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Sex Differences in Periodontal Disease in Catastrophic and Attritional Assemblages From Medieval London

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ABSTRACT Periodontal disease is one of the most common chronic diseases in living populations, and most studies that have examined sex differences in periodontal disease have found higher frequencies in men compared to women. This study examines sex differences in periodontal disease in two cemeteries from medieval London: the East Smithfield cemetery (c. 1349–1350), an exclusively Black Death cemetery that represents catastrophic mortality ($n = 161$), and the St. Mary Graces cemetery (c. 1350–1538), a post-Black Death attritional assemblage that represents normal medieval mortality ($n = 100$). The results reveal a significantly higher frequency of periodontal disease, independent of age, among males compared with females in St. Mary Graces, but no significant difference between the sexes in East Smithfield. The sex differences in the attritional assemblage might reflect heightened susceptibility to periodontal disease in the living population or sex differences in frailty. The differences in the sex patterns of periodontal disease between the two cemeteries might be the result of disproportionately negative effects of the Great Bovine Pestilence and consequent decreases in dairy availability on female oral health among victims of the Black Death. Am J Phys Anthropol 149:405–416, 2012.

Periodontal disease, one of the most common chronic diseases in living populations (Abdellatif and Burt, 1987; Beck et al., 1996; Pihlstrom et al., 2005), is characterized by inflammation and destruction of gum tissue (gingiva), the periodontal ligament, root cementum, and alveolar bone, and can be caused by a variety of pathogenic infectious agents that are found in oral biofilms (dental plaque), including the bacteria *Actinobacillus actinomycetemcomitans, Porphyromonas gingivalis*, and *Treponema denticola* and various herpes viruses (van Winkelhoff and Slots, 1999; Li et al., 2000; Slots, 2004). There is an abundance of evidence that periodontal disease is associated with increased risks of mortality in living populations and is a risk factor for a variety of other diseases, such as cardiovascular disease, respiratory disease, cancers, Alzheimer's disease, obesity, diabetes, renal disease, and osteoporosis (for example, see the following reviews: Hollister and Weintraub, 1993; Li et al., 2000; Kowolik et al., 2001; Slots, 2004; Pihlstrom et al., 2005; Johnson et al., 2006; Irwin et al., 2008; Williams et al., 2008). Recent work has also shown that periodontal disease was associated with elevated risks of mortality and with other skeletal evidence of inflammation in medieval populations (DeWitte and Bekvalac, 2010, 2011).

As is true of many other diseases, there is an apparent sex differential in the risk of developing periodontal disease. The majority of published studies of sex differences in periodontal disease in both living populations and in archaeological samples from past populations have revealed higher frequencies and greater severity of periodontal disease in males compared to females (e.g., Costa, 1982; y'Edynak, 1989; Sakki et al., 1995; Crossner and Unell, 1996; Genco, 1996; Šlaus, 2000; Pihlstrom, 2001; Desvarieux et al., 2004; Torrungruang et al., 2005; Delgado-Darias et al., 2006; Meisel et al., 2008; Holtfreter et al., 2009; Shiau and Reynolds, 2010b; Van Der Merwe et al., 2010; Jordan et al., 2011; Kundu et al., 2011; Rheu et al., 2011; Wasterlain et al., 2011).

The higher prevalence and greater severity of periodontal disease in males has been shown by some studies to be associated with behavioral differences between the sexes, such as higher rates of smoking and relatively poor oral hygiene in males (Shiau and Reynolds, 2010b). However, the sex differences in periodontal disease persist when such behavioral differences are controlled for, and there are significant sex differences in periodontal disease in other animals, both of which indicate that fundamental biological differences between the sexes play a role in the risk of developing periodontal disease (Shiau and Reynolds, 2010b). Studies have shown that there are no significant differences between males and females in the bacteria that cause periodontal disease, which suggests that sex differences in immune and inflammatory responses, rather than differences in the composition of oral flora, influence rates, and severity of periodontal disease (Schenkein et al., 1993; Shiau and Reynolds, 2010b).

Periodontal disease is just one example of many diseases for which the prevalence or severity is higher in males than females, and, as has been demonstrated for other diseases, sex hormones may greatly influence susceptibility to and severity of periodontal disease (Kaplan et al., 1989; Michael et al., 1996; Boisier et al., 2002;

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Laupland et al., 2003; Kaewpitoon et al., 2006; Teo, 2006; Rustgi, 2007; Falagas et al., 2008; Faleiros et al., 2009; Snider et al., 2009; Jonsson et al., 2010; Klein and Roberts, 2010; Oren et al., 2011; Case et al., 2012; Mobarak, 2012). In general, estrogens enhance immune competence, whereas androgens reduce it, and females thus tend to mount stronger immune responses (Ahmed et al., 2010; Klein and Huber, 2010). Estrogen inhibits the production of inflammatory cytokines that are important in the process of bone resorption, and in general, men appear to produce higher levels of inflammatory cytokines (e.g., IL-1β and TNF-α) in response to infection and trauma compared to females (Orwoll et al., 2009; Shiau and Reynolds, 2010b). This is potentially important in the context of periodontal disease because the destruction of alveolar bone that is characteristic of the disease is part of the inflammatory response to the presence of periodontal pathogens and functions to create additional space to accommodate immune defense cells (Preshaw et al., 2004). Thus, if men have exaggerated inflammatory responses to infection with pathogens, including those that cause periodontal disease, this might account for some of the sex differences in the disease. Studies have shown that estrogen is important both for the differentiation of periodontal ligament stem cells into osteoblast-like cells that can regenerate alveolar bone and for exerting bone-sparing effects by altering the expression of inflammatory cytokines in periodontal tissues and that estrogen deficiency in postmenopausal women is a risk factor for periodontal disease (Mascarenhas et al., 2003; Cao et al., 2007; Shu et al., 2008; Zhang et al., 2011). Progesterone similarly appears to play a significant role in the osteoblastic function of periodontal ligament cells and maintenance of alveolar bone mass (Mascarenhas et al., 2003; Yuan et al., 2010). In addition to being less prone to the bone destruction associated with periodontal disease, at least before menopause, females generally have more effective humoral immune responses (including heightened activation of B-lymphocytes and enhanced antibody production by B cells in response to antigens) compared with males, which might allow females to better clear infection with the pathogens that cause periodontal disease (Ahmed et al., 2010; Klein and Roberts, 2010; Shiau and Reynolds 2010b).

