

**CARDIOLOGY CLINICAL TRIAL PARTICIPATION IN COMMUNITY-BASED  
HEALTHCARE SYSTEMS: OBSTACLES AND OPPORTUNITIES**

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Funding Source: National Institutes of Health, Bethesda Maryland. Coordinated Clinical  
Studies Network (CCSN), Contract No. HHSN268200425216C, ADB Contract No. N01-HC-  
45216 (P.I.: Dr. Eric Larson)

## **ABSTRACT**

**Background:** The objective of our study was to examine cardiologists' and organizational leaders' interest in clinical trial participation and perceived barriers and facilitators to participation within ten diverse non-profit healthcare delivery systems. Trials play a pivotal role in advancing knowledge about the safety and efficacy of cardiovascular interventions and tests. Although cardiovascular trials successfully enroll patients, recruitment challenges persist. Community-based health systems could be an important source of participants and investigators, but little is known about community cardiologists' experiences with trials.

**Methods:** We interviewed 25 cardiology and administrative leaders and mailed questionnaires to all 280 cardiologists at 10 U.S. healthcare organizations.

**Results:** The survey received a 73% response rate. While 60% of respondents had not participated in any trials in the past year, nearly 75% wanted greater participation. Cardiologists reported positive attitudes toward trial participation; more than half agreed that trials were their first choice of therapy for patients, if available. Almost all leaders described their organizations as valuing research but not necessarily trials. Major barriers to participation were lack of physician time and insufficient skilled research nurses.

**Conclusions:** Cardiologists have considerable interest in trial participation. Major obstacles to increased participation are lack of time and effective infrastructure to support trials. These results suggest that community-based health systems are a rich source for cardiovascular research but additional funding and infrastructure are needed to leverage this resource.

**Keywords:** clinical trials; clinical trials recruitment; barriers to clinical trial participation; clinician participation in clinical trials

## INTRODUCTION

Clinical trials have played a pivotal role in identifying new treatments, refining therapeutic strategies, and forming the evidence base for the development of clinical practice guidelines [1,2]. Clinical trials also help advance our understanding of underlying disease mechanisms and processes and often serve as the final “proof of concept” for hypotheses regarding potentially modifiable risk factors. The National Institutes of Health (NIH), other non-profit organizations, and pharmaceutical and device companies, have all made substantial financial investments in the planning and conduct of cardiovascular trials over the past several decades, leading to a growing number of studies that enroll anywhere from several hundred to many thousands of participants for primary, secondary and tertiary prevention of cardiovascular diseases [3].

Despite the success of many trials that enroll large numbers of patients across the spectrum of acuity and disease complexity, recruitment challenges remain for trials, especially in enrolling the elderly, women, and minorities [2,4-9] as well as persons with important comorbidities (e.g., chronic kidney disease [10] ). Under-representation of various important subpopulations in trials may reduce the generalizability of results to larger target populations with cardiovascular risk factors or clinical conditions treated in typical practice settings [10,11]. Furthermore, investigators and sponsors are increasingly pursuing patient populations outside the U.S. to meet recruitment goals, particularly in larger clinical outcomes studies, which increases both methodological complexity and costs [12,13].

In its effort to close the gap between basic research and application, the NIH created a “roadmap” to “catalyze changes that must be made to transform our new scientific knowledge into tangible benefits for people [14] .” The initiative led to the agency’s release of a new approach to funding for biomedical research in 2006—the Clinical and Translational Science Awards (CTSAs) [15]. One requirement of the CTSAs is the development of community partnerships to increase the number of participants in trials. While historically the majority of

trial participants in the United States have come from academic centers, an increasing proportion of participants are now enrolled by community-based practices [1,12,16]. Numerous current community-based healthcare delivery systems have large populations of ethnically diverse enrollees who are followed for long periods of time, and employ many experienced researchers [17]. However, little is known about the attitudes and experiences related to trial participation of cardiologists who practice in these types of organizations, which are likely sources of participants and investigators.

To address this knowledge gap, we examined interest in trial participation, and perceived barriers and facilitators to participation, among cardiologists and cardiology and administrative leaders within ten diverse healthcare delivery systems that are members of the HMO Research Network [17]. Our overall goals were to provide insights into the perspectives of key stakeholders on cardiovascular trials and to identify high priority areas that could be targeted to increase participation in trials within community-based settings.

