A Review of the Alpha-1 Foundation: Its Formation, Impact, and Critical Success Factors

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Patient-advocacy organizations have proliferated because they can be an effective method to advance research and clinical care for those with the index condition, and can produce substantial benefits for the affected community, especially when the condition is uncommon. To clarify critical success factors in organizing a patient-advocacy organization and to provide a blueprint for others, including the respiratory-care advocacy community, this report examines features of one highly successful organization, the Alpha-1 Foundation, which is committed to helping those with the genetic condition alpha-1 antitrypsin deficiency. Features of the Alpha-1 Foundation that underlie its success include: consistently creating partnerships with key stakeholders, including the scientific and clinical communities, government, and pharmaceutical manufacturers; bringing passion to the cause (eg, by assuring that organizational leadership is provided by individuals affected by alpha-1 antitrypsin deficiency); and developing strategic business partnerships, as with a company that administers alpha-1 antitrypsin treatment (so-called intravenous augmentation therapy) and employs individuals with alpha-1 antitrypsin deficiency. Funds allocated by the company help to underwrite the foundation's research-funding commitment. The foundation also recruits and retains talent, including alpha-1 patients, to leadership roles (eg, on the board of directors) and has a voluntary group of committed scientists and clinicians. We believe that attention to these factors can help assure the success of patient-advocacy groups. *Key words: alpha-1 antitrypsin deficiency, patient advocacy, organization.* [Respir Care 2006;51(5):526–531.

Introduction

Patient-advocacy organizations can exert a powerful influence on the course of research and clinical care for those with the index condition, and can have substantial benefits for the affected community, especially when the condition is uncommon. Because such organizations have proliferated recently and may interface with the respiratory-care community, understanding the critical organizational success factors is important. Benchmarking by adopt-

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ing successful features from existing organizations can enhance the success of fledgling groups and can help avert pitfalls that thwart success. Yet little attention has been given to assessing the features of advocacy groups that promote success on the one hand or that lead to failure on the other. To address this need, this report analyzes the genesis, structure, and impact of the Alpha-1 Foundation, an advocacy organization regarding alpha-1 antitrypsin (AAT) deficiency,[1–3] whose mission is, "to provide the leadership and resources to increase research, improve health, promote worldwide detection, and to effect a cure for AAT deficiency."[4]

This paper briefly reviews the history of the Alpha-1 Foundation and analyzes the strengths of the organization, with the goal of identifying features of the foundation that warrant adoption. Another goal is to enhance the respiratory-care community's awareness of the foundation and of AAT deficiency. To emphasize the impact that such organizations can exert, we then review the foundation's major accomplishments. Finally, we suggest ways that the foundation's work has affected the respiratory-care community and describe lessons from the foundation for respiratory care.

Structure and Development of the Alpha-1 Foundation

The Alpha-1 Foundation began in 1995, when 3 committed founders with severe Pi phenotype ZZ AAT deficiency envisioned an organization that would allow patients to take an active role in fostering research to effect a cure for their disease. John Walsh, Susan Stanley, and Sandy Lindsey (the latter two of whom have since died of AAT deficiency) were all veterans of earlier AAT research studies at the National Institutes of Health.[5] They had experienced the power of research in characterizing the natural history of severe AAT deficiency and in developing AAT-augmentation therapy.[2] They realized that resource limitations would retard research progress. Accordingly, they organized the foundation as a by-invitation-only organization to raise money for research and to advocate in stakeholder communities such as government, academe, and the pharmaceutical industry, for more and better research.

In the context of these drivers, the founders convened an original 5-member board of directors composed entirely of AAT-deficient individuals, called "alphas." The board was expanded within 5 months to include members of the clinical and scientific community. John Walsh was the founding chairman of the board and has served as president and chief executive officer of the foundation since its inception. The bylaws require that at least half the members of the board be AAT-deficiency-affected, either by having severe AAT deficiency or by being a carrier of the AAT-deficiency gene.

