

**FOOT
DROP
TRIAL**



Federaal Kenniscentrum voor de Gezondheidszorg
Centre Fédéral d'Expertise des Soins de Santé
Belgian Health Care Knowledge Centre

The FOOTDROP trial

4TH KCE symposium

Hot topics and methods in publicly funded clinical trials

Christophe Oosterbos & Tom Theys

TABLE OF CONTENTS

1. BACKGROUND & RATIONALE

2. TRIAL DESIGN

3. PILOT STUDY: RESULTS AND LESSONS LEARNED

4. FULL STUDY



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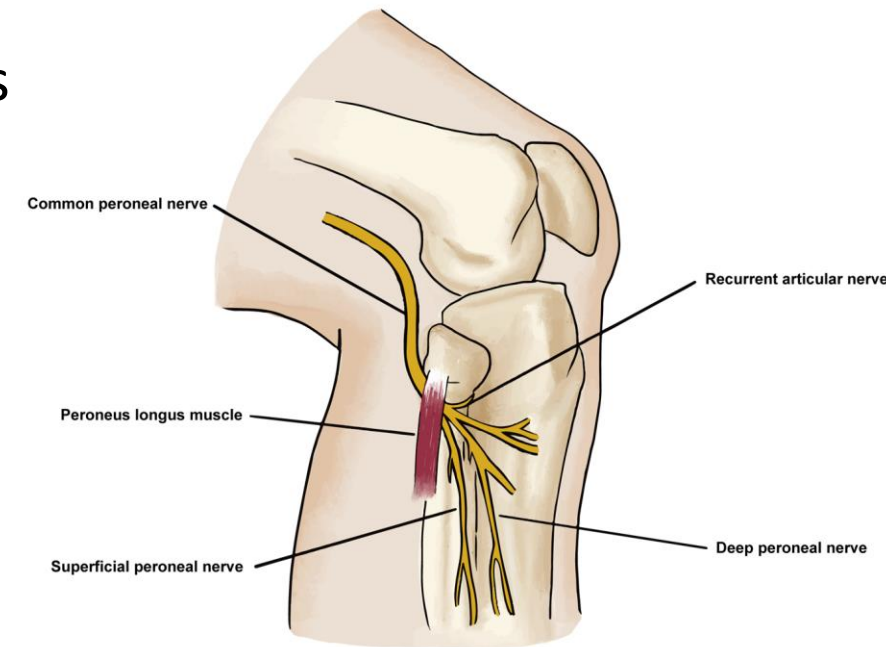
BACKGROUND & RATIONALE



BACKGROUND

■ PERONEAL MONONEUROPATHY

- 'Entrapment' of peroneal nerve at fibular head
- Most frequent mononeuropathy in the lower limbs
- Frequent cause of painless foot drop
 - Gait difficulties
 - Increased risk of falling
 - ! Increased risk in patients with subclinical entrapment

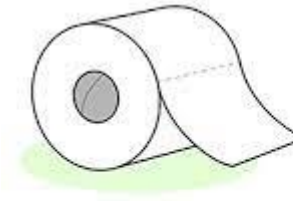




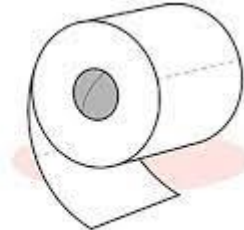
BACKGROUND

■ Treatment of peroneal neuropathy

- Non-invasive treatment
 - Mobilisation, muscle strengthening and stretching
 - Gait and proprioceptive training
- Neurolysis of the peroneal nerve



This is right.
(good)



This is wrong.
(bad)





VARIATION IN DAILY PRACTICE

“Operating on these patients is not ethical”

“Patients with foot drop due to important weight loss should always undergo surgery, I cannot randomize these patients”

“Patients always recover without surgery. Those who do not recover have important comorbidities”

“A no cross-over policy is not fair; you cannot deny surgery to half of the patients”



VARIATION IN DAILY PRACTICE



Contents lists available at [ScienceDirect](https://www.sciencedirect.com)

Brain and Spine

journal homepage: www.journals.elsevier.com/brain-and-spine



Controversies in treatment strategies in patients with foot drop due to peroneal nerve entrapment: Results of a survey among specialists



