Avoidance and Inhibition Do Not Predict Nonrespondent Bias Among Patients With Inflammatory Bowel Disease

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ABSTRACT

Background: It has been suggested that participant withdrawal from studies can bias estimates. However, this is only possible when withdrawers and nonwithdrawers differ in an important way. We tested the hypothesis that withdrawers are more likely than nonwithdrawers to be avoidant and negatively affected.

Methods: A total of 1160 participants with inflammatory bowel disease were recruited at different sites in Switzerland. Their levels of avoidance coping and negative affectivity were rated by means of 2 short baseline questionnaires. One year later, they were sent a longer follow-up questionnaire. The primary outcome was return versus non-return of the follow-up questionnaire within 3 months. After controlling for potential confounders identified in an extensive literature search, we estimated the odds of returning the follow-up questionnaire for 1 standard deviation of avoidance coping and negative affectivity.

Results: The odds ratio for 1 standard deviation was 1.03 (95% confidence interval: 0.89–1.18) for avoidance coping and 1.02 (0.89–1.17) for negative affectivity.

Conclusions: The odds of returning the questionnaires did not depend on avoidance coping or negative affectivity.

Key words: refusal to participate; behavior and behavior mechanisms; bias (epidemiology)

INTRODUCTION

Clinical researchers regularly face the problem of a significant number of patients refusing to participate in a study or subsequently failing to return a questionnaire containing important information. In randomized clinical trials with a reasonable sample size, adequate blinding and concealment, and intention to treat analysis, these difficulties may limit the generalizability of findings. In observational research, however, if nonresponse is selective, ie, nonrespondents are not just a random sample of the sample, then estimates might be biased.1

The term “nonrespondent bias” (also referred to as volunteer bias, nonresponse bias [also used with different meanings], or nonparticipation bias) was first used in 1979 in a classic paper describing 9 potential biases of interest,2 and usage of this term has increased over time.3 A clear divergence of nonrespondents from respondents is a necessary condition for nonrespondent bias.1 Given the high frequency and proportion of nonrespondents in studies, efforts have been made to find out if such divergences exist and, if so, whether they are associated with certain characteristics. Several demographic parameters have been thoroughly investigated.4–8 However, data on personality characteristics that potentially influence nonrespondent bias are scarce.

In this study, we examined 2 novel personality characteristics—avoidance coping and negative affectivity. In avoidant coping, individuals react to a demanding situation by distraction or social diversion, particularly if the situation constitutes a difficulty that must be solved.9 This strategy may be useful in moderation: gaining distance from an obstacle by participating in social activities may help in more easily finding a solution later on. However, extensive avoidance coping may result in unresolved situations. Highly avoidant patients might attempt to escape from anything suggestive of their illness and might thus be more prone to postpone completion of a questionnaire.

Negative affectivity implies that given situations or experiences are more likely to provoke negative emotions and a negative perception of those situations. Negative affectivity is associated with irritability, anxiety, depression, and general mental distress. Individuals who are negatively
affected have unfavorable opinions of themselves and other people.\textsuperscript{10} Negatively affected persons receiving a questionnaire, for example, might be more likely to consider possible burdens and needed time and less likely to believe in personal and social benefits. Additional reasons for assuming that avoidant coping and negative affectivity might be involved in nonresponse are that both have been shown to be related to diminished medication adherence.\textsuperscript{11,12}

We hypothesized that people with chronic diseases who show evidence of avoidance-oriented coping and/or a tendency to experience negative affect might be less likely to respond to a questionnaire. Confirming one or both of these hypotheses would suggest an elevated risk of bias in cases of personality-related exposures or outcomes (eg, subjective outcome measures), which would necessitate the assessment of personality characteristics and the comparison of outcomes in respondents and nonrespondents. Conversely, a rejection of both hypotheses, with sufficient statistical power, would indicate a low risk of selective bias related to personality or coping strategies. In both cases, however, it would be necessary to further investigate whether common personality characteristics are possible contributors of nonresponse (eg, overcommitment to work may decrease nonresponse). We would like to emphasize that this study was not conducted merely to test if some other findings of our group might be biased by nonresponse. Our main objective was to find out if nonresponse is associated with avoidance behavior and negative affectivity, in order to provide important information for future studies of exposures or outcomes that might be related to these personality characteristics.