Given observed patterns in living populations of higher prevalences of periodontal disease in males and recent evidence that periodontal disease was associated with elevated risks of mortality in a medieval sample from London (DeWitte and Bekvalac, 2010), this study examines whether frequencies of periodontal disease differ between the sexes in medieval samples from London; such sex differences in periodontal disease might, more generally, reflect differences in health and frailty between the sexes during this period. This study also compares the sex patterns of periodontal disease between a catastrophic (Black Death, c. 1349–1350) and attritional (i.e., normal medieval mortality) cemetery. Recent research has shown that patterns of mortality during the Black Death were similar in kind, if not in scale, to normal medieval mortality patterns, particularly in terms of targeting individuals in relatively poor health (DeWitte and Wood, 2008; DeWitte and Hughes-Morey, 2012). In the event that patterns in the attritional sample resemble those in living populations—that is, a higher frequency of periodontal disease in males—this study examines whether the pattern from the catastrophic assemblage conforms to the normal mortality pattern. Thus, this study examines not only the sex patterns of periodontal disease in the past, but also if and how catastrophic (i.e., Black Death) and normal mortality differentially influence those patterns.

MATERIALS AND METHODS

Skeletal samples

East Smithfield Cemetery. The catastrophic sample for this study comes from the medieval East Smithfield Black Death cemetery in northeast London, near the Tower of London. The East Smithfield cemetery is one of only a few excavated cemeteries with both documentary and archaeological evidence clearly linking it to the 14th-century Black Death (Grainger et al., 2008). The Black Death, which arrived in London in the fall of 1348 (Gottfried, 1983; Horrox, 1994), killed an estimated one third to one half (or more) of the city's population in under two years (Sloane, 2011). According to records from the Church of the Holy Trinity, which note the exact location and dimensions of the burial ground, the East Smithfield cemetery was founded in late 1348 in anticipation of the arrival of the Black Death (Hawkins, 1990). Archaeological excavations, carried out by the Museum of London's Department of Greater London Archaeology in the 1980s, disinterred over 600 individuals from East Smithfield, and the collection is currently in the care of the Museum of London's Centre for Human Bioarchaeology. Stratigraphic evidence indicates that the East Smithfield burials were completed in a single phase, and there is no evidence of interments after 1350 (Grainger et al., 2008); hence, it can be safely assumed that most, if not all, of the individuals interred in East Smithfield cemetery died as the result of the Black Death.

For this study, a sample of 161 adults (96 males and 65 females) was selected from the East Smithfield cemetery collection and analyzed at the Museum of London Centre for Human Bioarchaeology. This sample comprises all of the excavated adults from East Smithfield who were preserved well enough to provide sufficient data on age (using the method described below), sex, and periodontal disease. This study only includes adults because periodontal disease is not as common in children as in adults, and, more importantly, sex cannot be accurately determined from juvenile skeletal remains using existing methods.

St. Mary Graces Cemetery. The attritional sample for this study comes from the post-Black Death cemetery of St. Mary Graces. The Cistercian Abbey of St. Mary Graces was established in London in 1350, soon after the Black Death ended, and it was in use until the Reformation in 1538 (Grainger and Hawkins, 1988; Grainger et al., 2008). While the Abbey of St. Mary Graces was active, members of the general population were interred in a cemetery associated with the Abbey, and monks and important lay people were buried within the Abbey's church and chapels (Grainger and Hawkins, 1988; Rogers and Waldron, 2001; Grainger and Phillpotts, 2011). Excavation of St. Mary Graces in the 1980s by the Museum of London Archaeology Service revealed several hundred skeletons from within the Abbey church and chapels and from the larger lay cemetery (Grainger and Hawkins, 1988; Grainger and Phillpotts, 2011); the excavated collection is currently curated by the Museum of London's Centre for Human Bioarchaeology. The St. Mary Graces cemetery contains individuals of all ages,

both sexes, and both higher and lower socioeconomic statuses, and given that it comes from the same area as East Smithfield, it provides a good, post-Black Death normal-mortality comparison sample for the East Smithfield Black Death cemetery.

This study uses a sample of 100 individuals (67 males and 33 females) from the St. Mary Graces cemetery. This sample includes all the excavated individuals from the cemetery who were preserved well enough to be scored for skeletal indicators of age, sex, and the presence of periodontal disease, as described below.

Age estimation

Ages were estimated using the method of transition analysis described by Boldsen et al. (2002). The advantages of transition analysis include the avoidance of age estimates that are biased toward the known-age-reference sample, as occurs with traditional methods of age estimation, and the estimation of point estimates of age and individual standard errors for those point estimates, even for older adults (i.e., rather than the broad terminal adult age categories typical of traditional methods). In transition analysis, data from a known-age reference collection (in this case, the Smithsonian Institution's Terry Collection) are used to obtain the conditional probability that a skeleton will exhibit a particular age indicator stage or suite of age indicator stages given the individual's known age. Using Bayes' theorem, this conditional probability is combined with a prior distribution of ages at death to determine the posterior probability that a skeleton in the cemetery sample died at a particular age given that it displays particular age indicator stages. In transition analysis, the prior distribution of ages at death can either be an informative prior based on documentary data or a uniform prior; for this study, an informative prior is used, as described below. By combining the conditional probability from a known-age reference sample with a prior distribution of ages at death, transition analysis avoids imposing the age distribution of the reference sample on the target sample (Boldsen et al., 2002). For this study, transition analysis was applied to skeletal age indicators on the pubic symphysis and the iliac auricular surface and to cranial suture closure as described by Boldsen et al. (2002), and the ADBOU (Anthropological Database, Odense University) Age Estimation software was used to determine individual ages-at-death and the standard errors associated with those point estimates. The program uses an informative prior distribution of ages at death based on data from 17th-century Danish rural parish records (the Gompertz-Makeham parameter estimates for this prior are as follows: $\alpha_1 = 0.01273$, $\alpha_2 = 0.00002478$, and $\beta = 0.01618$).