Christophe Oosterbos^{a,b,*}, Lukas Rasulic^{c,d}, Sofie Rummens^{e,f}, Charlotte Kiekens^g,
Johannes van Loon^{a,b}, Robin Lemmens^{h,i,j}, Tom Theys^{a,b}

Survey among 181 specialists (50% Belgian) : **important variations** in clinical decision making

- Practice is mostly based on habits and beliefs
- Agreement on need for RCT
- Important variations in timing of neurolysis
- Important variations in (duration of) conservative treatment



CLINICAL EQUIPOISE

Evidence in peroneal nerve entrapment: A scoping review

Christophe Oosterbos , Thomas Decramer, Sofie Rummens, Frank Weyns, Annie Dubuisson, Jeroen Ceuppens, Sophie Schuind, Justus Groen, Johannes van Loon, Lukas Rasulic, Robin Lemmens, Tom Theys ... [See fewer authors](#) 

No good evidence to support either treatment strategy

	DESIGN level of evidence		NUMBER OF INCLUDED ARTICLES	SAMPLE SIZE
TREATMENT OUTCOME (26 articles)	Systematic review of randomized controlled trials or number of level 1 evidence articles	1	0	0
	Randomized controlled trial or observational study with dramatic effect	2	0	0
	Systematic review of all surgical techniques in peroneal neuropathy	3	1	189
	Poor quality narrative literature review on peroneal nerve entrapment due to weight loss		1	
	Non-randomized follow-up study		2	
	Case series mostly on surgical treatment	4	13	533
	Case series on conservative treatment and/or spontaneous evolution (predominantly)		9	

Mapping of available evidence. Level of evidence was assessed using the Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence. Size of the included study sample is reported.



CLINICAL EQUIPOISE

- **TREATMENT: key numbers**

- **Neurolysis of peroneal nerve**

- Good outcome: 40% to 100%
 - Time to surgery (11 papers): 9 days to 19,8 months; average 9,7 months (460 patients)
 - Time to recovery (7 papers): *weeks to months*

- **Conservative treatment**

- Good outcome: 0% to 100%
 - Time to recovery: 79% improvement at 6 months

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FOOTDROP TRIAL DESIGN



TRIAL DESIGN

Oosterbos et al. *Trials* (2022) 23:1065
<https://doi.org/10.1186/s13063-022-07009-x>

Trials

STUDY PROTOCOL

Open Access

Conservative versus surgical treatment of foot drop in peroneal nerve entrapment: rationale and design of a prospective, multi-centre, randomized parallel-group controlled trial



Christophe Oosterbos^{1,2*} , Sofie Rummens^{3,4}, Kris Bogaerts⁵, Sophie Hoornaert^{1,2}, Frank Weyns^{6,7}, Annie Dubuisson⁸, Robin Lemmens^{9,10,11} and Tom Theys^{1,2}

- 6 centers in *internal feasibility pilot study*
- 20-26 centers in full study



TRIAL OBJECTIVES

Primary objective

“To assess whether foot drop, caused by peroneal nerve entrapment in adult patients recovers better within 9 months after decompressive surgery compared to prolonged standard conservative treatment”



