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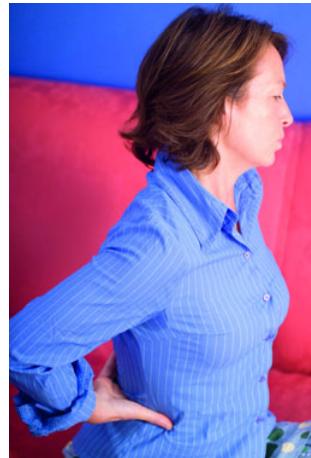
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Obesity, Physical Activity and Lower Back Pain: a genetically informative analysis

Health Promotion

Low back pain is one of the leading causes of disability. In Spain it affects 20.5 percent of the population over 15 years and is responsible for 12.5 percent of sick leave. In addition to the discomfort and suffering caused to millions of people, its economic cost is estimated at 160 million euros. This study, conducted on a sample of 1631 individuals registered as twins, seeks to establish the relationship between the variables of physical activity, Body Mass Index (BMI) and physical inactivity with the risk of having suffered back pain at some point, as well as determine whether such a relationship is maintained as genetic and environmental factors are shared.



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Lower back pain is one of the main causes of disability worldwide^[1] and has an important impact on the physical, social, psychological and economic spheres of people's lives^[2]. This impact also extends to their environment and society as a whole. Based on a 2011-2012 National Health Survey, in Spain 20.5 percent of people older than 15 admit to have suffered lower back pain during the last twelve months^[3], a proportion that seems to have stabilized in recent years^[4]. Between the years 2000 and 2004, this problem represented 12.5 percent of all lost work days and its average estimated cost per lost work day during this period was more than 160 million Euros per year^[5]. On the other hand, although the rate of recovery is 75 percent after 6 weeks, frequent relapses occur (where 33 percent result in lost work days)^[6, 7]. As a whole, given the magnitude and the extent of its implications, the identification of the causes of this problem as well as the preventive and effective rehabilitation strategies become especially relevant. However, the risk factors involved in lower back pain are not fully defined^[8] and currently, no decisive evidence exists regarding the efficiency of the preventive measures^[9].

Both obesity and low levels of physical activity have been

Obesity as well as physical activity have been considered possible factors affecting lower back pain, so the presence of obesity as well as lower physical activity have been associated, although not conclusively, to an increased risk of

linked, although inconclusively, with an increase in the risk of experiencing lumbar pain

modifiable factors, the nature of their association with lower back pain is especially of interest due to their role as possible preventive alternatives^[21] (references).

Several recent publications report the significant heritability of the phenotype, and state that genetic makeup accounts for between 30% and 67% of the individual differences observed in lumbar pain

cohort analysis disappeared when identical or monozygotic twins with different body weights were studied, which suggests that genetics could influence and confuse this relationship. Therefore the relationship between obesity and lower back pain is still not clear^[25, 30].

In turn, different studies have analyzed the relationship between physical activity and lower back pain with contradictory results^[12, 13, 21] and there is still no evidence regarding up to what point different types of physical activity may cause or prevent this problem^[31]. For example, while some studies associate intense physical activity with a low prevalence of lower back pain^[21, 32]; others have found that sedentary behavior as well as highly intense physical activity increases the risk^[33].

Studies on twins, in which the genetic factor can be controlled, can explain the real influence of modifiable environmental factors on lumbar pain

One of the possible explanations to this disparity in the results when associating obesity and physical exercise with lower back pain may be found in the impact of the genetic factors in these relationships. In reality, environmental as well as genetic factors seem to be associated with the occurrence of lower back pain^[24]. Several recent publications note a significant heritability in this phenotype^[24, 34-37]. In accordance with these studies, the variations in our different genetic constitution would explain between 30 percent and 67 percent of the individual

differences observed in lower back pain, where the effect of the genetic factor is greater in chronic and incapacitating pathologies than in acute episodes^[24]. Likewise, we have observed that the genetic factors that affect this problem are common to other related phenotypes such as the degeneration of the lumbar disc^[34]. A large number of studies have been conducted from a genetically informative point of view, which have researched further into the association of lower back pain with socio-demographic factors, occupational workload, being dissatisfied with life and personality variables^[36, 38-41].

In the same way, obesity as well as physical activity demonstrate genetic influences in the occurrence of lower back pain. Studies of twins have consistently found a significant contribution of genetic factors in the changes in BMI and related traits, in both sexes and in all ages. Currently a mean heritability of BMI near 70 percent is estimated with a range based on the sample between 50 percent and 90 percent^[42-44]. This distribution remains constant in different countries and cultures^[43, 45, 46]. Likewise, exercising also seems to have genetic influences^[19, 47, 48] and in fact, a recently conducted genome-wide association study (GWAS) concluded that physical exercise is probably influenced by multiple genes^[47].

Given the relevant contribution of genetic factors to the variance observed for lower back pain as well as obesity or physical activity, the use of designs that allow controlling the effect of said factors is especially interesting. Studies using twins where the genetic effect can be controlled may contribute to clarifying the relationships between these variables and determine the real impact of modifiable environmental factors regarding lower back pain.

