

# Enhanced clinical trial stratification in SCI: the value of electrophysiology

Paulina S Scheuren, PhD

International Collaboration on Repair Discoveries (ICORD)

The University of British Columbia, Vancouver, BC, Canada

*SCOPE Meeting Nov 11, 2025*



ICORD and the Blusson Spinal Cord Centre are located on the traditional, ancestral, unceded territory of the  $x^w m \theta k^w \text{əy} \text{ə} m$  (Musqueam),  $Skwxwú7mesh$  (Squamish) and  $səl'ílwətaʔt$  (Tseil-Waututh) peoples.

# Clinical trials in spinal cord injury (SCI)



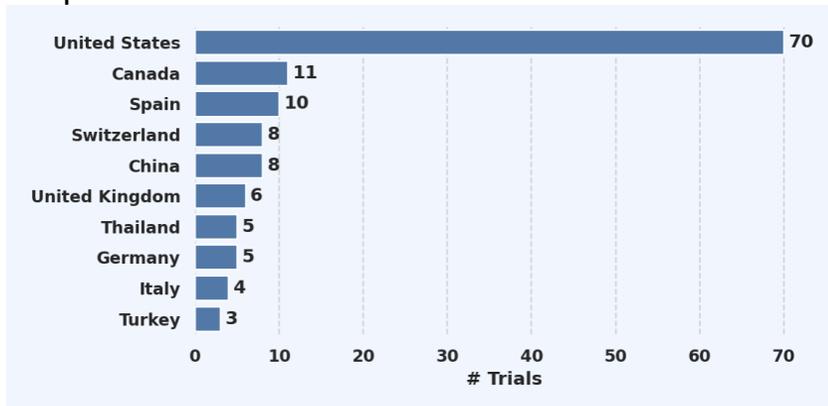
scitrialsfinder.net



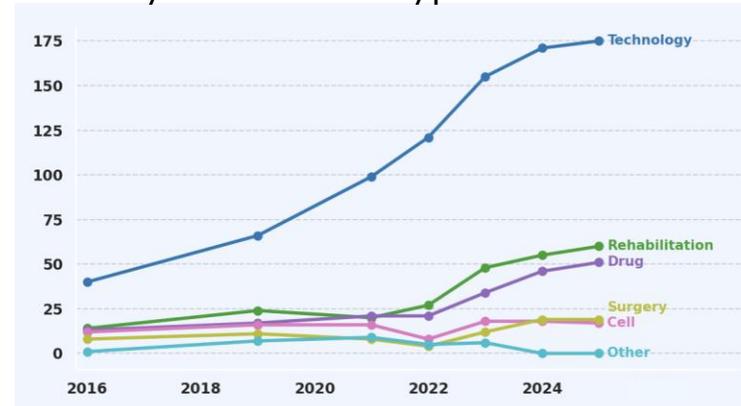
## Overview of SCI neurorestorative trials



