

How disease advocacy organizations participate in clinical research: a survey of genetic organizations

David C. Landy, MPH¹, Margaret A. Brinich, BA², Mary Ellen Colten, PhD³, Elizabeth J. Horn, PhD, MBI⁴, Sharon F. Terry, MA⁴ and Richard R. Sharp, PhD^{2,5,6}

Purpose: Disease advocacy organizations may assist in the conduct of research in a variety of ways. We sought to characterize how disease advocacy organizations participate in clinical research and perceive their contributions.

Methods: Postal and electronic surveys administered to leaders of disease advocacy organizations for genetic conditions identified through the Genetic Alliance's Disease InfoSearch.

Results: Of the 201 disease advocacy organizations approached, 124 (62%) responded. In the past 2 years, 91% of these organizations had assisted in participant recruitment, 75% collected data, 60% provided a researcher with financial support, and 56% assisted with study design. Forty-five percent of these organizations also supported a research registry or biobank. Few disease advocacy organization leaders (12%) reported regrets about research studies they

had supported. Most (68%) felt their involvement in clinical research had increased the amount of research on their condition and that researchers should consult organizations like theirs in deciding how to recruit participants (58%) and in selecting research topics (56%).

Conclusion: In addition to providing financial support, disease advocacy organizations participate directly in multiple aspects of research, ranging from study design and patient recruitment to data collection and analysis. Leaders of these organizations feel strongly that scientists and research sponsors should engage them as partners in the conduct of clinical research.

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INTRODUCTION

As our capacity to analyze the human genome continues to expand and enables a wider range of studies examining genetic contributions to human disease, the importance of adequately powered clinical studies has become increasingly clear.^{1,2} Well-designed clinical studies often require large numbers of human participants and the resources to monitor those individuals for extended periods of time.^{3,4} For many genetic disorders, particularly rare conditions that affect relatively small numbers of individuals worldwide, enrolling adequate numbers of research participants into large clinical trials can be an enormous challenge.^{5,6} These challenges will likely increase as a broader array of molecular methods are used to characterize human diseases and subtypes using genetic criteria.^{7,8}

The need to increase participation rates in clinical trials has been highlighted by others.^{9,10} Few effective strategies exist for addressing this need in the study of genetic conditions, where limited economic incentives exist to spur biopharmaceutical interest in the study of rare diseases.^{11,12} Although the efforts of the Office of Rare Diseases Research at the National Institutes of Health (NIH) and the Orphan Drug Act are examples of substantive US federal investments in research, major advances in

our understanding of rare genetic conditions will require additional strategies for promoting clinical research.^{13,14} This will also be true for common conditions as populations are stratified using genetic diagnostics.

In response to this need, networks of affected individuals and their families have emerged as key partners in the research enterprise, capable of connecting clinical scientists with large numbers of patients and providing financial support for research.^{15,16} Many disease advocacy organizations (DAOs), which enable individuals with a shared interest to pool their collective resources and shared knowledge of a medical condition, work closely with clinicians and scientists, particularly in the United States.^{17–19} DAOs are becoming more common in other countries as well, including the developing world.^{20,21} Although DAOs have traditionally been associated with patient education and support, recent evidence suggests that their involvement in clinical research may be expanding.^{22,23}

Despite the important role that DAOs seem to be playing in clinical research, little data are available on the nature of these collaborations with scientists, their frequency, or the specific contributions of DAOs to research. We report results from a survey intended to characterize DAOs' participation in clinical

¹MD/PhD Program, University of Miami Miller School of Medicine, Miami, Florida, USA; ²Department of Bioethics, Cleveland Clinic, Cleveland, Ohio, USA; ³Center for Survey Research, University of Massachusetts Boston, Boston, Massachusetts, USA; ⁴Genetic Alliance, Washington, DC, USA; ⁵Genomic Medicine Institute, Lerner College of Medicine, Cleveland Clinic, Cleveland, Ohio, USA; ⁶Center for Genetic Research Ethics and Law, Case Western Reserve University, Cleveland, Ohio, USA. Correspondence: Richard R. Sharp (sharp3@ccf.org)

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research and how leaders of these organizations view their collaborations with clinical scientists. Understanding the full extent and nature of collaborations among genetic researchers and DAOs is an important first step toward maximizing the benefits of this emerging form of research partnership.