## METHODS

### Setting

This study was conducted as part of the HMO Research Network Coordinated Clinical Studies Network funded through the NIH Roadmap initiative. The HMO Research Network is a consortium of 15 geographically diverse healthcare organizations in the U.S. with integrated research divisions committed to public domain research that advances population health [17]. The ten network members participating in this study include: Kaiser Permanente Northern California, Northwest, Colorado, and Georgia; Group Health, Washington; HealthPartners Research Foundation, Minnesota; Henry Ford Health System, Michigan; Harvard Pilgrim Health Care, eastern Massachusetts; Meyers Primary Care Institute, western Massachusetts; and Lovelace Clinic Foundation, New Mexico. These organizations provide comprehensive healthcare to a defined population of approximately 6.8 million people using a variety of financial

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models. Institutional review boards of all participating organizations approved this study, and informed consent was obtained from all respondents as described below.

### **Data Collection**

Utilizing a mixed-methods approach, we employed two methods to collect data [18,19]. First, between July 2005 and January 2006, we conducted in-depth, semi-structured, key-informant phone interviews with two to four cardiology and administrative leaders at each site. We interviewed a total of 25 administrative and cardiology leaders. At each of the 10 sites, we interviewed at least one administrative leader (AL) and one cardiology leader (CL). Administrative leaders were from health plans, medical groups, and research units, and were typically the Medical Director, Director of Quality, or Director of Research. Cardiology leaders were chiefs of service, directors of subspecialty cardiovascular services, and/or active clinical trialists. The number of interviewees per site was based on the recommendations of the site investigators/authors who were best aware of appropriate individuals to include in the interview.

Second, from February through June 2006, we conducted a mailed survey of all cardiologists associated with each healthcare system. The interviews were designed to describe the different organizational arrangements pertaining to trials within participating organizations and to explore how these may facilitate or hinder trial activity. The interviews assessed leaders' perceptions of the general state of cardiology trials at their site, the nature and extent of financial and administrative issues, their organization's research culture and relationships with local academic centers and the National Heart, Lung and Blood Institute (NHLBI). Interviews were conducted by the second author. Consent to participate in the interview and to be audiotaped was given orally by each participant.

Questions for the interviews and survey were based on those used in a previous similar study of organizational barriers and facilitators to trial participation among oncologists [20]. We additionally used initial findings from the interviews to modify the survey. The survey assessed clinician involvement in trials; their perception of the value of trials to themselves, their

organization and their patients; and the presence of infrastructure support and constraints for trials. Most survey questions were 5-point Likert scale items that ranged from “strongly disagree” to “strongly agree” or from “not at all helpful” to “very helpful,” with an option either of “no opinion” or “does not apply.” Cardiologists also were asked to provide basic demographic information, including age, gender, years in practice, and additional subspecialty, if applicable. The sample included the universe of cardiologists (n = 280) at the 10 healthcare organizations. Eligibility criteria included employment in the practice for at least one year and at least 50% effort devoted to clinical practice. We used these eligibility criteria to better ensure that respondents would have a good working knowledge of their organization’s practices. Surveys were returned anonymously to allay physician concerns about confidentiality. To make the survey anonymous and allow follow-up with non-respondents, cardiologists separately mailed back a postcard indicating that they completed the survey at the time that they mailed back the survey. Non-respondents at each organization were sent another survey and were reminded by the local investigator; an interviewer from Kaiser Permanente Northern California also offered to complete the survey over the telephone. A waiver of informed consent was obtained since returning the survey was considered informed consent.

### **Interview Analysis**

All interviews were tape recorded and transcribed. After completing an interview, the interviewer (A.A.) composed field notes about the content, focus and possible implications of the interview. Based on multiple reviews of the transcripts and field notes, two authors (C.P.S. and A.A.) developed a set of codes, and independently coded the transcripts and identified key themes that occurred throughout the interviews. Themes included such categories as the current state of cardiology trials, financial/administrative issues, and research culture, with codes such as staffing problems, valuing trials specifically versus research generally, and clinician interest in different types of trials. In the small number of cases when coding

disagreements occurred, the authors returned to the data and achieved consensus about how best to code the data. We used standard qualitative methods [21,22] to develop a set of analytic memos and developed the analysis from the series of readings, codings, and memos.

