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Improving Study Quality with PDV Codes

By Jamie Lucey

MAGI's Protocol Deviation and Violation (PDV) codes are a practical approach to easily categorize protocol deviations and violations in a systematic way.[1,2] With PDV codes, we can collect, categorize and analyze data to assess the problems in our studies so they can be addressed.

PDV Code Definitions

There are currently 119 PDV codes in 15 categories, such as Informed Consent, Enrollment and Adverse events. In the Documentation category, for example, there are seven PDV codes:

P1901 Documentation missing
P1902 Documentation incomplete
P1903 Documentation incorrect
P1904 Documentation signed by incorrect person
P1905 Documentation not signed correctly, other
P1906 Documentation back-dated
P1907 Documentation not dated correctly

The PDV lexicon suggests three Severity levels: Violation (major), Deviation (minor), and Progress Note (worth documenting). Severity levels are not regulatory definitions and different sites, sponsors, CROs and IRBs might interpret events of different types differently. They might also vary by protocol. For example, the failure to take a blood pressure reading might be a Deviation in a dermatology study but a Violation in a hypertension study.

The PDV lexicon also identifies seven Causations: Study Personnel, Subject, Sponsor, CRO, Ethics Committee, Other and None. The cause of a specific problem might affect the Severity level.

There might be disagreement as to what constitutes a test, an assessment, or a procedure. The important point is that useful analysis requires specific types of events to be classified consistently. Over time, it would be worthwhile to standardize classifications and interpretations so data can be compared across the clinical research enterprise.

Case Study

To test the PDV codes, I performed a retrospective analysis of five studies (A, B, C, D and E), all with similar, complex designs. The studies had five different sponsors and 29 subjects in total. Based on a retrospective analysis, the studies generated a total of 144 deviations and violations over a six-month period for which all five studies were actively enrolling subjects.

The data show that 59% of the deviations were (P1202) *Test not attempted*. For this analysis, "tests" included vitals, blood work, urine sample, EKG, etc.

Study personnel appear to have caused 63% of these deviations, and subjects caused 25% of them (although the data might have been biased by the study coordinators). As Chart 1 shows, the number and causation of the P1202 PDV code varied by study:

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Perhaps because Study D was the most demanding of the five studies, it had the highest number of P1202 deviations, with an exceptionally high number of deviations caused by subjects. (However, since the study coordinators performed the causation classification, the data might be biased.)

