

# INTREPAD

## A randomized trial of naproxen to slow progress of presymptomatic Alzheimer disease

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### Study objective and summary result

This study tested the efficacy of low-dose oral naproxen for preventing progression in measures of presymptomatic Alzheimer disease (AD) among cognitively intact persons at risk of AD, and it found that low-dose oral naproxen does not affect progression of these measures in such persons.

### Classification of evidence

Class I.

### What is known and what this paper adds

Observational studies have suggested an association between nonsteroidal anti-inflammatory drugs (NSAIDs) and a reduced risk of AD in relatively young older adults, but clinical trials have not shown any benefit in preventing AD. This study specifically characterizes the effects of an NSAID on the progression of presymptomatic AD in a relatively young group of cognitively intact at-risk individuals.

### Participants and setting

The Investigation of Naproxen Treatment Effects in Presymptomatic AD (INTREPAD) enrolled 195 individuals (26% male; mean age,  $63.3 \pm 5.6$  years) with strong family histories of AD but no evidence of cognitive deficits. The INTREPAD study was conducted at the Douglas Mental Health University Institute (Montréal, Québec). Recruitment occurred between November 2011 and March 2015, and data collection ended in March 2017.

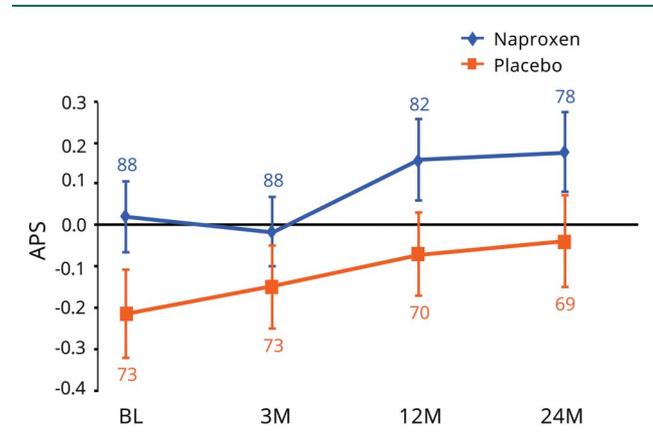
### Design, size, and duration

This double-blinded study used electronic randomization to assign participants to groups receiving 220-mg tablets of naproxen-sodium ( $n = 102$ ) or placebo ( $n = 93$ ) for 2 years. The tablets were taken twice daily. The progress of presymptomatic AD, if any, was assessed using the Alzheimer Progression Score (APS), which summarizes imaging, neurosensory, cognitive, and CSF markers. Higher APS values reflect greater progression. Participants were evaluated at baseline and after 3, 12, and 24 months.

### Primary outcome measures

The primary outcome was change from-baseline in the APS over the 2-year treatment period.

**Figure** APS measurements in the naproxen- and placebo-treated groups at various timepoints



### Main results and the role of chance

The naproxen- and placebo-treated groups exhibited similar APS change ( $p = 0.51$ ).

### Harms

Adverse events were more common in the naproxen-treated group ( $p = 0.015$ ).

### Bias, confounding, and other reasons for caution

This study had less statistical power than it had initially aimed for.

### Generalizability to other populations

This study's single-center nature may limit the generalizability of the results.

### Study funding/potential competing interests

This study was funded by McGill University, Pfizer, the Canadian federal and Québécois provincial governments, and various foundations. The authors report no competing interests. Go to [Neurology.org/N](http://Neurology.org/N) for full disclosures.

### Trial registration number

NCT02702817 on [ClinicalTrials.gov](http://ClinicalTrials.gov).

A draft of the short-form article was written by M. Dalefield, a writer with Editage, a division of Cactus Communications. The authors of the full-length article and the journal editors edited and approved the final version.

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## The genetic basis of undiagnosed muscular dystrophies and myopathies

Results from 504 patients

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In the article "The genetic basis of undiagnosed muscular dystrophies and myopathies: Results from 504 patients" by Savarese et al.,<sup>1</sup> the degree listed for the eleventh author, Dr. Alessandra Ruggieri, should be MSc rather than PhD. The authors regret the error.

### Reference

1. Savarese M, Di Fruscio G, Torella A, et al. The genetic basis of undiagnosed muscular dystrophies and myopathies: results from 504 patients. *Neurology* 2016;87:71–76.

## Congenital autophagic vacuolar myopathy is allelic to X-linked myopathy with excessive autophagy

*Neurology*® 2019;93:371. doi:10.1212/WNL.0000000000007478

In the article "Congenital autophagic vacuolar myopathy is allelic to X-linked myopathy with excessive autophagy" by Munteanu et al.,<sup>1</sup> the degree listed for the third author, Dr. Alessandra Ruggieri, should be MSc rather than PhD. The authors regret the error.

### Reference

1. Munteanu I, Ramachandran N, Ruggieri A, Awaya T, Nishino I, Minassian BA. Congenital autophagic vacuolar myopathy is allelic to X-linked myopathy with excessive autophagy. *Neurology* 2015;84:1714–1716.

## Congenital muscular dystrophies with defective glycosylation of dystroglycan

A population study

*Neurology*® 2019;93:371. doi:10.1212/WNL.0000000000007479

In the article "Congenital muscular dystrophies with defective glycosylation of dystroglycan: A population study" by Mercuri et al.,<sup>1</sup> the degree listed for the twenty-fifth author, Dr. Alessandra Ruggieri, should be MSc rather than PhD. The authors regret the error.

### Reference

1. Mercuri E, Messina S, Bruno C, et al. Congenital muscular dystrophies with defective glycosylation of dystroglycan: a population study. *Neurology* 2009;72:1802–1809.

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In the article "INTREPAD: A randomized trial of naproxen to slow progress of presymptomatic Alzheimer disease" by Meyer et al.,<sup>1</sup> first published online April 5, 2019, Dr. Lafaille-Magnan's name should appear in the author list as Marie-Elyse Lafaille-Magnan. The authors regret the error.

### Reference

1. Meyer PF, Tremblay-Mercier J, Leoutsakos J, et al. INTREPAD: a randomized trial of naproxen to slow progress of presymptomatic Alzheimer disease. *Neurology* 2019;92:e2070–e2080.