METHODS

Setting, design, and patients
Several studies have observed a higher response rate among individuals with a chronic condition, as compared with those without such a condition.\textsuperscript{7,13} Thus, we elected to examine psychological factors of nonresponse in a sample of participants who had the same chronic condition, ie, inflammatory bowel disease. In addition, emerging evidence suggests that this disease is associated with psychological factors.\textsuperscript{14} We therefore used data from a consecutive sample of adults with recurrent inflammatory bowel disease diagnosed according to the Lennard-Jones criteria.\textsuperscript{15} The data were collected from July 2006 through February 2008 by collaborators of the Swiss Inflammatory Bowel Disease Cohort Study in university hospitals, regional hospitals, and private practices in the Swiss cities of Basel, Bern, Geneva, Lausanne, St Gallen, and Zurich.\textsuperscript{16}

The ethical committees of all the study sites approved the study protocol, and the research was conducted in accordance with the Declaration of Helsinki of 1975. Once patients had provided written informed consent, we assessed avoidant coping and negative affectivity (the main predictors) by means of case report forms containing 2 self-rating scales, as outlined below.\textsuperscript{9,10} On the same case report forms, patients provided information on age, sex, marital status, education, employment, alcohol consumption, and smoking. One year after enrollment we sent them a longer questionnaire, which was sent directly to the participants by post. Those who did not return the questionnaire within 3 months were defined as nonrespondents to follow-up.

Because both rejection and confirmation of our hypothesis would provide important information to researchers, we were particularly concerned to adequately power our study. We enrolled 1150 participants, which yielded a power of 95% to detect an odds ratio (OR) for 1 standard deviation (SD) of 1.33 with projected proportions of 20% nonrespondents at baseline and 20% nonrespondents to follow-up and a 2-tailed \( \alpha \)-level of 0.05.\textsuperscript{17}

Examined predictors
To measure avoidance coping, we used the Task-Oriented Coping Scale of the Coping Inventory for Stressful Situations.\textsuperscript{9} Eight items are rated on a 5-point Likert-scale from “not at all” (1) to “very much” (5). The total value is equal to the mean of the items, and a minimum of 7 valid items is needed to compute a valid mean. To assess negative affectivity, we used the 7-item Negative Affect Subscale of the Type D Scale-14 because of its well-documented characteristics.\textsuperscript{10} Items are rated on a 5-point Likert-scale from false (0) to true (4), and the scores are summed. The total score ranges from 0 to 28. Up to 2 missing items can be replaced with the mean of the valid items, without significantly affecting the properties of the scale.

In the present study, the German and French versions had a variance of item means of 0.16 and a variance of item variances of 0.03, indicating good weighting of the Task-Oriented Coping Scale. Considering the brevity of the scale, a Cronbach’s \( \alpha \) of 0.79 indicated good overall reliability. The Negative Affect Subscale had even better quality measures: a variance of item means of 0.13, a variance of item variances of 0.05, and a Cronbach’s \( \alpha \) of 0.88. A shared variance of less than 1% showed very good distinction between the 2 personality questionnaires.

Since it has been demonstrated that avoidance coping and negative affectivity, as measured with the above described instruments, are consistent over time (test–retest reliability: 0.68\textsuperscript{9} and 0.72, respectively),\textsuperscript{10} we decided to wait a maximum of 9 months for questionnaires to be returned. In addition, every 3 months, we reminded late respondents at baseline to return the questionnaires, in order to minimize baseline nonresponse.

