



ORIGINAL ARTICLE

Association between the eruption of the third molar and caries and periodontitis distal to the second molars in elderly patients



Yu-Hsiang Chou ^a, Pei-Shan Ho ^b, Kun-Yen Ho ^c, Wen-Chen Wang ^c,
Kai-Fang Hu ^{d,*}

^a Division of Periodontics, Department of Dentistry, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan

^b Faculty of Dental Hygiene, College of Dental Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan

^c School of Dentistry, College of Dental Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan

^d Department of Dentistry, Kaohsiung Municipal Ta-Tung Hospital, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan

Received 29 August 2016; accepted 15 February 2017

Available online 27 March 2017

KEYWORDS

Elderly patients;
Periodontitis;
Second molar caries;
Third molar

Abstract The objective of this study was to verify whether caries and periodontal diseases, when present on the distal surface of the second molars (M2s), are associated with the eruption of the third molars (M3s). In this split-mouth study, we evaluated 70 elderly patients with unilateral maxillary or mandibular M3s who presented to the outpatient clinics of two hospitals. Patients underwent comprehensive oral examinations and radiographical measurements, and we assessed the outcomes of periodontal disease and caries. Periodontal measurements included plaque index, bleeding on probing, and periodontal probing pocket depth (PD). Moreover, caries were assessed through visual–tactile examination and radiography. We performed the χ^2 test to determine factors associated with M3 and non-M3 outcomes. Eighty-one unilateral erupted M3s were observed in the study patients. Both the distobuccal region ($p < 0.0001$) and the distolingual region ($p = 0.006$) had a higher PD on the nonextraction side than the extraction side, and the caries rate was significantly higher on the nonextraction side than on the extraction side ($p < 0.0001$ on M2 with caries and $p = 0.003$ on M2 with distal caries). M3 eruption, at the same or different occlusal plane levels of M2, is a risk factor for periodontal diseases and caries in M2s in elderly patients. M3s may continue to negatively impact dental health well into later life.

Conflicts of interest: All authors declare no conflicts of interests.

* Corresponding author. Department of Dentistry, Kaohsiung Municipal Ta-Tung Hospital, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Number 100, Tzyou 1st Road, Kaohsiung 807, Taiwan.

E-mail address: kaifang729@yahoo.com.tw (K.-F. Hu).

<http://dx.doi.org/10.1016/j.kjms.2017.03.001>

1607-551X/Copyright © 2017, Kaohsiung Medical University. Published by Elsevier Taiwan LLC. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Introduction

Eruption of the third molar (M3) is common in adults, and on exposure to the oral environment, M3s are more susceptible to periodontal infection, leading to greater periodontal tissue breakdown. Maintaining appropriate oral hygiene in the posterior areas of the arch is relatively difficult, and plaque accumulation causes diseases of the second molar (M2). Patients often develop deep periodontal pockets or decay on M2s. Previous studies have revealed that retained asymptomatic M3s are risk factors for diseases of M2s [1]. In a clinical study involving patients with a mean age of 28 years that was designed to monitor asymptomatic M3s over time, the prevalence of periodontal inflammation in the M3 region was high at enrollment at six periodontal probing sites around M3s and at probing depths (PDs) at distal M2s [2]. Moreover, 41% of patients had at least one PD ≥ 4 mm on the distal side of M2s.

Elter et al [3] studied M3-related oral health data in patients aged 18–34 years (mean, 26 years) enrolled in the Third National Health and Nutrition Examination Survey. No radiographs were available, and 40% of patients were current or former smokers. Furthermore, a ≥ 5 -mm PD on an M2 was twice as likely when an adjacent M3 was present. The odds of detecting a ≥ 5 -mm PD on an M2 were similar if an M3 was present or if the patient was a current or former smoker. Falci et al [4] observed that the prevalence rate of caries on the distal surface of M2s was 13.4% in patients with a mean age of 24.17 years.

Previous studies [5–7] have revealed that an M2 adjacent to malpositioned M3 increases the risk of distal caries, and carious lesions form on the distal cervical root surface of M2s. Retaining M3s promotes the formation of distal caries in M2s. In a previous longitudinal study, the lowest prevalence and incidence of M2 diseases occurred in the absence of an adjacent M3 [8].

