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The Impact of Axial Spondyloarthritis on Mental Health: Results from the Atlas

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Running head:

Axial Spondyloarthritis Mental Health

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Abstract

Objective: To assess the risk for mental disorders in patients with axSpA and to examine the associated factors with this.

Method: In 2016, a sample of 680 axSpA patients was interviewed as part of the development process for the Atlas of Axial Spondyloarthritis in Spain. The risk of mental disorders in these patients was assessed using the General Health Questionnaire (GHQ-12) scale. Additionally, the variables associated with the risk of mental disorders were investigated, including: sociodemographic characteristics (age, gender, relationship, association membership, job status, and educational level); disease status (BASDAI, spinal stiffness and functional limitation); and previous diagnosis of mental disorders (depression and anxiety). Bivariate correlation analyses were performed, followed by multiple hierarchical and stepwise regression analysis.

Results: A total of 45.6% patients were at risk of mental disorders. All variables except educational level and thoracic stiffness significantly correlated with risk of mental disorder. Nevertheless, disease activity, functional limitation, and age showed the highest coefficient ($r=0.543$, $p<0.001$; $r=0.378$, $p<0.001$; $r=-0.174$, $p<0.001$, respectively).

In the stepwise regression analysis, four variables (disease activity, functional limitation, association membership, and cervical stiffness) explained the majority of the variance for the risk of mental disorders. Disease activity displayed the highest explanatory degree ($R^2=0.875$, $p<0.001$).

Conclusions: In patients with axSpA, the prevalence of risk for mental disorders is high. Combined with a certain sociodemographic profile, high disease activity is a good indicator of the risk of for mental disorders.

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Keywords: Axial Spondyloarthritis, BASDAI, Spinal Stiffness, Functional Limitation, Depression, Anxiety, GHQ-12.

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INTRODUCTION

Axial spondyloarthritis (axSpA) manifestations, such as loss of mobility, chronic pain and fatigue have an impact on a patient's daily functioning and quality of life[1]. However, the same number and degree of manifestations does not always have the same impact on all patients. On the one hand, increasing evidence published during the last ten years has demonstrated the importance of psychosocial factors for patients adjusting to their physical limitations and chronic pain stemming from the disease[2,3,4]. Mental health problems, such as depression and anxiety, can worsen functioning and adherence to treatment[5]. A longitudinal study carried out over one year in patients with ankylosing spondylitis (AS) showed that depression is a mediating factor between the disease activity degree and functional limitation[6]. On the other hand, previous data suggest that the psychological health status of patients with axSpA may be influenced by the level of disease activity experienced, although these findings have not been confirmed[7].

A recent systematic review and meta-analysis reported that the prevalence of depression in patients with axSpA ranging from 11% to 64%[8]. This wide estimation in previous studies reflects the fact that very heterogeneous definitions and assessments of depression were employed in these studies. In addition, most of these studies mainly included male patients, with a very long disease duration and substantial radiographic damage and, therefore, their results are difficult to be extrapolated to all patients across the entire spectrum of axSpA.

The Atlas of Spondyloarthritis 2017[9] is a national initiative that seeks to better understand the current state of people suffering from axSpA. It utilizes an integrative approach based on scientific evidence, expert knowledge, and patient opinion. The Atlas population represents the entire spectrum of axSpA and is equally distributed in terms of gender. Additionally, the risk of mental disorders (RMD) was assessed by using the 12-item General Health Questionnaire 12 (GHQ-12). This is a valid screening tool for identifying minor psychiatric disorders in the general population

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within non-psychiatric clinical settings such as primary care or general medical out-patient facilities. Therefore, the Atlas 2017 provides a great opportunity to further explore the impact of disease outcomes on mental health in patients with axSpA. Moreover, the screening tool can shed light on the influence of explanatory variables related to mental health disorders in these patients.

Aims and scope

The objective of the present study was to determine the prevalence of risk for mental disorders in patients with axSpA and any associated factors. Our hypothesis was that greater disease activity is associated with a higher risk of suffering from mental disorders.

