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ABSTRACT

This report provides a review of reviews concerning the effects of stimulant medication on children with attention deficit disorders (ADD) conducted by a special federally funded center at the University of California (Irvine). Both computer searching and nomination by ADD experts were used to identify the 336 reviews examined. All reviews were systematically examined for information in 10 critical areas: (1) response rate, (2) effects on diagnostic symptoms, (3) effects of associated features, (4) side effects, (5) long term effects, (6) paradoxical response, (7) effects on high order processes, (8) prediction of response, (9) recommendations about clinical use, and (10) recommendations for multimodality treatment. Substantial consensus was found about the effects of stimulant medication--in most cases a clear and immediate short term benefit is perceived in symptoms and associated features of ADD. Persistent controversies about stimulant medication concern the lack of diagnostic specificity for short term effects, the lack of effects on learning or complex cognitive skills, potential side effects and adverse effects, and the lack of evidence of significant long term effects. A complete list of the reviews is provided. (DB)

THE EFFECTS OF STIMULANT MEDICATION ON CHILDREN WITH ATTENTION DEFICIT DISORDER: A REVIEW OF REVIEWS

Education of Children with Attention Deficit Disorder

THE EFFECTS OF STIMULANT MEDICATION ON CHILDREN WITH ATTENTION DEFICIT DISORDER: A REVIEW OF REVIEWS

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The UCI ADD Center: Final Report

The Effects of Stimulant Medication of Children with ADD: A Review of Reviews

James M. Swanson, Principal Investigator

Executive Summary

This report presents a review and synthesis of a large literature addressing the use of stimulant medication to treat children with Attention Deficit Disorder (ADD). This topic was chosen as one of the critical areas to be addressed by the four ADD Centers established in 1991 by the US Department of Education. The special expertise of the UCI staff, the priorities established during initial UCI Center meetings with national and local leaders (triads of parents, educators, and clinicians), negotiations among the Directors of the four Centers, and collaboration with the staff of the Office of Special Education Projects, combined to assign this topic to the UCI ADD Center.

In this report, **the term ADD** is used as the general label for a condition of childhood once commonly called "hyperactivity" and now generally called "attention deficit disorder" (ADD) or "attention-deficit hyperactivity disorder" (ADHD). Also, in this report **the term stimulant medication** will be used to refer to the class of drugs which includes d-amphetamine (Dexedrine), methylphenidate (Ritalin), and pemoline (Cylert).

Historically, the recognition of ADD as a disorder has been linked to the response of children with ADD to stimulant medication. In the face of diagnostic uncertainty and changing labels,

this has created a persistent controversy about the use of stimulant medication. **The definition of response** to stimulant medication and **the basis for controversies** about the use of medication were identified as important topics to be addressed in this report.

The UCI ADD Center decided to perform a "review of reviews", instead of performing just another traditional review, to synthesize the large literature which spans over 55 years of research on the use of stimulants to treat children with ADD. This literature is massive: a list of over 5,000 original articles has been accumulated for this report, and over 300 reviews of this literature have been located. The first study in the literature on the use of stimulant medication to treat children with ADD is commonly attributed to Bradley (1937), but rigorous research on this topic started in the 1960's (Lipman, 1970). By 1970, the use of stimulant medication had become so widespread that it created controversy (Freeman, 1970). Controversies have persisted for the last 2 decades (Cowart, 1988), but the prevalence of stimulant therapy has remained relatively high: the literature suggests that from 2% to 6% of all elementary school-aged children may be treated with stimulant medication (Jacobvitz, Stroufe, Stewart, and Leffert, 1990) and that from 60% to 90% of school-aged children with an ADD diagnosis are treated with stimulant medication for a prolonged period of time (Whalen and Henker, 1991).

A rigorous methodology (Cooper, 1985) was adapted for use in

this project to define the scope of the "review of reviews". Two search strategies were used: a search by a research librarian based on electronic data bases (a computer-search strategy which located 183 reviews) and a search by ADD experts based on the "invisible college" approach (an expert-search strategy which located 241 reviews). Only 87 reviews were identified by both search strategies, so this dual search strategy yielded a total of 338 unique reviews with an search-strategy overlap of 26% (87/338). The computer-search failed to identify 154 reviews considered to be important by the "invisible college" of experts, and this represented 46% of the dual search strategy total and 64% of the expert-search strategy total. The nominations by experts failed to identify 96 reviews which were retrieved by the computer-search, and this represented 28% of the dual search strategy total and 52% of the computer-search strategy total. Thus, the dual search strategy was important for defining a broad literature to be reviewed, and either single-method search strategy would have missed a significant percentage of the 338 specific reviews located for this "review of reviews".

At an initial step in the evaluation of reviews, another measure of overlap ("source overlap") was estimated. Logically, in a literature that spans a half century and several disciplines, not all reviews would be expected to address the same literature defined by the articles in each review's reference list. However, even when reviews were performed at about the same time and were focused on similar topics, low (25% to 40%)

source-overlap was documented. Surprisingly, even though source overlap was relatively low in several sets of topic-matched and time-matched reviews, agreement across these reviews was high for the conclusions about the effects of stimulant medication on children with ADD. This consensus in the face of low source-overlap suggests that the effects of stimulant medication are robust. However, despite this consensus on medication effects, clear differences were expressed across these selected reviews a bout the clinical use of stimulant medication. I several different eras, some reviews supported the established clinical practice of symptomatic treatment that has resulted in widespread use of stimulant medication, but others did not or recommended major changes.

As part of the synthesis of the literature, a set of critical topics was selected which outlined consensus views on what should and what should not be expected when stimulant medication is used to treat children with ADD. Following the recommendations of Cooper (1985), a coding sheet was used to extract systematic information from the 338 reviews. Agreement across reviews was calculated from the coding sheets, and summaries of the ten critical topics are presented below:

1. Response Rate. Not all children with ADD respond favorably to stimulant drugs. Across a subset of reviews which addressed this topic, the prevalence of a favorable response was about 70% and was about the same across 55 years despite changes over time in the diagnostic criteria and labels used to define

the disorder.

2. Effects on Diagnostic Symptoms. In the majority of ADD children who responded favorably to stimulants, the response included temporary management of the diagnostic symptoms of ADD (ie., a decrease in inattention, impulsivity, and hyperactivity) and a time-limited increase in concentration and goal-directed effort. Across relevant reviews, 97% agreed with this description of short-term effects.

3. Effects of Associated Features. In reviews which addressed associated features of ADD (such as deviant deportment, high levels of aggression, inappropriate social interaction, and poor academic productivity) which occur in some affected children, 94% agreed that a component of response to stimulant medication was a decrease in the manifestation of these disruptive behaviors.

4. Side Effects. In reviews which addressed side effects (such as minor problems of anorexia and insomnia, serious problems associated with motor and verbal tics, and psychological impairment in the areas of cognition and social interaction), almost all (99%) acknowledged the existence of side effects and the clinical necessity to monitor and manage these effects.

5. Long Term Effects. In the reviews which addressed the issue of long-term effects of stimulant medication, 88% acknowledged the lack of demonstrated long-term effects on important outcome domains (ie., social adjustment and academic achievement).

6. Paradoxical Response. Some early influential reviews asserted that stimulant medication "calmed or subdued" children with ADD, which was represented as a paradoxical response. However, in reviews which addressed this topic, 78% concluded that in children with ADD the behavioral, physiological and psychological responses (ie., increased concentration and goal-directed effort) to clinical doses of stimulant medication were not qualitatively different from the responses of normal children and adults to equivalent doses, and thus these responses should not be considered paradoxical.

7. Effects on High Order Processes. A subset of reviews addressed the effects of stimulant medication on complex behavior requiring high order skills (eg., learning, reading, etc.) as well as on simple behavior requiring low order skills (eg., performing rote tasks, monitoring a repetitive display, etc.). Most (72%) of these reviews acknowledged the lack on a demonstrated beneficial effect on performance of complex tasks or behaviors which required the use of high order processes.

8. Prediction of Response. Some reviews addressed the methods of evaluating a trial response to stimulant medication, and the prediction of response on the basis of behavioral, cognitive, physiological, biochemical, or neurological measures. Most reviews (68%) acknowledged poor prediction by these measures.

9. Recommendations about Clinical Use. Across the past half century, most reviews were written by clinicians and most (91%) supported some clinical use of stimulant medication to

treat children with ADD. However, in each era of the past half century, some reviews have addressed the same issues which generate controversy and have questioned this established clinical practice.

10. Recommendations for Multimodality Treatment. Many reviews ended with a recommendation for combinations of psychosocial and pharmacological interventions, but in most (70%) of these reviews, specific references to support this common-sense recommendation were not provided, and when references were specified they provided little empirical data to support this specific recommendation.

This report evaluated agreement across reviews and interpreted high levels of agreement as consensus about the effects of stimulant medication. Specific disagreements which endured over time were interpreted as controversy about the use of stimulant medication. The literature covered by the reviews suggested that in most (but not all) cases a clear and immediate short-term benefit was perceived by parents, teachers, and physicians in terms of the management of symptoms and associated features of ADD. The controversies which have persisted over time (and are consistent with acknowledged effects of stimulant medication) are the lack of diagnostic specificity for short-term effects, the lack of effects on learning or complex cognitive skills, potential side effects and adverse effects, and the lack of evidence of significant long-term effects.

The consensus about the effects of stimulant medication and

the enduring controversies about its widespread use suggest a careful approach be taken in the clinical decision to treat a child with ADD. In this report, recent reviews are identified which recommend a systematic approach to assessment of response, including the use of double-blind procedures, the evaluation of response across home and school settings, and the consideration of cognitive as well as behavioral domains of behavior. Also in this report, reviews are identified which discuss methodological issues and point out important qualifications of the existing literature. Finally, three reviews of current areas of investigation (with focuses on academic productivity, aggression, and social interaction) are identified which promise to make important additions to the existing literature on the effects of stimulant medication on children with ADD.

Chapter 1: Introduction and Background

1.1 ADD: Revised Criteria and Labels

In this report, ADD is used as the general label for a condition of childhood once commonly called "hyperactivity" and now generally called "attention-deficit hyperactivity disorder" (ADHD). These definitions changed over the 55 years covered by this review. Initially, much of the defining literature on ADD was contributed by pediatrician, and reviews appeared in journals for the profession of Pediatrics (eg., Bradley, 1950; Werry, 1968; Wender, 1973). The labels were based on a presumed association with brain damage and motor dysfunction and learning disabilities. In the 1950's and 1960's, a succession of labels including "hyperkinetic impulse disorder" (Laufer and Denhoff, 1957), "minimal brain damage" (Bax and McKeith, 1963), and "minimal brain dysfunction" (Wender, 1971).

In the 1970's, the defining literature began to be contributed by psychologists and psychiatrists, and reviews began to appear in journals for the professions of Psychology (eg., Conners, 1971; Douglas, 1972; Sprague, 1972) and Psychiatry (eg., Fish, 1971; Cantwell, 1975). In 1980, the American Psychiatric Association (APA) took the lead by incorporating the research finding into revised psychiatirc defintions in the Third Edition of the Diagnostic and Statistical Manual (DSM-III, 1980). Based on the literature, the label "hyperkinetic reaction of childhood" (DSM-II, 1968) was replaced by the label Attention Deficit Disorder with or without Hyperactivity (ADD or ADDH), based on the

assumption that the core symptoms of the disorder were due to a cognitive rather than motor dysfunction. The leadership role of the APA was confirmed when the DSM-III-R (1987) manual was published and the revised criteria and the label Attention-deficit Hyperactivity Disorder (ADHD) were proposed as a refinements of the ADD/ADDH criteria and labels. In 1990, the need for an education definition of ADD, to complement the psychiatic definition of ADD, was recognized in responses to the Notice of Inquiry on ADD. The Professional Group for Attention and Related Disorders PGARD) offerred and educational definition of ADHD (PGARD, 1990; Fowler, 1992; Swanson, 1992).

