Measurement of ADHD Outcomes: Implications for the Future

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Introduction

Many questions arise when considering the outcomes of attention deficit hyperactivity disorder (ADHD) and exploring the ways treatment may affect those outcomes. The other papers in this supplement outline issues that affect assessment of specific aspects of ADHD and its outcomes. However, some overarching issues have implications for future research on ADHD outcomes. They relate to: 1) the definition of the condition(s) itself and its manifestations; 2) the natural history of the condition(s) and the morbidity that it causes; 3) the choice of outcomes and their relative importance; 4) the nature of the treatments; 5) the implementation of evaluation research; and 6) research priorities. In the commentary that follows I address each of these briefly.

Clarity in Definitions

The lack of clarity in defining ADHD affects all past and current work. ADHD differs from many other conditions in that it lacks biological markers for making the diagnosis and hence the criteria for diagnosis of affected individuals were developed by expert consensus. To date, in the overwhelming majority of studies, ADHD remains a purely clinical label and the criteria for its diagnosis and for inclusion in studies are somewhat subjective.[1] Moreover, many, if not all, investigators do not think that ADHD is a single homogenous condition.

All practitioners who evaluate and care for children with ADHD have encountered children given that label who do not in fact have ADHD. The diagnosis of a child's mental health condition is a challenging task, and relatively few children undergo comprehensive evaluations. As a result, many clinical trials are conducted without sufficient attention to baseline diagnosis and co-morbidities in both the treatment and control groups. Therefore, a central issue in any work on ADHD is the stability of classification of subjects based on the definitional framework. With only 12 years since the last major change in the way that the condition is defined and given the lag time in implementing and publishing studies, publications more than a decade old are likely to include some subjects who would not be classified as having ADHD today and exclude others who would be included today.

Related to this issue of classification is the decision about what symptoms or features of the condition are inherent in the condition itself and what features are parts of co-morbid conditions that are commonly found in the population of children who are diagnosed with ADHD.[2] The challenge of differentiating the ADHD-related outcomes from those due to common co-morbidities can make outcome research difficult. This problem is made more complicated because many of the co-morbid conditions also lack biological markers. The net effect is that assessing outcomes of ADHD in a sample of children or adolescents may include some subjects with a range of other conditions, or alternatively, if those with obvious co-morbidities are excluded, the study may under represent the consequences of ADHD, because they do not include the full range of subjects with the condition.

Those involved with the International Classification of Functioning are working to separate the elements that are inherent in the condition itself from those that occur as a result of interactions with the environment.[3] This effort, if widely adopted and applied to DSM classification schemes, may help to disaggregate some of the definitional elements and the outcomes. In addition, it may help with the development of descriptive data about the symptoms and the contextual variables as well as the development of phenotypic descriptions of ADHD.

Beyond these purely descriptive efforts, it is likely that efforts to define ADHD and its phenotypic variation based on improved understanding of the underlying genetic and gene environment interactions

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will significantly enhance the field in the next decade. Hopefully, these efforts will produce information about the different subtypes of ADHD. A recent example of such research is Rob Kahn's work showing that mothers with a particular mutation who smoke during pregnancy have a far greater incidence of ADHD in their young children.[4] This is clearly the tip of the iceberg and of likely complicated genetic and environmental interactions. As understanding of these phenomena improves, new avenues will open up for preventive interventions to minimize risk and severity of ADHD. However, the field will once again be challenged to reclassify the condition and its co-morbidities and to re-describe the elements of impairment and their effects on functioning and participation of each of the newly disaggregated subtypes of ADHD. Hopefully, this new understanding may also lead to new treatment modalities, as well as new understanding of the mechanisms of action of current treatments.

Natural History of the Condition in Current Society

Many unanswered questions about the natural history of ADHD remain. Although many small studies of specific clinical populations exist, the absence of longitudinal data on a population-based sample of children with ADHD who are identified in early childhood means that there is very little generalizable information about the effects of ADHD on overall developmental trajectories, morbidity, self esteem, learning, etc. Similarly there is a paucity of robust data on its effects on adolescents and young adults and their school functioning except in clinical samples, which, while helpful, are clearly biased toward children whose conditions were severe or persistent enough to bring them to care. Moreover, data are often lacking in how treatment affects (in both positive and negative ways) the natural history of the condition. Some new data that may help in this regard are emerging from the ALSPAC study.[5] Long term population-based information is needed on educational outcomes[6], risk taking behavior, adult functioning, employment, relationships, substance use, use of health, educational, social and justice system resources[7], and effects, if any, on lifetime mortality rates. The last has become a growing concern, both because of risk taking behaviors and increased accidents during driving and because of growing concern about the long-term cardiovascular issues of stimulant treatment. Here again, it will be important to disentangle the effects of the condition(s) from those of treatments and stigma.

A related issue in understanding the natural history is the extent to which the condition and its manifestations and outcomes result from a cycle of interactions between the biology of the affected individuals and their environments. Children do not grow up in a vacuum; they have important interactions with their families, communities, and physical environments.[8] Will meaningful changes in the environmental demands placed on a child alter this cycle? To what extent can the outcomes of ADHD be modified through environmental changes such as by altering the social and physical environments in which children are raised? What, for example, are the effects of sitting in crowded versus small classes, permitting or restricting recess and gym, or having parents who themselves may or may not have ADHD? What are the effects of electronic media on ADHD or its manifestations? Relatively little is known about these issues.

Definition of Outcomes

Which outcomes to measure and their relative importance remain unresolved issues. Specifying and prioritizing these variables and creating robust measures for them are formidable tasks. These tasks are especially daunting because of the tradeoff between studying everything and having sufficient depth and diversity of perspectives (and reporters) to enhance understanding of the underlying processes on the one hand, and having the power, resources, and participant cooperation to conduct the studies on the other.

