

WELCOME

Welcome to the first issue of the BEACON Registry Newsletter for Investigators & Coordinators. The newsletter is published quarterly and will provide you with current registry information, related clinical practice information and answers to your frequently asked questions.

On behalf of the sponsor, HeartScape Technologies, Inc., and the Academic Research Organization, C5Research, we would like to thank you for joining the BEACON Registry as a clinical site.

The primary objective of the BEACON Registry is to assess and ultimately improve the process of care and health outcomes of patients presenting with chest pain suspected to be of cardiac origin. The secondary objective is to determine the impact of new technologies, practice patterns and initiatives on patient care. One of the technologies that will be used is the 80-lead PRIME ECG®.

We are excited that you will be part of this registry and that we will be working with you!

The BEACON Registry Team

A Message from the Principal Investigator

BEACON Reflections: Guidelines, quality metrics and suspected acute coronary syndromes

Exactly what do guidelines from the large cardiology and emergency medicine societies say about the early evaluation of suspected acute coronary syndrome (ACS)? They are pretty straightforward, essentially saying “get an ECG quick and measure some biomarkers”. When either the ECG or biomarker testing results in an MI diagnosis, the guidelines then provide detailed and validated instructions for patient care. However, as to the type of ECG and which specific biomarker or platform is best, they are intentionally vague. This pathway represents the state of the art in medical care for AMI and for patients meeting entry criteria; it standardizes care and optimizes outcomes. Unfortunately, the number of patients with a diagnostic ECG or biomarker represent no more than about 10% of the patients presenting to the ED with a chief complaint chest pain.

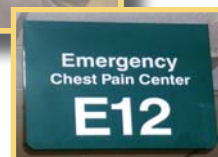
That leaves about 90% of the remaining patients without a clearly articulated strategy. What do the guidelines say about the patients with a non-diagnostic ECG and undetectable biomarkers? They give us a menu of many things that may work, but guidance as to the best strategy is unclear. In fairness to guideline writing committees, there is a serious lack of data on what is the most efficient and optimal evaluation. There are very few randomized controlled comparative trials reporting outcomes between the different evaluation strategies for patients with suspected acute coronary syndromes. Thus, in the absence of data, rather than picking a single course, the guidelines simply acknowledge that many strategies may be adequate.

BEACON may provide opportunities to better define the early ACS evaluation. For the “get an ECG quick” recommendation, the highest risk patients are currently identified by the 12 lead ECG that identifies some of the most critical types of STEMI. While the 12 lead is simple, non-invasive and fast, it suffers a significant sensitivity deficit for posterior, high

THE CLEVELAND CLINIC TEAM



Beth Gaul, Research Nurse Coordinator, Tracy Barbour, Clinical Research Assistant II and Dr. Frank Peacock, PI, in the Emergency Department with their PRIME ECG Unit.



continued on page 6.

INSPIRATIONS

There will be some revisions made to the InSpire system in the near future that will eliminate redundant queries as well as provide for the collection of the quality measures for myocardial infarctions. The sites will be notified once these changes become available.

If you find it necessary to enter or change data on an existing, locked page in InSpire, please contact your site manager and request that the page be unlocked.

There is a new, large “L” icon on the InSpire home page in the upper right hand corner of the page. This Featured Form Listing icon can be used to access certain documents or pages from your site on some or all of your subjects enrolled in BEACON. For example, this icon could be used to look up all of the forms with queries for all of the subjects at your site.

To review all the InSpire FAQs noted so far, access the FAQ document on the BEACON Website home page under BEACON EDC, or look under the documentation library tab on the InSpire home page.

INSPIRE FAQs

Here are a few of the more frequently asked questions regarding data entry in the InSpire system:

Q: If the subject goes to the Clinical Decisions Unit (CDU)/ Observation Unit from the ED, is this considered an admission?

A: Technically, the Centers for Medical & Medicaid Services (CMS) do not consider CDU and chest pain units (or any observation status) admissions. The definition is based on the status that the transfer occurs. It is not a geo-

graphical consideration, as you can admit a subject to any hospital ward as observation status, and he/she isn't considered an admission. So, a subject in an observation status is considered to have an outpatient visit, no matter where the subject is in the hospital.

Q: Not all of our subjects have the onset of ischemic symptoms time recorded. We have been putting 00:00 as the time -- is this OK?

A: We would rather that a time is used that is closest to the time that the symptoms occurred. Does the chart note how many hours ago the chest pain started? If so, please estimate using this time. You could also use the time that the subject called 911 or decided to come into the ED. If the symptoms are stuttering then use the time that the symptoms became severe.

Q: How should we enter troponin results of <0.01, since I have not found a way to display this?

