# ARTIGOS

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# DOES TREATMENT FOR PAIN REDUCE WILLINGNESS TO PARTICIPATE IN RESEARCH?

**Caroline Freiermuth[1], Gisselle Mani[2], Wei-Ying Drake[3], Debra Freeman[4], Paula Tanabe[5], Alex Limkakeng[1]**

1- **Duke University Medical Center**
2- **University of North Carolina at Chapel Hill**
3- **PRA Health Sciences**
4- **Duke Clinical Research Institute**
5- **Duke University**

## ABSTRACT

Research participation by patients is critical to the improvement of medical care. Prior work has suggested that treatment for pain may influence patient participation in research, although this has not been studied in a rigorous quantitative way. We hypothesized that receiving prior treatment for pain would not independently increase the participation rate for patients approached for cardiac biomarker research studies.
DESIGN-Retrospective observational cohort study. SETTING–academic urban tertiary care emergency department (ED) with annual census of approximately 70,000 visits. PARTICIPANTS–Patients who were approached for enrollment into 1 of 2 IRB approved, cardiac biomarker research studies between 12/2010 and 11/2011. To be eligible, patients had to be 18 years of age, present with chief complaint of chest pain, and have experienced chest pain within 12 hours of presentation. Trained clinical research coordinators approached eligible patients from 8 am-10 pm on weekdays with intermittent sampling on weekends. OBSERVATIONS–Pain treatment data was abstracted from electronic medical records by a single reviewer who was blinded to study hypothesis. Patient demographics and participation outcomes were recorded from a research screening log. DATA ANALYSIS-Simple descriptive statistics were calculated and a multivariate logistic regression model was created with participation as outcome, pain treatment as a binary predictor variable, and age, race, gender, and self-reported pain score as confounding variables. All analyses were performed using JMP (Version 9.0, SAS Institute, Cary, NC).
A total of 396 patients were approached, with 3 excluded patients for missing data. Median age was 55 years, 39.2% Black, and 50.1 % male. Eighty percent of patients participated in the research studies. A total of 67.3% of patients had been provided pain treatment prior to approach; only 10% of those patients received opiates. Treated patients had an 80.8% participation rate versus 78.3% for those not receiving treatment. After adjusting for confounding variables, treated patients had odds ratio of 1.14 (95%CI 0.66-1.94) of participating.
Treatment for pain does not seem to affect participation ED research studies. This study is limited by being restricted to one type of pain and research study. Other factors that do influence participation should be explored.

**Keywords:** Healthy and Unhealthy Organizations, Wellbeing, Psychosocial Phenomena

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## INTRODUCTION

Each year, almost 6 million people present to emergency departments (ED) with chest pain.1 The differential for this complaint is broad and encompasses time-sensitive life threats including acute coronary syndrome (ACS).2 Currently, multiple approaches have been proposed to help risk stratify patients with chest pain3, but ACS remains an important cause of morbidity and mortality.4 Therefore, diagnosis of acute coronary syndrome in the ED remains an active area of research.

Advances in ACS diagnostics are dependent on the willingness of chest pain patients to participate in research. In previous qualitative studies patients cited pain in general as a reason for refusal of research participation.5, 6 Pain has also been cited as a cause of a compromised informed consent process by interfering with patients' ability to understand what is involved in participating in research.7, 8 It is therefore possible that prior studies in patients with chest pain may have been systematically biased. If level of pain influences participation, it would also suggest that addressing a patient's pain prior to approaching them for research would improve enrollment rates for research studies. No prior study has quantitatively explored the relationship between pain treatment and research study refusal rates in a sample of ED patients.

We sought to describe the relationship between patient-reported pain scores and consent rates in a cohort of chest pain patients approached for 2 "parent" research studies. We hypothesized that patients with higher self-reported pain scores at emergency department triage or at the time that they were approached for research consent would be less likely to consent to participate in research.

## METHODS

### Study Design

We performed a secondary analysis of 2 prospective diagnostic test trials, examining the relationship between patient-reported pain scores and consent to participate in research. This study was approved by our institutional review board; Individual patient informed consent was waived.

