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# RESEARCH ARTICLE



# An observational analysis of risk factors associated with

# symptomatic third molar teeth [version 1; peer review:

# awaiting peer review]

# Douglas Bruce<sup>1</sup>, Tom Dudding<sup>1,2</sup>, Mark Gormley<sup>1,2</sup>, Rebecca C Richmond<sup>2</sup>, Simon Haworth<sup>1,2</sup>

<sup>1</sup>Bristol Dental School, University of Bristol, Bristol, UK <sup>2</sup>The MRC Integrative Epidemiology Unit at the University of Bristol, University of Bristol, Bristol, UK

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## Abstract

Background: Third molar teeth (wisdom teeth) are a common cause of pain and infection in young adults. The study aimed to describe the prevalence of symptomatic third molar teeth and identify factors which predispose to third molar symptoms in a birth cohort. Methods: An observational study was undertaken nested in the Avon Longitudinal Study of Parents and Children (ALSPAC), a birth cohort based in south west England. The main outcomes were self-reported third molar pain, swelling and treatment for third molar problems, taken from guestionnaires completed at age 23 years. The exposures including sex, dental history, socioeconomic status, diet, and genetic factors were obtained from earlier ALSPAC data. Results: In total 4,222 ALSPAC participants responded to one or more questions about third molar teeth. The final sample included more female participants than male participants. The majority of participants (56.6%) reported at least one episode of pain associated with their third molars. Females had greater odds than males of reporting swelling (adjusted odds ratio (OR) 1.97; 95% confidence interval (CI) 1.56, 2.51), pain (adjusted OR=1.96; 95%CI 1.56, 2.51) and receiving both non-surgical and surgical treatment (adjusted OR=2.30; 95%CI 1.62, 3.35, adjusted OR=1.54; 95%CI 1.17, 2.06 respectively). Participants with previously filled teeth had greater odds of third molar extraction. There were no strong associations between index of

multiple deprivation (IMD) score or sugar intake and the third molar outcomes. There was weak evidence for a genetic contribution to third molar pain.

Conclusions: Symptomatic third molars are common in this age group, with over half of the participants reporting pain or other symptoms. Female participants had greater odds for third molar pain, swelling and treatment.

## **Open Peer Review**

Approval Status AWAITING PEER REVIEW

Any reports and responses or comments on the article can be found at the end of the article.

## **Keywords**

Third molars, wisdom teeth, pericoronitis, risk factors, genetics, ALSPAC



This article is included in the Avon Longitudinal

Study of Parents and Children (ALSPAC)

gateway.

Corresponding author: Simon Haworth (Simon.Haworth@bristol.ac.uk)

Author roles: Bruce D: Conceptualization, Formal Analysis, Writing – Original Draft Preparation, Writing – Review & Editing; Dudding T: Conceptualization, Formal Analysis, Supervision, Writing – Original Draft Preparation, Writing – Review & Editing; Gormley M: Conceptualization, Data Curation, Formal Analysis, Writing – Original Draft Preparation, Writing – Review & Editing; Richmond RC: Data Curation, Formal Analysis, Supervision, Writing – Review & Editing; Haworth S: Conceptualization, Supervision, Writing – Review & Editing; Editing – Review & Editing; Haworth S: Conceptualization, Supervision, Writing – Review & Editing

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#### Introduction

Third molars, also known as wisdom teeth, are usually the last teeth to develop in humans, erupting in the late teenage years to early twenties<sup>1</sup>. These teeth are often developmentally absent<sup>2</sup> or unfavorably positioned<sup>3</sup>, and have highly variable crown and root morphology<sup>4</sup>. Third molar impaction is a common problem<sup>5</sup>, which can result in communication between the residual follicle space and the oral cavity, leading to bacterial ingress and infection<sup>6,7</sup>.

The management of impacted third molars remains an area of ongoing debate. In the United Kingdom, the National Institute of Health and Care Excellence (NICE) published guidance in 2000, suggesting third molar teeth should only be removed under specific clinical situations, discontinuing the practice of prophylactic removal<sup>8</sup>. Two decades later, there is a growing body of evidence which challenges this guidance. While prophylactic surgery has problems, there are also risks associated with leaving third molars in situ, including pericoronitis, caries, periodontitis, and cyst development9-14. A Cochrane review by Ghaeminia et al. concluded there was insufficient evidence to determine whether asymptomatic, disease-free impacted third molars should be removed or retained<sup>15</sup>, and clinicians need to weigh up the risks and benefits of different management approaches on a case by case basis in discussion with the patient. At the present time, common management strategies for mandibular third molar teeth range from clinical review and surveillance, to extraction of opposing maxillary third molar, coronectomy and surgical removal<sup>6</sup>.

