Allocating treatment options to patient profiles: clinical art or science?

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ABSTRACT

Background For many researchers, the disappointing results of Project MATCH were the death blow for any further activities in the field of patient–treatment interactions. On the other hand, we have an increased knowledge of patient heterogeneity and a greater variety of treatment options than before, and allocation guidelines for an ongoing process of patient-placement decisions are of high practical relevance. Aims To analyse deficits in the current research and to provide suggestions for future action. Findings It is argued that (1) certain major design aspects of Project MATCH and other research studies—such as stringent patient exclusion criteria and low treatment ‘dosage’—minimize the chances of detecting possible patient–treatment interactions and (2) Project MATCH obscures our view of previous treatment-allocation research findings. Conclusions Several research strategies and specific research topics are suggested for (1) improving the theoretical and methodological basis for detecting possible patient–treatment interactions and (2) stimulating research on major treatment decision needs, such as site, setting, time in treatment (extensiveness and intensity), service components and specific treatment modules. More international research cooperation is needed to clarify the inconsistent findings.

Keywords Addiction, patient heterogeneity, treatment allocation.

INTRODUCTION

In Finney’s (1999) comment on the legendary Project MATCH, ‘matching individual patients to treatment will remain more of a clinical art than a science’ was his final conclusion (for an overview and introduction to more than 100 articles, see Babor & Del Boca 2003) and in a series of commentaries in Addiction, many authors expressed more or less the same opinion (Gordis & Fuller 1999; Lindström 1999; Orford 1999; San 1999). What are the core conclusions? Should we aim for better research concepts and designs, or should we prevent further activities in the field?

This paper (1) analyses some of the possible deficits in current research designs for detecting patient–treatment interactions (using Project MATCH as an example) and (2) provides some suggestions for future research strategies and research designs. First, a comment on the terminology: As a general concept, the term ‘allocation processes’ instead of ‘matching’ is preferable because it (1) covers a broad range of treatment decision needs, e.g. out-patient versus in-patient, short- versus long-term, in addition to the selection of specific intervention techniques, such as Cognitive Behavioural Therapy (CBT) or Motivational Enhancement Therapy (MET); and (2) stresses the process character of decision making within an individual patient’s period of treatment. Other terms are ‘patient placement’ and ‘targeted’ or ‘tailored treatment’, sometimes amounting to a difference between ‘selective’ treatment-decision procedures (pre-treatment decisions among different options) and ‘adaptive’ treatment protocols (allocating treatment components according to treatment progress towards specific goals; McLellan et al. 2005). In both cases, allocating treatments to individual patient profiles is needed. The ‘stepped-care’ approach is not discussed (e.g. Sobell & Sobell 1999) because this concept allocates sets of interventions, gradually increasing in intensity, but in the same way to all patients.
THE NEED FOR ALLOCATION GUIDELINES

Research in the past provided evidence for patient heterogeneity. Patients with substance-use disorders were shown to differ among themselves in many respects, all of which have potential relevance for treatment decisions: e.g. in areas such as genetic vulnerability, substance use patterns, degree of dependence, comorbidity, cognitive deficits, cue-reactivity, motivation for change or type of social support. On the other hand, compared to the 1960s and 1970s a much broader range of effective treatment options have become available for alcohol, nicotine and other kinds of drug dependence. Both developments laid the groundwork for research and practical treatment questions, such as: should a heroin-dependent patient with some social support be detoxified in a standard in-patient setting, or would an out-patient intervention be equally effective and more efficient? Would it be helpful to provide a smoker with a pre-contemplation profile with a motivational treatment component first, and one with an action profile with just the behavioural technology to manage smoking cessation and to cope with craving? Or should an alcohol-dependent patient whose drinking is maintained by positive reinforcements (such as individual rewards and social support) receive a different treatment regimen than a patient whose drinking is primarily reinforced negatively? The underlying need for allocation guidelines in practical settings and for further research on this topic is neither new nor specific to the addiction field. Nearly 40 years ago, Paul (1967) published his challenge for future psychotherapy research in a frequently cited question: ‘What treatment by whom is most effective for this individual with that specific problem, and under which set of circumstances?’ (Paul 1967, p. 111). As usual, Freud (1905) was among the first to discuss this issue.

