

Are Less Active Sites More Likely to Deviate from Study Protocol and Procedures?

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PEDIG

- Multi-center network conducting studies in strabismus, amblyopia, and other eye disorders that affect children.
- Grant-funded by the National Eye Institute.
 - NIH grants EY011751 and EY018810
- Over 130 Ophthalmology and Optometry based sites participating in multiple research studies.

Background

- The Central Coordinating Center routinely evaluates protocol and procedural deviations as a component of quality control monitoring
- Forms are reviewed weekly to monitor adherence to protocol and procedures
- Feedback given to sites in real time to try and change behavior and prevent future problems

Objective

- Anecdotal observations
 - A trend that sites with only a few patients seemed to have the most number of deviations
 - Sites who were engaged with a high level of activity rarely deviated from the protocol
- Led us to hypothesize that the frequency of deviations would be related to the level of site activity

Methods

- The network conducts concurrent protocols
- Sites choose to participate in one or more protocols
- To test our hypothesis, we reviewed the *deviation rate per visit* for each of 117 sites participating in the last 8 randomized trials

Definition of Deviation

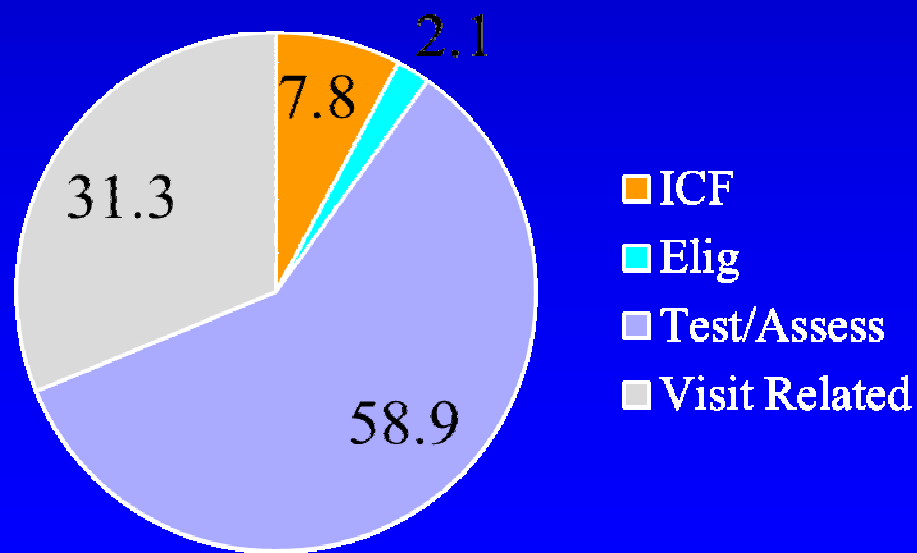
- Any deviation to the study protocol or procedure during the study
- Deviations can occur at any time
 - During the screening process (informed consent)
 - Upon completion of each enrollment, randomization, or study follow up visit