METHODS

Study design and population

A sample of 680 patients diagnosed with axSpA was interviewed between 1 May and 15 August 2016 as part of the Atlas on Axial Spondyloarthritis in Spain[9], which seeks to promote early diagnosis, improved healthcare, and the use of effective treatments in patients with axSpA. The anonymous questionnaire included a series of items related to disease status (disease activity as measured by the BASDAI self-administered questionnaire, spinal stiffness, and functional limitation) and psychological aspects related to coping with the disease. All of the methodologies upon which the Atlas is based have been previously published in detail. This specific study includes data from 474 patients with recorded information about risk for mental disorders using the GHQ-12.

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Independent variables

Disease activity

Disease activity was measured using the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) with a range between 0 and 10[10].

In addition, spinal stiffness levels in the three areas of the vertebral column (cervical, dorsal, and lumbar) were collected, measured on a scale from lower to higher levels using an ordinal variable (1 = without limitation, 2 = mild limitation, 3 = moderate limitation, and 4 = severe limitation). Using this information, an index of spinal stiffness was created by adding, but without weighting, the degree of stiffness in each of the three areas. The resulting values ranged between 3 and 12. The Cronbach alpha value of this scale was 0.85, which attest to its consistency for assessing general stiffness.

Function limitations in daily activities

To determine the degree of functional limitation a composite index was employed, which included the sum of recorded limitation in 18 daily activities (dressing, grooming, bathing, tying shoelaces, moving about the home, walking up and down stairs, getting into/out of bed, using the toilet, shopping, preparing meals, eating, housework, walking, using public transportation, going to the doctor, driving, physical exercise, and sexual relations) using an ordinal variable (0 = none, 1 = little, 2 = some, and 3 = moderate). The resulting values oscillate between 0 and 54; thus, a value between 0 and 18 was set as a low limitation, that between 18 and 36 as a medium limitation, and that between 36 and 54 as an indication of high limitation. The Cronbach alpha value of this scale was 0.964, guaranteeing its reliability as a means for assessing limitation.

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Sociodemographic aspects

The following demographic aspects were also collected: gender, age, living as a couple, education level, employment status, and whether the individual belonged to a patient association.

Comorbidity of mental health

Finally, patients were queried about any previous mental health diagnosis (made by psychologist or psychiatrist), including anxiety or depression. Such diagnoses of depression and/or anxiety referred only to some point(s) in the past and patients were asked to provide a positive answer only when said diagnosis had been made by a psychologist/psychiatrist based on clinical criteria.

Dependent variable

Risk of mental disorder

The risk of mental disorder (RMD) was determined by using the GHQ-12[11], which consists of 12 items, each one assessing the severity of a mental health problems during the previous four weeks using a Likert scale (0-1-2-3). Thus, a maximum score of 36 was obtained; higher scores reflected an increased risk of psychiatric morbidity. However, to determine the risk of patients suffering with poor mental health, these scores were transferred to a GHQ scale, where 0 or 1 = 0, and 2 or 3 = 1. Following this methodology, the majority of studies found that scores equal to or greater than 3 indicated a high risk of poor mental health; therefore, we used this cut-off point for the present study[12]. The GHQ-12 offers reliability in studies developed within the Spanish population, resulting in a Cronbach's alpha that oscillated between 0.76 and 0.90[11,13]. In our study, a Cronbach's alpha of 0.934 was obtained, which supported the reliability hypothesis of this scale.

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Statistical analysis

The statistical analysis was conducted in three stages. The first step focused on the descriptive statistics for the sample and the study variables. The second step consisted of bivariate regression analyses of each predictor vis-à-vis the risk of poor mental health (GHQ-12) was performed. Here, nonparametric contrasts were made since the GHQ-12 values obtained did not follow a normal distribution pattern. For quantitative variables, Mann-Whitney tests for two categories and Kruskall-Wallis tests for more than two categories were performed. For categorical variables, chi square independence or Fisher tests were employed. In addition, the Spearman correlation coefficient was utilized to assess whether there was a relationship between mental health status (GHQ-12) and the different quantitative factors, such as the level of disease activity as measured by BASDAI.