A: Enter 0.01 for results that are < 0.01 since you would be unable to enter the < sign.

Q: Do you want the initial or the second ECG recorded on the 12 Lead ECG page?

A: We would like all ECGs recorded that were done in the ED. On the ECG form, on the left, under “FORMS,” there is an “add” button. Click on the “add” button, and you will get another ECG form. You can put in as many ECGs as you have for each subject.

Q: Can I enter the same subject more than once in the InSpire system?

A: If the same subject had more than one ED visit for chest pain, he/she can be entered more than once. Be sure that the date and time of arrival at the ED are different.



WWW.BEACONREGISTRY.COM

There are many features on the BEACON Website – have you seen them all? We invite you to take a few minutes to explore the webpage, including the Message Board!

The BEACON electronic data collection (InSpire) can be accessed via the webpage. The Frequently Asked Questions document has lots of information for your reference. The questions and answers are presented page by page for your convenience.

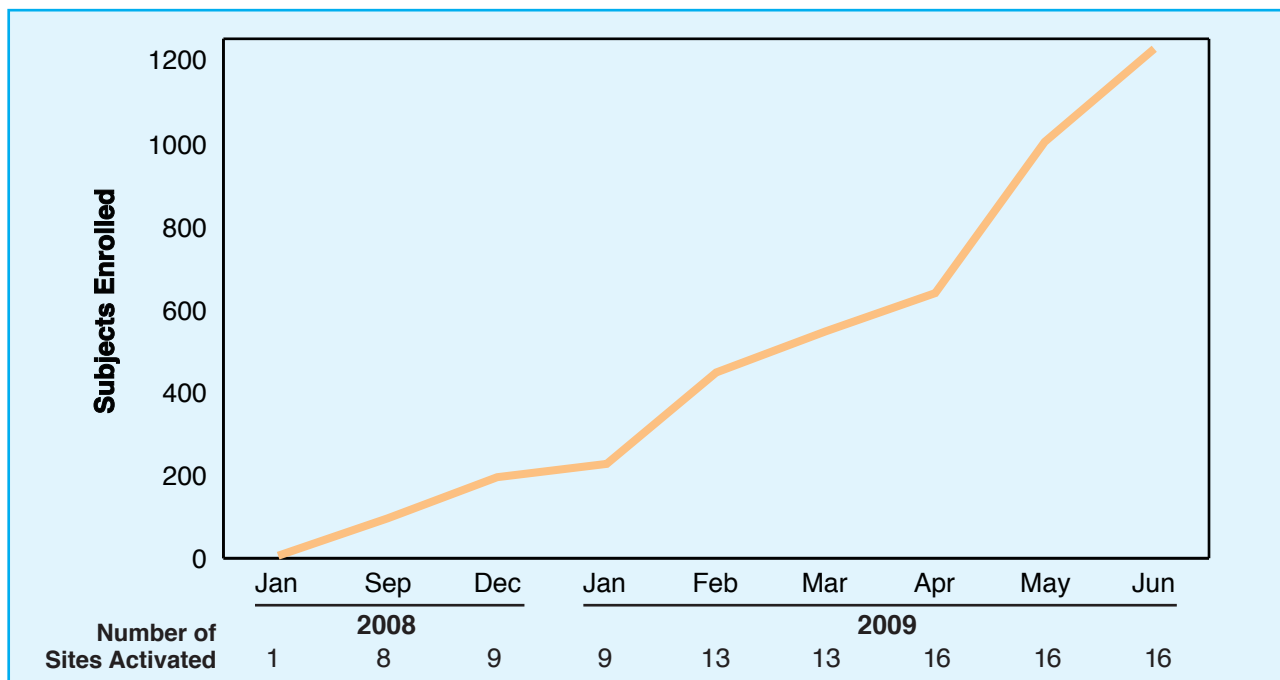
A new section has been added - “Case Studies from BEACON Sites.” This section will provide a forum for investigators to share some of their interesting cases with other BEACON sites. The first presentation is three case studies submitted from Site 04 – Wake Forest University by Cedric Lefebvre MD, Adam Langenbrunner, MD, James Hoekstra, MD and Jane Kilkeny – thank you!