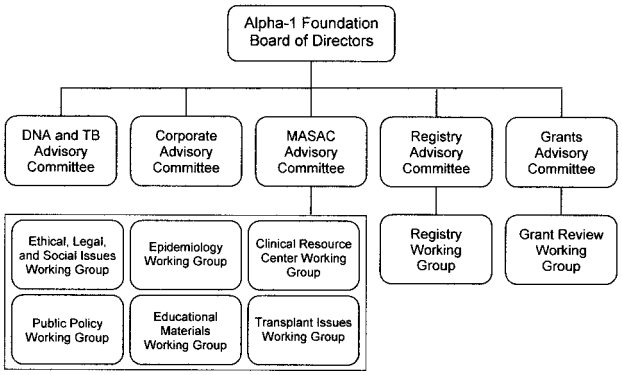

Fig. 1. Organization chart of the Alpha-1 Foundation. DNA = deoxyribonucleic acid. TB = tuberculosis. MASAC = Medical and Scientific Advisory Committee.

As shown in the organization chart (Fig. 1), the foundation has developed a number of functioning committees and working groups (eg, Medical and Scientific Advisory Committee, Grants Advisory Committee, and Epidemiology Working Group) to support its mission. In the context of this structure, major efforts of the foundation include providing an infrastructure for conducting research and for identifying affected individuals, securing funds for and funding research, advocating regarding AAT deficiency in strategic forums, and assuring ethical oversight of all activities.

Research Infrastructure and Funding

For the first 3 years, resources were directed to building a research registry to serve as a source of recruitment of subjects for clinical studies; developing a network of Clinical Resource Centers headed by investigators with expertise in AAT deficiency and in clinical research; establishing a dedicated academic research center to house an international genetics reference laboratory and translational research laboratory to support clinical trials; organizing the foundation's deoxyribonucleic acid (DNA) and tissue bank; and building scientific credibility by hosting a series of critical issues workshops. These workshops were meant to be at the leading edge of knowledge. Their programs (eg, focusing on computed tomography in assessing emphysema, conformational diseases, development of a functional and antigenic AAT standard, and others, as listed on the foundation's Web site, http://www.alphaone.org) included scientists who are not working on AAT deficiency but whose work had relevance to the field; the purpose was to encourage scientists to shift some of their effort to AAT research, to foster research collaborations, and to facilitate progress in research. Attending scientists were invited to apply for research support from the foundation.

It was this deliberate commitment to building a responsible and effective research program that provided the credibility to initiate the foundation's research grants and awards program. Within the first year of the foundation, a group of distinguished investigators was recruited to form the foundation's Medical and Scientific Advisory Committee, which has guided the foundation in decisions and policies regarding science and clinical care. Also, a Grants Advisory Committee was created to generate grant policies and procedures, to establish a formal peer-review and grants-administration process. A grants-review working group, whose work is overseen by the Grants Advisory Committee, was appointed to review grants. Grants are awarded once a year.

Since its inception, the foundation has given priority to thorough bioethical review and oversight in its operations and key decisions. Initially, a bioethicist from the National Institutes of Health served as a consultant. Subsequently, the foundation developed an ethical, legal, and social issues working group that advises and leads deliberation on issues involving confidentiality, conflict of interest, program-structure, board oversight, volunteer management, and relations with the pharmaceutical industry.

As another important dimension of its mission, the foundation has invested the resources to develop and validate patient and professional-education materials (available at http://www.alphaone.org). Available brochures include: "A Healthcare Provider's Guide to Alpha-1," "What Is Alpha-1? Should I Be Tested?," "A Guide for the Recently Diagnosed Individual," "A Guide for the Recently Diagnosed Alpha-1 Carrier," "The Research Registry Questionnaire," "Family Linkage in the Alpha-1 Research Registry," "Alpha-1 DNA and Tissue Bank," "Taking Part in Alpha-1 Research," and "Issues in End-of-Life Care." The foundation continues to revise and develop new materials under the direction of their Education Materials Working Group. The foundation's educational materials have been adopted by the Alpha-1 International Patient Congress and are being translated into 6 languages. The foundation founded the Alpha-1 International Patient Congress in 2003, to foster collaboration and resource-sharing in less-developed countries.