Ideally, a shared decision making process about treatment options would involve accurate assessment of risk factors for third molar pathology in addition to discussion of patient symptoms and preferences. People with multiple risk factors may benefit from early surgical management, as the complexity of third molar removal increases with age<sup>16</sup>, while those with fewer risk factors might benefit from a period of active surveillance and conservative management. This would enable resources to be directed towards patients who are most likely to require future surgical management<sup>17</sup>, while avoiding surgery for patients who are unlikely to develop problems.

There is, therefore, a need to understand the risk factors for developing third molar problems. Both host and environmental factors affect other dental diseases such as periodontal disease and caries<sup>18,19</sup>, but there is relatively little evidence to show which risk factors are associated with third molar pathology. We aimed to investigate a wide range of factors including socio-economic status (SES), diet, host genetic susceptibility, previous dental attendance, and anxiety, to identify risk factors for symptomatic third molar teeth.

### Methods

### ALSPAC cohort

The Avon Longitudinal Study of Parents and Children (ALSPAC) is a large population-based birth cohort study<sup>20</sup>. Pregnant women living in the former county of Avon (South West England, UK) with expected dates of delivery between 1<sup>st</sup>

April 1991 and 31st December 1992 were invited to take part in the study. A total of 14,541 pregnancies were enrolled in the study, resulting in 14,062 live births and 13,988 children who were alive at 1 year of age. When these children were approximately 7 years of age, an attempt was made to enlarge the ALSPAC study by recruiting additional eligible people who had failed to join the study originally. A total of 913 additional children were enrolled though these efforts. This means the total initial sample size for the present study (with outcomes after the age of 7 years) is 15,454 pregnancies resulting in 14,901 children alive at 1 year of age. The ALSPAC study is ongoing, and the indexed children are now adults, many with children of their own. The study recruitment and design has been described in detail previously<sup>20-22</sup>. Study data was collected and managed using REDCap electronic data capture tools hosted at the University of Bristol. REDCap (Research Electronic Data Capture) is a secure, web-based software platform designed to support data capture for research studies<sup>23</sup>. Comprehensive phenotype, genetic and environmental information has been collected from both mothers, their partners and offspring at multiple time points. Ethical approval for the ALSPAC study was obtained from the ALSPAC Ethics and Law Committee. Informed consent for the use of data collected via questionnaires and clinics was obtained from participants following the recommendations of the ALSPAC Ethics and Law Committee at the time. Consent for biological samples has been collected in accordance with the Human Tissue Act (2004). Approval for the analysis reported in this article was obtained from the ALSPAC study executive (project reference B3482).

#### Data collection

The host and environmental factors examined for this study were measured at numerous time points throughout the study. Some questionnaires were completed by the participant's parents and others by the participant themself.

Sex was recorded by the midwife at the time of birth and recorded as either male or female. IMD scores were assigned according to a participant's home post code at age 13.8 years when they completed the *Travelling Leisure and School* questionnaire. To minimize disclosure risks, the scores were divided into quintiles 1 to 5, with 1 being the least deprived and 5 the most deprived, and the quintiles were used as an ordered categorial variable in subsequent analysis.

Sugar intake was measured at the *Teen Focus 2* research clinics which were open to all members of the ALSPAC cohort from ages 12.5 years to 15.2 years. The mean age of participants at these clinics was 13.8 years. Sugar intake was reported via means of three-day dietary diaries and coded as a continuous variable with the units being grams of sugar per day.

Dental anxiety, and record of previous extractions were measured at the *Teen Focus 4: Focus at 17* research clinic. The age range was 16.25 years to 20 years with the mean age being 17.8 years. The questions regarding dental anxiety mirrored those used in the Corah anxiety scale, with 4 question stems asking how the participant would feel in different situations (see extended data<sup>24</sup>). Each question stem had multiple responses, where lower scores indicate low levels of anxiety. Two question stems included options for reporting they had never received dental treatment. If participants selected this option (692 individuals) their response for these two question stems was replaced with the median response.

