Adaptive Treatment Strategies: an Emerging Approach for Improving Treatment Effectiveness

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Adaptive Treatment Strategies

In the treatment and prevention sciences it has long been evident that there is individual heterogeneity in need for treatment in terms of disorder severity, background characteristics and co-occurring problems. Indeed the need for treatment may vary across time. For example, there is increased recognition that addictions have many of the characteristics of chronic disorders (McLellan et al., 2000), in particular addictions are characterized by interweaving time intervals of high and low risk. The heterogeneity in need translates into heterogeneity in response to various aspects of any treatment program, both across individuals and within individuals across time. Researchers have come to realize that it is possible to utilize this heterogeneity when designing treatment programs, potentially improving the effectiveness of these programs. Rather than focusing on the traditional "one-size-fits-all" approach to program development, treatment and prevention theorists are recommending integrated approaches that link services across various levels of intensity and allow for greater individualization in programming over time (Dryfoos, l994; Weissberg & Greenberg, l998; Brooner & Kidorf, 2002). This individualization in programming occurs via *adaptive treatment strategies* (Conduct Problems Prevention Research Group, 1992; Sobell and Sobell, 1993,1999,2000; Brooner & Kidorf, 2002, Collins, Murphy & Bierman, 2002).

In adaptive treatment strategies the treatment level and type is repeatedly adjusted according to the individual's need. For example, consider an addiction maintenance study for alcohol dependent subjects. Following an intensive outpatient program, alcohol dependent subjects are prescribed the opiate antagonist naltrexone, which has been shown in prior research to reduce alcohol use, particularly episodes of "heavy"drinking (5 or more drinks per sitting) (O'Brien & McKay, 2002). Then over the next months, subjects are monitored. If during a defined period, the subject has more than one heavy drinking day (yet is compliant with naltrexone medication) then the subject receives an increase in care via a combined motivational enhancement therapy and cognitive behavioral therapy (CBI) in addition to the naltrexone

medication. In this adaptive treatment strategy only the subject who exhibits need (as defined by heavy drinking days) is offered an increased level of treatment (naltrexone + CBI).

In adaptive treatment strategies, the goal is to provide treatment that optimizes response. In this respect this treatment strategy more closely simulates real world clinical practice than the standard one-size-fits-all treatment. In the standard, or fixed, treatment strategy, the composition and dosage of the treatment is not varied in response to the needs or characteristics of individual subjects. In contrast, in an adaptive treatment strategy, both the dosage and treatment type may vary across individuals and within an individual over time. This variation reflects the needs of individual subjects.

An example of a fixed treatment strategy is a school-based drug abuse prevention curriculum that is to be delivered to all sixth through ninth graders in a particular school. Every component of the multi-component intervention that may be necessary for any particular subject is included in the curriculum, and each child is offered the same treatment. Contrast this with an adaptive treatment strategy used in the Fast Track (Conduct Problems Prevention Research Group, 1992, 1999a, 1999b) program. This is a multi-year, multi-component program designed to prevent conduct disorders in high-risk children. The Fast Track program included a core intervention delivered to all study subjects, plus several adaptive components. One of the adaptive components was home visits for family counseling, where the number of home visits assigned to each family varied depending upon level of family functioning. The dosage assignment of the adaptive components in Fast Track was time-varying, that is, family functioning were reassessed three times per year and dosage was readjusted accordingly.

Below we describe adaptive treatment strategies in greater detail; we review why and when we would want to use adaptive treatments. This is followed by an outline of design goals. See Collins et al., (2002) for further discussion.

What is an Adaptive Treatment Strategy?