## Top 10 countries



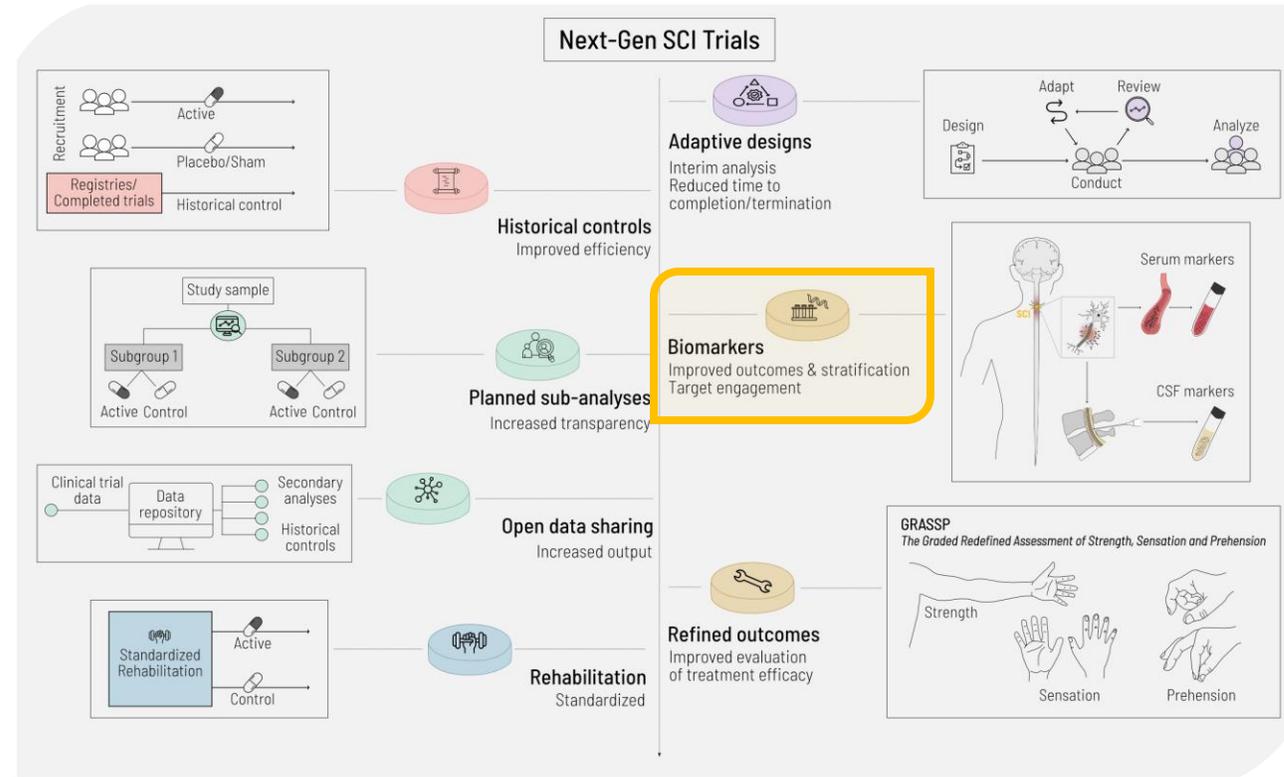
## Primary intervention type



# Lessons learned & opportunities for future success

## CHALLENGES EMERGING OPPORTUNITIES/SOLUTIONS

SCI heterogeneity  
Slow Recruitment  
...

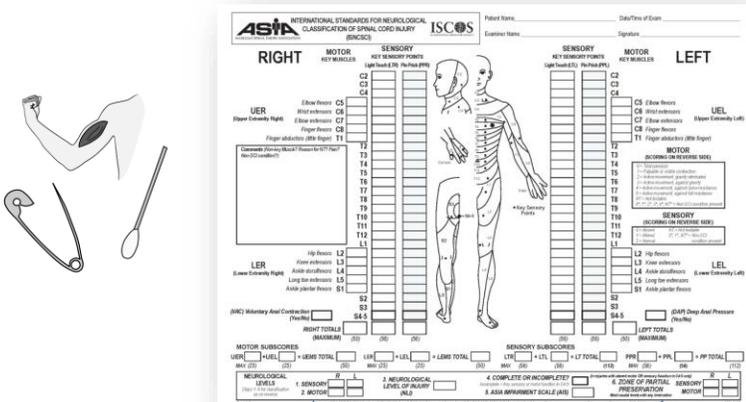


Scheuren PS, Kramer JLK. Next-gen spinal cord injury clinical trials: lessons learned and opportunities for future success. EBioMedicine. 2024 Nov;109:105381.

# The need for biomarkers

The ISNCSCI exam was not designed as a prediction tool... but it's the best we have (so far)

*International Standards for the Neurological Classification of SCI (ISNCSCI)*

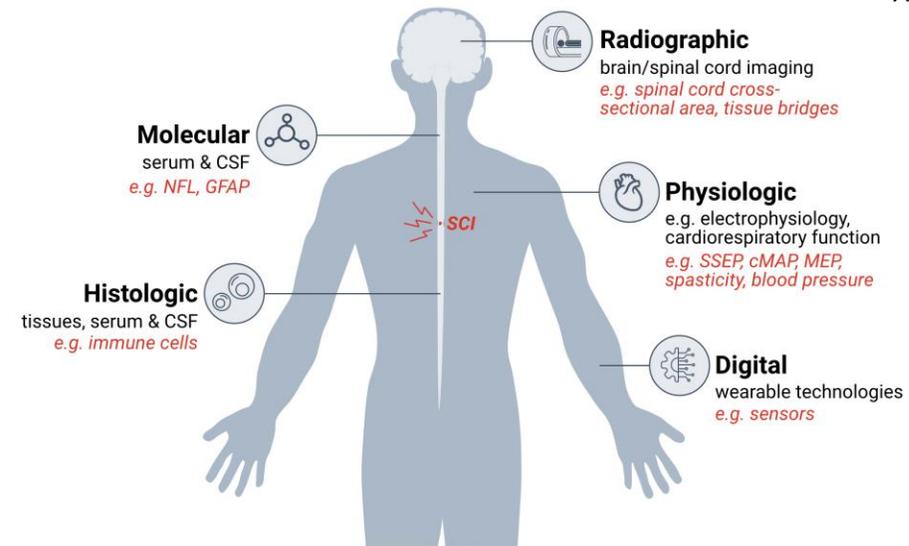


Complete SCI      Incomplete SCI

**Biomarkers** are needed to identify an individual's likelihood to respond to intervention

## Exploring the Landscape of Biomarkers in Spinal Cord Injury

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SCOPE sponsored Biomarker pre-course, ASIA 2024 Annual Meeting

# Can electrophysiological biomarkers fill this gap?

→ identify participants who will respond best to plasticity enhancing regenerative therapies in SCI.