### **Survey Analysis**

For questions with categorical or ordinal responses, the data are summarized as frequencies and percentages. When the responses were on a 5-level Likert scale we combined categories resulting in a 3-level response variable to facilitate ease of reading tables. For questions with an integer or continuous outcome, many of the response distributions were not normally distributed and therefore for consistency all such responses are summarized using medians and interquartile ranges (IQR)

## **RESULTS**

### **Sample and Characteristics**

Among 280 eligible cardiologists, 73% responded; among these, 82% practiced clinical cardiology, 37% performed echocardiography, and 24% performed interventional cardiology, (Table 1). The majority of respondents worked within an integrated delivery system; however, there was notable variation in the types of clinical practice arrangements across participating organizations. For example, one site operates as an integrated healthcare delivery system, but contracts with three groups for cardiovascular care. Eighty-three percent of survey respondents were men. Respondents spent a median of only 10% of their time on non-clinical activities, and reported that only a minimal amount of their time was devoted to research.

### **Trial Activity and Interest**

Sixty percent of respondents reported no participation in any trials during the past year (Table 2). The reported number of open trials at each site varied considerably; 35% of

respondents reported they had no open protocols at their site, while 1% reported 16 or more open trials. Thirty-seven percent reported ever having served as a site principal investigator for a trial. Approximately 25% had arrangements with an academic medical center to provide patients access to trials.

Clinicians voiced substantial interest in participating in a wide range of trials (Table 2). About three quarters of respondents expressed interest in participating in pharmacological prevention or treatment trials and almost two-thirds were interested in health-system or physician-based interventions (Table 2). More than half were interested in participating in lifestyle or behavioral interventions, educational interventions, and device trials. Though 73% indicated they would like to participate in more trials, less than 40% were able to identify any specific trials in which they would have liked to enroll patients but were not able to do so.

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**Comment [cps3]:** Remove these numberstoo?

Cardiologists expressed greater interest in enrolling patients into federally-funded trials than in industry-sponsored protocols, but interest was high for both types (78% and 66%, respectively). While leaders at sites where trials currently take place estimated that they received three times more industry than federal funding, several leaders expressed a desire for greater participation in federally-funded trials and little interest in participating in post-marketing studies:

“Some studies are seen as just marketing exercises: ‘Use my drug instead of their drug.’ But if the study offered a true advantage, I have a feeling there would be interest. But I think, unfortunately, pharma-based trials, historically, have an aura of skepticism, of ‘Why do we need another statin?’ that kind of thing.” (Administrative Leader)

Cardiologists reported positive attitudes toward trial participation (Table 2). Approximately two thirds agreed that “enrolling patients is important to me” and “participating in trials keeps me current with state of the art treatment.” More than half agreed that trials were their first choice of therapy if available, although a similar proportion also agreed that trial

eligibility requirements excluded most of their patients. About one third reported that they have a strong trial program in their practice (Table 2), while a similar proportion stated that trials were not available (Table 3).

Consistent with the survey data (Table 2), leaders described a wide range of cardiology trial activity at the 10 sites. Leaders discussed the importance of evaluating trials in terms of their medical importance, scientific interest, and financial viability. Cardiology leaders at most sites indicated that decisions about whether or not to initiate or participate in a particular trial are made by individual investigators, sometimes with informal input from colleagues. While one site uses a more formal group process to make these decisions, an administrative leader's response elaborates on the more typical decision making process and draws the distinction between trials in oncology and cardiology:

"Unlike oncology, where [offering clinical trials is] something that we have deliberately organized to do, and really need to do in order to provide clinical care, [cardiology trials are] something that's much less well-organized, more haphazard, depending on the interest of one person, or opportunities presented by industry or others."

Interview data also showed more interest in inpatient than outpatient trials. Comments by several administrative leaders about the availability of better treatment options for cardiovascular conditions treated in the outpatient setting support a stronger focus on inpatient trials. For example, one administrative leader described the situation in this way:

"...while there's always some way to improve lipid lowering in some patients... it feels like the current treatments are pretty good for almost everybody. And similarly, in hypertension, it's pretty good for almost everybody...cardiology has a pretty good repertoire, and I'm just not aware of the outpatient part of cardiology where they would perceive an urgency to do trials. Inpatient medicine, I can imagine, with people with

congestive heart failure and other kinds of more dramatic diseases, in which the standard of care maybe is not great.”