In this study, our aim was to study the relationship between BMI and different levels of physical activity with lower back pain in a sample using twins. Particularly, the objective consisted in conducting a case-control study using twins with differences regarding the studied condition. In other words, pairs where only one of the members is experiencing lower back pain. Given the perfect pairing by gender, age and family environment, to which we add the control of the genetic factors in the case of monozygotic twins, this type of study provides evident advantages for controlling confusing variables^[49] and determining the effect of the studied variables.

Material and method

Design, subjects and procedures

A cross-sectional study using a co-twin case-control design was carried out. The subjects were taken from the Registro de Gemelos de Murcia / Murcia Twin Registry (RGM is the Spanish acronym). This is a population-based registry of twins comprised of adults born from multiple births between 1940 and 1966, and residing in the Region of Murcia. The RGM is a joint initiative lead by the University of Murcia and the Health Department of the Autonomous Community. Information about the characteristics of the RGM and its development are described in another publication.^[50] Participation in the Registry is voluntary and subject to consent. The Registry procedures have been approved by the Ethics Committee of the University of Murcia.

developing this condition^[10-13]. In turn, Body Mass Index (BMI) and physical activity are clearly related^[14-18] and in fact, a relationship has been suggested between the genetic ability to lose weight by exercising and the adherence to regular exercise^[19] or an interaction between low physical activity and the FTO gene to increase the risk of obesity^[20]. Since obesity and physical activity are

Obesity is considered a pandemic^[22] and is a growing public health problem^[23], and also seems to be associated with different musculoskeletal disorders such as lower back pain^[10]. However, its association with this problem continues to be controversial^[8, 24, 25]. For example, while some studies have demonstrated that obesity increases the prevalence of chronic^[11, 26] and recurrent^[26] lower back pain and a relationship has been identified between BMI and lower back pain^[10, 11], other studies have not been able to observe an association between them^[27-29]. On the other hand, in a study of twins with controls^[26], the positive association between BMI and lower back pain that was found in the general

cohort analysis disappeared when identical or monozygotic twins with different body weights were studied, which suggests that genetics could influence and confuse this relationship. Therefore the relationship between obesity and lower back pain is still not clear^[25, 30].

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The data used in this study was obtained in 2013 through telephone interviews. The sample for this study includes a total of 1,613 individuals participating in the registry, which were grouped in different zygosity categories (Table 1). Women represented 55.1 percent of the participants and the average age of the sample was 56.7 (SD: 7.1) years, without any significant differences noted between genders.

Table 1. Characteristics of the sample, prevalence of lower back pain and BMI; by gender and total

	Men	Women	Total		
General sample					
n (percent)	725 (44.9)	888(55.1)	1,613 (100)		
Age [mean, (DE)]	56.4 (6.9)	56.9 (7.3)	56.7 (7.1)		
Zygosity (Subjects) [n, (percent)]					
MZ	225 (31.0)	341 (38.4)	566 (35.0)		
DZ (Same gender)	261 (36.0)	309 (34.8)	570 (35.4)		
DZ-OG	239 (33.0)	238 (26.8)	477 (29.6)		
Prevalence of lower back pain [n, (percent)]	211 (29.1)	323 (36.4)	534 (33.1)		
BMI [media, (SD)]	27.8 (3.9)	26.6 (4.6)	27.2 (4.3)		
Case-control					
Discordant pairs for lower back pain	MZM 38 (36.5)	DZM 49 (41.9)	MZF 49 (31.9)	DZF 63 (45.0)	DZ-OG 99 (46.9)
n (percent)					
Age [mean, (SD)]	54.0 (6.0)	56.3 (7.6)	55.6 (6.8)	58.1 (7.6)	57.5 (6.2)

BMI: Body Mass Index; **SD:** Standard Deviation; **MZ:** Monozygotic; **DZ:** Dizygotic; **MZF:** Monozygotic female; **MZM:** Monozygotic male; **DZF:** Dizygotic female; **DZM:** Dizygotic male; **DZ-OG:** Dizygotic opposite gender.

Determining the zygosity

The zygosity was assessed by means of a 12-point questionnaire focused on specific anthropometric characteristics and the physical similarity of the pair. This questionnaire was previously validated and its results properly correspond to the zygosity determined by the DNA analysis, reaching a concordance above 95 percent^[50].

Instruments and measurements

The interview was based on an epidemiological type questionnaire that among other things included aspects related with back pain, anthropometric data and physical activity. The prevalence of lower back pain was assessed by means of two questions taken from the National Health Survey^[51] asking if they have ever experienced lower back pain in their lives and if they required medical attention. It was defined as presence of lower back pain at some time when a positive response was given to both questions. On the other hand, the height and weight were provided by the subjects and the BMI was calculated by dividing the body weight of the individuals in kilograms by the square of their height in meters. Regarding physical activity, a questionnaire was used that was based on the International Physical Activity Questionnaire (IPAQ)^[52] which included measuring the frequency with which mild physical activity is practiced (i.e., walking for at least 10 continuous minutes), moderate (i.e., moderate physical activity for at least 10 minutes such as a relaxing swim or playing golf) and intense physical activity (i.e., physical activity that causes rapid breathing or gasping for at least 10 minutes) as well as time dedicated weekly to each one of these activities. Additionally, a sedentary lifestyle measurement was considered, implemented as time spent sitting down during a workday. Measuring of the frequency of physical activity was recorded as the number of times per week. The duration measurements were recorded in minutes and subsequently, given their concentration around specific points corresponding to hours, they were transformed into 11 time groups (from less than 1 hour up to more than 10 hours). In the case of sedentary lifestyle, the duration is grouped into four levels (less than 3 hours; between 3-6 hours; between 6-10 hours; more than 10 hours).

