

GLOBAL VISION RESEARCH NEEDS AND OPPORTUNITIES

Highlights of a National Eye Institute Workshop

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Introduction

The National Eye Institute was established for the purpose of conducting and supporting medical research leading to increased understanding of normal and abnormal visual function, and the development and improvement of prevention strategies, diagnostics, and treatments across the full spectrum of eye diseases/conditions. The mission includes provision of research resources and infrastructure to provide access to advanced instrumentation and technologies in vision research laboratories, and access to requisite biological material for clinical studies. Extensions to international collaborations represent a bridge linking complementary research resources available in developed and developing countries.

Increasingly, access to affordable, high-quality eye care is seen as a worldwide challenge. In cooperation with professional eye care societies and non-governmental organizations, the NEI is supportive of health services and operations research that stresses the use of knowledge already gained to improve the world's eye health, including furthering the application of vision research results in clinical practice to improve the delivery of quality eye care. Global awareness of the economic and disability burden of visual impairment is fundamental to appreciating the societal relevance of the NEI research mission.

BACKGROUND

The NEI has been actively engaged in the direct support of international research collaborations in a number of ways. A central component is the twenty-five year history of providing funding to the Prevention of Blindness Unit of the World Health Organization under contract N01-EY-9-2103 (Strengthening the WHO Program for the Prevention of Blindness). Under this contract, financial support, often accompanied by technical assistance, has been awarded to numerous eye care institutions in developing countries for a variety of epidemiological, clinical and health services research projects. Notable projects have included: i.) a randomized clinical trial in India to compare safety, efficacy, and quality of life outcomes after intracapsular cataract extraction with aphakic glasses versus extracapsular cataract extraction with posterior chamber intraocular lens; ii.) population-based adult visual impairment/blindness and cataract surgery outcome surveys in Nepal, China, India, and Brazil; iii.) development and validation in India of an international vision function questionnaire (similar to the widely used NEI-VFQ) for use in developing country settings; iv.) population-based childhood visual impairment and refractive error surveys in Nepal, China, Chile, India, South Africa, Malaysia, and Brazil, and v.) translation and adaptation of AAO Preferred Practice Patterns for implementation in China.

Direct investigator-to-investigator initiated collaborations aimed at understanding disease mechanisms and the development of therapeutic interventions continue to be an important feature of the NEI intramural research portfolio. Twenty senior intramural investigators are currently engaged in basic and clinical international research collaborations spanning as many countries. Similarly, the NEI grantee community has established wide-ranging international research collaborations involving 62 currently funded U.S. grants with a funded foreign component and 7 grants to foreign principal investigators.

With funding from NEI under a cooperative agreement with ARVO, workshops were held at three sites in India in February 2005 and in the U.S in April 2005 in a concerted attempt to expand vision research collaborations between scientists in the U.S. and India. A US-India Statement of Intent for collaboration on expansion of vision research was subsequently signed by the Secretary of the India Department of Biotechnology and the Director of the U.S. National Institutes of Health on August 24, 2005. Implementation of this agreement will involve cooperation in scientific review and joint funding of collaborative priority research proposals.

WORKSHOP THEMES

Complimentary and Collaborative Activities

Furthering the development of an international research agenda for the NEI was the underlying theme for the workshop. Twenty workshop participants from the international eye care and vision research community were charged with considering what medical science in a global context might look like in 2020 and to address three topical areas:

- Basic, translational, and clinical vision research where international collaborations offer unique opportunities and leverage.
- Research capacity and infrastructure development needs for enhancing global vision research productivity.
- Operations and health services research in bridging international disparities and improving eye care worldwide.

Additionally, the participants were invited to elaborate on:

- Non-governmental organization and professional society responsibilities and roles in fostering international cooperation and collaboration.
- The specific role of the NEI in advancing the development and support of international research collaborations.

Basic, Translational, and Clinical Vision Research

Participants were asked to consider ways in which the NEI can leverage the international vision science community and its resources to improve and accelerate basic, translational and clinical research.

Basic and Translational Research

Internationally, genomics opportunities abound. Countries with histories of social caste systems and consanguinity have created population isolates where rare diseases occur with greater frequency than in the United States. These rare disease populations have already proven helpful in identifying genes and in correlating genotype/phenotype relationships. The variation in phenotype for common complex diseases among ethnicities presents further opportunities to

examine the underlying genetics and environmental factors that influence genotype/phenotype relationships.

