EPILEPSY WITH AUDITORY FEATURES (EAF): long-term outcome in a large cohort
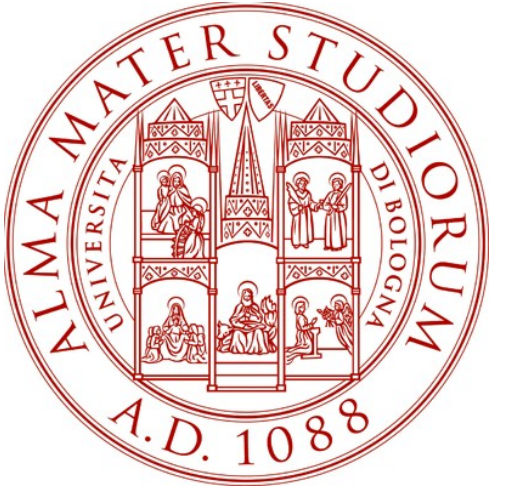
Bisulli F[1,2], Menghi V[1,2], Stipa C[1,2], Gizzi M[2], Vignatelli L[1,2], Licchetta L[1,2], Leta C[1,2], Tinuper P[1,2]

[1] IRCCS Institute of Neurological Sciences of Bologna, Italy
[2] Department of Biomedical and Neuromotor Sciences, University of Bologna, Italy

Purpose:
- To define the outcome of EAF in terms of 5-year seizure freedom rate (Terminal Remission, TR)
- To identify possible prognostic factors

Methods:

Inclusion criteria
- Diagnosis of EAF → clinical history of at least 2 lifetime seizures with auditory and/or aphasic features as first symptoms
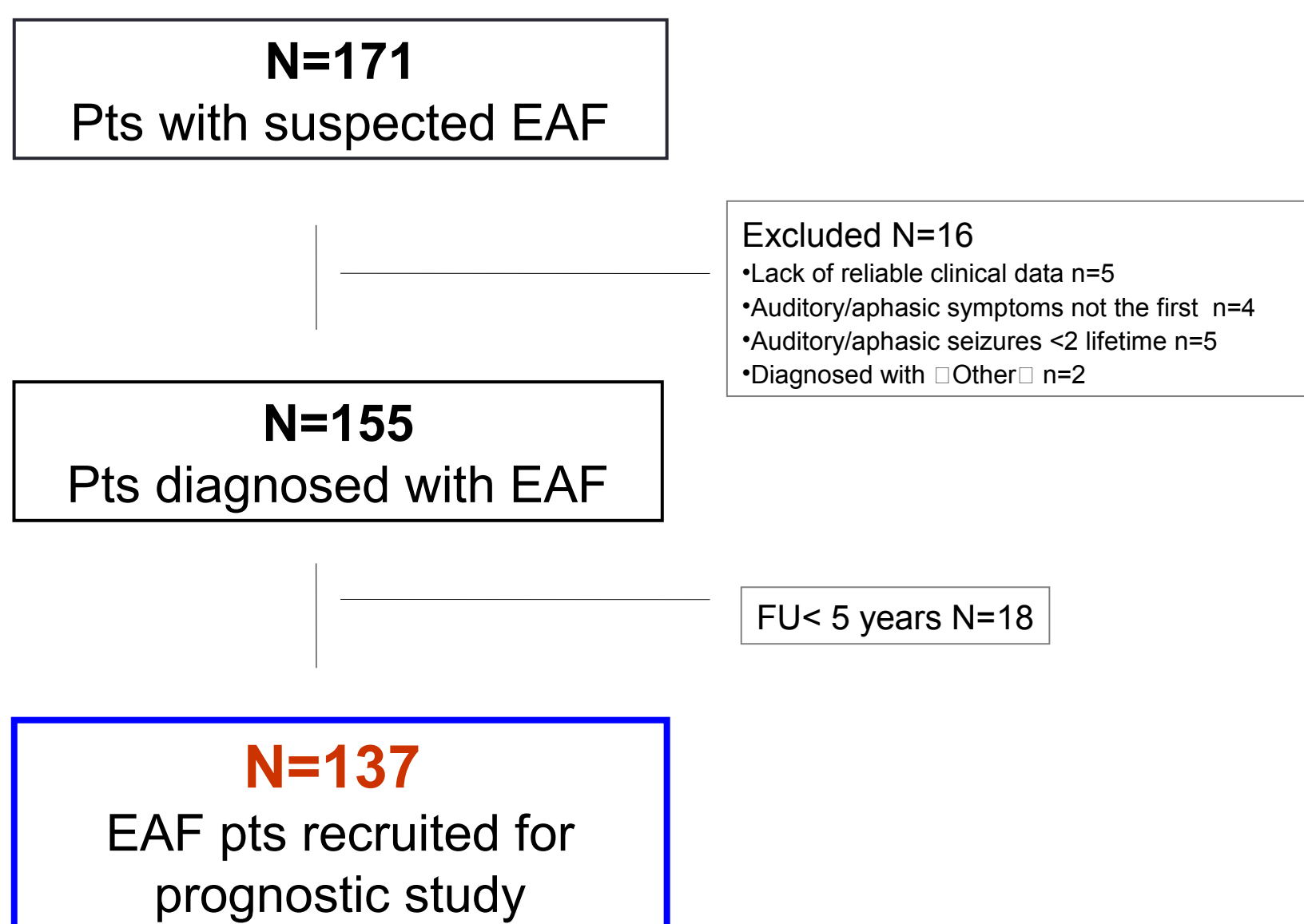- Follow-up period ≥ 5 years