Additional working groups (see Fig. 1) were established to create the appropriate oversight and organize the professional expertise to guide the foundation in its programs: epidemiology, research registry, Clinical Resource Centers, transplant issues, public policy, and the DNA and Tissue Bank.

Fund-Raising

An important success factor has been the foundation's entrepreneurial approach to fund-raising. The founders realized the need for consistent revenue and for comprehensive patient care. At the very outset of the foundation, a unique not-for-profit health-management company, called AlphaNet, was formed, with a separate board and management. The AlphaNet company mission was to establish the ability to provide health-management services exclusively to alphas, and to contribute any profits from third-party service fees to support the foundation's mission.

Since 1995, AlphaNet has contributed $13 million to the foundation and over $1 million to the Alpha-1 Association, which is a sister, membership organization whose mission is "to identify those affected by AAT deficiency and to improve the quality of their lives through support, advocacy, and research."[6] AlphaNet currently provides disease-management services to over 2,500 individuals with AAT deficiency. The company has developed a comprehensive disease-management program under the direction of its medical director, disease-management director, nursing staff, and a group of consultants. Outcomes research on the efficacy of the disease-management program is under way.[4]

The foundation has also implemented a strategy to promote matching research grants that enable the foundation to leverage its investment in research. Matching grant programs have been established with the American Liver Foundation (> $750,000), American Thoracic Society ($50,000/y) American Lung Association ($35,000/y), American Association for the Study of Liver Diseases ($25,000/y), and National Heart, Lung, and Blood Institute ($65,000/y). A standing matching challenge grant to the foundation's Clinical Resource Centers for up to $150,000 in matching funds has been taken up by 2 Clinical Resource Centers to date. The foundation has attracted over $4 million from family and private foundations.

An Alpha-1 research program was established at the University of Florida College of Medicine, with a $600,000 grant that was matched by $420,000 from the State of Florida and a commitment of $1.3 million from the University of Florida College of Medicine. For the past 4 years, the State of Florida has provided funding to support the foundation's Florida targeted-detection program. Preliminary results of the targeted-detection project are promising. Also, a recent cost-effectiveness analysis suggests that targeted detection satisfies traditional criteria for cost-effectiveness when the prevalence of the condition in the population being tested resembles that observed in the targeted-detection project to date.[7]

Although the foundation has been reluctant to ask alphas to contribute because of the burden of their healthcare costs, in the past 3 years the foundation has established an increasing volume of contributions from the community in an annual appeal program. Several alphas are now dedicating themselves to help raise funds to support additional research.

A number of fund-raising efforts have been sponsored that reach out to the community. Team Alpha is a bicycle team that is headed by an alpha who is now an 11-year lung-transplantation veteran. Team Alpha conducts several bike rides each year, many with the American Lung Association, that help to increase awareness of the disease as well as raise money. Each year in Miami a golf outing and dinner, known as "The Celebration of Life," also serves fundraising.

Overall, in 9 years, the foundation has funded more than $15 million worth of research in 42 institutions in North America and Europe. The research portfolio covers a broad range of research, from basic science to translational and clinical research to research on psychosocial issues. The vigilance of alphas on the board and on each advisory committee and working group has led to a responsible and productive research-grants program, which has been a defining success factor for the foundation.

Summary of Selected Accomplishments

To emphasize the power of the organizational structure to effect important change on behalf of AAT deficiency, some additional details of selected accomplishments of the foundation are offered in this section.

To assure confidentiality and appropriate administration, the Alpha-1 Registry[8] is located under a university institutional review board, with the direction of a principal investigator who is a faculty member. The registry is currently operating under a management agreement with the Medical University of South Carolina. The registry also operates a confidential testing program, known as the Alpha-1 Coded Testing Trial,[4] which allows family members to get tested confidentially, thereby avoiding any potential exposure to genetic discrimination. Blood-spot samples are submitted to the registry, with a research questionnaire. The blinded samples are forwarded by the registry to the foundation's genetics laboratory at the University of Florida College of Medicine; results are reported back to the registry and are reported confidentially to the person who submitted the sample.