Statistical analysis

The analysis was carried out in two stages: analysis of the general sample and cases and controls study. All the variables, except gender, were used as continuous variables. To analyze the general sample we studied the association between BMI and the physical activity measurements (in other words, weekly frequency and duration of mild, moderate and intense physical activity and sedentary lifestyle) and the prevalence of lower back pain, including all participants regardless of the type of pair; if the pair was complete or incomplete, or the similarity of the lower back pain. Gender was included as a possible confusion factor. The effects of the predictor variables were calculated using Generalized Estimation Equations using a rough estimator. This method takes into account the structure that is dependent on family data so that all the members of each family can be included in the study. Gender was considered a factor while all the rest of the predictors were included as covariates.

The sample on which the study

Subsequently, for the purpose of controlling the possible confusing effect of the genetic factors and the family or shared environment, a case and controls study

was conducted included 1,613 individuals of different categories of zygosity, 55.1% of whom were female and the average age of whom was 56.7 years

was conducted using only pairs of twins of the same gender, complete and discordant for lower back pain (both twins had answered the questionnaire and only one of them mentioned having experienced lower back pain on some occasion), using the same statistical procedure. Gender and age were not taken into account since there was a perfect pairing in both variables. Additionally, separate studies were conducted for monozygotic (MZ) and dizygotic (DZ) pairs of twins. In these types of designs, when the magnitude of the association between two variables (for example BMI and lower back pain) sequentially decreases between the analysis of the general sample (not adjusted for genetic factors or early shared environment) and the case and control studies of DZ pairs (adjusted for early shared environment) and MZ pairs (adjusted for genetic factors and shared environment), the relationship between the two variables would be indirect and mediated by confounding factors. By the contrary, the maintaining of the association in the case-control studies would be a solid indicator of a possible direct causal pathway^[49]. The data analysis was carried out using statistical software SPSS v.19.

Results

Characteristics of the sample

Detailed information about the characteristics of the sample are listed in Table 1. The prevalence of lower back pain in the total sample was 33.1 percent, with a greater presence in women (36.4 percent) than in men (29.1 percent). No significant differences in the prevalence by zygosity was found ($p < .05$).

The mean BMI of the sample was 27.2 (SD: 4.3), being significantly higher in males (F: 26.4; $p < .001$). In this case, no significant differences were observed by zygosity between individuals of the same gender.

The physical activity that is carried out is listed in Table 2. The average frequency of the mild activity was 3.7 times per week and was practiced an average of 6.5 hours per week. The frequency of the moderate activity did not reach once per week although those that practiced it, did so for 8.5 hours a week. Regarding intense physical activity, the frequency was also less than once per week with an average duration of less than 7 hours. On a normal workday, the participants in the study spent an average of 4.5 hours sitting down. In all cases except the frequency of engaging in mild physical activity, which did not show any differences by gender, males presented significantly higher values of frequency [Moderate (F: 33.3; $p < .001$); Intense (F: 110.1; $p < .001$)] as well as duration [Mild (F: 6.4; $p < .01$); Moderate (F: 26.6; $p < .001$); Intense (F: 9.8; $p < .01$)]. Likewise, males spent more hours sitting down during a workday (F: 61.7; $p < .001$). Also in this case we did not observe any significant differences by zygosity in individuals of the same gender except for a tendency in males of mixed pairs to spend more time sitting down (F: 4.8; $p < .01$).

Table 2. Frequency and duration of mild, moderate and intense physical activity and time sitting down during a normal work day. Total and by gender

	Men		Women		Total	
	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)
Walking (Times/week)	716	3.7 (4.3)	883	3.7 (3.6)	1,599	3.7 (3.9)
Walking (Hours/week)	471	7.2 (9.5)	553	5.9 (5.1)	1,024	6.5 (7.5)
Moderate activity (Times/week)	699	0.7 (1.8)	883	0.3 (1.2)	1,582	0.5 (1.5)
Moderate activity (Hours/week)	109	11.5 (12.0)	70	3.7 (5.1)	179	8.5 (10.6)
Intense activity (Times/week)	708	1.2 (2.2)	882	0.3 (1.1)	1,590	0.7 (1.7)
Intense activity (Hours/week)	218	7.6 (9.2)	84	4.2 (5.9)	302	6.7 (8.6)
Time spent sitting down (Hours/day)	710	5.2 (3.3)	871	4.0 (2.5)	1,581	4.5 (2.9)

Analysis of the general sample

Differentiated analyses by gender showed that the risk of experiencing lumbar pain was greater at a lower age in men, while the opposite was true for women

Table 3 lists the results obtained in the analysis of the general sample as it relates to the object being studied. As was expected, gender showed a relevant association with lower back pain. Age on the other hand did not have any effect on this condition in the total sample. Therefore, the analyses conducted afterwards were adjusted by gender. In the case of the total sample, a high BMI, low frequencies of moderate and intense physical activity and a sedentary lifestyle showed to be significantly associated to a higher risk of suffering lower back pain. The duration of the activity did not have any effect on lower back pain regardless of the type of activity that was carried out.