Deviation Types

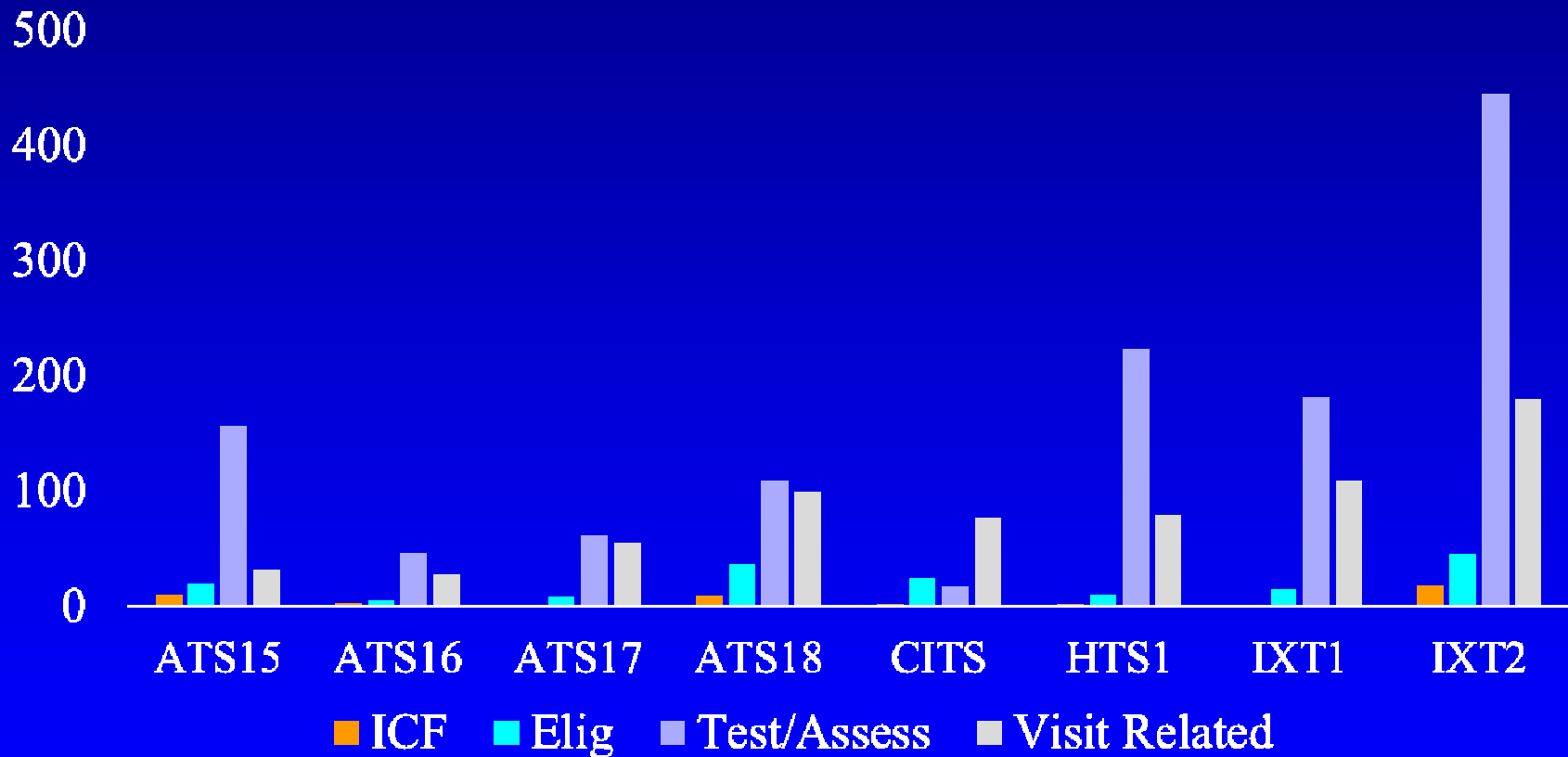
- Related to the informed consent process
- Related to eligibility
- Related to adherence to treatment protocol
- Related to required tests or assessments
 - Failure to perform an assessment or performed but deviated from protocol
- Related to visit completion
 - Visits completed out of window or missed visits

Number of Deviations In 8 RCT's

Deviation Type	N	%
Informed Consent Process	163	7.8%
Eligibility / Enrollment	43	2.1%
Tests/Assessments	1238	58.9%
Visit Completion	657	31.3%
Total	2101	



Number of Deviations Stratified by RCT



Define Site Activity?

1. # randomized - Easily understood

- Con – Weights each patient equally across studies
 - Sites with less randomized into a study with many FU visits could be more active than sites with the same number randomized in a study with fewer visits

2. # of potential visits (# completed + # missed)