Outcomes
One year after enrollment, the patients received a longer follow-up questionnaire assessing disease-related quality of
Consumption22,23 and smoking status2,23 are believed to play a
predictors of nonresponse or late response. Moreover, alcohol
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and employment 13 have often been reported as possible
gender,6,13,19,20 marital status,6,21 educational level,5,6,13,19,20
potential source of selection bias,1
Although nonresponse is considered an important
mechanisms underlying response and nonresponse. Age,6,13,19
and alcohol, they showed the difference between those
smokers, respectively; for education, employment status,
and alcohol consumption, and smoking. Because
with negative affectivity as the main independent variable
and nonrespondents to follow-up. Second, we estimated
outcome) as a function of avoidance coping and negative
changes in the odds of response to follow-up (primary
and nonrespondents to follow-up. Therefore, as a proxy for
baseline. It was not possible to compute the relation between
the examined predictors (avoidance behavior and negative
and nonresponse at baseline, because these
d predictors were assessed in the baseline questionnaire.
Therefore, as a proxy for this relation, we examined the
relation between the suspected predictors and late response
at baseline, the time needed to respond to the baseline
questionnaires, in 1-month units). To test whether this proxy
(i.e., the continuum of the resistance model) was satisfactory,7
we also analyzed the relation between late response at baseline
and nonresponse to follow-up.

Control variables
Although nonresponse is considered an important
potential source of selection bias,1–3 little is known of the
mechanisms underlying response and nonresponse. Age,6,13,19
gender,6,13,19,20 marital status,6,21 educational level,5,6,13,19,20
and employment13 have often been reported as possible
predictors of nonresponse or late response. Moreover, alcohol
consumption22,23 and smoking status2,23 are believed to play a
role in response to surveys on alcohol consumption and
smoking. Because we found no external evidence to suggest
that nonresponse is different among patients with Crohn’s
disease, ulcerative colitis, and indeterminate colitis, we did not
control for different forms of inflammatory bowel disease.
However, for interested readers, we report the proportions of
patients with these disease forms.

Data analysis
First, we presented our sample and identified respondents
and nonrespondents to follow-up. Second, we estimated
changes in the odds of response to follow-up (primary
outcome) as a function of avoidance coping and negative
affectivity and computed the linear relation between both
avoidance coping and negative affectivity and time to base-
line questionnaire return (late response at baseline). We
used SPSS 15 for Windows (Chicago, IL, USA) for these
analyses.

Continuous variables were described by using means and
SD; categorical variables were described by percentages and
absolute values. Respondents and nonrespondents to follow-
up were compared by using mean or percentage differences.
For all differences, we supplied asymptotic 95% confidence
intervals (CIs) and 2-sided $P$ values, using the Mann-Whitney
U test for questionnaire scores, the independent $t$ test for age,
and Fisher’s exact test for sex, marital status, education,
employment, alcohol consumption, and smoking. Because
time to baseline questionnaires return was very skewed, we
used the Mann-Whitney U test despite the large sample size.

In a first model (model 1), we estimated the OR for 1 SD
of avoidance coping, while controlling for all described
control variables. The dependent variable was the odds of
returning the follow-up questionnaire. In a second model
(model 2), the same procedure was used for negative
affectivity. For avoidance coping, negative affectivity, and
age, the ORs referred to the factor by which 1 standard
deviation multiplied the odds of returning the questionnaires;
for sex, marital status, and smoking, they indicated the odds
for females divided by that for males, the odds for married
individuals divided by that for unmarried individuals,
and the odds for smokers divided by that for nonsmokers,
respectively. For the variables of education, employment
status, and alcohol, the OR referred to the odds of belonging
to a category compared with not belonging to that category.

In a third model (model 3), we computed linear regression
coefficients with time to return of baseline questionnaire as
the dependent variable and avoidance coping plus control
variables as independent variables. The same was done
with negative affectivity as the main independent variable
(model 4). For avoidance coping, negative affectivity, and age,
coefficients indicated additional months needed for 1 standard
deviation; for sex, marital status, and smoking, coefficients
showed the average difference in months between women
and men, married and unmarried people, and smokers
and nonsmokers, respectively; for education, employment status,
and alcohol, they showed the difference between those
who did and did not belong to the respective category
(e.g., fulltime employment vs no fulltime employment). All
ORs and linear relationships were provided with their
Corresponding 95% CIs and 2-sided $P$ values. The
significance level was 0.05.