Recently, the APA published a draft of DSM-IV (1993). In this latest version of the criteria, the ADHD label from DSM-III-R (1987) was retained but the criteria changed by returning to multiple symptom lists to define the disorder. The DSM-IV subgroups are characterized by two classes of symptoms and three subgroups based on predominant symptom-type (inattentive, hyperactive/impulsive, or both).

The DSM-IV criteria for ADHD are listed under the general heading of "Disorders of Infancy, Childhood, or Adolescence" and the subheading of "Disruptive Behavior and Attention-deficit Disorders". The criteria for the categorical diagnosis of "Attention-deficit/Hyperactivity Disorder" are the following:

A. Either 1 or 2:

(1) Inattention: At least six of the following symptoms of inattention have persisted for at least six months to a degree that is maladaptive and inconsistent with

developmental level:

(a) often fails to give close attention to details or makes careless mistakes in schoolwork, work, or other activities

(b) often has difficulty sustaining attention in tasks or play activities

(c) often does not seem to listen to what is being said to him or her

(d) often does not follow through on instructions and fails to finish schoolwork, chores, or duties in the workplace (not due to oppositional behavior or failure to understand instructions)

(e) often has difficulties organizing tasks and activities

(f) often avoids or strongly dislikes tasks (such as schoolwork or homework) that require sustained mental effort

(g) often loses things necessary for tasks or activities (e.g., school assignments, pencils, books, tools, or toys)

(h) is often easily distracted by extraneous stimuli

(i) often forgetful in daily activities

(2) Hyperactivity-Impulsivity: At least four of the following symptoms of hyperactivity-impulsivity have persisted for at least six months to a degree that is maladaptive and inconsistent with developmental level:

Hyperactivity

(a) often fidgets with hands or feet or squirms in seat

(b) leaves seat in classroom or in other situations in which remaining seated is expected

(c) often runs or climbs excessively in situations where it is inappropriate (in adolescents or adults, may be limited to subjective feelings of restlessness)

(d) often has difficulty playing or engaging in leisure activities quietly

Impulsivity

(e) often blurts out answers to questions before the questions have been completed

(f) often has difficulty waiting in lines or awaiting turn in games or group situations

B. Onset no later than seven years of age.

C. Symptoms must be present in two or more situations (e.g., at school, work, and at home).

D. The disturbance causes clinically significant distress or impairment in social, academic, or occupational functioning.

E. Does not occur exclusively during the course of a Pervasive Developmental Disorder, Schizophrenia or other Psychotic Disorder, and is not better accounted for by a Mood Disorder, Anxiety Disorder, Dissociative Disorder, or a Personality Disorder.

These criteria are used to specify the following subtypes:

314.00 Attention-deficit/Hyperactivity Disorder, Predominantly Inattentive Type; if criterion A(1) is met but not criterion A(2) for the past six months

314.01 Attention-deficit/Hyperactivity Disorder, Predominantly Hyperactive-Impulsive Type; if criterion A(2) is met but not criterion A(1) for the past six months

314.01 Attention-deficit/Hyperactivity Disorder, Combined Type: if both criterion A(1) and A(2) are met for the past six months

314.19 Attention-deficit/Hyperactivity Disorder, Not Otherwise Specified; for disorders with prominent symptoms of attention-deficit or hyperactivity-Impulsivity that do not meet criteria for Attention Deficit/Hyperactivity Disorder.

Coding Note: For individual (especially adolescent and adults) who currently have symptoms that no longer meet full criteria, "In partial remission" should be specified.

1.2 The Notice of Inquiry on ADD

In 1990, Congress issued a Notice of Inquiry on Attention Deficit Disorder (ADD). In response to this Notice, PGARD formu-

lated and educational definition of ADD based on a two tiered process of verifying categorical diagnosis and determining educational impairment. The PGARD criteria for ADD are presented below:

On the basis of extensive review of the literature and broad consultation, the following educational description of ADD has been formulated:

The condition 'attention deficit disorder' refers to a developmental disorder involving one or more of the basic cognitive processes related to orienting, focusing or maintaining **attention**, resulting in a marked degree of inadequate attention to academic and social tasks. The disorder may also include verbal or motor impulsivity and excessive non-task related activities such as fidgeting or restlessness. The inattentive behavior of ADD most commonly has onset in early childhood, remains inappropriate for age, and persists throughout development.

ADD adversely affects educational performance to the extent that a significant discrepancy exists between a child's intellectual ability and that child's productivity with respect to listening, following directions, planning, organizing, or completing academic assignments which require reading, writing, spelling, or mathematical calculations.

Inattentive behaviors, if caused by cultural differences, socioeconomic disadvantage, or lack of adequate exposure to the language of educational instruction, are not evidence of ADD. Inattentive behaviors with acute onset are not evidence of ADD if they arise directly from (1) stressful events associated with family functioning (e.g., parental divorce, or the death of a family member or close friend) or environmental disruption (e.g., a change in residence or school); (2) post-traumatic stress reactions caused by abuse (e.g., physical, psychological, or sexual) or natural disasters; (3) noncompliance due solely to opposition or defiance; (4) frustration resulting from inappropriate tasks beyond intellectual ability or level of achievement skills; or (5) emotional disorders (e.g., anxiety, depression, schizophrenia).

ADD can co-exist with other handicapping conditions (i.e., specific learning disabilities, serious emotional disturbance, or mental retardation).

The following definitions are given for the terms stated above:

1. "a marked degree" means, at a minimum, disproportionate for

the child's age as measured by well-standardized and unbiased rating scales or structured interviews which result in functional impairment.

2. "onset in early childhood" means that when a careful developmental history of the child is obtained, it confirms that parents, teachers, or other involved adults have observed the development of the age-inappropriate inattentive behaviors before the age of 7 years. The onset of these persistent inattentive behaviors should not to be confused with the educational manifestations of ADD, because onset of educational impairment may occur at any time in the child's life when school tasks tax the child's underlying attentional deficit.

As set forth in the proposed educational definition of ADD, the criteria for ADD are quite comparable to those used to determine eligibility for other disabilities currently recognized in part B of the EHA/IDEA. The proposed ADD definition is based on a two-tier framework: (1) first, it must be confirmed that the child has the ADD disorder based on specific criteria which include cardinal characteristics, early onset, chronic duration, and exclusion conditions; (2) second, it must be determined that the educational manifestation of ADD (which may have an onset at any point in the ADD child's life) is severe enough to have an adverse impact on educational performance.

The following operational criteria for qualifying an ADD child for special education services are in keeping with the intent and scope of EHA to address the educational needs of children with disabilities: ADD adversely affects educational performance to the extent that a significant discrepancy exists between a child's intellectual ability and that child's educational productivity with respect to listening, following directions, planning, organizing or completing academic assignments that require reading, writing, spelling or mathematical calculations.

Although ADD appears to occur with uniform prevalence among all racial, ethnic and linguistic groups, safeguards are required to protect minority children from being misclassified and over identified under any definition of the EHA/IDEA. The basic safeguards of our approach would include: (1) involving in the evaluation team at least one member of the child's minority who is knowledgeable regarding potential bias; (2) comparing the minority child being evaluated with children of similar minority status; (3) addressing the manifestations of the conditions and circumstances noted above which alone would not be evidence of ADD. In general, it was recommended that to the extent possible, evaluation teams should strive to use broad-based assessment procedures and instruments which minimize biases against minority children, are sensitive to cultural nuances of different ethnic groups, take into consideration the level of the child's acculturu-

ration, and are conducted in the child's primary language.

In 1991, the Department of Education issued a memorandum (Davila, Williams, and MacDonald, 1991) which changed the interpretation of the regulations established by a prior memorandum by Bellamy (1987). The educational regulations governing ADD now indicate that students may be considered disabled "...soley on the basis of the disorder within the 'other health impaired' category" and that "...a full continuum of placement alternatives, including the regular classroom, must be available for providing special education and related services required in the IEP" (Davila, et al, 1991, p. 3).

The use of stimulant medication to treat children with ADD may affect this placement and the services provided in the school setting. Since the new interpretation of the educational regulations governing ADD is so recent, no literature is available on the impact and implication of the changes associated with implementation of the Davila et al (1991) memorandum.

1.3 The DOE ADD Centers

The responses to the 1990 Notice were interpreted by the US Department of Education (DOE), which concluded that extensive information existed on ADD but was not readily accessible to educators and parents who must deal with children who have ADD. To remedy this, the DOE proposed to establish ADD Centers. According to the guidelines published by the Department of Education for the Attention Deficit Disorder (ADD) Centers, each Center should (1) identify critical issues, (2) analyze current

research, (3) foster interaction among clinicians, educators, and parents to synthesize current knowledge, and (4) disseminate these syntheses at the national forum and through existing channels. Two types of Centers were established: (1) Centers for the Identification of Children with ADD and (2) Centers for the Intervention with Children with ADD.

The University of California at Irvine (UCI) Child Development Center (CDC) was chosen as an ADD Intervention Center. For a variety of reasons, most ADD research has been conducted by clinicians in clinical settings, rather than by eucators in educational settings. One purpose of the UCI ADD Center was to review the large body of clinical research and to distill from it what is most relevant for educational purposes. To accomplish this, the UCI ADD Center filtered the existing literature through the eyes of experienced leaders in education and parent advocacy, with the expressed intent to make the available knowledge relevant and accessible to consumers -- the parents and teachers who are directly responsible for its application in the school setting.

1.4 The Local Participants

The UCI ADD Center had local and national participants. Some of the local participants were individuals on the UCI Child Development Center staff, who are listed below:

1. Four psychologists: a cognitive psychologist (James M. Swanson, Ph.D.), an educational psychologist (Ron Kotkin, Ed.D.), a clinical neuropsychologist (Keith McBurnett, Ph.D.), a clinical behavioral psychologist (Linda Pfiffner, Ph.D.), and a develop-

mental psychologist (Tim Wigal, Ph.D.).

2. Three part-time physicians: a consultant child psychiatrist (Dennis Cantwell, M.D.) and 2 behavioral pediatricians (Marc Lerner, M.D. and Angie Stampe, M.D.).

3. Two counselors: a social worker (Rose Zoccoli, M.A.) and a graduate student (Julie Elliot).

4. Four transition classroom aides who work in the IUSD and SAUSD: (new individuals are trained each year).

5. Consultants: a child clinical psychologist (Carol Whalen, Ph.D.), educator (Alan Hoffer, Ed.D.), a child psychiatrist (James Satterfield, M.D.), a social worker (Brenna Satterfield, M.A.), a school psychologist (Steve Forness, Ed.D.), and a child clinical neuropsychologist (Mike Lopez, Ph.D.), and a behavioral pediatrician (Martin Baren, M.D.).

Some local participants were staff of the collaborative UCI-UCLA (Irvine Unified School District), who are listed below:

1. A part-time principal: John Brady.
2. A part-time school psychologist: Steve Simpson.
3. Three full-time teachers: Dan Flynn, David Agler, and Jennifer Ross.
4. Three specially-trained classroom aides (new individuals are trained each year in UCI courses.