Third-party payers for treatment, such as health insurance companies, are a second source of pressure for allocation guidelines. They aim to avoid mismatches between patients and treatments which might lead to under- or over-treatment and the related adverse treatment effects and waste of financial resources. In the United States, the most widely used method for meeting these needs is use of ‘patient placement criteria’ (American Society of Addiction Medicine 2001). The guidelines define five levels of care (e.g. Level III: Residential Inpatient services), and within each service there are additional levels of intensity (e.g. staff–patient ratio) according to patient needs along six dimensions: need for detoxification, medical complications, emotional/behavioural complications, treatment acceptance, relapse potential and recovery environment. The guidelines are available separately for adolescents and adults and in a computerized version that includes a decision-making algorithm.

THE DISCREPANCY BETWEEN HOPE AND EVIDENCE

Research progress on treatment allocation guidelines has been disappointing, and for many researchers Project MATCH was at first a milestone and a source of high expectations. However, after the data had been analysed it became the death blow for any further action in the field. While it is not necessary to repeat or summarize the extensive discussion on this enormous, 28-million-dollar project (for an introduction, see Commentaries 1999), one of the major results is worth pointing out: only four of 21 well-selected, a priori matching predictions were supported; the results are inconsistent between the out-patient and aftercare treatment arms of the study; and together the predictions have a limited theoretical basis and limited clinical relevance (Project MATCH Research Group 1997a; Project MATCH Research Group 1997b).

Some critical commentaries on Project MATCH argued that the design itself minimized the possibility of obtaining support for the matching hypotheses: (1) the patient exclusion rate was somewhat high (61%), reducing external validity (patient variability) for the sake of internal validity; (2) aftercare patients were exposed to ‘an intensive initial treatment prior to randomisation...’ (Project MATCH Research Group 1998, p. 636); and (3) the three different interventions had a low intensity for patients with a Diagnostic and Statistical Manual version III (DSM-III) diagnosis of alcohol dependence [e.g. average utilization figures were 3.3, 8.3 and 7.5 sessions in the out-patient arm of MET, CBT and 12-Step facilitation (TSF), respectively]. Such low figures reduced the chances of finding matching effects from the outset. Additionally, the standardized assessment and follow-up procedures were extremely intensive (six interviews in the first 15 months, or about 15 hours), so that the ‘treatment’ commonalities exceeded the differences, again with the effect of reducing the chances of detecting any existing matching effects. The baseline and follow-up assessment ‘interventions’ could have been the major source of impact on treatment outcome rates. Unfortunately, however, there was no control group that would allow this possibility to be confirmed. In short, the critical point is that major aspects of the study design may have minimized the probability of detecting possible existing matching effects, and the interventions might have been too short to yield differential treatment effects and for patient–treatment interactions to unfold.

It would be short-sighted to blame the Project MATCH design for the current discrepancy between hope and
evidence; many other patient-placement studies have shown similar disappointing results, including those for the treatment of alcohol use disorders (Finney 1999), smoking cessation among alcohol-dependent patients (Kröger, Metz & Bühler 2004) and heroin/methadone maintenance among heroin-dependent patients (Blanken et al. 2005). Research on the American Society of Addiction Medicine Patient Placement Criteria (ASAM-PPC) has found few effects (McKay et al. 1997) or limited evidence (Konsanke et al. 2002; Magura et al. 2003) in specific areas such as the level of care, but overall ‘the initial results on the validity of the ASAM-PPC are rather mixed’ (Gustafson 2005; for a comprehensive review of the research, see Gastfriend 2003).

Some researchers have argued that even refining the treatment design such as that used in Project MATCH would not lead us to better results for allocation processes, because patient–environment–treatment interactions are of a much higher complexity than can be addressed by our current research technology (e.g. Finney 1999). What does this mean for the future of allocation guidelines and research directions? Does the present situation call for an end to asking which patient needs which intervention? Should practitioners forget about patient differences, disregard questionnaires on individual differences and be concerned only about providing care with treatment modalities whose overall effectiveness has been demonstrated (e.g. as described by Miller & Wilbourne 2002)?