Participants discussed the opportunities in their own countries to conduct genomic research. NEI intramural researchers have been collaborating with scientists in Pakistan to collect DNA samples and have identified new loci and genes for nonsyndromic deafness and rare retinal diseases. In China, an estimated 10 million people have glaucoma with primary closed angle glaucoma accounting for 80% of cases. In Japan, 91% of glaucoma is normal tension. Yet in the United States, open-angle glaucoma is the most common form of the disease. A young twin registry involving nearly 20,000 twins is being developed in China which offers unparalleled opportunity for clarifying gene and environmental interactions and gene tracking in myopia. With a very low incidence of macular degeneration and high incidence of proliferate diabetic retinopathy, the Meztiso population in Mexico offer unique opportunities for genetic studies.

Clinical Research

The participants stated that international research collaborations should be focused on issues of clinical relevance in reducing the burden of blindness and visual disease worldwide.

International collaborations provide for a critical increase in the number and diversity of potential subjects, a large range of phenotypes, a greater variety of environmental histories and a potentially large number of co-investigators. Complex diseases require collaborative groups in conducting clinical trials. The internet facilitates linkage of clinics from around the world.

International collaborations provide cost-effective opportunities for multi-centered clinical trials. Clinical trials to support the evidence base for interventions tailored to genetic characteristics can be optimized in distinct international populations.

Standardization and Classification

With the possibility of a global research network comes the challenge of standardizing phenotype classifications and phenotypes. There is a need for global consensus on disease phenotype classification and methods to standardize such classification. The question is not whether a classification system is perfect, but whether it is an improvement. If a consensus cannot be reached, the field is not ready. Standardization of grading or phenotype classification is needed for the development of biobanks or patient repositories for collaborative research. Collaborations require standardization of terminology, case definitions, and data collection.

Standard disease phenotype descriptors need to be developed disease-by-disease by a specialized team for each one. We need to get the phenotype right if we are to get the genotype-phenotype connection right. To get the phenotype right, we need morphological/pathological information. The ICD-11 (International Classification of Diseases) will be a completely different disease descriptor system. We should explore this further to ensure that eye diagnoses are addressed properly.

There is a need for the development, implementation, and wide-spread dissemination of disease severity scales for the most important ocular disorders. Quality data are important in developing disease scales, as was the case for diabetic retinopathy. Nomenclature, imaging and communication standards are needed for the expansion of networks of information exchange.

Images are important in disease documentation as they don't require judgment and a predetermined classification system.

Research Resource Capacity and Infrastructure Development

A critical appraisal of national research capacity, including the volume and quality of research, is needed in middle and low income countries. Countries with a large variety and magnitude of vision problems and the necessary science infrastructure offer the greatest scope for international collaboration. Only a few institutions in any country will have the infrastructure needed for international vision research collaborations.

Building research capacity in low and middle income countries is a daunting task. Participants suggested that international capacity building could become an integral part of a regular research grant. Training programs like the NEI's intramural Overseas Scholars Program, where participants receive training and return to their home countries, are a good source for capacity building. Fogarty grant programs—Fogarty International Research Collaboration Awards (FIRCAs) and Global Health Research Initiative Program for New Foreign Investigators (GRIPs)—also help to build capacity by training researchers and clinicians and then sending them back to home country with NIH grant support to collaborate with NIH grantees.

Databases and Registries

As antibiotic resistance grows and infections play an even greater role in the ocular disease burden, the need and opportunities for data banks and registries that span countries will grow. Countries with large populations offer the greatest scope and opportunity for establishing databases of DNA, biological tissues, and patients.

Datasets from the WHO/NEI supported multi-country surveys of visual impairment in children and adults could be made available to other researchers through the WHO website. The large number of WHO/NEI-supported prevalence surveys all used the same standardized protocol, which is critically important in enabling the merging of the individual study data sets.

Education/Training/Exchange

It is important to establish a culture of critical thinking and scientific inquiry at all levels of training. Enhancement of postgraduate research training and research capacity development is an important priority. There is a general need to expand scientist/student exchange programs and long-distance educational programs for graduate students and clinician scientists. Collaborative international research should be fostered with pilot projects, support for international travel to meetings, and funding of sandwich programs for scientists and clinician scientists.

Post-doctoral training and development of organizational networks/structures requires further attention. There is also a need to enhance skills and resources through training for the conduct of clinical and health services research. The potential exists for national, regional and international groups to work together to develop standards for ophthalmic resident and fellow education.

Operations and Health Services Research

Service Delivery

Considering the 70-90 percent of global blindness is avoidable or preventable with current knowledge, operational research is needed to understand the barriers to knowledge implementation and the availability and uptake of eye care. There are country- and region-specific factors affecting eye care delivery, but also common factors across cultures.