### Study Setting and Population

We included all patients who were approached for enrollment into one of two parent industry-funded, IRB approved, cardiac biomarker research studies between

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December 2010 and November 2011. The adult ED volume at the study site is approximately 70,000 visits per year. To be eligible for either study, patients had to be 18 years of age, present with chief complaint of chest pain, and have experienced chest pain within 12 hours of presentation. Patients were not eligible if they were not competent to consent or could not speak English. Trained clinical research coordinators approached eligible patients from 8 am to 10 pm on weekdays with intermittent sampling on weekends.

## DATA COLLECTION, PROCESSING AND MEASURES

All study personnel were trained in responsible conduct of clinical research as well as protocol specific procedures. As part of ongoing parent study activities, patients meeting inclusion criteria were approached for consent. The time that they were approached was recorded, in addition to age, race, gender, and when possible, reason for non-enrollment for eligible patients in a structured screening log. Clinical care was not changed by the current study.

For enrolled patients, coordinators collected all relevant demographic and clinical data including laboratory and radiographic study results. Study personnel also drew blood samples up to four times during their hospital stay. Patients' clinical course was then followed for the duration of their stay and they were contacted for follow-up outcomes at one year. Neither study offered any form of financial compensation for participation.

All pain scores used for the current study were abstracted retrospectively from patients' clinical charts. Pain scores were recorded as part of routine clinical care by clinical nursing staff, who had received standard training on assessing patients' pain levels. Pain scores were recorded using a 0-10 verbal descriptor scale (VDS). The patient was instructed to provide a rating corresponding to their current level of pain, with 0 representing no pain and 10 representing the most severe pain they have ever felt. Pain scores were routinely recorded at triage, after any pain medication administration, and at other times as per usual clinical care. Two reviewers who were blinded to study hypothesis retrospectively extracted pain scores from triage (Triage) and from the time closest to approach for consent for the parent research studies (Approach) from electronic clinical records for both enrolled and non-enrolled patients. Because pain scores were not collected prospectively, the

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time difference between the pain score report and time patients were approached was measured for reporting.

## DATA ANALYSIS

Demographic data are reported as proportions. All patient pain scores are presented as simple integers with medians and interquartile ranges (IQR). Because presence of pain treatment or not was a simple, quantitative data point we did not perform inter-rater reliability assessment on the data abstraction. Demographics were compared using simple proportions. We analyzed the association between consent rates and patient pain treatment using a multivariate logistic regression model. Because our sample was derived from two parent research studies, our sample size was fixed. Our model contained age, race, gender, and self-reported pain score as confounding predictor variables. These predictor variables were selected based on prior research on this topic.9-19. We identified research participation as our outcome variable.

A Chi-square statistic was computed by taking twice the difference in negative log-likelihoods between the fitted model and a reduced model that has only intercepts. Goodness of fit for the models was determined via Chi-square statistic for 2 times the negative log-likelihood for error. Odds ratios were calculated for each predictor variable. A p-value < 0.05 was considered statistically significant, with no adjustment for multiple comparisons. All analyses were performed using JMP (Version 9.0, SAS Institute, Cary, NC).

## RESULTS

Overall, 396 patients were approached to participate in the two cardiac biomarker studies. A total of 390 charts were included in the final analysis, with 3 charts excluded due to lack of documentation. Demographics are described in Table 1. Overall, 274 patients (80.1%) consented to participate in the parent research studies. Demographics were similar between those who consented to participate and those who refused participation (Table 1). We recorded specific reasons for refusal for 32 eligible patients; none cited pain as the reason for refusal. The most common reason given for refusal (10 patients) was that the study required too much blood to be drawn.