Adaptive treatment strategies tailor the dosage and/or type of treatment to each subject by use of prespecified decision rules. The rules provide the mechanism whereby we translate subject's values on key characteristics, called tailoring variables, to dosage amount and type. Rather than delivering the same dosage and treatment type to every subject, an adaptive treatment strategy assigns different dosages/ treatment types across individuals, and within individuals across time according to their values on the tailoring variables. A subject may even be assigned no treatment at a particular time. For example, there may be individuals who do not receive certain components of a multi-component treatment or at certain times do not receive one of the treatment components. The assignment of a particular level of dosage and/or type of treatment is based on the individual's values on the tailoring variables**.** The logic is that the level or type of treatment required to address the needs of individuals varies according to these tailoring variables. For example, individuals who are characterized by a particular risk factor may require an intensive treatment, whereas less treatment will be sufficient (and perhaps optimal) for individuals who do not have this characteristic. In the Fast Track example above, family functioning is the tailoring variable; the treatment dosage is the number of assigned home visits for family counseling. In the addiction maintenance study, the number of heavy drinking

days is the tailoring variable and the treatment type is naltexone alone or naltrexone in combination with CBI.

Further Examples of Adaptive Treatment Strategies

In a wide sense adaptive treatment strategies are actually quite old. In any medication trial, ethical considerations require that researchers establish a protocol to monitor subjects for side effects and if necessary take the subject off treatment. In many cases, "safety net" interventions are provided to patients who do not respond to the experimental treatment. Such protocols can be termed adaptive treatment strategies, although the goal is to prevent morbidity rather than to provide treatment that optimizes response. Adaptive treatment strategies with the aim of optimizing response have been occurring with increasing frequency in the literature. For example, stepped care approaches as advanced by Brownell & Wadden (1991) and Sobell & Sobell (1999) and the expert system approaches as advanced by Velicer, Prochaska, Bellis, DiClemente, Rossi, Fava, & Steiger (1993) and Kreuter, Strecher & Glassman (1996) are adaptive treatment strategies.

The stepped care approach (Sobell & Sobell,1999, 2000) starts all clients on the lowest level of treatment and then steps up the treatment on the basis of the client's functioning during treatment. Breslin, Sobell, Sobell, Cunningham, Sdao-Jarvie & Borsoi (1999) describe and evaluate a stepped care approach for problem drinkers. A primary outcome was the percentage of days between the end of treatment and six months on which the clients consumed no alcohol (i.e., "percent days abstinent"). Initially all clients are assigned to a relatively low intensity intervention, Guided Self Change counseling (Sobell & Sobell, 1993). If a client consumed more

than 12 drinks per week prior to the third treatment session, the client was assigned a supplemental intervention that included an additional counseling session and progress reports at the 1 and 3 month aftercare contacts. Clients were not offered the supplemental intervention if they did not meet the drinking cutoff. Thus the tailoring variable was the number of drinks per week, which is a proximal measure of the primary outcome, days abstinent.

A second example of an adaptive strategy is given by Brooner and Kidorf's (2002) treatment of opioid-dependent individuals. This adaptive strategy is composed of two adaptive components. The first component is a stepped care approach in that all clients are provided methadone treatment and begin with the lowest level of counseling sessions (once per week). In this strategy the number of counseling sessions (dosage) is tailored to a proximal outcome, namely presence/absence of drug free urinalyses and to attendance at assigned counseling sessions. Clients are moved between higher and lower numbers of counseling sessions depending on these proximal measures. That is, the tailoring variables are outcomes of urinalyses tests and attendance at assigned counseling sessions. The absence of drug free urines and/or missed counseling sessions is interpreted as evidence of greater need for treatment (i.e. more counseling). The rationale for using attendance is that attendance at assigned counseling sessions is an indicator of progress toward abstinence. Assigning more counseling to subjects who miss sessions requires a second adaptive treatment component: "encouragement to adhere." Brooner and Kidorf link attendance at counseling to treatment features or characteristics that subjects value, in this case preferred time slots for daily methadone dosing and avoidance of a 30-day methadone taper combined with discharge from the program. It should be noted that discharged individuals are given a "second chance," in that they are guaranteed readmission to

the program within 24 hours if they agree to attend counseling sessions. Regular attendance at counseling sessions results in earlier daily methadone medication dosing and continued access to methadone. In this second adaptive treatment component, the tailoring variable is attendance at counseling sessions; the encouragement (dosage) is the timing of methadone dosing or discharge. Note that the second adaptive treatment component uses attendance at counseling sessions as a tailoring variable whereas the first adaptive treatment component uses both attendance and urinalysis as tailoring variables.