Most studies were conducted in young patients. Limited evidence is available regarding the risk of caries and periodontitis in M2s adjacent to retained M3s, particularly in elderly patients. The objective of this split-mouth study was to verify whether caries and periodontal diseases, when present on the distal surface of M2s, are associated with the presence of erupted M3s.

Methods

This study was designed to evaluate patients with unilateral maxillary or mandibular M3s in the outpatient clinic of the Department of Periodontology, Kaohsiung Medical University Chung-Ho Memorial Hospital and Department of Dentistry, Kaohsiung Municipal Ta-Tung Hospital, Kaohsiung, Taiwan. The exclusion criteria were age < 25 years, pregnancy, symptomatic M3s, active periodontal treatment

or M3 extraction in the preceding 6 months, a history of smoking, and a systemic condition (uncontrolled diabetes mellitus and using Ca^{2+} channel blockers and immunosuppressive medications) that may affect gingival enlargement. Patients underwent comprehensive oral examinations by a trained, calibrated periodontist. Both clinical and radiographical measurements were performed by a single, trained investigator for eliminating interexaminer variability. The protocol was approved by the Institutional Review Board of Kaohsiung Medical University Chung-Ho Memorial Hospital.

Clinical examinations

Clinical measurements were performed at distobuccal and distolingual sites around M2s in test and control patients. The following factors were examined:

- (1) Plaque index (PLQ) [9]: presence or absence
- (2) Bleeding on probing (BOP) [10]: presence or absence
- (3) Periodontal PD: measured using a manual periodontal probe
- (4) Caries, as assessed by visual–tactile examination [11], and radiographic detection: presence or absence
- (5) M3 position:
 - Group A: the occlusal plane of M3 is at the level the same as that of the adjacent tooth (Figure 1)
 - Group B: the occlusal plane of M3 is at a level different from that of the adjacent tooth (Figure 2)

Radiological examinations

High-quality periapical or bitewing radiographs of bilateral M2s were obtained using a parallel long-cone technique for detecting proximal caries (Figures 1 and 2).

Statistical analysis

The collected data were recorded and organized in a database using SPSS, Version 19.0 (SPSS, Chicago, IL, USA). The paired *t* test was used to compare the clinical index at extraction and nonextraction sides. The χ^2 test was used to compare the distribution of related factors in different groups. A *p* value < 0.05 was considered significant for all analyses.

Results

This study examined 70 patients with 81 unilaterally erupted M3s. Table 1 shows patient characteristics and the M3



Figure 1. M3 position Group A (lower left 3rd molar). M3 = third molar.



Figure 2. M3 position Group B (upper left 3rd molar). M3 = third molar.

distribution status. The mean patient age was 45.12 years (26–73 years). Forty-two (51.9%) M3s were observed in the mandible, and 51 (63%) patients were women. In total, 46 (56.8%) and 35 (43.2%) M3s were in Group A and B, respectively. The average number of restored or carious teeth was 6.68 (2–15) and the mean PD of full mouth teeth was 3.16 mm (2.22–4.88 mm) in our enrolled patients.

Table 2 shows the M2 condition on the extraction and nonextraction sides of the patients at enrollment. Regarding periodontal parameters, at both the distobuccal and distolingual sites of M2s, the periodontal PD was significantly greater on the nonextraction side than on the extraction side ($p < 0.0001$ in distobuccal region vs. $p = 0.006$ in distolingual region). Plaque accumulation was significantly higher at the distobuccal site of the nonextraction side than at that of the extraction side ($p = 0.041$); however, no significant difference was observed in the PLQ of the distolingual site. Furthermore, although BOP was high on the nonextraction side, no significant difference was noted compared with the extraction side. Regarding dental caries, the caries rate was significantly higher on the nonextraction side than on the extraction side ($p < 0.0001$ on M2 with caries and $p = 0.003$ on M2 with distal caries).

The clinical parameters of M2 in the maxilla and mandible were compared (data not shown) and, except for BOP, the parameters exhibited no significant differences. At the distolingual site, the BOP prevalence was significantly higher in the maxilla than in the mandible (64.1% vs.

Table 1 Characteristics of study sample ($n = 81$).