→ Secondary Analysis of the Nogo Inhibition in Spinal Cord Injury (NISC) clinical trial

*Lancet Neurol* 2025; 24: 42–53



**Safety and efficacy of intrathecal antibodies to Nogo-A in patients with acute cervical spinal cord injury: a randomised, double-blind, multicentre, placebo-controlled, phase 2b trial**



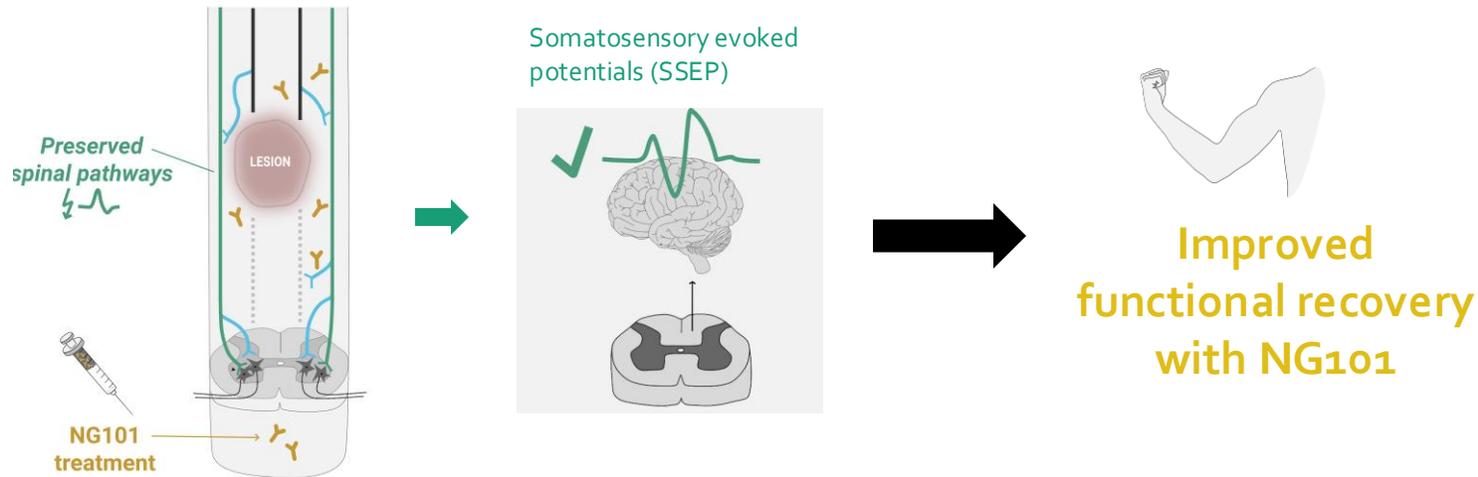
Norbert Weidner, Rainer Abel, Doris Maier, Klaus Röhl, Frank Röhrich, Michael Baumberger, Margret Hund-Georgiadis, Marion Saur, Jesús Benito-Penalva, Kerstin Rehahn, Mirko Aach, Andreas Badke, Jiri Kriz, Katalin Barkovits, Tim Killeen, Lynn Farner, Maryam Seif, Michèle Hubli, Katrin Marcus, Michael A Maurer, Bérénice Robert, Rüdiger Rupp, Paulina S Scheuren, Martin Schubert, Christian Schulz, Christina Sina, Bettina Steiner, Tanja Weis, Andreas Hug, Marc Bolliger, Nikolaus Weiskopf, Patrick Freund, Torsten Hothorn, Martin E Schwab, Armin Curt, for the Nogo Inhibition in Spinal Cord Injury Study Group\*

# Can electrophysiological biomarkers fill this gap?

→ identify participants who will respond best to plasticity enhancing regenerative therapies in SCI.