Sex determination

Sex was determined based on sexually dimorphic features of the skull and pelvis using the standards described in Buikstra and Ubelaker (1994). The following dimorphic features of the skull and pelvis were scored: glabella/supraorbital ridge, supraorbital margin, mastoid process, external occipital protuberance/nuchal crest, mental eminence, ventral arc of the pubis, subpubic concavity, ischiopubic ramus ridge, and the greater sciatic notch. The accuracy of these individual skeletal features, or various combinations thereof, for the purposes of sex determination has been shown to range from 68 to over 96% (Phenice, 1969; Sutherland and Suchey, 1991; Graw et al., 1999; Ubelaker and Volk, 2002; Rogers, 2005; Walker, 2005; Williams and Rogers, 2006). Multiple skeletal indicators of sex were used for this study given that including more than one indicator improves the accuracy of sex determination (Meindl et al., 1985; Rogers, 2005; Williams and Rogers, 2006; Walker, 2008). Because sex determinations based on features of the pelvis alone have been shown to be more accurate than those based on features of the skull alone (Meindl et al., 1985; Walrath et al., 2004), for individuals in this study for which the skull and pelvis indicated different sexes, the pelvic scores were subjectively weighted more heavily than features of the skull.

Periodontal disease

Periodontal disease can result in the gradual destruction of periodontal tissues and alveolar bone (Irfan et al., 2001) and is thus often identified in skeletal material by the loss of alveolar bone which exposes the underlying trabecular bone and thereby produces porosity (Clarke and Hirsch, 1991; Larsen, 1997) or causes the alveolar crest (AC) to recede relative to the cementoenamel junction (CEJ) of the associated dentition (Larsen, 1997). This study uses periodontal disease data gathered by researchers at the Museum of London Centre for Human Bioarchaeology (WORD database, 2010). Data are available from the WORD database on periodontal disease at the level of individual alveoli. In preliminary work for this study, data were pooled for entire quadrants, and sample sizes of individuals with preserved alveoli and who could also be scored both for sex and age were found to be largest for the left mandible; so for this study, only data from the left mandible are analyzed in order to maximize the power of the analyses. Periodontal disease was scored as present if the distance between the CEJ and AC was >2 mm. For an individual to be scored for periodontal disease, alveoli in the left mandible had to be present and lack postmortem damage.

The use of the distance between the CEJ and the AC as an indicator of periodontal disease is potentially problematic, given that nonpathological processes associated with aging can increase the distance beyond 2 mm (Costa, 1982; Clarke et al., 1986; Clarke, 1990; Clarke and Hirsch, 1991; Hildebolt and Molnar, 1991; Varrela et al., 1995; Hillson, 1996; Ogden, 2008). For example, the distance between the CEJ and AC can increase because teeth continue to erupt throughout adulthood (i.e., super-eruption) in response to reduced tooth height caused by normal wear with age and the processing of certain foods (Clarke and Hirsch, 1991; Hildebolt and Molnar, 1991). Super-eruption of teeth maintains lower facial height and the occlusal level of teeth, but it occurs without the simultaneous growth of the AC, thereby increasing the distance between the CEJ and AC (Whittaker et al., 1990; Clarke and Hirsch, 1991; Hildebolt and Molnar, 1991; Varrela et al., 1995; Ogden, 2008). Continued eruption of the teeth, without concurrent growth of the AC, also occurs in response to the continued growth of the facial skeleton in adulthood, and such super-eruption functions to maintain dental occlusion (Clarke and Hirsch, 1991; Hildebolt and Molnar, 1991).

Because the distance between the CEJ and AC can increase because of super-eruption of teeth and without any pathological destruction of the alveolar bone, use of this distance alone to identify cases of periodontal disease can lead to the overestimation of the prevalence of

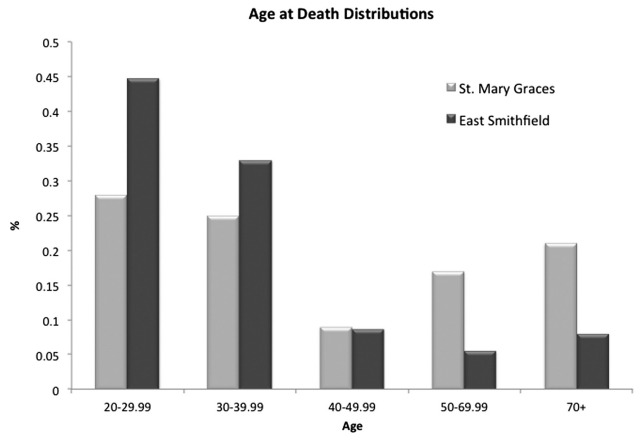

Fig. 1. Age at death distributions.

periodontal disease in past populations. Some of the individuals in the samples used for this study who were scored as having periodontal disease might not actually have had it. Because the distance between the CEJ and AC can occur because of nonpathological processes that are primarily associated with aging, the individuals who are incorrectly diagnosed with periodontal disease on the basis of the CEJ-AC distance are most likely to be older adults. Therefore, age must be included in the analysis of the association between periodontal disease and sex. If a significant association exists between periodontal disease and sex, and that association is consistent across age groups (i.e., the association is not restricted to older adults), this indicates that the observed relationship is not simply the result of including false positives for periodontal disease in the sample.