Age (y)	45.12 ± 12.22
Sex	
M	30 (37)
F	51 (63)
Position	
Maxillary	39 (48.1)
Mandibular	42 (51.9)
Third molar position	
Group A	46 (56.8)
Group B	35 (43.2)

Data are presented as mean ± SD or n (%).

F = female; M = male; SD = standard deviation.

38.1%, $p = 0.026$ on the extraction side and 82.1% vs. 45.2%, $p = 0.001$ on the nonextraction side). In the mandible and maxilla of the nonextraction sides, the prevalence of distal caries in M2s was 35.7% and 30.8%, respectively.

In maxillary Group A (**Table 3**), the mean PDs on the extraction sides were 3.84 ± 1.30 mm (distobuccal) and 4.84 ± 1.26 mm (distolingual). However, the mean PDs on the nonextraction sides were 5.42 ± 2.24 mm (distobuccal) and 6.11 ± 2.28 mm (distolingual), exhibiting a significant difference ($p = 0.001$ and $p = 0.003$). The caries percentages for the nonextraction (82.6% with caries and 34.8% with distal caries) and extraction (51.2% with caries and

Table 2 Association between presence of M3 and clinical parameters in M2.

	Extraction site	Nonextraction site	<i>p</i>
PD (mm)			
Distobuccal	3.90 ± 1.44	5.05 ± 1.84	< 0.0001
Distolingual	4.60 ± 1.86	5.37 ± 2.34	0.006
PLQ			
Distobuccal	44 (54.3)	54 (66.7)	0.041
Distolingual	49 (60.5)	51 (63)	0.815
BOP			
Distobuccal	36 (44.4)	44 (54.3)	0.201
Distolingual	41 (50.6)	51 (63)	0.078
Caries			
M2 with caries	47 (58)	64 (79)	< 0.0001
M2 with distal caries	10 (12.3)	27 (33.3)	0.003

Data are presented as mean ± SD or *n* (%).

BOP = bleeding on probing; M2 = second molar; M3 = third molar; PD = pocket depth; PLQ = plaque index; SD = standard deviation.

10.9% with distal caries) sides were significant ($p = 0.005$ and $p = 0.042$). PLQ and BOP measurements were similar on the extraction and nonextraction sides.

In maxillary Group B, the mean PD of the distobuccal site was significantly higher on the nonextraction side than on the extraction side (4.70 ± 1.69 mm vs. 3.55 ± 1.01 mm; $p = 0.011$). Furthermore, the PLQ percentage was significantly higher for the nonextraction side than for the extraction side (70% vs. 45%, $p = 0.021$). The distal caries percentage for the nonextraction (35%) and extraction (5%) sides were significant ($p = 0.03$).

In mandibular Group A, the mean PD of the distobuccal site was significantly higher on the nonextraction side than on the extraction side (4.59 ± 1.82 mm vs. 3.89 ± 1.83 mm; $p = 0.039$). The caries percentages for the nonextraction (81.5% with caries and 40.7% with distal caries) and extraction (55.6% with caries and 14.8% with distal caries) sides were significant ($p = 0.017$ and $p = 0.05$). PLQ and BOP measurements were nonsignificant.

In mandibular Group B, the mean PD of the distobuccal site was higher on the extraction side than on the nonextraction side (4.47 ± 1.19 mm vs. 5.87 ± 1.19 mm; $p = 0.004$). PLQ and BOP measurements and the caries percentage were nonsignificant.

Discussion

The results of the present study show that an erupted M3 negatively affects the periodontal and caries statuses of the adjacent M2. Regarding the periodontal status, irrespective of the position of the erupted M3, at the distobuccal site, the PD of M2 was greater on the nonextraction side than on the extraction side. However, BOP and the PLQ were not significantly different. Although BOP has a strong negative correlation with disease progression and PLQ is a reliable indicator of a successful daily

Table 3 Clinical parameters in M2 adjacent to different M3 positions.