## HYPOTHESIS

Preserved electrophysiology



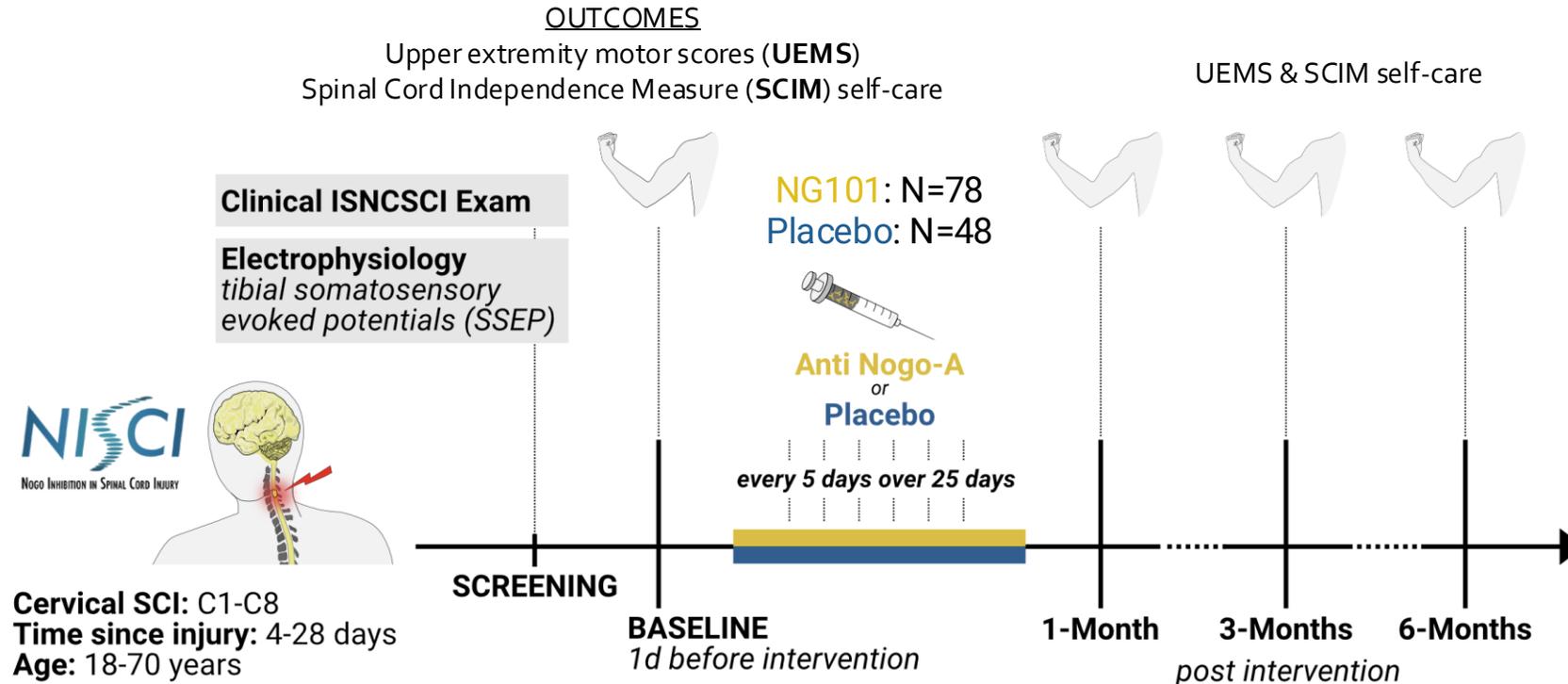
*NG101, a recombinant human antibody that neutralizes the neurite outgrowth protein Nogo-A*

