# Social and Clinical Risk Determinants of Oral Lichen Planus – a Case Control Study

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**Abstract**

To examine potential social and clinical risk determinants of Lichen Planus.

Data was collected during the five years' time period and information was available about 133 patients with Oral Lichen Planus (OLP) and 133 gender, age and urbanization matched controls. Information about social (marital status, education, occupation) and clinical determinants (general health, medications, addictions, allergies, experience of negative life events and family history of systemic diseases) was collected from questionnaires. The presence of local etiological factors was assessed clinically. Bivariate and multivariate analyses were used to compare the study groups and the threshold for statistical significance was set at $P<0.05$.

There were more females than males with Lichen Planus. There were no statistically significant differences between OLP cases and their controls regarding social determinants, but OLP cases were statistically significantly worse in terms of local dental etiological conditions, systemic diseases, medications and allergies. In the logistic regression, all clinical risk determinants were statistically significantly related to OLP.

Oral Lichen Planus was not associated with social risk determinants. The associations between Lichen Planus and clinical risk determinants such as local dental-related etiological conditions, systemic diseases, medication use, and allergies were statistically significant.

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## Introduction

Oral Lichen Planus (OLP), most commonly found in middle-aged women; is a rare disease affecting about 0.1–4% of the population[1–3]. The pathogenesis of this mucocutaneous disease has been linked to cell-mediated immunological dysfunction[4,5]. Several local as well as systemic factors have been associated with OLP. Local etiological risks have been attributed to risks within the oral environment such as periodontal pathology, dental restorations or poor oral hygiene[6–11]. Systemic etiological factors risks have been related to Hepatitis C, thyroid diseases, gallbladder diseases, diabetes or stress[12–15].

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Addictions such as smoking and alcohol abuse have also been proposed as etiological agents[13]. However, no definite evidence has been established regarding the association between OLP and other autoimmune diseases[16]. Concomitantly, it has been suggested that there may still be unknown etiological factors for OLP[17]. Seemingly, there is a multiple array of risk determinants for OLP; thus, it is important to comprehensively explore a number of the potential risks for this rare disease.

OLP lesions commonly have a distinctive clinical morphology but sometimes they may present clinical patterns mimicking other diseases[2]. Consequently, the differential diagnosis of OLP may be problematic, e.g. OLP and Oral Lichenoid Lesions are clinically indistinguishable [18,19]. In most cases, a biopsy is recommended to confirm the diagnosis of OLP and exclude dysplasia or malignancy[20]. However, the majority of dentists (>85%) do not routinely take biopsies and have difficulty in differentiating among different types of oral mucosal lesions[21]. Moreover, when biopsies are taken by

inexperienced dental professionals these biopsies tend to be of low quality[22]; consequently, strict clinical and histological criteria are needed for a definite diagnosis of OLP[23].

In Lithuania, there is a deficiency of oral pathologists, therefore dentists from different locations around the country refer patients with suspected OLP to the Dental Clinic of Vilnius University. Due to the centralization of OLP cases in one location for diagnosis and treatment, a study focusing on multiple OLP risk determinants is feasible and standardization of biopsies, including oral histopathology, can be ensured.

For studying multiple risk determinants for rare chronic diseases such as Oral Lichen Planus where complex relationships among a multitude of risks may occur, it is important to examine local and systemic etiological risk determinants as well as evaluate the summative burden of risks. The majority of epidemiological OLP studies are case reports or case series, but these study designs are weak for studying the risks inherent in the development of rare diseases. The best primary study design for studying risks would be a prospective cohort study. However, such design is impractical for the study of rare diseases where the prevalence is relatively low. A practical and feasible study design for examining risks in OLP patients is a case control study where the distribution of diverse risks can be compared between patients with OLP (cases) and well-matched controls, i.e. patients without OLP.

Therefore, the present case control study examined a number of potential social and clinical risk determinants for Lichen Planus in a sample of patients with Oral Lichen Planus and in a similar sample of patients without this rare systemic condition.

## Materials and methods

The present study was approved by the Research Ethics Committee, the Faculty of Medicine, Vilnius University and by the Ministry of Health of Lithuania.