Age must also be considered in these analyses because the prevalence of periodontal disease increases with age (Abdellatif and Burt, 1987). This occurs in some cases because of changes in oral hygiene or the increased use of medications that reduce salivary flow (Abdellatif and Burt, 1987; Sjögren and Nordström, 2000; Leal et al., 2010). Behavioral factors alone, however, do not explain the increase in periodontal disease with age (Streckfus et al., 1999). Increases in the prevalence of periodontal disease with age are also thought to be influenced by age-related changes in inflammatory status. That is, the accumulated effects of years of exposure to oral pathogens and their byproducts lead to elevated levels of proinflammatory cytokines, which are associated with periodontal tissue destruction, and the reduced production of anti-inflammatory cytokines in periodontal tissues (Benatti et al., 2009; Liang et al., 2010). Because the prevalence of periodontal disease increases with age, variation in the age-at-death distributions by sex may obscure the true relationship between peridontal disease and sex. For example, the overall frequency of periodontal disease may appear higher in one sex simply because there is a higher proportion of older adults of that sex in the sample. By accounting for age in these analyses, I avoid such potential confounding. The potential effects of hormonal changes in postmenopausal women (i.e., a reduction in the protective effects of estrogen) on sex-patterns of periodontal disease are described in the Discussion section.

Because the early stage of periodontal disease is not detectable in dry skulls (Strohm and Alt, 1998), it is possible that the samples used in this study include false negatives for periodontal disease. The possible effect of the presence of such false negatives on the results of this study is described in the Discussion section.

Statistical analyses

Kolmogorov-Smirnov. The age at death distributions from the East Smithfield and St. Mary Graces cemeteries are compared using a Kolmogorov-Smirnov test to identify differences between the two distributions that might have influenced patterns of periodontal disease, which, as mentioned above, has been observed to increase in frequency with age.

Hierarchical log-linear analysis. The associations among periodontal disease, sex, and age within each cemetery are evaluated using hierarchical log-linear analysis with SPSS version 19. This approach is used because the data include both categorical (i.e., age-interval) and binary (i.e., presence/absence of pathological conditions and male/female sex) variables. Hierarchical log-linear analysis is used to test the significance of the three-way interaction among age, periodontal disease, and sex, as well as all other lower order interactions (e.g., the interaction between age and periodontal disease, and between age and sex). Backwards elimination is used to remove non-significant interactions among variables with a statistical significance criterion of 0.05. Because hierarchical log-linear analysis allows for the evaluation of interactions between more than two variables, it is possible to determine whether a significant association between periodontal disease and sex exists in the absence of age. In the event that a significant association is observed between periodontal disease and sex, this approach is informative about whether the relationship is consistent across all age groups or if it is dependent on age (Green, 1988).

To test differences in the relationships among age, sex, and periodontal disease between the two cemeteries, hierarchical log-linear analysis is also done using a pooled-cemetery sample with "cemetery" as a fourth variable (i.e., to test the associations among cemetery, age, sex, and periodontal disease).

Statistical significance is reported here, despite recommendations by major epidemiological and medical journals to avoid doing so (Lang et al., 1998; Rothman, 1998; Goodman, 1999; Cohen, 2011). For both the hierarchical log-linear analysis and the Kolmogorov-Smirnov test, P-values <0.10 are considered here to be suggestive of a real effect.

Because of a lack of people with signs of periodontal disease at some ages in the East Smithfield and St. Mary Graces samples, age estimates are collapsed into three age intervals, as shown in Tables 2 and 3, to minimize the number of cells with counts of <5 in the analysis.

RESULTS

The age-at-death distributions from East Smithfield and St. Mary Graces are shown in Figure 1. Based on the results of the Kolmogorov-Smirnov test, the two distributions are significantly different (K-S test, $P < 0.05$). There are a higher proportion of individuals between the ages of 20 and 39.99 and a lower proportion of individuals above the age of 50 in East Smithfield compared to St. Mary Graces.

The frequencies of periodontal disease by sex and age in St. Mary Graces and East Smithfield are shown in Tables 1 and 2. In St. Mary Graces, the frequency of periodontal disease is higher in males than females; it is also higher, though less dramatically so, in males in East Smithfield. The absence of a strong sex difference in periodontal disease in East Smithfield is the result of a

TABLE 1. Periodontal disease (PD) frequencies by age and sex in St. Mary Graces

Age	Sex	No PD	PD	% with PD
20–39.99	Male	13	16	55
	Female	19	5	21
40–59.99	Male	1	7	88
	Female	0	4	100
60+	Male	16	14	47
	Female	5	0	0
Total	Male	30	37	55
	Female	24	9	27
	Both	54	46	46

TABLE 2. Periodontal disease frequencies by age and sex in East Smithfield

Age	Sex	No PD	PD	% with PD
20–39.99	Male	34	36	51
	Female	30	25	45
40–59.99	Male	5	6	55
	Female	3	2	40
60+	Male	6	9	60
	Female	3	2	40
Total	Male	45	51	53
	Female	36	29	45
	Both	81	80	50

higher frequency of the condition among females in East Smithfield compared to St. Mary Graces, that is, not because of a significantly lower frequency of periodontal disease in East Smithfield males compared to St. Mary Graces males (the frequencies of periodontal disease among males in each sample are quite similar).

The results of the hierarchical log-linear analysis for each cemetery are shown in Table 3. The results indicate that in St. Mary Graces, the three-way interaction between age, periodontal disease, and sex is not significant, but that all two-way interactions are significant. Importantly, for this study, there is a significant association between sex and periodontal disease in the St. Mary Graces cemetery (with a higher frequency in males, as shown in Table 1). Given the lack of a significant three-way association between all three variables, the association between sex and periodontal disease appears to be independent of age in St. Mary Graces. The results for the East Smithfield cemetery indicate that there are no significant associations among any of the variables within the catastrophic cemetery.

The results of the four-way hierarchical log-linear analysis using the pooled-cemetery sample are shown in Table 4, and they indicate that there is not a significant association among all four variables (i.e.. cemetery, age, sex, and periodontal disease). However, there is a significant association among cemetery, sex, and periodontal disease ($P = 0.047$), which indicates a significant difference in the sex patterns of periodontal disease between East Smithfield and St. Mary Graces. There is also a significant association among cemetery, age, and periodontal disease ($P = 0.008$), which indicates a significant difference between the two cemeteries in their age distributions of periodontal disease.