Chart 1. P1202 Protocol Deviations

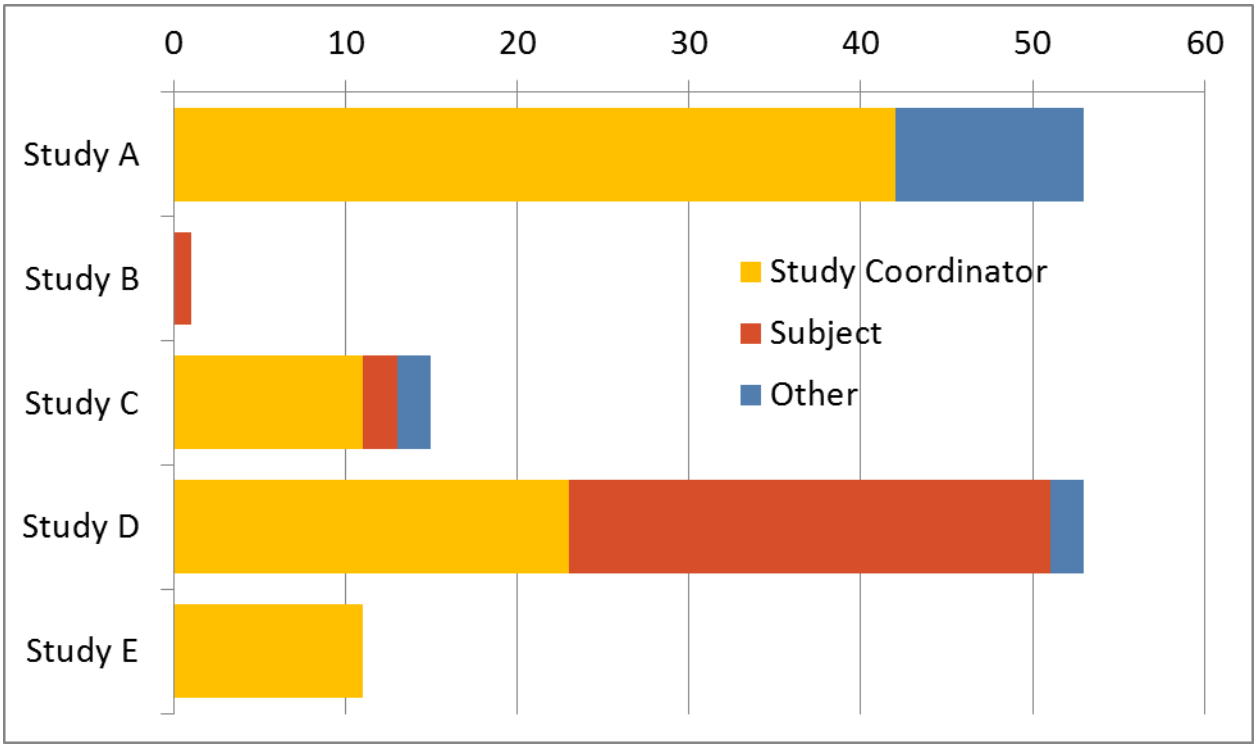

Table 1 shows the number of subjects, visits and P1202 protocol deviations for each study. In two of the five studies, the number of P1202 deviations exceeded the total number of visits because each missing data point counted as a violation.

Table 1. Subjects, Visits and P1202 Protocol Deviations

Study	Subjects	Visits/ Subject	Total Visits	P1202s	P1202s/ Visit
Study A	3	6	18	20	111%
Study B	1	2	2	1	50%
Study C	6	2	12	12	100%
Study D	6	3	18	49	272%
Study E	10	2	20	2	10%

Armed with this analysis, we can now search for the actual cause of these deviations.

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Root Cause Analysis

Root cause analysis (RCA) is a methodology to dig down to the root cause(s) of a problem. In a meeting with the study coordinators, we investigated six areas: Environment, Methods, Machines, Materials, Measurement and People. We discovered the following:

Some tests were not being performed because the test equipment was not available.

> The test equipment was not available because it had to be transported from the storage area to the exam room.
>
> > The test equipment had to be transported because there was no place to store it in or near the exam room.
> >
> > > There was no place to store it in or near the exam room because study equipment has to be kept separate from other equipment.
> > >
> > > > Study equipment has to be kept separate from other equipment to prevent using study equipment for regular patients.

Based on this information, we instituted three initiatives:

- Dedicate an exam room to research.
- Special scheduling parameters and "flags" for research subjects.
- Hold "feasibility" and "launch meetings" to determine the specific requirements and logistics of each study.

One month after implementing these initiatives, we started analyzing the data for the five studies for the following six months. P1202 protocol deviations/violations with both "study coordinator" and "study subject" causation codes both decreased by 80% vs. the pre-initiative period.

Conclusion

It is remarkable that nobody at the time appears to have done anything to correct these problems or call them to management's attention. Only one site monitor mentioned these deviations in a monitoring visit follow-up letter, and it was the site monitor for Study B, which had only one P1202 deviation.

We are currently phasing in PDV codes and root cause analysis across all studies at our site and are seeing substantial improvement in quality.

References

1. "Bringing Method to the Madness: Protocol Deviation & Violation Codes," Norman M. Goldfarb, Journal of Clinical Research Best Practices, November 2005.
2. Protocol Deviation & Violation (PDV) Codes, 2004-2016, available at https://www.magiworld.org/standards

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