Primary endpoint → 5-year SF at last follow-up (Terminal Remission)

Study design: cohort-study **Recruitment:** prospective (since 2001)/retrospective
Participants and setting/eligibility criteria: patients of any gender and age, referred between 1975 and 2016 to our Epilepsy Center with a history of epileptic seizures with auditory and/or aphasic features
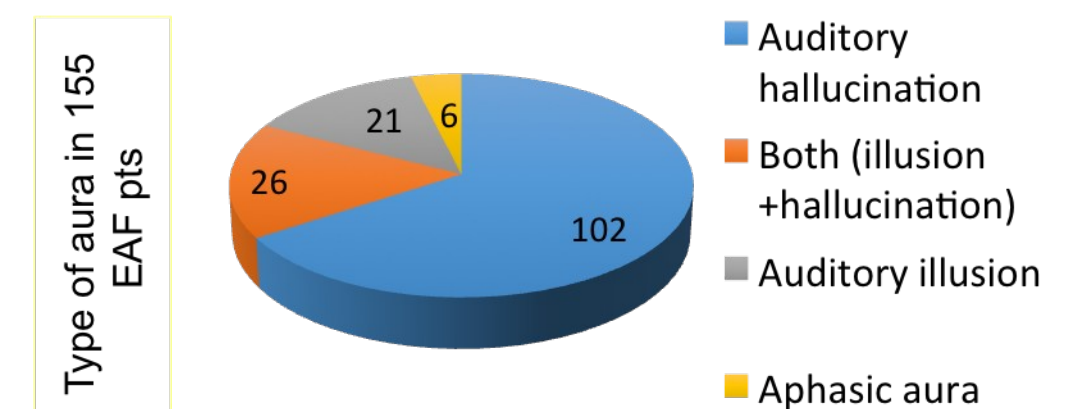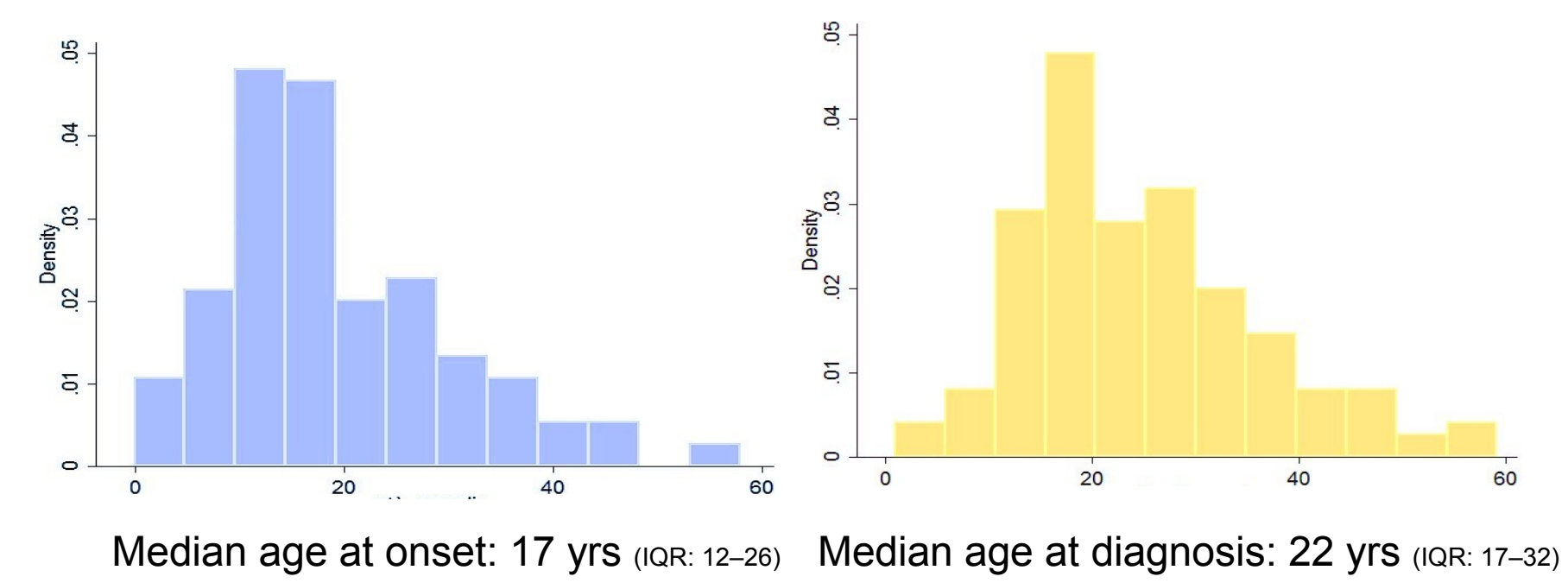**Data collection:** semi-structured interview (direct/telephonic) from Dec, the 1st 2014 to July, the 8th 2016 and review of medical records (last visit recorded)