Collaborations by the foundation with the National Institutes of Health have fostered increased investment in lung and liver diseases related to AAT deficiency and have helped support the establishment of the Rare Lung Disease Clinical Research Network, one of the main studies of which is on the role of computerized densitometry as an outcome measure of AAT deficiency.

The foundation's mission to promote worldwide detection is being addressed by its funding of an International Laboratory Fellowship to foster detection laboratories in several countries other than the United States. To help establish and promulgate clinical management standards for individuals with AAT deficiency, the foundation provided financial support for the preparation and publication of the American Thoracic Society/European Respiratory Society Standards for the Diagnosis and Management of Individuals With AAT Deficiency, an evidence-based systematic review of the literature, published in the *American Journal of Respiratory and Critical Care Medicine* in October 2003.[3] Among other important recommendations, this document endorsed AAT-deficiency testing for all individuals who have chronic obstructive pulmonary disease. Furthermore, in compliance with this recommendation, the foundation launched a national targeted-detection program in May 2004 that seeks to assure AAT-deficiency testing for all individuals with chronic obstructive pulmonary disease. Also directed at promoting detection, a large-scale effort is under way to educate both physicians and patients about the importance of AAT testing.

Overall, in its 10-year history, the Alpha-1 Foundation has made important advances to achieve its mission. Critical success elements for the organization merit emulation and include:

- The creation of partnerships with key stakeholders, including the scientific and clinical communities, government, and pharmaceutical manufacturers
- The ability to sustain initiatives, aided by bylaws that require leadership by AAT-deficiency-affected individuals who have "skin in the game"
- Affiliation with a partner (AlphaNet) that helps to underwrite its research-funding commitment
- The ability to recruit and retain talent, including a voluntary group of committed scientists and clinicians

Physician Experiences on the Alpha-1 Foundation Board

Inclusion of physicians and scientists on the foundation's Board of Directors is another critical success element because it juxtaposes the voices of science and clinical care with the voices of advocacy. Indeed, the experience of the clinician authors of the present paper (GLS and JKS) highlights the special effects of this joining of voices and its unique effect on our perspective.

Two of us (GLS and JKS) are physician/scientists experienced in AAT deficiency, but we had never, before our experience with the foundation, sat on a board with people not trained in medicine or science, and who suffered from the disease of interest. It was not too long before we heard foundation board members asking pointed questions of the scientists. They wanted to know, for instance, how an apparently esoteric cell-biology project designed to study the abnormal folding of the Z AAT protein was going to lead to a cure. Why was that

project recommended for funding in preference to a project that had more obvious and immediate connection with AAT deficiency? We found ourselves explaining that the latter project would provide information that would have only limited importance. On the other hand, the project dealing with Z protein folding could lead to a major therapeutic breakthrough—although the breakthrough might not occur for many years.

We initially had difficulty using or endorsing the word "cure" (which was liberally used by the alphas on the board), because we did not want to create false expectations with use of that word. Our concern was that only a small percentage of the best research initiatives lead to breakthroughs in any one year, or, for that matter, in any 10-year period. Given scientists' general aversion to invoking "cure," we were keen to avoid misleading or giving the impression of naïve hope. Yet the striking power of joining with affected individuals and of developing and promoting a strong research agenda has allowed us to embrace and now use the word "cure" in our own discussions of AAT deficiency.

As we got to know the alphas, we realized that they were expressing cautious hope and were not expressing unrealistic expectations. How else do you live with knowing that your disease is relentlessly progressive? How else do you live through the deaths of your friends and colleagues? And then we found that a strange change in our attitude was occurring. Rather than the dispassionate attitude about science that we had always cultivated, we found ourselves becoming increasingly concerned about the chances of success of every project we reviewed. The alphas on the board were becoming our friends. Their concerns were becoming ours and we were developing a new perspective of immediacy and advocacy. The "cure" word began rolling off our tongues more easily. We became passionate about science as the way we could best understand the disease, alleviate suffering, and find a cure to help our friends; indeed, this perspective became contagious among the scientists and clinicians associated with the foundation, whose commitment has been another critical success factor.

