



PREVENTABLE RISK FACTORS ASSOCIATED WITH ORAL POTENTIALLY MALIGNANT DISORDERS: A STUDY IN SAUDI ARABIA

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AUTHORS' CONTRIBUTIONS

This work was carried out in collaboration among all authors. Author MM designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors FK and FK managed the analyses of the study. Author AAA managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Background: Oral potentially malignant disorders, (OPMDs) include a highly diverse forms of lesions and conditions with an increased risk for malignant transformation to oral cancer. The exact etiology of OPMDs is not fully understood yet, however, some preventable risk factors have been reported. The objective of this study is to recognize the correlation of preventable risk factors with OPMDs.

Patients and Methods: A prospective cross-sectional study was conducted at King Salman Hospital, Riyadh, KSA. A total of 1340 patients were screened with 6.49% (n=87) showing OPMDs. All Saudi and non-Saudi patients above fifteen years of age having suspicious lesions were included in the study after evaluation.

Results: The sample comprised 50 (58%) males and 37 (42%) females. Out of 87 patients, 75(86%) were Saudi and 11(14%) were non-Saudi. Buccal mucosa was the most common site for OPMDs (51.72%), followed by the tongue (31.03%). The results of our study reveal that the most prevalent age group was from 25 to 35 years followed by 36-45 years age group. Records of medical history showed that (3%) of patients had Type I Diabetes, Type 2 Diabetes was observed in 16%, anemia in 10% and 2% had history of Hepatitis C. The highest number of OPMDs lesion was lichen planus (51%) followed by leukoplakia (19%). Smoking was found to be the most prevalent risk factor. Results showed that (11%) of OPMDs has soft tissue odontogenic trauma, (7%) of patients are on antihypertensive and antidiabetic medicines, (19%) were multifactorial and (30%) reported with unknown etiology.

Conclusion: On the basis of our findings, we suggest that all general practitioners and physicians should have enough knowledge about OPMDs. Healthy life style can prevent diabetes, anemia and hypertension. Early management of OPMDs can prevent major complications and progression into cancer.

Keywords: Oral potentially malignant disorders; risk factors; leukoplakia; erythroplakia; lichen planus; dental trauma; erosive lichen planus; proliferative verrucous leukoplakia; candidiasis.

1. INTRODUCTION

Oral potentially malignant disorders (OPMDs), can be defined as “the risk of malignancy being present in a lesion or condition either at the time of initial diagnosis or at a future date” [1]. OPMDs include a highly diverse forms of lesions and conditions with an increased risk for malignant transformation (MT) to oral squamous cell carcinoma (OSCC) [2]. OPMDs are generally reported in 5th and 6th decade of life. However, in the last few years, a new pattern of OPMDs has emerged in which there is a greater incidence of younger age groups [3]. Overall population-base studies on the prevalence of OPMDs are limited but it has been estimated that the worldwide prevalence of OPMDs is 4.47% with higher male predilection. Moreover, the highest prevalence rates of OPMDs were found among the Asian populations [4]. In Saudi Arabia specifically, the prevalence of OSCC which is usually preceded by OPMDs varies from 21.6% to 68.6%, it is considered a major public health issue in the southern region of Saudi Arabia especially in Jizan province due to common practice of smokeless tobacco, namely Shammah [5].

The exact etiology of OPMDs is not fully understood yet [6]. However, some preventable risk factors such as tobacco chewing, tobacco smoking, alcohol and diet deficient in fruit and vegetables have a strong correlation with the development of such conditions [7]. Metabolic disorders associated with OPMDs includes Diabetes [8], abnormal body mass index [7] and patients on different medication [9]. Local factors may also have an etiological role in the development of OPMDs include odontogenic trauma, prosthesis mucosal trauma and malocclusion [10]. In addition, various inherited and acquired diseases like xeroderma pigmentosum, dyskeratosis congenita, Fanconi's anemia, chronic iron deficiency anemia and immunodeficiency are also enlisted as OPMDs preceding oral carcinoma [1].

