Euro-HSP
Federation of European HSP Associations

Disease Alliance of Italian Spastic paraplegia researchers for You

“Daisy”, the Italian HSP database

Euro-HSP Annual Meeting June 17, 2017
Alghero (SS) Italy

Hereditary spastic paraparesis (Strümpell-Lorrain)

Hereditary spastic paraparesis is a genetically heterogeneous disorder of the CNS of which slowly increasing spastic paraparesis is the pivotal clinical hallmark

R.P.M.Bruyn and PH.Scheltens

Handbook of Clinical Neurology, Vol. 15 (59), 1991

Strümpell, A.: Beiträge zur Pathologie des Rückenmarks. Arch. Psychiatr. Nervenkr. 10 (1880) 676-717

Strümpell, A.: Über eine bestimmte Form der primären combinierten Systemerkrankung des Rückenmarks. Arch. Psychiatr. Nervenkr. 17 (1886) 217-238

Lorrain, M: Contribution a l'étude de la paraplégie spasmodique familiale. Thesis. Steinheil, Paris (1898)

664

Pazients harboring *SPAST/SPG4* mutations

>97

Families

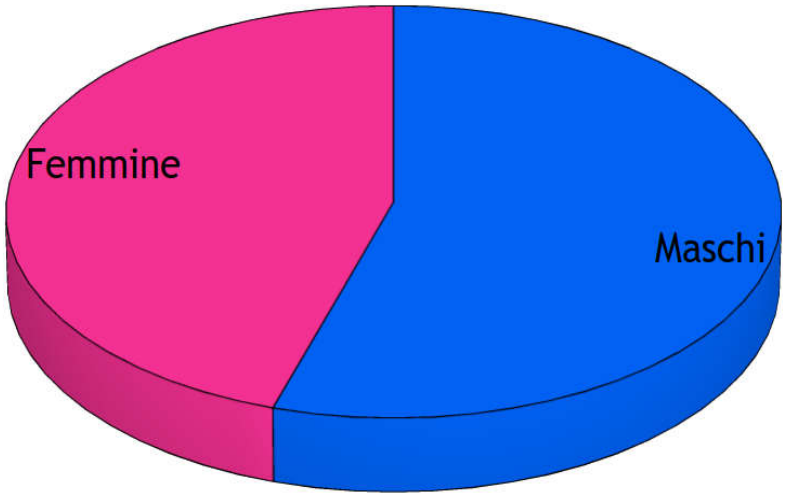
Gender and Onset distribution

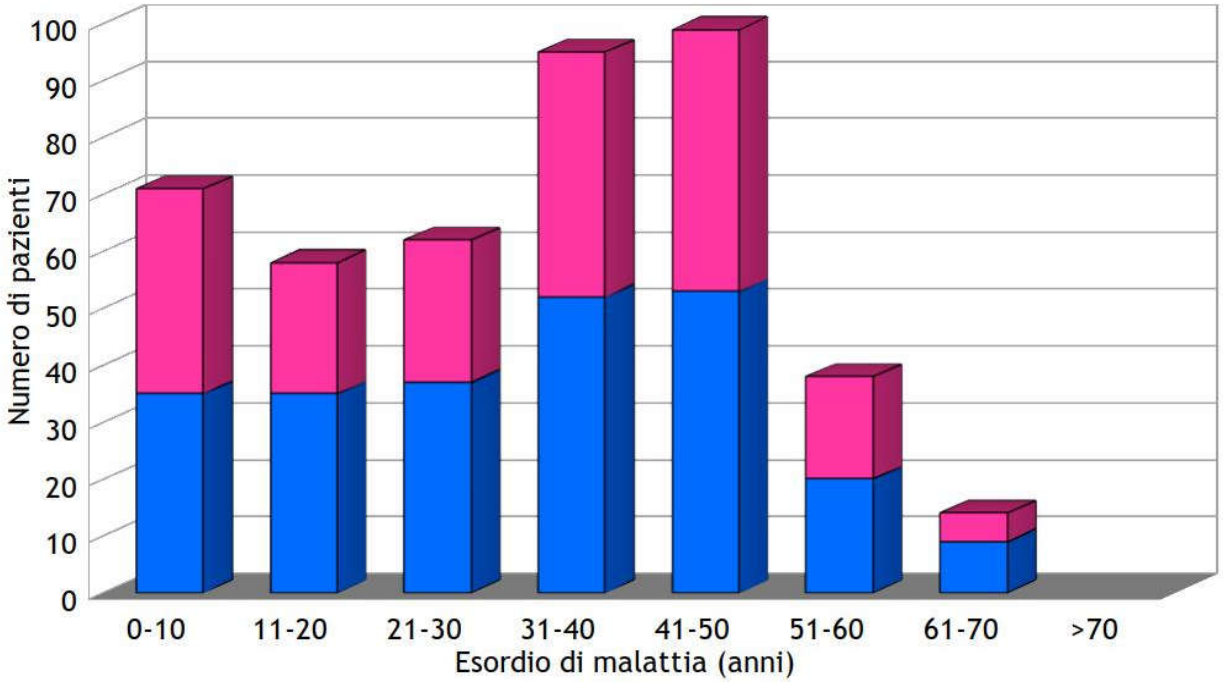