Results:

N=171
Pts with suspected EAF

Excluded N=16
- Lack of reliable clinical data n=5
- Auditory/aphasic symptoms not the first n=4
- Auditory/aphasic seizures <2 lifetime n=5
- Diagnosed with □Other□ n=2

N=155
Pts diagnosed with EAF

FU< 5 years N=18

N=137
EAF pts recruited for prognostic study

Clinical features of 155 EAF pts			Valid %
Male			47%
Negative family history of epilepsy			*83%*
Etiology	Structural	Focal cortical lesions	12.3%
		Gross/Multiple Abnormalities	3.2%
	Genetic		9%
	Unknown		*75.5%*
Personal history	Developmental delay		0.6%
	Intellectual disability		*1.3%*
	Febrile Seizures		11%
Low seizure frequency at onset			*78.7%*
Bilateral convulsive seizures			*84.5%*
Seizures in sleep			53%
Interictal EEG	Epileptiform		35%
	Normal or Aspecific		*65%*
AED ≥ 2			*28.4%*
Surgical treatment			6.5%
Relapse after drug withdrawal			*78.7%*

Diagnostic delay in 81/155 pts: median 5 yrs
For no medical counseling (42) or misdiagnosis (39)

Median age at onset: 17 yrs (IQR: 12–26)   Median age at diagnosis: 22 yrs (IQR: 17–32)

Type of aura in 155 EAF pts:
- Auditory hallucination — 102
- Both (illusion +hallucination) — 26
- Auditory illusion — 21
- Aphasic aura — 6

Prognostic study on 137 pts:
- Mean of follow-up duration: 19 yrs
- M:F=64:73
- Median age at last follow-up: 42 yrs
- Mean age of seizure remission: 35.4±12.7 yrs

Cumulative time-dependent TR rate:
50% after a 40-year f-u

50.1%
24.4%

% of remission — Follow-up (years) from disease onset

Univariate analysis (Log-rank test)

Age at seizures onset (p= 0.003)   Seizure frequency at onset (p 0.018)