DISCUSSION

The results of this study indicate that in the St. Mary Graces sample, periodontal disease and sex are significantly associated (i.e.. there is a significantly higher frequency in males), and that the association between the two is not explained by age. In contrast, in the East Smithfield cemetery, periodontal disease and sex are not significantly associated, and the frequency of periodontal disease is similar between the sexes. The results of the four-way hierarchical log-linear analysis suggest that the differences between the two cemeteries indicate a real trend and are not simply an artifact of sample size differences.

A review of the available literature reveals a wide range of periodontal disease frequencies in medieval cemeteries. Unfortunately, direct comparison among these studies is not possible in every case, given that some studies examine periodontal disease at the level of the individual, while others examine the disease at the level of the tooth. Nonetheless, of those studies using medieval skeletal samples that report results by individual, periodontal disease frequencies range from 27 to 83% (Sagne and Olsson, 1977; Power, 1985–1986; Kerr, 1991; Djurić Srejić, 2001; Vodanović et al., 2012), and the overall frequencies observed in East Smithfield and St. Mary Graces (50 and 46%, respectively) fall within that range. Only a few studies of medieval periodontal disease report sex-specific frequencies either by individual or by tooth (Sagne and Olsson, 1977; Šlaus et al., 1997; Šlaus, 2000; nović et al., in press). Šlaus et al. (1997, 2000) found a significantly higher frequency of periodontal disease by tooth in males in samples from medieval Croatia. Vodanović et al. (2012) did not find a significant sex difference in periodontal disease by individual in medieval Croatian samples, although they did find a significantly higher frequency by tooth in males. Sagne and Olsson (1977) found a higher frequency of periodontal disease by individual in males (52.1 vs. 45.5%), but it is not clear from their report whether this difference is statistically significant. Given the small number of studies with which it is possible to compare the results from St. Mary Graces and East Smithfield, it is difficult to state definitively which cemetery conforms to the norms for medieval populations.

The results of this study also reveal that in the St. Mary Graces cemetery, periodontal disease is associated with age, which is consistent with the findings from a previous examination of the association between periodontal disease and periosteal lesions in St. Mary Graces (DeWitte and Bekvalac, 2011), and more generally with findings in living populations that the prevalence of periodontal disease increases with age, for the reasons described above (Abdellatif and Burt, 1987). As can be seen in Table 1, the highest frequency of periodontal disease in St. Mary Graces is observed in the 40–59.99 age interval and not in the oldest age category; hence, although there is an increase in the disease from young adulthood to middle adulthood that trend is not maintained in the transition from middle to older adult ages. Whether this lack of a consistent increase in periodontal disease with age is a real trend awaits confirmation using a larger sample size. The significant association between sex and age in St. Mary Graces reflects the higher proportion of females ages 20–39.99 and lower proportion of females over the age of 60 compared to males; such a relatively high proportion of females at reproductive ages in the sample might reflect maternal mortality.

As mentioned above, the early stages of periodontal disease are not detectable in skeletal material (Strohm and Alt, 1998); hence, it is possible that the samples used in this study include people who did had periodontal disease but were not scored as having it. However,

TABLE 3. Results of the three-way hierarchical log-linear analyses (PD = periodontal disease; age groups: 20–39.99, 40–59.99, and 60+)

Cemetery	Variables	*P*
St. Mary Graces	Age × sex × PD	0.132
	Age × sex	0.003
	Age × PD	0.001
	Sex × PD	0.002
East Smithfield	Age × sex × PD	0.848
	Age × sex	0.2
	Age × PD	0.928
	Sex × PD	0.315

TABLE 4. Results of the four-way hierarchical log-linear analyses (age groups: 20–39.99, 40–59.99, and 60+)

Variables	*P*
Cemetery × age × sex × PD	0.206
Cemetery × age × sex	0.273
Cemetery × age × PD	0.008
Cemetery × sex × PD	0.047
Age × sex × PD	0.544

the potential for inclusion of false negatives for periodontal disease is not really a problem for this study, as it focuses primarily on the association between periodontal disease and sex. Given that there is no reason to suspect that false negatives are more likely to occur in one sex compared with the other, the possible existence of false negatives in these samples will likely not obscure the relationship between periodontal disease and sex.

Explanations for sex differences in periodontal disease in St. Mary Graces. The higher frequency of periodontal disease in males compared with females in St. Mary Graces might indicate that males in this population faced higher risks than females of developing periodontal disease for a variety of reasons. Biological explanations include the negative effects of testosterone on male immune competence (i.e., reduced abilities to effectively fight oral pathogens associated with periodontal disease) or the relative absence, in males, of the positive effects of estrogen on bone destruction in response to inflammation, both of which have been suggested to explain sex differences in periodontal disease in living populations (Mascarenhas et al., 2003; Cao et al., 2007; Shiau and Reynolds, 2010a,b; Zhang et al., 2011).

The existence of sex differences in periodontal disease at older ages might be surprising given evidence from living populations that the risk of periodontal disease increases in postmenopausal women who no longer benefit from the protective effects of female sex hormones (Haas et al., 2009). Studies have found an association between decreased bone mineral density and alveolar bone loss (Sultan and Rao, 2011; Vishwanath et al., 2011), which suggests that postmenopausal osteopenia is a risk factor for periodontal disease. There are some studies from living populations that fail to find a significant sex difference in periodontal disease at older adult ages (Skudutytė et al., 2001; Shah, 2003; Eustaquio et al., 2010; Thaweboon et al., 2010). Similarly, Šlaus et al. (1997) found overall that there was a significantly higher frequency of periodontal disease in males in medieval Croatia but that the sex differential decreased in the oldest age category.

