

**NATIONAL INSTITUTES OF HEALTH
NATIONAL INSTITUTE OF NURSING RESEARCH**

**Working Group
Increasing Opportunities in Biobehavioral Research
July 15-16, 2004
Four Points Sheraton
Bethesda, Maryland**

Executive Summary

The National Institute of Nursing Research (NINR) sponsored a two day working group meeting with behavioral, biological, and immunological science experts to examine current knowledge and provide recommendations to further advance biobehavioral research. The rare disease, allergic bronchopulmonary aspergillosis (ABPA) was used as an exploratory model.

ABPA was used as an example during presentations and discussions to illustrate the challenges in biobehavioral research. Discussions focused on areas for future science directions and on the need for educating researchers in biobehavioral methods of measurement and analysis. The use of interdisciplinary/biobehavioral approaches was emphasized.

I. WELCOME

Dr. Patricia Grady, PhD, RN, FAAN, Director of the National Institute of Nursing Research (NINR), welcomed participants on behalf of the Institute and working group Co-Chairs, Karen Huss, DNSc, RN, FAAN and Pamela Mitchell, PhD, RN, FAAN. NINR has supported interdisciplinary/biobehavioral research for many years. NIH is now emphasizing biobehavioral studies within the Roadmap themes. Dr. Grady went on to highlight the work of selected NINR funded researchers who are emphasizing biobehavioral themes.

II. SUMMARY

There are many facilitators and barriers to research using biobehavioral approaches. Some of the barriers are related to the nature of diseases with small patient populations and some are broader concerns associated with carrying out biobehavioral research with patients along the natural history of an illness. Presenters discussed these barriers and identified gaps and approaches for future research. Key discussion points and conclusions of the working group members are as follows:

Biobehavioral Research Designs

- Use alternatives to randomized clinical trials especially crossover designs.
- Utilize Bayesian techniques.
- One conceptual model suggested (“Biopsychosocial Interactive Paradigm”) consisted of 3 intersecting circles representing biological, social, and psychological domains set within a larger circle representing the environment. Behavior is the manifestation of the interaction of the 3 circles. Mid-level theories or concept models could guide handling of variables of interest in a study. Interdisciplinary approaches permeate the model.

Biobehavioral Research Analysis

- Employ structural equation modeling for disparate measures in self-report.
- Use longitudinal repeated measurements to assess magnitude & pattern of change in outcomes especially before and after exacerbations of disease.
- Make use of discriminant analysis to sort out most significant factors and potential weights within a given health condition/population.
- Apply repeated measures of variance and longer periods of assessment for small sample size research.

Research Suggestions Relevant to Designs Involving Small Sample Sizes

- Add psychosocial/behavioral outcome variables to research aims such as changes in functional abilities, social support (family, community resources), and adherence.
- Use pooled data analyses.
- Explanatory case study models may be useful.
- Consider sequential trials.
- Examine alternate clinical outcomes including hospital/ED admissions, length of hospital stay, and cost of care.
- Study patients along various stages of disease; detail remissions and exacerbations either spontaneously or with treatment.
- Find ways to minimize burden of study participation for vulnerable populations.
- Have the community participate early in the research design; enrollment, adherence to a regimen, and follow-up will increase.

Biobehavioral Approaches to Assessment of Variables

- Use composite scores when using measurements for variables such as stress, depression, and anxiety rather than measuring each individual component.
- Encourage development of new methods for studying variables from an integrated approach.
- Develop condition specific measures such as adherence that can be used across studies and address biologic and behavioral components of the variables.
- Use general and specific disease Quality of Life measures for short and long term cross sectional and longitudinal studies.
- Use ambulatory monitoring techniques to make setting more like natural experiences.
- Use non-invasive measures like diaries along with objective biological measures.

Biobehavioral Instruments

- Health Related Quality of Life (HRQL) – supplemented with specific psychosocial and behavioral measures and physiologic markers.
- Biologic responses indicating exacerbation of disease; including immune responses and immune function.
- Disease specific physiologic measures.

- Electronic monitoring of symptoms (electronic diaries, activity monitors).
- Objective measures of biological endpoints.
- Gene and protein chip studies; other genetic markers to complement behavioral assessments.
- Adherence measures.
- Psychobiologic assessment measures followed over time; tools to assess coping skills of patients; trajectory of confidence in healthcare; discrete outcomes (death, decline in FEV1, change in respiratory status).
- Consider magnitude of subject burden; instruments appropriate for all developmental stages.
- Robust measures of symptoms, biomarkers, and adherence to medications instruments that are standardized.
- Tool development for valid/reliable instruments.
- Develop a national data base of current measures.

Biobehavioral Instruments; Problem Issues

- Difficulty locating biobehavioral instruments that are valid, reliable, and discriminate across populations and in longitudinal designs.
- Systematic and random errors in measurement; in small n studies must be fewer errors, more reproducibility.
- Difficulty of standardizing self-report measures.