Table 3. Analysis of the general sample (Total and by gender). Estimate of the effect on lower back pain and confidence interval 95 percent for demographic, anthropometric (BMI) and physical activity variables.

n	B	CI 95 percent	p
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Gender				
General sample	1,605	0.367	0.148, 0.585	0.001
Age				
General sample	1,605	0	-0.02, 0.02	0.990
Men	722	-0.037	-0.06, -0.01	0.002
Women	888	0.023	0.01, 0.04	0.021
BMI				
General sample	1,482	0.030	0.00, 0.06	0.027
Men	705	0.008	-0.03, 0.05	0.707
Women	777	0.038	0.01, 0.07	0.037
Walking (Times/week)				
General sample	1,593	-0.018	-0.05, 0.01	0.203
Men	713	-0.018	-0.06, 0.02	0.400
Women	880	-0.019	-0.06, 0.02	0.370
Walking (Minutes/week)				
General sample	1,019	-0.023	-0.07, 0.02	0.296
Men	468	-0.042	-0.11, 0.02	0.185
Women	551	0.006	-0.05, 0.07	0.850
Moderate activity (Times/week)				
General sample	1,576	-0.078	-0.15, -0.01	0.045
Men	696	-0.085	-0.19, 0.02	0.114
Women	880	-0.062	-0.17, 0.05	0.268
Moderate activity (Minutes/week)				
General sample	179	-0.036	-0.15, 0.08	0.525
Men	109	-0.049	-0.19, 0.09	0.491
Women	70	-0.157	-0.47, 0.16	0.330
Intense activity (Times/week)				
General sample	1,584	-0.073	-0.14, -0.01	0.044
Men	705	-0.065	-0.15, 0.02	0.122
Women	879	-0.083	-0.22, 0.06	0.239
Intense activity (Minutes/week)				
General sample	301	-0.021	-0.10, 0.06	0.625
Men	217	-0.013	-0.09, 0.11	0.800
Women	84	-0.010	-0.01, 0.01	0.255
Time spent sitting down (Per day)				
General sample	1,575	0.160	0.02, 0.30	0.026
Men	707	0.230	0.04, 0.42	0.016
Women	868	0.051	-0.15, 0.26	0.628

Note: The models of the total sample are adjusted by gender. The models for the samples of men and women are adjusted by age.

Given the important effect of gender, we decided to carry out this same analysis independently for men and women. In this case, age showed to have a significant effect, although in the opposite direction for each gender. Thus, a younger age increased the risk of suffering lower back pain in males while for women, the risk increases, as they get older. For this reason the rest of the predictor variables were adjusted for age. The subsequent analyses limited the effect of a sedentary lifestyle in men and BMI in women.

Case and control study

A total of 199 complete and discordant pairs of twins were studied in the case and control studies. As would be expected, the discordance occurred with less frequency in MZ pairs of twins (Table 1). The conducted analyses showed that none of the variables that had shown to have an effect on the general sample had a significant effect when the sample was analyzed as a pair (Table 4). Regardless of the sub-sample that was used, the BMI as well as the variables of physical activity or sedentary lifestyle lost their statistical significance.

Table 4. Case-control study. Main effects of the covariates with a significant influence in the analysis of the general sample

	Wald χ^2	gl	p
Discordant pairs (n = 199)			
BMI	0.027	1	0.870
Moderate activity (Times/Week)	0.533	1	0.466
Intense activity (Times/Week)	0.007	1	0.932
Time spent sitting down (Per day)	0.308	1	0.579
Discordant Dz pairs (n = 112)			
BMI	0.563	1	0.453
Moderate activity (Times/Week)	0.103	1	0.749
Intense activity (Times/Week)	0.081	1	0.776
Time spent sitting down (Per day)	0.183	1	0.669
Discordant MZ pairs (n = 87)			
BMI	1.71	1	0.191
Moderate activity (Times/Week)	0.612	1	0.434
Intense activity (Times/Week)	0.200	1	0.655
Time spent sitting down (Per day)	1.63	1	0.202
Male Discordant pairs (n = 87)			
Time spent sitting down (Per day)	0.018	1	0.892
Male DZ discordant pairs (n = 49)			
Time spent sitting down (Per day)	0.019	1	0.892
Male MZ discordant pairs (n = 39)			
Time spent sitting down (Per day)	0.101	1	0.750
Female discordant pairs (n = 112)			
BMI	0.014	1	0.906
Female discordant DZ pairs (n = 63)			
BMI	0.535	1	0.464
Female discordant MZ pairs (n = 49)			
BMI	1.19	1	0.273

Discussion

The object of this study was to analyze, in a genetically informative model, the possible relationship between anthropometric variables (BMI), physical activity (mild, moderate and intense) and a sedentary lifestyle, with the risk of having suffered lower back pain on some occasion. This way we expected to determine if an association existed between these variables and if said association was maintained after the genetic and shared environmental factors were controlled.

The results indicated that relationships exist between the considered predictor variables and the risk of suffering lower back pain. Thus, a higher BMI, spending hours sitting down and engaging in moderate or intense physical activity with less frequency are related with a greater risk of suffering lower back pain. On the other hand, the analyses also suggest that all these relationships are mitigated by genetic and shared environmental factors. None of the associations found in the analysis of the general sample maintained the significance in the case-control study, where the pairing of twins controls the effect of said factors. These results are in consonance with a prior study which also found a positive association between BMI and lower back pain in the general cohort analysis; this association disappeared when the case-control study was

conducted using MZ twins, which suggests that genetic factors could affect and confuse this relationship^[26]. Similarly, the inconsistency of the results found with respect to the association that exists between a sedentary lifestyle and physical activity (moderate as well as intense) with lower back pain suggest that this association is not direct; instead, it is affected by other factors.