**FUTURE RESEARCH OPTIONS**

Simply having more refined and extended Project MATCH designs, despite some general scientific scepticism (e.g. Hall 1999; Lindström 1999; Negrete 1999; Orford 1999), might increase our knowledge of allocation processes, but financial and other resource limitations will certainly keep the number of studies using this type of research design small. As an alternative or additional approach, I suggest a combination of conceptual and methodological changes for future research strategies and designs. These are neither new nor ground-breaking suggestions, but together they would allow us, in a heterogeneous manner, to learn more about (1) the factors that influence current practitioners’ decision making and the outcomes and results of these decisions and (2) the relevance of specific patient characteristics and other factors for treatment-allocation procedures. In part, the suggestions refer to the methodology and results of long-term research activities on patient–treatment interactions that were almost forgotten because they were overshadowed by Project MATCH (e.g. Mattson et al. 1994; Gastfriend & McLellan 1997; Gastfriend 2003).

**Suggestions for conceptual changes in allocation research**

*Extend the scope of relevant factors in change processes*

Most research designs are based on the assumption that the type of treatment intervention (the independent variable) is the major source of change in a defined problematic behaviour (the dependent variable). Other possible relevant causal factors (such as social support, patient–therapist interaction and treatment site) are neglected or, at best, are considered as a moderating source of outcome variance.

*Clarify the relevance of social support for maintaining or reducing problematic substance use.* In his or her daily routine, a patient’s social support system seems to be a critical factor in treatment outcome. The impact might be negative (maintaining contact with a drinking or drug-using culture) or positive (supporting reduced use or abstinence). Such external factors are difficult to measure, control and manipulate in treatment designs, and many studies ‘neutralize’ these influences as nuisance moderator variables by excluding problematic patients (e.g. Project MATCH required that patients have some level of support system and housing stability). However, the level of change-orientated social support might also be a mediating variable. There is preliminary evidence that developing a positive social support network would improve addiction treatment outcome (Galanter 1999; Copello et al. 2002). Individual differences in the type and degree of social support might be highly relevant for allocation procedures.

*Study patient–therapist interactions.* There is some general agreement that patient–therapist interactions might be relevant for treatment outcome, and some researchers believe that allocating patients with specific profiles to specific therapists might improve outcome. ‘Interaction’ effects are a complex group of mediating and moderating processes, and might include treatment climate, perceived competence and interest in the patient’s recovery (from the patient’s viewpoint) or cooperation and perceived willingness to change (from the therapist’s viewpoint). More knowledge about this ‘old’ topic might also improve allocation guidelines.

*Study site effects.* Project MATCH represents a high degree of methodological rigour for avoiding critical intervening variables, such as variations in staff training or treatment delivery. Nevertheless, intervention × site interactions did occur (Project MATCH Research Group 1998, p. 633) and should be studied in greater detail. Some patients with specific disorder profiles probably fare better at a specific site within a particular type of setting.
Our general understanding of allocation procedures (as discussed earlier) is that they cover such decisions about patients’ needs, which are also relevant for patients’ daily routine.

**Clarify the relevance of patient decision making for treatment allocation**

Allocation procedures are usually based on ‘objective’ variables, such as type and severity of the disorder or severity of the living conditions (e.g. homelessness). However, research on patient choices as potential ‘subjective’ variables is scarce, with the exemption ‘motivation for change, as discussed next’.

**Analyse the relevance of motivation/readiness for change.**

There is some agreement that a willingness to change a problematic behaviour is a basic prerequisite for entering treatment. Therefore, the stages-of-change (SOC) model of DiClemente & Prochaska (1998) gained much scientific interest, and the first empirical support from smokers was promising. However, later results with other types of substance abuse were mixed. Project MATCH did not support the relevance of the concept, nor did a study in Germany on smoking cessation among alcohol-dependent patients (Kröger, Metz & Bühler 2004). It is probable that our measurement technology should be refined (see Sutton 1999), or individual variations in ‘readiness for change’ are highly dependent on complex interactions among treatments, clients and environments which would lead us to intervention programmes with multiple MET components, according to specific but changing characteristics during the course of treatment. The SOC model is possibly too simple to be adequate in specific situations; West (2005), in fact, even suggested totally abandoning the model.