MATERIALS AND METHODS

An initial list of DAOs was obtained by reviewing Genetic Alliance's Disease InfoSearch, a directory of DAOs for genetic conditions, as it existed on March 20, 2007. Genetic Alliance is a network of health-related organizations, including DAOs, that works to improve health through genetics.²⁴ For the purpose of this study, an organization was considered a DAO if it met the criteria described by the International Alliance of Patients' Organizations.²⁵ We excluded organizations for which a functional website could not be identified through either Disease InfoSearch or Google. DAOs that did not represent individuals with a condition originating from a genetic mutation or chromosomal abnormality were excluded. If the genetic or chromosomal origin of a condition was unknown, the DAO's website description of the condition was examined. DAOs that described their condition of interest as the product of a genetic or chromosomal defect were included. DAOs seeking to represent the genetic or chromosomal component of a condition of multifactorial origin were included. No consideration was given to whether the organization indicated a commitment to supporting clinical research on its website.

Contact information was obtained from the DAO's website with the organization leader identified by one of the following titles: president, board chairman, executive director, or chief executive officer. In cases where two or more different individuals were identified, the individual who appeared most likely to be responsible for the overall direction of the organization was selected. If contact information was not available on an organization's website (which occasionally resulted when an embedded contact link was the only method available through the site), additional Google searches and reviews of information available through Genetic Alliance were used to identify an organizational contact. If, during the course of the study, a functioning website or contact person could no longer be identified for an organization, the DAO was removed from the sample.

An eight-page survey was developed to assess the involvement of DAOs in clinical research and organizational leaders' attitudes about these activities. Individual items consisted mainly of "Yes" or "No" questions, although there were several open-response items and questions eliciting a response on a Likert scale. The survey instrument was validated via pilot testing and cognitive interviews with seven leaders of DAOs for genetic conditions.

Surveys were administered between February and June 2008. Hard copies of the survey were distributed via postal mail and accompanied by a postage-paid, return-addressed envelope. Two weeks after the initial mailing, an email reminder was sent to nonresponders. Three weeks later, the survey was remailed to all nonresponders and followed by another, similarly timed

email reminder. In April and May 2008, a study coordinator attempted to contact remaining nonrespondents by telephone. A final reminder was sent at the end of May. Participants were not compensated.

Survey responses were entered into an electronic database and descriptive statistics calculated. Because recent reports suggest that DAO involvement in clinical research may be expanding, the association between the organization's age and self-reported organization's emphasis on research was examined. Spearman's rho was used to examine the association between the year in which the DAO was founded and the emphasis DAO leaders assigned to their organization's promoting of research. All statistical analyses were performed with Stata 9.2 (College Station, TX).

RESULTS

Of the 201 DAOs that met the study's eligibility criteria, surveys were received from 124 (response rate, 62%). Respondents often had held their DAO leadership position for more than 5 years (67%). Respondents most often had been elected to their position (43%), but many had been self-appointed (27%) or hired (19%). Relatively few respondents had been in their current leadership position for less than 1 year (9%). DAO leaders frequently were affected individuals or family members of a patient (77%).

Characteristics of these DAOs for genetic conditions are described in **Table 1**. Most of these organizations were at least 10 years old at the time of response (66%). Most provided information about their annual budget (82%). The median annual budget of those responding was \$200,000 dollars, with an interquartile range of \$30,000 to \$700,000. Forty-eight DAOs reported receiving more than half of their last fiscal year's total operating budget from a single type of funding source, and of these, 86% reported that their primary funding source was private donations or membership dues.

DAOs reported involvement in a range of traditional patient support activities, including development of educational materials (90%), distribution of newsletters (86%), organization of support groups (73%), and sponsorship of patient education events (69%). DAOs also reported sponsoring educational events for healthcare professionals (53%) and lobbying elected officials or public policy makers (44%).

