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High prevalence of personality disorders among healthy volunteers for research: implications for control group bias

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Abstract

Individuals who volunteer as control subjects for clinical studies are regularly screened for Axis I diagnoses, but seldom screened for Axis II disorders. This study examined the relative rates of Axis II diagnoses among 341 volunteers passing an initial telephone screen for entry into biological research studies. Axis I and II diagnoses by DSM-IV were assigned by best estimate after structured clinical interview, and subjects were categorized into one of three groups based on their diagnostic profiles: (1) volunteers without lifetime Axis I or II diagnoses (''healthy controls''), (2) personality-disordered volunteers without any history of Axis I pathology, and (3) personality-disordered volunteers with past (but not current) Axis I pathology. The results revealed a high prevalence of personality disorders (44.4%) among these volunteers. Several clinically relevant self-report inventories were used to demonstrate important characterological differences between the three comparison groups. Although inventory results demonstrated multiple differences between all three groups, most scales revealed differences between healthy controls and the two personality-disordered groups (with or without lifetime Axis I diagnoses), suggesting that most of the variance was accounted for by the presence or absence of an Axis II disorder, not a past Axis I disorder. These results suggest that personality-disordered volunteers may bias a control group due to the infrequent screening for Axis II disorders among volunteers for medical and psychiatric research. Implications are discussed for routine Axis II screening of volunteers for research with specific diagnostic instruments.

Keywords: Control group bias; Psychiatric research; Subject recruitment; Healthy volunteers; Personality disorders

1. Introduction

One of the defining characteristics of effective psychiatric or medical research is the use of ''healthy controls'' against which the population of interest may be compared. Although no clear consensus establishes what constitutes a healthy control, control groups are generally designed with two goals in mind. First, control groups may serve to represent the general population as a random sampling. A true randomization ensures that the control group accurately reflects the population from which it is drawn. Second, control group design involves screening to ensure that members lack the defining characteristic of the experimental group or other characteristics that may bias experimental results. Both of these goals are taken into consideration when recruiting volunteers for psychiatric or medical research.

Recruiting volunteers from a large non-clinical population supports the goal of random sampling. However, controls are frequently recruited from the community using advertisements offering incentives, such as payment or course credit. The initiative to respond to an

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advertisement and be willing to participate in research may itself distinguish volunteers from the general population. Similarly, the seeking of the particular incentive may distinguish volunteers from those in the population who do not seek the incentive. Multiple studies have determined that standardized personality rating scales conducted on research volunteers yield means that differ from general population means. For example, Eysenck Personality Questionnaire (EPQ; Eysenck et al., 1985) extraversion and neuroticism have been shown to correlate with willingness to volunteer in college students (Cowles and Davis, 1987), and the Freiburg Personality Inventory dimensions of extraversion, neuroticism, and nervousness correlate with medical student participation in pharmacology studies (Meyer et al., 1995). An Italian publication demonstrated that ''healthy volunteers'' for clinical trials differ significantly from Italian national means on the three validity scales and nine of 10 clinical scales from the Minnesota Multiphasic Personality Inventory (Berto et al., 1996). In light of their findings, the authors advocate the use of this instrument in evaluating volunteers for Phase I clinical trials. Using an inmate population, Walsh and Nash (1978) found that volunteers for medical research were more impulsive, manipulative, and exhibited more disordered thought processes than inmates who elected not to volunteer. Among a sample of putative healthy control subjects, individuals who chose to participate in a potentially painful procedure (lumbar puncture) were found to be more impulsive than those who declined (Gustavsson et al., 1997). This demonstrates an inherent problem in subject recruitment; namely, the research topic advertised in the recruitment advertisement differentially piques the interest of potential subjects, thus biasing respondents in a way that conforms to particular personality dimensions.

The aforementioned studies provide evidence that research volunteers may differ from the general population, and assist in describing these differences. However, they do not address whether volunteers' personality rating scale differences translate into clinically relevant differences. That is, it is unclear if these personality rating scale differences reflect significant volunteer biases in control groups. Also, these studies do not classify personality rating scale differences into diagnoses based on Diagnostic and Statistical Manual of Mental Disorders (DSM-IV; American Psychiatric Association, 1994) criteria; as such, they provide a limited contribution to the process of screening volunteers for potential exclusion from control groups.

The second goal of control group design involves screening to ensure that members lack the defining characteristic of the experimental group or other characteristics that may bias experimental results. Unfortunately, it is not always obvious what factors are relevant and have the potential to bias results. Furthermore, the ability to create an appropriate control group hinges on the ability to identify such factors in the first place. For this purpose, psychiatric research often utilizes standardized diagnostic instruments to screen for Axis I disorders and excludes diagnosed volunteers from serving as controls. Personality disorder diagnoses tend to be neglected during this process, although the suggestion that volunteers differ in ''personality features'' from the general population has been in the literature since the 1950s (Pollin and Perlin, 1958). Screening for Axis II disorders is not standard practice, perhaps due to the additional time, expertise, and expense necessary for diagnosis. This is an unfortunate trend, as no research to date has demonstrated that personality disorders do not introduce clinically relevant biases into control groups.

Research has addressed the prevalence of Axis I psychopathology among volunteers recruited to serve as controls in medical and psychiatric research, indicating a higher prevalence of psychopathology as compared to epidemiological population estimates. Prevalence rates of Axis I pathology among research volunteers have been estimated at 16.5–27.7% for current diagnoses and 35.6–41.2% for past (without current) diagnoses according to two studies which administered the Schedule for Affective Disorders and Schizophrenia (SADS) using Research Diagnostic Criteria (Halbreich et al., 1989; Schechter et al., 1994). These same studies report prevalence rates of 2.2–7% for personality disorder diagnoses, although they did not employ diagnostic tools specifically sensitive to Axis II symptomatology. A study seeking healthy subjects for paid research at a university hospital found that 26.9% of respondents passing a telephone screen were subsequently excluded due to Axis I diagnoses or psychoactive substance use, and 6.7% were excluded due to personality disorders (Shtasel et al., 1991). Diagnoses were made by psychiatric interview employing the Structured Clinical Interview for DSM-III-R: Non-Patient Version, while instruments more specific to personality disorder diagnoses were not utilized. The authors suggested that their telephone screening procedure was more rigid than in other studies, thereby minimizing the number of volunteers with psychopathology that proceeded to interview assessment. A small study of 49 research volunteers that employed the Structured Interview for Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) Personality Disorders (SIDP), as well as the SADS, diagnosed lifetime Axis I disorders at a prevalence of 32.6% and Axis II disorders (in the absence of lifetime Axis I diagnoses) at a prevalence rate of 20.4% (Thaker et al., 1990). By employing a diagnostic tool specific to Axis II disorders, this study more clearly demonstrates the potential for a high proportion of personality disorders among research volunteers.

The aforementioned studies imply a lifetime prevalence rate of mental illness as high as 69% (Halbreich