**Clarify the role of patients’ treatment choices.**

It is possible that that the choices of drug-dependent patients have traditionally played a much greater role in treatment allocations (e.g. to methadone maintenance or abstinence therapy) than those of alcohol-dependent patients. However, little objective information is available either on this point or on the relevance of patients’ decision-making in their treatment outcome.

**Search for mediator and moderator effects**

A plea for conceptual changes demonstrates the need for a renaissance in theory-driven statistical analyses of mediators (intervening mechanisms that are responsible for the link between treatment and outcome, such as increased patient self-efficacy) and moderators (patient or social factors that influence the association between treatment and outcome, such as the degree of comorbidity). We need this type of information to understand more effectively the relevance of change factors and patient variables for treatment outcome. The study by Finney, Hahn & Moos (1996) analysing treatment-setting effects is a good example of this type of research need, as are the ‘causal-chain’ analyses of the Project MATCH data set (Longabaugh & Wirtz 2001).

**Consider treatment ‘macro-level’ allocation needs in practice**

Choices between CBT and MET are of limited relevance compared to much more controversial and—at least in some countries—much-debated treatment placement decisions, such as the setting, duration and intensity of treatment and the choice of relevant problem areas to be targeted.

**Determine the need for in-patient/residential interventions.**

In-patient/residential interventions play a much greater role in Europe than in the United States, especially in some countries such as Germany. However, Europe is currently seeing a rapid shift to day-care or out-patient treatments. We know of some patient characteristics that favour in-patient/residential/day-care settings (e.g. sociopathy, severe psychopathology, a negative social climate, low social stability and low social competence; Finney, Hahn & Moos 1996; Gastfriend & McLellan 1997), but our knowledge of one of the major decision needs in addiction treatment is somewhat limited.

**Improve the knowledge on duration versus intensity of interventions.**

Dosage of intervention is probably related to outcome and is highly relevant for treatment-decision processes. However, the evidence is mixed: some studies have not found a significant relationship (e.g. Edwards et al. 1977; Miller & Hester 1986); other studies have found a positive relationship (e.g. McLellan et al. 1993; Süß 1995; Monahan & Finney 1996; Sonntag & Künnzel 2000). It is probable that the very short duration of treatment in the United States, compared to Germany, has not allowed enough statistical variance within studies conducted in the United States to detect significant effects. In most cases ‘dosage’ is operationalized as ‘time-in-treatment’, but we need more knowledge about the effects of systematic variations in the duration versus intensity of treatment. It might be that for patients with deficits in behavioural competences (e.g. the ability to cope with cognitive and social drinking cues), greater treatment intensity is required, whereas for patients with motivational deficits, time in treatment might be more important than intensity. In a similar manner, Finney (1999) and Humphreys & Tucker (2002) argue for more ‘extensity’ of treatment delivery (less intensity over longer periods of time). Again, this suggestion might apply only to patients with specific profiles.
Determine the choice of relevant problem areas for treatment. Traditional ‘broad-spectrum’ intervention programmes were based on a philosophy that a maximum number of problem areas should be treated within a maximum period of time. However, in order to improve treatment efficiency, we now try to select and allocate only necessary service components. Vocational therapy is a case in point. We agree that many patients do not need this treatment component, but a long-term heroin addict with no vocational competences might have a strong need for it. Friedmann et al.’s (2004) study on matching patients’ needs with service delivery is a good example of how to improve the basis for treatment-allocation decisions. Addiction Severity Index (ASI) ratings might be a basis for deciding the types of treatment that patients need.

Methodological suggestions

Maximize patient heterogeneity

Many researchers ‘streamline’ their research patients by excluding a large proportion of cases during the assessment procedure. Technically speaking, they reduce the variance in hypothetically relevant patient characteristics. This strategy reduces both the chances of detecting patient-placement information, and the external validity of the study. Reducing the external validity limits the transfer of research outcomes into practice; in fact, many practitioners complain that research patients do not reflect actual patient heterogeneity. Humphreys & Weisner (2000) showed that typical patient exclusion criteria result in treatment research samples of participants that do not reflect ‘real-world samples of substance abuse patients seen in clinical practice, potentially compromising the generalizability of results’. Therefore, patients with a broad range of characteristics should be studied, at least in Phase III clinical trials, in order to assess the adequacy of a treatment for particular subgroups of patients.