# NISCI – Nogo Inhibition in Spinal Cord Injury

## Trial design

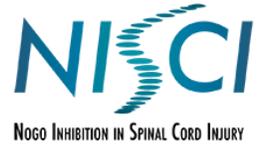
EMSCi

European Multicenter Study about Spinal Cord Injury

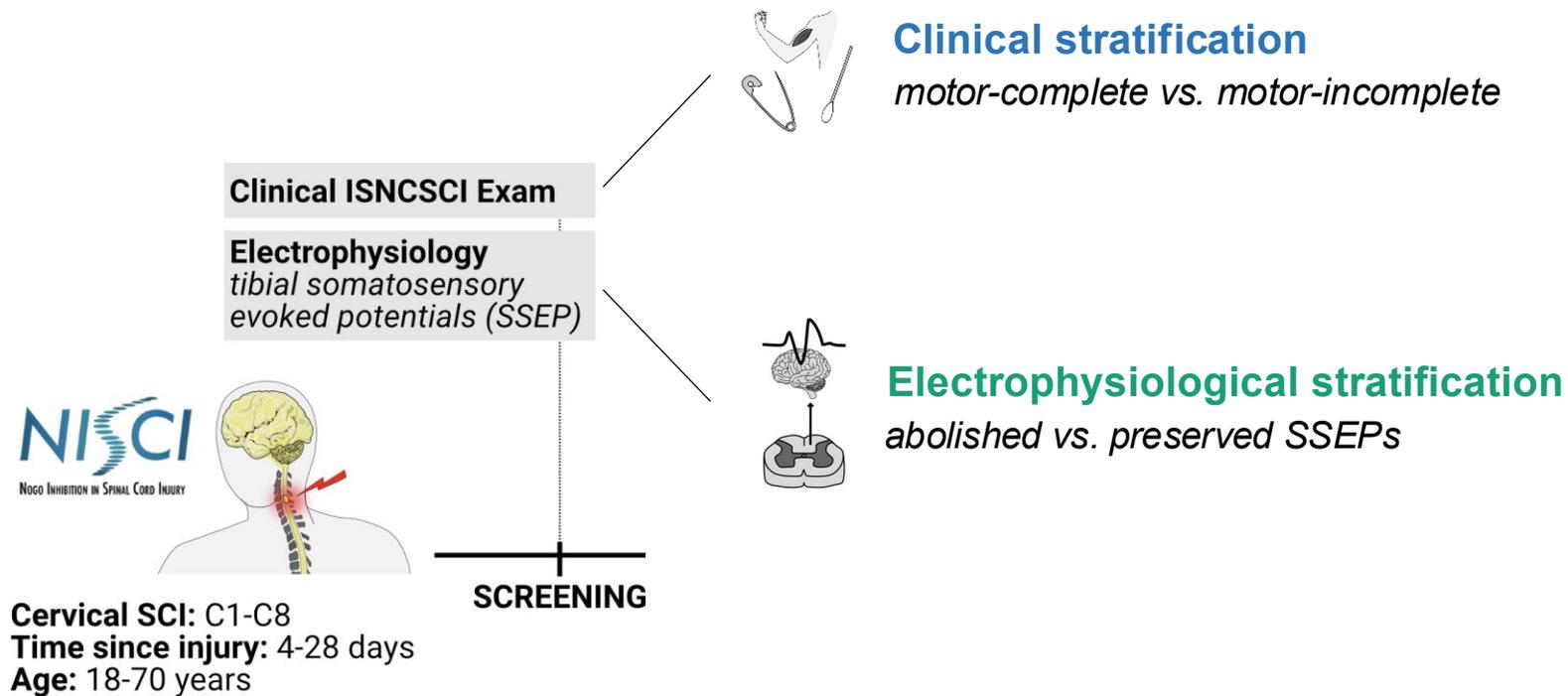


# Biomarker-driven participant stratification

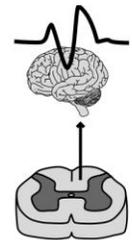
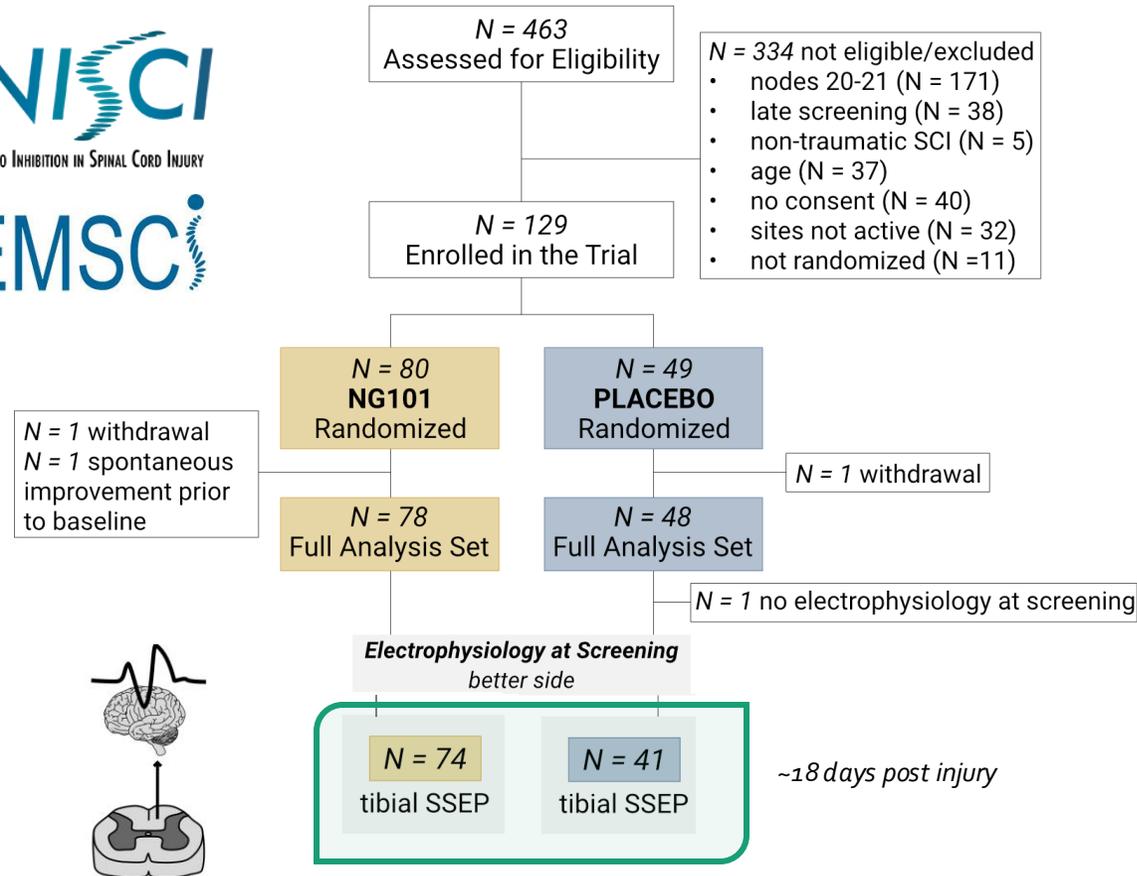
## NISCI – Secondary Analysis