RESULTS

Descriptive results
Of the 1149 enrolled patients, 1% died or left Switzerland
(mean age ± SD, 54.7 ± 19.4 years; proportion of women,
63.6%; proportion of patients with Crohn’s disease,
72.7%), and 15.9% returned no baseline questionnaire
(i.e., questionnaire-level nonrespondents) or an insufficiently
completed baseline questionnaire (i.e., item-level non-
respondents) (mean age ± SD, 38.7 ± 14.4 years; proportion
of women, 45.3%; proportion of patients with Crohn’s disease, 64.8%). As compared with respondents at baseline, the participants who died or left Switzerland were 12.4 years older on average (95% CI, 3.8–21.0 years; \( P = 0.005 \)), had a 12.1% higher proportion of women (−17.7% to 41.9%; \( P = 0.549 \)), and a 15.1% higher proportion of patients with Crohn’s disease (−14.3% to 44.5%; \( P = 0.373 \)). Nonrespondents at baseline were on average 3.6 years younger (1.3–5.9 years; \( P = 0.002 \)), had a 6.2% lower proportion of women (−1.7% to 14.1%; \( P = 0.146 \)), and a 7.2% higher proportion of patients with Crohn’s disease (0.6%–15.0%; \( P = 0.071 \)). For nonrespondents at baseline, there was no information on marital status, employment status, education, or alcohol intake, because this information was assessed with avoidance behavior and negative affectivity in the baseline questionnaire. The Figure summarizes the selection of the 955 participants for analysis.

Of the 955 analyzed patients, 594 (62.2%) returned the follow-up questionnaire within 3 months and 361 (37.8%) did not. On average, participants who did not return the follow-up questionnaire were 1.52 months later in returning the baseline questionnaires. Apart from the time span until baseline questionnaires were returned, smoking was the only characteristic that distinguished the patients who returned the follow-up questionnaire from those who did not (Table 1).

Main results
The odds of returning the follow-up questionnaire (models 1 and 2 in Table 2) showed no relevant or significant logit-linear dependence from avoidance coping (OR for 1 SD, 1.03; 95% CI, 0.89–1.18) or negative affectivity (1.02; 0.89–1.17).

Secondary results
Each additional SD (= 2.82 months) needed to return the baseline questionnaires decreased the odds of returning the follow-up questionnaire by 1.76 times (95% CI, 1.48–2.09; \( P < 0.001 \)). Because there were no data on avoidance coping and negative affectivity for nonrespondents at baseline, we used late response at baseline as an approximation for nonresponse at baseline (Table 3). Time to return of baseline questionnaire (models 3 and 4 in Table 3) showed no relevant or significant linear dependence from avoidance coping (linear increase for 1 SD, 0.15 months; 95% CI, 0.05–0.36) or negative affectivity (0.06 months; 0.14–0.26).

DISCUSSION
In a meta-analysis of response rates for 68 internet-based surveys, the average ± SD was 39.6 ± 19.6%.\(^{24}\) Providing overall estimates for participation rates in randomized clinical trials and cohort studies, or response rates for questionnaire studies, is difficult because rates vary greatly. Most researchers will agree, however, that response rates below 60% are not unusual and that 80% is very good.\(^{24}\) For this reason, it is essential for clinical research to investigate if nonresponse is accidental and, if not, whether it is systematically associated with particular characteristics to a relevant degree. Conclusive data are lacking, and
methodologists have focused almost exclusively on common
demographic parameters: younger age,7,19 and male gender,4,19
predicted later responses. Other studies performed in different
parts of the world found that younger age,6,13 male gender,6,13
being single or divorced,6,8,21 and a lower educational
level5,6,13 were associated with reduced participation. In

Quantitative variables are presented as mean ± standard deviation, and qualitative variables as percentages (absolute numbers). There were 955 (100%) valid responses for age, sex, marital status, and diagnosis; 953 (99.8%) for negative affectivity and smoking; 952 (99.7%) for employment status; and 944 (98.8%) for education and alcohol consumption.

Abbreviations: CI, confidence interval; ISCED, international standard classification of education (www.uis.unesco.org; last access September 16, 2010); levels 1 and 2 are obligatory in Switzerland, and levels 3 and 4 allow access to 4-year higher education (level 5B) and university study (levels 5A and 6).