It has been established that 15-48% of OSCC cases had an associated history with OPMDs [11]. There is a wide spectrum of oral mucosal lesions which possess a higher tendency to evolve into malignancies, the World Health Organization has identified these lesions as OPMDs including leukoplakia, erythroplakia, palatal lesion of reverse cigar smoking, oral lichen planus, oral submucous fibrosis, and discoid lupus erythematosus. It has been reported in the literature that of the previously mentioned lesions; leukoplakia, erythroplakia, erosive

lichen planus and submucous fibrosis [12] have more tendency for malignant transformations as compared to other OPMDs. Moreover, Superimposed Candida infections in some recognized OPMDs have a synergistic effect in the development of OSCC, for example, a Leukoplakia lesion with candida infection has more potential for malignant transformation as compared to uninfected leukoplakic lesion [13].

Oral leukoplakia (OL) is the most common among potentially malignant disorders of oral mucosa [14]. According to the World Health Organization in 1978, it is a white patch or plaque which cannot otherwise be characterized clinically or pathologically as any other disease. In studies reported in recent years, the prevalence of oral leukoplakia varies between 1.1% and 11.7%, with a mean value of 2.9% [15]. Risk factors for malignant transformation include longer duration of leukoplakia, non-smokers, non-homogenous type, size greater than 200 mm² and presence on the tongue and floor of mouth [16]. *Erythroplakia* is a bright red velvety plaque, it is generally associated with the underlying epithelial dysplasia and carries a greater risk of turning into malignancy than leukoplakia [1]. *Oral Lichen Planus* prevalence is less than 1%, most affected individuals are middle aged with (0 to 10%) malignant transformation rate [17]. Although oral lichen planus is still under debate to consider as OPMD, however, literature reports erosive lichen planus indicates higher than expected rate of malignant transformation over period of time [18]. The oral cancer progression has also been reported at molecular level in the erosive lichen planus lesions [19].

Oral submucous fibrosis (OSF) has a strong established association with betel quid and nut chewing especially in Indian subcontinent and south East Asia. OSF has greater risk of malignant transformation estimated between (2% to 8%) [20]. It is conspicuous that early diagnosis and management of OPMDs can prevent their possible progression into OSCC [21]. Restriction of preventable risk factors decrease the risk of developing OSCC [3]. Therefore, the purpose of this study is to observe the correlation of preventable and predictable factors with the development of oral potentially malignant disorders in Saudi population. In order to provide health-care providers with the latest reported data about the high-risk OPMDs, to be utilized as an aid in identification of these lesions at their early stage thus reducing the morbidity and mortality of oral cancer.

2. PATIENTS AND METHODS

This prospective cross-sectional study was conducted after the approval of Hospital’s Ethical Review committee in Oral Surgery and Oral Medicine Clinics at King Salman Hospital, Riyadh, Saudi Arabia from May 2018 to May 2020. Referrals accepted included other specialty clinics inside the hospital, dental OPD diagnostic, Tanseeq system acceptance, indoor patients’ consultations and referral from other public or private sectors and primary health care centers. Most patients were referred with their biopsy report which was carried out at their primary centers and any further remaining suspicious lesions biopsy was carried out at our clinics. All patients were kept under follow up and conservative treatment.

All Saudi and non-Saudi patients above fifteen years of age having suspicious lesions persisting for more than two weeks were included in the study after evaluation. Laboratory investigations included complete blood count, vitamins profile and folic acid deficiency to rule out the systemic diseases as these may interfere with the oral lesions. The body mass index was calculated using the formulae $BMI = \text{height}/\text{weight}^2$, it was then categorized according to the International Classification of Obesity into three strata as follows; underweight, normal, and overweight/obese.

3. RESULTS

The collected data was entered and analyzed using Statistical Package of Social Science (SPSS version 23). A p value ≤ 0.05 was considered significant. Chi-

square analysis and likelihood ratio was calculated to find out if there is any association between the variables. A total of 1340 patients attended the dental clinics from May 2018 to May 2020 and from those only 87 patients were identified with OPMDs showing a prevalence of 6.49%. Among these 87 patients (81%) were biopsy proven and have been referred to our OMFS and OM clinics for consultation. The sample comprised 50 (58%) males and 37 (42%) females with a ratio of 1.35:1. Patients having OPMDs were divided into five age groups. Group I: 15-25, Group II: 26-35, Group III: 36-45, Group IV: 46 -55 and Group V: Above 55 years. The results of our study revealed that the most prevalent age group was from 25 to 35 years followed by 36-45 years age group. The distribution of data according to age is depicted in Fig. 1.