European Multicenter Study about Spinal Cord Injury



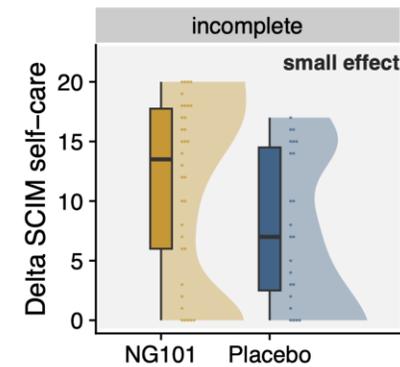
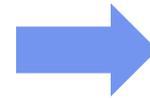
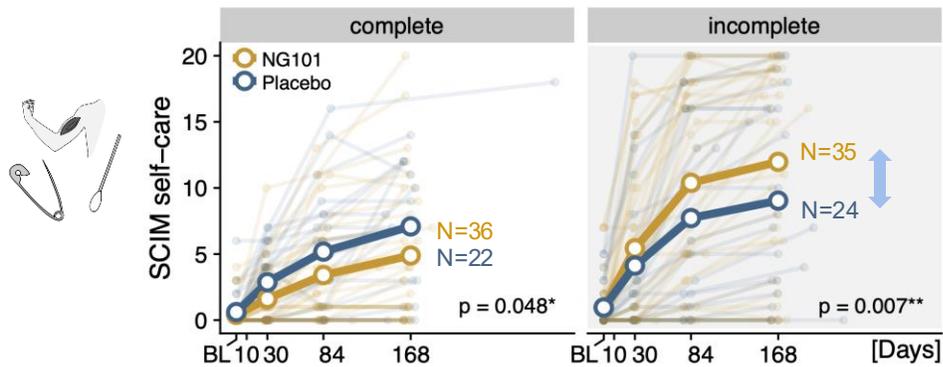
# Electrophysiology - feasible in a multi-center SCI trials



## Electrophysiology @ Screening

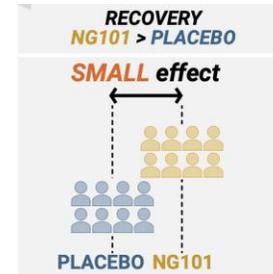
# Electrophysiology improves participant stratification

## Clinical stratification

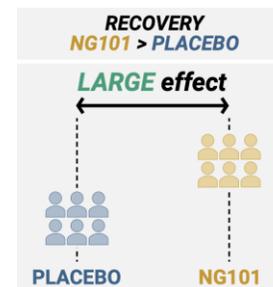
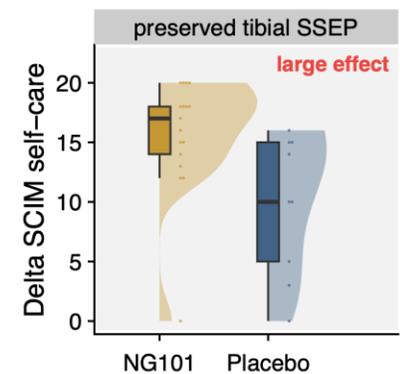
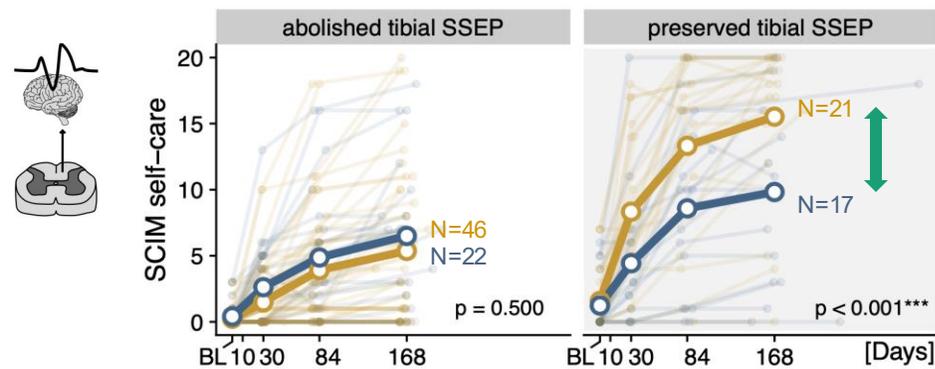