Participants at the *Teen Focus 4* clinic were asked how many teeth they have had taken out because they were 'bad', which was used as a proxy for previous treated dental caries experience. This variable was coded as a categorical variable with 3 levels (none, 1-4 and more than 4 previous extractions).

Data regarding the outcomes relating to third molar pathology and treatment were collected in the Me @ 23 questionnaire which was completed sent to participants at age 23 years. Participants were asked if they had had pain or swelling from their wisdom teeth and, if so, how many episodes they had (1, 2-3, 3-4 or 5 or more times). They were also asked if they had any wisdom teeth removed or any other treatment to wisdom teeth when they were causing pain. Responses to these questions were summarized as binary variables of symptoms or no reported symptoms, and treatment or no reported treatment. The Me@23 questionnaire also asked when the last time the young person went to the dentist. This was used as a proxy for dental attendance frequency, reported as either irregular (greater than two years between appointments) or regular (less than two years between appointments). They were also asked how many of their teeth had fillings or other restorative treatment such as crowns. This was treated as a proxy for previous caries experience and was coded as a categorical variable with 4 levels (no, 1-4, 5-9 and more than 9 teeth filled).

The questions asked in the ALSPAC surveys can be found in the extended  $data^{24}$ .

Please note that the study website contains details of all the data that is available through a fully searchable data dictionary and variable search tool<sup>25</sup>. Data were retrieved in August 2020.

## Statistical analysis

Continuous variables were described using means and standard deviation. Categorical variables were described as counts and percentages. Logistic regression analysis was conducted using the glm() function to investigate the association between host and environmental exposures and self-reported outcomes. Logistic regression included unadjusted models, and models adjusted for age, sex and IMD Score. Analysis was performed using R (version 4.0.2).

#### Genetic susceptibility

The variation in each outcome attributable to common single nucleotide polymorphisms (SNPs) was estimated with genetic restricted maximum likelihood analysis (GREML) using Genome-wide Complex Trait Analysis (GCTA)<sup>26,27</sup>. This analysis tests whether people who are more genetically similar are

also more phenotypically similar, to infer whether genetic factors influence a trait.

The genotype data used for this analysis was originally generated in collaboration between the Wellcome Trust Sanger Institute in the UK and the Laboratory Corporation of America using the Illumina HumanHap550 genotyping platforms. Quality control filtering was done with the PLINK (v1.07) software. SNPs with a minor allele frequency of < 1%, call rate < 95%and Hardy-Weinberg equilibrium (HWE)  $P < 5 \times 10-7$  were removed. The initial data included 9.912 individuals with 609,203 SNPs. Those with extreme or undetermined autosomal heterozygosity, those with insufficient sample replication (0.1)and >3% missingness have been removed leaving 9,115 individuals and 500,527 SNPs<sup>28</sup>. ALPSAC children were phased using ShapeIt V2 to phase the Haplotype Reference Consortium (HRC) panel (39,235,157 SNPs)<sup>29</sup>. Genotype imputation was performed with the Michigan Imputation Server using the Haplotype Reference Consortium (HRCr1.1) panel.

A subset of common genetic variants (minor allele frequency of 0.05 or greater) was then used to construct a genetic relatedness matrix and participants related at the first-degree level or closer (identity by state 0.125 or greater) were excluded. The final sample size with non-missing phenotypic data included 2,771 participants.

Variation in the outcomes attributable to genetic factors was expressed as a proportion of the total phenotypic variance.

#### Results

A total of 9,394 participants were sent the 'Me @ 23' questionnaire. Participants who submitted a valid answer to at least one of the four questions related to third molar symptoms were included in the study (Figure 1.).

The final study sample contained more female participants than male (66% female) and were predominantly from a less deprived background (the most common IMD quintile score was 1 with 30% of participants being from this quintile). Most participants reported attending a dentist regularly (82%) (Table 1).

Over half the participants (57%) reported experiencing pain from their third molar teeth on at least one occasion (Table S1<sup>24</sup>, while 17% reported experiencing facial swelling on at least one occasion (Table S1<sup>24</sup>). A smaller proportion of the cohort reported receiving surgical management (10%) or non-surgical treatment (7%) for their third molars (Table S2<sup>24</sup>).