Almost all the leaders described their organization as placing a high value on research, but for a few respondents, this meant research in general, not necessarily trials. Several respondents talked about the importance of research that addresses patient care, and the importance of translational research, health services, and epidemiological research that more directly supports their organizational mission of providing population-based healthcare. As one administrative leader said:

“Remember, our primary directive as physicians, and as [an organization], is to take care of patients, to prevent, detect, evaluate and manage disease. As certain clinical trials tend to support that in a very advanced, high quality way, that’s perfect as far as our mission goes. To divert our attention from our prime focus of taking care of patients to research is probably not quite compatible with what we are.”

Several respondents said that they would like the NHLBI to develop a clear research agenda and set priorities for cardiology research. Some leaders were also interested in NHLBI’s supporting research that more directly optimizes cardiology practice:

“The NHLBI, what drives them is not the questions that we’re trying to ask, and this is this whole issue of transferring research into practice. When you talk about it that way, research is the client not practice. If you say, well how do we optimize practice through research? Practice is the client ...” (Cardiology Leader)

Assuming adequate funding and research infrastructure is available, leaders see their organizations as ready and willing to participate more fully in trials.

“There’s a benefit in conducting trials in a real practice environment, unlike an academic practice, and we are certainly a real practice environment. So, if trials could be fitted into

a practice environment, both from the perspective of making it feasible so that it doesn't encumber the clinical practice so heavily that it can't function, but also from a perspective of being able to test real things in real situations, that would be beneficial...I think we've all seen times where what looks like a particular result in what I sometimes call a "hothouse trial" just doesn't pan out when you get it in a real garden instead of in a greenhouse." (Administrative Leader)

Respondents at several sites discussed the value of trials regarding the prestige they bring related to "being more than just physicians out to make money" and elevating the reputation of the organization. However, one cardiologist stated that while this might be true for trials in other areas, what improves prestige for cardiology is achieving excellent outcomes.

### **Barriers to Enrollment**

Major reported barriers to trial participation were organizational, including lack of time due to clinical or administrative responsibilities; lack of adequate skilled support staff and information about available trials; and effort and time needed to obtain informed consent (Table 3). Leaders' answers amplified the problem of inadequate resources to attend to trial demands, especially regarding inpatient trials:

"A major issue is actually availability of research nurses and coordination. Particularly for studies on acute patients and patients who are enrolled after hours, we and most of the sites that we work with, are really facing a tough challenge, (being) able to recruit, hire and staff research positions after hours." (Cardiology Leader)

### **Perceived Facilitators to Enrollment**

Among 15 possible sources of support for enhancing participation in trials, cardiologists who participated in trials were most likely to rate the following as helpful: research nurses

(61%), physician colleagues (55%), and their organization's research department (44%) (Table 4).

Interviewees at most sites reported good relationships with their research departments. However, in most cases, research departments were minimally involved in trials. Several sites reported that they had worked with university-based partners to recruit patients in the past. Sites that participated in few to no trials reported that there was inadequate time and financial resources to cover clinical duties and the requirements of participation.

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## DISCUSSION

Despite the expanding role of non-academic practices in conducting trials, little is known about the perceptions about trials among cardiologists and leaders in these settings. Thus, our study provides novel insights into the interest and experiences in conducting trials among cardiologists in community-based practices throughout the U.S. We found that cardiologists had considerable interest in participating in trials across a wide variety of topics including health system or physician-based interventions, lifestyle and behavioral interventions, and the study of pharmacological agents and devices. The major reported obstacles to trial participation were lack of time due to clinical or administrative responsibilities and lack of infrastructure to support trials, especially an insufficient number of skilled research nurses to help conduct studies. Only a minority of cardiologists reported significant experience as principal investigators and/or enrolling patients in trials.

Almost 75% of respondents expressed interest in greater trial participation. These results suggest considerable opportunities for conducting research in community-based settings, which offer a large pool of patients and investigators. The interviews highlight the widespread interest in conducting the kind of "real world" practical trials that answer questions relevant to daily practice and for which these settings are especially well suited [23-25].