Table 2. Relation between suspected predictive factors and nonresponse to follow-up on logistic regression analysis

| Variable                      | Model 1                     | Model 2                     |
|-------------------------------|-----------------------------|-----------------------------|
|                               | Odds ratio (95% CI)         | P                           | Odds ratio (95% CI)         | P                           |
| Avoidance coping score        | 1.03 (0.89–1.18)            | 0.379                       | —                           | —                           |
| Negative affectivity score    | —                           | —                           | 1.02 (0.89–1.17)            | 0.742                       |
| Age                           | 1.04 (0.87–1.24)            | 0.652                       | 1.06 (0.89–1.26)            | 0.523                       |
| Female sex                    | 1.09 (0.81–1.46)            | 0.572                       | 1.11 (0.84–1.67)            | 0.310                       |
| Married                       | 1.16 (0.86–1.57)            | 0.335                       | 1.12 (0.84–1.67)            | 0.310                       |
| ISCED 5A and 6                | 0.85 (0.32–2.25)            | 0.746                       | 0.79 (0.30–2.07)            | 0.632                       |
| ISCED 5B                      | 0.77 (0.27–2.16)            | 0.626                       | 0.74 (0.27–2.04)            | 0.558                       |
| ISCED 3 and 4                 | 0.80 (0.28–2.26)            | 0.675                       | 0.76 (0.27–2.11)            | 0.594                       |
| Full-time                     | 1.27 (0.80–2.00)            | 0.310                       | 1.29 (0.82–2.03)            | 0.279                       |
| Part-time                     | 1.13 (0.75–1.71)            | 0.553                       | 1.15 (0.76–1.74)            | 0.503                       |
| Daily consumption             | 1.04 (0.77–1.40)            | 0.800                       | 1.04 (0.77–1.40)            | 0.786                       |
| Weekly                        | 1.02 (0.60–1.72)            | 0.964                       | 1.03 (0.61–1.74)            | 0.916                       |
| Smoking                       | 0.67 (0.50–0.89)            | 0.007                       | 0.65 (0.49–0.88)            | 0.004                       |

Model 1 included 926 cases (97.0%) and examined the hypothesis that individuals with avoidant behavior are less likely to return a follow-up questionnaire; model 2 included 934 cases (97.8%) and tested the hypothesis that individuals with negatively affectivity might be less likely to do so. Abbreviations: CI, confidence interval; ISCED, international standard classification of education (for additional information please refer to the legend for Table 1).
Table 3. Relation between suspected predictive factors and late response at baseline on linear regression analysis

| Variable                | Model 3                              | Model 4                              |
|-------------------------|--------------------------------------|--------------------------------------|
|                         | Coefficient (95% CI)  | P          | Coefficient (95% CI) | P |
| Avoidance coping        | 0.15 (−0.05 to 0.36) | 0.139  | 0.06 (−0.14 to 0.26) | 0.556 |
| Negative affectivity    | —                                    | —          | —                    | — |
| Age                     | −0.27 (−0.53 to −0.00) | 0.048  | −0.24 (−0.50 to 0.03) | 0.080 |
| Female sex              | −0.59 (−1.02 to −0.15) | 0.009  | −0.52 (−0.95 to −0.08) | 0.020 |
| Married                 | −0.31 (−0.76 to 0.14) | 0.180  | −0.35 (−0.80 to 0.10) | 0.129 |
| Education               | ISCED 5A and 6 | 1.74 (0.27 to 3.22) | 0.020  | 1.43 (−0.01 to 2.88) | 0.051 |
|                         | ISCED 5B | 1.34 (−0.12 to 2.80) | 0.072  | 1.06 (−0.37 to 2.48) | 0.146 |
|                         | ISCED 3 and 4 | 1.23 (−0.15 to 2.61) | 0.082  | 0.91 (−0.43 to 2.26) | 0.181 |
| Employment status       | Full-time | −0.59 (0.84 to 1.67) | 0.058  | −0.56 (−1.17 to 0.05) | 0.072 |
|                         | Part-time | 0.03 (0.84 to 1.67) | 0.034  | 0.03 (−0.65 to 0.70) | 0.936 |
| Alcohol consumption     | Daily | −0.29 (−1.11 to 0.52) | 0.477  | −0.30 (−1.11 to 0.51) | 0.474 |
|                         | Weekly | −0.48 (−0.92 to −0.03) | 0.034  | −0.47 (−0.91 to −0.03) | 0.038 |
|                         | Smoking | 0.32 (−0.11 to 0.76) | 0.145  | 0.26 (−0.18 to 0.69) | 0.249 |