Expert systems in smoking cessation are adaptive treatment strategies. For example, the Pathways to Change (Velicer et al., 1993; Velicer & Prochaska, 1999; Prochaska, Velicer, Fava, Rossi & Tsoh, 2001) program is based on the Transtheoretical Model of Change (Prochaska, & DiClemente, 1983); this model describes how individuals can modify problem behaviors and acquire positive behaviors. In this smoking cessation program, smokers complete questionnaires that are used to classify the smoker into one of five stages of change[1] and collects information on recent failed quit attempts. The treatment takes the form of a individualized report that includes information on individuals in the same stage who went on to successfully quit smoking, strategies the subject can use to progress to the next stage and if indicated, relapse issues associated with a failed quit attempt. When the treatment strategy is time varying, that is, individuals are assessed repeatedly over time, the reports also include indications of the progress the smoker is making through the stages of change. The tailoring variables include the stage of change and recent failed quit attempts; the treatment is the report. Similarly Kreuter and Strecher (1996) evaluate a one-time intervention that involved individually-tailored feedback to a health risk appraisal. Subjects completed a questionnaire that included assessments of a wide

[1] These are Precontemplation, Contemplation, Preparation, Action, and Maintenance; see Velicer et al., 1993.

range of health-related behaviors such as smoking and exercise, and perceived barriers and benefits of the health-related behaviors. Each subject's answers to the assessments served as the tailoring variables. These answers were used to select printed behavior change information targeted at the individual's health risks and perceived barriers to behavior change. The rationale behind the tailoring in these expert system approaches is that selected, personally relevant information will be attended to and thoughtfully processed, and thus will be more efficacious (Kreuter, Strecher & Glassman, 1999). Another example of an adaptive treatment is the Systolic Hypertension in the Elderly Program (SHEP; Cooperative Research Group, 1988; Borhani et al., 1991). See Lavori, Dawson and Rush (2000) for the rationale in designing adaptive treatment strategies for use in treating mental illness.

Why use an Adaptive Treatment Strategy?

Adaptive treatment strategies are promising alternatives to fixed treatments whenever subjects are heterogeneous in their need for treatment. Thus in order to optimize response, the type or dosage of treatment should vary by subject. In psychiatry, for example, some subjects respond well to medication alone whereas other subjects may require a talk therapy to respond well. Adaptive treatment strategies are also promising alternatives to fixed treatments whenever subjects are heterogeneous in their response to treatment; for example, some may respond best to a high level of treatment while others respond best to a low level of treatment, and some will respond best to longer periods of treatment rather than shorter. Heterogeneity in need is common in the management of chronic relapsing disorders (addictions, mental illnesses, etc.) since some individuals can go long periods without treatment and maintain health while others require more

frequent treatment to maintain their health. If the treatment is expensive, either in staff or subject time or money, adaptive treatment strategies can be used to reduce waste by avoiding giving low-risk individuals a higher dose when a lower dose would have been as effective. We would consider using an adaptive treatment strategy when there are several useful interventions, all equally efficacious but differing in the type of side effects or demands on the subject. In these cases, adherence or lack thereof may be the difference between an effective treatment and ineffective treatment. One potential way to increase adherence is to tailor the treatment to the subject's preference. As mentioned above another important reason to use an adaptive treatment strategy is to avoid side effects due to over treatment. Such side effects can be obvious and life threatening as in the overdose of a medication. However often the side effects are subtle. For example, in a multi-component intervention, attempting to provide too much of one component may result in reduced adherence to other components of the intervention and thereby reduce the overall effectiveness of the multi-component intervention.

When should we consider an Adaptive Treatment Strategy?

We should consider an adaptive treatment strategy whenever significant moderators of the effect of the treatment are available. These moderators can serve as tailoring variables in an adaptive treatment. The list of potential tailoring variables is almost endless, and naturally will depend on the study. Potential tailoring variables include both time invariant and time varying individual, family, or contextual characteristics that represent risk or protective factors which influence responsivity to (or need for) various types or intensity of treatment. Potential tailoring variables also include proximal outcomes measuring treatment responsivity or mediators of treatment. For further elaboration and explanation of the relationship between moderators and

tailoring variables see Collins et al. (2002). For example, if some individuals (e.g., those characterized by high values on the tailoring variable) will not respond to low levels of a treatment but will respond to higher levels, whereas others (e.g., those characterized by low values on the moderator) will respond about the same, or even better, to low levels as they will to high levels, an adaptive design allows for the cost-effective and efficient delivery of different levels of treatment to these groups.