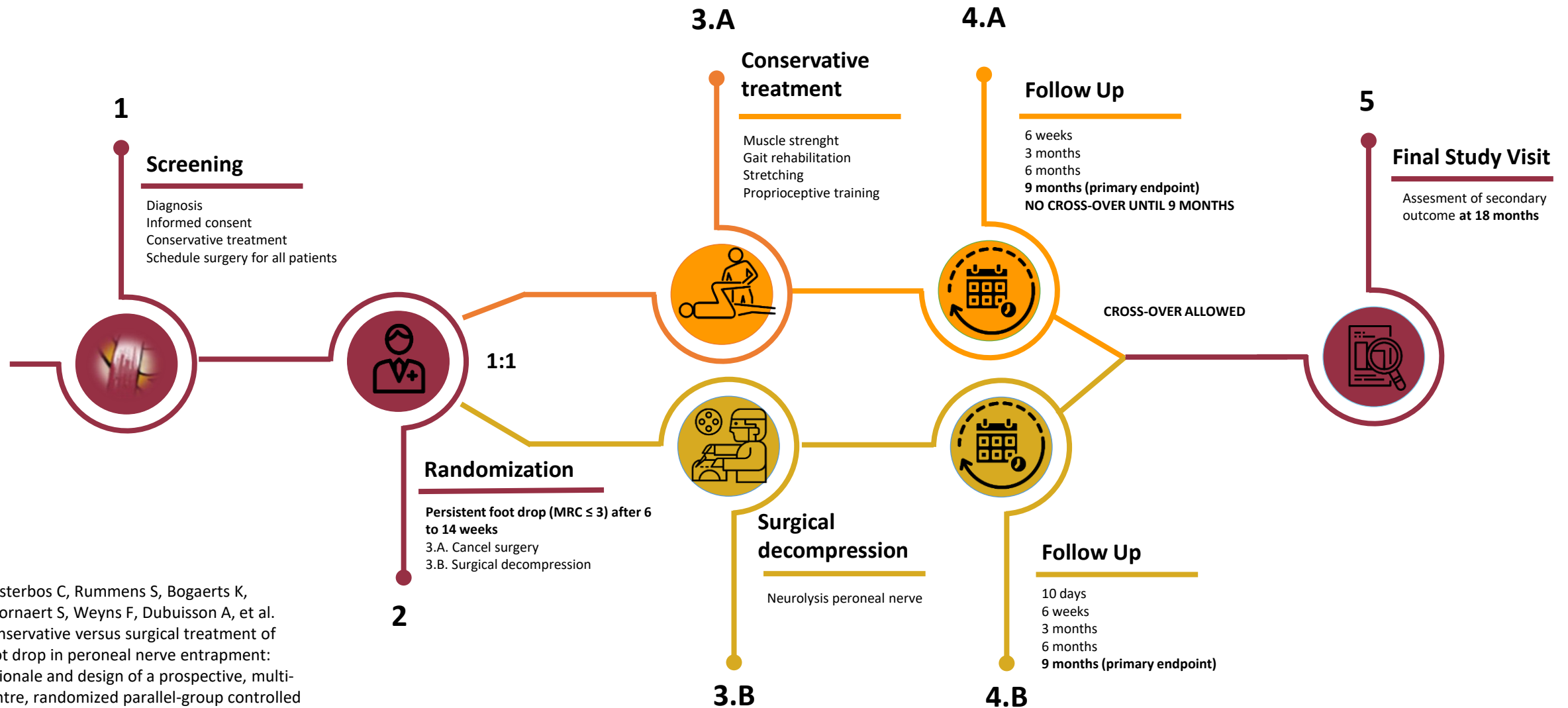
TRIAL OBJECTIVES

Secondary objectives

- Quality of life
- Return to work
- Gait assessment
- Risk factors
- Electrophysiological data
- Long-term follow-up
- Cost-effectiveness



TRIAL FLOW



Oosterbos C, Rummens S, Bogaerts K, Hoornaert S, Weyns F, Dubuisson A, et al. Conservative versus surgical treatment of foot drop in peroneal nerve entrapment: rationale and design of a prospective, multi-centre, randomized parallel-group controlled trial. *Trials*. 2022;23(1):1065.



TRIAL ASSESSMENTS

Table 2 Data collection and outcome measures. *d* days, *w* weeks, *m* months

Time since randomization	0	10d	6w	3m	6m	9m	18m
6-min walk test	X		X	X	X	X	X
10-m walk test	X		X	X	X	X	X
Isometric dynamometry	X	X	X	X	X	X	X
Muscle strength (MRC score)	X	X	X	X	X	X	X
Electrodiagnostics				X		X	
Functional ambulation categories	X		X	X	X	X	X
Stanmore questionnaire	X		X	X	X	X	X
Sensory changes	X	X	X	X	X	X	X
EQ5D-5L questionnaire	X	X	X	X	X	X	X
Return to work			X				
Surgical complications		X	X				X
Treatment record	X		X	X	X	X	X
Ability to walk barefoot	X		X	X	X	X	X
Need for orthosis	X		X	X	X	X	X
WPAI questionnaire	X		X		X		

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FEASIBILITY PILOT STUDY RESULTS & LESSONS LEARNED



FEASIBILITY OF TRIAL DESIGN

- **Recruitment:**
 - Are patients willing to participate?
 - Are treating physicians willing to participate?
 - Number of eligible patients?
- **Feasibility of**
 - no-cross over policy?
 - blinding measures?
 - trial assessments