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Yet given the lack of time to devote to research and relative lack of investigator experience, what can be done to increase the ability of community-based cardiologists to participate in research? Above all, our findings highlight the need for ongoing funding for and investment in infrastructure to support trials, especially in expanding the number of skilled research nurses and personnel arrangements that would provide dedicated time for interested cardiologists to participate in trials at no financial loss to physicians or health plans. To maximize the personnel and patient resources within these community-based healthcare systems, these barriers need to be addressed explicitly for both federally-funded and industry-sponsored trials.

Our findings also suggest an opportunity for research departments in these and similar healthcare organizations to play a greater role in working with cardiologists to facilitate their participation in trials. This study was conducted in 10 healthcare organizations that have independent research departments which conduct primarily publicly-funded, peer-reviewed research, yet we found less than half of survey respondents involved in trials found them helpful in supporting their participation. Research departments can support clinicians in a variety of ways – by providing methodological training; helping to prepare grant applications and institutional review board applications; and providing consultation for budgeting and grant administration. Research departments also could offer support by using increasingly prevalent electronic medical records to identify pools of potentially eligible participants.

One strength of our study was our mixed methods approach. We surveyed cardiologists and interviewed administrative and cardiology leaders. The interviews were particularly useful in providing concrete examples of general issues captured in the survey. Overall, we found remarkable consistency between leader and clinician attitudes toward trials as well as the types of research considered most supportive of the missions of the organizations we studied. This consistency should facilitate future efforts to increase trial participation. Our respondents and their organizations are both a strength and a limitation. These organizations provided a

diversity of population size (171,000 to 3,260,000 members per site), geography, and financing structures. However, this sample may not be generalizable to all community-based health settings and physicians. Our results may be affected by non-responder bias, but we achieved a response rate of 73% which exceeds the usual response rate for physician surveys [26].

Another potential limitation is our use of self-reported data on selected outcomes. However, our main objective was to evaluate cardiologists' and leaders' perceptions of issues surrounding trials which likely directly influences subsequent behaviors.

Community-based healthcare systems provide a largely untapped resource for conducting cardiovascular trials. This study's results suggest considerable opportunities for conducting research in community settings, which offer a large pool of diverse patients, clinical data, and investigators. The results also point to ways physicians and community-based health care systems can help create and sustain a "culture of research" [27] in the United States. Given the current and growing challenges of recruiting patients into cardiovascular trials, innovative efforts are needed to address key barriers within community-based health systems that will leverage their unique strengths and capabilities and facilitate greater participation in clinical trials.

Acknowledgements: We thank the following people either for their intellectual or administrative contributions to the paper: David Brand, Jeff Brown, Katherine Dodd, Jerry Gurwitz MD, Tom Kottke, MD, Betty Haggerty, Aikya Param, and Janine Simpkins.

## References

- [1] Armstrong PW, Newby LK, Granger CB, Lee KL, Simes RJ, Van de WF et al. Lessons learned from a clinical trial. *Circulation* 2004 Dec 7 ;110 (23):3610 -4 2004; 110: 3610-4.
- [2] Yancy CW, Benjamin EJ, Fabunmi RP, Bonow RO. Discovering the full spectrum of cardiovascular disease: Minority Health Summit 2003: executive summary. *Circulation* 2005; 111(10): 1339-49.
- [3] Ridker PM, Torres J. Reported outcomes in major cardiovascular clinical trials funded by for-profit and not-for-profit organizations: 2000-2005. *JAMA* 2006; 295(19): 2270-4.
- [4] Mitka M. Efforts needed to foster participation of blacks in stroke studies. *JAMA* 2004; 291(11): 1311-2.
- [5] Mitka M. Help wanted: participants for clinical trials. *JAMA* 2003; 290(12): 1567-8.
- [6] Peterson ED, Lytle BL, Biswas MS, Coombs L. Willingness to participate in cardiac trials. *Am J Geriatr Cardiol* 2004 Jan -Feb ;13(1):11-5 2004; 13: 11-5.
- [7] Ding EL, Powe NR, Manson JE, Sherber NS, Braunstein JB. Sex differences in perceived risks, distrust, and willingness to participate in clinical trials: a randomized study of cardiovascular prevention trials. *Arch Intern Med* 2007 May 14;167 (9 ):905 -12 2007; 167: 905-12.
- [8] Harris DJ, Douglas PS. Enrollment of women in cardiovascular clinical trials funded by the National Heart, Lung, and Blood Institute. *N Engl J Med* 2000; 343(7): 475-80.