The third step evaluated the independent influence of disease outcomes on mental health by using a hierarchical multiple regression analysis with those that had shown a significant relationship with mental health status in the bivariate analyses conducted during the second step. For the hierarchical regression analysis, variables were grouped into three conceptual categories: (1) sociodemographic variables, (2) comorbidities, and (3) physical variables. This analysis introduced the variables of each category in a step-by-step fashion, thereby allowing for model comparison by building several regression models. Each model added variables to the previous one at each step; later models always included smaller models in their previous steps. In this case, our interest was to determine whether newly added conceptual categories of variables showed a significant improvement in R^2 (the proportion of explained variance in GHQ-12 by the model). Finally, a stepwise forward regression multivariable analysis was carried out, which included the variables that passed an F test, in order to ascertain the best associated factors.

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All contrasts were bilateral and considered statistically significant when the p value was <0.05. The data was analysed using SPSS software, version 24 for 64 Bits.

RESULTS

Characteristics of the study participants

A total of 838 patients with axSpA anonymously accessed the online questionnaire between May 1 and August 15, 2016. After validation and normalization of the information, the sample consisted of 680 patients who responded to the majority of the questionnaire (the completion rate exceeded 75%) and made up the total valid sample of the Spanish Atlas of Spondyloarthritis[9]. From these, a total of 474 patients had valid data for the GHQ-12 and comprised the group under evaluation for this study; characteristics of the sample are summarized in Table 1. The characteristics of this subgroup were similar compared with the entire population, with the exception of having more frequently a partner relationship. In the studied population, the mean GHQ-12 score was 18.3 ± 8.0. Furthermore, 310 (65.4%) patients were classified as having risk of mental disorder (RMD), while 164 (34.6%) had no RMD.

Table 1.

Socio-demographic data, disease outcomes, and comorbidity sample characteristics (n = 474, unless otherwise specified). Results are expressed as the mean (standard deviation) or n (percentage).

Bivariate analyses

Tables 2, 3 and 4 depict the results for the bivariate analyses. Mental health showed a statistically significant association with the following variables: older age, male gender, no partner

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relationship, unemployment, no patient association membership, anxiety and/or depression diagnosis, high level of disease activity (BASDAI), high degree of spinal stiffness (cervical and lumbar), and worse functional limitations in daily activities.

Table 2.

Bivariate analysis of demographic factors associated with risk of mental disorders measured by GHQ-12.

Table 3.

Bivariate analysis for comorbidity factors associated with risk of mental disorders measured by GHQ-12.

Table 4.

Bivariate analysis for disease activity and functional limitation factors associated with risk of mental disorders measured by GHQ-12

Hierarchical modelling with successive conceptual categories

To evaluate the independent influence of disease outcomes on mental health, a hierarchical multiple regression analysis with those variables that had shown a significant relationship with GHQ-12 in the bivariate analyses was performed (see Table 5). This analysis demonstrated how, among sociodemographic variables, membership in a patient association had a significant regression coefficient while the rest did not.

In the first step, all sociodemographic attributes were included and established as control variables. That model explained patient mental health to a great extent (R^2 = 83.2%). In a second step, diagnoses of depression and anxiety were added to this model but the R2 value only

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increased by 0.6% (p = 0.001) and yielded no significant regression coefficients (p-values equal to 0.08 and 0.8, respectively). In a third step, disease activity (BASDAI and stiffness) and function were also included in the model, which added 5.5% (p < 0.001) to the variance of the GHQ-12 scores. However, of these last variables only BASDAI and limitations experienced in daily life had a coefficient significantly different from zero: 0.52, p <0.001 and 0.14, p <0.01, respectively. This means that once the sociodemographic characteristics and psychiatric/psychological comorbidity (depression and anxiety) were established, a change in BASDAI levels or functional limitation is reflected a change in the GHQ-12.