- M/F ratio

  54,79%

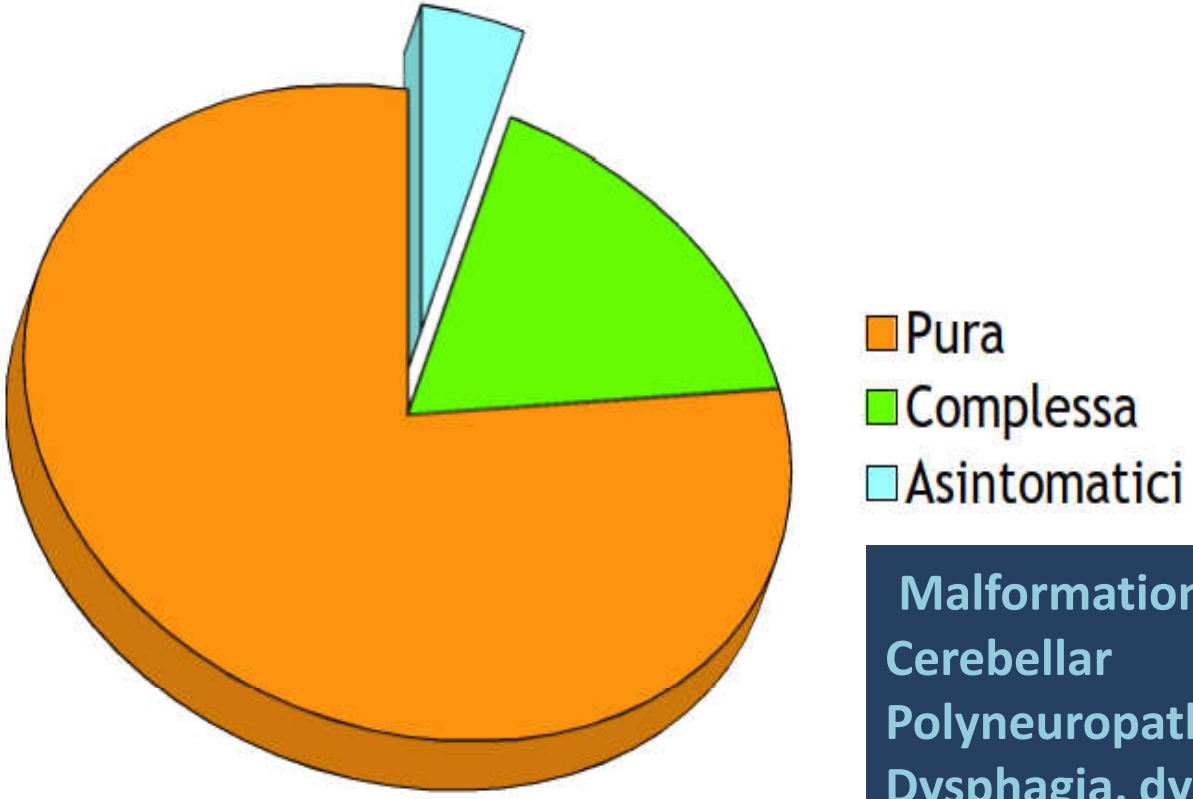
- Bimodal distribution

  <10 yrs
  30-50 yrs



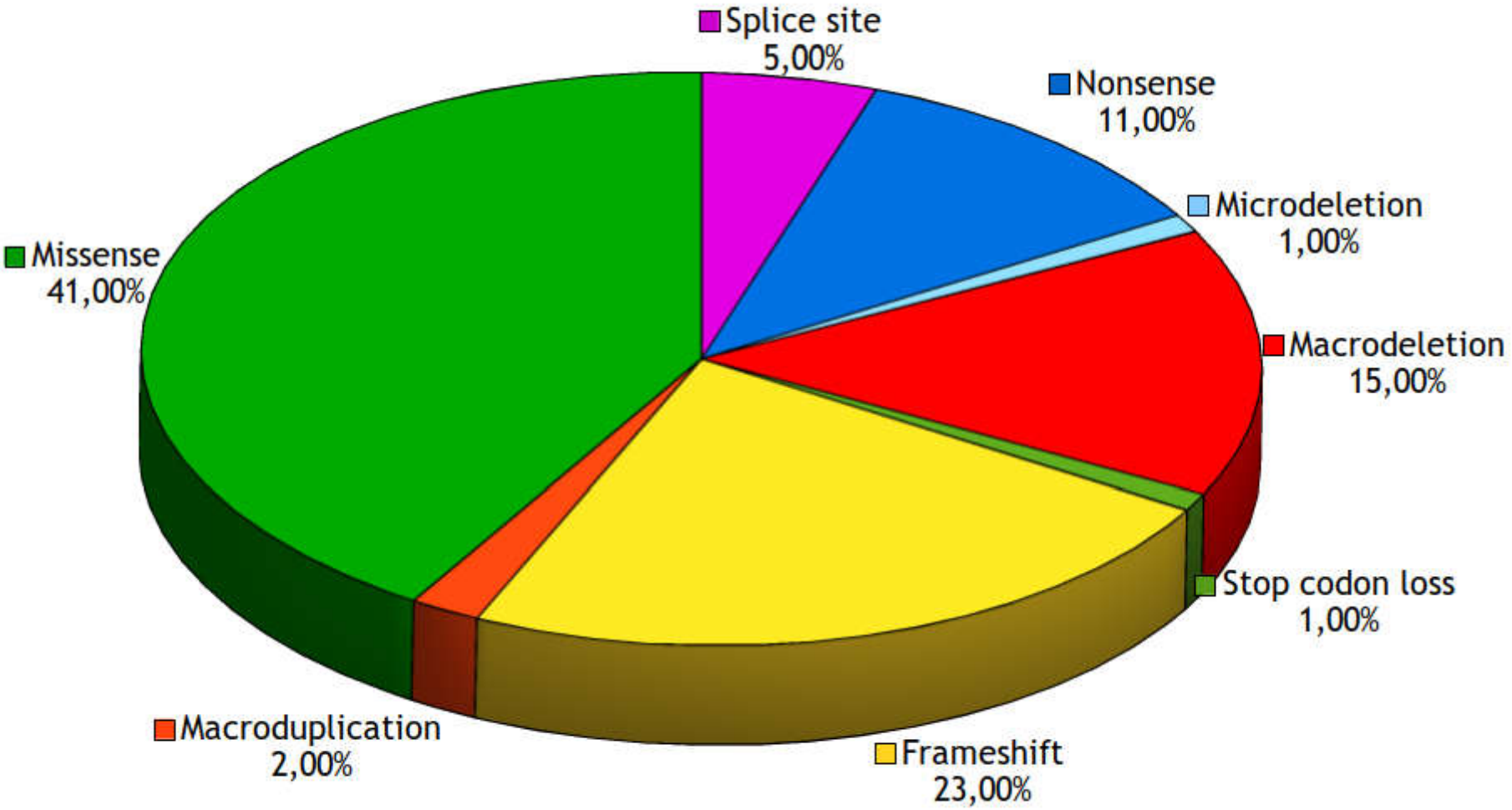


Clinical presentation

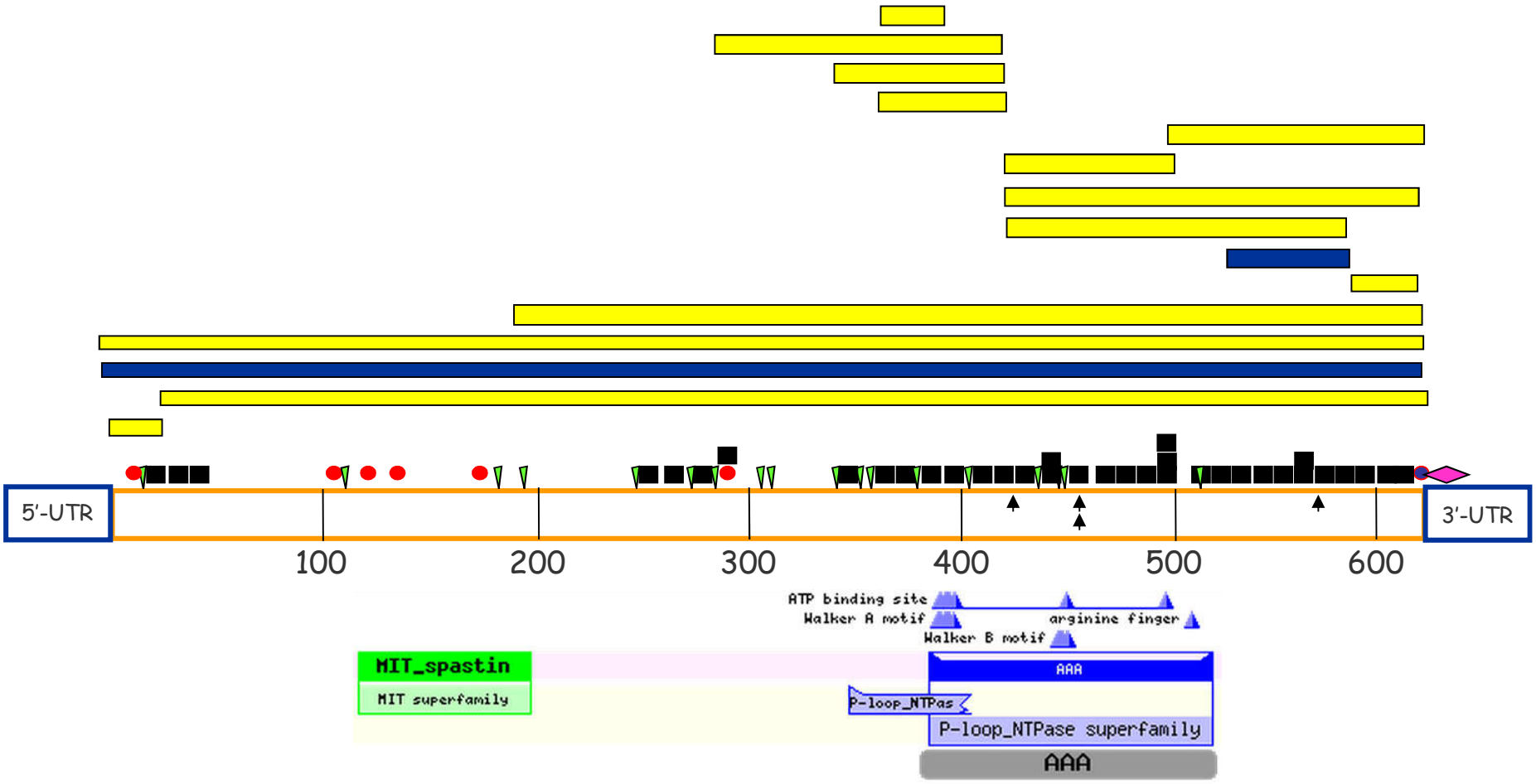


Malformations
Cerebellar
Polyneuropathy
Dysphagia, dysarthria
Delayede psichomotor milestones
Cognitive
Epilepsy