The fact that lumbar pain is influenced by genetic factors suggests that individual characteristics should be considered in research and interventions in order to resolve it

This study also provides other results worth mentioning. This way we have found a higher prevalence of lower back pain in women than in males, which is normal in the literature^[40, 53-56] but also, we have found a different pattern as far as the influences of predictor variables by gender. This way while in women the BMI was related with the risk of suffering lower back pain, in males this risk was associated with a sedentary lifestyle and a very low frequency of engaging in physical activity. Moreover, age also seemed to have a differentiated impact. While older age entailed an increased risk in women, in males it had the opposite effect. Until now, different explanations have been offered for this

higher prevalence of lower back pain in women but the reason for this is still not clear. Some authors have suggested that women may be more prone to report feeling pain^[40], feeling pain for longer periods^[40], seeking medical attention more often^[57], or are more prone to suffering pain^[58, 59] than males. Our data suggests another possible explanation. It is possible that males and females represent specific sub-groups of patients with lower back pain and which, due to their body constitution and lifestyles, require a differentiated analysis, at least in this age group. For example, the distribution of body fat is different in adult women and men, where being overweight could cause a greater impact in some people than in others. On the other hand, the type of job and the intensity with which a sport is practiced also differ by genders, which could explain part of the differences that are found.

Men and women can represent specific subgroups of lumbar pain patients that require different analyses due to their physical characteristics and lifestyles

Another relevant question is one related with the effect that physical activity and a sedentary lifestyle have on lower back pain. In our study, although a protective effect seemed to exist between the frequency of moderate and intense physical activity and lower back pain, this association was not strong enough for it to be maintained in the analysis by gender. As mentioned above, it did not have a significant effect in the case-control study. On the other hand, the number of hours per week engaged in physical activity was irrelevant. In the case of a sedentary lifestyle, the risk of suffering lower back pain increased as

the person spent more hours sitting down during the day but only in males. This condition implies a complex and possibly reciprocal relationship between physical activity and lower back pain with non-generalized effects and important changes based on the characteristics of the subject. This would also explain the results found by other authors. For example, De la Cruz *et al.*^[21], found that the total amount of normal physical activity does not seem to have an effect on back pain. However, subjects that had experienced back pain during the past 12 months, had more frequently engaged in a low or moderate activity pattern. Other authors found that intense physical activity had a preventive effect^[32], while others found that a sedentary lifestyle as well as intense activity were associated with the risk of developing lower back pain^[33]. In other words, the literature provides contradictory evidence regarding what type and degree of physical activity may cause or prevent lower back pain^[31], which is consistent with the noted explanatory model, according to which different types and degrees of activity would have different effects based on the characteristics of the individual. Worth adding to this is that the discrepancies can also be a result of the different definitions and categories used for lower back pain as well as for physical activity.

This study presents certain limitations that must be taken into account when interpreting the results. First of all, the definition used for lower back pain is basic and does not include information about the different degrees, frequencies of appearance, origin of the episode or functional impact, which could contribute to grouping cases with different characteristics in the same category. On the other hand, the information obtained regarding lower back pain as well as the predictors that were taken into account were self-reported. It is known that the frequency as well as the duration of the physical activity as well as the weight and height can be over-estimated (e.g. height) or under-estimated (e.g. weight)^[33, 60]. Additionally, our study uses a cross-sectional model that limits the possibility of identifying the causal relationships between variables^[33]. This design prevents accurately determining if for example, the sedentary lifestyle is what causes a higher risk for suffering lower back pain or if it is the presence of this pain what generates a higher possibility of spending more time sitting down. Any of these interpretations would be plausible in light of the current literature^[61-63]. However, we believe that our study provides valuable information for understanding the individual differences regarding the prevalence of lower back pain, with important practical implications for preventing and rehabilitating this condition.

In summary, while the literature provides many different strategies for handling cases after an episode of lower back pain^[64, 65], it offers a limited evidence regarding the strategies for preventing these episodes from occurring. Given the important impact of lower back pain on the individual and on their environment, its functional effects and the consequences it has on peoples jobs and income, having information available on preventive strategies and rehabilitation is especially relevant. The current lack of clear evidence regarding the effectiveness of these type of interventions may be attributed to a certain lack of knowledge on the causal factors that are responsible for lower back pain^[66]. The conclusions of this study, although far from answering the questions that exist, may contribute to gaining a more in depth knowledge of these aspects. Thus, our results suggest a greater relevance of the frequency of physical activity than the duration of the activity, provides information on the role of moderate or intense physical activity and points to the avoidance of a

sedentary lifestyle and excess weight as areas that should be further explored due to their potential for preventing lower back pain. Also, our study suggests the need to take the individual (e.g. age) as well as group (e.g. gender) characteristics into account instead of assuming that any strategy and with any intensity should have the same preventive or rehabilitating impact on all persons. Finally, our study also suggests that we should take into account the role played by genetic factors on the analyzed associations. The fact that lower back pain as well as BMI or engaging in physical activity are influenced by these types of factors leads us to consider the weight of individual characteristics and the interest in conducting further research on personalized interventions.