ENROLLMENT STATUS AS OF JUNE 30

Institution	Investigator	Study Coordinator	Subjects Enrolled
Cleveland Clinic	Dr. Frank Peacock	Beth Gaul	211
Tampa General	Dr. Richard Paula	Daryl DeNittis	201
Christiana Care	Dr. Charles Reese	Barbara Davis	183
Wake Forest	Dr. Cederic Lefebvre	Jane Kilkenny	163
Minneapolis Heart	Dr. David Larson Dr. Tim Henry	Jeanne Oelfke	143
Mayo Clinic	Dr. David Nestler	Lindsay Wiebusch	102
University Community Hospital	Dr. Steven Lay	Gloria Stagi-Coyle	54
Vanderbilt University	Dr. David Maron Dr. Allan Storrow	Karen Miller	40
Henry Ford	Dr. Richard Nowak	Michele Moyer	40
Ohio State	Dr. Brian Hiestand	Lynn White	31
University of Virginia	Dr. Lawrence Gimple Dr. William Brady	Lea Becker	23
University of Cincinnati	Dr. Gregory Fermann	Cendi Dahl	17
William Beaumont	Dr. Carol Clark	Cindy Huckabone	12
UC Davis	Dr. Debra Diercks	Allyson Sage	4
St. Francis Hospital	Dr. Shahriar Dadhka	Korosh Sharain	2
Pennsylvania Hospital	Dr. Charles Pollack	Dr. Chris Rees	0

Total Enrollment as of June 30 - 1,226

ENROLLMENT GRAPH



COORDINATORS' CORNER

CLARIFICATION OF PROTOCOL PARTS 1A, 1B AND 2

Part 1a includes the **first 30 subjects** that are entered into the electronic data collection system, InSpire. These subjects (0001 – 0030) meet the inclusion criteria and were seen in your ED prior to having the **PRIME ECG®** available. You can pull charts from several months ago and enter those subjects.

No subjects with numbers 0001 through 0030 will have had a PRIME ECG® performed.

Part 1b includes the **second 30 subjects** that you enter into InSpire (0031 – 0060). These are subjects who meet inclusion criteria and were seen in your ED and had the PRIME ECG® performed.

All subjects with numbers 0031 through 0060 will have **had a PRIME ECG®** performed.

Part 2 can be started after Parts 1a and 1b have been completed. Enter “all comers” with chest pain who present to your ED suspected to be of cardiac origin or equivalent.

Some of these subjects will have a PRIME ECG® and others will not.

Inclusion criteria (any 1 constitutes eligibility) for Part 1a & 1b

1) Suspected acute coronary syndrome and a positive troponin as defined by the local institutional standard

OR 2) At least 10 minutes of symptoms believed to represent a myocardial ischemic equivalent within 24 hours of presentation, and any one of the following:

- a) ST elevation > 1mm on 12-lead electrocardiogram, in any 2 anatomically contiguous leads
- b) Presumed new left bundle branch block
- c) ST depression of at least 0.5 mm on 12 lead ECG, in any 2 anatomically contiguous leads
- d) Age ≥ 55
- e) History of PTCA, PCI, CABG, AMI or myocardial ischemia diagnosed by stress testing
- f) Receiving treatment for diabetes or hyperlipidemia
- g) More than 20 pack years of cigarette smoking

SUBJECT LOG

Please be sure to use the revised Subject Log which was sent to Sites in March, 2009. This log includes a column for the subject's Social Security number. This will assist you when performing the Social Security Death Index Inquiry at 18 months from ED presentation for mortality status at 1 year. As the Registry moves forward, the completeness and accuracy of your Subject Log will be extremely important.

Please contact Karen Mrazek at Mrazek@ccf.org if you have not received your site's Subject Log.

BENCHMARK REPORTS

We will send each site quarterly benchmark reports which will contain the following information from that site:

- Enrollment information
- Key BEACON variables
- Outcomes
- National Hospital Quality Measurements
- Rates of compliance with AHA/ACC 1A recommendations for the care of the ACS patients

The report will include the following demographic information:

- Procedures performed (ECG, PRIME ECG, echocardiogram, PCI, CABG, etc)
- Length of stay in the emergency department (ED) and hospital
- Time to disposition in ED
- National Hospital Quality Measures such as the use of ASA, lipid lowering agents, LDL assessment, Beta Blockers, PCI etc.



TECHNICALLY SPEAKING FROM HEARTSCAPE TECHNOLOGIES, INC. —

DIAGNOSTIC ALGORITHM vs. ST0 FILTER



Why do they sometimes disagree?

The ST0 Filter map is a very intuitive display and often becomes the main port of call for novice users of PRIME. Generally, a totally green Filter map will be accompanied by a “Normal” diagnosis from the Diagnostic Algorithm, and strong coloration on the Filter map by an “Acute MI” from the Diagnostic Algorithm. However, there are times when you will be presented by an apparent discordance:

Why is this?