The distribution of oral potentially malignant disorders according to the involved site is illustrated in Fig. 2, buccal mucosa was the most common site (51.72%), followed by the tongue (31.03%).

Majority of our participants had normal Body Mass Index (82%), with only 18% having either low or high BMI. Records of medical history showed that (3%) of patients had Type I Diabetes, Type 2 Diabetes was observed in 16%, anemia in 10% and 2% had history of Hepatitis C. Risk factors contributing in development of OPMDs observed in our study are depicted in Fig. 3, smoking was found to be the most prevalent risk factor. Results showed that (11%) of OPMDs had soft tissue odontogenic trauma, (7%) of patients are on antihypertensive and antidiabetic medicines, (19%) were multifactorial and (30%) reported with unknown etiology.

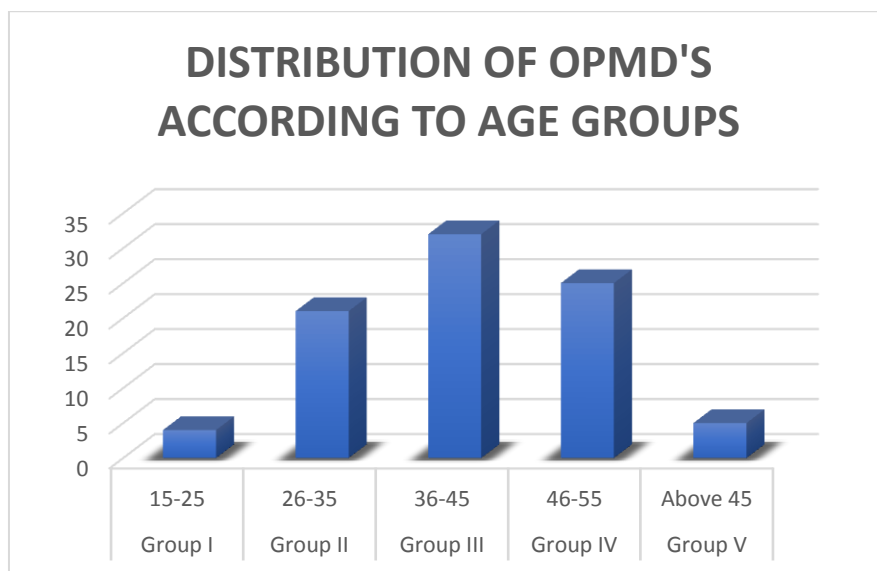


Fig. 1. Distribution of OPMD’s according to age group

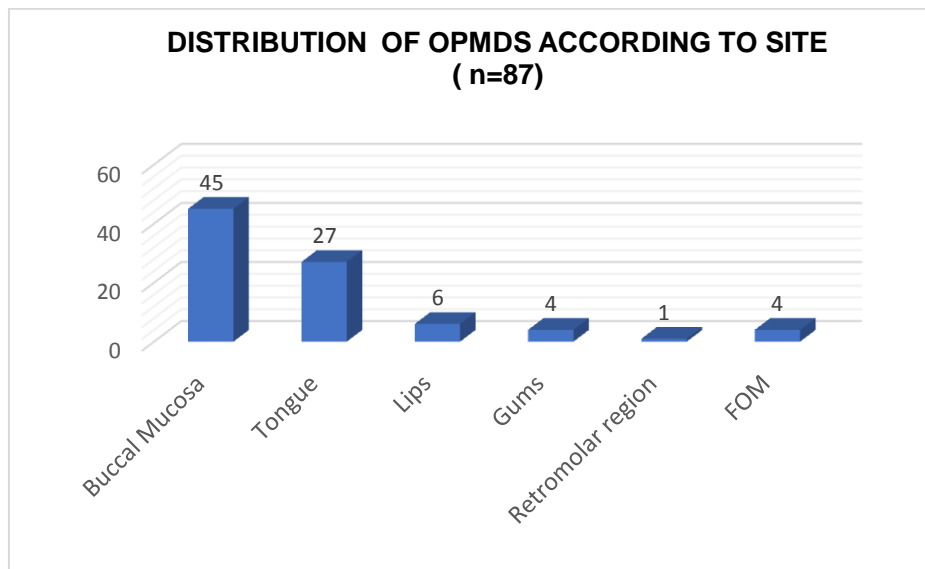


Fig. 2. Distribution of OMPDs according to site

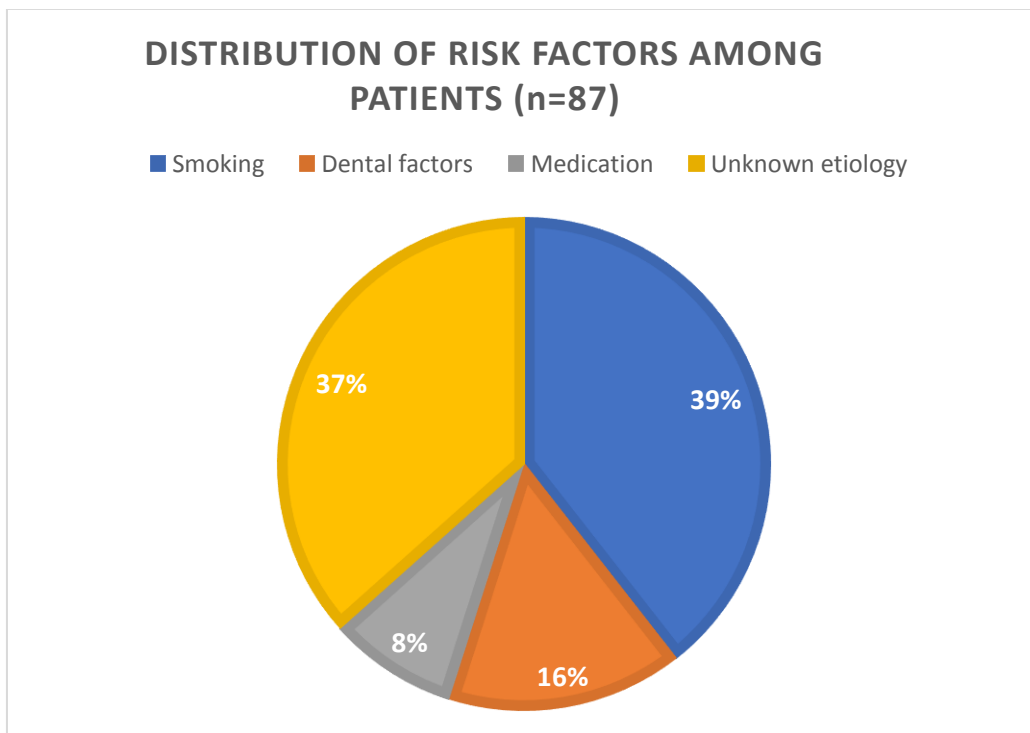


Fig. 3. Distribution of OMPDs according to risk factors

A distribution of the cases according to their exact pathology is given in Fig. 4. It was seen that highest number of OPMDs lesion was lichen planus (51%) followed by leukoplakia (19%).

Clinical pictures of oral lichen planus and leukoplakia and are shown in Fig. 5 and Fig. 6.

In the study Pre-malignant Disorder was found associated with BMI, Diabetes II, Medication,

Anemia, Smoking, Unknown and Location. The data of statistical analysis is depicted in Table 1.

4. DISCUSSION

The objective of this study is to observe the correlation between diverse predictable and preventable risk factors and OPMDs. The two terms, “precancerous lesions and precancerous conditions”

had been used since 1978 to identify morphologically altered tissue that is more prone to develop cancer as compared to its apparently normal counterpart. In 2005, the WHO introduced a new terminology “oral

potentially malignant disorders” in replacement of the previously used two terms. OPMDs are lesions which are at more risk to develop into malignancy [22].