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**Table 1 - Demographics of Patients Approached for Research Consent**

| | Total | | Consenters | | Non-consenters | |
|---|---|---|---|---|---|---|
| Total | 396 | | 317 | | 79 | |
| Age, Mean (years) | 57 | | 56 | | 60 | |
| Male | 201 | 50.8% | 163 | 51.4% | 38 | 48.1% |
| Race | | | | | | |
| Black | 155 | 39.1% | 118 | 37.2% | 37 | 46.8% |
| White | 230 | 58.1% | 192 | 60.6% | 38 | 48.1% |
| Other | 11 | 2.8% | 7 | 2.2% | 4 | 5.1% |

**Table 2 - Pain Score Summary Statistics**

| | Total | Consenters | Non-Consenters |
|---|---|---|---|
| Triage Pain Score (median, (IQR)) | 4 (0-6) | 4 (0-7) | 4 (0-7) |
| Approach Pain Score (median, (IQR)) | 2 (0-5) | 3 (0-6) | 2 (0-6) |
| Change in Pain Score, (median, (IQR)) | 0 (0-2) | 0 (0-2) | 0 (0-0) |

IQR = interquartile range

For the total sample, the median (IQR) Triage, Approach, and change in pain scores are summarized in Table 2. The majority of patients reported a "0" pain rating at time of Triage and Approach, with the remaining scores normally distributed. Overall, there was a small difference in time between when pain scores were obtained compared to Approach (median 34 minutes IQR 14-68 minutes). Generally, there was very minimal change in pain scores between Triage and Approach.

Consent rates by tertiles of Triage and Approach pain scores are shown in Table 3. Consent rates did not differ significantly across race or gender subgroups nor was there a clear trend based on change in pain scores between Triage and Approach (Table 4).

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**Table 3 - Consent Rates by Pain Scores at Triage and Approach**

| Pain Score | 0 | 1-3 | 4-6 | 7-10 |
|---|---|---|---|---|
| Triage (n, consent rate (%)) | 105, 77.1 | 86, 84.9 | 104, 79.8 | 95, 80.0 |
| Approach (n, consent rate (%)) | 139, 76.3 | 61, 85.2 | 76, 80.3 | 69, 78.3 |

For the logistic regression model, the Chi square statistic for the whole model test (comparing model to intercepts only) was 13.02 ($p<0.043$) indicating improved fit for the model over intercepts only. The model's Chi square statistic for lack of fit was 325.41 ($p>0.72$), indicating good fit. In multivariate analysis, after adjusting for age, race, and gender, and pain scores, pain treatment did not predict participation by effect likelihood ratio tests (odds ratio 1.13; 95% CI 0.65-1.94).

**Table 4 - Consent Rates by Change in Pain Scores between Triage and Approach.**

| Change in Pain Score | n | Consent rate |
|---|---|---|
| Pain Worsened | 36 | 77.8% |
| 0 | 231 | 80.1% |
| 1 | 26 | 84.6% |
| 2 | 29 | 89.7% |
| 3-10 | 68 | 79.4% |

## DISCUSSION

ACS remains a vexing problem and further research is needed to improve the current diagnostic paradigm20. In order to accomplish this research, patient participation is necessary. However, there have been no evidence-based methods proposed for increasing the likelihood of patient participation. In this quantitative analysis, we did not find a relationship between pain treatment and likelihood of participating in a research study of a diagnostic test. This study stands in contrast to qualitative work5, 7 suggesting that patients' pain levels or inherent gratitude from receiving treatment might influence their likelihood of participating in research. In part this may be due to the fact that the data obtained in this study reflect actual behavior with regard to research participation and not responses to hypothetical scenarios or a posteriori interviews. The current study is also differentiated from prior work on research consent in that we examined a potentially modifiable factor (pain treatment) rather than a patient demographic characteristic.

Even after adjusting for known demographic factors9-12, 14-18 that might influence likelihood of participation, there did not appear to be a relationship between pain treatment and consent to research participation. Overall the majority of patients agreed to participate regardless of treatment. These findings suggest that addressing patients' pain prior to approach for research is not likely to unduly influence or coerce patient and that research

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enrollment for diagnostic studies is highly feasible in emergency care environments, even in patients with pain.