*Selection of Cases and Controls*

Cases were patients who were referred to the Vilnius University 's Dental Clinic from different locations around the country who had a Lichen Planus diagnosis histologically confirmed and who agreed to participate. Controls were patients not having OLP who were recruited from the patient pool attending the same University Clinic. The cases and controls were matched by gender, age and urbanization. The final sample included a total of 266 patients, of which 133 were cases and 133 were matched controls, all treated in the Žalgiris Dental Clinic of Vilnius University Hospital.

The level of matching was assessed by Chi-Square Test and is presented in Table 1. There were no statistically significant proportional differences regarding age, gender or urbanization between the cases and controls, thus matching was considered satisfactory.

| | Controls | | Lichen Planus Patients | | |
|---|---|---|---|---|---|
| Matching Criteria | Number | % | Number | % | Total: No (%) |
| **Matching by Gender** | | | | | |
| Males | 25 | 18.8 | 24 | 18.0 | 49 (18.4) |
| Females | 108 | 81.2 | 109 | 82.0 | 217 (81.6) |
| Total | 133 | 100.0 | 133 | 100.0 | 266 (100.0) |
| Chi Squared Test, P=0.500 | | | | | |
| **Matching by Age Group** | | | | | |
| ≤ 30 years | 12 | 9.0 | 12 | 9.0 | 24 (9.0) |
| 31-40 years | 12 | 9.0 | 9 | 6.8 | 21 (7.9) |
| 41- 50 years | 24 | 18.0 | 21 | 15.8 | 45 (16.9) |
| 51 -60 years | 34 | 25.6 | 38 | 28.6 | 72 (27.1) |
| 61 -70 years | 30 | 22.6 | 29 | 21.8 | 59 (22.2) |
| >70 years | 21 | 15.8 | 24 | 18.0 | 45 (16.9) |
| Total | 133 | 100.0 | 133 | 100.0 | 266 (100.0) |
| Chi Squared Test, P=0.957 | | | | | |
| **Matching by Urbanization** | | | | | |
| Urban | 104 | 78.2 | 102 | 76.7 | 206 (77.4) |
| Semi-urban/rural | 29 | 21.7 | 31 | 23.3 | 60 (22.6) |
| Total | 133 | 100.0 | 133 | 100.0 | 266 (100.0) |
| Chi Squared Test, P=0.441 | | | | | |

**Table 1.** Matching of Cases and Controls.

| Study Variables | Operationalization |
|---|---|
| DEMOGRAHIC FACTORS | |
| Age | Measured in age ranges: 30 years or less=1, 31-40 years=2, 41-50 years=3, 51-60 years=4, 61-70 years=5 and > 70 years=6. |
| Gender | Male=1 and Female=2. |
| Urbanization | Urban =1 and Semi-urban / Rural=2. |
| SOCIAL DETERMINANTS | |
| Marital Status | Single=1, married/common-law partner=2 and widow or widower=3 |
| | |
| Education | Secondary school or less=1, Trades education=2, College / University=3. |
| Occupation | Based on self-reports regarding occupation, three occupational groups were created: Low=1, Moderate=2 and High=3. |
| CLINICAL DETERMINANTS | |
| Local etiological conditions | Bimetallism, sharp tooth edges, poor oral hygiene, defective fillings, root tips, chronic endodontic or periodontal infections, untreated dental caries, silver amalgams, fixed prostheses (crowns, bridges) and removable prostheses. A total number of conditions was recorded. |
| Systemic Diseases | Presence of a systemic disease=1.<br>The total number of systemic diseases was recorded. |
| Medications Use | A total number of medications was recorded. |
| Addictions | A total number of addictions (smoking, alcohol abuse and/or drug-related addictions) was recorded. |
| Allergies | Allergies to any of the following: local anesthetics, antibiotics, sulfanilamide's, sleeping medications, anti-inflammatory, iodine, dental materials, food and other (specified). A total number of allergies was recorded. |
| Negative Life Events | A total number of negative life events was recorded (partner's death, death of a family member, divorce, financial problems, legal problems, severe morbidity or trauma). |
| Family History of Systemic Diseases | The presence of one or more systemic diseases in a family was reported. |

**Table 2.** Operationalization of the study variables.

*Social & Clinical Risk Determinants*

Social and clinical risk determinants were studied and the operationalization of them is

presented in Table 2. Information regarding social and clinical determinants except for local dentally-related risk determinants was collected by means of a structured questionnaire. In order to reduce the number of missing answers, personal interviews complemented questionnaires when information was incomplete. The information about local dentally-related etiological factors was obtained by a clinical assessment performed by one examiner (R.A).