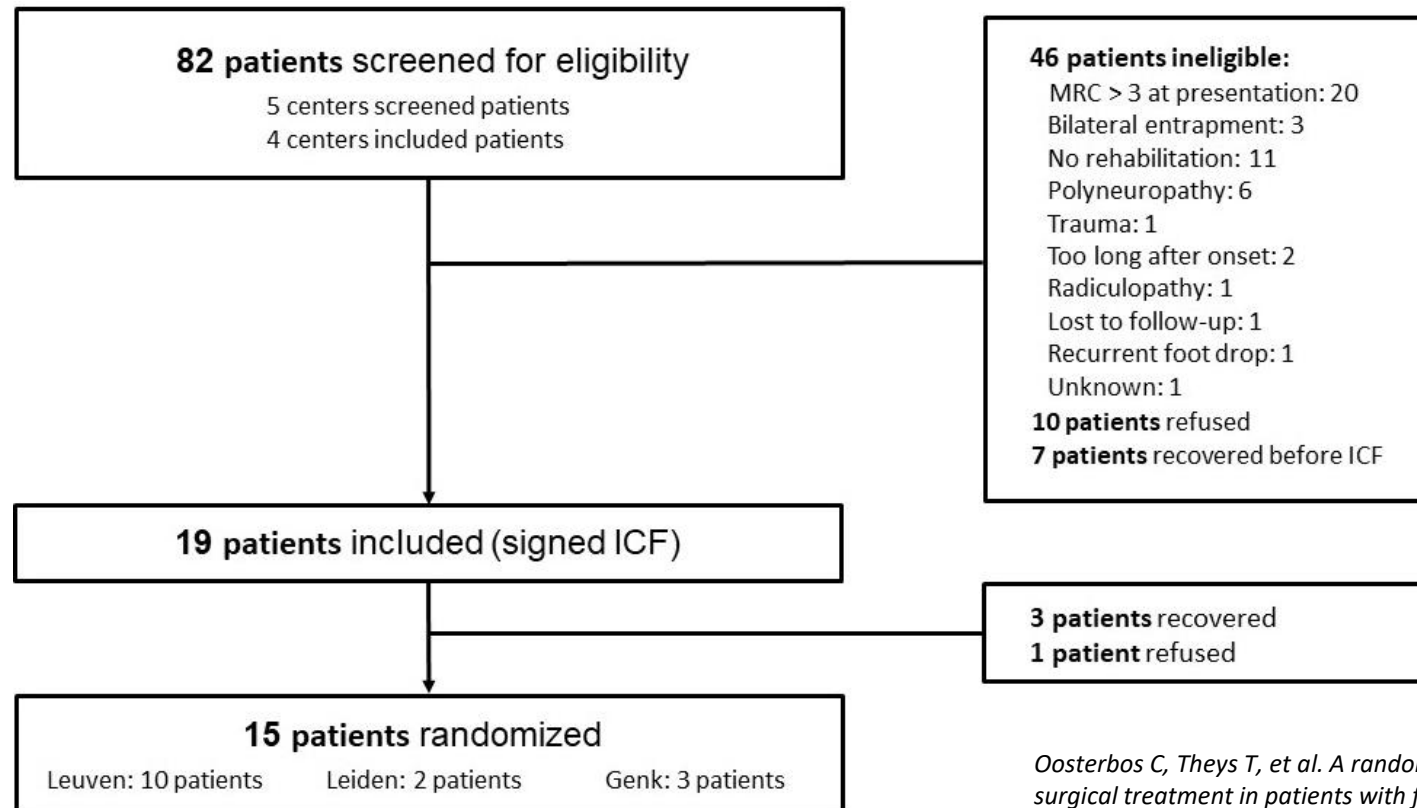




PILOT STUDY: RESULTS

- **Patient recruitment**

- Go-criterion: *“to randomize at least 14 patients in 6 centers within 6 months”*

