Response to managing editor

1. Please provide a structured abstract as shown here:
http://bmjopen.bmj.com/site/about/guidelines.xhtml#research

Abstract has been revised.

Responses to Dr. Adrian Boyle

1. The study is very US centric and patterns of cardiac investigation and cocaine usage are very different outside North America. This limits the paper for an international readership.

We understand the US centric nature of the database may not be relevant to international readers regarding chest pain treatment. However, while our specific clinical problem was the treatment of cocaine related chest pain, our general point is that well-constructed registry databases can be instrumental in directing research towards what are actually clinically important questions that need answering. This underlying point is relevant to all readers interested in conducting clinical research.

2. The study is very underpowered to detect important differences. There is no a priori sample size calculation.

The study is a retrospective descriptive study using an already constructed database. Our power and sample sizes are limited by the data available to us and we readily acknowledged that we were under-powered to detect any differences in clinical outcomes. Please see "Discussion" paragraphs 7 and 8.

3. My main concern, however, is recall bias. They found few cases of cocaine users. How can the authors be sure that there were no cocaine users in the control group? I would imagine this slightly sensitive illicit activity might not always be reported to a physician or entered into a database.

We agree that our prevalence based on patient reports is lower than that from prior studies based on laboratory confirmation, which is very likely due to under-reporting by patients either due to reluctance or forgetfulness. We believe that physicians do not routinely order cocaine testing on chest pain patients and therefore in the real-world setting, a patient's subjective report, not any objective evidence, is what clinicians use in their decision-making process. And as our focus was on factors affecting physicians' decisions on testing and not on factors affecting patients' outcomes, we belief self-report more closely mimics real-world conditions and give our results more clinical relevance. Also, please see "Discussion" paragraph 6 sentence 4.

4. I am slightly struggling to see the usefullness of their results are. Basically, they have failed to find a significant difference in an underpowered sample.

Our point is exactly that we did not find a difference in testing. Our study was not primarily focused on finding a difference in patient outcomes and indeed was not powered to do so. We had assumed that reported cocaine use would have led to more testing, which is the assumption that likely resulted in studies that have come out over the past decade (see ref 9-13 and "Discussion" paragraph 4). We believe that if the lack of difference had been found and reported earlier, there may have been less research conducted over the past decade.

5. The term 'propensity' has a precise statistical use and I suggest the authors use a better term, such as 'tendency.'

Thank you for the distinction, and we have made the recommended change. Please see revised manuscript.

6. Though the sample is underpowered they should consider performing a McNemar's test to evaluate the difference in baseline groups.

We appreciate the recommendation. From our table 2 results, again since our primary outcome was tendency of testing:

Control group: 229 no test, 20 yes test
Case group: 225 no test, 24 yes test

498 discordant pairs. 245 (49.197%) pairs where the control underwent testing but the case did not, and 253 (50.803%) pairs where the case underwent testing but the control did not.

The two-tailed P value equals 0.7538

The odds ratio is 1.033, with a 95% confidence interval 0.863 to 1.236

This does not change our conclusion.

Response to Dr. Luke K. Hermann, MD

This paper nicely demonstrates the importance of using registry data to determine what clinical research questions actually warrant answering.

We thank Dr. Hermann for his time and comments.

Response to Dr. Jon W. Schrock MD FAHA FACEP

1. In the Methods section please clarify the inclusion criteria as based on ECG findings. The methods state that patients with ST segment elevation were excluded and in the first sentence of the discussion the population is described as those ‘without ECG suggestive of new ACS’. Does this mean patients with ECG findings of possible ACS including flipped T waves and ST depression were included or not? Please clarify this in the methods.

We have clarified the first sentence of our discussion. We did not include patients with new ST elevations on ECG or patients with a physician's initial impression of AMI as we stated in the methods sections. Please see change to "Discussion" paragraph 1 sentence 1.

2. In the results please list the number and percentage of patients lost to 30 day follow up for the cocaine related population and the registry as a whole.

For the entire registry - 647 patients (4.6%) were lost to follow up; for our study - 40 patients (8.0%) were lost to follow up, 20 patients from the control and 20 patients from the case groups. This has been added to the "results" paragraph 1.

3. Results section third paragraph please list the actual odds ratio and confidence intervals in the results section as this was the primary objective of the study.

This is added. Please see "Results" paragraph 3.

4. Discussion page 7 line 4. The sentence starting with “our study” is misleading as you list in your limitations that the registry only asked people to report if they used cocaine not if they used it recently. You

may say ‘chest pain in patients with self reported cocaine use’. The use of the phrase ‘cocaine associated chest pain’ implies that the pain began shortly after the cocaine use. Since we do not know the exact timing of the cocaine use one cannot infer that the chest pain is directly due to cocaine use.

Corrected. See "Discussion" paragraph 1 sentence 2.

5. Funding disclose states that no specific grant money was used however in the initial ITRACTs study the sponsor was listed as Millenium Pharmaceuticals and Schering-Plough Pharmaceuticals. As this study is using data from that initial endeavor the funding should be disclosed. The Authors can note that although the current analysis was not funded, the initial registry was supported by a grant in part by Millenium Pharmaceuticals and Schering-Plough Pharmaceuticals as cited in your reference #16.

This is now added. See text.

6. Table 3 the row listing ‘any testing’ was listed in table 2. This is redundant and should be deleted from table 3.

This has been removed. See table 3.