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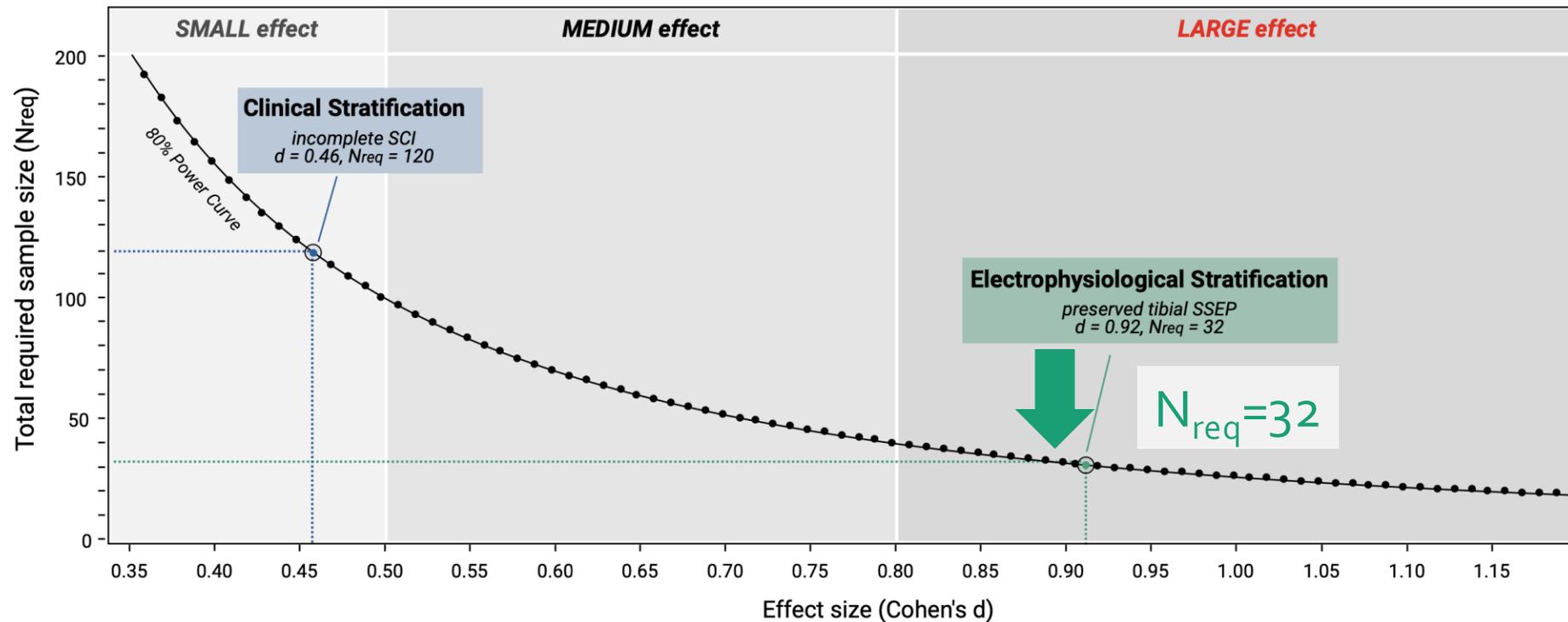
## Electrophysiological stratification