	Extraction site	Nonextraction site	<i>p</i>
Maxillary			
Group A			
PD (mm)			
Distobuccal	3.84 ± 1.30	5.42 ± 2.24	0.001
Distolingual	4.84 ± 1.26	6.11 ± 2.28	0.003
PLQ (%)			
Distobuccal	52.6	57.9	0.667
Distolingual	57.9	63.2	0.578
BOP (%)			
Distobuccal	52.6	63.2	0.494
Distolingual	68.4	78.9	0.429
Decay (%)			
M2 with caries	51.2	82.6	0.005
M2 with distal caries	10.9	34.8	0.042
Group B			
PD (mm)			
Distobuccal	3.55 ± 1.01	4.70 ± 1.69	0.011
Distolingual	4.50 ± 1.82	5.25 ± 2.67	0.321
PLQ (%)			
Distobuccal	45.0	70.0	0.021
Distolingual	55.0	45.0	0.330
BOP (%)			
Distobuccal	50.0	65.0	0.267
Distolingual	60.0	85.0	0.021
Decay (%)			
M2 with caries	60.0	70.0	0.330
M2 with distal caries	5.0	35.0	0.030
Mandibular			
Group A			
PD (mm)			
Distobuccal	3.89 ± 1.83	4.59 ± 1.82	0.039
Distolingual	4.07 ± 1.54	4.78 ± 2.42	0.079
PLQ (%)			
Distobuccal	51.9	59.3	0.425
Distolingual	63.0	63.0	1.000
BOP (%)			
Distobuccal	33.3	37.0	0.713
Distolingual	29.6	37.0	0.425
Decay (%)			
M2 with caries	55.6	81.5	0.017
M2 with distal caries	14.8	40.7	0.050
Group B			
PD (mm)			
Distobuccal	4.47 ± 1.19	5.87 ± 1.19	0.004
Distolingual	5.40 ± 2.72	5.67 ± 1.59	0.717
PLQ (%)			
Distobuccal	73.3	86.7	0.334
Distolingual	66.7	86.7	0.271
BOP (%)			
Distobuccal	46.7	60.0	0.499
Distolingual	53.3	60.0	0.751
Decay (%)			
M2 with caries	73.3	80.0	0.581

(continued on next page)

Table 3 (continued)

	Extraction site	Nonextraction site	<i>p</i>
M2 with distal caries	26.7	26.7	1.000

BOP = bleeding on probing; M2 = second molar; M3 = third molar; PD = pocket depth; PLQ = plaque index; SD = standard deviation.

plaque control procedure in patients, both parameters are not specific, sensitive markers of periodontal health [12].

In a longitudinal study, Nunn et al [8] observed that retained M3s, particularly erupted and soft-tissue-impacted M3s, are associated with an increased risk of M2 diseases. Elter et al [3] demonstrated that a visible M3 was associated with a twofold increased risk of a ≥ 5 -mm periodontal PD on the adjacent M2. Similarly, in the Dental Atherosclerosis Risk in Community Study [13], M3s were associated with a 50% increased likelihood of a PD ≥ 5 mm on adjacent M2s in elderly patients (age 52–74 years). Our results are in accordance with those of this study. Furthermore, Moss et al [14] observed a significantly greater overall mean PD calculated from all other teeth in patients with visible M3s than in those with no visible M3s. In the present study, the PDs of the distal M2 were significantly greater on the non-extraction side than on the extraction side, independent of the position of the molar. Moreover, irrespective of the M3 position, the mean PDs of distobuccal sites were significantly greater on the nonextraction side than on the extraction side. These results are in accordance with those of previous studies [13,14].

Nunn et al [8] reported that only M2s adjacent to erupted M3s had a significantly increased caries risk. Previous studies have reported prevalence rates of distal caries on mandibular M2s associated with mandibular M3s of 7% [15], 17.2% [16], 20% [17], and 32% [5]. Accordingly, in the present study, we observed that M2s adjacent to erupted M3s were at significantly higher risk of caries and distal caries. In maxillary M2s, regardless of the occlusal plane level of M3 and M2, erupted M3s increased the distal caries rate of M2s. Furthermore, in mandibular M2s, when M3s and M2s were at the same occlusal plane level, the caries or distal caries rate of M2s increased. The prevalence rates of distal caries in M2s on the nonextraction side were 35.7% and 30.8% in the mandible and maxilla, respectively; the difference in rates may be related to age and cultural differences, including socioeconomic and education levels, between patients. Furthermore, the high mean age of patients possibly contributed to the high prevalence of distal caries in M2s in this study. The mean patient age in our study is high, probably because of an increasing incidence of distal caries in elderly patients, which is consistent with the findings of previous studies [18,19]. Because it is directly related to increasing age, Toedtling et al [20] argue that dental caries is significantly linked to the length of time a wisdom tooth is in a partially erupted state; consequently, these patients are older. A previous study revealed that the contact point between M2 and M3 had significant effects on caries formation [17]. Knutsson et al