SPAST/SPG4 gene: **142** identified variants



Morbidity Map



Missense

Nonsense

Frameshift

MacroDeletion

MacroDuplication

Splice-site

UTR/micro

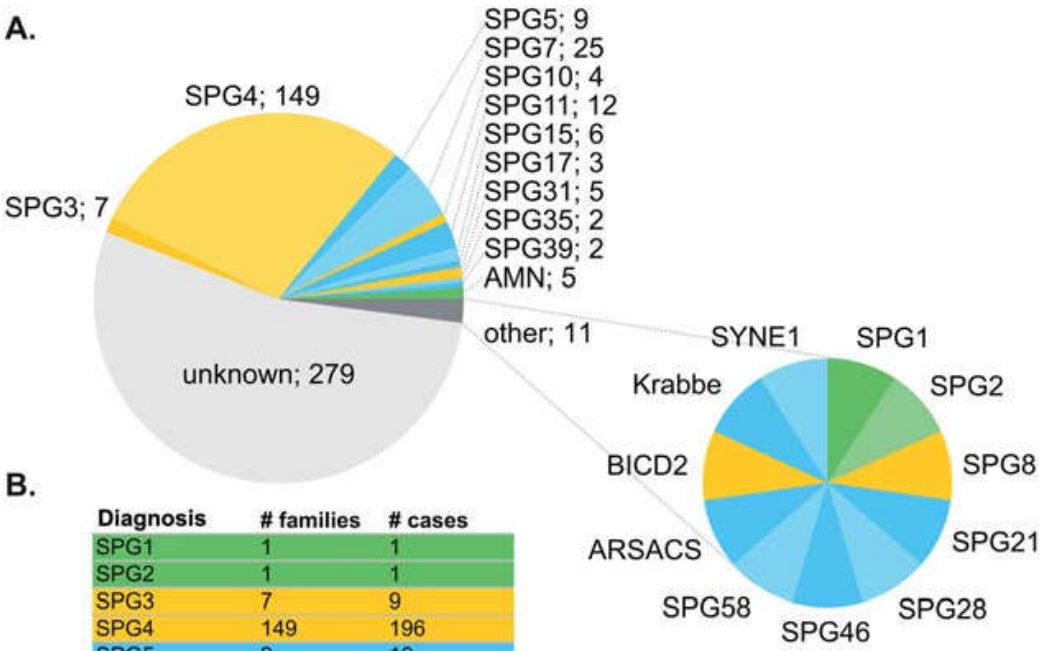
Stop Codon Loss

Hereditary spastic paraplegia: Clinicogenetic lessons from 608 patients

Schüle et al Annals of Neurology, 2016

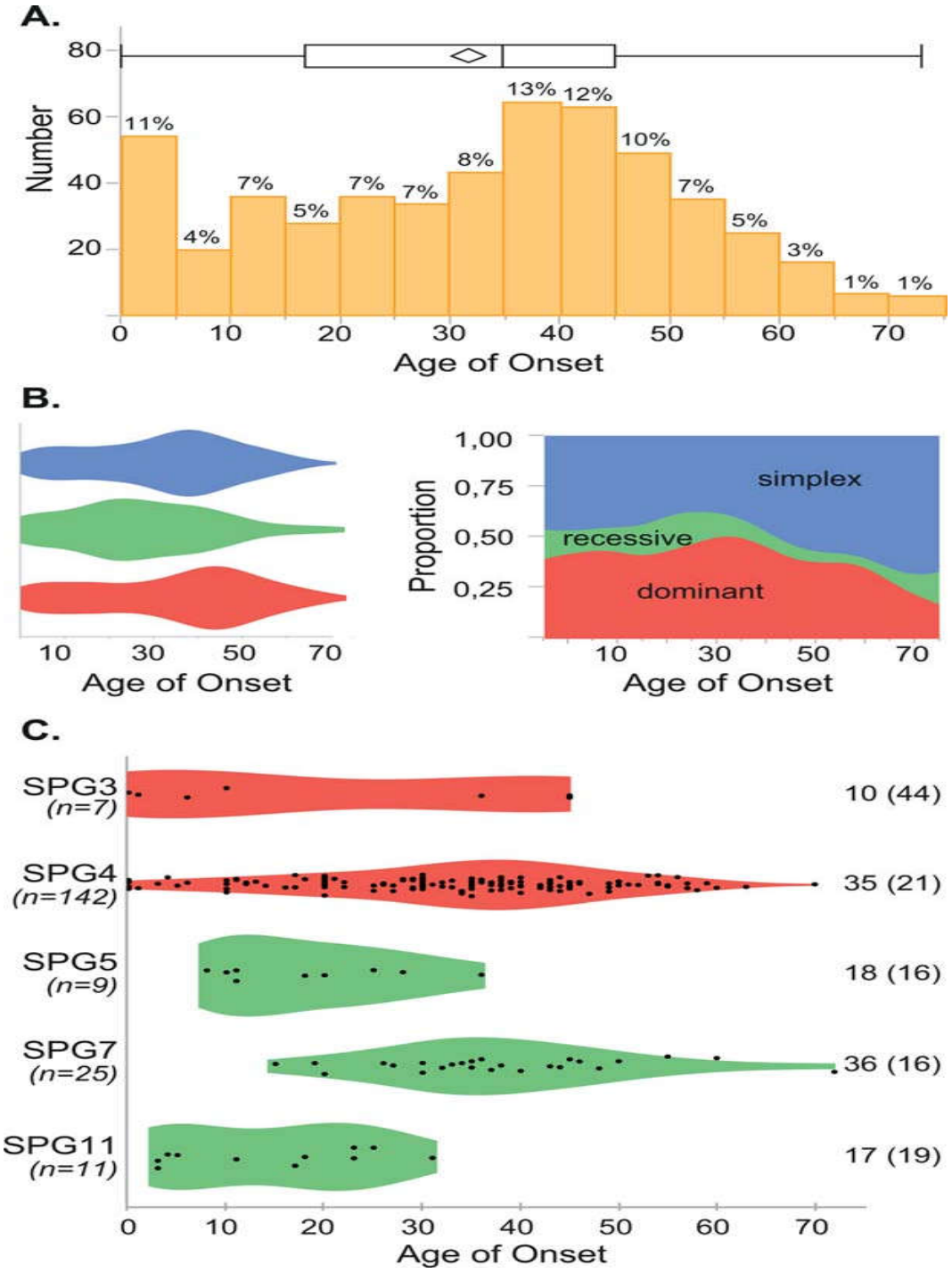
Cohort of 608 pazients with HSP - 519 index cases

- 196 SPG44 di SPG4 (149 IC)
- Others: SPG7, 15, 10, 3.
- 279 pazients without molecular diagnosis



B.

Diagnosis	# families	# cases
SPG1	1	1
SPG2	1	1
SPG3	7	9
SPG4	149	196
SPG5	9	10
SPG7	25	28
SPG8	1	1
SPG10	4	5
SPG11	12	15
SPG15	6	7
SPG17	3	3
SPG21	1	2
SPG28	1	1
SPG31	5	5
SPG35	2	2
SPG39	2	2
SPG46	1	1
SPG58	1	1
AMN	5	5
ARSACS	1	1
BICD2	1	1
Krabbe disease	1	1
SYNE1	1	1


A.
Number
80
60
40
20
11%
4%
7%
5%
7%
7%
8%
13%
12%
10%
7%
5%
3%
1%
1%
0
10
20
30
40
50
60
70
Age of Onset
B.
10
30
50
70
Age of Onset
Proportion
1,00
0,75
0,50
0,25
simplex
recessive
dominant
10
30
50
70
Age of Onset
C.
SPG3
(n=7)
10 (44)
SPG4
(n=142)
35 (21)
SPG5
(n=9)
18 (16)
SPG7
(n=25)
36 (16)
SPG11
(n=11)
17 (19)
0
10
20
30
40
50
60
70
Age of Onset

Future challenges:

- Clinical data
  - Intrafamilial variability
  - Modifying factors
    - Genetic
    - Non genetic
- Assessing efficacy of treatments
  - Clinical trials
  - Rehabilitation protocols
- Building european network
  - Assessing epidemiological data across countries