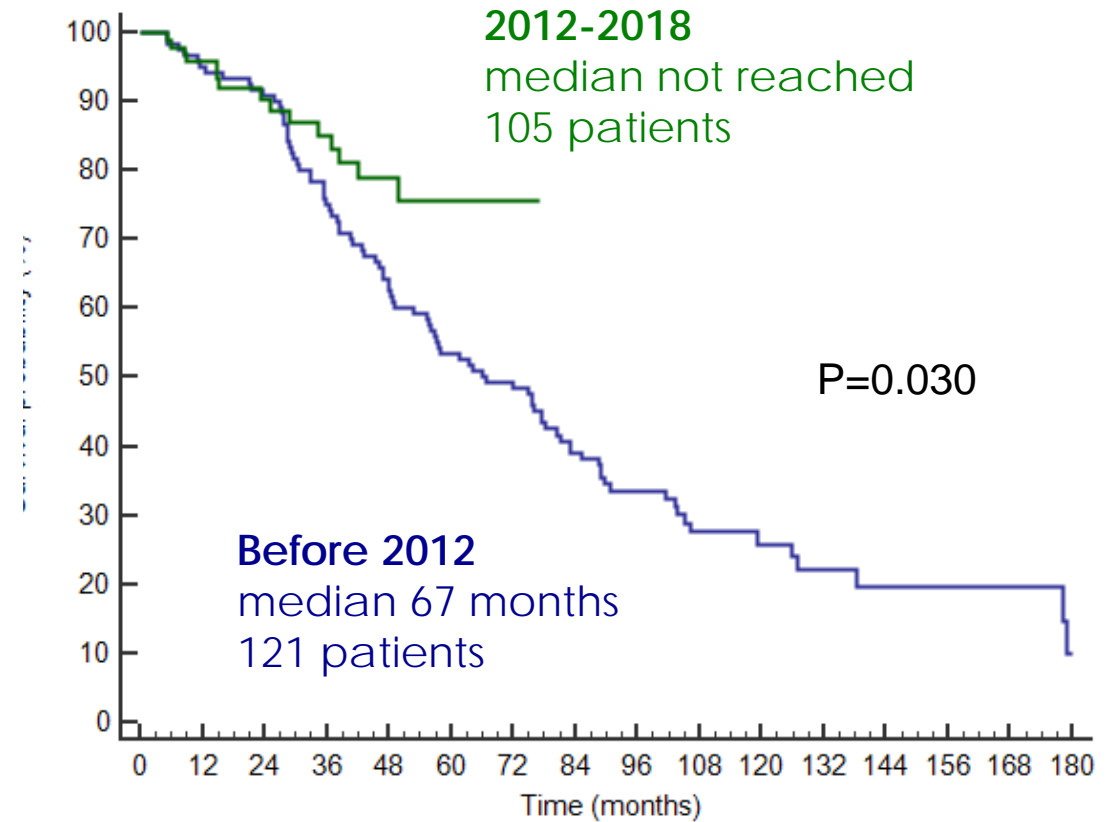
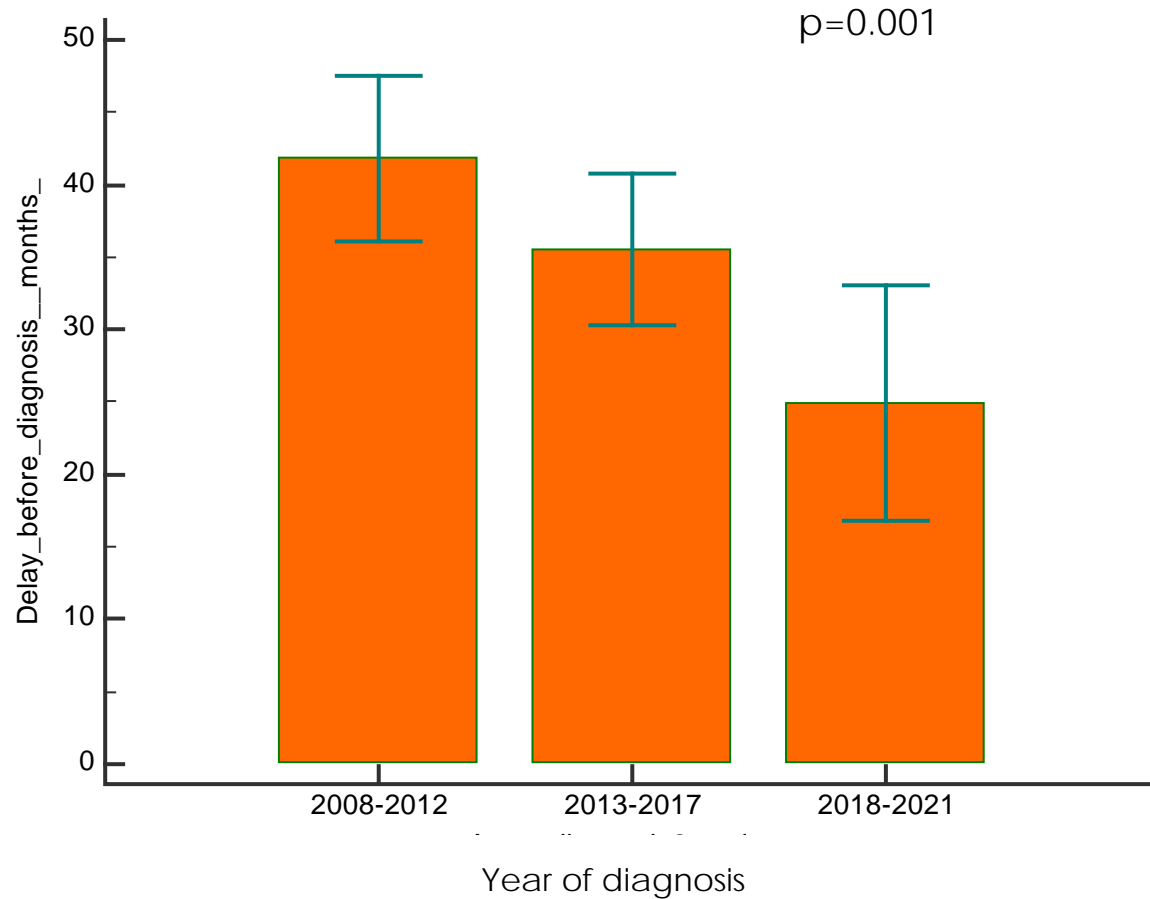
Andrea Foli
Paolo Milani
Alessandro Lozza
Roberta Mussinelli
Francesca Lavatelli
Mario Nuvolone

