Utilizing Human Subjects Research Protection Trainings and Site Initiation Visits to Improve Participant Safety in Clinical Neurology Research

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1 – Introduction

- The protection of human participants in clinical research is of critical importance. As a result, regulations have been developed to ensure that the rights, safety, and welfare of participants are addressed and research protocols are designed in a manner that minimizes the risks to participants.
- Non-compliance occurs when the protocol and/or the regulations governing the clinical research are not adhered to. This can: 1) Expose participants to harm; 2) Compromise data integrity; and 3) Result in disciplinary action from regulatory bodies.
- We have identified three tools to support clinical investigators when conducting clinical research (i.e., Human Subjects Training, Events Reporting Training, and site initiation visits [SIVs]).
- This study advances the field by investigating the effect of clinical research training and SIVs on the occurrence of non-compliance – ultimately improving participant safety and reducing potential harm.

2 – Statement of Purpose

- The aim of this study was to investigate a database of non-compliance findings to determine the effects of clinical research trainings and SIVs on the occurrence of non-compliance identified during protocol audits at National Institute of Neurological Disorders and Stroke (NINDS).

3 – Materials and Methods

- Non-compliance findings, identified by auditors from January 2003 to December 2019, were included and analyzed.
- The three tools, shown below in **Table 1**, created three distinct groups. The "Late 2017-2019" group was further divided into protocols that did not receive a SIV and protocols that did receive a SIV.

	Early	Middle	Late	
	2003-2012	2013-2016	2017-2019	
			No SIV	SIV
Human Subjects Training		✓	✓	✓
Events Reporting Training			✓	✓
Site Initiation Visits*				✓

Table 1. The evolution of policies governing protocol audits in NINDS to increase regulatory oversight from 2003 to 2019 (additional details are shown in **Supplemental Table 1**).
* Site initiation visits were offered for all protocols, but not required.

- Non-compliance events were then categorized by type, primary category, and cause, shown below in **Table 2**.

	Non-Compliance	Definition
Type	Major	Non-compliance which may affect participant safety or data integrity
	Minor	Non-compliance which does not affect participant safety or data integrity
Primary Category	Procedural	A deviation from protocol procedures
	Consent	A deviation pertaining to participant consent
	Eligibility	Failure to document participant meeting inclusion/exclusion criteria
	Policy	Failure to follow NIH policies
	Personally Identifiable Information (PII)	Breach of PII or failure to protect participant's identity
Cause	Study Team	Non-compliance caused by Principal Investigator or study team member

Table 2. Non-compliance classifications and definitions used in this study.

4 – Results

	Early	Middle	Late		Total
	2003-2012	2013-2016	2017-2019		
			No SIV	SIV	
Protocols	49	17	17	14	97
Non-Compliance Events	370	279	274	29	952
Participants	606	220	187	67	1080
Non-Compliance Events per Participant	0.61	1.27	1.47	0.43	0.88

Table 3. Descriptive statistics across groups.

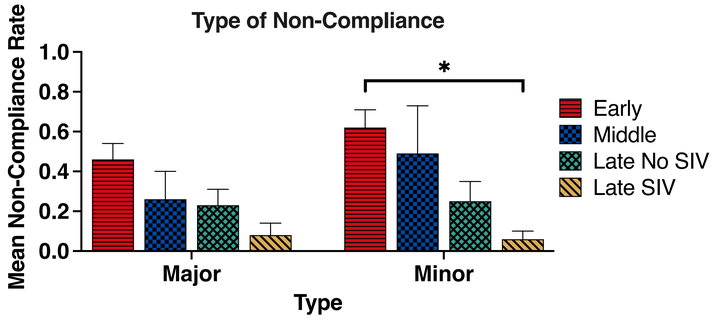

Figure 1. Mean non-compliance rates across protocols for major and minor non-compliance shown by time period. Error bars represent standard error.
*$p = 0.03$.

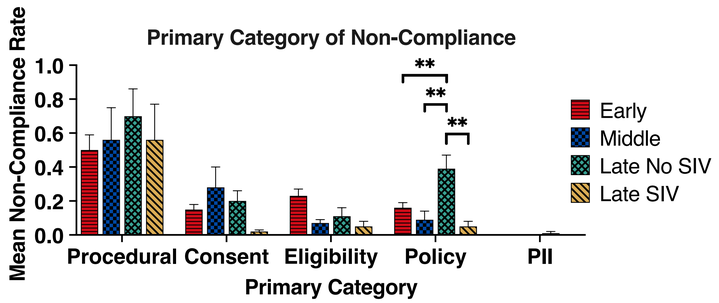

Figure 2. Mean non-compliance rates across protocols for each primary category of non-compliance shown by time period. Error bars represent standard error.
**$p = 0.001$.

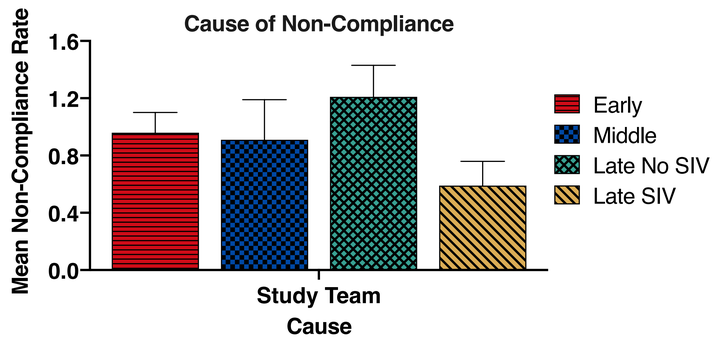

Figure 3. Mean non-compliance rates across protocols for study team-caused non-compliance shown by time period. Error bars represent standard error.

5 – Conclusions

- Results indicated a general reduction in non-compliance events and fewer study team-caused events across all time periods. Even with a lack of statistical significance between the Late No SIV and Late SIV groups, there were fewer non-compliance events found in protocols that had a SIV, compared to protocols that did not have a SIV.
- This study shows the importance of clinical research training and SIVs in clinical research and should be implemented for all levels of clinical neurology protocols.
- Additional studies are needed to analyze the specific qualities in SIVs that most greatly impact protocol compliance.

6 – Acknowledgements

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- To access supplemental information, please use an Apple/Android Camera application and place the QR code, on right, in the frame.
- Please contact us to continue the conversation: Matthew.Gooden@nih.gov.