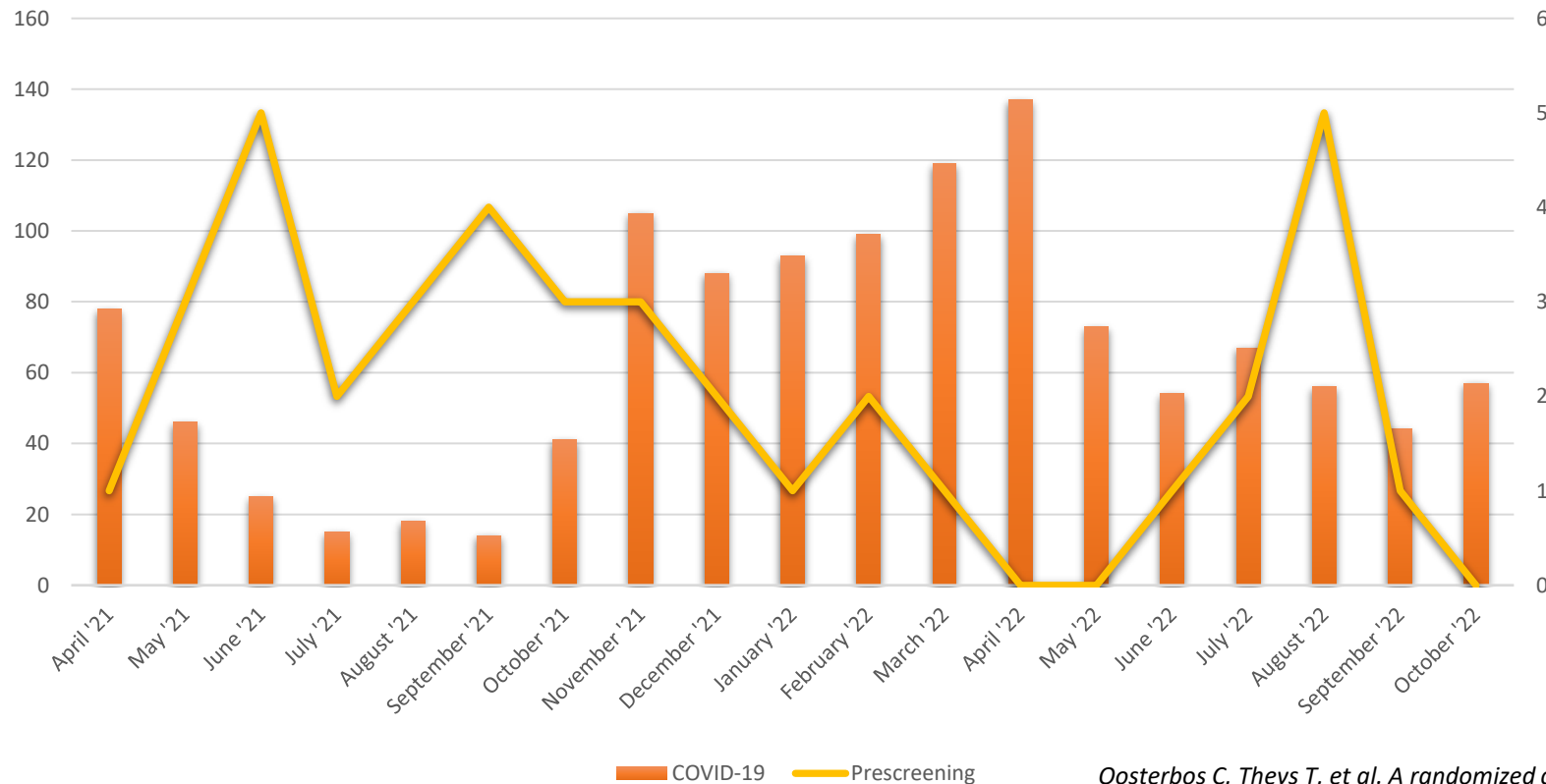


Oosterbos C, Theys T, et al. A randomized controlled trial comparing conservative versus surgical treatment in patients with foot drop due to peroneal nerve entrapment: results of an internal feasibility pilot study. Pilot and Feasibility Studies. 2023. Under review.



PILOT STUDY: RESULTS

- **Patient recruitment**
 - Study prolongation due to ongoing COVID-19 pandemic



Oosterbos C, Theys T, et al. A randomized controlled trial comparing conservative versus surgical treatment in patients with foot drop due to peroneal nerve entrapment: results of an internal feasibility pilot study. *Pilot and Feasibility Studies*. 2023. Under review.