Marco Basset
Francesca Benigna
Stefano Perlini
Paola Rognoni
Simona Casarini
Pasquale Cascino
Margherita Bozzola
Jessica Ripepi

Alice Nevone
Anna Carnevale Baraglia
Claudia Sforzini
Elona Luka
Eleonora Di Buduo



Diagnostic delay (months) and survival in 281 patients with hATTR amyloidosis according to year of diagnosis

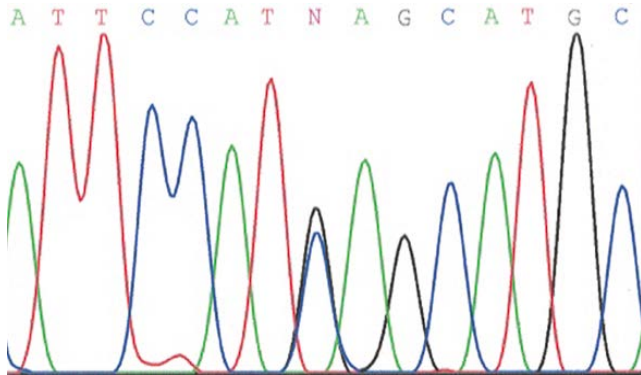


Diagnostic approach to transthyretin amyloidosis

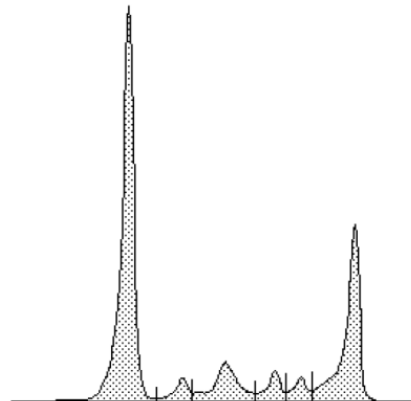
Symptoms and signs
Abnormal NCS/Abnormal echo/MRI
GI/renal function