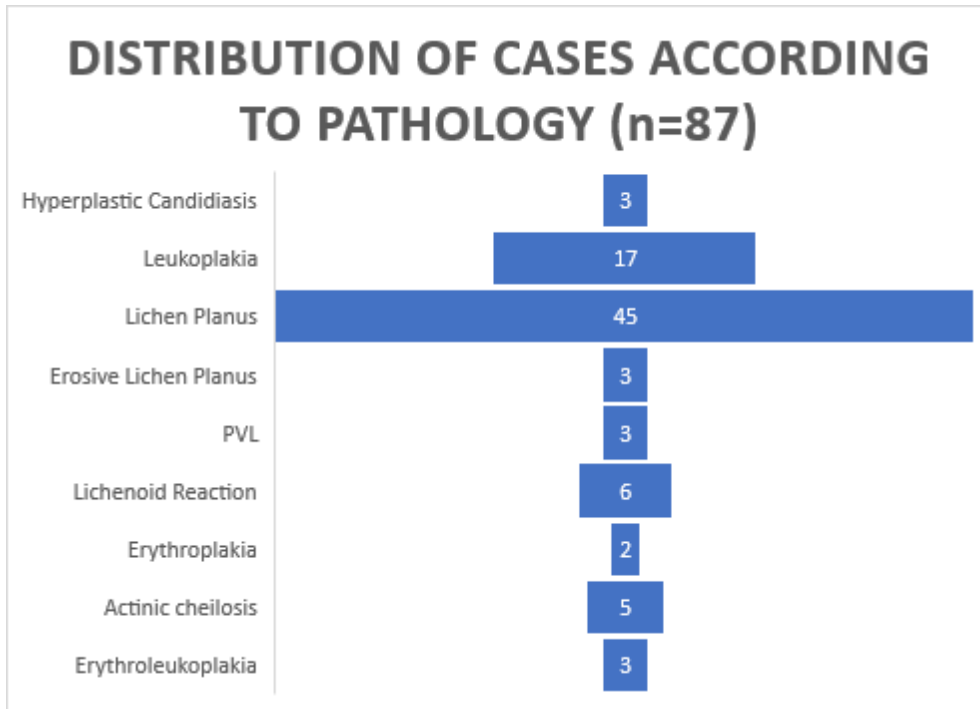


Fig. 4. Distribution of cases according to pathology



Fig. 5. Lichen Planus involving buccal mucosa and alveolar ridge bilaterally.



Fig. 6. Leukoplakia at right buccal mucosa

Table 1. Likelihood ratio for oral potentially malignant disorders

Oral Potentially Malignant Disorders		AC	ELP	EL	E	HC	L	LP	LR	PVL	P- value
Gender	Male	5(11.1%)	1(2.2%)	2(4.4%)		1(2.2%)	12(26.7%)	19(42.2%)	3(6.7%)	2(4.4%)	0.003
	Female		2(4.8%)	1(2.4%)	2(4.8%)	2(4.8%)	5 (11.9 %)	26(61.9%)	3(7.1%)	1(2.4%)	
BMI	Low			2(28.6%)		1(14.3%)	1(14.3%)	3(42.9%)			0.004
	Normal	5(7.0%)	3(4.2%)	1(1.4%)	2(2.8%)	2(2.8%)	15(21.1%)	38(53.5%)	2(2.8%)	3(4.2%)	
	High						1(11.1%)	4(44.4%)	4(44.4%)		
Diabetes	No	5(6.8%)	3(4.1%)	3(4.1%)	2(2.7%)	3(4.1%)	14(19.2%)	40(54.8%)		3(4.1%)	<0.001
	Yes						3(21.4%)	5(35.7%)	6(42.9%)		
Medication	No	5(6.2%)	3(3.7%)	3(3.7%)	2(2.5%)	3(3.7%)	17(21.0%)	45(55.6%)		3(3.7%)	<0.001
	Yes								6(100.0%)		
Anemia	No	5(6.4%)	3(3.8%)	1(1.3%)		2(2.6%)	15(19.2%)	43(55.1%)	6(7.7%)	3(3.8%)	0.003
	Yes			2(22.2%)	2(22.2%)	1(11.1%)	2(22.2%)	2(22.2%)			
Smoking	No		3(5.1%)		2(3.4%)	2(3.4%)	7(11.9%)	37(62.7%)	5(8.5%)	3(5.1%)	<0.001
	Yes	5(17.9%)		3(10.7%)		1(3.6%)	10(35.7%)	8(28.6%)	1(3.6%)		
	Yes										