- [9] Lee PY, Alexander KP, Hammill BG, Pasquali SK, Peterson ED. Representation of elderly persons and women in published randomized trials of acute coronary syndromes. JAMA 2001; 286(6): 708-13.
- [10] Coca SG, Krumholz HM, Garg AX, Parikh CR. Underrepresentation of renal disease in randomized controlled trials of cardiovascular disease. JAMA 2006 Sep 20 ;296 (11):1377 -84 2006; 296: 1377-84.
- [11] Kandzari DE, Roe MT, Chen AY, Lytle BL, Pollack CV, Jr., Harrington RA et al. Influence of clinical trial enrollment on the quality of care and outcomes for patients with non-ST-segment elevation acute coronary syndromes. Am Heart J 2005; 149(3): 474-81.
- [12] Topol EJ, Califf RM, Van de WF, Simoons M, Hampton J, Lee KL et al. Perspectives on large-scale cardiovascular clinical trials for the new millennium. The Virtual Coordinating Center for Global Collaborative Cardiovascular Research (VIGOUR) Group. Circulation 1997; 95(4): 1072-82.
- [13] Drennan KB. Patient recruitment: the costly and growing bottleneck in drug development. Drug Discov Today 2002 Feb 1;7 (3):167 -70 2002; 7: 167-70.
- [14] Overview of the NIH Roadmap. 2007. Available at <http://nihroadmap.nih.gov/overview.asp>. Accessed August 21, 2007.
- [15] RFA-RM-06-002: Institutional Clinical and Translational Science Award RFA. 2007. Available at <http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-06-002.html>. Accessed August 21, 2007

- [16] Davidson RM, McNeer JF, Logan L, Higginbotham MB, Anderson J, Blackshear J et al. A cooperative network of trained sites for the conduct of a complex clinical trial: a new concept in multicenter clinical research. *Am Heart J* 2006; 151(2): 451-6.
- [17] Vogt TM, Elston-Lafata J, Tolsma D, Greene SM. The role of research in integrated healthcare systems: the HMO Research Network. *Am J Manag Care* 2004; 10: 643-8.
- [18] National Institutes of Health, Office of Behavioral and Social Science Research. Qualitative Methods in Health Research: Opportunities and Considerations in Application and Review. 1999. National Institutes of Health. Available at <http://obssr.od.nih.gov/Documents/Publications/Qualitative.PDF>. Accessed August 21, 2007.
- [19] Creswell JW, Fetters MD, Ivankova NV. Designing a mixed methods study in primary care. *Ann Fam Med* 2004 Jan -Feb ;2(1):7 -12 2004; 2: 7-12.
- [20] Somkin CP, Altschuler A, Ackerson L, Geiger AM, Greene SM, Mouchawar J et al. Organizational barriers to physician participation in cancer clinical trials. *Am J Manag Care* 2005; 11(7): 413-21.
- [21] Charmaz K. *Constructing Grounded Theory: A Practical Guide Through Qualitative Analysis*. Thousand Oaks: Sage Publications Inc. 2006.
- [22] Strauss A, Corbin J. *Basics of Qualitative Research: Techniques and Procedures for Developing Grounded Theory*. Newbury Park, CA: Sage Publications. 1998.

- [23] Tunis SR, Stryer DB, Clancy CM. Practical clinical trials: increasing the value of clinical research for decision making in clinical and health policy. *JAMA* 2003; 290(12): 1624-32.
- [24] Tunis SR. A clinical research strategy to support shared decision making. *Health Aff (Millwood)* 2005; 24(1): 180-4.
- [25] Califf RM, Harrington RA, Madre LK, Peterson ED, Roth D, Schulman KA. Curbing the cardiovascular disease epidemic: aligning industry, government, payers, and academics. *Health Aff (Millwood)* 2007; 26(1): 62-74.
- [26] Asch DA, Jedrzewski MK, Christakis NA. Response rates to mail surveys published in medical journals. *J Clin Epidemiol* 1997; 50: 1129-36.
- [27] Avins AL, Goldberg H. Creating a culture of research. *Contemp Clin Trials* 2007 Jul ;28(4):557 -62 Epub 2007 Feb 27 2007; 28: 557-62.