PILOT STUDY: RESULTS

- **No cross-over policy**
 - No cross-over after randomization
 - No cross-over was never a reason to decline participation
- **Blinding measures**
 - No accidental unblinding throughout pilot study
- **Evaluation of trial assessments**
 - Patient perspective: questionnaire at 6 weeks and 3 months after randomization
 - Too many repetitive questionnaires: exclusion of SF-36 from full study
 - Physician perspective: trial steering committee
 - Variability in range of motion measurements: exclusion from full study



PILOT STUDY: LESSONS LEARNED

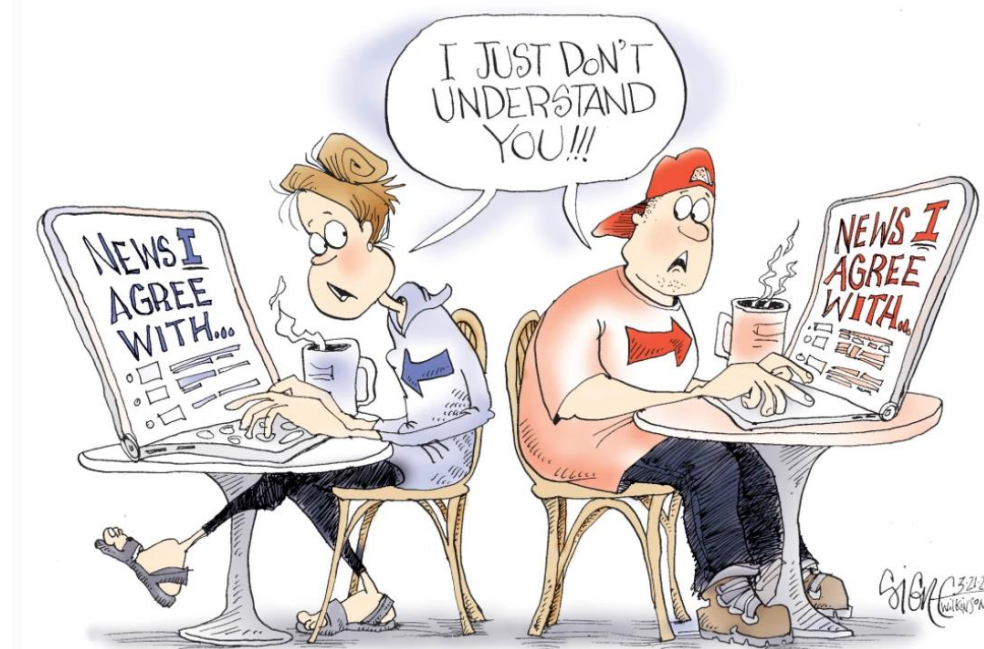
- **LESSON 1: MULTIDISCIPLINARY COLLABORATION IS KEY TO SUCCESS**
 - Low number of patients per treating specialism
 - Active involvement of all specialisms in local study team
 - Active roll for electrophysiologists!
 - 'Adjunct PI'





PILOT STUDY: LESSONS LEARNED

- **LESSON 2: BIAS IS REAL**
 - Initiate study only when clinical equipoise is supported
 - Take time to inform patients
 - Patient brochure



Oosterbos C, Theys T, et al. A randomized controlled trial comparing conservative versus surgical treatment in patients with foot drop due to peroneal nerve entrapment: results of an internal feasibility pilot study. *Pilot and Feasibility Studies*. 2023. Under review.



PILOT STUDY: LESSONS LEARNED

- **LESSON 3: EVERY INCLUSION COUNTS**
 - Recruitment potential was overestimated in pilot study
 - Eligible patients are not encountered on a daily base
 - Anticipate low numbers of patients in each center
 - Study visibility
 - Posters & pocket cards
 - Frequent communication
 - Monthly newsletters

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FOOTDROP TRIAL FULL STUDY



FULL STUDY

- **Currently being enrolled in 20 centers**
- **Feasibility exercise in new centers**
 - Questionnaire based on lessons learned
 - Feasibility meeting in selected centers
 - In collaboration with Keyrus
- **Study in 2 phases**
 - Opportunity to initiate additional 6 centers based on recruitment rate

Phase 1

6 pilot study centers
14 additional centers



**Yearly minimum
randomization rate not
reached**

Phase 2

+ 3 Belgian centers
+ 3 Dutch centers

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Thank you for your attention!

christophe.oosterbos@uzleuven.be

www.footdroptrial.com