Other local participants were staff from other programs of the IUSD, who are listed below:

1. Bruce Givner, Ph.D., Assistant Superintendent, IUSD
2. John Brady, Ph.D., Program specialist, IUSD
3. Marsha Mortkin, M.A., School Psychologist, El Toro
4. David Prince, Counselor, El Toro
5. Dan Graham, Principal, El Toro
6. Carol Lloyd, Teacher, El Toro
7. Ruth Jarvis, Teacher, El Toro
8. Josette Macaluso, Teacher, El Toro
9. Suzzane Wiegand, Principal, Deerfield
10. Helen Holahan, School Psychologist, Deerfield
11. Peggy Belitz, Teacher, Deerfield

Local parent groups are well-established, with over 500 members in several groups. Members of the UCI staff serve on the professional advisory boards of 2 large groups (Ladders and South Coast). The following parents of ADD children participated in the proposed ADD Center:

1. Debbie Del Rio (Ladders).
2. Maggie Brewer (Ladders)
3. Peggy Carnow (Long Beach)
4. Connie Bacerra (Parent of Children who Learn Differently)
5. Denise and Ray Ruiz (UCI)
6. Bertha and Adelbert Walker (UCI)
7. Linda Phillips (ADDA)
8. Kathy Staymates (ADD of North Orange County)

1.5 The National Participants

A national group of clinicians, educators, and parents was selected from locations from around the country. These individuals were paired with the local UCI-CDC staff and parents to get a broader input from 3 different perspectives.

The national group of clinicians, listed below, was composed of individuals who have made career commitments to the study and treatment of ADD:

1. Sally Shaywitz, M.D. and Bennett Shaywitz, M.D., pediatricians from Yale University who wrote the scholarly monograph on ADD for the National Conference on Learning Disabilities.
2. Peter Jensen, M.D., a child psychiatrist and the Chief of the Child and Adolescent Disorders Research Branch of the National Institute of Mental Health in Washington, DC.
3. Ben Lahey, Ph.D., a clinical psychologist at Miami University who is the Director of the ADD component of the DSM-IV field trial which will result in a revised definition of ADD in 1992.
4. Russ Barkley, Ph.D., a clinical psychologist at the University of Massachusetts and the author of the most widely used handbook on ADD.
5. William Pelham, Ph.D., a behavioral psychologist and the Director of a large Summer treatment program at Western Psychiatric Institute and Clinic in Pittsburgh, PA.
6. Kytja Voellar, M.D., a child neurologist at the University of Florida who recently edited a special issue on ADD for the Journal of Child Neurology.
7. Harvey Parker, Ph.D., a clinical psychologist in private practice in Plantation, FL who founded the CH.A.D.D support group.

The national group of educators, chosen based on experience and interest about ADD, included the following individuals:

1. Fred Weintraub, Assistant Executive Director, Department of Communication of the CEC.
2. Patrick Campbell, the State Director of Special Education for California.
3. Carl Smith, of the Mountain Plains Regional Resource Center in Des Moines, Iowa.
4. Hill Walker, Prof.& Assoc. Dean of the Division of Special Ed at the University of Oregon.
5. Frank Gresham, Professor of Education, UC Riverside who focuses on social skills training.
6. Margaret Dawson, the past president of the National Association of School Psychologists.
7. Marco Pena, of OC Head Start who is interested in intervention with preschool ADD children.

The national group of leaders of ADD parent groups, chosen on the basis of participation in the Notice of Inquiry on ADD, included the following individuals:

1. Sandy Thomas, the President of Children with Attention Deficit Disorders (CH.A.D.D.), a large national parent support group.

2. Nancy Cornish, the President of the Attention Deficit Disorder Association (ADDA), a national coalition of a large number of local and regional parent support groups.

3. Debra Maxey, President of Attention Deficit Disorder Association of Virginia (ADDAV), a statewide network of 34 parent support groups.

4. Julie Doy, the President of the Iowa ADD Coalition which represents over 2000 households and professionals interested in ADD.

5. Mary Fowler, a CH.A.D.D. Board Member in charge of government Affairs, an experienced teacher of ADD children, and the author of a parent book on ADD.

6. Pamela Murray, the Executive Director and past president of ADDA and a member of Colorado's committee for America 2000.

7. Jean Harrison, an ADDA Board Member and the Editor of Challenge, the ADDA Newsletter.

1.6 Organization of the UCI ADD Triads

The individuals from the 3 groups of national participants were assigned to clinician-educator-parent triads, as shown below:

Clinicians	Educators	Parents
Russell Barkley (MA)	Hill Walker (OR)	Sandra Thomas (CN)
Ben Lahey (FL)	Carl Smith (IA)	Julie Doy (IA)
William Pelham (PA)	Frank Gresham (CA)	Debra Maxey (VA)
Sally/Ben Shaywitz (CN)	Fred Weintraub (VA)	Mary Fowler (NJ)
Peter Jensen (DC)	Patrick Campbell (CA)	Pamela Murray (CO)
Kytja Voellar (FL)	Margaret Dawson (NH)	Nancy Cornish (TX)
Harvey Parker (FL)	Marco Pena (CA)	Jean Harrison (MA)

Similar triads were formed for the local UCI groups, drawing on the groups of clinicians from the UCI-CDC, the educators from OCDE and IUSD, and parents from the various support groups. Each of the national clinician-educator-parent triads will be linked with a local (UCI) triad, as shown below:

Local Triads	National Triad
Pfiffner, Ross, Brewer	Barkley, Walker, Thomas
Satterfields, Ferrari, Ruiz	Lahey, Smith, Doy
Levin/Lerner, Simpson, Phillips	Shaywitzs, Weintraub, Fowler
McBurnett, Holcombe, Walker	Jensen, Campbell, Murray
Kotkin, Givner, Del Rio	Pelham, Gresham, Maxey
Whalen, Zoccoli, Bacerra	Parker, Pena, Harrison
Cantwell, Mortkin, Carnow	Voellar, Dawson, Cornish

The 42 individuals specified above participated in the

identification of critical issues, analysis of research, and synthesis of the literature. From the beginning of the UCI ADD Center, all three groups -- clinicians, educators, and parents -- were involved. Clinical information was filtered through the eyes of the educators and the parents, which is intended to direct the development of practical intervention programs with a strong empirical basis.

1.7 Operation of the UCI ADD Center

As directed by OSEP, an initial set of critical issues defined by the local and national participants in the UCI ADD Center. Four critical components of intervention were identified: (1) parent involvement for home-based contingency management and reward programs; (2) physician involvement for selective use of medication; (3) classroom teacher involvement in token systems for behavior modification in the classroom; (4) clinical and educational staff involvement for social skills and cognitive training for small group training. These interventions were considered in a hierarchical fashion: (1) parent involvement is essential for all ADD children, regardless of the level of severity; (2) medication is tried to treat most children with ADD, but in a significant minority either a non- or adverse response or parental objection precludes pharmacological intervention; (3) classroom token systems are effective but time consuming, which may restrict use to the most severe cases; (4) group therapy for social skills and cognitive training forms a clear interface

between clinical and educational interventions, but it is expensive which may limit its use.

The initial list of critical issues, with detailed description of each issues, is presented in Appendix A.

1.8 Refinement of the Goal of the UCI ADD Center

The initial activities of the UCI ADD Center will be described in terms of 3 phases: (1) the First Center Meeting, (2) the Collaborative Activity with OSEP, and (3) the Revised Center Activity. The stated purposes of these initial activities were the following: (1) To bring groups of parents, educators, and clinicians/researchers together to define critical issues; (2) To circulate the set of critical issues to get additional input from a broad selection of interested individuals.

Meetings were organized, based on the concept of "triads" (parents, educators, clinicians). As described above, Center participants were organized into 7 triads, and the following steps were taken to accomplish the initial purposes of the project:

1. In October, 1991, the initial list of 25 critical issues (from the grant application) was circulated to 21 Center participants (representing the 7 triads).
2. In early November, 1991 the Center participants read an critically evaluated the initial list, and based on this each participant formed a smaller list of critical issues representing the most important topics on ADD from his or her own perspective.
3. In late November, the Center Director telephoned and discussed the individual list of critical items with each Center Participant, and written notes of these telephone conversations were kept.
4. During October and November 1991, local professionals representing minority groups were identified to address cultural, ethnic, linguistic, and racial issues about ADD, and they read

and discussed the initial critical issues list.

5. In early December, 1991 the Project Director revised the set of critical issues to represent the consensus views of the 3 groups of participants in the Center (educators, researchers/clinicians, and parents).

6. On December 6-8, 1991, the first Center meeting was held in California, and the revised list of 7 critical issues was distributed to initiate the in-depth review by each group (educators, researchers/clinicians, and parents).

7. The Center meeting was divided into 2 workshops. Instead of organizing as triads (as originally planned), the participants decided to organize these workshops as three working groups representing educators, parents, and researchers/clinicians. The parents' group was chaired by Sandy Thomas; the educators' group was chaired by Carl Smith; the researchers'/clinicians' group was chaired by William Pelham.

8. After the workshops, each working group submitted a revised set of critical issues and a suggested format for information products on the critical issue.

9. The Director used the material derived from the workshops to form a list of Draft Critical Issues to be discussed at the first Project Directors Meeting.

10. To obtain additional input from minority professionals, Dr. Harold Dent was contacted. A visit to his office was arranged, and a meeting was held in mid-January, 1992 to discuss the issue of over representation of minority children in Special Education classes. The prior history of this practice, based on the misuse of the Serious Emotional Disturbed (SED) and Educable Mentally Retarded (EMR) categories, was outlined by Dr. Dent, and the legal action taken to stop this practice was discussed. Department of Education data was presented showing a recent trend to misuse the Learning Disabled (LD) category in the way the SED and EMR categories had been misused in the past. The potential misuse of any Attention Deficit Disorder (ADD) of Other Health Impaired (OHI) category was discussed.

As outlined in the Cooperative Agreement which provided funding for the UCI ADD center, collaboration with and direction by the Office of Special Education Programs (OSEP) of the U.S. Department of Education was an integral part of the operation of the UCI ADD Centers. OSEP held a meeting in Washington on January 23-24, where all 4 Center Directors presented their respective lists of critical issues. Since the ADD Centers are funded by the "cooperative agreement" mechanism, OSEP personnel play an

active part in developing the program to meet the stated goals (ie., to organize, synthesize, and disseminate information about ADD). The following items describe key aspects of this collaborations:

1. OSEP personnel, Marty Kaufman (Director of OSEP Innovation and Development), Ellen Schiller (Acting Branch Chief, OSEP Directed Research Branch), and Jane Hauser (OSEP Project Officer), organized the Directors meeting and participated in all phases of it. They also designated 2 consultants for the project (Harris Cooper, from the University of Missouri and Rodney Ogawa, (from the University of Utah) who are experts in the area of rigorous literature review.

2. At the January Directors meeting, a decision was made to alter the course of the Centers. Instead of each Center dealing with a different set of critical issues, a single set of 6 critical issues was selected. Each Center was assigned at least one critical issue as a focus of its work for the second phase of the project. The UCI Intervention Center accepted an assignment to take the lead role in synthesizing the literature on the efficacy of medication for children with ADD.

3. The Directors meeting was very helpful in defining how this synthesis was to be performed. Based on the discussions at the meeting and excellent input from the consultants, a decision was made to perform an integrative research review of the literature on effects of stimulant medication instead of a traditional literature review. A specific methodology, described by Cooper (1982) in the paper "Scientific Guidelines for Conducting Integrative Research Reviews" (Cooper, 1982, Review of Educational Research, 52, 291-302), was selected for use.

4. The first steps were outlined in a memorandum to Ellen Schiller, dated February 10, 1992, which reviewed the issues discussed at the Directors' meeting. This memorandum was guided by a letter from Ellen Schiller, dated February 3, 1992, in which she outlined the purpose of a site visit to the UCI Center scheduled for February 10, 1992. The outcome of this site visit was summarized in a letter from her dated March 17, 1992, outlining discussions and possible directions for conducting a literature review on the efficacy of stimulant medication.