The following social determinants were assessed: marital status and socio-economic status-related variables such as education and occupation. Given some of the study participants were either jobless, retired, still at school or staying at home, the information about these subjects was excluded from the socio-economic occupation-based grouping. This omission was necessary to have an accurate socio-economic occupation-based grouping into low, medium or high.

Data about clinical determinants was collected in seven domains: 1) local dental-related etiological conditions, 2) systemic diseases, 3) medication use, 4) addictions, 5) allergies, 6) experience of negative life events, and 7) family history of systemic diseases. Each of these domains was represented by several indicators; for specifics refer to Table 2. The present study took into consideration the overall burden of potential clinical risk determinants. Therefore, the total number of clinical risk determinants within each domain was calculated e.g. a total number of local dental etiological conditions, a total number of systemic diseases or a total number of allergies.

*Statistical analyses*

All statistical analyses were performed employing the SPSS Version 21.0 statistical software. Bivariate and multivariate analyses were employed to compare the study groups. Bivariate analyses were used to evaluate the quality of matching (Chi Square Test), the proportional difference between the study groups regarding potential social risk determinants (Chi Square Test), and differences in means regarding clinical risk determinants (Independent Sample t Test).

The multivariate logistic regression analysis examined the joint effect of both potential social and clinical risk determinants with the presence or absence of Lichen Planus being a dependent binary outcome. The threshold of statistical significance for all tests was set at $P<0.05$.

## Results

The present case control study included a total of 133 patients with Lichen Planus and a total of 133 matched controls. Bivariate analyses presented in Table 3 compared controls with cases regarding potential social risk determinants such as marital status, education and occupation and regarding a number of domains with clinical determinants such as local dental-related etiological factors, systemic diseases, medication use, negative life events, allergies, addictions and a family history of systemic diseases. There were no statistically significant proportional differences in social risk determinants, but there were statistically significant differences between cases and controls in a few domains of clinical determinants. The mean numbers of local dentally-related etiological conditions, systemic diseases, medication use, allergies and addictions differed statistically significantly between the cases and the controls. The most pronounced differences related to the mean number of systemic diseases and to the mean number of medications with subjects with OLP having worse general health and using more medications than their matched controls.

| | Matched Controls | | Lichen Planus Patients | | |
|---|---|---|---|---|---|
| | Number | % | Number | % | P values |
| **SOCIAL RISK DETERMINANTS #** | | | | | |
| **Marital Status** | | | | | |
| Single | 16 | 12.1 | 17 | 12.8 | |
| Married⁄Common Law | 98 | 74.2 | 97 | 72.9 | 0.971 |
| Widow⁄Widower | 18 | 13.6 | 19 | 14.3 | |
| **Education** | | | | | |
| Secondary school or less | 33 | 24.8 | 40 | 30.1 | |
| Trades education | 33 | 24.8 | 44 | 28.9 | 0.081 |
| College⁄University | 67 | 50.4 | 49 | 36.8 | |
| **Occupation** | | | | | |
| Low | 7 | 8.0 | 3 | 4.1 | |
| Medium | 13 | 14.9 | 12 | 16.2 | 0.575 |
| High | 67 | 77.0 | 59 | 79.7 | |
| **CLINICAL RISK DETERMINANTS *** | **Number** | **mean±SD** | **Number** | **mean±SD** | **P values (95%CI)** |
| Local etiological conditions | 133 | 2.6±1.9 | 133 | 3.3±1.8 | 0.002(-1.15;-0.26) |
| General Health | 133 | 1.5±1.6 | 133 | 2.8±2.4 | <0.001 (-1.81; -0.83) |
| Medication Use | 133 | 0.6±1.1 | 133 | 1.2±1.0 | <0.001(-0.81;-0.29) |
| Negative Life Events | 133 | 2.1±1.4 | 133 | 1.8±1.4 | 0.106 (-0.06;0.62) |
| Allergies | 133 | 0.2±0.5 | 133 | 0.5±0.9 | <0.001 (-0.48;-0.15) |
| Family History of Systemic Diseases | 133 | 1.1±0.8 | 133 | 0.9±0.8 | 0.258 (-0.08;0.31) |
| Addictions | 133 | 0.3±0.6 | 133 | 0.1±0.4 | 0.002 (0.08;0.33) |