If in a given situation, we are uncomfortable with the implicit assumptions or requirements made by using a fixed treatment strategy we would consider adaptive treatment strategies. Some of these assumptions follow. In using standard or fixed treatment strategies, we assume that although individuals may have different treatment needs, the treatment is in no way diluted or made counterproductive for an individual if components that are particularly relevant for that individual are embedded in components that may have less relevance. In a fixed treatment strategy all subjects receive the same dose of treatment; we assume that side effects from overtreatment are minimal. Therefore, fixed treatment can be appropriate if the concentration of services is not counter productive in some way. However, fixed treatment strategies may be prohibitive from an economic standpoint, even if they do not "harm" some patients through overtreatment. Indeed a requirement of a fixed multi-component treatment is that all components must delivered to all subjects, thus often treatment components that are expensive in terms of money, expertise, time, or logistics cannot be included. Or, certain treatment components that might help some individuals are not included because they would have a harmful effect on other subjects. For example, some individuals might benefit from additional counseling, but if an attempt were made to administer this to all subjects, those who

do not need the counseling would forgo other opportunities such as participation in pleasurable social or recreational pursuits, mutual support groups, or other health promoting activities. In addition such individuals may drop out of the study, thus depriving them of the benefits of other treatment components.

Designing Adaptive Treatment Strategies

In designing and evaluating an adaptive treatment we have two primary goals. These are first to maximize the strength of the adaptive treatment strategy and second to maximize replicability. The first goal is obvious! The second goal is less obvious and thus requires some discussion. Replicability means that when a study is repeated on different samples, the same population-level treatment effect is being estimated in each sample. The idea of replicability is an important one in the evaluation of treatment effects. We have the most confidence in a treatment when its effects are replicable with different experimenters, different clinical staff, different locations, etc. In fact, one aspect of replicability is what Flay (1986) has termed "effectiveness," the ability of the treatment to maintain the desired effect under real-world implementation conditions. This is the ultimate goal of most treatment researchers.

Replicability in an adaptive treatment strategy is closely linked to fidelity of implementation of the decision rules. When the rules in an adaptive treatment strategy are not well implemented, there is a resulting reduction in replicability. This is because it is possible to attribute the obtained results to factors other than the treatment. These factors are called alternative explanations. These alternative explanations stem from lack of specificity or clarity concerning the adaptive procedures, or unknown or known reasons why there was implementation infidelity. For example, suppose in one study, clinical staff occasionally use

considerations other than the established decision rules to make dosage/treatment assignments. This means that we are unable to attribute any treatment-control differences (or lack thereof) solely to the treatment; differences may be due in part to any undocumented and unplanned procedures followed by the clinical staff. To the degree that clinical staff in all other implementations of the treatment strategy do not make use of these same considerations, the results obtained in this study will not be replicable. The principles outlined below can be used to establish clear definitions of fidelity, thereby helping researchers to encourage and maintain implementation fidelity and, by extension, replicability.

In order to identify some fundamental principles of the design of adaptive treatment strategies, we need to highlight an essential difference between fixed treatment strategies and adaptive treatment strategies with respect to exactly what constitutes the treatment. In the adaptive case, the treatment strategy consists of not only the treatments, but the treatments inextricably coupled with the entire system for assigning treatment type and dosage. In other words, the choice of tailoring variables, the measures of the tailoring variables, the decision rules linking tailoring variables to treatment type and dosage assignment, and the implementation of these rules *are a part of the treatment strategy*. (Note that according to this framework, individual staff, treatment sites, etc. are not part of the treatment strategy. Rather, they are sources of extraneous variance.) Each of the following four parts of the treatment strategy are important: choice of tailoring variables, measurement of tailoring variables, derivation of decision rules, and implementation of the decision rules. Below we provide brief discussions of each of these parts; a more in-depth discussion can be found in Collins et al. (2002).