Table 5.

Hierarchical multivariate analyses of socio-demographic, comorbidity, and disease status factors in relation to the risk of mental disorders, measured by GHQ-12 (n = 474).

Stepwise regression analysis without successive conceptual categories

Stepwise regression analysis resulted in the inclusion of four variables: BASDAI, functional limitations in daily activities, membership in a patient association, and cervical stiffness. All four of these variables contributed to a significant change in R^2 (p <0.001 for BASDAI, belonging to a patient association, and functional limitations in daily activities, and p = 0.03 for cervical stiffness, where p is the p-value for a change test in R^2). Out of these variables, BASDAI was found to have remarkably more explanatory power (contribution to R^2 = 0.875) (see Table 6).

Table 6.

Stepwise forward multivariate analyses of socio-demographic and disease status variables in relation to GHQ-12 (n = 474).

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DISCUSSION

According to the data from the 2017 Atlas survey, 45.6% of patients with axSpA experience risk of mental disorder (RMD). Furthermore, this study identifies several disease-specific factors associated with the RMD. Among all factors, the most relevant is disease activity. Higher disease activity is associated with higher RMD. In addition, other factors associated with RMD are worse functional limitation in daily life, not belonging to a patient association and a higher degree of cervical stiffness. Moreover, 20% of patients reported having a clinical diagnosis of anxiety and 15% of depression. Although the prevalence of anxiety and depression varied depending on the definition employed, the prevalence of these diseases in this study are within the published ranges (11-64% for depression)[8] and (16-20% for anxiety)[14,15,16].

These findings are consistent with other evidence suggesting a relationship between disease activity and negative psychological factors associated with axSpA. This relationship has been proven to have a bidirectional character. On the one hand, it shows how negative psychological factors (depression, anxiety, passive coping style, insomnia, and negative affective states) explain the significant variability of disease activity when self-reported by patients, beyond what is explained by the clinical and demographic variables[17,18,19,20]. On the other hand, it is evident how disease activity and functional limitation can explain some variability in patient mental health status (anxiety, depression, and insomnia)[7,16,21,22].

The high prevalence of RMD found in this study is discouraging. Nevertheless, taking into account that the identified factors associated with RMD, especially the most influential (disease activity), are not fixed and can be modified with a more appropriate and intensive treatment strategy. Indeed, these results should encourage physicians to develop strategies for improving this situation during the coming years.

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In the field of chronic disease, of great importance is an adequate assessment of the information given by patients in addition to their quality of life, since a patient's perspective can guide resource allocation, the design of interventions, and pharmacological treatment[23,24,25]. The results of this study add to the evidence that supporting the relationship between disease status (disease activity, spinal stiffness), psychosocial factors (functional limitation in daily activities), and the mental health status of patients with axSpA. However, it is important to understand the mechanism underlying this type of relationship before considering how to use this knowledge in clinical practice. These findings also raise the question of whether a psychological intervention, perhaps directed at certain subgroups of patients, may be useful in the treatment of axSpA. In this context, there is some evidence as to the influence of certain psychological interventions on these pathologies, although they are more commonly observed in patients who have rheumatoid arthritis than those with axSpA[26,27,28,29].

This study has several limitations. First, the use of non-previously validated scale or indices for assessing certain factors, such as functional limitations in daily life and stiffness, should be thoroughly considered. The reason for utilizing such scales or composite indices originated during the preliminary phase of the survey development, when patients expressed their concern about not being able to report all aspects of their disease if other scales or indices were to be employed. In any case, a good Cronbach alpha value was obtained for the index employed in our study, which testifies to the reliability of these instruments. Second, the bi-directional nature of these relationships is another limitation of this study, since it is not possible to establish causality using this cross-sectional approach. In fact, it is difficult to assess whether the RMD stems the problems related to the disease, the underlying inflammatory processes, or other factors associated with this chronic pathology (spinal stiffness or functional limitations in daily life). Conclusions can only be drawn based on the relationship between variables. To establish a causality, it would be