Maximize intervention heterogeneity

There is some doubt that only a few treatment sessions (e.g. from three to eight, as in Project MATCH) will have a significant 12-month follow-up effect on the percentage of patients with a long-term diagnosis of alcohol dependence (see above). Alternatives could be (1) to have a larger variation in the time and intensity of treatment and (2) to intensify the exposure of specific intervention techniques, in order to achieve larger between-treatment effects. In statistical terms, the more that the prevalence of the treatment outcome to be predicted departs in either direction from a 50/50% split in a sample (i.e. in samples where almost all or very few patients had the outcome being predicted), the lower will be the chances of detecting existing matching effects.

Implement more adequate research designs

Most patient–treatment interactions are analysed post hoc, based hopefully on a priori hypotheses. Miller & Cooney (1994) argued that such retrospective analyses are an equally valid strategy for analysing matching effects. However, very few hypothetical interactions have been tested and replicated later, using a prospective design in which patients have been allocated systematically to treatment options. Knowledge is limited if interactions identified through post hoc analyses (hindsight matching; Gastfriend & McLellan 1997) can be replicated using prospective allocation procedures (foresight matching). However, such procedures would be the critical test for utilizing research results in practical settings. In a research network that explores allocation issues (Bühringer et al. 2002), we are currently developing randomized controlled trials (RCTs) specifically for (1) cannabis-use disorders (see Zimmermann et al. 2004) and (2) heroin-dependent patients in methadone maintenance programmes (see Küfner et al. 2004), in order to consider a broad range of patient-disorder profiles. Participants in the cannabis study will be assigned randomly to standardized treatment (ST) or targeted standardized treatment (TST). The TST allocates systematically the same treatment components as those in ST, but it does so contingent on specific patient characteristics (e.g. ASI scores); Steingberg et al. (2002) used a similar design. The study of heroin-dependent patients on methadone maintenance, which is currently being carried out, uses a comparable design. Another approach for maximizing treatment outcome variations when evaluating allocation procedures is to compare patients who have been assigned randomly to interventions with those who have been matched or mismatched to particular interventions.

FINAL COMMENTS

Future options for post-MATCH allocation research and practice were the starting point for this paper. There is no simple answer, nor is there a single research strategy. There is, however, a clear need for more information about how to improve treatment decision requirements in daily practice. In my view, allocation covers a broad range of topics, from the selection of site and setting and duration and intensity of interventions, to the choice of specific treatment components. Environmental-, treatment-, patient- and disorder-specific characteristics all play a part. It has to be accepted that such complex multifactorial interactions cannot be teased apart with one or even several large-scale studies. The proposed research topics and strategies are more demanding in terms of scope and practical relevance, but they are more modest in terms of study design and speed of progress.
This paper is also a plea to researchers to recognize that complex issues need a greater variety of research strategies than classic RCTs allow. A variety of strategies is needed for the analysis of individual factors in naturalistic and observation studies, and for statistical modelling in order to integrate complex mediating and moderating effects on treatment outcome. Papers by Simpson (2001) from the drug field and Humphreys & Tucker (2002) from the alcohol field are exemplars of such an approach. In the case of long-term epidemiological designs, clinical trials and evaluation research will probably need to be merged in order to address allocation questions more thoroughly. Finally, we need more effective international cooperation for analysing discrepancies in the relevance of major patient–treatment interactions, such as duration and intensity of treatment or setting effects. Such a cooperation could also stimulate coordination between national activities in the development of evidence-based allocation guidelines (e.g. see Gastfriend 2003; Havemann-Reinecke et al. 2004). It is a long but worthwhile path from art to science.

Acknowledgements

This paper was written within the framework of the addiction research network 'Allocating Substance Abuse Treatments to Patient Heterogeneity (ASAT)'; contact information: asatkoordination@mpipsykl.mpg.de (http://www.asat-verband.de). ASAT is supported by grant no. 01 EB 0140–0142 from the Federal Ministry of Education and Research. The author thanks C. Metzner for assistance in preparing the manuscript. M. Cox, Ch. Kröger, H. Küßner and H.-U. Wittchen for their critical comments and M. Cox for assistance with the language.

References


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Addiction, 101, 646–652