We maximize the strength of the treatment strategy by using appropriately chosen tailoring variables, measuring the tailoring variables well and by using appropriately chosen decision rules. We maximize replicability in future experimental and real-world implementation conditions by clearly specifying the treatment strategy (tailoring variables and decision rules) and by maximizing implementation fidelity.

Choice of tailoring variables

The identification of key individual (or group) characteristics that would be associated with different responses to treatment outcome in a fixed treatment, and that can serve as tailoring variables, is an important factor leading to a strong adaptive treatment strategy. In the case of preventive-interventions, key risk and protective factors and indicators of the developmental processes associate with the maladaptive behavior are all potentially useful tailoring variables. Other potential tailoring variables are mediators of the treatment or proximal measures of distal outcomes.

Consider the family counseling component of Fast Track (Conduct Problems Prevention Research Group, 1992, 1999a, 1999b) again. Recall that the goal of Fast Track was to prevent conduct disorders in high-risk children. This program is based on longitudinal research that suggests the developmental course of conduct disorders involves the interaction of multiple risks, including child characteristics, parenting difficulties, community factors, and academic and social maladjustment (Dodge, Bates, & Pettit, 1990; Offord, Alder, & Boyle, l986; Patterson, Capaldi, & Bank, l991). Any one family and child may exhibit only some of the risks. The purpose of the family counseling component is to address the parenting difficulties and general

family functioning. Past family functioning was expected to moderate the effect of family counseling on later child behavior.

It was expected that families with a high level of problems would benefit from intensive family counseling, and that this level of intensity was needed to promote positive intervention effects. In contrast, for families with few of these problems, it was anticipated that less family counseling would be sufficient to promote positive child outcomes, and higher levels might have a negative impact (e.g., stigmatizing families, reducing parent self-efficacy, fostering dependence on home visits for solving everyday problems). An additional risk was that families might feel burdened by family counseling they felt were excessive and intrusive, fueling resentment of the program and reducing participation in other intervention components, thereby reducing intervention effects. Hence, the optimal impact of intervention was expected when the level of family counseling was tailored to the time varying level of family functioning, avoiding the potential loss of intervention effects associated with insufficient or excessive home visiting. Additionally during intervention family functioning was expected to mediate the effect of past family counseling on later child behavior thus family functioning is indicative of responsivity to the intervention.

Next consider the addiction management study for alcohol dependent subjects. A primary outcome is percent heavy drinking days and the treatment strategy is to increase from naltrexone medication alone to naltrexone + the more comprehensive behavioral treatment protocol (e.g., CBI), on the basis of a measure of heavy drinking (number of heavy drinking days within a defined period). So here the tailoring variable is a proximal outcome. The rationale is that heavy drinking days are indicative of responsivity to treatment and thus should be used to decide if the treatment should be changed. Contrasting the two examples we see that in the family counseling component a

moderator/mediator, family functioning, is the tailoring variable yet in the addiction management study a proximal measure of the primary outcome is the tailoring variable. Although proximal measures of the primary outcome of conduct disorder, such as teacher ratings of daily oppositional-aggressive behavior, were available, these proximal measures were not used as tailoring variables in the assignment of family counseling. This is because not all children with problem behaviors come from families possessing the risk factor of family problems and parenting difficulties; such children exhibit deficits in other domains such as social and academic functioning. Thus a high level of oppositional-aggressive behavior does not necessarily indicate family problems and thus need for family counseling.

These two examples also highlight an additional important factor in designing adaptive treatment strategies—whether changes in treatment are done proactively or reactively. Ideally, it is better to adjust treatment to optimal levels before a "bad" initial outcome occurs. This approach is taken in the Fast Track example, where intensity of family functioning is determined by family functioning. However, this requires a strong theory or prior research findings that point to tailoring variables with high sensitivity and specificity as markers of future outcomes. In the case of naltrexone, such predictors of response to this medication have not yet been identified. Therefore, the addiction management protocol had to make use of proximal outcome variables to determine whether changes in treatment were warranted—a "reactive" rather than proactive approach. Note that like Fast Track, the expert systems approach in smoking cessation also uses strong theory to form markers of future outcomes (e.g. stages of change) and uses these markers as tailoring variables.

