



Building an Ethics Foundation for Future Spinal Cord Injury Clinical Trials



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MEND THE GAP

OBJECTIVE

To examine the landscape of participation criteria for spinal cord injury (SCI) clinical trials registered on ClinicalTrials.gov.

BACKGROUND

- There are 250,000 – 500,000 SCI cases worldwide each year.¹
- The incidence of depression and anxiety can be as high as 40%, and 20% for substance use in people with lived experience (PWLE) of SCI.²
- Numerous interventions – biologicals, drugs, devices, procedural, rehabilitation, or a combination – have improved quality of life but none have provided a solution.
- Potential trial participants rely on the public database, ClinicalTrials.gov, for information on novel interventions and ongoing clinical trials.

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METHODS

- ClinicalTrials.gov mined for SCI clinical trials registered up to December 2022 using the search term "spinal cord injury" and variants.
- Inclusion and exclusion criteria manually populated for each trial and coded using thematic analysis.
- Criteria cross-coded with geographical region and intervention type.

RESULTS

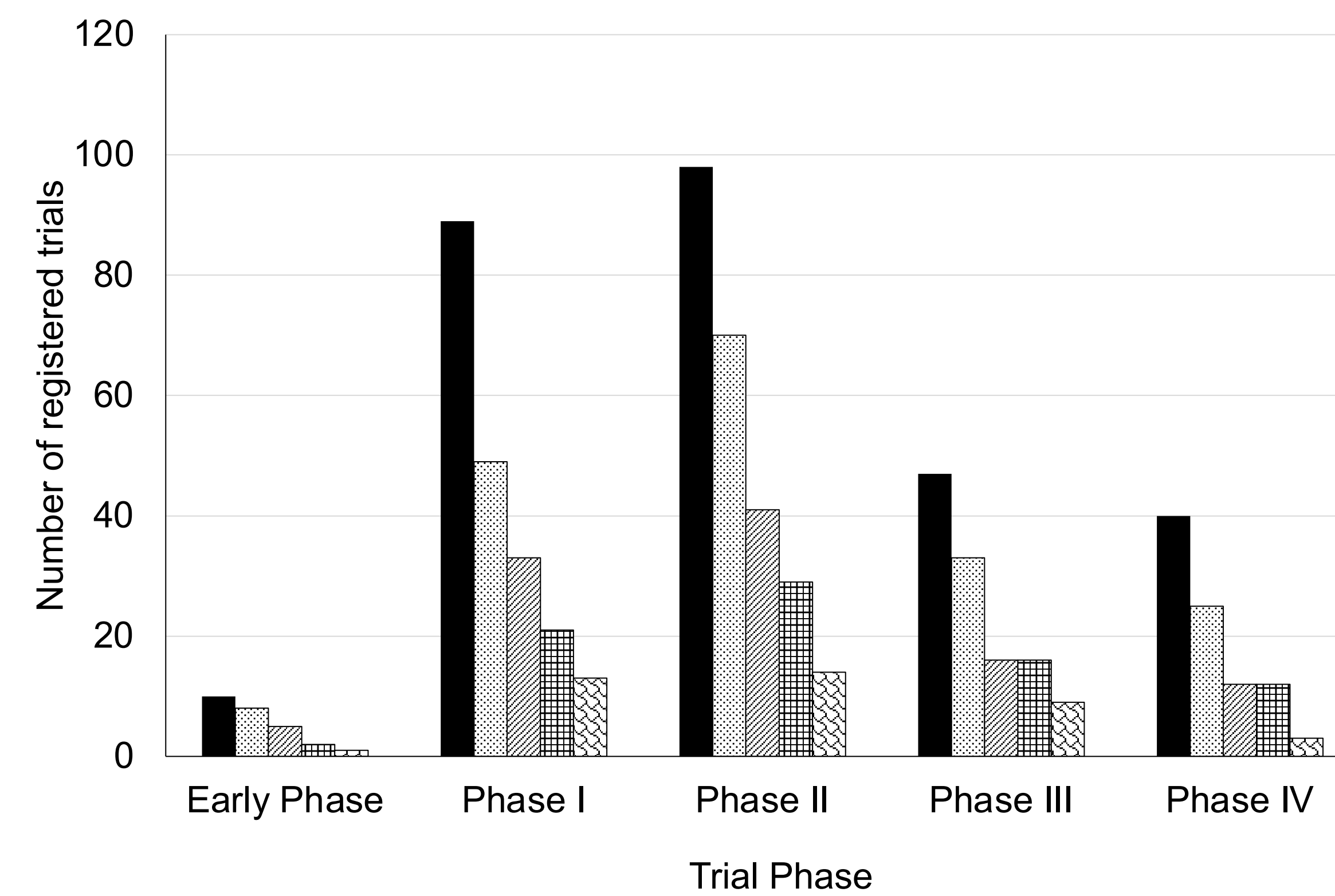


Figure 1: Distribution of exclusion criteria across trial phases. Solid black bars - total number of trials assessed for the identified phase. Dotted bars - number of trials that exclude participants on the basis of reproductive potential. Black slanted line bars - exclusion for mental illness. Hatched bars - exclusion for substance use. Black fish-scaled bars - exclusion at the investigator's discretion.

	North America				Asia				Europe				Multi-site			
	Drug	Biol	Device	Comb.	Drug	Biol	Device	Comb.	Drug	Biol	Device	Comb.	Drug	Biol	Device	Comb.
Phase 0																
Rep. Pot.	67		75	100												
Ment. Ill.	0		75	67												
Subst. Use	0		25	33												
Inv. Disc.	33															
Phase I																
Rep. Pot.	74	70	46	38	60	45	33	33	67	57	0	100				
Ment. Ill.	42	40	31	50	0	55	0	0	29	50	100	0				
Subst. Use	32	10	23	25	40	27	0	0	29	33	0	0				
Inv. Disc.	35	20	15	13	80	0	33	0	14	17	0	0				