5. On April 6, James Swanson met with Jane Hauser before the Federal Resource Center meeting at the University of Kentucky in Lexington. In this meeting, three meta analyses of medication effects were presented and discussed (Kavale, 1982; Ottenbacher and Cooper, 1983; Thurber and Walker, 1983), along with several other traditional literature reviews. One topic of discussion was the number of articles found for review and subsequently excluded by the operational definition of an acceptable study in the meta analyses by Kavale, 1983 (365/500) and Ottenbacher and

Cooper, 1984 (770/831).

6. A new direction for the formulation of the draft methodological approach was established during the April 9-10, 1992 consultation meeting with Harris Cooper. The wisdom of conducting another review or meta analysis was questioned. When the consultant realized that such a large number (25 or more) of high-quality reviews on the topic of efficacy of medication already were published, and that at least three were formally meta analyses (ie., Kavale, 1982; Ottenbacher and Cooper, 1983; Thurber and Walker, 1983), the discussion turned toward the idea of performing a "review of reviews" instead of a review of individual studies.

7. In his role as a consultant, Cooper discussed two examples of a "review of reviews": the review of the literature on homework and the review of the literature on class size. Based on his experience in these two areas, Cooper suggested that a "review of reviews" would uncover agreements and disagreements in the existing large literature on the efficacy of medication for the treatment of ADD children. There seemed to be agreement that another meta analysis would likely be considered just one voice in a choir, while a well executed "review of reviews" had the potential to have a greater acceptance and impact than another meta analysis.

8. On April 22-23, 1992 4 experts (William Pelham, Russell Barkley, Dennis Cantwell, and James Satterfield) attended a Center meeting at UCI to discuss Cooper's recommendations. The recommendation to conduct a "review of reviews" was endorsed by this group.

Chapter 2: Defining the Literature

2.1 The Initial Literature. The existing clinical literature on ADD is so extensive that its size may overwhelm simple attempts to distill critical issues from it, or to organize and synthesize it. Fortunately, the ADD Center had several individuals in key positions to facilitate the interface of clinical and educational research. The following individuals initiated the review of critical issues as outlined below:

1. Sally Shaywitz and Bennett Shaywitz contributed a review of a recently published special series on ADD which they edited for the Journal of Learning Disabilities.
2. Kytja Voellar contributed a review the recent special issue on ADD which she edited for the Journal of Child Neurology.
3. Margaret Dawson contributed a review the recent special issue on ADD in the School Psychologist Review.
4. Peter Jensen contributed a review the current research projects on ADD currently funded by the various Institutes of the US Department of Health and Human Services (NIMH, NIDA, NIAAA, NICHHD, NINDS).
5. Ben Lahey and Keith McBurnett contributed a review the DSM-IV definition of ADD developed from the Field Trial.
6. James Swanson and Lewis Bloomingdale contributed a review the Bloomingdale series on Attention Deficit Disorder, which they edit and now includes 5 books covering 10 years of annual meetings by a group whose members specialize in ADD.
7. Russ Barkley and Linda Pfiffner contributed a review their chapter on educational interventions with ADD children which was published in the most widely used handbook on ADD.
8. William Pelham and James Satterfield contributed a review the literature on combined pharmacological and behavioral (multimodality) treatment of ADD.
9. Harvey Parker and Linda Phillips contributed a review the current collection of information provided to parents and teachers by CH.A.D.D. and ADD.
10. Marco Pena and Mike Lopez contributed a review the literature on cultural and ethnic issues in the identification of ADD children and their access to services.

The revised objective of the UCI ADD Center was to use rigorous integrative review techniques to complete the "review of reviews" on effects of stimulant medication on ADD children. The

literature on using medication to treat ADD children spans over 55 years and includes thousands of empirical articles and hundreds of reviews of these articles. As described above, the UCI ADD Center decided that another review was not needed. Instead, our analysis suggested that a "review of reviews" would provide a better methodology for organizing and synthesizing the literature.

A broad focus was taken to capture the historical trends manifested in the literature on stimulants and ADD which spanned the 56 years from 1937 to 1993. To capture the accumulated knowledge derived from the thousands of articles published on the effects of stimulant medication on ADD children, a broad definition of "review" was formulated. Also, a narrow definition of "review" was formulated to be consistent with established definitions in the area of integrative research. The two operational definitions of "review" are presented below:

(1) BROAD DEFINITION (must meet all of these criteria)

a. The article contains a summary of knowledge about the effects of stimulant medication on children with hyperactivity, ADD, or a related term which refers to the conditions currently termed ADHD or UADD.

b. The primary purpose of the article is to present a secondary report of published findings from original sources in the literature or a report of generalizations formed from the literature, rather than to provide the background for an initial report of new empirical findings.

c. The article attempts to integrate findings into conclusions regarding the literature at large, which have a broader scope than the conclusions found in the source articles.

d. The article is published in the English language or is translated into the English language.

e. The article is retrievable in its entirety either through a request to the author, a colleague, or a librarian.

(2) NARROW DEFINITION (also meets one or both of these criteria)

f. The article reports or critiques at least five original sources which present the effects of stimulant medication in school-age children. (Tutorials or presentations of generalizations which are not based on individual reports would not meet this criterion).

g. The article was classified as a "REVIEW ARTICLE" by an electronic database, either as publication type or document type, or under a subject heading or descriptor.

2.2 Electronic Search Procedures. Both primary channels and secondary channels were utilized in our search for reviews. Four electronic data bases were searched to cover the published literature in the medical (Medline), educational (ERIC), psychological (PsychInfo), and government (GPO) publication arenas. The jargon of data bases (i.e., Field, Descriptor, Key Word, etc.) is complicated but important for communicating how the search of these sources was conducted. In these data bases, the definition of review is incorporated at the highest level of organization (as a Field, Document Type or Publication Type). This specification, as well as a Key Word ("review"), was used in the search.

To specify the disorder, an entry in the Descriptor Field was used. A thesaurus defines terms which are entered in the Descriptor Field to specify the population for the search. In the search, which covered a time period when labels for problem were

changing, 2 terms were used: Minimal Brain Dysfunction (MBD) and Attention Deficit Disorder with Hyperactivity (ADDH). In the electronic search of data bases, the use of the term MBD captures articles published between 1966 and 1980 which address groups of subjects also described by the terms Minimal Brain Damage, Hyperkinesis, or Hyperactivity). The use of the term ADDH captures articles published between 1980 and the present time which address the groups of subjects also described by the terms Attention Deficit Disorder (ADD), Attention Deficit Disorder without Hyperactivity (ADDnoH), Attention-deficit Hyperactivity Disorder (ADHD), and Undifferentiated Attention Deficit Disorder (UADD).

Key Words were used to operationalize the term "stimulant medication". Multiple Key Words were linked by the "OR" operators. Specifically, the generic and trade names of the amphetamines, methylphenidate, and pemoline were used. The Descriptor Field (which specified the diagnoses considered) was combined with the Key Word group (which specified the medications considered) with an "AND" operator.

2.3 The Review Location Method. As recommended by Cooper (1989, p. 57), multiple channels of source identification were used to minimize biases and in order to increase the probability of capturing the universe of pertinent reviews. An a priori decision was made to restrict the search to published studies, primarily because of the number of published reviews. In the electronic database searches, review were identified by either

(1) identification as a review artical in a database "publication type" field, or occurrence in the title or abstract the word "review" (as in the original MEDLINE search, see below). In the archival identification strategy, a liberal working definition of "review was utilized. This required that a source either (1) attempted to summarize existing knowledge or integrate research reports as its primary goal, rather than to discuss previous research as background to presenting new data, (2) attempted to summarize an area of clinical practice with stimulants in a tutorial or encyclopedic style, (c) attempted to select critical issues in stimulant treatment of hyperactivity and address these from information in primary papers, or (d) took a particular stance or "point of view" toward some aspect of stimulant treatment and referred to other sources in support of that stance.

The initial identification of reviews was derived from collections of journals, books, and articles for sources that fit the stated conception of review. First-hand acquaintance with the ADD medication literature retrieved some review articles. Some informal inquiries were conducted of research colleagues as to their awareness of recently published reviews or reviews in development. In this aspect of the search, location of meta-analyses, classic (well-known or widely cited) reviews, large-scale reviews, and very recently published review articles of any type were addressed. This stage, which was not intended to be exhaustive, resulted in a list of 25 review articles which were subsequently examined by the UCI ADD Center's technical consult-

ant (Cooper) and a subset of the UCI ADD Center's panel of clinicans (Barkley, Cantwell, Pelham, & Satterfield).

The reference lists of all 25 review articles were inspected and references that were not medication articles (e. g., methodology or nosology sources) and sources known to be primary reports of original research were deleted. The retained references were those which fit the liberal definition of "review." The results of the initial Medline search (see below) was merged with the list of primary sources, which resulted in a collection of 241 review articles. Research assistants then retrieved the remaining references from the UCI library and through inter-library loan arrangements.

2.3 Computer Searchs of Electronic Databases. Four electronic databases were searched, covering the medical, psychological, educational, and government publication literatures. The search strategies are detailed below:

1. Initial search on UCI Melvyl Medline. Campus computer networks allow access to the UCI library's electronic reference system, Melvyl, which was utilized for the initial search. Melvyl permits access to a medical database, Medline, which is updated monthly and which extends back to 1966.

The search strategy used the term "attention deficit disorder with hyperactivity" as a subject heading. The various diagnostic labels and other terms applied to ADD children are cap-

tured by this subject heading back to 1981. The subject heading "minimal brain dysfunction" achieves this purpose from 1966 to 1980. Medications were captured by using the following list as key words with "or" as the logical operator:

stimulant
stimulants
methylphenidate
Ritalin
amphetamine
dextroamphetamine
d-amphetamine
d,l-amphetamine
Benzedrine
Dexedrine
pemoline
Cylert

This grouping of medication keywords was crossed with the diagnostic subject headings ("and" as logical operator). The resulting references were downloaded directly into our microcomputers using Endlink and were read into our bibliography software, EndnotePlus. The search was repeated limiting the publication type to Review ("and" as logical operator). A study was retained in the review list if it met the following criteria:

a. The review was not primarily an original report of empirical findings, but instead was a secondary report of findings from at least 5 original reports. A review was retained if it reported original data as long as the chief purpose clearly was to present data from a larger literature, and the literature review was not restricted to the background of the empirical report.

b. The review made some attempt at integrating findings into conclusions regarding the literature at large, and thus provided conclusions broader in scope than the conclusions found in the source articles.

c. The original sources which provided the data for the review study were primarily original reports of empirical studies of stimulant effects in school-age children.

d. The review was published in English or translated into English.

e. The review had been retrievable in its entirety either through the efforts of UCI ADD staff or those of the UCI research librarians.

2. Research librarian-conducted multiple database search. The assistance of a UCI research librarian experienced in electronic searches (Ms. Woo) was enlisted. The librarian conducted a simultaneous search of four electronic databases: MEDLINE, PsychINFO, ERIC, and GPO Monthly Catalog using the DIALOG online service. The "master strategy" assembled by Ms. Woo was the following:

SET I. Attention Deficit Disorder set: all thesaurus terms identifying the disorder from all of the individual databases, "or'ed" together.

SET II. Drug set: all thesaurus terms from the four files identifying the stimulants or stimulant treatment, plus free-text names of individual drugs, "or'ed" together.

SET III. Merging Sets I and II together AND English language (total of 1464 records).

SET IV. Set III with duplicates among database sources removed.

SET V. Database field document types (review or equivalent), and thesaurus terms from four files "or'ed" together.

SET VI. Set V AND Set IV.
The result was 183 records, which were downloaded and read into ENDNOTE.