Measurement of tailoring variables

Every dosage assignment decision made about an individual in an adaptive treatment strategy begins with the individual's value on the relevant tailoring variable. To the extent that the tailoring variable is well measured (and the theory is correct), the appropriate dose of the treatment will be assigned; to the extent that the tailoring variable is measured poorly, it is possible that inappropriate or even insalubrious doses will be assigned. Thus the quality of the measurement of tailoring variables in an adaptive treatment strategy is critical.

In some settings, the tailoring variable may be relatively straightforward to measure, such as whether a urinalysis is positive for opiod use. However in many studies, the tailoring variables are more difficult to measure. Take for example, the measurement of number of heavy drinking days. In order to produce a reliable and valid measure of number of heavy drinking days it may be important to corroborate self-reports of heavy drinking; for example using reports by the spouse or significant others or via biological measurements such as blood or breath tests. Sometimes the tailoring variables are of considerable theoretical interest quite apart from their role in treatment assignment; they may play the role of a mediator or intermediate outcome, and therefore the researchers have already thought through how best to measure them. However often well-established measures of important tailoring variables may not be available, and research is needed to develop reliable and valid measurement instruments. An important constraint is that results from assessments that yield tailoring variables should be available rapidly, so that decisions regarding therapeutic dosage can be made in a timely fashion.

Derivation of decision rules

The decision rules form the basis for assigning the optimal dose or type of each treatment component to each subject, based on that subject's values on the relevant tailoring variables. With effective decision rules, each component of the intervention is delivered in the intended intensity to the intended individuals. With ineffective decision rules, some individuals will receive an inappropriate dosage of some components, or possibly even an inappropriate treatment. Thus ineffective decision rules reduce the effectiveness of adaptive treatment strategies.

There are three important characteristics of good decision rules. First, such rules are based on an accurate model of the relations among tailoring variables, treatment dosage, and outcome. Thus the clear and thoughtful articulation of this model is very important. Second, good decision rules are objective. They clearly operationalize the type of treatment and dosage to be given and the value (or range of values) on the measure of the tailoring variable. For example, an decision rule that states "individuals who return to heavy drinking should receive CBI in addition to naltrexone" is insufficient; a better decision rule states " individuals who experience greater than 1 heavy drinking day within a two month period after 10 consecutive days of taking naltrexone medication during the first month should receive weekly CBI in addition to naltrexone." This statement contains an operational definition for the rule connecting the tailoring variable (days of heavy drinking) to treatment (naltrexone plus CBI) and the dosage of treatment. Third, good design rules are as comprehensive as possible, covering anticipated situations that can occur in practice, including situations where the measure of the tailoring variable is missing or ambiguous.

As has been discussed above, the philosophy underlying adaptive treatment strategies is that a given treatment will not have the same effect for all individuals. Instead, for a given treatment individuals with certain values of the tailoring variable will enjoy a more beneficial treatment effect, or suffer a less beneficial effect, than individuals with other values. Another way to think of this is that in order to achieve a particular desired treatment effect, different dosages or types of treatment may be needed for different individuals.

Consider the addiction management study for alcohol dependent clients. In order to derive the decision rule relating the tailoring variable (number of heavy drinking days) to the timing of a step up in treatment from the medication naltrexone to naltrexone + CBI, researchers used the results of past trials. In the past trials, clients who experienced more than one heavy drinking day within the first two months while taking naltrexone rarely if ever improved if maintained on the medication alone (unpublished data, personal communication from David Oslin, Treatment Research Center, University of Pennsylvania). This led to the rule: as soon as the client experiences more than one heavy drinking day (within first two months) then the more comprehensive behavioral intervention is added to naltrexone treatment. In general, prior research is particularly valuable in articulating the decision rule, but is not the only appropriate source of information; in fact, in many areas in treatment there will be little or no prior research to draw upon. Other sources likely to be helpful are scientific theory in the area and prior clinical or treatment experience. In most cases, the task of articulating the model will require gathering any and all available information, assembling the research team and clinical staff, and carefully thinking through and discussing “If we were to give this dosage to people

with this characteristic on the dosage moderator, what treatment effect would be expected?" See Collins et al. (2002) for further discussion.