Phase II																
Rep. Pot.	77		11	30	90	50	0	100	80	100		50	100	100		
Ment. Ill.	44		22	40	70	25	100	100	40	50		50	0	0		
Subst. Use	35		0	10	30	0	0	0	40	100		50	25	100		
Inv. Disc.	8		11	30	30	0	0	0	20	50		0	50	0		
Phase III																
Rep. Pot.	91		0	100	50											
Ment. Ill.	18		100	0	0											
Subst. Use	9		0	0	25											
Inv. Disc.	9		0	0	25											
Phase IV																
Rep. Pot.	71		100	50	40											
Ment. Ill.	14		100	50	20											
Subst. Use	5		0	0	0											
Inv. Disc.	5		0	0	0											

Table 1: Heat map of exclusion criteria distribution by trial phase, intervention type, and geographic region. Values are represented as percentages of the total number of trials registered as that intervention type, in the specified region and phase.



DISCUSSION

- Inconsistent phase designation and intervention categorization challenge usability of the database.
- Fewer than 15% of trials benchmarked criteria for mental illness and substance use to clinical assessments. This is both a serious scientific and ethical concern, and pose a challenge to powering trials from a limited participant pool.
- Leaving undefined criteria to the investigator's discretion lacks transparency and leaves room for biases.
- Drug trials overall and trials conducted in Europe were more likely to exclude participants on the basis of reproductive potential, mental illness, substance use, and at the investigator's discretion.
- Review of participation criteria for future SCI trials is needed to meet the goals of both ethical and scientific rigor.

REFERENCES

1. World Health Organization (2013, November 19) Spinal cord injury. Accessed July 31, 2023.
2. Management of Mental Health Disorders, Substance Use Disorders, and Suicide in Adults with Spinal Cord Injury. *J Spinal Cord Med* 44, 102-162 (2021).

RELATED PUBLICATIONS

1. Barretto T., Tetzlaff W., Illes J. Ethics and accountability for clinical trials. *Nature – Spinal Cord* 2024 (Published 18 March 2024).
2. Barretto T., Manohara V., Illes J. An examination of exclusion criteria in spinal cord injury clinical trials (in preparation).