

S Cheng, R Li, KL Shiu, E Yeung, CN Lee, M AuYeung, CM Cheung

Department of Medicine, Pamela Youde Nethersole Eastern Hospital, Hong Kong



## Correspondence

Dr. Stephen Cheng  
PYNEH, Hong Kong  
Email: coronis\_@hotmail.com

## Background

Multiple sclerosis (MS) and neuromyelitis optica spectrum disorders (NMOSD) are now recognized as clinically distinct entities with different prognoses and management strategies. In recent years, there has been raised awareness to these CNS demyelinating diseases in Hong Kong, and cases of clinically isolated syndrome (CIS) were monitored more closely.

In 2013, we reported the local conversion rates of MS and NMO as 32% and 12% respectively. With the 2015 revised Wingerchuk criteria and better diagnostic approaches, we conducted this study to review the latest conversion rate of CIS in Hong Kong. We specifically target cases with a disease duration of at least 5 years, and analyzed their mid to long term outcome. We also had a subgroup analysis to compare with risk factors and outcome of MS and NMOSD.

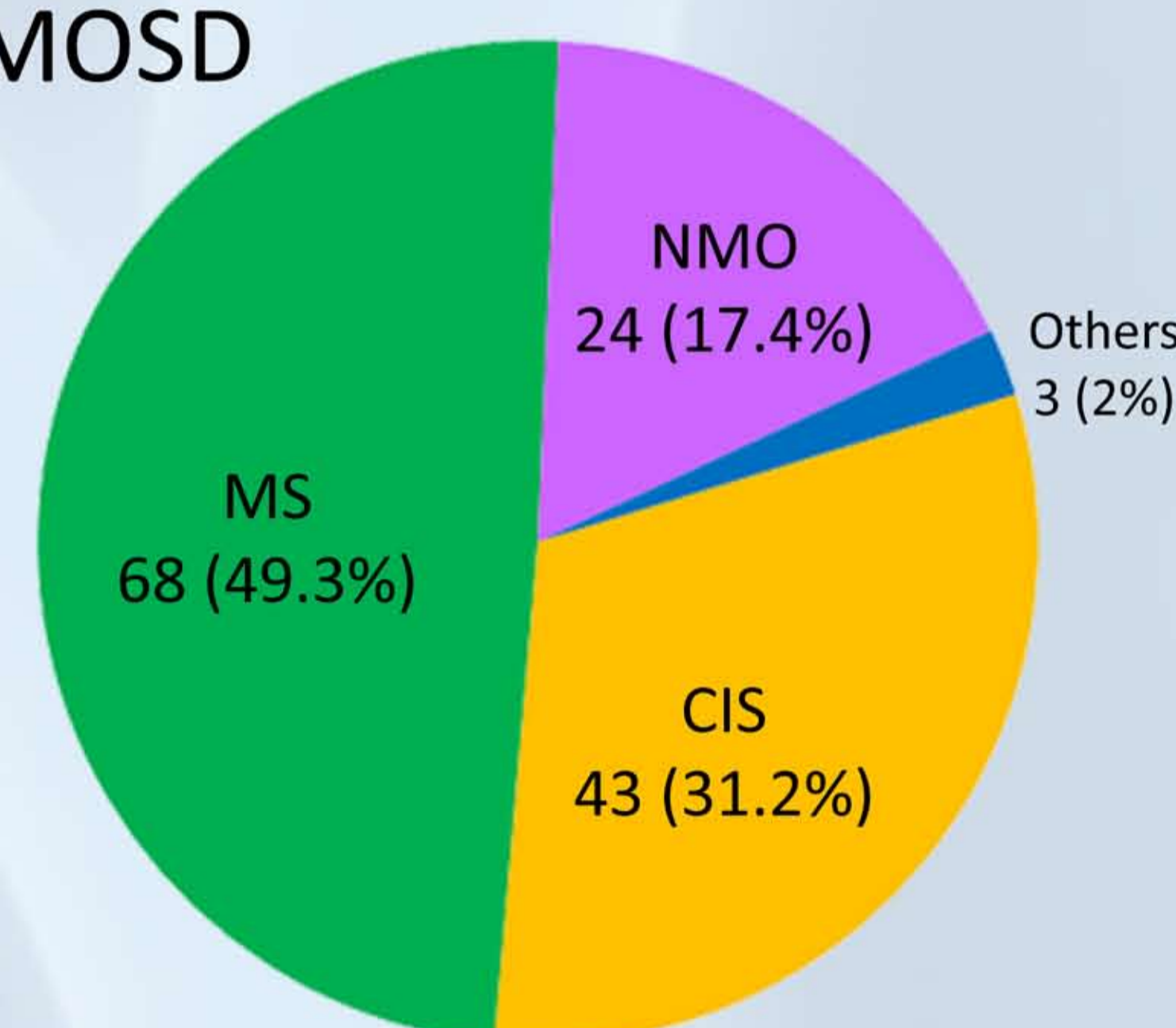
## Methods

Between 1996 and 2017, all patients with CIS who have been followed in **Pamela Youde Nethersole Eastern Hospital**, a Hong Kong tertiary hospital, with a disease duration of at least 5 years were recruited. They were analyzed based on their most updated diagnosis and clinical status as of September 2017, applying the **2010 McDonald Criteria** and the **2015 revised Wingerchuk Criteria**.

## Results

Total of **138** CIS patients were identified. After a median disease duration of 129 months, 92 have converted to MS or NMOSD