DAOs reported involvement in multiple aspects of clinical research, including research design, conduct, and dissemination (**Table 2**). The most common research activity reported was recruitment of research volunteers, which 113 DAOs (91%) had performed over the past 2 years. Other forms of participation in clinical research reported by DAOs included collecting research data (75%), supporting a research registry or biobank (45%), preparing research reports (44%), and analyzing data (37%). Many DAOs reported that they disseminated research findings by using their websites (89%), supporting scientific conferences (60%), and presenting results at scientific conferences (30%). In addition, more than half of these DAOs had provided advice on study design and some had written funding proposals to allow the organization to conduct its own research (13%).

Table 1 Characteristics of 124 disease advocacy organizations representing genetic conditions

Characteristic	N (%)
<i>Leader type</i>	
Patient or family member	96 (77)
Healthcare provider	10 (8)
Researcher	15 (12)
<i>Organization's age</i>	
<5 years	11 (9)
5–10 years	27 (22)
>10 years	82 (66)
<i>Annual budget</i>	
<\$50,000	31 (25)
\$50,000–\$499,000	33 (27)
\$500,000–\$5,000,000	23 (19)
>\$5,000,000	5 (4)
No response	22 (18)
<i>Paid employees</i>	
0	49 (40)
1–2	25 (20)
3–5	26 (21)
6–15	19 (15)
>15	4 (3)
<i>Medical or scientific advisory board</i>	
Yes	107 (86)
<i>Organization's activities</i>	
Developed patient education materials	111 (90)
Distributed newsletter	106 (85)
Organized support groups	91 (73)
Sponsored patient education events	86 (69)
Maintained toll-free support line	66 (53)
Sponsored healthcare professional education events	66 (53)
Educated or lobbied public policy makers	55 (44)
Provided financial assistance to patients	25 (20)

Not all respondents completed all items, so responses may not sum to 124.

Seventy-four DAOs (60%) reported that they had provided financial support to at least one researcher in the last 2 years. Of these organizations, the median amount of research support provided in the past fiscal year was \$135,000 with an interquartile range from \$50,000 to \$460,000. In the past two fiscal years, these DAOs reported that they had supported an average of four research projects with an interquartile range of 2 to 11 projects. The majority of DAOs that provided financial support to a researcher (84%) reported that they had asked scientific and medical experts who were not involved with these studies to review their scientific quality. Nine organizations (12%) reported that they regretted having provided financial assistance for at least one research project in the past. These regrets

Table 2 Research involvement among 124 disease advocacy organizations in the past 2 years

Research activity	N (%)
<i>Planning</i>	
Provided an investigator with financial support	74 (60)
Provided advice on the design of a research project	70 (56)
Provided researcher with a letter of support	67 (54)
Wrote funding proposal to conduct own research	16 (13)
<i>Conduct</i>	
Helped recruit research subjects	113 (91)
Participated in data collection	93 (75)
Involved with research registry or biobank ^a	56 (45)
Helped prepare a research report or article	55 (44)
Participated in data analysis	46 (37)
<i>Dissemination of research results</i>	
Presented research via a website or newsletter	110 (89)
Organized or supported a scientific conference	75 (60)
Helped disseminate research through the press	38 (31)
Presented research at scientific conference	37 (30)

^aThis question was not specific to the past 2 years.

were due to researchers having made less progress than anticipated or from lack of follow-up communication with the investigators supported.

Leaders of DAOs felt their organization's involvement in research had a substantial and positive effect on the research studies in which they were involved (Table 3). Of DAOs involved in research, 69 (68%) felt their involvement had increased the amount of research relevant to their condition. In this same group, 59 (58%) felt their organization's involvement had increased participation rates "a lot." Although it was less common for respondents to report that their organization's involvement in research had reduced financial costs significantly or helped to minimize research-related risks to subjects, a majority felt their organization's involvement had at least some impact on these outcomes.

Leaders of DAOs considered research to be an important activity in relation to other organization priorities. Many respondents described their organization's emphasis on research, when compared with other activities, as "extremely important" (48%) or "very important" (28%). These opinions of the importance of research in relation to other organization's priorities were independent of the year in which a DAO was founded, with 78% of DAOs founded before 1990 viewing research as very/extremely important compared with 75% of DAOs founded after 1990 ($Rho = -0.07, P = 0.45$).