# Chi Squared Test or Fischer,s Exact; *Independent Sample t test or Mann-Whitney U test

**Table 3.** Risk Determinants in Lichen Planus Patients and Controls – Bivariate Analyses.

Figures 1-5 demonstrate in more detail the distribution of study subjects regarding the clinical risk domains, where differences between the study groups and their variations can be

observed. Although in both groups around 75% of patients presented with at least one potential local dental-related etiological condition, an overall trend was that cases had more of these local etiological risks than a group of their matched controls (Table 4, Figure 1).

| RISK DETERMINANTS | P values | Odds Ratio |
|---|---|---|
| Gender | 0.733 | 0.9 |
| Education | 0.461 | 0.9 |
| Age | 0.700 | 1.0 |
| Local etiological factors | 0.002 | 1.3 |
| Systemic Diseases | 0.001 | 1.4 |
| Medication Use | 0.001 | 1.6 |
| Allergies | 0.003 | 2.3 |
| Negative Life Events | 0.003 | 0.7 |
| Family History of Systemic diseases | 0.080 | 0.7 |
| Dependent Binary outcome: Controls=0; Lichen Planus Cases=1 Model Summary: Chi Square=59.9; -2 Log Likelihood=308.841; Nagelkerke R Square=0.269; P<0.001. | | |