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References

1. Vos T, Flaxman AD, Naghavi M, Lozano R, Michaud C, Ezzati M, et al. Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet.* 2013 Dec 15;380(9859):2163-96.
2. Kumar S, Beaton K, Hughes T. The effectiveness of massage therapy for the treatment of nonspecific low back pain: a systematic review of systematic reviews. *International journal of general medicine.* 2013;6:733-41.
3. INE. *Encuesta Nacional de Salud 2011/12.* . Instituto Nacional de Estadística / Ministerio de Sanidad, Servicios Sociales e Igualdad 2012.
4. Fernandez-de-Las-Penas C, Alonso- Blanco C, Hernandez-Barrera V, Palacios-Cena D, Jimenez-Garcia R, Carrasco-Garrido P. Has the prevalence of neck pain and low back pain changed over the last 5 years? A population-based national study in Spain. *Spine J.* 2013 Sep;13(9):1069-76.
5. Salvans MM, Gonzalez-Viejo MA. [Disability by low back pain in Spain from 2000 to 2004]. *Medicina clinica.* 2008 Sep 13;131(8):319.
6. Hestbaek L, Leboeuf-Yde C, Manniche C. Low back pain: what is the long-term course? A review of studies of general patient populations. *Eur Spine J.* 2003 Apr;12(2):149-65.
7. Andersson GB. Epidemiological features of chronic low-back pain. *Lancet.* 1999 Aug 14;354(9178):581-5.
8. Leboeuf-Yde C. Body weight and low back pain. A systematic literature review of 56 journal articles reporting on 65 epidemiologic studies. *Spine.* 2000 Jan 15;25(2):226-37.
9. van Poppel MN, Koes BW, Smid T, Bouter LM. A systematic review of controlled clinical trials on the prevention of back pain in industry. *Occupational and environmental medicine.* 1997 Dec;54(12):841-7.
10. Guh DP, Zhang W, Bansback N, Amarsi Z, Birmingham CL, Anis AH. The incidence of co-morbidities related to obesity and overweight: a systematic review and meta-analysis. *BMC Public Health.* 2009;9:88.
11. Shiri R, Karppinen J, Leino-Arjas P, Solovieva S, Viikari-Juntura E. The association between obesity and low back pain: a meta-analysis. *Am J Epidemiol.* 2009 Jan 15;171(2):135-54.
12. Heneweer H, Staes F, Aufdemkampe G, van Rijn M, Vanhees L. Physical activity and low back pain: a systematic review of recent literature. *Eur Spine J.* 2011 Jun;20(6):826-45.
13. Schiltenwolf M, Schneider S. Activity and low back pain: a dubious correlation. *Pain.* 2009 May;143(1- 2):1-2.
14. Malis C, Rasmussen EL, Poulsen P, Petersen I, Christensen K, Beck- Nielsen H, et al. Total and regional fat distribution is strongly influenced by genetic factors in young and elderly twins. *Obesity research.* 2005 Dec;13(12):2139-45.
15. Heitmann BL, Kaprio J, Harris JR, Rissanen A, Korkeila M, Koskenvuo M. Are genetic determinants of weight gain modified by leisure- time physical activity? A prospective study of Finnish twins. *The American journal of clinical nutrition.* 1997 Sep;66(3):672-8.
16. Heuch I, Heuch I, Hagen K, Zwart JA. Body mass index as a risk factor for developing chronic low back pain: a follow-up in the Nord-Trondelag Health Study. *Spine.* 2013 Jan 15;38(2):133-9.
17. Karnehed N, Tynelius P, Heitmann BL, Rasmussen F. Physical activity, diet and gene-environment interactions in relation to body mass index and waist circumference: the Swedish young male twins study. *Public health nutrition.* 2006 Oct;9(7):851-8.
18. Nelson MC, Gordon-Larsen P, North KE, Adair LS. Body mass index gain, fast food, and physical activity: effects of shared environments over time. *Obesity (Silver Spring, Md.* 2006 Apr;14(4):701-9.
19. Stubbe JH, Boomsma DI, Vink JM, Cornes BK, Martin NG, Skytthe A, et al. Genetic influences on exercise participation in 37,051 twin pairs from seven countries. *PloS one.* 2006;1:e22.
20. Andreasen CH, Stender-Petersen KL, Mogensen MS, Torekov SS, Wegner L, Andersen G, et al. Low physical activity accentuates the effect of the FTO rs9939609 polymorphism on body fat accumulation. *Diabetes.* 2008 Jan;57(1):95-101.
21. de la Cruz-Sanchez E, Torres-Bonete MD, Garcia-Pallares J, Gascon- Canovas JJ, Valero-Valenzuela A, Pereniguez-