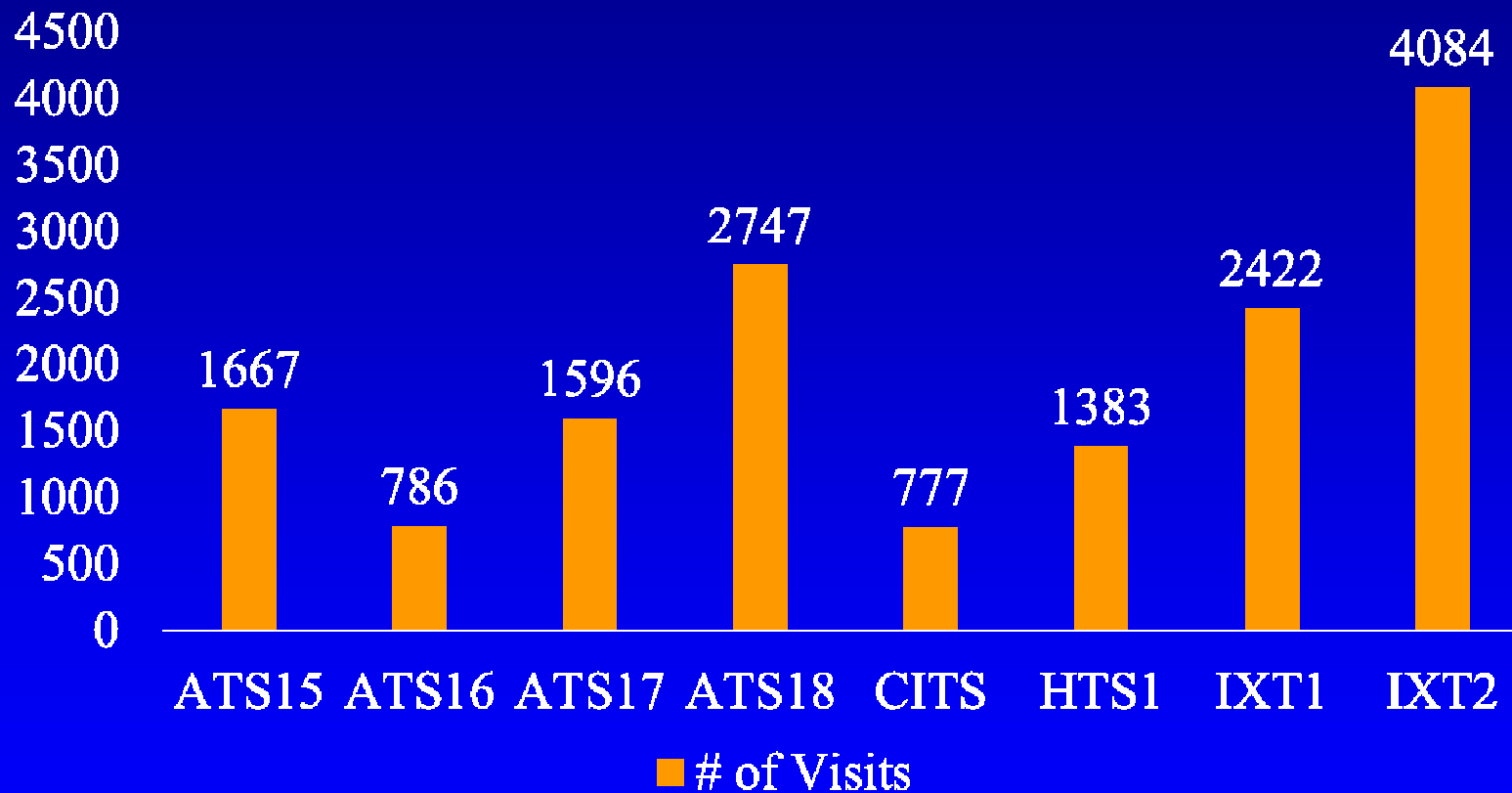
- Better than completed visits alone since missed visits are in denominator
- Con – still possible that higher missed visit rate is associated with lower rate of other deviations for visits completed

Define Site Activity?

3. # of visits completed – Better than randomized

- Con – higher missed visit rate is associated with lower rate of other deviations for visits that were completed
- We chose # 3
 - Site Activity defined as # of visits completed

