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The Influence of Genotype Information on Psychiatrists' Treatment Recommendations: More Experienced Clinicians Know Better What to Ignore

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ABSTRACT

Background: This study applies attribute nonattendance to medical decision making. We aimed to demonstrate how this type of analysis can be used in medical decision making to assess whether psychiatrists were influenced in their treatment recommendations by information on the genotype of a patient, despite knowing the patient's response to treatment as measured by the Positive and Negative Syndrome Scale. A patient's genetic information may be used to predict their response to therapy; such information, however, becomes redundant, and should not influence decisions, once a clinician knows the patient's actual response to treatment. **Methods:** Sixty-seven psychiatrists were presented with patients' pre- or post-treatment scores on the Positive and Negative Syndrome Scale for two hypothetical treatments for schizophrenia. Psychiatrists were also informed whether the patient possessed a genotype linked to hyper-responsiveness to one of the treatments, and were asked to recommend one of these two treatments. Attribute nonattendance assessed whether the information on genotype influenced psychiatrists' treatment recommendations. **Results:** Years of experience predicted whether psychiatrists were influenced by the genetic information. Psychiatrists with 1 year or less of experience had a 46% probability of considering genetic information, whereas psychiatrists with at least 15 years of experience had a lower probability (7%). **Conclusions:** Psychiatrists and other clinicians should be cautious about allowing a patient's genetic information to carry unnecessary weight in their clinical decision making.

Keywords: attribute nonattendance, discrete choice, medical decision making.

Introduction

Clinicians are becoming increasingly aware of how a patient's genotype can influence their response to treatment [1]. Tailoring treatments according to this anticipated response is known as stratified, or personalized, medicine [2]. In psychiatry, some genetic profiles in the population are associated with an increased risk of schizophrenia. Furthermore, some genetic profiles signal higher potential benefits of particular antipsychotic treatments [3,4], suggesting that for some patients psychiatric treatments could, in the future, be tailored to their genetic profile. Nevertheless, whether or how information about a patient's genetic profile influences psychiatrists' treatment recommendations is still unclear.

Genetic information may indicate the potential benefits that a patient could receive from a treatment but is redundant when the patient's actual response to a treatment is known. Thus, in certain circumstances, genetic information about a patient could bias the psychiatrist's clinical decision making. In particular, clinicians may view treatment outcomes differently when they are aware that the patient possesses a genotype that is indicative of hyper-responsiveness to a treatment. Consequently, when aware of a patient's genetic profile, a clinician may be less or more likely to recommend or continue a treatment even though the treatment may have been shown to be effective in the patient's pre- or post-treatment scores on a given symptom report scale. The potential for genetic information to bias clinical decision making in respect of a patient's treatment is known as *pharmacogenetic exceptionalism* [5]; this may result in an inefficient allocation of resources for public health. This article explores the topic by using a choice-format conjoint analysis (referred to as a discrete-choice

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experiment [DCE]) administered to psychiatrists in Northern Ireland.

In the practice of DCEs, respondents are presented with a sequence of choices for alternative options and are asked to select the one they prefer, with each alternative being described by different attributes and attribute levels [6–9]. A recent review showed a substantial increase in the application of DCEs in health economics and medical decision making and a desire to incorporate patients' and doctors' preferences in the study of effectiveness of treatments [10]. Indeed, the Food and Drug Administration recently stated that new cancer treatments must first assess patient preferences before becoming widely available to all patients [11]. The conventional underlying assumption of DCEs is that when choosing between alternatives, respondents rationally consider all the attributes presented and select the alternative that maximizes their utility. Nevertheless, research has seen an increasing focus on decision-making heuristics [12–14]. One particular type of heuristic widely explored by choice modelers in transportation [15–17] and environmental economics [18–20] is attribute nonattendance (ANA). In ANA, respondents may ignore one or more attributes that they believe are not relevant so as to simplify the process of choosing the best alternative [21]. The importance of ANA in modeling respondents' choices and preferences has been highlighted by its influence on both coefficient estimations and welfare analysis [17,22]. Recently, ANA has also been extended to health economics [14,23] in which researchers warn that not accounting for ANA may lead to biased health policies [24]. Within the context of medical decision-making research, however, ANA has not been widely used to assess which attributes (if any) are nonattended [23]. Researchers consider ANA a nonrational heuristic that should be included in the analysis to avoid bias, but should not be included if respondents acted rationally, as assumed by the framework in which DCE operates. This study departs somewhat from this perspective, because ANA is considered the correct heuristic that a clinician should apply because the patient's response to treatment is already known, making the patient's genotype information redundant.