Further, Agarwal (2012) found significant vertebral bone loss between middle (30–49.99) and old age (50+) in East Smithfield females but not in males. Given the association between bone loss and periodontal disease, one might expect to see relatively steep increases in periodontal disease with age among females, and thus decreased sex differences in periodontal disease at older ages in these populations. It is possible that in the living population of St. Mary Graces, postmenopausal females had frequencies of periodontal disease more similar to those of their male peers and, thus, that the observed sex difference at older ages in the cemetery is an artifact of small sample sizes. However, many studies in living populations have also found that sex differences in periodontal disease persist at postmenopausal ages (Douglass et al., 1993; Ogawa et al., 2002; Desvarieux et al., 2004; Owotade et al., 2005; Mamai-Homata et al., 2012; Talwar et al., 2012). Given these patterns in living populations, it is reasonable to expect consistent sex differences in periodontal disease at all adult ages in skeletal samples from past populations.

In addition to possibly reflecting intrinsic biological differences, the sex differences in periodontal disease in St. Mary Graces might also have resulted from differences in oral care and hygiene similar to those that have been observed in living populations (Furuta et al., 2011). During the middle ages, some physicians understood the etiology of gum disease. For example, in the Ottoman Empire, the physician Şerafeddin Sabuncuoğlu recognized calculus deposits as a risk factor for periodontal disease and the need to remove them via scaling (Yilmaz et al., 1994). However, according to Yilmaz et al. (1994), even though the benefits of such procedures were understood during the middle ages, they were rarely performed. Anderson (2004) describes various dental care practices that were recommended in medieval literature. For example, in the 13th-century Compendium of Medicine, Gilbert advises cleaning teeth after eating to prevent the buildup of food debris, the removal of rotten flesh from the mouth, the use of various herbal mouthwashes and dentifrices, and other treatments for bad breath and toothaches. Guy de Chauliac, in the 14th-century *Chirurgia Magna*, advocated the removal of excess calculus and the use of antiseptic gargles (Anderson, 2004).

In addition to potentially effective recommended treatments for periodontal disease, there were also rather questionable theories of, and associated treatments for, oral pathologies during the middle ages. For example, throughout medieval Europe, dental caries and periodontal disease were believed to be caused by "tooth-worms," and there were numerous treatments that, according to popular medicine, would eliminate them, such as holding burning candles near infected teeth and the application or consumption of various herbs (Gerabek, 1999; Anderson, 2004).

From these sources, it is clear that at least some medieval people were aware of oral hygiene practices and dental care that might have served to reduce the risks of periodontal disease, but it is not clear whether most people knew about or actually heeded such advice. According to Anderson (2004: p 424) the vast majority of the population would not have had access to medical texts and would not have "come into contact with the recipes or procedures mentioned" therein. Although, according to Fischman (1997: p 7) mechanical tooth cleaning and mouth rinsing were "established practices" among Europeans by the 16th century.

In addition to potential sex differences in personal oral hygiene, access to professional dental care (for what it was worth) might have varied between the sexes. Lopez

et al. (2012) suggested sex differences in dental care when they found higher frequencies of dental caries in females from early modern Spain; such sex differences might indicate that females were excluded from professional dental care (e.g., tooth extraction), which at that time was mostly provided by barber-surgeons in shops frequented primarily by male clientele. Although it is possible that there were sex differences in oral care or the use of herbal or chemical treatments for gum disease in medieval Europe, a search of the literature reveals no explicit information regarding such sex differences in this population.

It is also possible that dietary differences between the sexes in St. Mary Graces led to the observed differences in periodontal disease. Diets high in carbohydrates and those high in protein have both been associated with the accumulation of calculus, which is a risk factor for periodontal disease (Delgado-Darias et al., 2006); on the other hand, deficiencies of protein, calcium, vitamins A and D, and other micronutrients have also been associated with periodontal disease (Shaw, 1962). To explain observed sex differences in periodontal disease in medieval Croatia, Šlaus et al. (1997) suggests that males had greater access to highly cariogenic foods (e.g., cereals) and thus both developed more caries and suffered more alveolar bone loss than females. Hillson (1979) suggests that slightly higher frequencies of plaque-related diseases (including periodontal disease) in females in ancient Egypt and Nubia might have resulted from greater consumption of sugar by females (or from physiological differences between the sexes). Delgado-Darias et al. (2006) suggest that sex differences in periodontal disease in pre-Hispanic Gran Canaria resulted from higher protein consumption and thus greater calculus accumulation among males. Y'Ednyak (1989) found higher frequencies of periodontal disease in females in a Mesolithic sample from Yugoslavia, and suggests that dietary calcium deficiencies or less nutritionally varied (i.e., cereal-based) diets shaped the observed patterns. Differences in the physical consistency of foods consumed by each sex may have also affected patterns of periodontal disease in St. Mary Graces, as more highly abrasive foods might better cleanse the teeth and gums and stimulate gingival keratinization (i.e., producing tougher gums), and thus lead to less alveolar resorption than softer foods (Lavelle and Moore, 1969). Perhaps in St. Mary Graces, there were sex differences in diet similar to those suggested in other studies; unfortunately, there are currently no data from this cemetery to test this directly.

Rather than indicating sex differences in periodontal disease in the living St. Mary Graces population, the observed sex differences in the cemetery might be an artifact of variation in frailty. That is, the prevalence of periodontal disease among living males and females might have been similar, but there might have been significant sex differences in frailty that resulted in a skeletal sample with a higher frequency of the disease among interred males. A previous study of sex differences in the excess mortality associated with a variety of skeletal stress markers (tibial periosteal lesions, cribra orbitalia, porotic hyperostosis, and linear enamel hypoplasia), using a sample from the East Smithfield cemetery, found significant differences between adult males and females in medieval London (DeWitte, 2010). For both sexes, individuals with the stress markers faced elevated risks of dying; however, there is evidence that the excess mortality associated with skeletal stress markers was higher for males than females. These results suggest that females with a history of exposure to physiological stress were better able to resist dying than similarly stressed males, and thus that males were frailer than females. If males were similarly frailer than females in the St. Mary Graces population, males with periodontal disease might have been more likely to die than females with it, thereby increasing the proportion of males with the disease in the cemetery relative to the once-living population.