Implementation of Decision Rules

The final link in the chain constituting an adaptive intervention is the optimal implementation of the decision rules. The optimal way to implement decision rules is universally, in other words, to apply them consistently across study subjects, time, implementation site, staff member, and every other set of circumstances, so that the decision rules are applied identically to any subject with the same values on the tailoring variables. In an optimal intervention design, design rules are established before the intervention begins, so that there is no variability or "drift" in how they are carried out as a study progresses. Another important implication is that when decision rules are optimally implemented there are no changes or exceptions made on an ad hoc basis. In suboptimal implementation of decision rules, some persons are treated differently from others, because the dosage assignment is based in part on factors that do not figure in the decision rules and may be unique to a certain individual, time, or situation. Suboptimal implementation of decision rules can introduce random error into the treatment, thereby lessening its effectiveness. It also can introduce unknown, systematic error into the treatment, thereby reducing our ability to replicate the comparison of the adaptive treatment strategy with other conditions.

Suboptimal implementation may occur for many reasons. Clinical staff may perceive that the decision rules are inappropriate or less appropriate in a particular case due to extenuating circumstances. Important tailoring variables may be omitted or the decision rule uses the tailoring variables in an inappropriate way, or the tailoring variable is poorly measured so that

staff perceive that the tailoring variable does not emphasize the appropriate aspects of client need. Staff may also feel that the design rules were stated ambiguously, or due to insufficient training or supervision, the staff may lack a clear understanding or acceptance of the rationale for the decision rules. The last reason indicates a need for additional staff training and supervision, or clarification of the rules whereas the prior reasons indicate a need for a change to the decision rules themselves.

One approach to deal with staffs' desire to deviate from the decision rules, is for the research project to hold regular meetings of the scientific and clinical staffs, on an ongoing basis, for the express purpose of discussing cases in which staff wish to deviate from the decision rules. This will require staff to present a carefully thought-out argument why the rule should be not followed for a particular client. In many cases, this will lead to clarification of the decision rules. In some cases, the scientific and clinical staff may be convinced that it is necessary to make an exception to these rules. If a careful log of such cases is kept, including a detailed explanation of why an exception was made, this information can be used to describe the implemented treatment with the aim of maintaining replicability, by using it to make sure that the same procedure is followed in any future implementations of the treatment. Furthermore, the information in this log will be helpful in fine-tuning the decision rules for future studies. However, to the extent that individuals with the same tailoring variable values are assigned treatment dosage and type by relying on ad hoc procedures rather than the established decision rules, there will still be problems with replicability. The log will help to assess the extent of the problem, and possibly to prevent it in the future, but will not help to ameliorate it in the current study.

Summary and Future Directions

As discussed here, adaptive treatment strategies are an exciting and potentially very powerful approach to optimizing treatment. These adaptive strategies represent a vehicle whereby scientists can seek to improve the tailoring of treatment and dosage used in clinical practice. In comparison to fixed treatment strategies, adaptive treatment strategies utilize the heterogeneity in response to treatment to increase potency, improve adherence, reduce side effects and reduce waste. Certainly as treatment and prevention programs move in the direction of more comprehensive, multi-layered systems, adaptive components should become more common. At the same time, adaptive treatment strategies raise considerable scientific and methodological challenges. A challenging and contentious issue is the degree to which clinical judgment should be incorporated into the decision rules. Research is needed to identify the best ways to utilize clinical judgment: should this primarily be in the formulation of the rules? and/or should clinical judgment be a tailoring variable? and/or should the rules explicitly allow for clinical judgment? There is little research on this in the context of adaptive treatment strategies (see however Breslin, et al., 1997). Research is needed to build an empirical literature that can provide guidance in areas such as the identification of powerful tailoring variables and the development of measures that can serve as reliable and valid indices of these tailoring variables in the course of repeated clinical assessments. Research is needed on how we can better design and analyze experimental trials for identifying powerful tailoring variables and estimating the best decision rules so as to optimize response (for an analysis method see Murphy, 2002). Fulfilling the potential promise of the adaptive treatment strategies will require innovation and

technological refinement, with thoughtful conceptual articulation and careful empirical evaluation.

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