- Barranco JE. [Back pain and restricted daily physical activity in the Spanish adult population]. *Anales del sistema sanitario de Navarra*. 2012 May-Aug;35(2):241-9.
22. Vismara L, Menegoni F, Zaina F, Galli M, Negrini S, Capodaglio P. Effect of obesity and low back pain on spinal mobility: a cross sectional study in women. *J Neuroeng Rehabil*. 2010;7:3.
 23. Haslam DW, James WP. Obesity. *Lancet*. 2005 Oct 1;366(9492):1197-209.
 24. Ferreira PH, Beekenkamp P, Maher CG, Hopper JL, Ferreira ML. Nature or nurture in low back pain? Results of a systematic review of studies based on twin samples. *European journal of pain (London, England)*. 2013 Aug;17(7):957-71.
 25. Mirtz TA, Greene L. Is obesity a risk factor for low back pain? An example of using the evidence to answer a clinical question. *Chiropr Osteopat*. 2005 Apr 11;13(1):2.
 26. Leboeuf-Yde C, Kyvik KO, Bruun NH. Low back pain and lifestyle. Part II--Obesity. Information from a population-based sample of 29,424 twin subjects. *Spine*. 1999 Apr 15;24(8):779-83; discussion 83-4.
 27. Hestbaek L, Leboeuf-Yde C, Kyvik KO. Are lifestyle-factors in adolescence predictors for adult low back pain? A cross-sectional and prospective study of young twins. *BMC Musculoskelet Disord*. 2006;7:27.
 28. Tsuritani I, Honda R, Noborisaka Y, Ishida M, Ishizaki M, Yamada Y. Impact of obesity on musculoskeletal pain and difficulty of daily movements in Japanese middleaged women. *Maturitas*. 2002 May 20;42(1):23-30.
 29. Riihimaki H, Wickstrom G, Hanninen K, Luopajarvi T. Predictors of sciatic pain among concrete reinforcement workers and house painters--a five-year follow-up. *Scand J Work Environ Health*. 1989 Dec;15(6):415-23.
 30. Wright LJ, Schur E, Noonan C, Ahumada S, Buchwald D, Afari N. Chronic pain, overweight, and obesity: findings from a community- based twin registry. *J Pain*. 2010 Jul;11(7):628-35.
 31. Sitthipornvorakul E, Janwantanakul P, Purepong N, Pensri P, van der Beek AJ. The association between physical activity and neck and low back pain: a systematic review. *Eur Spine J*. 2011 May;20(5):677-89.
 32. Hartvigsen J, Christensen K. Active lifestyle protects against incident low back pain in seniors: a population-based 2- year prospective study of 1387 Danish twins aged 70-100 years. *Spine*. 2007 Jan 1;32(1):76-81.
 33. Heneweer H, Vanhees L, Picavet HS. Physical activity and low back pain: a U-shaped relation? *Pain*. 2009 May;143(1-2):21-5.
 34. Livshits G, Popham M, Malkin I, Sambrook PN, Macgregor AJ, Spector T, et al. Lumbar disc degeneration and genetic factors are the main risk factors for low back pain in women: the UK Twin Spine Study. *Annals of the rheumatic diseases*. 2011 Oct;70(10):1740-5.
 35. Williams FM, Popham M, Sambrook PN, Jones AF, Spector TD, MacGregor AJ. Progression of lumbar disc degeneration over a decade: a heritability study. *Annals of the rheumatic diseases*. 2011 Jul;70(7):1203-7.
 36. Nyman T, Mulder M, Iliadou A, Svartengren M, Wiktorin C. High heritability for concurrent low back and neck-shoulder pain: a study of twins. *Spine*. 2011 Oct 15;36(22):E1469-76.
 37. Battie MC, Videman T, Levalahti E, Gill K, Kaprio J. Heritability of low back pain and the role of disc degeneration. *Pain*. 2007 Oct;131(3):272-80.
 38. Ropponen A, Svedberg P, Huunan-Seppala A, Koskenvuo K, Koskenvuo M, Alexanderson K, et al. Personality traits and life dissatisfaction as risk factors for disability pension due to low back diagnoses: a 30-year longitudinal cohort study of Finnish twins. *Journal of psychosomatic research*. 2012 Oct;73(4):289-94.
 39. Kristman VL, Hartvigsen J, Leboeuf- Yde C, Kyvik KO, Cassidy JD. Does radiating spinal pain determine future work disability? A retrospective cohort study of 22,952 Danish twins. *Spine*. 2012 May 15;37(11):1003-13.
 40. Leboeuf-Yde C, Nielsen J, Kyvik KO, Fejer R, Hartvigsen J. Pain in the lumbar, thoracic or cervical regions: do age and gender matter? A population-based study of 34,902 Danish twins 20-71 years of age. *BMC Musculoskelet Disord*. 2009;10:39.
 41. Pietikainen S, Silventoinen K, Svedberg P, Alexanderson K, Huunan-Seppala A, Koskenvuo K, et al. Health-related and sociodemographic risk factors for disability pension due to low back disorders: a 30-year prospective Finnish Twin Cohort Study. *Journal of occupational and environmental medicine / American College of Occupational and Environmental Medicine*. 2011 May;53(5):488-96.
 42. Maes HH, Neale MC, Eaves LJ. Genetic and environmental factors in relative body weight and human adiposity. *Behavior genetics*. 1997 Jul;27(4):325-51.
 43. Ordonana JR, Rebollo-Mesa I, Gonzalez-Javier F, Perez-Riquelme F, Martinez-Selva JM, Willemsen G, et al. Heritability of body mass index: a comparison between the Netherlands and Spain. *Twin Res Hum Genet*. 2007 Oct;10(5):749-56.
 44. Nan C, Guo B, Warner C, Fowler T, Barrett T, Boomsma D, et al. Heritability of body mass index in preadolescence, young adulthood and late adulthood. *European journal of epidemiology*. 2012 Apr;27(4):247-53.
 45. Hur YM, Kaprio J, Iacono WG, Boomsma DI, McGue M, Silventoinen K, et al. Genetic influences on the difference in variability of height, weight and body mass index between Caucasian and East Asian adolescent twins. *International journal of obesity (2005)*. 2008 Oct;32(10):1455-67.
 46. Schousboe K, Willemsen G, Kyvik KO, Mortensen J, Boomsma DI, Cornes BK, et al. Sex differences in heritability of BMI: a comparative study of results from twin studies in eight countries. *Twin Res*. 2003 Oct;6(5):409-21.
 47. De Moor MH, Posthuma D, Hottenga JJ, Willemsen G, Boomsma DI, De Geus EJ. Genome-wide linkage scan for exercise

