

Methodological Diversity and Theory in the Stage Model: Reply to Kazdin

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We thank Dr. Kazdin for his erudite explication of some of the many critical issues on which our stage model has been “silent.” He points to three major omissions: (a) the lack of emphasis on theory-driven components to stage model research, (b) a failure to address the need for research on “what are the mechanisms through which therapy operates and under what conditions is therapy likely to be effective and why,” and (c) an exclusive reliance on randomized clinical trials as the basis for evidence of efficacy/effectiveness of a treatment under study. Given these omissions, he expresses pessimism that the sequence of studies outlined in the model will achieve the goal of “identifying treatments that can be used effectively in clinical settings.”

We can only reply that our “silence” on these matters does not mean that theory, mechanisms of action, and methodological diversity are excluded from or even peripheral to the stage model. In fact, we agree that they are fundamental to psychotherapy efficacy and effectiveness research. Our own convictions on the need for a scientific, theoretically informed basis for behavioral therapies research is embodied other publications (Onken, 1997; Onken & Bootzin, 1998; Onken and Blaine, 1997). We will describe where they fit into the model in this response.

AIMS OF THE STAGE MODEL

The stage model of behavioral therapies research was developed to provide a framework that would broaden the research agenda beyond what we believe to be an over-

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emphasis on single-site, efficacy testing in randomized clinical trials (RCTs), which we now describe as stage II. To use Kazdin’s analogy, the pipeline of behavioral therapies research (or, more broadly, psychotherapy research) is clogged in two places.

At the front end, creative clinicians have preferred literally hundreds of new treatments, but few of these treatments’ originators have had or taken the opportunity to subject these approaches to systematic, empirical testing. Many promising, potentially effective approaches may be ignored (or worse, broadly adopted with marginal or no evidence of efficacy) because these clinicians lack the resources to develop their treatments in a form that is subject to efficacy testing. Stage I was designed to address this blockage and includes a wide range of research activities aimed at yielding the minimal elements required for efficacy testing with randomized clinical trials, most importantly including an operationalized set of treatment procedures (i.e., the treatment manual). By providing guidelines for stage I research, our hope is to encourage clinicians and clinical investigators with good ideas to systematize them and move them along the pipeline. As Kazdin points out, stage I research may be an ideal format for collaboration between experienced investigators and clinicians unfamiliar with research methods.

Further along the pipeline, a growing number of new psychotherapies are seldom practiced outside research settings despite having a track record of efficacy demonstrated by two or more RCTs. Stage III is conceptualized as a program of research that addresses a wide range of questions crucial to the technology transfer process: Will the treatment work with real-world patients, therapists, and treatment settings? What kind of training and supervision are required for clinicians to practice the new treatment with skill and safety? What are the costs and cost

offsets of introducing the new treatment? It is important to articulate stage III research as part of the research agenda so that investigators will be encouraged to think of technology transfer issues even at stage I and to recognize that their work is not completed when they have demonstrated efficacy in randomized clinical trials. We emphasize that stage III research questions are not best or exclusively answered by large-scale, treatment demonstration trials in multiple clinical settings. Rather, stage III research is best seen as a multiplicity of studies and research strategies addressing treatment-specific issues arising from results from stage I and II findings. Kazdin poses the hypothetical situation in which cognitive therapy is shown to work in RCTs but not through mechanism of changes in cognition. Should the next step be clinical trials in other settings, studies of improved measures of targeted cognitive processes, or laboratory studies of alternative possible mechanisms of action? We agree that all three directions are desirable in this case and would be conceived of in the model as late stage II or stage III research. Also, stage III research does not necessarily mark the end of the line, as findings on a treatment's shortcomings in stage III may point to the need for new interventions to be developed at the stage I level.

While the stage model encompasses a broad research agenda and a diversity of research designs, RCTs retain a pivotal role in early stage II. Efficacy demonstration in early Stage II is a hurdle that a treatment must clear to justify further research that attempts to address mechanisms of action and the host of other questions Kazdin poses. We agree with him that even the most clearly refined and specified behavioral treatments represent a package of elements that is likely to contain active, inert, and perhaps even toxic ingredients in quantities that are not known by its developers. Only after such a package is shown to be efficacious, is it reasonable to pursue research that attempts to identify, purify, and amplify the active kernel of the treatment and to sort out the inert and toxic elements. Thus, in this model, RCTs represent an essential litmus test to identify those treatment packages that are worth unpacking.