Models 3 and 4 investigated if time to baseline questionnaire response was associated with avoidance coping and negative affectivity, respectively. Abbreviations: CI, confidence interval; ISCED, international standard classification of education (for additional information please refer to the legend for Table 1).
Are the present results reliable? Due to the fact that the rate of nonresponse to follow-up was higher than expected, the statistical power of the present study was not 95%, as we had planned, but 99%. Thus, even very small effects were statistically significant, and additional statistical power was not necessary. With respect to bias in the present estimates, the most important weakness of this study was that represented by the studied topic. We investigated potential relationships between personality characteristics (avoidance behavior and negative affectivity) and nonresponse; however, we could not assess those characteristics in the 183 (15.9%) nonrespondents at baseline (see Figure legend). We attempted to overcome this limitation by using late response at baseline as a proxy for nonresponse at baseline. As mentioned above, the association between late response at baseline and nonresponse to follow-up was insufficient for the use of late response as a proxy for nonresponse. Two hypotheses emerged from this observation. First, some patients may never respond, regardless of the time they are allotted. Second, the relation between response at baseline and response to follow-up could be weak, which, if true, suggests that nonresponse is not consistent within one person (this would diminish the risk of systematic differences between respondents and nonrespondents). We achieved a good baseline response rate (83.1%) and our outcome of interest was not rare (37.8% nonresponse to follow-up). However, our estimates could still be biased if nonrespondents do indeed differ systematically from respondents, which is as yet unproven. Specifically, we found that, on average, nonrespondents at baseline were 3.6 years younger than respondents. This difference is somewhat more pronounced than the age effect for late response to follow-up, but still small.

Given that bias is a systematic deviation from the truth and not a random deviation, nonrespondents can only bias estimates if at least one relevant characteristic systematically divides respondents and nonrespondents. Until such a characteristic is identified, there is insufficient evidence that nonrespondents bias estimates, and it remains reasonable to assume that nonresponse is random. This does not mean, however, that outcome estimates will necessarily be the same for nonrespondents and respondents. For example, a study found that, despite equally distributed smoking habits, respiratory symptoms, and lung function, the outcome—hospital admissions during follow-up—was twice as high in nonrespondents (9.9%) as in respondents (5.0%). The authors concluded that estimates were biased by nonresponse. We computed exact 95% CIs for the estimates of this study using STATA 11 for Windows and found that the estimate for the whole sample (5.6%, n = 1070) was within the 95% CIs for both the nonrespondents (5.5%–16.0%, n = 142) and the respondents (3.6%–6.6%, n = 928). If estimates vary randomly, i.e., not because of bias, the true value will stay within the 95% CI in 95% of cases. We conclude that the difference between nonrespondents and respondents in that study can be explained by random variance alone. We nevertheless agree with the principal conclusion of the authors, that equal distribution of baseline characteristics is not sufficient to exclude nonresponder bias. Research must continue to move forward and analyze more than common baseline characteristics.

Meta-analytic methods might be useful in distinguishing random differences from biases. In an email survey of 2127 clinicians, nonrespondents received as many as 5 email reminders and, if necessary, a sixth by fax. The outcome was the prescribing of contraindicated medications. Subgroups were defined by number of reminders needed. The estimate for the total group was within the 95% CIs of all 7 subgroups. An I2 statistic of zero indicated that there was no inconsistency among groups, other than random differences. To summarize, our findings show that avoidance coping and negative affectivity are unlikely to differ among respondents and nonrespondents to a questionnaire survey. In addition, our survey of the literature findings revealed no decisive factors underlying nonresponse. Further study of this topic is important because nonresponse is very frequent.

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