There is little consensus about which outcomes are most important. Should studies assess personal, short term outcomes such as symptom control, school performance, self esteem, peer interactions, and/or risk taking behavior? Sometimes several of these may follow the same pattern, but at other times they may not. To what extent are these outcomes more or less critical than longer term outcomes such as better long term relationships, better educational success, and lower levels of physical and mental health morbidity?

Alternatively, instead of focusing on the outcomes for the child, should studies place priority on reducing the toll on the family, for example on parental perception of symptom control, improvement of parental and sibling stress, or family function, or their physical and mental health? And if so is it more important to assess and improve these outcomes in the short or long term? In the face of growing awareness that ADHD is a condition that affects substantial numbers of adults[1,9], these questions become even more complex.

Other lenses to assess outcomes include societal impact and cost? What should the calculations consider? Should it be only those costs of treatment or should it be those that relate to the education system, to time lost from work by family members or additional costs of supervision or enrollment in special programs? And what cost-benefit issues merit consideration? If the immediate costs of treatments result in longer term benefits, such as a more functional adult population with better self esteem and mental health, how should the short and long term costs be weighed in the assessment?[10] ADHD, like many other health conditions, has tradeoffs between positive and negative aspects of treatments, both for the patient and for the family.[11] These outcome-related issues are not unique to ADHD, but the large impact of this condition, together with its somewhat hard to measure or subjective features compounds these issues.

Measurement and Standardization of Treatment

Important questions arise in intervention trials about the delivery and standardization of treatments under evaluation. The MTA trial clearly demonstrates that even with the use of familiar pharmacological agents, differences in outcomes, probably related to lack of standardization of the dosage, arose between those in the pharmacologic arms and those treated in the community.[12] With the exception of the MTA, few trials involve direct comparisons of different treatment modalities (i.e., that test both pharmacological agents and behavioral modalities), and few test the whole spectrum of patients or consider both the therapeutic and side effects. Very few studies look at long term treatment effects.

However difficult it may be to standardize pharmacological trials and to be sure that samples, methods, and outcomes are comparable, it is even more difficult to do so for interventions that aim to change behavior through other means or ones that take a more public health approach. Problems of standardizing interventions escalate when the treatments involve behavioral and social skills training or modifications of the environment. In part this is because many consider that the replication must follow a cookbook approach rather than implement the conceptual model as proposed by Bauman et al.[13] Thus researchers find it very difficult to examine such questions as whether there modifications of the environment or of demands on behavior would improve ADHD symptoms, as for example, a school environment that does not require children to sit and work quietly all day, or one that provides more frequent recess. Researchers also struggle to assess interventions that aim to alter family behavior or peer interactions that may exacerbate symptoms and impairment.

Research Implementation Issues

All these considerations would make the study of outcomes of ADHD difficult enough, but the possible development of mental health co-morbidities over time compound the known problems that still pervade the literature related to the accuracy of baseline diagnosis, comorbidity, and condition stability. Beyond problems related to treatment and to whether or not patients adhere to their prescribed regimen, issues abound as well around the other interventions that may co-occur, especially during a long-term trial as families seek additional help. The consequence is that the results of a trial cannot always be ascribed entirely to the intervention being tested. All these issues suggest the need to measure the systems of care within which intervention studies are conducted. It is important to begin to understand the nested context for the research, as well as the nested treatments and outcomes.

Studies should increasingly address subgroup effects, mechanisms of action, and the roles of mediators and moderators of outcomes in ADHD, as so well discussed by Hinshaw.[14] Racially- and culturally-diverse families are generally underrepresented in current studies. With the escalating rates of immigrant children in the population, little is known about the models of parental beliefs about ADHD and the role of these factors in the expression of the condition and in access of children with ADHD in these subgroups to appropriate treatment.

Finally, how do genes and the environment interact to influence child behavior? And given the sizable contribution of genetic predisposition to ADHD, with many children with ADHD living with parents who also have ADHD, how do these factors affect both the outcomes being evaluated and participation in research?

Challenges in the Choice of Questions

Challenges in caring for children with ADHD and their families and in studying outcomes of ADHD include financing health and behavioral services for children with ADHD and their families; splitting out the subtypes and co-morbidities; preventing and limiting the manifestations of ADHD; sustaining interventions; and moving efficacious treatments into the real world to bring them to scale.

Identifying the questions to answer is an important first step. This compendium of papers has identified many important issues that call for further research.

All the questions are important, but some require higher priority. Of highest priority is developing a reliable method of identifying and classifying the condition(s) without impairment; that is, to separate the measurement of ADHD as a health condition from the impairment it causes. Currently impairment is a fundamental component of diagnosis. Does a child whose impairment is controlled still have ADHD? Without resolution of this issue and reliable methods of classifying the condition(s) without impairment, the field faces a somewhat circular set of issues. Separating the condition and the impairment would enable studies of whether efforts in early childhood to minimize the chances of manifesting ADHD and later on to alter its persistence.

Another consideration is whether modifying expectations for the tasks and behaviors of children will minimize the disability that children with ADHD exhibit. The current level of diagnosis of ADHD suggests considering public health approaches to environmental modification that might reduce the level of impairment of many children.

Studies should also determine whether cognitive capacities of children with ADHD are impaired compared to those without ADHD and, if so, to what extent differences in outcomes reflect differences in cognition? Finally, while much has been achieved in studies of ADHD to date, few of these are focused on long-term outcomes. Investigators must work toward improvement in the long-term outcomes, not just short-term symptoms.

These questions will keep the field busy for a long time. This compendium of state of the art papers shows that the field has come a long way but still faces major challenges.

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