We believe this experience has relevance for many scientific committees advising lay groups who are supporting research. Including in leadership and advisory committees some individuals who have the disease has a subtle but powerful effect on the scientists. The research problems somehow acquire greater urgency.

Critical Success Factors and Lessons To Be Learned

Analysis of the experience and accomplishments of the Alpha-1 Foundation permits identification of several critical success factors that offer important lessons for fledgling organizations seeking similar success. These critical success factors include:

- The creation of partnerships with key stakeholders, including the scientific and clinical communities, government, and pharmaceutical manufacturers
- The ability to bring passion to the cause, aided by mandating that leadership be provided by alpha-1-affected individuals
- Development of a partner (such as AlphaNet) that helps to underwrite the organization's research-funding commitment and that employs affected individuals in service of other affected individuals
- The ability to recruit and retain talent, including affected individuals, to leadership roles (eg, on the board of directors) and a voluntary group of committed scientists and clinicians

Each of these elements is briefly discussed below.

Cultivation of strategic partnerships has been a distinctive success element. The foundation's leadership has been able to identify and articulate ways in which its partners' agendas align closely with the foundation's, thereby allowing extraordinary collaboration and cementing the foundation's role as a "broker."

Leadership involvement by alphas in the foundation is another critical success factor, because it has brought immediacy and passion to the foundation's activities and has lent credibility and force to the foundation's roles, such as in testifying before government and Congress. The fact of the organization's having "skin in the game" is powerful and leads us to recommend that all like organizations seek leadership service by affected individuals.

Developing a partnership with a service company, in this case AlphaNet, has been of signal importance to the foundation, because it provides a mechanism to assure research funding and to harvest the talents and activities of alphas in service of other alphas. All organizations should consider the possibility of developing a service company, although it is recognized that specific conditions of each disease may affect what the service company does and ways in which it interfaces with the foundation.

As with all organizations, the ability to identify, recruit, and retain talent in service of the organization's mission has been an important success factor. While admittedly difficult to reproduce, the foundation has been blessed with impassioned and capable alpha leaders who have successfully engaged others, including clinicians and scientists, in their cause. In part, this success in recruiting relates to the foundation's ability to align agendas. Examples include: providing research funding that engages research scientists; sponsoring stimulating, cross-disciplinary educational conferences that bring high-caliber scientists

who are working on other topics into the field of AAT deficiency, by demonstrating the relevance of their work to AAT deficiency and the prospects of research funding to support those efforts; and providing a forum for meaningful work that makes a difference for alphas seeking such opportunities.

We believe that these critical success factors offer a road map for nascent organizations, which, if followed, can help assure similar successes to those achieved over the first decade of the Alpha-1 Foundation's existence. Offering such lessons will, we hope, be yet another important contribution.

Finally, the work of the Alpha-1 Foundation has had important impact on the respiratory-care community and the story of the foundation's development and success elements offers several important lessons for the respiratory-care community and for respiratory therapists:

As an important example of the impact of the Alpha-1 Foundation on respiratory care, the foundation, along with the American Respiratory Care Foundation, the American Thoracic Society, and the European Respiratory Society, was an important sponsor of the recent standards document regarding the diagnosis and management of individuals with AAT deficiency.[3] These standards have provided important guidelines for respiratory-care practice. Also, competitive grant opportunities funded by the Alpha-1 Foundation offer opportunities to the respiratory-care community to investigate basic, clinical, ethical, legal, and social aspects of AAT deficiency.

Regarding lessons for the respiratory-care community, the success of the foundation demonstrates how passion, savvy, and organization can be brought to bear in service of an important cause. Challenges facing respiratory care, such as how to optimize the delivery of respiratory care services, how to grow the profession to confer the benefits of respiratory care in other countries, how to increase the scientific basis of respiratory care, and how to maintain and grow professionalism, can all be served by similar resources.

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