Biobehavioral Research Gaps

- Mentoring expertise for faculty.
- Integrating biological and behavioral variables into research designs.
- Research designs and data analysis techniques for small samples.
- Understanding of disease processes & pharmacology.
- Psychosocial factors and relationship to health outcomes.
- Training clinicians on impact of patients' behaviors on their QOL.
- Screening & surveillance issues including who to screen, frequency, role of long term monitoring.
- Helping patients accomplish indoor environmental control measures such as reducing mold growth in homes.
- Understanding factors that promote or decrease adherence.

Initiatives to Address Biobehavioral Research Gaps

- Support for biobehavioral research curricula at universities.
- Biobehavioral Workshops.
- Formulate interdisciplinary hypotheses; collaboration is critical to do biobehavioral research.

- Standardize response variables; give attention to heterogeneous populations (age, ethnicity, etc.); measures must reflect intent or goals of research and be appropriate for populations studied.
- Encourage that longitudinal studies have consistent measurements over time.
- Clarify cross discipline knowledge base necessary to conduct biobehavioral research.
- Establish collaborative relationships with colleagues across disciplines, e.g. journal clubs, professional affiliations.
- Promote improved laboratory methods for biomarker measurements (e.g. IgE anti-Aspergillus f antigen for ABPA).
- Interdisciplinary investigators meet early in proposal plan; explicitly state how research and specific discipline sheds light on project and what each investigator will contribute; maintain the team.

Enhancing Skills of Biobehavioral Researchers to Create Opportunities for Interdisciplinary Research

- Provide cross training in physiology, immunology, genetics, microbiology, biochemistry and other relevant disciplines.
- Provide adequate laboratory time to teach assays, techniques, and basic science procedures.
- Educate researchers about available training mechanisms including small grants for pilot testing of biological measures and tools.
- Identify existing biobehavioral resources such as inter-laboratory sabbaticals and summer programs.
- Utilize T32, P20, and P30 grant mechanisms as starting point for collaborators.
- Address barriers needing change to further interdisciplinary biobehavioral research.
- Write PAs and RFAs that encourage collaboration with basic scientists.
- Encourage institutions to focus on multidisciplinary problem issues.
- Through collaboration, facilitate researchers to speak a common language (basic scientists and behavioral scientists must learn to speak to each other).

Suggestions to Enhancing Skills of Basic Science Researchers to Create Opportunities for Interdisciplinary Research

- Become familiar with behavioral measures such as adherence, quality of life, and functional status.
- Be aware of developmental and ethnicity factors and relationship to measurement (e.g. cognitive development, language skills, SES, acculturation).
- Recognize statistical analyses, human subjects' regulations, selection of tools, measures and study designs for behavioral research.

Areas Ready for Interdisciplinary Collaboration

- NIH Roadmap encourages collaboration of investigators. Researchers must overcome differences in perspective, incentives, methods, and primary and secondary outcomes.
- Researchers must go beyond usual collaborations to engage others to solve problems creatively and efficiently.
- Anticipate novel technologies, imaging probes, or instrumentation including broader chemical diversity, assay flexibility, more sensitive noninvasive imaging, extension of robotics and supercomputing networks to expand biobehavioral approaches.
- Utilize nanotechnology which may herald a new paradigm for investigating behavioral/biological interfaces, predicting and preventing diseases, and personalizing therapies to improve and maximize health. Nanotechnology may be cross linked to other health care disciplines to provide a quantitative measurement of biological processes.
- Explore pharmacogenetics which may affect the physiological responses to therapeutic interventions in a clinical trial.

Suggestions for Further Biobehavioral Research

- Collaborate with bioengineers to offer new ways to look at biological problems.
- Form interdisciplinary partnerships for data analysis, detection of changes in variables, and monitoring.
- Utilize registries (e.g. cystic fibrosis) as sources for subjects or retrospective data.
- Utilize collaborative partnerships based on a conceptual framework encompassing a mixed methods approach to qualitative and biological research.

III. CONCLUSIONS AND RECOMMENDATIONS

1. More communication is needed between scientists in biologic and behavioral fields. This working group is one step in fostering communication, sharing information, and addressing complex issues between disciplines.
2. Patients with complex diseases have both behavioral and biologic problems. New science initiatives should encourage investigator consideration of the interaction of psychosocial, behavioral, cultural, and biological issues.
3. Biobehavioral models and frameworks should be used to guide research related to biobehavioral problems.
4. The research skill of varied scientists to do biobehavioral research is a problem. Many ideas on enhancing these skills were addressed.
5. A number of biobehavioral measures were discussed. The group recommended methodological studies to improve the robustness of findings.

6. Expertise in mentoring new investigators in biobehavioral research is needed. The group recommends exploration of NINR and community approaches to address this issue.

V. ATTACHMENTS

1. Agenda
2. Participant list

- NINR acknowledges the partial support of this working group from Office of Rare Diseases, NIH