A common framework is needed for operations research study protocols. The relevance of an international perspective in operation research comes from the added value provided by comparisons across international settings, while recognizing that the communication of findings is a local, cultural issue.

There is a need for evaluation of eye care system weaknesses in the public health management in developing country settings. Evaluating actual skills and performance in the care process, as opposed to just knowledge, is paramount in assessing the uptake and impact of new information and technology introduced to the eye care community.

Outcomes research is needed to determine what happens there in the community, and operations research is needed to address barriers in eliminating infectious diseases such as trachoma from a population.

Clinical Guidelines

The introduction of guidelines is a way to integrate state of the art research findings into education and clinical care. Translation and adaptation of ICO/AAO eye care guidelines for implementation where needed would be helpful.

Overall, clinical performance (process of care) guidelines provide a framework for evaluation and ultimately improvement of the quality of care for patients.

Economic Analyses

There is a need for epidemiological data on the prevalence of blinding diseases especially in countries and regions where reliable data are not available. Economic and manpower analyses, relevant to influencing country expenditures for health, will become an important part of operational research. Global health economic assessments of the financial cost and quality of life burden of visual impairment are needed to support advocacy, and prioritization of eye care services in resource poor settings. There is a need for cost of illness and cost of failure to treat studies from a macroeconomic perspective, in contrast to studies at the household level.

Non-Government Organizations, Professional Societies, and the NEI

Organizations such as ARVO could use information technology to foster networking among researchers. U.S. based research associations could establish chapters in other countries to assist in defining the nature and scope of research needed to promote world wide eye health.

Scientific and clinical meetings could be shifted to affordable locations to increase attendance from developing countries. Societies/associations can encourage non-US membership by reducing dues in innovative ways. Improving the quality of residence education on an international scale may be an important goal for professional societies, as is the continuing education of physicians.

The National Eye Institute

Fostering international collaborations that cut across disciplinary boundaries and inter-professional politics will increasingly become an NIH activity. NEI should encourage, where possible, the training of young researchers from all over the world at leading ophthalmic research centers, in developed as well as developing countries. NEI could fund the organization of international/regional meetings, symposia and seminars to provide opportunities for collaboration and cross-fertilization of ideas among researchers working on similar goals. Enlargement of participation in scientific exchange through NEI merit-fellowships and travel award programs would be of value.

NEI could consider funding new investigators to establish research laboratories/programs in their native countries upon completion of NIH post-doctoral training by increasing support of the Global Research Initiative Program [GRIP].

The NEI is in a unique position to encourage the development of international harmonization/standards and disease classification systems. There are multiple ways for the NEI to support international collaborations within existing NIH/FIC mechanisms. The NIH is an active supporter of health services research, as evidenced particularly by the substantial funding NIA and NIDDK provide for projects of this nature.

Continuing NEI support of consultations in cooperation with the World Health Organization—where high caliber international public health collaborations are developed—is enormously productive. NEI could increase its impact on world health by directing more resources to research on optimizing health care delivery models.

SUMMARY

The workshop highlighted the unique genetic research advantages and opportunities within the global arena. The global arena also presents opportunities to increase clinical research opportunities and efficiency.

Much of global blindness is preventable or treatable with current knowledge, and therefore, research is needed to understand delivery system failures and barriers to the provision and utilization of quality eye care services. Quantitative analyses of the economic and quality of life burden of visual impairment and blindness on a global scale are also essential for an informed public and for increasing support of vision research.

Adequately trained manpower is required if the unique advantages offered by international vision research collaborations are to be realized. Workshop participants recognized that a host of additional resources are needed to leverage existing efforts to reduce global blindness.

For its part the NEI, with the assistance of its global partners and advice from the National Advisory Eye Council, is committed to maximize its role as a leading collaborator and facilitator in the international vision research community.

The participants developed a summary table outlining how the NEI and other key organizations fit into the effort to foster international research efforts. The table below identifies the workshop themes and the roles each organization might consider playing in enhancing complimentary and collaborative activities directed toward improving vision health and reducing the global burden of blindness.

ORGANIZATION =====	NEI	Other NIH	CDC	Other Govts.	WHO	ARVO	Prof. Soc.	NGOs
TOPIC								
Basic, translational & clinical research	P	P		P	F	C,F	F	
Health services & operations research	P,C	P,C	C	P	P	F	C	P,C,F
Economic analysis & QOL burden of visual impairment	P		P,C	P	C			P,C
Research education & training	C	P			C	P	P,C	
Other research resources & capacity building	P	P		P	C,F			P,C

P = Primary funding responsibility C = Collaborator role F = Facilitating role

ANNEX 1
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