- ❖ Monophasic disease: 43
- ❖ Converted: 92 (MS: 68, NMOSD: 24 <seropositive=14>)
- ❖ Recurrent optic neuritis: 2
- ❖ 1 case revised as CLIPPERS  
(Chronic lymphocytic inflammation with pontine perivascular enhancement responsive to steroids)



Overall conversion rate: 66.7%

### Key findings:

- higher conversion change if young age and first CIS was myelitis ( $p < 0.01$ )
- less likely to convert if 1st CIS was optic neuritis ( $p = 0.04$ )
- no significant difference in mortality, EDSS at 5 years and proportion that are walking aid dependent ( $EDSS \geq 6$ )
- more likely convert into MS if young and 1st CIS was brain syndrome
- more likely convert into NMOSD if 1st CIS was ON
- time to conversion (diagnosis) significantly longer for NMOSD

7 NMOSD patients were previously labelled and treated as MS

### Treatment:

No CIS cases received immunotherapy. 43 (63.2%) MS patients and 19 (79.2%) NMOSD patients have been on immunomodulation.

## Discussion

The revised 2015 Wingerchuk criteria expanded the spectrum of NMOSD, encompassing more seronegative cases which did not fulfill the previous criteria. It was therefore not surprising that the conversion rate of NMOSD has increased from 12% to **17%** in our center. However, it was striking to note that the MS conversion rate has risen from 32% to **49%**, which was comparable to those reported in the placebo arm of previous interferon studies (ETOMS: 45%, CHAMPS: 37%, BENEFIT 45%). This was likely due to the overall heightened awareness but also due to incomplete catchment of CIS patients who have not been referred to neurology team for follow up.