Explanations for a lack of sex difference in periodontal disease in East Smithfield. In this study, one of the main differences between the two cemeteries is a lack of significant sex differences in periodontal disease in East Smithfield, and this difference exists primarily because of a relatively high proportion of females with the disease in East Smithfield compared with St. Mary Graces. This might indicate differences in selective mortality during the Black Death versus during conditions of normal medieval mortality. Recent research has suggested that the Black Death disproportionately killed people who were already in poor health, but that it was perhaps less strongly selective than normal medieval mortality. That is, although it apparently targeted people in poor health, the Black Death was nonetheless highly virulent and likely killed many relatively healthy people who would not have been likely to die under nonepidemic conditions (DeWitte and Wood, 2008). The higher proportion of females with periodontal disease in East Smithfield compared with St. Mary Graces might have resulted from the deaths of a greater number of otherwise healthy females (with periodontal disease) during the Black Death compared to conditions of normal mortality. This assumes that under conditions of normal mortality, women would be less likely to enter the skeletal sample with periodontal disease compared to men, as suggested above. However, this explains the lack of a sex difference in East Smithfield only if the epidemic disproportionately affected females. Given previous findings that the Black Death did not disproportionately kill either sex (DeWitte, 2009), reduced selectivity during the epidemic does not likely explain the patterns of periodontal disease in East Smithfield.

The difference between the two cemeteries might reflect the negative effects of the Great Bovine Pestilence (c. 1319–1320) and the resulting decreases in dairy availability that persisted until about 1340 (Slavin, 2012). The cause of the Great Bovine Pestilence is not yet known conclusively, and suspected causes include anthrax, foot-and-mouth disease, and *rinderpest*. Regardless of the cause, the bovine pestilence resulted in the deaths of over 60 percent of bovine animals in England and Wales alone, and thus a significant reduction in dairy resources; in some areas, milk output fell by over 80%. It took decades for herds of bovine animals to be restored to their pre-1319 levels, and milk output was depressed through the 1330s (Slavin, 2012).

The Great Bovine Pestilence might have affected frequencies of periodontal disease in the East Smithfield cemetery by reducing the amount of protein in the diets of people who lived through the pestilence and the resulting protracted period of reduced dairy product availability. Dairy products were among the most important sources, if not the single most important source of protein for medieval peasants (Slavin, 2012), and pro-

TABLE 5. Periodontal disease frequencies using prereproductive versus reproductive ages (P-values are provided for Chi-square tests or Fisher's exact test, where appropriate)

Cemetery	Age	Males with PD (%)	Females with PD (%)	*P*
St. Mary Graces	20–24.99	3 (30%)	1 (17%)	0.5
	25+	34 (60%)	8 (30%)	0.01
	P	0.08	0.5	
East Smithfield	20–24.99	9 (41%)	4 (17%)	0.08
	25+	42 (57%)	25 (60%)	0.77
	P	0.19	0.001	

TABLE 6. Results of hierarchical log-linear analyses using pre-reproductive versus reproductive ages (age groups: 20-24.99, 25+)

Cemetery	Variables	*P*
Both	Cemetery × age × sex × PD	0.286
	Cemetery × age × sex	0.289
	Cemetery × age × PD	0.856
	Cemetery × sex × PD	0.053
	Age × sex × PD	0.187
St. Mary Graces	Age × sex × PD	0.728
	Age × sex	0.945
	Age × PD	0.066
	Sex × PD	0.008
East Smithfield	Age × sex × PD	0.091
	Age × sex	0.134
	Age × PD	0.001
	Sex × PD	0.523

tein-malnutrition is associated with poor periodontal status in living populations (Russell et al., 2010).

The Great Bovine Pestilence might also have affected frequencies of periodontal disease by dramatically reducing the availability of dietary calcium. Calcium plays an important role in the development and severity of periodontal disease. Low dietary intake of calcium is associated with greater severity of periodontal disease and increased risks of tooth loss associated with the disease (Nishida et al., 2000; Al-Zahrani, 2006; Amarasena et al., 2008; Adegboye et al., 2010; de Andrade et al., 2011; Van der Velden et al., 2011), and higher levels of calcium are associated with reduced alveolar bone loss (Krall, 2001). Some researchers have suggested that the relationship between dietary calcium intake and periodontal disease progression is mediated by bone mineral density, that is, low calcium levels result in lower bone mineral density, and lower alveolar bone mass, in particular, in turn exacerbates the bone destruction associated with periodontal disease (Amarasena et al., 2008). Using a rat model, Shoji et al. (2007) found that decreased calcium intake was associated with lower alveolar bone mineral density and decreases in alveolar bone height. The magnitude of the relationship between calcium intake and alveolar bone height in animal models is higher in pregnant and lactating females than in other individuals (Shoji et al., 2007).

Given the association between low calcium intake and risk of periodontal disease (Nishida et al. 2000), and the high calcium needs of pregnant and lactating women (Prentice, 2000; Gold, 2005), the Great Bovine Pestilence might have disproportionately affected the oral health of females who were at childbearing ages before the Black Death. This might explain why there is a relatively high frequency of periodontal disease among females in East Smithfield compared with St. Mary Graces. It is likely that a greater proportion of females buried in East Smithfield, compared to St. Mary Graces, suffered through long-term dairy depravations while they were at reproductive ages, and such depravations could have increased their risks of developing periodontal disease. Although there might be some females in the St. Mary Graces cemetery who could have been of reproductive ages during times of low dairy availability about 1319–1340, given the relatively long period of use of St. Mary Graces (1350–1538), such females are not likely to make up as large a proportion of the cemetery sample compared with East Smithfield. Furthermore, no sustained and dramatic decreases in dairy availability similar in scale to the Great Bovine Pestilence occurred during the time the St. Mary Graces cemetery was in use. As noted above, the frequency of periodontal disease among males in East Smithfield and St. Mary Graces is similar (53 and 55%, respectively). Assuming low calcium availability caused an increase of periodontal disease in females in East Smithfield, it would not have done so for males given their lower calcium requirements during adulthood.