AC: Actinic Cheilosis, ELP: Erosive Lichen Planus, EL: Erythroleukoplakia, E: Erythroplakia, HC: Hyperplastic Candidiasis, L: Leukoplakia, LP: Lichen Planus, LR: Lichenoid Reaction, PVL: Proliferative Verrucous Leukoplakia

Oral cancer is a serious condition with high morbidity and mortality rate. It is an established fact that oral cancer is mostly preceded by OPMDs. Moreover, in recent years there has been a significant increase in the number of OSCC cases in Saudi Arabia [5, 23]. It is noteworthy that if these OPMDs are diagnosed at earlier stages, they are more likely to be treated more easily with very good prognosis. These OPMDs include: erythroplakia, non-homogeneous leukoplakia, erosive lichen planus, oral submucous fibrosis and actinic keratosis. Moreover, erythroplakia, non-homogeneous leukoplakia, erosive lichen planus, oral submucous fibrosis and actinic keratosis possess the most likely potential of transforming to carcinoma [2, 24]. The results of our study demonstrated that Lichen planus (51%) is the most prevalent OPMD followed by leukoplakia (19%), this finding is in contrast with Mortazvi and Saman Warnakulasuriya et al studies which concluded that leukoplakia is the most common OPMD encountered in clinical practice [24].

Our findings revealed higher male predilection in patients presenting with OPMDs which is in accordance with Ferreira et al study that also revealed male predominance [25]. Moreover, average age of patients having OPMDs is 50–69 years, however, recent studies have shown a new pattern of OPMDs with greater incidence of younger patients from 30 to 50 years [1], this finding is in agreement with our study which showed highest number of cases in the age group ranging from 30 to 40 years. Nevertheless, our study findings are in contrast with Ferreira et al study in which the mean age for OPMDs was 60 years. Also, studies show that people having low BMI are more prone to develop OPMDs as compared to healthy individuals. Our study results showed that (8%) had low BMI and (10%) had high BMI whereas majority (82%) of patients developed OPMDs in spite of their normal BMI which is in contrast with Sandeep Kumar et al. [26] study in which an inverse relationship was reported between the BMI and the development of oral potentially malignant disorders in underweight individuals. The most common involved site in our study was buccal mucosa (51.72%) followed by the tongue (31.03%) which is in agreement with Manthapuri et al. [27] and Nega et al study in which the most common site recognized for the occurrence of OPMDs was buccal mucosa followed by tongue [28].

The etiology OPMDs development is multifactorial. Results of our study showed that a great number of patients who developed OPMDs practiced the habit of smoking (smoked and smokeless variations) which is in accordance with Vidya Kadashetti et al study in which they also concluded that smoking and chewing

tobacco is a strong risk factor associated with the development of OPMDs and oral cancer [29]. One of the emerging risk indicators for occurrence of OPMDs are dental factors such as sharp tooth cusp, broken tooth, ill-fitted dentures with sharp clasp, broken restorations or crowns, all of the previously mentioned situations are sources of constant trauma and can be regarded as etiological factors giving rise to OPMDs. Our study also showed that (11%) of patients had history of different dental factors which is in agreement with Eduardo David Piemonte et al study which suggests that chronic trauma, together with other factors, is considered an important risk factor in patients with oral cancer more compared to those with OPMDs [30]. In addition, diabetes is a metabolic disorder effecting the oral mucosa. There is a positive association between diabetes and development of OPMDs [31]. Our results demonstrated that (19%) of patients having OPMDs had history of diabetes which is similar to the findings reported by Sandeep et al. in which diabetes was found to be a major risk factor for the occurrence of OPMDs.

5. CONCLUSION

Interception of preventable factors should be always prioritized. All general practitioners and physicians should have enough knowledge and awareness about the development of oral potentially malignant lesions. Our study showed that the use of smoked and smokeless tobacco is a major preventable risk factor. Healthy life style including a balanced diet and regular physical activity can prevent diabetes, anemia and hypertension. Early management of OPMDs can prevent major complications and progression into cancer.

CONSENT AND ETHICAL APPROVAL

This prospective cross-sectional study was conducted after the approval of Hospital's Ethical Review committee in Oral Surgery and Oral Medicine Clinics at King Salman Hospital, Riyadh, Saudi Arabia from May 2018 to May 2020. Verbal consent was taken from all the participants before enrollment.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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