15,462 Visits in 8 RCT's



Deviation Rate

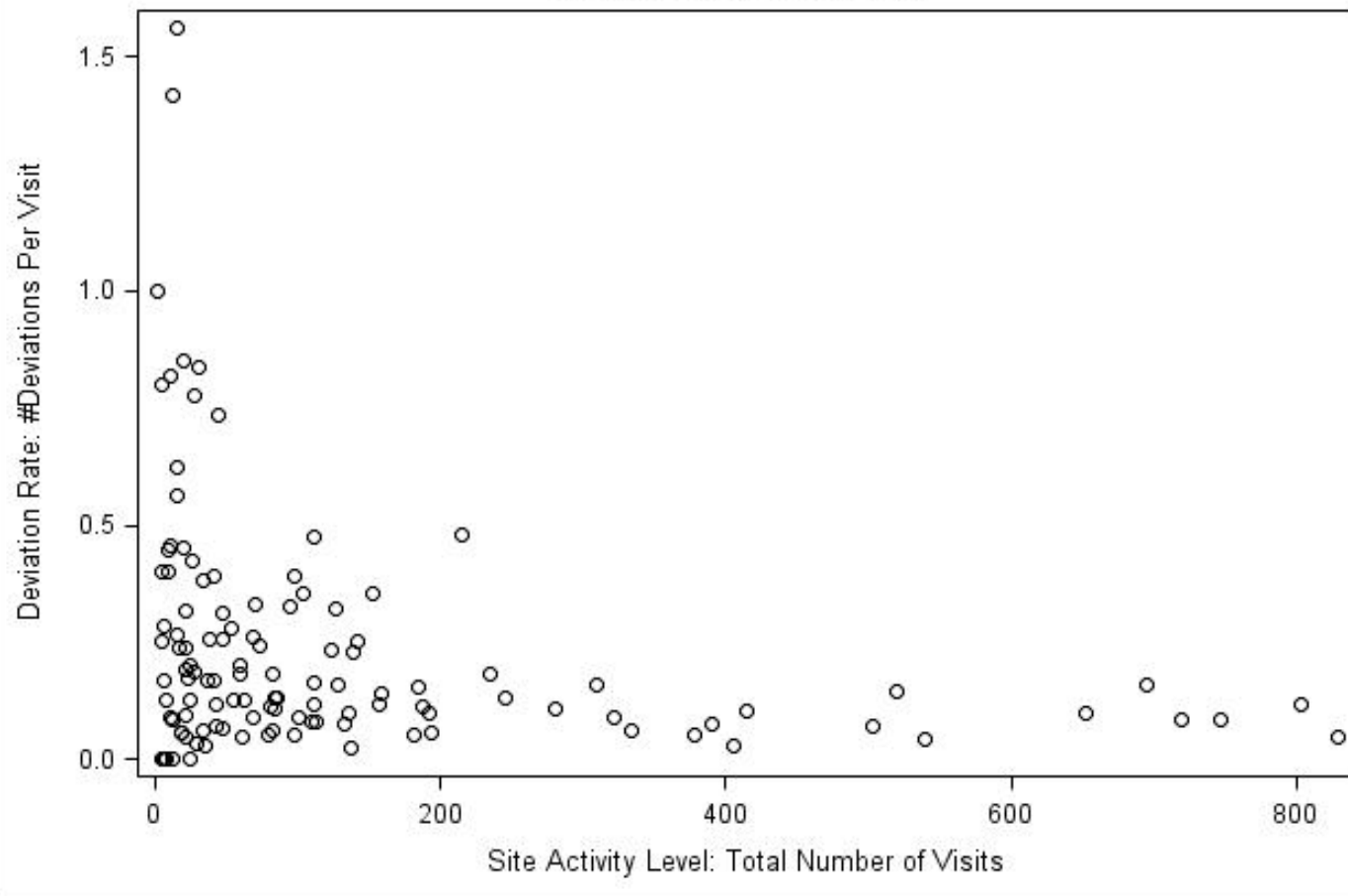
- Rate = # of deviations / # visits completed
- Excludes missed visit deviations
- Reasonable since we want to judge sites based upon the number of deviations that occurred for the number of visits they completed

Results

- 118 sites enrolled 2439 subjects into the last 8 randomized trials
- 15,462 visits were completed
 - Median 61 visits per site, range 1 to 829
- 2,101 protocol and procedural deviations were identified
 - Median 10 deviations per site, range 0 to 111