**Table 4.** Risk Determinants in Lichen Planus Patients (Logistic Regression of.

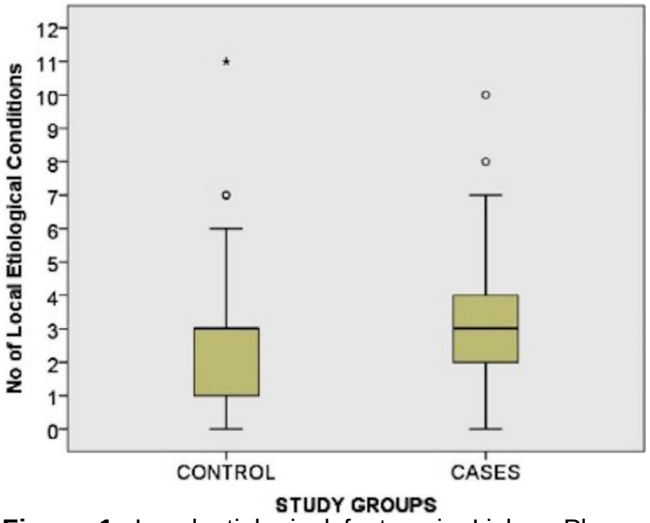


**Figure 1.** Local etiological factors in Lichen Planus Patients $ Matched Controls.

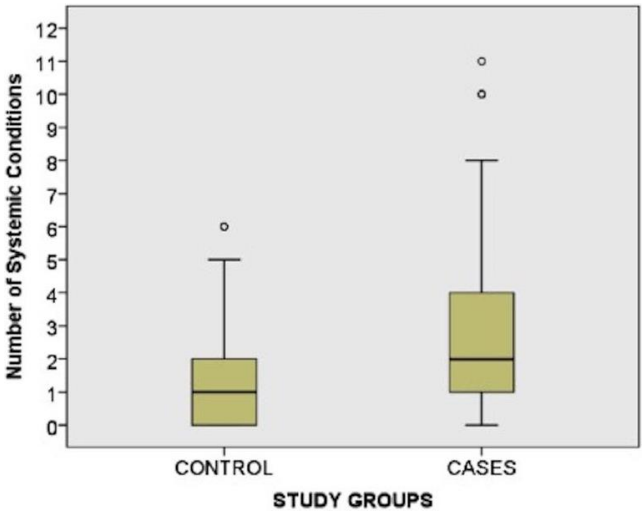


**Figure 2.** Systemic Conditions in Lichen Planus Patients & Matched Controls.

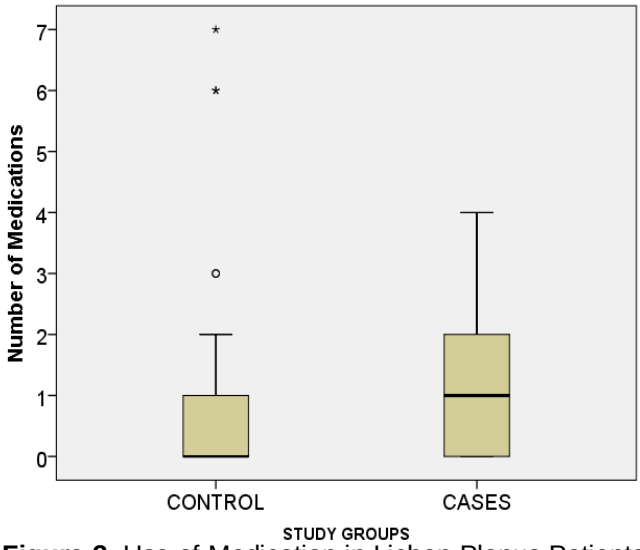


**Figure 3.** Use of Medication in Lichen Planus Patients & Matched Controls.

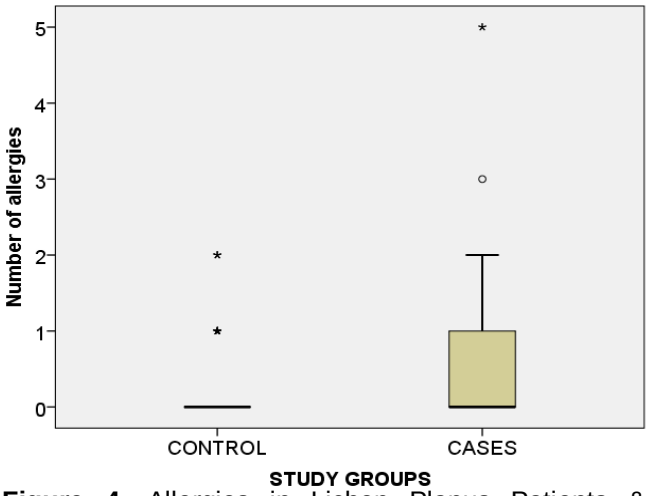


**Figure 4.** Allergies in Lichen Planus Patients & Matched Controls.

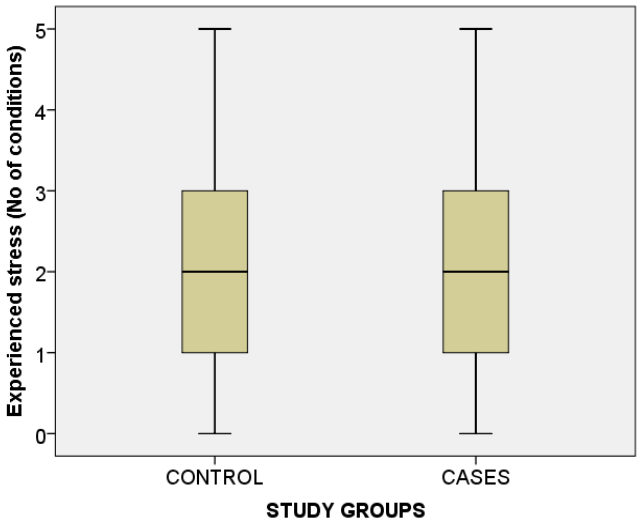


**Figure 5.** Negative Life Events in Lichen Planus Patients & Matched Controls.

Similar differences can be observed regarding the number of systemic conditions (Figure 2) or regarding the medication use (Figure 3). One can see that higher proportions of OLP patients had more systemic diseases and used more medications than controls. The clearest trend was observed when mean numbers of allergies and their distribution was compared among the two study groups (Figure 4), demonstrating that allergies were rare in the control group, while the cases presented with a considerable number of allergies. The Figure 5 illustrates the distribution within each group as it relates to experiencing negative life events. Seemingly both study groups had similar stress-related experiences. As there were only a few patients with addictions in both groups, no graph illustration is presented.