**Table 1. Respondent and Practice Characteristics**

	Median (IQR)*	N
Age, years	50 (42-56)	195
Years in practice as a cardiologist	15.5 (8-25)	202
Years in healthcare organization	8 (4-18)	199
Activity distribution, %		
Clinical Activities	90 (80-99)	201
Administrative Activities	4 (0-10)	201
Teaching	0 (0-5)	201
Research	0 (0-1)	201
Reported number of patients treated in past 12 months	1000 (500-1500)	178
	n (%)	N
Male gender	168 (83.2)	202
Type of clinical practice <sup>†</sup>		
Clinical cardiology	168 (82.0)	205
Echocardiography	76 (37.1)	205
Interventional cardiology	50 (24.4)	205
Electrophysiology	9 (4.4)	205
Other (cardiac/transplant surgery, nuclear cardiology, pediatric cardiology)	24 (11.7)	205
Practice setting		205
Group/staff model health plan	136 (66)	

	n (%)	
Multi-specialty group	52 (25)	
Specialty group	17 (8)	
Healthcare organization		205
Kaiser Permanente Northern California	105 (51.2)	
Henry Ford Health System	23 (11.2)	
Kaiser Permanente Georgia	17 (8.3)	
Kaiser Permanente Northwest	12 (5.9)	
Fallon/Meyers Primary Care	10 (4.9)	
Kaiser Permanente Colorado	11 (5.4)	
HealthPartners Research Foundation	9 (4.4)	
Group Health Cooperative	8 (3.9)	
Harvard Pilgrim Health Care	5 (2.4)	
Lovelace Clinic Foundation	5 (2.4)	

\*IQR = Interquartile range (25<sup>th</sup> and 75<sup>th</sup> percentiles)

† Not mutually exclusive

**Table 2. Clinical Trials Experience and Interest**

	n (%)	N
Reported number of trials open for		202
enrollment in practice		
0	70 (34.7)	
1-5	69 (34.2)	
6-10	20 ( 9.9)	
11-15	6 (3.0)	
16-20	1 (0.5)	
> 20	1 (0.5)	
Don't know	35 (17.3)	
Reported number of trials participated in during 2005		181
0	109 (60.2)	
1	25 (13.8)	
>1	47 (26.0)	
Reported number of patients enrolled in trials in past 12 months		69
0	4 (5.8)	
1-5	20 (29.0)	
6-10	7 (10.1)	
11-15	8 (11.6)	
16-20	4 (5.8)	
>20	26 (37.7)	
Types of trials interested in		
Pharmacological prevention or treatment trials	150 (76.9)	195
Health-system or physician-based interventions	127 (65.8)	193

	n (%)	N
Device therapies	111 (58.1)	191
Lifestyle, behavioral interventions	107(57.2)	187
Educational interventions	107 (56.0)	191
Percutaneous coronary interventions	85 (44.5)	191
Surgical interventions	63 (33.9)	186
Preferred funding sources, % yes <sup>†</sup>		
Federally-sponsored/ funded trials	150 (78.1)	192
Industry-sponsored/funded trials	125 (66.1)	189
Interest and experience, % yes		
In general, would you like opportunity to participate in more trials than now?	148 (73.3)	202
In past 12 months, were there any trials in which you would have like to enroll patients but were not able to do so?	76 (39.0)	195
Ever been trial site PI	74 (36.6)	202
If no, interest in being site PI	39 (31.0)	126
Collaborative trial arrangement with academic medical center	53 (26.4)	201

	Agree	Disagree	No	N
	Opinion			
	%	%	%	
Attitudes and beliefs				
Cardiology clinical trials	96.5	2.5	1.0	201
improve care in general				

Trials provide high quality care whether or not patients receive experimental intervention	86.5	9.0	4.5	200
Participating in trials keep me current with state of the art treatment	69.0	20.8	10.1	197
Enrolling patients in trials is important to me	63.8	28.1	8.0	199
Trials first choice of therapy if available	54.0	41.5	4.5	200
Information about open trials available to me	37.5	60.0	2.5	200
There is a strong clinical trials program in my practice	35.5	64.0	0.5	200
I am regularly approached by industry representatives about trials	26.1	71.4	2.5	199

\*IQR = Interquartile range (25<sup>th</sup> and 75<sup>th</sup> percentiles)