Deviation Rate by Site Activity Level

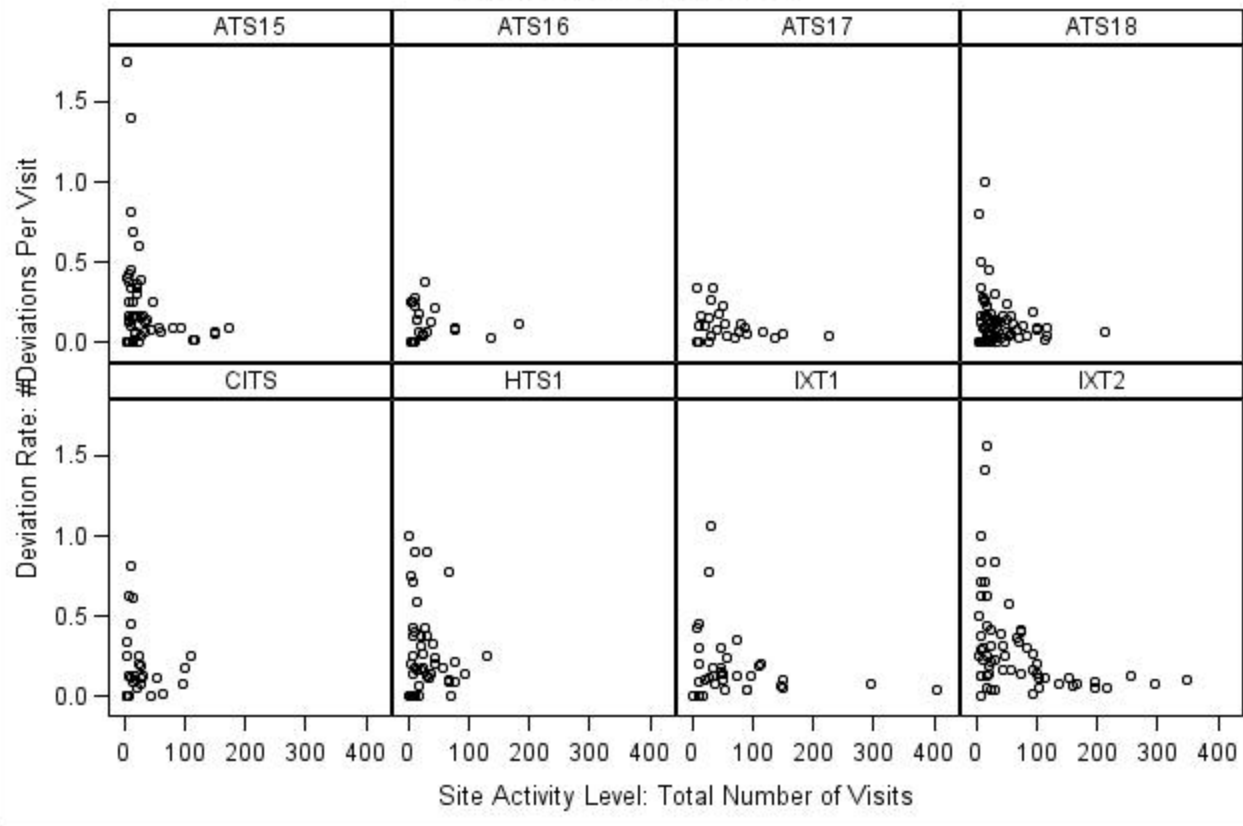
FIGURE 1 - NUMBER OF PROTOCOL AND PROCEDURAL DEVIATIONS PER VISIT BY NUMBER OF VISITS AS MEASURE OF ACTIVITY ACROSS ALL PROTOCOLS



Deviation Rate by Site Activity

Stratified by Protocol

FIGURE 2 - NUMBER OF PROTOCOL AND PROCEDURAL DEVIATIONS PER VISIT BY NUMBER OF VISITS AS MEASURE OF ACTIVITY STRATIFIED BY PROTOCOL



Summary

Site Activity Level (quintiles) Lowest to Highest	# of Sites	# of Devs	# of Visits	Deviation Rate (devs/visit)	Unadj. Rate Ratio	Adj.* Rate Ratio
1 to <17 visits	23	102	217	0.47	4.7	6.3
17 to <41 visits	24	159	614	0.26	2.6	3.5
41 to <84 visits	22	248	1317	0.19	1.9	2.8
84 to <184 visits	25	540	3021	0.18	1.8	2.2
>=184 visits	24	1052	10293	0.10	1.0 (ref)	1.0 (ref)
Across Network	118	2101	15462	0.14		

* Adjusted rate ratio from Poisson regression model controlling for protocol (P<0.0001)

Conclusions

- Sites with the least activity have six times more deviations than sites with the highest level of activity
- PEDIG leadership defined thresholds for site activity that must be maintained in order to remain active in the network and to remain active in a given protocol

Conclusions (cont.)

- Investigators must enroll one subject every six months or complete an online based protocol question and answer session to remain active in a protocol
- Sites must enroll 4 subjects or complete 15 or more visits each year to maintain active status in the network

Questions?

Thank You

*For a list of PEDIG studies and more
information*

<http://www.pedig.net>

Email: pedig@jaeb.org