3. Merging of primary and secondary sources. The 241 reviews derived from the combination of the primary sources and the original MEDLINE search were cross-referenced with the 183 reviews identified from the multi-database (secondary source) search. This identified 85 duplicates. A total of 156 reviews were found to be unique to the first set (primary sources plus original MEDLINE search), and a total of 88 sources were found to

be unique to the multi-database search. The total of sources across both search strategies was 336.

A perusal of the sources which were unique to the initial (ancestral plus MEDLINE) found that a number of these sources were book chapters, general tutorially-oriented papers, point of view or opinion papers, and papers which limited their discussion to a narrow set of critical issues. Inspection of the list unique to the multi-database results suggested that a number of these sources appeared in educational journals not accessed by MEDLINE.

As shown in Figure 1, most of these reviews located were published in a time period (1966 to 1990) covering about a quarter of a century. To show the trend over time, the time period was divided into five 5-year intervals, with additional intervals specified for pre-1966 publications and post-1990 publications. There were very few reviews published before 1970. Perhaps due to publicity in the media (e.g., newspapers and magazines) and in congressional hearing, the number of reviews increased dramatically after 1970. The numbers of reviews leveled off (or actually dropped) after 1976. Perhaps due to another round of negative publicity and threatened court cases, the number increased in the mid-1980s and reached a peak in 1985. Another leveling off occurred. Perhaps due to the congressional hearings in 1989 and the Notice of Inquiry on ADD in 1990, a large number of reviews (21) appeared in 1991.

Chapter 3: Methods for Describing Reviews

3.1 Introduction. Not all reviews of the effects of stimulant medications on ADD children arrive at the same conclusions. The reviews were characterized in meaningful ways to help organize the similarities and interpret the differences manifested in the conclusions of multiple reviews of this common topic. Two methods were used to characterize the reviews: a taxonomy of reviews (Cooper, 1988) and a coding sheet (Cooper, 1989) relevant to the specific information in the reviews of stimulant medication and ADD.

After retrieving potential reviews and retaining those which fit our operational definitions, the reviews were processed using three trial procedures. Each review was formally classified by placing it in a modification of Cooper's (1988) taxonomy of reviews. Each review was then subjected to rigorous descriptive analysis using review methodology adapted from Cooper (1989) to fit our particular level of analysis (a "review of reviews.") Finally, each review was coded for its consideration of selected critical issues in order to describe the time course or historical progression of the importance accorded to each issue by reviewers. Each of these processing procedures (summarized below) was conducted for a different purpose:

Classification	Taxonomy of Reviews
Description	Coding Sheet for Rigor
Trends	Progression of Critical Issues

a. Classification. Cooper's (1988) taxonomy of reviews for

was adapted for the "review of reviews". An initial classification scheme was developed by Cooper in consultation with the UCI ADD Center participatns, with a purpose of discovering whether reviews could fit into Cooper's categories. The taxonomy is based on six characteristics (Focus, Goal, Perspective, Coverage, Organization, and Audience). Each characteristic is associated with several more specific categories (e. g., the Audience characteristic is separated into the four categories of General Scholars, Specialized Scholars, Practitioners or Policymakers, and General Public). For this application, an additional level of description was added to this taxonomy to make it appropriate for the UCI ADD Center's "review of reviews" (e. g., the Specialized Scholars category of the Audience characteristic was subdivided to specify the three professions most interested in this topic: Educators, Physicians, Psychologists, and Other).

b. Rigorous descriptive analysis. The purpose in using this approach was to empirically examine the review methodologies and the relationships between selected independent variables and review conclusions. Cooper (1989) detailed a comprehensive methodology for conducting integrative literature reviews. This methodology is heavily weighted toward quantitative analysis and uses empirical reports (i. e., individual studies, hypothesis tests, etc.) as the unit of analysis.

No comparable methodology for conducting an integrative review of literature reviews exists. The Cooper (1989) methodology is not directly applicable to this different level of

analysis for several reasons. For example, in a review of reviews, the unit of analysis is the review article. There is no analog to the hypothesis test or other statistic for purposes of quantitative synthesis at this level of analysis; in fact, the majority of review articles themselves do not provide any quantitative synthesis of findings. In several other respects, the characteristics to be extracted from reviews differ from the characteristics to be extracted from articles. Another example is that for the most part, the historical era in which a particular experiment or study was conducted is secondary in importance to the question posed and the design characteristics. Review articles, however, may address the same problem with similar methods, but differ greatly in the data they examine and the conclusions they reach precisely because of the time in which they were conducted.

Cooper's (1989) process was adapted for conducting the level of analysis required by the "review of reviews". This process follows five stages: Problem Formulation, Data Collection, Data Evaluation, Analysis/Interpretation, and Public Presentation. Cooper's (1989) detailed descriptions of these stages was applied to the "review of reviews" project, and Cooper's (1989) coding sheet development scheme and examples were adapted by substituting analogs for the "review of reviews" level of analysis and by devising appropriate categories to capture data needed to address the stated problems. The list of problems (generated during the Problem Formulation stage) and a coding sheet was generated by

this process.

c. Trends. Another area of interest addressed how certain issues first become introduced, how interest in these issues developed or waned, and how conclusions about these issues become either focuses of a reviewer's efforts or assumption which are accepted without further investigation. For example, during the initial years after Bradley's (1937) report, the response of children with ADD to stimulant medication was considered to be "paradoxical". This changed over time, and even before a consenus was reached, several reviews (eg., Wiess and Laties, 1962; Cole, 1969) pointed out that this clinical response of childrenw ith ADD to relatively low doses of stimulant medication was not paradoxical. The appearance and consensus of this view of the paradoxical response was an initial topic of interest for the "review of reviews".

After the initial work on these three approaches, it became clear that some combination of these approaches would be best for synthesizing the literature on the effects of stimulant medication on children with ADD. The initial evaluations yielded ten important topics in the literature on which a consensus seems apparent. These topics are discussed below in a separate section.

After the rigorous "review of reviews" was initiated, it became apparent that the size of the literature on this specialized topic had been underestimated. The dual search strategies described above (the expert-search strategy and the computer-

search strategy) located over 300 reviews (see Appendix A). The appearance of these reviews over time is shown in Figure 1. The pattern described by Cooper (1989) for other areas holds for this literature on ADHD and stimulants: the number of reviews is increasing.

The literature covered in a "review of reviews" is defined by the references lists of the reviews. The number of unique references in the 336 reviews is over 5,000. These references are listed in Appendix B. This product of the "review of reviews" may be valuable to clinicans, educators, and parents who are interested in a broad list of the orign=inal studies already published on the effects of stimulant medication on children with ADD.

3.2 Overlap of Sources. For the rigorous analysis of reviews, a few key reviews were chosen which appeared in the literautre at about the same time and addressed similar topics. The initial evaluation of these selected reviews was to determine if they addessed the same literature as defined by the specific references contained in the references lists of each review.

As an example or the concept of "overlap", the general literature (articles, reviews, chapters, etc.) retrieved from four different electronic data bases was considered as an exercise within the computer-search process. This literature was constrained by the combination of the disorder (defined by the multiple terms used over the years) and the treatment (defined by the multiple names of the multiple stimulants). A service

callled "Dialogue" gives access to 4 relevant data bases (Medline, Eric, PsychLit, GPO). A simultaneous search of the 4 data bases revealed 1462 articles, of which 1161 were unique. Thus, only 301 (20.6%) of the located articles appeared in any 2 of the 4 data bases. The lack of overlap, shown below, from computer searches of electronic databases was surprising:

Data Bases:	Medline	ERIC	PsychLit	GPO
# of articles retrieved:			total of 1462	
# unique articles:			total of 1161	
# articles with at least pairwise overlap:			301	

This pattern of a lack of overlap was investigated in subsets of review articles located by our search. To do this, review articles were chosen which were equated reviews for time of publication and method of review. For example, in 1982-1983, three meta analyses were published on the effects of stimulant medication: Kavale (1982), Ottenbacher and Cooper (1983), and Thurber and Walker (1983). The overlap of the references from any 2 reviews is presented below:

	K (1982)	O&C (1983)	T (1983)
K (1982)	74	6	4
O&C (1983)	6	86	9
T (1983)	4	9	33

By applying rigorous methods for reviewing the reviews, the ovrlap was documented for the reference list of any two of these reviews. The pair-wise overlap was low (20% to 30%), and it was

very surprising to find that no article in the combined list appeared in all 3 reference lists.

The same pattern held from a set of reviews selected from the 1970's and which all had a similar purpose (to criticize the use of stimulants). As shown below, the overlap of the reference lists from Fish (1971), Stroufe and Stewart (1973), and Grinspoon and Singer (1973) was minimal. Comparisons of pairs of reference lists indicated a 4% to 34% overlap, and only 2 of the articles were included in all three reference lists.

	F(1971)	S&S (1973)	G&S (1973)
F (1971)	29	3	10
S&S (1973)	3	77	14
G&S (1973)	10	14	99

The later reviews by Whalen and Henker (1976), Barkley (1977), and Adelman and Compas (1977) covered more articles, reflecting the increased research activity in this area. As shown below, the overlap of literature reviewed was also relatively low. Comparison of pairs of reference lists reveal overlaps from 24% to 38%, but only 23 of the articles appeared in all three reference lists, representing from 15%, 16%, and 20% of the articles on the reference lists.

	W&H (1976)	B (1977)	A&C (1977)
W&H (1976)	113	38	42
B (1977)	38	158	54
A&C (1977)	42	54	143

Of course, there are many reasons for low overlap of reviews, including different sub-topics being addressed, representative inclusion of a typical article from multiple exemplars from a specific topic domain, or selective inclusion of a single review when several are published by a specific author. In our synthesis of the literature, this important methodological point is being emphasized: not all reviews of the effects of stimulant medication on ADHD children are based on the same literature. One of the products of UCI ADD Center's literature synthesis (see Appendix B) is an "exhaustive" list that can be used to evaluate the degree to which any review covers the literature.

3.3 Set of Observations Derived from Selected Reviews. The "review of reviews" revealed that reviews may acknowledged very similar patterns of benefits and limitations of stimulant medication but still draw very different conclusions and make very different recommendations about pharmacological treatment of ADD children. Consider the recent review by Jacobvitz, Stroufe, Stewart, and Leffert (1990), which criticizes current clinical practice, and the review by Stevenson and Wolraich (1989), which supports current clinical practice. As shown below, both reviews describe a pattern pattern of expected benefits which is expressed in the literature. Also shown below is a summary of the limitations which were acknowledged in both reviews.

WHAT SHOULD BE EXPECTED:

1. Temporary Management of Diagnostic Symptoms:

a. overactivity (improved ability to modulate motor behavior)
b. inattention (increased concentration or effort on tasks)
c. impulsivity (improved self-regulation)

2. Temporary Improvement of Associated Features:

a. deportment (increased compliance and effort)
b. aggression (decrease in physical and verbal hostility)
c. social interactions (decreased negative behaviors)
d. academic productivity (increased amount and accuracy of work)

WHAT SHOULD NOT BE EXPECTED:

1. Paradoxical Response

a. responses of normal children are in same directions
b. responses of normal adults are in same direction
c. responses of affected adults and children are similar

2. Prediction of Response

a. not by neurological signs
b. not by physiological measures
c. not by biochemical markers

3. Absence of Side Effects

a. infrequently the appearance or increase in tics
b. frequently problems with eating and sleeping
c. possible psychological effects on cognition and attribution

4. Large Effects on Skills or Higher Order Processes

a. no significant improvement of reading skills
b. no significant improvement of athletic or game skills
c. no significant improvement of positive social skills
d. improvement on learning/achievement < behavior/attention

5. Improvement in Long-term Adjustment

a. no improvement in academic achievement
b. no reduction in antisocial behavior or arrest rate

Jacobvitz, Stroufe, Stewart, and Leffert (1990) acknowledged the short-term benefits outlined above but focused on the limitations. As a conclusion, they urged a "...greater caution and a more restricted use of stimulant treatment" (p. 685). In contrast, Stevenson and Wolraich (1989) acknowledged the limitations outlined above but focused on the temporary suppression of symptoms. As a conclusion, the stated: "Stimulant medications are an effective treatment modality for most children with ADHD" (p. 1193).