# Power analysis

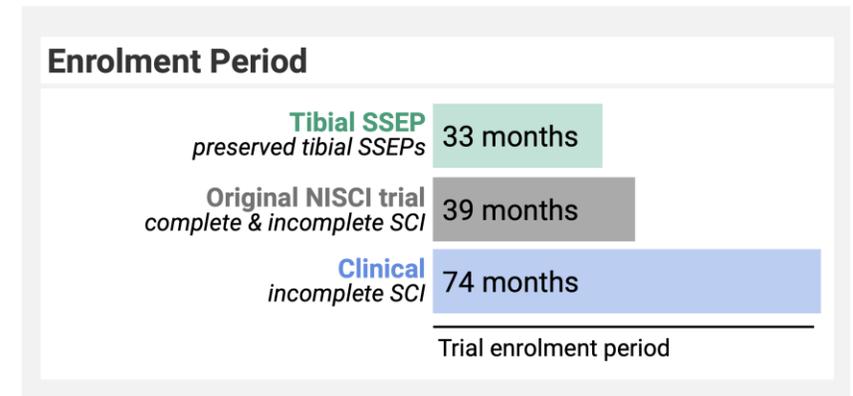
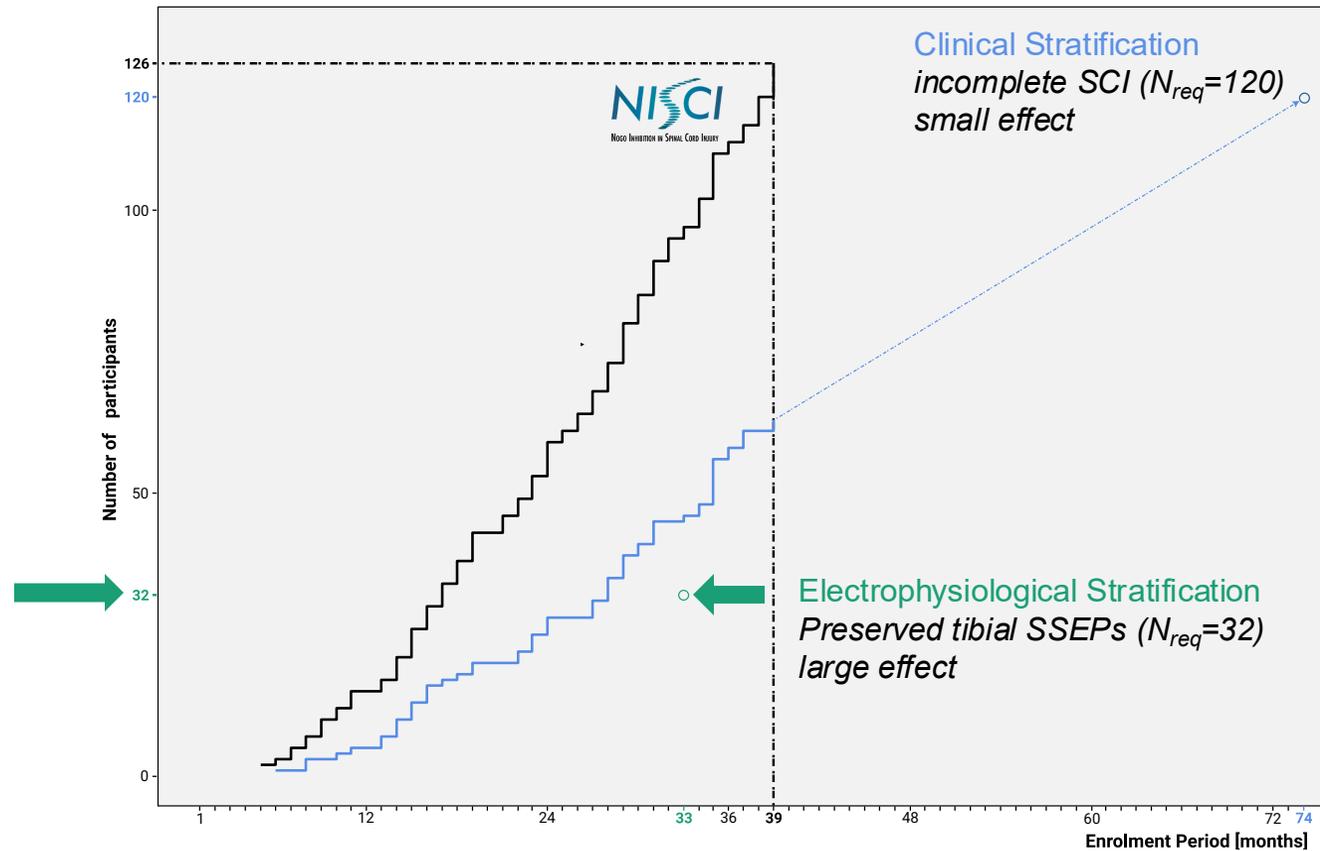
Electrophysiological stratification reduces the required sample size ( $N_{req}=32$  vs. 120)

## A. Power Analysis

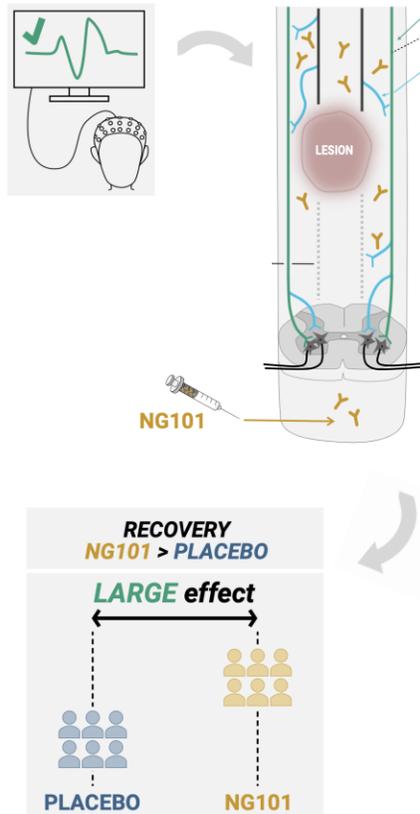


# Power analysis

Electrophysiological stratification **reduces the trial enrolment period** (33 vs. 74 months)



# Informing the design of future clinical trials



- **Electrophysiological biomarkers improved participant stratification** compared to clinical measures in an acute SCI clinical trial.
  - increased effect sizes & shorter trial duration
- **Biological importance of preserved neuronal pathways**, which may serve as key substrates for plasticity-inducing therapies.
- **Biomarker-driven stratification approach** to inform future SCI clinical trial design.

# ACKNOWLEDGEMENTS

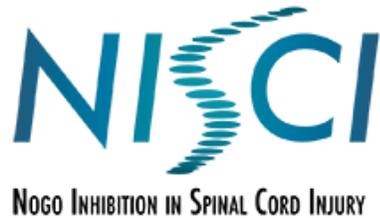


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Schweizer  
Paraplegiker  
Stiftung



Faculty of Medicine  
Bluma Tischler Fellowship



Thanks to all co-authors

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Brain, awaf354, <https://doi.org/10.1093/brain/awaf354>

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