Auditory aura (p 0.018)   Any underlying brain disorder* (p 0.023)
*pathological NE or positive MRI or ID
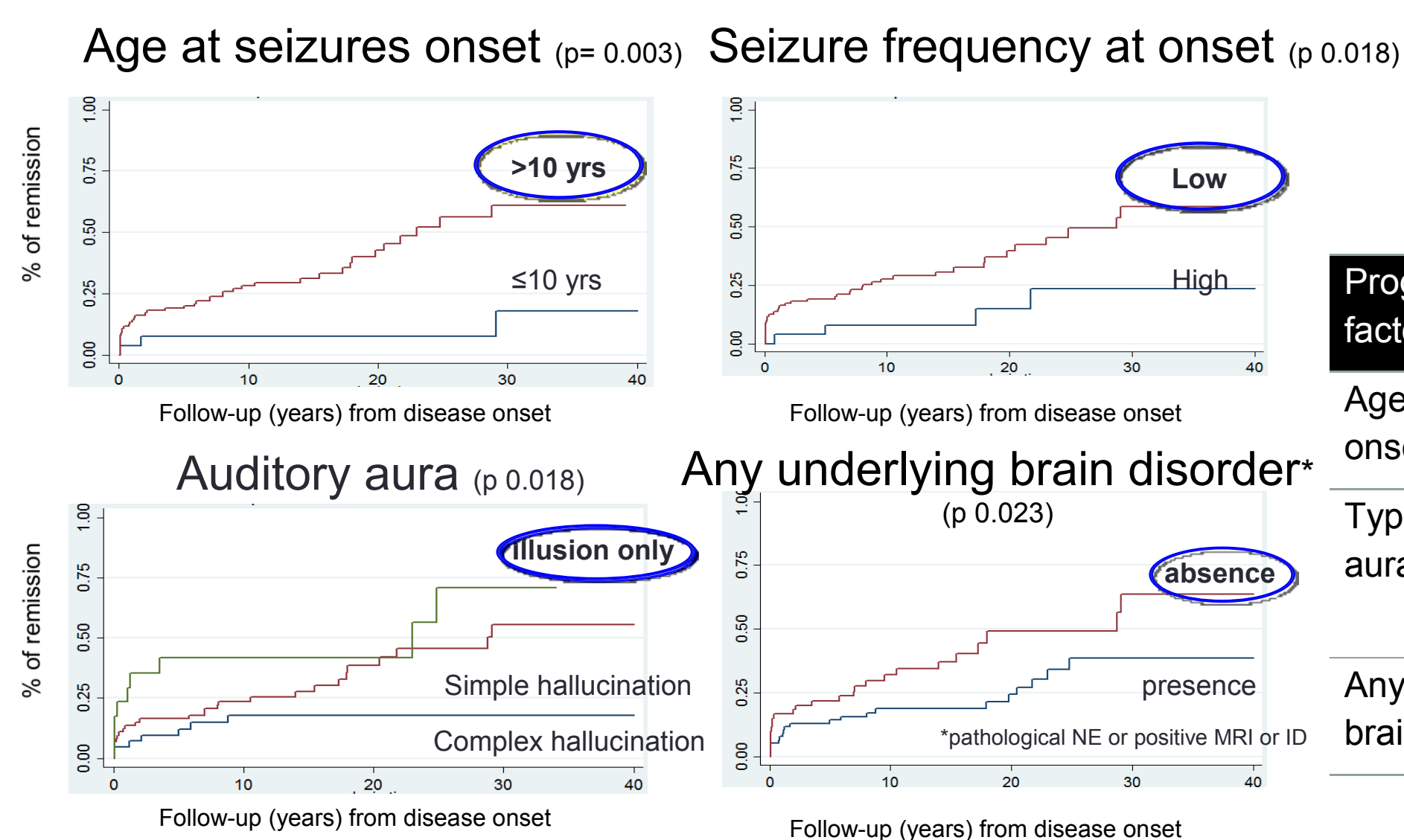
Multivariate analysis

Prognostic factors		HR adjusted (95% CI)	p-value
Age at seizures onset	<10 yrs	ref.	0.012
	>10 yrs	4.5 (1.4-14.3)	
Type of auditory aura	Complex hallucination	ref.	0.004
	Simple hallucination	2.2 (0.9-5.3)	
	Illusion only	4.1 (1.6-10.8)	
Any underlying brain disorder*	Presence	ref	0.039
	Absence	3.2 (1.1-9.5)	

Conclusion: prognostic features of EAF

- Cumulative Terminal Remission (TR) rate   → ≅ 25% after 10 yrs of follow-up
  → 50% after 40 yrs of follow-up

- Positive predictors of TR (multivariate analysis)   → age at onset > 10 yrs
  → absence of any underlying brain disorder
  → auditory illusions

Diagnostic delay not associated with increased risk of NTR