† = Not mutually exclusive

**Table 3. Perceived Barriers to Trial Enrollment**

	Agree	Disagree	Does Not Apply	N
	%	%	%	
Lack of time	92.6	5.9	1.5	203
Lack of adequate support staff	81.3	16.8	2.0	203
Lack of adequate information	74.8	23.8	1.5	202
Inadequate support staff	70.9	27.1	2.0	199
Time to obtain informed consent	63.4	30.2	6.4	202
Lack of space	43.7	44.2	12.2	197
Lack of experience with trials	41.4	53.7	4.9	203
Lack of continuity of care if trial occurs outside my practice	34.7	56.4	8.9	202
Lack of interest among acute patients	32.2	61.4	6.4	202
Lack of interest among outpatients	29.6	65.0	5.4	203
Lack of interest in trials available to my practice	29.5	58.5	12.0	200
Trial participation not part of my role	26.6	70.9	2.5	203
Concern about inadequate reimbursement	23.4	57.7	18.9	201

	Agree	Disagree	No Opinion	N
	%	%	%	
Concern about making less money	10.4	71.8	17.8	202
No time to participate	59.3	38.2	2.5	199
Eligibility requirements exclude most of my patients	58.2	35.3	6.5	201
Trials not available in my practice	36.0	61.4	2.5	197
Trials usually not right choice for most patients	24.0	73.0	3.0	200
Trials not of interest to my patients	17.8	78.2	4.0	202
Not role of our practices to participate in trials	12.6	84.9	2.5	199
Trials rarely benefit my patients	11.9	84.1	4.0	201

**Table 4. Perceived facilitators to trial enrollment among cardiologists involved in clinical trials (N=72)**

	Helpful %	Not Helpful %	Not Available %	N
Research nurses	87.0	11.6	1.5	69
Physician colleagues	62.3	34.8	2.9	69
Research department	62.1	31.8	6.1	66
Industry representatives	56.5	36.2	7.3	69
Clinic nurses	55.8	38.2	5.9	68
Briefings by chief	39.7	45.6	14.7	68
Clerical staff	39.7	42.7	17.7	68
Computer databases	38.8	47.7	13.4	67
Statisticians	36.8	41.2	22.1	68
Data managers	35.3	44.1	20.6	68
Hospital nurses	33.3	57.6	9.1	66
Flyers in exam and waiting rooms	32.4	50.0	17.7	68
Hospital	32.3	53.9	13.9	65
Pharmacists	26.9	56.7	16.4	67
Medical School	10.3	55.9	33.8	68

**Appendix. Interview Questions**

Domain	Question
Logistics/processes of patient enrollment	<ol style="list-style-type: none"> <li>1. Does your organization initiate and/or participate in cardiology clinical trials? What is process for deciding on specific trials? Is there a group of cardiologists within your health plan who specifically work on clinical trial-related issues What type/number of trials?</li> <li>2. How are doctors and patients made aware of available trials?</li> <li>3. How are patients enrolled in trials, i.e. what is usual process that occurs?/ How often do your patients participate in cardiology CTs not conducted by [your organization]? What is the process of approval for patients' participation in clinical trials <u>not</u> conducted within your organization?</li> <li>4. Do you have staff currently available to assist in clinical trials activities? If yes, what types, what do they do, is there sufficient staffing</li> <li>5. To what extent is your research department involved in any type of clinical trials? If yes, is your research department involved in cardiology trials? What other types of clinical trials?</li> </ol>
Financial issues	<ol style="list-style-type: none"> <li>6. How much do financial issues or concerns influence [your organization's] interest and ability to enroll patients in CTs? If so</li> </ol>

	how/ if not why not?
Values and goals	<p>7. To what extent, if at all, would you say the opportunity for patient enrollment in clinical trials is considered a key element to the provision of high quality medical care?</p> <p>8. To what extent, if at all, would you say patient enrollment in CTs is an explicit organizational value or goal?</p> <p>9. Are CTs promoted in [your organization]? If yes: How and by whom? How well are CTs promoted?</p>
Influence of outside organizations	<p>10. How could the NHLBI (NIH) or the research community be helpful to health plan leaders in your decision making regarding participation in clinical trials overall or in specific types of clinical trials? Is there anything you would like to tell NHLBI about your experience with trials at [your organization]? What do you think is most important for the NHLBI (NIH) to know about conducting cardiology trials in your health plan?</p>