A joint effect of both social and clinical risk determinants was analyzed by means of logistic regression, where a dependent binary outcome was either a control designated with a ´0´ value or a case given a value ´1´. The overall logistic regression model was highly statistically significant (P<0.001) and the predictors (risk determinants) jointly explained around 27% of the variation (Nagelkerke R Square=0.269) in the dependent binary outcome. Similar patterns emerged in the multivariate analysis (logistic regression) as in the bivariate analyses, i.e. social risk determinants did not associate with Oral Lichen Planus, while OLP associations were statistically significant with all clinical risk determinants except for the family history of systemic diseases. In the logistic regression, the following statistically significant positive associations with OLP were found (OR>1.0, P<0.05): local dentally-related etiological conditions, systemic diseases, medication use and presence of allergies. An unexpected statistically significant negative relationship with OLP (OR<1.0, P<0.05) was observed in multivariate analysis regarding the negative life events.

## Discussion

The present case control study examined a number of potential risk determinants for Oral Lichen Planus (OLP). Due to ethical and practical reasons, to study rare diseases such as OLP a case control study design is the only feasible option. The inherent challenge in case control studies is to recruit a good control group, i.e. to have well-matched cases with controls. Cases with controls are commonly matched by gender and age. In addition to matching by gender and age, we also added residency as a matching criterion. Our matching was successful as there were no statistically significant differences between cases and controls related to any of the three matching criteria: gender, age and urbanization.

We examined a number of social and clinical potential risk determinants and associated them with OLP. As it relates to social determinants, there were no observable either bivariate or multivariate associations between social risk determinants such as marital status, education or occupation and Lichen Planus. A comprehensive approach to study the clinical risk determinants has been taken in the present study, i.e. instead of focusing only on a few risk determinants, we examined several domains of them and included both local as well as systemic clinical risk determinants in both bivariate as well as multivariate analyses. To enable comparisons between the cases and the controls we examined summative risks within each clinical domain. For example, the summative risk in the domain of local dental-related etiological conditions was indicated by a total number of these conditions such as trauma from sharp tooth corners, dental restorations, presence of periodontal or endodontic infections, poor oral hygiene, etc. Similarly, a burden of systemic general health-related risks was measured as a total number of systemic diseases or a total number of medications used. This way, a total of seven domains of potential clinical risk determinants were analyzed both bivariately and multivariate. In the bivariate analyses, five of the clinical determinants associated statistically significantly with OLP (local dental-related etiological conditions, systemic diseases, medication use, addictions and allergies).

In the multivariate logistic regression analysis, where joint effect of multiple social and clinical risk determinants was studied, none of the social risk determinants related statistically significantly to OLP, while all risk determinants from the clinical domains presented statistically significant associations. Some associations between Oral Lichen Planus and clinical determinants such as the number of systemic diseases, use of medications and allergies were

expected, while the association between OLP and experiencing negative life events such as a partner's death, death of another family member, divorce, financial problems, legal problems, severe morbidity or trauma was unexpected. As it relates to experiencing negative life events, both groups had a similar mean number of them and only a relatively small proportion of the study participants reported the presence of a family history of systemic diseases. Our findings are in accordance to other studies, where co-morbidities of systemic diseases or a family history of them was rather low in OLP patients[14], or where no association between OLP and systemic diseases or medication use[24] or between OLP and addictions (smoking, alcohol abuse) were found[25]. As it relates to coping with negative life events, it is important to consider that interindividual variations in effective coping with stressful events as well as in OLP itself exist [26]. Possibly, despite that both study groups experienced similar levels of negative life events, the controls were worse in coping with these negative life events. As to both unexpected multivariate associations, future studies are needed to answer why these unexpected results were obtained.

It is also important to consider some limitations of the present study. A study design we chose (a case control study) was ethical and practical but this study design due to its inherent nature does not allow any causal inferences of the study findings. Another limitation relates to a relatively small sample size; a larger sample size may be necessary for sub-analyses or to ask more specific questions, particularly given that there was little variation in risk determinants from some of the clinical domains. As the patterns of diverse risk determinants and their relationship to Lichen Planus seem to be complex, future studies with larger sample sizes than in the present study should be considered.

## Conclusions

There were more females than males with Lichen Planus, but this rare systemic disease was not associated with social risk determinants such as marital status, education or occupation. There were statistically significant associations among Lichen Planus and a number of systemic conditions such as more systemic diseases, medications or allergies in a group of cases as compared to their matched controls were found.

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## Declaration of Interest

All authors declare they don't have any conflict of interest. All authors have made substantive contribution to this study and/or manuscript, and all have reviewed the final paper prior to its submission.

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