Leaders of DAOs felt strongly that clinical researchers and funding agencies had an obligation to consult their organizations about the design and conduct of research. This was especially true with regard to the need for investigators to consult DAOs about what information to give participants, which topics to study, and

Table 3 How leaders of 107 disease advocacy organizations view the impact of their organizations on clinical research

Reported effect on research	A lot	Some	None
Increased the amount of relevant research	69 (68)	29 (29)	3 (3)
Increased participation rates	59 (58)	34 (34)	8 (8)
Increased the quality of data produced	42 (42)	45 (45)	12 (12)
Helped participants understand informed consent	42 (42)	43 (43)	14 (14)
Reduced time for research completion	32 (33)	37 (38)	28 (29)
Reduced financial costs of research	21 (21)	48 (49)	29 (30)
Minimized research participant risks	20 (21)	29 (30)	48 (49)

Values are expressed as *N* (%). Respondents who indicated that their organization had not been previously involved with research were not asked this series of questions.

how to recruit subjects (**Table 4**). Seventy-eight percent of respondents also felt that the NIH should consult DAOs in setting funding priorities, although most felt that NIH leaders had not done a good job of involving organizations like theirs in selecting areas to give funding priority (59%). Most respondents (55%) also felt that funding organizations such as the NIH had an obligation to consult their organizations about the acceptability of controversial types of research. Leaders of DAOs reported involvement in research-policy debates as well, with 19 (15%) having taken a public position on stem cell research and 7 (6%) having taken a public position opposing a particular research study.

DISCUSSION

The DAOs we surveyed showed considerable variation in organization size and budgets, which is characteristic of the spectrum of DAOs for genetic conditions and reflective of their unique histories.²⁶ These organizations provide a range of patient-centered activities, such as the production of educational materials and organization of support activities for affected individuals. Our results show that in addition to these traditional DAO activities, a large proportion of DAOs are involved in clinical research. This involvement extends well beyond the financing of research or endorsement of specific projects. Most of the DAOs we surveyed had participated in multiple aspects of the research process, ranging from study design and patient recruitment to data collection, analysis, and dissemination of results.

Our results reveal much more extensive and direct forms of collaboration among DAOs and clinical researchers than may be appreciated outside of those with personal experience. Nearly all the DAOs we surveyed had helped recruit research volunteers and many had also participated in data collection. The advantages and limitations of these forms of collaboration, particularly those in which DAOs are involved in the direct recruitment of research volunteers or collection of study data, are dependent on many factors. For example, researcher-DAO collaborations may hold the potential to increase research participation rates and improve patients' understanding of study benefits and risks.^{27,28} On the other hand, active forms of DAO

Table 4 How leaders of disease advocacy organizations view the obligation of clinical researchers to consult their organization about the conduct of research

Research issue	How strongly do you feel clinical researchers have an obligation to consult with organizations like yours regarding ... ^a				
	Very strongly, 1	2	3	4	Not strongly at all, 5
Information to give subjects	45 (38)	29 (24)	20 (17)	6 (5)	19 (16)
How to recruit subjects	40 (34)	29 (24)	21 (18)	12 (10)	17 (14)
Topics to study	40 (34)	27 (23)	26 (22)	13 (11)	13 (11)
The goals of the study	35 (29)	37 (31)	26 (22)	6 (5)	15 (13)
How a study is designed	24 (20)	16 (13)	40 (34)	16 (13)	23 (19)

Values are expressed as *N* (%).

^aThis language prefaced the individual research issues listed below.

participation in volunteer recruitment and data collection may create unintended social pressures to participate.²⁹ As partnerships between DAOs and clinical researchers continue to expand, it is important to examine the impact of these collaborations on patients' decisions about research participation.