THEORY, MECHANISMS OF ACTION, AND METHODOLOGICAL DIVERSITY IN THE STAGE MODEL

We also recognize that it is not essential that behavioral therapies efficacy research encompassed by the stage

model be informed by theory or hypotheses about why a given treatment works. A set of techniques noted to be efficacious could be explicated in a manual and pilot tested in stage I, subjected to RCTs in stage II and evaluated for generalizability in stage III without any attention paid to why the techniques work. Such a line of research has frequently taken place in the development of pharmaceutical treatments, with aspirin (acetylsalicylic acid) providing a well-known example. Salicylates have been the active ingredients of folk medicines, including willow bark, that have been used since ancient times for fever and pain. Aspirin, derived from the kernal ingredient of willow bark, was repeatedly shown to be efficacious and was disseminated into widespread use to reduce fever, inflammation, and pain for more than 100 years before its effect on prostaglandins was shown to be its primary mechanism of action. If a psychotherapist developed a behavioral treatment as efficacious, reliable, and inexpensive as aspirin to address mental disorders, this would be hailed as a breakthrough even if the discovery were completely atheoretical and serendipitous.

However, the aspirin example also illustrates Kazdin's points about the power and importance of knowing why a treatment works. To start with, aspirin's wide-ranging effects helped guide research on the role of prostaglandins once these previously unknown compounds were discovered. This is one of many examples in which the actions of efficacious drugs have provided clues for discovering general principles of human physiology. Conversely, the knowledge that aspirin's effects were mediated by prostaglandins provided the basis for development of more potent salicylate derivatives, such as ibuprofen (Motrin). Further research on mediators of prostaglandin effects has led to the recent development of a new class of aspirinlike medications, the Cox-2 inhibitors, (e.g., celecoxib/Celebrex), which retain aspirin's anti-inflammatory and pain-reducing properties while avoiding gastric side effects that have made aspirin intolerable to many. Thus, discovery of the aspirin's mechanism of action has resulted both in expanded scientific knowledge and improvements on the original treatment.

As Kazdin notes, theory can be a powerful tool to guide a program of research on the efficacy of behavioral treatments, and we believe that research guided by the stage model is strengthened if grounded in theory. Within the stage model, the manual development activities of early stage I is the most typical place for "specifying a con-

ceptual view of the processes or factors responsible for change [and] . . . developing measures of these processes,” in Kazdin’s words. Thus, stage I work can entail many theory-driven research activities under the rubric of manual development, including development and validation of methods to measure theoretically relevant factors hypothesized to mediate outcomes of a newly proposed treatment. At stages I–III, the treatment can be enriched and improved on the basis of findings that verify that theoretically important changes mediate or moderate the effects of a new treatment under study. As noted above, verification of efficacy with RCTs in early stage II represents a pivotal element of the model. Hence, once a treatment package is developed, first priority is placed on demonstrating that the treatment works. It is an assumption of the model that effective ingredients of change are more likely to be discovered in efficacious packages than in those for which efficacy is not yet established. Hence, extensive effort to discover why a treatment works may not be justified until we demonstrate that it works.

Once efficacy is established in early stage II, the direction for further study can take many paths, only one of which may involve replication RCTs in diverse clinical settings to address generalizability issues. At this point, the path is best dictated by findings from earlier research and the particular challenges that stand in the way of more widespread dissemination of that treatment. Before dissemination, an efficacious new behavioral treatment typically needs to be simplified and abbreviated to make it easier to learn and apply in typical clinical settings. Research on effective ingredients is essential for making decisions about what can be removed from the treatment without undermining its efficacy. This is a place for dismantling studies or targeted laboratory studies evaluating the impact of elements hypothesized to underlie the treatment’s effects. If findings from clinical trials conducted in stages I and II do not confirm the mediating and moderating effects of hypothesized change processes, further exploration of other possible mechanisms of action may be most fruitful at this point.

Although RCTs retain pride of place for efficacy testing in early stage II, this design is not an essential element of research at any other stage. Initial stage I studies of a new approach may most fruitfully and efficiently use a range of experimental and quasi-experimental designs including single-case designs and the multiple-baseline design described by Kazdin. We agree that research designs should be tailored to the questions posed and that RCTs may not be the most efficient way to identify effective and essential elements in a given treatment.

THE STAGE MODEL IS A TREE, NOT A PIPELINE

Implicit in Kazdin’s characterization and reaction to the stage model is a cut-and-dried, assembly line view of the process, which moves inexorably from small-scale pilot studies, to full-scale RCTs to large-scale, multisite RCTs in clinical settings without pausing for breath or reflection. He likens the psychotherapy efficacy research process to a clogged pipeline. Like a pipeline, the stage model is intended to be directional, following a logical sequence of steps toward a universally accepted goal. However, it is an outline only, and the series of studies that may be encompassed is not machine made and prespecified but an organic outgrowth of results of studies conducted along the way. We would prefer to compare the stage model to a tree, which has a directional, upward course, but a course that branches to catch the most light and to bear more than one fruit.

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