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necessary to carry out longitudinal studies in order to evaluate over time the evolution of physical variables and their relationship to mental health or vice versa. Third, a possible overlap between GHQ-12 and the diagnosis of depression and anxiety cannot be completely excluded. However, the diagnosis of depression and anxiety in these respondents was made by a psychologist/psychiatrist based on clinical criteria while GHQ-12 is a self-reported measure of the RMD. The GHQ-12 values show the current RMD during the survey period while, the diagnoses of depression and anxiety referred to points in the past. Finally, the possible effect of biological therapy on depressive symptoms and mental health-associated quality of life could have influenced the results of this study.

CONCLUSIONS

The results of this study underscore the high prevalence of mental disorders in patients with axSpA and its clear association with disease status. Approximately, one of every two patients with axSpA reports RMD. Furthermore, this RMD seems to be explained, to a great extent, by the degree of disease activity and, to a lesser extent, to such factors as the degree of functional limitation in daily life, cervical stiffness and patient association membership. These findings highlight the benefit of rheumatologists promoting psychiatric evaluations of patients with high disease activity and who are at risk of mental disorders. It is posited that this will contribute to a more integral treatment strategy.

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Table 1. Socio-demographic data, disease outcomes, and comorbidity sample characteristics (n = 474, unless otherwise specified). Results are expressed as the mean (standard deviation) or n (percentage).

Variables	Values (means ± SD or percentage)
Socio-demographic:	
Age, years	45.4 ± 10.7
Gender, Male	233 (49.1%)
Having a Partner (N=444)	386 (86.9%)
Education Level, University	185 (39.0%)
Job Status, Employee	234 (49.4%)
Patient Association Membership	227 (47.8%)
Disease Outcomes:	
BASDAI (0-10)* (N=442)	5.4 ± 2.1
Spinal Stiffness, Moderate or Severe	
Cervical (1-4) (N=447)	201 (44.9%)
Thoracic (1-4) (N=435)	186 (42.7%)
Lumbar (1-4) (N=458)	288 (62.8%)
Functional Limitations in Daily Activities (0-54) (N=473)	27.5 ± 12.7
Treatment	
NSAIDs	363 /76.6%)
sDMARDs	181 (38.2)
bDMARDs	240 (50.3)
Comorbidity:	

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Self-reported Depression Diagnostic	99 (20.8)
Self-reported Anxiety Diagnostic	134 (28.2)
*GHQ**-12 score (0-36)*	18.3 ± 8.0

* BASDAI = Bath Ankylosing Spondylitis Disease Activity Index.

**GHQ-12 = General Health Questionnaire.

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Table 2: Bivariate analysis of demographic factors associated with the risk of mental disorders measured by GHQ-12.

Factors	Homogeneity Test: (1) Kruskall-Wallis (2) Mann-Whitney	Chi- square
Socio-demographic		
Age, Years	0,001 (1) [Corr. Spearman= -0,174]	0.001
Gender, Male	0.013 (2)	0.025
Having a Partner	0.009 (2)	0.021
Education Level, University	0.607 (1)	0.43
Job Status, Employee	≤0.001 (1)	≤0.001
Patient Association Membership	0.001 (2)	0.001

GHQ-12 = 12-items General Health Questionnaire;

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Table 3: Bivariate analysis for comorbidity factors associated with risk of metal disorders measured by GHQ-12.

Factors	Homogeneity Test: (1) Kruskall-Wallis (2) Mann-Whitney	*Chi-square*
Comorbidity:		
Self-reported Depression Diagnostic	≤0.001 (2)	≤0.001
Self-reported Anxiety Diagnostic	≤0.001 (2)	≤0.001

GHQ-12 = 12-items General Health Questionnaire;

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Table 4: Bivariate analysis for disease activity and functional limitation factors associated with risk of mental health disorders measured by GHQ-12*.