In the "review of reviews", several organizing principles were used, including a taxonomy of reviews (Cooper, 1988) and a coding sheet of reviews (adapted from Cooper, 1989), to reconcile different conclusions of reviews. A description of these methods and a more detailed description on the organization and synthesis of the literature on the effects of stimulant medication on children with ADD, is presented in the next chapters of this report.

Chapter 4: History of 5 Decades of Reviews

To illustrate the history of reviews, 7 time periods were selected for emphasis: pre-1966, 1966-1970, 1971-1975, 1976-1980, 1981-1985, 1986-1990, post-1990. The pattern of primary topics addressed by reviews in these 7 eras was contrasted.

The classification of reviews by era gives a brief description of the stated main purpose or critical issue addressed by each review. From this evaluation, the following main trends have been identified which ahve emerged over the past half centry:

1. The initial period (pre-1966) addressed basic clinical issues about how to define the patient population and what forms of stimulant medications to use.

2. The next era (1966-1970) represents the development of scientific methods in a new discipline (pediatric psychopharmacology).

3. The third era (1970-1975) was an era of public controversy, sparked by newspaper articles and congressional hearings on this topic.

4. The fourth era (1975-1980) was marked by the introduction of methodologies for measuring the differential effects of stimulants on activity, attention, cognition, and social interaction, as well as the difference between dramatic short-term effects and negligible long-term effects.

5. The fifth era (1981-1985) emphasized refined methods for the investigation of time course and dcse effects of the stimu-

lants.

6. The sixth era (1986-1990) emphasized the combination of psychosocial treatments with stimulants.

7. The current era (post-1990) seems to be emphasizing the effects of stimulants on academic productivity and aggression, as well as the definition of boundary conditions which may limit the long-term effects of stimulants.

Chapter 5: Interpretation of reviews

The organization of the multiple reviews and some of the historical trends have been described above. Based on this organization, ten topics were selected to synthesize the information contained in the multiple reviews. These ten topics are (a) response rate, (b) effects on diagnostic symptoms, (c) effects on associated features, (d) side effects, (d) long term effects, (e) paradoxical response, (f) effects on high order processes, (g) prediction of response, (h) recommendations for clinical use, (i) recommendation for multimodality treatment.

For the "review of reviews", these ten topics were incorporated into a coding sheet for the systematic evaluation of the 336 reviews. Each review was analyzed to determine if itaddressed each topic, and each review was evaluated with respect to whether it agreed or disagreed with the topic. Then, the infromation derived from this evaluation was summarized across reviews to determine the degree of consensus in the literature covered by the 336 reviews and over 5,000 original references listed in Appendix A and Appendix B.

The coding sheets were completed by four of the staff of the UCI ADD Center: James Swanson, Tim Wigal, Keith McBurnett, and linda Pfiffner. The coding sheets are presented in Appendix C. The review articles evaluated by use of the coding sheets are presented in Appendix D, volumes 1 to 5. The results of the coding sheet evaluation are summarized below:

1. Response Rate. Not all children with ADD respond fa-

vorably to stimulant drugs. Across a subset of reviews which addressed this topic, the prevalence of a favorable response was about 70% and was about the same across 55 years despite changes over time in the diagnostic criteria and labels used to define the disorder.

2. Effects on Diagnostic Symptoms. In the majority of ADD children who responded favorably to stimulants, the response included temporary management of the diagnostic symptoms of ADD (ie., a decrease in inattention, impulsivity, and hyperactivity) and a time-limited increase in concentration and goal-directed effort. Across relevant reviews, 97% agreed with this description of short-term effects.

3. Effects of Associated Features. In reviews which addressed common associated features of ADD which occur in some affected children (such as deviant deportment, high levels of aggression, inappropriate social interaction, and poor academic productivity), 94% agreed that a component of response to stimulant medication was a decrease in the manifestation of these disruptive behaviors.

4. Side Effects. In reviews which addressed side effects (such as minor problems of anorexia and insomnia, serious problems associated with motor and verbal tics, and psychological impairment in the areas of cognition and social interaction), almost all (99%) acknowledged the existence of side effects and the clinical necessity to monitor and manage these effects.

5. Long Term Effects. In the reviews which addressed the

issue of long-term effects of stimulant medication, 88% acknowledged the lack of demonstrated long-term effects on important outcome domains (ie., social adjustment and academic achievement).

6. Paradoxical Response. Some early influential reviews asserted that stimulant medication "calmed or subdued" children with ADD, which was represented as a paradoxical response. This probably was because the response to high doses of stimulant drugs in other literatures (eg., the abuse literature) commonly was described as an euphoric or "speeding" response. However, in reviews which addressed this topic, 78% concluded that in children with ADD the behavioral, physiological and psychological responses to clinical doses of stimulant medication (ie., increased concentration and goal-directed effort) were not qualitatively different from the responses of normal children and adults to equivalent doses. Thus, most reviews of the use of stimulant medication to treat children with ADD did not classify the typical cinical response as a paradoxical response.

7. Effects on High Order Processes. A subset of reviews addressed the effects of stimulant medication on complex behavior requiring high order skills (eg., learning, reading, etc.) as well as on simple behavior requiring low order skills (eg., performing rote tasks, monitoring a repetitive display, etc.). Most (72%) of these reviews acknowledged the lack on a demonstrated beneficial effect on performance of complex tasks or behaviors which required the use of high order processes.

8. Prediction of Response. Some reviews addressed the methods of evaluating a trial response to stimulant medication, and the prediction of response on the basis of behavioral, cognitive, physiological, biochemical, or neurological measures. Most reviews (68%) acknowledged poor prediction by these measures.

9. Recommendations about Clinical Use. Across the past half century, most reviews were written by clinicians and most (91%) supported some clinical use of stimulant medication to treat children with ADD. However, in each era of the past half century, some reviews have addressed the same issues which generate controversy and have questioned this established clinical practice.

10. Recommendations for Multimodality Treatment. Many reviews ended with a recommendation for combinations of psychosocial and pharmacological interventions, but in most (70%) of these reviews, specific references to support this common-sense recommendation were not provided, and when references were specified they provided little empirical data to support this specific recommendation.

This evaluation produced a qualtative estimate of agreement across reviews. The agreement across reviews may be interprted as reflecting a consensus about the effects of stimulant medication. Specific disagreements which endured over time were interpreted as controversy about the use of stimulant medication. The literature covered by the reviews suggested that in most (but not all) cases a clear and immediate short-term benefit was per-

cieved by parents, teachers, and physicians in terms of the management of symptoms and associated features of ADD. The controversies which have persisted over time (and are consistent with acknowledged effects of stimulant medication) are the lack of diagnostic specificity for short-term effects, the lack of effects on learning or complex cognitive skills, potential side effects and adverse effects, and the lack of evidence of significant long-term effects.

The consensus about the effects of stimulant medication and the enduring controversies about its widespread use suggest a careful approach be taken in the clinical decision to treat a child with ADD. In the next chapter, recent reviews are identified which recommend a systematic approach to assessment of response, including the use of double-blind procedures, the evaluation of response across home and school settings, and the consideration of cognitive as well as behavioral domains of behavior. Also in the next chapter, reviews are identified which discuss methodological issues and point out important qualifications of the existing literature. Finally, three reviews of current areas of investigation (with focuses on adademic productivity, aggression, and social interaction) are identified which promise to make important additions to the existing literature on the effects of stimulant medication on children with ADD.

Chapter 6: Comparison of Sets of Reviews

6.1. Introduction. In the prior chapters of this report, the methods for specifying invariant findings were edescribed which were used to extracted information from 336 reviews covering the half century of work in this area. Also, the consensus about progress in this area was discussed, based on changes over time in the understanding of the effects of stimulant medication on children with ADD. In addition, trends over time in research on ADHD and stimulants were identified and discussed, and boundary conditions were identified which may limit the immediate and long-term effects of stimulant medication. A subsequent chapter will address some unanswered questions about the effects of stimulant medication on ADD children which are now under investigation.

In this chapter, to synthesize the information contained in the multiple reviews, will be presented of differences in conclusions stated in selected sets of reviews. Some of the differences in conclusions may be simply related to the time of publication. This can be interpreted as a reflection of progress (as defined above). Observed differences in the conclusions of reviews from the same era may be due to reviews being conducted on a different subset of articles. This possibility is quanitfied by the measurement of overlap of the literature reviewed. In addition, some differences in conclusions of reviews may result from different purposes of the review (as defined by the taxonomy of reviews), different methods of conducting reviews (as defined

on the coding sheet), or different ways or organizing the information from the reviews. These four methods of organizing reviews are summarized below:

Era	Time of Publication in 5 Year Intervals
Overlap	Number of Common Articles
Taxonomy	Characteristics and Categories
Coding Sheet	Independent and Dependent Variables

In this chapter, examples will be presented to demonstrate how differences across reviews may be resolved by the "review of reviews" methodology.

6.2 A Comparison of 3 Traditional Reviews. In the late 1970's, three influential reviews were published: Whalen and Henker (1976), Barkley (1977), and Adelman and Compas (1977). These three reviews differed in their stated purposes and conclusions, as outlined below:

A & C (1977)	to counteract the premature, widespread application of stimulants as a treatment
B (1977)	to formulate conclusions and generalizations based on a vast literature on stimulant drugs and hyperactivity
W & H (1976)	to offer a sociocognitive analysis of the effects of stimulant drugs on children

Adelman and Compas (1977. p. 377) stated "...our purpose is not to simply summarize and organize the work being done in this field. We are critical of some of the research and most of the current applications; therefore, portions of the presentation are intended to help counteract the premature, widespread application of stimulants as a treatment for learning problems. We

believe such an approach is a justified reaction to the pro-drug bias which permeates the massive body of literature in this area". They concluded that "...the research related to treatment efficacy has emphasized that is remains unproven that the children taking stimulant drugs manifest important positive changes (p. 409).

Barkley (1977, p. 137) stated two aims of his review: "First, to review the results of a vast number of research reports on stimulant drugs and hyperkinesis. And second, to attempt to formulate conclusions and generalizations regarding the number of specific questions". He concluded that in the short term "...most children are judged as improved on drugs" (p. 158).

Whalen and Henker (1976) stated three purposes of their review: "...to review current methodologies and empirical evidence on the effects of stimulant drugs with children" (p. 1113), to offer "...a sociocognitive analysis of the drug effects" (p. 1114), and "...to suggest the process of giving medication to children for behavioral regulation presents, in crucible form, an ecosystem for the evaluation of sociopsychological theories of attribution, personal causation, and expectancy" (p. 1114). They accepted that "...number of well-designed and carefully executed studies attest clearly and consistently to drug-induced gains in a substantial portion of children taking stimulant medication" (p. 1113), but that "...the successful medication responses have powerful attributional consequences" (p. 1126).

Thus, these three reviews provide different messages about

the clinical practice of using stimulant to treat children with problems at home and in school. The Barkley (1977) review provides supports for the clinical practice by defining the areas of functioning in which positive change has been documented. The Adelman and Cooper (1977) review discounts the reported positive changes and suggest that the clinical practice is premature. The Whalen and Henker (1977) review defines limitations of the standard clinical practice and suggest nonpharmacological procedures which may improve it.