[6] reported that mesioangular and horizontally positioned M3s are more likely to be associated with caries development in the adjacent M2s. Second molar distal caries has been observed in association with partially erupted lower M3s [5,7,21]. All of our enrolled patients had erupted M3s. The influence of M3s on the health status of its adjacent M2s appears to be greater when the occlusal plane of M3s is at the same level as that of M2s (Group A), as compared to teeth with occlusal planes at different levels (Group B). We speculate that this is related to the contact point between M2s and M3s, with which this study is not concerned. Nonetheless, these results provide additional information indicating that, even if a M3 and M2 are in the same occlusal plane, and the M3 can perform the normal occlusion function, the M3 may still cause periodontal or dental problems in the M2 of elderly patients.

Most relevant studies have focused on younger populations. Our study provides additional evidence for the association of M3s with caries and periodontal disease risk in the M2s of elderly patients. Compared with the patients in a previous study, the patients in our study were relatively healthy and had no smoking history. Thus, after eliminating the interfering factors of systemic diseases and smoking habits, this study confirmed that retained erupted M3s caused more damage to M2s in elderly nonsmokers.

Previous studies have revealed an association between the distal surfaces of the mandibular M2s and M3s. Prevalence data in these studies were based on panoramic radiographs, which were used for diagnosing caries [16,17]. Panoramic radiographs are adequate for planning M3 extraction; however, they are not as precise as periapical or bitewing radiographs for caries diagnosis [22]. Unlike previous studies [16,17], our study obtained radiographs of all patients, enabling the identification of proximal caries. Falci et al [4] used periapical radiographs of mandibular M2s and revealed a 13.4% prevalence rate of caries on the distal surface of M2s. Our study revealed a higher percentage (35.7%) of distal caries in mandibular M2s, possibly because the mean patient age was higher in this study compared with that in the study by Falci et al [4] (45.12 years vs. 24.17 years). However, few studies have focused on maxillary teeth [8,23]. Periapical and bitewing radiographs enabled us to observe that the prevalence rate of caries on the distal surface of maxillary M2s was 30.8%.

Our study has some major limitations. The study involved hospital outpatients, who may pay close attention to their general health, including oral health, and practice positive health behaviors. Hence, our results may be biased toward underestimating the prevalence and incidence of diseases of M2 in the community-dwelling elderly population. Furthermore, the patients in this study were adults who had undergone M3 removal. Hence, we could not determine whether, or why, the patients had had any M3s removed before participating in the study. Finally, angulation of erupted M3s is associated with the risk of caries or periodontal diseases in M2s, and determining this association may require a large sample size.

Despite the aforementioned limitations, we conclude that M3 eruption is a risk factor for periodontal diseases and caries of M2s, irrespective of the occlusal plane level of M2s and M3s. M3s may continue to have a negative impact on M2 health well into later life. Therefore, if optimizing M2

health is a primary desired outcome, removing erupted M3s is the most suitable option.