Our findings also have implications for medical geneticists, genetic counselors, and other healthcare providers who refer patients to DAOs for education and support. In contrast to traditional understandings of DAOs as organizations that are concerned primarily with support and educational outreach,²⁵ our data suggest that many of these organizations view the promotion of clinical research as central to their organization's missions and goals. Healthcare providers should be aware that DAOs are active participants in many aspects of clinical genetics research. Connecting affected individuals with clinical researchers and opportunities to participate in clinical trials may be an additional benefit of referring individuals to DAOs, although for some healthcare providers this may also be a source of concern.^{30,31} How best to work with DAOs, and decide when to refer individuals to these organizations for help, will be increasingly important for healthcare providers in the future, to the extent that although each of the approximately 7,000 known rare diseases affects a small number of individuals, in aggregate they affect a considerably larger proportion of the population.³²

Our results reveal that most DAOs for genetic conditions consider research to be an important organization activity in relation to other core values and organization priorities. We did not find that organization support for research was associated with the year a DAO was founded, suggesting that these attitudes do not reflect the emergence of newer DAOs focused more narrowly on research activities. It is possible that as genetics research has become more concerned with clinical translation and the production of diagnostic tests and potential therapies, DAOs have become more interested in promoting clinical studies. It is also possible that DAOs are in part responsible for

some of the shift in focus toward translational and more clinically oriented research. Given the limited resources of many DAOs, these organizations may struggle to balance increased involvement in clinical research with more traditional patient-support activities.

Our results also clarify the contributions that leaders of DAOs believe their organizations make to clinical research. Leaders of DAOs felt their organization's participation in clinical research had increased the amount of research performed on their condition of interest and had improved the overall quality of the data produced. In addition, DAO leaders felt strongly that scientists and research funding agencies should seek their advice about studies of potential interest to the communities these organizations serve, particularly regarding the recruitment of research volunteers. Interestingly, leaders of these organizations felt their involvement had a less significant impact with respect to minimizing research-related risks and reducing costs. These may be aspects of researcher-DAO collaborations that should be examined more closely, particularly because they suggest new ways in which DAOs might contribute to research.

Finally, our results suggest that the experiences of DAOs that partner with clinical investigators are not always positive. A small but significant number of DAO leaders reported that they regretted having provided financial support to a clinical investigator. These regrets may reflect the relative novelty of researcher-DAO partnerships, poor communication, or lack of shared expectations regarding the nature of these collaborations. By learning more about these prior experiences, it may be possible to help organizations avoid problems in the future. Additional studies might also help in clarifying how best to implement prior recommendations for building and maintaining strong researcher-DAO partnerships.¹⁵

The results of this study are strengthened by a high response rate and the diverse group of DAOs represented in our sample. As an exploratory study of DAO participation in clinical research, there are several limitations to the results we report. Of particular note is that we sought to describe the experiences of DAOs that were associated with genetic conditions. It is unclear to what extent our findings may be typical of other DAOs, such as organizations that represent nongenetic conditions that affect much larger numbers of individuals. It also is possible that respondents to this survey may have self-selected for more active involvement in research and that their responses are not typical of other DAOs although respondents and non-respondents were not compared. In addition, it may be the case that members of Genetic Alliance network are more supportive of clinical research than other DAOs.

Future research should seek to characterize the involvement of other types of DAOs in clinical research. Studies examining researcher and clinician perspectives on collaborations with DAOs can also help to provide a more comprehensive picture of these relationships. These and other studies are essential for providing a more complete account of the involvement of DAOs in research and can serve as the basis for forging strong researcher-DAO partnerships in the future.

CONCLUSION

More extensive and direct forms of collaboration among DAOs and clinical researchers may help to alleviate some of the burdens associated with genetic disease research, particularly challenges related to identifying sources of research support and recruiting research participants. Our results show that most DAOs for genetic conditions are involved directly in many aspects of clinical research and do far more than simply provide financial resources or informal support for investigators. Many DAOs participate directly in subject recruitment and impact the outcomes of research by participating in study design, data analysis, and presentation of scientific results. Leaders of DAOs feel these activities improve the overall relevance and quality of the research done and that investigators and research funding agencies should partner with them in carrying out their research. Future studies should assess the impact of DAOs on clinical research and develop practical guidance to maximize the benefits of these new research partnerships.

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DISCLOSURE

The authors declare no conflict of interest.

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