Identify the amyloid protein

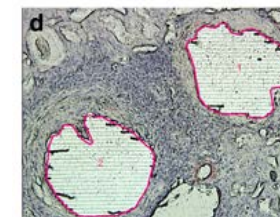
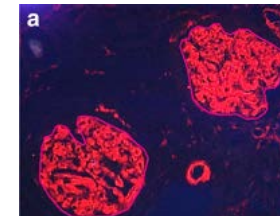
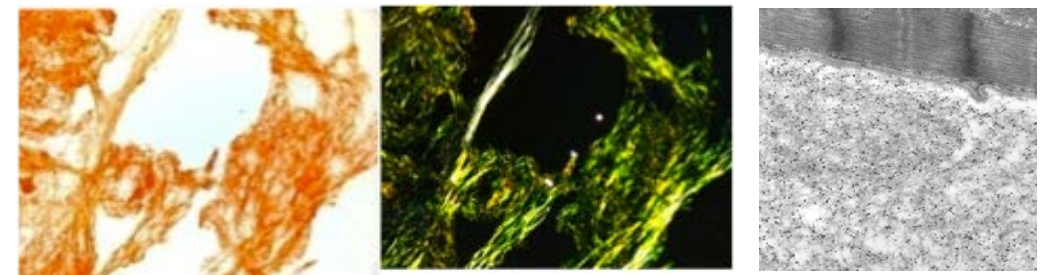
Document and type amyloid deposits



TTR gene analysis



Serum and urine
immunofixation



Probability Legend:		Patient				
over 95%	Green					
80% to 94%	Yellow					
50% to 79%	Orange					
20% to 49%	Red					
0% to 19%	Grey					
Bio View:						
Identified Proteins (517)						
Apolipoprotein E OS=Homo sapiens GR=...	36 kDa	10	10	10	10	10
Serum amyloid P-component OS=Ho...	25 kDa	19	26	11	13	12
Transthyretin OS=Homo sapiens GR=...	16 kDa	42			34	
Ig kappa chain C region OS=Homo sa...	12 kDa		31			
Serum amyloid A protein OS=Homo s...	14 kDa					
Ig lambda chain C regions OS=Homo ...	11 kDa					22
Ig lambda chain V-VI region WIT OS=...	12 kDa					13
Leukocyte cell-derived chemotaxin-2...	16 kDa			12		
Ig kappa chain V-IV region Len OS=H...	13 kDa				13	
Apolipoprotein A-1 OS=Homo sapien...	31 kDa					
Ig kappa chain V-III region SIE OS=H...	12 kDa					1
Ig kappa chain V-I region Gal OS=Ho...	12 kDa					
Vitronectin OS=Homo sapiens GR=VT...	54 kDa	35	70	21	1	8
Apolipoprotein A-IV OS=Homo sapien...	45 kDa	16	6		63	5
Actin, aortic smooth muscle OS=Hom...	42 kDa	26	4	15	41	14
Serum albumin OS=Homo sapiens GR=...	69 kDa	26	13	12	55	1
Collagen alpha-3(VI) chain OS=Homo ...	344 kDa	32			23	9
Collagen alpha-1(I) chain OS=Homo s...	139 kDa	21	8	11	9	7
Collagen alpha-2(I) chain OS=Homo s...	129 kDa	16	8	13	10	8
Clusterin OS=Homo sapiens GR=CLU ...	52 kDa	11	17	6	6	3
Vimentin OS=Homo sapiens GR=VIM ...	54 kDa	24	2	3	5	3
Pyoxin-7 OS=Homo sapiens GR=PYX...	223 kDa	17				40
Desmin OS=Homo sapiens GR=DES PE...	54 kDa	3			18	15
Katanin p60 ATPase-containing subun...	55 kDa	3	2	1	3	2
Complement C3 OS=Homo sapiens GR...	187 kDa	17				
Filamin-A OS=Homo sapiens GR=FLNA_HUMAN	281 kDa	1			16	
Cartilage intermediate layer protein ...	133 kDa	19				
Actin, cytoplasmic 1 OS=Homo sapien...	42 kDa	10	4	6	5	1
Collagen alpha-1(VI) chain OS=Homo ...	109 kDa	4	2	2	2	1
Collagen alpha-1(III) chain OS=Homo...	139 kDa					

Free light chains
(FLC) measurement