If dairy depravations explain the relatively high frequency of periodontal disease in East Smithfield females, the highest frequency of the disease among females in East Smithfield should be in those who were between the reproductive ages of 15–50 during the Great Bovine Pestilence and resulting dairy depravations (i.e., no older than 50 at the beginning of the Great Bovine Pestilence in 1319 and at least 15 at the end of the dairy depravations around 1340; Amundsen and Diers, 1973a,b). That is, periodontal disease frequencies should be highest in individuals between the ages of 25 and 80 at the time of the Black Death, with relatively low frequencies in those below the age of 25 and above the age of 80. Unfortunately, in this dataset, there are no individuals with age estimates above 80, so frequencies of periodontal disease at ages above 80 cannot be evaluated. However, comparison of individuals who were at prereproductive versus reproductive ages during the dairy depravations is possible.

Age estimates were pooled into two age groups, 20–24.99 and 25–80, and periodontal frequencies were compared between such older and younger individuals in each cemetery. As shown in Table 5, for each sex in both cemeteries, there is an increase in periodontal disease with age, but the increase is most dramatic (and is statistically significant) for East Smithfield females. Further, the frequency of periodontal disease in older East Smithfield females is significantly higher than that of older St. Mary Graces females ($P = 0.015$); no other within-sex, between-site comparison yielded significant results. These results might suggest that dairy depravations negatively affected periodontal status in East Smithfield females who were at reproductive ages during the period of dairy depravations, and that a lack of similar dairy depravations in the St. Mary Graces population resulted in a less dramatic difference in periodontal disease between older and younger females compared with East Smithfield.

To assess intersite differences, these data were analyzed using a four-way hierarchical log-linear analysis of cemetery, sex, age, and periodontal disease; the results are shown in Table 6. Analysis of the associations among all four variables revealed no significant relationship. However, there is a significant association among cemetery, sex, and periodontal disease, indicating that St. Mary Graces and East Smithfield have significantly different sex patterns of periodontal disease, as was indicated by the analyses using three age groups and shown

in Table 4. Hierarchical log-linear analysis within St. Mary Graces revealed a significant association between sex and periodontal disease, and a significant association between age and periodontal disease. In East Smithfield, age and periodontal disease are significantly associated, as are sex, age, and periodontal disease. The latter association suggests that the age distribution of periodontal disease differs between the sexes in East Smithfield and that the increase in periodontal disease with age in females is the result of something more than just age (e.g., dairy depravations). However, the lack of a significant association among cemetery, sex, age, and periodontal disease using the pooled-cemetery sample indicates that the greater increase in periodontal disease with age in East Smithfield females compared with males is not significantly different from the analogous comparison in St. Mary Graces, as one would expect if dairy depravations were driving the patterns in East Smithfield.

Further, given the positive relationship between periodontal disease and age (using two age groups) in East Smithfield, it is not clear whether the dramatically higher frequency of periodontal disease in females' ages 25+ reflects the effects of dairy depravations or is simply the result of increases in periodontal disease that typically occur with age. To help discriminate between these two options, a relatively large sample of women who would have been postreproductive during the dairy depravations (i.e., over 80 in the East Smithfield sample) is needed. Such a sample would allow for a test of whether the frequency of periodontal disease in females ages 80+ is similar in East Smithfield and St. Mary Graces, which would suggest that the difference between the two cemeteries at younger ages (25–80) was the result of dairy depravations in the East Smithfield population. Unfortunately, such a sample is not currently available.

Recent analyses of skeletal stress markers in East Smithfield have shown a trend of higher frequencies of the markers among individuals who would have been at the ages vulnerable to developing them during the period of dairy depravations compared with individuals who were already past those vulnerable ages by the beginnings of the food crisis (DeWitte and Slavin, in press). These results are consistent with the idea that periodontal disease frequencies might have been relatively high in East Smithfield females because of the Great Bovine Pestilence. However, most of the skeletal stress marker analyses yielded results that are not statistically significant, and thus the effect of the Great Bovine Pestilence on periodontal disease requires further investigation.

As a final note, it was assumed for this study that St. Mary Graces is representative of normal medieval morbidity and mortality patterns, and that variations from that pattern in East Smithfield would reflect the effects of the Black Death. However, as described above, the dearth of details on sex patterns of periodontal disease from other, roughly contemporaneous sites makes it difficult to determine which, if either, cemetery most closely conforms to normal medieval patterns. St. Mary Graces, as a product of the selective sweep of the Black Death, might itself differ from the medieval norm with respect to periodontal disease. It is possible that frailty decreased in the post-Black Death population because of the epidemic or because of increased standards of living following the epidemic. It is further possible that improvements in diet and health might have more strongly benefitted females compared to males in the post-Black Death population, thus resulting in large decreases in periodontal disease in females but not in males. However, testing this will require the assessment of sex differences in periodontal disease in a pre-Black Death normal mortality sample from London, as well as further examination of other signs of frailty and sex differences thereof following the Black Death.

CONCLUSION

The results from the St. Mary Graces attritional sample are consistent with observations made in the majority of studies of sex differences in periodontal disease in both living and past populations—that is, a significantly higher frequency of the disease in males compared with females. The results from the catastrophic East Smithfield sample, however, failed to reveal significant differences in periodontal disease between the sexes, and the lack of sex differentials is the result of a higher frequency among females compared to St. Mary Graces. The lack of sex differences in the East Smithfield cemetery might reflect the differential effects of diet on males and females in the pre-Black Death population.

The results of this study hint at the effects of early 14th-century food crises on the population of London right before the Black Death. Given that the results of this study might indicate that female health was negatively affected by dairy shortages in the first half of the 14th century, it is possible that events like the Great Famine (Russell, 1966; Jordan, 1997) and the Great Bovine Pestilence broadly affected health and thereby contributed to the extraordinarily high mortality levels observed during the Black Death itself.

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