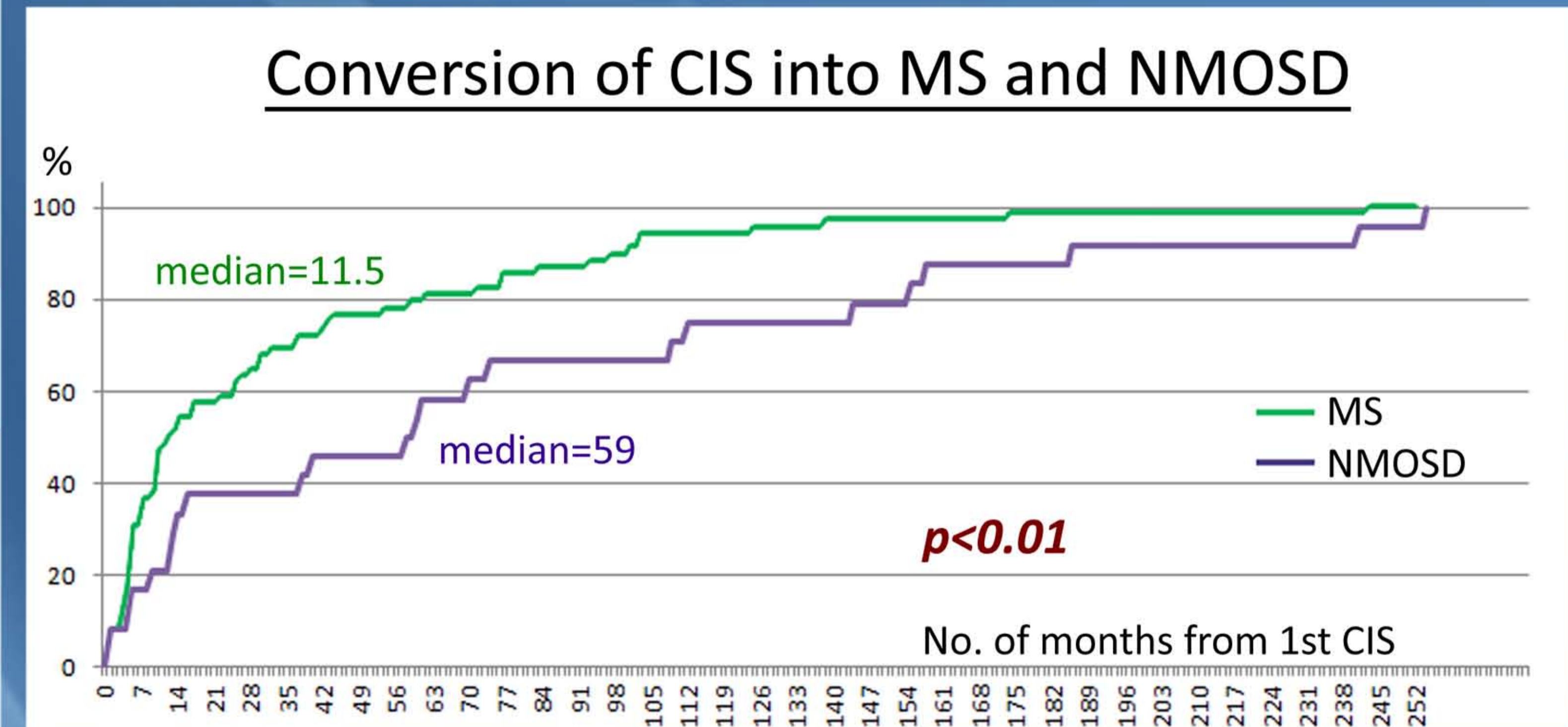
## Conclusion

The CIS conversion rates of our center were comparable with international data. Risk factors of conversion were young age and having myelitis as the first CIS.

Baseline Comparison	Monophasic (N=43)	MS/NMOSD (N=92)	Odds Ratio	p value
1st CIS median age	42.1	33.5	Z=-2.25	<b>0.02</b>
Female gender	26 (60.1%)	67 (72.8%)	0.57	0.16
1st CIS nature				
- Optic neuritis	5 (11.6%)	25 (27.2%)	0.35	<b>0.04</b>
- Transverse myelitis	27 (62.8%)	32 (34.8%)	3.16	<b>&lt;0.01</b>
- Brain syndrome	11 (25.6%)	35 (38%)	0.56	0.18
Disease duration				
- Median (months)	141	138.5	Z=0.49	0.62
Outcome	Monophasic (N=43)	MS/NMOSD (N=92)	Odds Ratio	p value
Mortality	4 (9.3%)	11 (12%)	0.75	0.77
EDSS $\geq 6$	10 (23.3%)	32 (74.4%)	0.57	0.23
Mean 5-year EDSS	2.9	3.7	Z=1.62	0.1

MS vs NMOSD	MS (N=68)	NMOSD (N=24)	Odds Ratio	p value
1st CIS median age	32	43.5	Z=-2.55	<b>0.01</b>
1st CIS ON	13	12	0.24	<b>&lt;0.01</b>
1st CIS brain synd.	31	4	4.19	<b>0.01</b>

\*No difference in gender, mortality, 5-year EDSS or proportion with



In our cohort, the conversion time to NMOSD was significantly longer than that of MS ( $p < 0.01$ ), which had several reasons. 7 cases were previously managed as MS, and were revised to be NMOSD afterwards. The unavailability of anti-NMO checking in our locality in earlier years also delayed the diagnosis in certain cases.

In reality, the 'conversion time' actually reflected the 'time to correct diagnosis', which called for a better diagnostic approach to delineate recurrent CNS demyelinating disorders in Hong Kong.

## Literature

- 1) Effect of early IFN treatment on conversion to definite MS: a randomised study. Comi et al. Lancet, 2001
- 2) IFN beta-1a for early MS: CHAMPS trial subgroup analysis. Beck et al. Ann Neurol, 2002
- 3) Treatment with IFN beta-1b delays conversion to CDMS in patients with CIS. Kappos et al. Neurology, 2006
- 4) Diagnostic criteria for MS: 2010 revisions to the McDonald criteria. Polman et al. Ann Neurol, 2011
- 5) International consensus diagnostic criteria for NMOSD. Wingerchuk et al. Neurology, 2015
- 6) Clinically isolated syndrome in HK and long term outcomes. Li et al. PACTRIMS (poster), 2009
- 7) Long term outcome of clinically isolated syndrome in HK. Cheng et al. AAN (poster), 2013