A "review of reviews" provides some explanation and reconciliation of the apparent discrepancies of these three reviews. First, the three reviews were based on different samples of the literature. The review that challenged the established clinical practice of using stimulant medication, Adelman and Compas (1977), reviewed only 34% (54/158) of the articles references by Barkley (1977) and only 37% (42/113) of the articles reviewed by Whalen and Henker (1977). However, the overlap of the literature reviewed by the two review that supported the established clinical practice, Barkley (1977) and Whalen and Henker (1977), was not much greater: Barkley's (1977) review included 34% (38/113) of the articles referenced by Whalen and Henker (1977) and 38% (54/143) of the articles referenced by Adelman and Cooper (1977), and Whalen and Henker's (1977) review included 24% (38/158) of the articles referenced by Barkley (1977) and 29% (42/143) of the articles referenced by Adelman and Compas (1977). Second, due to an inconsistent use of multiple diagnostic labels in vogue at the

time of the reviews, the three reviews emphasized different subgroups of subjects: Barkley (1977) used the labels "hyperactivity" and "hyperkinesis" without further description of the disorder; Whalen and Henker (1977) used the label "hyperactivity" but pointed out that this was an "unfortunate misnomer" since inattention, impulsivity, and emotional lability accompany high activity levels; Adelman and Compas (1977) used the term "learning problems" but emphasized the multiple labels used in the literature they reviewed. Third, the conclusions of the reviews emphasized different aspects of outcome: Adelman and Compas (1977) emphasized long-term outcome on measures of learning and performance, while Barkley (1977) emphasized the short-term outcome on measures of manageability and Whalen and Henker (1976) emphasized outcome measures of attribution.

The purpose (criticism) of the Adelman and Compas (1977) article led them to reject the clinical practice of using stimulant medication: We "...do not support the widespread use of stimulant drugs as a treatment of learning problems. This conclusion is based on the absence of evidence supporting drug effectiveness as an aid to academic learning and performance" (p. 409). In our review of reviews, we noted that Adelman and Compas 91977) acknowledged that some children were "...viewed as dramatically different after taking stimulants. This phenomena obviously occurs" (p. 409). However, they noted that no long-term effects had been reported in the literature, and they questioned whether the short-term effects were due to pharmacological action

of stimulants, proposing instead that the perceived effects were due to "halo" effects resulting from awareness of drug/placebo differences (even when double-blind procedures were used).

Barkley's (1977) analysis of the literature led to a similar conclusion about the effects of stimulant medication, but very different recommendations for clinical practice. With respect to drug effects, Barkley (1977) concluded the following: "While the drugs seem to facilitate the short-term management of hyperactive children, they have little impact on the long-term social, academic, or psychological adjustment of these children" (p. 158). With respect to clinical practice, he stated that "...stimulant drugs offer an effective treatment for the short-term management of hyperactivity but are not the answer to long-term treatment of these children" (p. 157).

Whalen and Henker (1977) draw the same conclusions about the effects of stimulants from their analysis of the literature: "What we do know is that stimulant treatment results in enhanced socially appropriate behavior as perceived by teachers and often parents and physicians as well. It is easier for adults, and presumably for peers, to get along with hyperactive children when they are taking stimulants than when they are unmedicated. These results have emerged repeatedly from carefully controlled double-blind studies and thu cannot be altogether discounted an experimental artifacts" (p. 1119). However, they pointed out that "We also know that a substantial proportion of children who do show drug-related gains fail to maintain academic or behavioral im-

provements" (p. 1120). The suggestions for clinical practice (based on their hypotheses about attributional consequences of short-term positive medication responses) were tentative, but lead them "...to question the customary medical practice of capitalizing on placebo effects by enhancing positive expectancies about drug potency" (1120).

Despite these differences in purpose, coverage, and emphasis, the three reviews present a surprising consensus about the actual effects of stimulant medication on ADD children:

1. The three reviews agree that in a large majority of cases (about 75%), after treatment with stimulant medication the parent and teacher perceptions of positive change and performance on tests that require concentration and attention after treatment with stimulant medication will occur immediately and will be dramatic.

2. The three reviews acknowledge that placebo and expectancy effects, as well as pharmacological effects, contribute to the perceived effects of stimulants on children.

3. The three reviews agree that the short-term percieved positive change cannot be predicted by pre-medication physiological or psychological profiles of the children being treated.

4. The three reviews agree that the effects of stimulant medication on long-term adjustment (academic achievement or prosocial behavior) are neglible.

Based on adjustment for purpose and emphasis, our "review of reviews" presents a consistent view of the effects of stimulant medication on children but a substantial difference in conclusions of the reviews. The differencec in the conclusions seem to be associated with the purposes of the review.

It is surprising thatIn this light, the documented difference in coverage (less than 30% overlap of articles reviewed)

does not seem to account for the different conclusions stated in the reviews. Thus, our "review of reviews" approach for organization and synthesis identifies some invariant features of the literature on stimulant and ADD.

6.3 A Comparison of 3 Meta Analyses. The influential reviews of Barkley (1977), Whalen and Henker (1976) and Adleman and Compas (1977) meet Cooper's (1989) definition of a "literary summary". Cooper (1979, 1989) uses this term to designate a review based on qualitative analysis of a selected set of studies. Cooper (1979) observed that the traditional review process typically lacks analytical precision because of biases associated with a reviewers idiosyncratic perspective, failure to assess the size of the effects reported by studies reviewed, and imprecise combination of the volume of evidence avaliable across the studies reviewed.

Meta analysis (Cooper, 1989) offers a method which avoids some of the problems of traditional "literary summaries". In the early 1980's, three meta analsyes were published based on the literature on the short-term effects of stimulants on "hyperactive" children: Kavale (1982) published a meta-analysis in the educational literature, Ottenbacher and Cooper (1983) published a meta-analysis in the medical literature, and Thurber and Walker (1983) published a meta-analysis in the psychological literature. In the UCI ADD Center's "review of reviews", we contrasted these three reviews which appeared at about the same time, used a similar methodological approach, and addressed the

same general topic. Despite these similaries, the conclusions of the three meta analyses were quite different:

1. Kavale's (1982) conclusions support the clinical practice of using stimulants: the overall effect was significant and not due to methodological weaknesses ("...drug therapy appears to be an effective intervention for the treatmeneffects on academic performance" (p. 287)); an effect on learning was verified ("Assessments of academic learning were improved by drug treatment" (p. 288)); the placebo effect was neglible ("...the present findngs indicate that the placebo effect accounted for only 3% of the improvement shown by drug-treated subjects" (p. 286)).

2. Thurber and Walker (1983) conclusions offer weaker support for clinical practice: "...although stimulants certainly appear to 'work' (drug-related imprvements are highly statistically reliable), the degree of treatment impact is comparatively small" (p. 83).

3. Ottenbacker and Cooper (1983) agreed with Kavale (1982) in term of the overall medication effect ("...pharmacological management produces effects on the behavior and performance of children identified as hyperactive" (p. 362)), but clearly disagreed about the drug effect on academic performance ("...drug therapy reduces hyperactive behavior and increases attention but has relatively little effect on improving overt academic performance" (p. 363) and the lack of a placebo effect ("...approximately 30 per cent of the effect found in the drug versus control

conditions could be attributed to the placebo phenomenon" (p. 363)).

The UCI ADD Center's "review of reviews" reconciles these apparent discrepancies in the three meta analyses. Our use of a coding sheet (which equates the definitions of independent and dependent variables of the reviews) reveals that the actual effects sizes reported across the studies were very similar. Since the three meta-analysis reported effect sizes for different classes of dependent measures, selective comparisons are necessary to make the comparisons across reviews on an equivalent dependent variable. For this purpose, we used 2 classes of effects size: the average effect size based on ratings of behavior and measures of attention (which individual comparisons indicated did not differ) and the average effect size based on measures of academic variables (IQ and achievement tests). The following pattern was extracted from these 3 meta-analyses:

	Behavior and Attention	IQ and Achievement
Kavale (1982)	.84	.39
O & C (1983)	.90	.47
T & W (1983)	.75	.19

Despite the similarities mentioned above, our description of these 3 meta-analyses on our coding sheet revealed important differences. Thurber and Walker (1983) performed the simplest analysis by emphasizing an overall drug-placebo effect size in a small number of existing studies free of methodological flaws. Kavale (1982) performed the most complicated analysis by evaluat-

ing the impact of a number of subject (i.e., diagnosis, age, etc.) and design (i.e., control, blinding, etc.) variables to evaluate their impact on the drug-placebo effect size. Ottenbacher and Cooper (1983) asked the most specific question: they formulated effect sizes based on three comparisons (drug-control, drug-placebo, and placebo-control) to evaluate evidence of a "placebo effect" on outcome.

The differences between the Kavale (1982) and Ottenbacher and Cooper (1983) estimate of effect size for the "placebo effect" remain unexplained. The Ottenbacher and Cooper (1983) meta-analysis specifically included a contrast of Placebo versus Control, which yielded an effect size of .32, or about 30% of the reported Drug versus Placebo effect size. Even though this comparison was not a major part of the Kavale (1982) meta-analysis, an estimate of the placebo effect was estimated and was small (an effect size of .07, or about 3% of the reported drug-placebo effect size). The "review of reviews" measure of reference overlap was low for these two meta analyses (despite the stated purpose of reviewing the literature as it existed in 1980): Ottenbacker and Cooper (1983) referenced 86 articles, and Kavale (1982) referenced 74 articles, but only 6 of these overlapped across the two meta analyses. (Kavale (1982) noted that 135 studies had been included in the meta analysis, but personal contact be letter and telephone revealed that this list had been lost and was no longer available). Apparently, the placebo-control comparisons from these two meta analyses were derived

from different studies. Since Ottenbacker and Cooper (1983) specifically addressed this issue, and the magnitude of the placebo effect they reported is consistent with the report of an important "literary summary" (e.g., Barkley, 1977 reports about a 30% placebo response rate), the UCI ADD Center's "review of reviews" accepts the conclusion that a significant and large placebo effect is manifested in the short-term response to stimulant medication.

In summary, the "review of reviews" indicates that despite the different literatures covered (shown by the overlap analysis), the different purposes (shown by our use of the taxonomy of reviews), and the different detailed methods used (shown by our use of the coding sheet), the results of these 3 meta-analyses were quite consistent. When reported, the average ages and IQs of the subjects in the studies reviewed were about the same (Ottenbacher and Cooper, 1983: age = 8.3 years, IQ = 102.2; Kavale, 1982: age = 8.75, IQ = 102). The effect sizes for behavior and attention (.90 and .84) and academics and learning (.39 and .47) are similar in size and are only 1 SD apart. Since these similarities are manifested in almost non-overlapping samples of the total literature, these effects seem to be quite robust.

These meta analyses were consistent with the conclusions of the literary summaries about the differential effect of stimulant medication on short-term (on the average, 7 to 18 week) outcome measures: the effect on measures related to the symptoms of the

disorder (behavior ratings and performance on attention tests) is about twice as large as the effect on measures which are not abnormal in subjects with the disorder (performance on IQ and achievement tests).

6.4 A Comparison of 3 Reviews for the General Public. One of the characteristics of reviews in Cooper's (1988) taxonomy is Audience, and one of the categories is General Public. In the UCI ADD Center's "review of reviews", it was noted that the conclusion of most reviews for the General Public was different than the conclusion of most reviews for General or Specialized Scholars: the reviews intended for the General Public did not support the clinical practice of treating children with stimulants. It was also noted that in the taxonomy of reviews, the characteristic of most reviews for the General Public with respect to Goal was Criticism. Furthermore, it was noted that the profession of the first author of a review for the General Public was usually different (i.e., journalist) than the profession of the first author of reviews for General or Specialize Scholars (i.e., physician or psychologist). An analysis of three well-known reviews for the General Public will be presented to isolate the reason for criticism of the clinical practice of treating children with stimulants.