References

- [1] Marciani RD. Is there pathology associated with asymptomatic third molars? *J Oral Maxillofac Surg* 2012;70:515–9.
- [2] Blakey GH, Jacks MT, Offenbacher S, Nance PE, Phillips C, Haug RH, et al. Progression of periodontal disease in the second/third molar region in subjects with asymptomatic third molars. *J Oral Maxillofac Surg* 2006;64:189–93.
- [3] Elter JR, Cuomo CJ, Offenbacher S, White Jr RP. Third molars associated with periodontal pathology in the Third National Health and Nutrition Examination Survey. *J Oral Maxillofac Surg* 2004;62:440–5.
- [4] Falci SG, de Castro CR, Santos RC, de Souza Lima LD, Ramos-Jorge ML, Botelho AM, et al. Association between the presence of a partially erupted mandibular third molar and the existence of caries in the distal of the second molars. *Int J Oral Maxillofac Surg* 2012;41:1270–4.
- [5] van der Linden W, Cleaton-Jones P, Lownie M. Diseases and lesions associated with third molars. Review of 1001 cases. *Oral Surg Oral Med Oral Pathol Oral Radiol Endodont* 1995;79:142–5.
- [6] Knutsson K, Brehmer B, Lysell L, Rohlin M. Pathoses associated with mandibular third molars subjected to removal. *Oral Surg Oral Med Oral Pathol Oral Radiol Endodont* 1996;82:10–7.
- [7] McArdle LW, Renton TF. Distal cervical caries in the mandibular second molar: an indication for the prophylactic removal of the third molar? *Br J Oral Maxillofac Surg* 2006;44:42–5.
- [8] Nunn ME, Fish MD, Garcia RI, Kaye EK, Figueroa R, Gohel A, et al. Retained asymptomatic third molars and risk for second molar pathology. *J Dent Res* 2013;92:1095–9.
- [9] O’Leary TJ, Drake RB, Naylor JE. The plaque control record. *J Periodontol* 1972;43:38.
- [10] Lenox JA, Kopczyk RA. A clinical system for scoring a patient’s oral hygiene performance. *J Am Dent Assoc* 1973;86:849–52.
- [11] Radike AW. Criteria for diagnosis of dental caries. In: Proceedings of the conference on the clinical testing of cariostatic agents. Chicago, Illinois: American Dental Association; October 14–16, 1968. p. 87–8. Chicago: ADA Council on Dental Research; 1972.
- [12] Lang NP, Joss A, Orsanic T, Gusberti FA, Siegrist BE. Bleeding on probing. A predictor for the progression of periodontal disease? *J Clin Periodontol* 1986;13:590–6.
- [13] Elter JR, Offenbacher S, White RP, Beck JD. Third molars associated with periodontal pathology in older Americans. *J Oral Maxillofac Surg* 2005;63:179–84.
- [14] Moss KL, Oh ES, Fisher E, Beck JD, Offenbacher S, White Jr RP. Third molars and periodontal pathologic findings in middle-age and older Americans. *J Oral Maxillofac Surg* 2009;67:2592–8.
- [15] Chu FC, Li TK, Lui VK, Newsome PR, Chow RL, Cheung LK. Prevalence of impacted teeth and associated pathologies—a radiographic study of the Hong Kong Chinese population. *Hong Kong Med J* 2003;9:158–63.
- [16] Chang SW, Shin SY, Kum KY, Hong J. Correlation study between distal caries in the mandibular second molar and the eruption status of the mandibular third molar in the Korean population. *Oral Surg Oral Med Oral Pathol Oral Radiol Endodont* 2009;108:838–43.
- [17] Ozc I, Herguner Siso S, Tasdemir U, Ezirganli S, Goktolga G. Prevalence and factors affecting the formation of second molar distal caries in a Turkish population. *Int J Oral Maxillofac Surg* 2009;38:1279–82.
- [18] Bruce RA, Frederickson GC, Small GS. Age of patients and morbidity associated with mandibular third molar surgery. *J Am Dent Assoc* 1980;101:240–5.
- [19] McArdle LW, Renton T. The effects of NICE guidelines on the management of third molar teeth. *B Dent J* 2012;213:E8.
- [20] Toedtling V, Coulthard P, Thackray G. Distal caries of the second molar in the presence of a mandibular third molar—a prevention protocol. *Br Dent J* 2016;221:297–302.
- [21] Punwutikorn J, Waikakul A, Ochareon P. Symptoms of unerupted mandibular third molars. *Oral Surg Oral Med Oral Pathol Oral Radiol Endodont* 1999;87:305–10.
- [22] Akarslan ZZ, Akdevelioğlu M, Güngör K, Erten H. A comparison of the diagnostic accuracy of bitewing, periapical, unfiltered and filtered digital panoramic images for approximal caries detection in posterior teeth. *Dentomaxillofac Radiol* 2008;37:458–63.
- [23] Coleman M, McCormick A, Laskin DM. The incidence of periodontal defects distal to the maxillary second molar after impacted third molar extraction. *J Oral Maxillofac Surg* 2011;69:319–21.