Our study contrasts with prior work indicating that the informed consent process itself may impart a systematic bias on research participant selection and enrollment. One prior analysis of a trauma registry indicated that among patients presenting to a level I trauma center, the most severely injured would be less likely to be able to consent to a hypothetical trial due to their acute illness and lack of availability of a legally authorized representative.21 Another study examining patients being tested for venous thromboembolism found that the prevalence of disease was lower (6% vs. 13%) among participants than nonparticipants.22 Furthermore, an analysis of a stroke registry requiring explicit consent found through a routine audit that there were important differences between those who did consented and those who did not.23

The needs of patients experiencing pain at the time of approach for the research informed consent process have been well described.24 Prior research has indicated that patients can participate in the informed consent process for treatment despite acute pain.25 Although chronic pain patients' willingness to enroll in research was related to pain severity and a desire for better pain management, cancer patients' willingness to enroll was not.26 Our study differs from this prior work in that we examined patients presenting with acute pain in the emergency department. To our knowledge, this study is the first to quantitatively examine the relationship between pain treatment and research participation in the emergency care milieu.

These results should serve to assuage the fears of reviewers and sponsors that enrollment in emergency care environments is ethically and logistically feasible. It is not known what sort of “chilling effect” such fears may have had on proposals or funding of studies performed in emergency care settings. There are many reasons why patients who are in pain might agree to participate in research.27 Patients who are well informed are more likely to participate than those who are not, regardless of the level of pain involved. In one empiric study, patients who understood the level of risk or pain associated with a hypothetical protocol were twice as likely to participate than those who did not.28 In our particular case, another explanation might be that the study for which we were approaching patients was a minimally invasive study. Thus, even patients in severe pain did not consider it a

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burden to participate. Alternatively, there might be other factors that influence patients' decisions to participate. Prior qualitative research has indicated numerous other reasons why patients with emergent health conditions participate in research including altruism, trust in the healthcare institution, and perceived self-benefit5-8, 29-34.

### LIMITATIONS

There are several limitations to this analysis of consent rates. This was a retrospective study of a single center's experience. Furthermore, we studied only patients with one type of pain, for a particular type of research study. Our sample was noted to report relatively low levels of pain overall. Our results thus might not be broadly generalizable to all types of pain or research studies. We were also limited in terms of sample size due to the retrospective nature of this analysis. However, we did have ample numbers of consent outcomes to allow for a logistic regression analysis. Due to the retrospective methods, we were unable to obtain pain scores for the entire sample, and the approach pain scores were collected at a different time than when the patient was actually approached (median, 34 minutes). We tried to control for this by measuring the time difference and removing outliers and it did not appear to affect results. This discrepancy should be corrected in future prospective studies. Furthermore, we did not control for all potential confounders, such as time spent waiting in the ER or whether any pain treatment was given. However, prior work suggests that amount of time spent waiting for clinical benchmarks do not influence participation.19

## CONCLUSIONS

Prior treatment for pain is not associated with higher rates of consent for research. It is feasible to enroll patients in research trials in the emergency department setting despite the presence of pain. Other, perhaps more subjective factors, likely influence patients' decisions to participate in research and these relationships should be further explored.

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## Contato

**Caroline Freiermuth MD, FACEP**
**Division of Emergency Medicine**
**Duke University Medical Center**
**Durham NC 27710**
**Email: caroline.freiermuth@duke.edu**

**Gisselle Mani MD**
**Department of Surgery**
**University of North Carolina at Chapel Hill**
**Chapel Hill NC 27599**
**Email: gisselle.mani@unchealth.uc.edu**

**Wei-Ying Drake MD**
**Clinical Research Associate**
**PRA Health Sciences**
**Raleigh NC 27612**
**weiying2005@gmail.com**

**Debra Freeman BSN**
**Duke Clinical Research Institute**
**Durham NC 27710**
**Email: debra.h.freeman@duke.edu**

**Paula Tanabe RN, PhD**
**School of Nursing**
**Duke University**
**Durham NC 27710**
**Email: paula.tanabe@duke.edu**

**Alex Limkakeng MD, FACEP**
**Division of Emergency Medicine**
**Duke University Medical Center**
**Durham NC 27710**
**Email: alex.limkakeng@duke.edu**