One of the first reviews for the General Public was published as a chapter of a book by Schrag and Divoky (1975). Ten years later, another review for the General Public was published

as a chapter of a book by McGuinness (1985). Recently, a review for the General Public was part of a magazine article by Kohn (1989).

The goals and conclusions of these reviews were quite similar:

1. The goal of the Schrag and Divoky (1975) review was to expose the "myth of the hyperactive child" and to show the inappropriateness of "...chemical intervention as a legitimate solution to the classic problem of controlling and making acceptable the behavior of children who annoy teachers, upset classroom routines, or otherwise fail to conform to adult expectations" (p. 71). They acknowledged that, judged by parent or teacher reports, "...the drugs clearly worked for a certain percentage of children: there was no shortage of positive reports, and there would be no shortage of people suggesting or demanding medication, and no shortage of doctors or clinics ready to prescribe" (p. 107). Despite that admission, their main message and conclusion was that treatment of children with stimulants was viewed in the realm of behavioral control and thus was considered unacceptable for political and social reasons: "In the final analysis, all the controversies about efficacy, safety and side effects, though highly significant, tend to be misleading. They turn attention from social and political considerations to individual medical questions and therefore conceal the most fundamental issue. From a political and social perspective, the most dangerous psychoactive drug is precisely the one that is medically the

safest and psychologically the most effective" (p. 105).

2. The goal of the McGuiness (1985) review was to propose and test critical questions about the link between diagnosis of hyperactivity and treatment with stimulant drugs, which (as expected by the author) were answered negatively would offer "...a powerful argument for abandoning our current practices of diagnosis and treatment" (p. 196). It was noted that the literature reports many clear effects of medication ("The noticeable changes in behavior and the dramatic effects on the peripheral and central nervous system are reflections of the drug's action on the brain" (p. 225)), but an emphasis was placed on the consensus view that these effects were not specific to hyperactive children or any specific physiological or neurological abnormality. McGuiness concluded that 25 years of research had failed to "...pin down a disorder that does not exist" and that "...drugs do not work. They help the teachers and parents, but they do nothing for children" (p. 229).

3. The goal of the Kohn (1989) review was to question the impact of the emphasis among researchers on biological causes and explanations of hyperactivity: "The most striking consequence of assuming that an unusually distractible or impulsive child is suffering from a disease is the tendency to turn to medication to solve the problem" (p. 96). Kohn (19890 acknowledged that in most children stimulants are efficacious, but "...that drugs do absolutely nothing for 25% to 40% (depending on whose estimate

you trust) of hyperactive children", that "...a large proportion of children who do respond to Ritalin also improve on a placebo", that "...drugs do nothing to enhance actual academic achievement", and that "...the effect is a temporary suppression of symptoms, not a cure" (p. 98). The conclusion of this review was to question why Ritalin is used i the first place: At best, the drug "...may have much greater relevance for stress reduction in caregivers than intrinsic value to the child" (p. 98).

These reviews for the General Public, with Criticism are a goal, make about the same points:

1. The literature does not support the notion of a paradoxical response of hyperactive children: normal children show increased attention and decreased undirected movement in response to stimulants.

2. The assumption that brain damage (or some other organic cause of the symptoms) predicts response to medication has not been supported in the literature.

3. The stimulants have effects on attention, concentration or motivation, but no clear effect on academic performance or learning.

4. The long-term adjustment of hyperactive children is not affected by treatment with stimulants.

5. When they work in the short-term, drugs are used as a crutch and may postpone or prevent the use of more effective long-term interventions.

The conclusions of the General Public reviews (i.e., that the clinical practice of treating children with stimulants is unjustified) conflicts with the conclusions of the General and Specialized Scholar reviews (i.e., that the use of stimulants to achieve short-term reduction of symptoms is an effective and legitimate clinical treatment. Why do the conclusions of these reviews differ?

The UCI ADD Center's review documented that the two types of reviews acknowledged the presence of the similar drug-induced effects and the absence of the same effects. Thus, a different understanding of the drug effects is not the reason for the different conclusions. Instead, different interpretations of the same drug effects may account for the difference in conclusions.

Chapter 7: Current Questions and Investigations

7.1 Introduction. The following critical questions have been addresses by the most recent reviews:

1. What are some boundary conditions which limit the effects of medication on school behavior and performance (Swanson, Cantwell, Lerner, McBurnett, Pfiffner, and Kotkin, 1992)?

2. Does stimulant medication have an effect on the academic performance of ADHD children (Carlson and Smith, in press)?

3. Does stimulant medication have an effect on the aggression manifested by some ADHD children (Hinshaw, 1991)?

4. Does the combination of psychosocial and pharmacological interventions improve the long-term outcome of ADHD children treated with stimulant medication (NIMH-RFA, 1991)?

In this chapter of the "review of reviews", each of these important reviews will be discussed to provide examples of current critical questions being addressed by investigators studying ADHD and stimulant medication.

7.2 Boundary Conditions. The purpose of the Swanson et al (1992) review was to emphasize the "...limitations that are not usually emphasized but have important implications for educators" (p. 13). The seven issues addressed in this selective review are presented below:

1. Is stimulant medication overused?
2. Does the short length of action critically limit the benefits of typical treatment with stimulants?
3. At what dose (if any) does cognitive toxicity occur?

4. How many ADHD cases are adverse responders to stimulants?

5. Why does treatment with stimulants stop in most cases?

6. Does treatment with medication have any residual effects that continue after the pharmacological effects dissipate?

7. Are double-blind assessments or laboratory assessments useful in the treatment of ADHD children with stimulants?

These issues were discussed in the context of what we know about task specificity of response to stimulants, U-shaped dose-response patterns, effortful tests, and multiple measures of response. The purpose, conclusions, and speculations of the Swanson et al (1992) paper are presented below:

PURPOSE: to emphasize the limitations of the effects of typical treatment with stimulant medication

CONCLUSIONS: the short-term effects of stimulants should not be considered "...to be a permanent solution to chronic ADD symptoms"

SPECULATIONS: stimulant medication may improved learning in some cases but impaired learning in other cases, in practice, prescribed doses of stimulants may be too high for optimal effects on learning, the length of action of most stimulants is too short to produce an affect on academic achievement

7.3 Academic Productivity. The purpose of the Carlson and Smith (in press) article was to exam "...whether short-term gains can be translated into long-term improvements in academic achievement" (p. 3). To accomplish this, they proposed to "...describe some of the research relevant to this topic, attempt to draw conclusions about many of the important questions related to stimulant effects on learning, and provide suggestions that may assist school personnel in helping to collaborate with physi-

cians in evaluating these effects" (p. 1). Early reviews (Barkley, 1977; Whalen and Henker, 1976; O'Leary, 1980) concluded that treatment of ADHD children with stimulant medication did not improve long-term academic achievement, but more recent work reviewed by Carlson and Smith (in press) provide clear evidence of short-term improvement in performance on academic tasks, in both the laboratory and the classroom settings. Investigations of ADHD children with comorbid learning problems (e.g., specific reading deficits or general academic deficits) were reviewed, pointing out the lack of a long-term effect of medication combined with specific interventions (e.g., reading remediations or cognitive therapy). However, in ADHD cases without concurrent academic problems, stimulant medication clearly improves practice to a degree that should improve learning. Serious methodological problems in the literature were reviewed by Carlson and Smith (in press), including lack of random assignment of comparison groups, lack of control of dose or length of treatment with stimulants, psychometric properties (lack of sensitivity, ceiling effects, etc.). In the absence of any definitive answer about the long-term effects of stimulants on ADHD children, Carlson and Smith (in press) recommended ways to avoid the limitations suggested by the methodological weaknesses, including "...performing thorough, individualized medications evaluations" using standardized procedures for administering "real life" academic tasks, the results of which are communicated to the physicians to titrate dose.

The purpose, conclusions, and recommendations of the Carlson and Smith (in press) article are summarized below:

PURPOSE: to examine "...whether short-term gains can be translated into long-term improvements in academic achievement" (p. 3).

CONCLUSION: clear evidence of short-term improvement in performance on academic tasks, in both in the laboratory and the classroom settings.

SPECULATIONS: ways to avoid the limitations suggested by the methodological weaknesses, including "...performing thorough, individualized medications evaluations" using standardized procedures for administering "real life" academic tasks, the results of which are communicated to the physicians to titrate dose.

7.4 Effects of Stimulant Medication on Aggression. The purpose of the Hinshaw (1991) review was to "(a) assess the role of the most prevalent treatment for children with attentional deficits -- stimulant medication -- in the amelioration of aggressive behavior; and (b) discuss relevant methodologic, clinical, and theoretical issues that pertain to the role of medication in treating aggressive acts" (p, 301). He reviewed the literature on subcategories of aggressive acts (e.g., eruptive/impulsive versus antisocial/hostile and covert versus overt), the weak effects of stimulants on aggression in the artificial settings of laboratory testing or playroom observation, and the strong effects of stimulants on aggression in the natural setting of the classroom and playground. He also reviewed the role of aggression in the long-term outcome of ADHD children, the minimal effects of stimulant medication on impor-

tant areas of functioning related to aggression (e.g., peer status and academic achievement), the role of environmental factors (e.g., low SES and conflictual family environments) in maintaining an aggressive pattern of behavior, and the effects of combined (e.g., psychosocial and pharmacological) treatments on aggression in ADHD children. Hinshaw (1991) challenged the accepted belief in the field that " ...whereas the core deficits of ADHD -- which are presumably biologically based -- are best treated with pharmacological agents, aggressive behavior requires psychosocial intervention, preferably family-oriented, behavioral treatment" (p. 303). He concluded that the literature suggests "...small and usually nonsignificant effects of medication in the laboratory or playroom" but large effects in "...naturalistic observations of aggression in classroom or outdoor play settings" (p. 307). However, Hinshaw (1991) also concluded that any short-term amelioration of aggressive acts with stimulant medication is likely to be counteracted by (a) compliance problems, (b) unmedicated periods in peer and neighborhood environments, and (c) the continuous, stressful interchanges that occur in the lives of the children" (309).

The purpose, conclusions, and recommendations from the Hinshaw (1991) are presented in Table 15:

PURPOSE: to assess the role of stimulant medication in the amelioration of aggressive behavior

CONCLUSION: stimulants have small effects on performance in the laboratory or playroom settings but large effects on naturalistic observations of aggression in classroom or playground

SPECULATIONS: any short-term amelioration of aggressive acts with stimulant medication is likely to be counteracted by medication compliance problems, length of action problems (resulting in periods when medication is not acting in peer and neighborhood environments), and the continuous stressful interchanges that occur in real life associated with low SES and conflictual family environments

7.5 Research in Progress. The Request for Applications (RFA) for a "Multi-site, Multimodality Treatment Study of ADHD", issued by the National Institute of Mental Health (NIMH) Child and Adolescent Research Branch, provided a comprehensive discussion and review of the dramatic short-term but negligible long-term effects of stimulant medication on ADHD children. The NIMH-RFA listed 10 topics that should be addressed in future studies of the effects of stimulants on ADHD children. These topics are presented below:

1. Why have no long-term effects been demonstrated?
2. In the short-term, how many ADHD children are nonresponders?
3. Do high doses impair learning?
4. Does state-dependent learning occur?
5. Do effects depend on age and IQ?
6. Do effects depend on comorbid conditions?
7. Are the effects of different stimulants the same?
8. Do attributions of success to the pill offset benefits?
9. Why are links to biological factors not well established?
10. Why has length of treatment in most cases been so limited?

These issues are being addressed in the NIMH Multi-site Multimodality treatment study which is now in the protocol development stage. One of the most important issues addressed by this study will be the effect of combined intervention which is recommended by almost all reviews on the effects of stimulant medication on ADHD children.

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