The answer lies in the nature of the two mechanisms:

- **ST0 Filter Map:** The ST0 Filter map is a simple visual cue to understand the general levels of ST0 (or J point) elevation/depression, and if they warrant further investigation. However:
 - The thresholds used are general approximations for each region.
 - The Filter map shows every electrode that exceeds the threshold. It does not necessarily mean that there are enough to call an MI. (In a 12-lead, you require 2 contiguous leads >2mm to call MI. With so many more electrodes in PRIME, you would not expect to call an MI on 1 or 2 electrodes).
- **Diagnostic Algorithm:** The Diagnostic Algorithm is far more subtle than just an ST0 elevation detector. It considers:
 - The amount of ST0 elevation, how widespread it is and looks for a similar amount of reciprocal depression, in the right area.
 - The ECG morphology: T wave inversion, lack of R wave progression, QRS:ST ratios, hyperacute T wave etc. The more morphology changes there are, the lower the ST0 changes have to be before calling MI.

So, trust the Diagnostic Algorithm over the ST0 Filter map, but use the explanations, pop ups and map displays to check that the diagnosis is based upon sound data.

For more information about PRIME ECG please visit Facebook and search “PRIME ECG.”



BE ON TARGET

Enrollment goal for Part 2 is
60 subjects/month/site

Message from page 1.

lateral, or inferior myocardial infarction, or if there is left bundle branch block. Newer 80 lead ECGs improve sensitivity, so one of the important questions BEACON will address is the impact of this technology for evaluating chest pain.

It should also be noted that while early identification of STEMI provides great benefit to the individual, from a system perspective, STEMI represent only 2% of all chest pain presentations, and ultimately only 1% of all ED patients. Since a sensitive test may exclude disease, improving ECG sensitivity may allow a far greater number of patients to forego unnecessary evaluations. How improving the ECG sensitivity will impact ED management will also be addressed by BEACON.

BEACON may also define the best of the various biomarker strategies currently employed. Existing guidelines do not define which troponin assay (I or T) should be used, whether a high sensitivity or standard platform is best, and in which clinical scenario is more rapid serial sampling adequate. While both the European Society of Cardiology and the American College of Emergency Physicians guidelines agree that selected patients may have myocardial infarction ruled out by a single marker, which patients constitute "selected" is sometimes unclear. This is because troponin, generally accepted as the most specific myocardial necrosis marker, has such poor early sensitivity that discharging a patient after a single negative test may miss an evolving myocardial infarction. Thus, to avoid inappropriate discharge of a chest pain patient with initially negative cardiac marker, serial marker testing is commonly performed. This "waiting for a positive", found in only 8% of all chest pain patients require more hours after which we still haven't excluded myocardial ischemia and myocardial perfusion evaluation may be needed.

Finally, while the application of a multimarker strategy (the simultaneous combination of a necrosis, ischemia, and stress markers) would theoretically provide superior data compared to any single marker strategy, the lack of comparative studies limits understanding which strategy should be universally adopted. Which markers, how often they should be repeated, and what is the definition of a clinically significant change or rate of change, is poorly defined. This lack of data hurts. While many studies have investigated various aspects of the ACS evaluation, few have compared overall outcomes between competing strategies.

The lack of data as to what work up provides the best outcomes not only results in non-specific guideline recommendations, it also limits quality metrics to evaluate the process of care. What are the metrics of quality in the evaluation of chest pain when the ECG and necrosis markers are negative? Most of the currently used metrics focus on the patient who has "ruled in" and lack specifics regarding the majority of patients who "rule out".

The hope for BEACON is that it will allow the comparison of outcomes that result from various testing strategies. Prior registries have literally evaluated millions of patients with STEMI or NSTEMI. While this represents the low hanging fruit for determining therapeutic interventions, it has not provided sufficient guidance for what constitutes the best evaluation of patients with suspected acute coronary syndromes who don't have STEMI or NSTEMI. In fact, no recent large registry has ever examined patients presenting with suspected ACS. With BEACON we hope to determine the optimum evaluation of the chest pain patient, which ECG provides the best data, which marker strategies provide the most efficient and accurate results, what is the best method and timing of myocardial perfusion evaluation, and what quality improvement metrics are associated with the best outcomes within a hospital system.

Thanks for your interest,
W. Frank Peacock, MD, FACEP

C5 RESEARCH CONTACTS



Susan Jasper, RN, BSN, CCRC Project Manager	jaspers@ccf.org	216.445.3484
Patricia Hodge, RN, BSN, CCRC Project Manager	hodgep@ccf.org	216.445.2849
Karen Mrzeck Project Specialist	mrzeck@ccf.org	216.445.5081

EDC Help

Inspire Helpdesk
Call 1.866.342.0693 or email Sitesupport@PharmalinkFHI.com