Factors	Spearman Correlation Coefficient	*Significance (p)*
Disease Activity		
*BASDAI** (0-10)*	0.543	≤0.001
Spinal Stiffness, Moderate or Severe, No. (%)		
Cervical (1-4)	0.120	0.011
Thoracic (1-4)	0.073	0.130
Lumbar (1-4)	0.165	≤0.001
Limitations in Daily Activities (0-54)	0.378	≤0.001

*GHQ-12 = 12-items General Health Questionnaire

**BASDAI = Bath Ankylosing Spondylitis Disease Activity Index.

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Table 5. Hierarchical multivariate analyses of socio-demographic, comorbidity, and disease status factors in relation to the risk of mental disorders, measured by GHQ-12 (n = 474).

Step	Factors	*β*-Weights	C.I. (95%)	*Standard β*-Weights	*P*	R^2 (%) (*p*+)**	ΔR^2 (%)(*p*+)***
1	**Socio-demographic:**					0.832	0.832
	Age, Years	-0.137	-1.143, 0.870	-0.016	0.789		
	Gender, Male	0.424	-0.953, 1.800	0.033	0.545		
	Being in a Relationship	0.606	-0.548, 1.760	0.042	0.302		
	Education Level, University	0.663	-0.192, 1.518	0.107	0.128		
	Job Status, Employee	0.237	-0.083, 0.557	0.041	0.146		
	Patient Association Membership	2.113	0.770, 3.456	0.168	0.002		
2	**Comorbidity:**					0.838	0.006
	Self-reported Depression Diagnostic	-1.705	-3.590, 0.181	-0.155	0.076		
	Self-reported Anxiety Diagnostic	-0.260	-2.020, 1.500	-0.023	0.772		
3	**Disease Outcomes:**					0.893	0.055
	BASDAI (0-10)	1.796	1.424, 2.167	0.527	0.000		
	Functional limitations in Daily Activities (0-54)	0.092	0.030, 0.154	0.140	0.004		
	Cervical Stiffness (1-4)	0.392	-0.439, 1.224	0.051	0.354		
	Lumbar Stiffness (1-4)	0.429	0.393, 1.250	0.063	0.306		

Note: Only values that were statistically significant in the bivariate analysis (or marginally significant, p<0.09) were included in this analysis. All β-weights, 95% confidence intervals, and p values for individual variables were estimates derived in the context of the full model (i.e., with all three conceptual blocks entered into the equation).

** Overall R-square (%) after adding each conceptual block and accompanying P value for the test of the overall R-square.

*** Incremental R-square change due to the addition of the conceptual block and accompanying P value for the test of the incremental R-square change

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Table 6. Stepwise forward multivariate analyses of socio-demographic and disease status variables in relation to GHQ-12 (n = 474).

Step	Predictors	*β*-Weights	C.I. (95%)	*Standard β*-Weights	*P*	R^2 (%) (*p*+)**	ΔR^2 (%)(*p*+)***
1	*BASDAI (0-10)*	1.912	1.551, 2.274	0.562	0.000	0.875	0.875
2	*Patient Association Membership*	2.028	1.012, 3.044	0.161	0.000	0.883	0.008
3	*Functional Limitations (0-54)*	0.112	0.053, 0.171	0.170	0.000	0.888	0.005
4	*Cervical Stiffness (1-4)*	0.610	0.054, 1.166	0.080	0.032	0.889	0.001

Note: Only values that were statistically significant in the bivariate analysis (or marginally significant, p<0.09) were included in the analysis. All β-weights, 95% confidence intervals, and p values for individual variables were estimates derived in the context of the full model (i.e., with all three conceptual blocks entered into the equation).

** Overall R-square (%) after adding each conceptual block and accompanying P value for the test of the overall R-square.

*** Incremental R-square change due to the addition of the conceptual block and accompanying P value for the test of the incremental R-square change.

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