This article's contribution to the literature is twofold. From a methodological viewpoint, ANA is applied in a new, present, and highly relevant context—stratified medicine—tackling the issues of coherence of information assessment in the psychiatrist's treatment selection. The novel methodological aspect here is the use of ANA to improve the understanding of the extent to which medical decision making incorporates irrelevant information. From a clinical perspective, the article aims to contribute to the topical issue of whether genotype information influences the treatment recommendations of psychiatrists when a patient's treatment response (in terms of symptom improvement) is already known to the psychiatrist.

Analytic Framework

The analysis of a DCE is based on the random utility maximization theory [25,26] in which the underlying assumption is that individuals select the alternative that offers them the highest utility. In this context, it is possible to denote with i the treatment that psychiatrist n recommended when considering the vignette t. The utility function that psychiatrists maximize when recommending a treatment can be described by characterizing each vignette using a vector of attributes (X) and a vector of parameters (β) to be estimated as follows:

$$U_{nit} = \beta' X_{nit} + \varepsilon_{nit}, \tag{1}$$

where ε represents the part of the utility function that the researcher cannot observe and is assumed to be an independent and identically Gumbel-distributed error term. With these definitions and assumptions, it is possible to mathematically specify the choice probability for each psychiatrist n selecting treatments i over j alternatives in the vignette t as a multinomial logit (MNL) selection probability [26,27]:

$$\Pr(nit) = \frac{\exp(\beta' X_{nit})}{\sum_{j=1}^{J} \exp(\beta' X_{njt})}. \tag{2}$$

This model is estimated as a benchmark and is the simplest starting point for behavioral analysis. Notwithstanding the importance and practicality of the MNL model results, the MNL has several restrictive assumptions. For example, preferences are homogeneous across respondents and choices are independent from irrelevant alternatives. These assumptions are often considered unrealistic and are likely to bias the results [28]. The mixed logit (MXL) model relaxes the restrictive assumptions underlying the MNL model and accommodates for the possibility that respondents may have different preferences [29]. Furthermore, the model fit to observed data is typically improved when estimating MXL models [30]. The models derived within the general framework of the MXL allow for taste parameters β to vary across respondents and to account for the fact that in the DCE, each respondent is observed across a series of T vignettes and can therefore be represented as a balanced longitudinal panel of responses on experimentally designed choice tasks (vignettes). If the value of β was known for each of the nth respondents, the probability of a sequence of choices would be given by Equation 3:

$$\Pr(y_{Tn}|\beta, X_{nit}) = \prod_{t=1}^{T} \frac{\exp(\beta' X_{nit})}{\sum_{j=1}^{J} \exp(\beta' X_{njt})} \tag{3}$$

Because it is impossible to know the value of β with certainty for each respondent, heterogeneity of preferences is estimated by allowing for random variation in β across respondents [7,31]. To address the research question, it is essential to understand whether psychiatrists are influenced by information about a patient's genotype in making their treatment recommendations. Therefore, we were interested in modeling ANA in this context while addressing preference heterogeneity. In this article, ANA was analyzed by means of behavioral latent class (LC) models, which are semiparametric variants of the MNL model. In LC models, it is assumed that each individual respondent can be implicitly sorted into a set of C behaviorally defined classes associated with certain estimated probabilities, with each class characterized by a unique class-specific pattern of ANA embedded in the utility parameters, β_c. With membership to class c, the probability of respondent n's sequences of choices y_{Tn} over T choice occasions is as follows:

$$\Pr(y_{Tn}|\beta_c, x_{nit}) = \prod_{t=1}^{T_n} \frac{[\exp(\beta_c')]X_{nit})}{\sum_{j=1}^{J} [\exp(\beta_c')] X_{njt})}. \tag{4}$$

Considering that the membership probabilities π for each behavioral LC c are also defined according to an MNL process, we have

$$\pi_c = \frac{\exp(\alpha_c + \gamma_c' z_n)}{\sum_{c=1}^{C} \exp(\alpha_c + \gamma_c' z_n)}, \tag{5}$$

where z_n is a vector of covariates characterizing respondent n, γ_c is a vector of associated parameters subject to estimation, and α_c is a class-specific constant. In the estimation of LC models, for identification purposes, only $C - 1$ set of coefficients can be independently identified (e.g., for one arbitrary class c, the vector $< \alpha_c : \gamma_c = 0 >$).