- participation in Dutch sibling pairs. *Eur J Hum Genet*. 2007 Dec;15(12):1252-9.
- 48. De Moor MH, Stubbe JH, Boomsma DI, De Geus EJ. Exercise participation and self-rated health: do common genes explain the association? *European journal of epidemiology*. 2007;22(1):27-32.
 - 49. Goldberg J, M F. Co-Twin Control Methods. *Encyclopedia of Statistics in Behavioral Science*: Wiley Online Library 2005.
 - 50. Ordonana JR, Rebollo-Mesa I, Carrillo E, Colodro-Conde L, Garcia- Palomo FJ, Gonzalez-Javier F, et al. The Murcia Twin Registry: a population-based registry of adult multiples in Spain. *Twin Res Hum Genet*. 2013 Feb;16(1):302-6.
 - 51. Ministerio de Sanidad Servicios Sociales e Igualdad. *Encuesta Nacional de Salud de España 2011/12*. . 2012.
 - 52. Hallal PC, Victora CG. Reliability and validity of the International Physical Activity Questionnaire (IPAQ). *Medicine and science in sports and exercise*. 2004 Mar;36(3):556.
 - 53. McBeth J, Jones K. Epidemiology of chronic musculoskeletal pain. *Best Pract Res Clin Rheumatol*. 2007 Jun;21(3):403-25.
 - 54. Biglarian A, Seifi B, Bakhshi E, Mohammad K, Rahgozar M, Karimloo M, et al. Low back pain prevalence and associated factors in Iranian population: findings from the national health survey. *Pain Res Treat*. 2012;2012:653060.
 - 55. Fernandez-de-las-Penas C, Hernandez- Barrera V, Alonso-Blanco C, Palacios-Cena D, Carrasco-Garrido P, Jimenez-Sanchez S, et al. Prevalence of neck and low back pain in community-dwelling adults in Spain: a population-based national study. *Spine*. 2011 Feb 1;36(3):E213-9.
 - 56. Ferreira ML, Ferreira PH, Latimer J, Herbert RD, Hodges PW, Jennings MD, et al. Comparison of general exercise, motor control exercise and spinal manipulative therapy for chronic low back pain: A randomized trial. *Pain*. 2007 Sep;131(1-2):31-7.
 - 57. Weimer MB, Macey TA, Nicolaïdis C, Dobscha SK, Duckart JP, Morasco BJ. Sex differences in the medical care of VA patients with chronic non-cancer pain. *Pain Med*. 2013 Dec;14(12):1839-47.
 - 58. Berkley KJ. Sex differences in pain. *Behav Brain Sci*. 1997 Sep;20(3): 371-80; discussion 435-513.
 - 59. Schneider S, Randoll D, Buchner M. Why do women have back pain more than men? A representative prevalence study in the federal republic of Germany. *Clin J Pain*. 2006 Oct;22(8):738-47.
 - 60. Rzewnicki R, Vanden Auweele Y, De Bourdeaudhuij I. Addressing overreporting on the International Physical Activity Questionnaire (IPAQ) telephone survey with a population sample. *Public health nutrition*. 2003 May;6(3):299-305.
 - 61. Verbunt JA, Seelen HA, Vlaeyen JW, van de Heijden GJ, Heuts PH, Pons K, et al. Disuse and deconditioning in chronic low back pain: concepts and hypotheses on contributing mechanisms. *European journal of pain (London, England)*. 2003;7(1):9-21.
 - 62. Jacob T, Baras M, Zeev A, Epstein L. Physical activities and low back pain: a community-based study. *Medicine and science in sports and exercise*. 2004 Jan;36(1):9-15.
 - 63. van den Berg-Emons RJ, Schasfoort FC, de Vos LA, Bussmann JB, Stam HJ. Impact of chronic pain on everyday physical activity. *European journal of pain (London, England)*. 2007 Jul;11(5):587-93.
 - 64. Airaksinen O, Brox JI, Cedraschi C, Hildebrandt J, Klaber-Moffett J, Kovacs F, et al. Chapter 4. European guidelines for the management of chronic nonspecific low back pain. *Eur Spine J*. 2006 Mar;15 Suppl 2:S192-300.
 - 65. Thomassen J, Tulder MWv, Bekkering GE, Oostendorp RAB, Heniks HJM, Koes BW, et al. Dutch physiotherapy guidelines for low back pain. *Physiotherapy* 2003;89(2):15.
 - 66. Burton AK, Balague F, Cardon G, Eriksen HR, Henrotin Y, Lahad A, et al. Chapter 2. European guidelines for prevention in low back pain : November 2004. *Eur Spine J*. 2006 Mar;15 Suppl 2:S136-68.