Female sex was associated with greater odds for all four outcomes examined, with adjusted odds ratios (OR) between OR 1.54 (95% confidence interval (CI) 1.17, 2.06) and OR 2.30 (95%CI 1.62, 3.35) for these outcomes (Table 2). People who reported dental anxiety had greater odds for extraction (adjusted OR= 1.70; 95%CI 1.05, 2.66) although with wide confidence intervals. Patients with previously restored teeth had greater odds of having had at least one third molar extracted, compared to those with no previous restorations. This association was

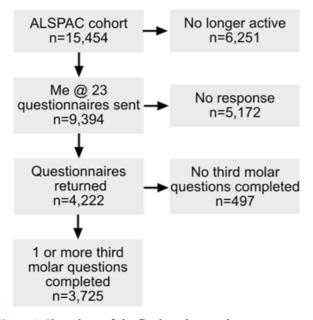


Figure 1. Flow chart of the final study sample.

stronger for participants with a greater number of previous restorations: 5-9 previously restored teeth (adjusted OR= 1.79; 95% CI 1.25, 2.52) and > 9 previously restored teeth (adjusted OR= 2.73; 95% CI 1.56, 4.58) (Table 2).

Heritability analysis yielded imprecise estimates, likely reflecting the low statistical power of this analysis in the available sample size. For pain, the estimated heritability was 0.17 (standard error 0.17), while the remaining traits had points estimates near zero.

#### Discussion

This study aimed to describe the prevalence of third molar symptoms in a birth cohort study and describe host and environmental risk factors for developing symptomatic third molar teeth or requiring treatment, with the assumption that self-reported pain, swelling and treatment for third molar teeth would serve as proxies for underlying pathology such as caries or pericoronitis. In this group of young adults, pain associated with third molar teeth was common, affecting a much higher proportion of people than those who received treatment for third molar teeth, suggesting that there may be a large burden of sub-clinical third molar problems in this age group.

In this study, female participants had greater odds for receiving surgical and non-surgical treatment than male participants. In part, this may reflect differences in health-seeking behaviour. It is reported that women are more active in seeking help with dental problems than men<sup>30,31</sup>. This mechanism, however, would not explain the finding that female participants had greater odds of reporting pain and swelling. Other possible explanations include differences in the perception or recollection Table 1. Descriptive characteristics of the study population(SD: standard deviation).

	Reported
	third molar symptoms or treatment Total=3725
Sex (%)	
Male	1,257 (33.7)
Female Missing	2,455 (66.2)
	13 (0.002)
Index of multiple deprivation (IMD) (%)	
1	1,126 (30.2)
2	760 (20.4)
3	507 (13.6)
4	349 (9.4)
ح Missing	185 (5.0)
	798 (21.4)
Dental attendance (%)	
Regular attender	3,048 (81.8)
Irregular or non-attender	636 (17.1)
Missing	41 (1.1)
Dental anxiety	
(COHRA scale) (%)	
<13	1,356 (36.4)
13 or above	219 (5.9)
Missing	2,150 (57.7)
Filled Teeth (%) No filled teeth	
1 - 4	1,711 (45.9)
5 - 9	,615 (43.4)
>9	312 (8.4)
Missing	87 (2.3)
	0 (0)
Teeth extracted due to decay (%)	
None	1,336 (35.9)
1 -4	149 (4.0) 90 (2.4)
>4	2,150 (57.7)
Missing	,
Diet	
Mean daily sugar intake in Gram (SD)	115g (49g)
(n=1432)	
(11-1452)	

of pain, differences in the mechanics of tooth eruption (for example related to the smaller size of the female mandible<sup>32</sup>, or sex-related differences in the chronology of tooth eruption).

 Table 2. Logistic regression models for host and environmental risk factors on third molar symptoms and treatment outcomes (OR, Odds Ratio; CI, Confidence Intervals; Ref, Reference; IMD, index of multiple deprivation, \*adjusted for age, sex and IMD quantile).

	Swe	Swelling	Pa	Pain	Non-surgical	Non-surgical management	Surgical m	Surgical management
	Crude	Adjusted*	Crude	Adjusted	Crude	Adjusted	Crude	Adjusted
Exposure	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Sex	P = 3.1x10-12	P = 1.86 ×10-8	P=0.44	P=0.44	P=0.79	P=0.73	P=0.24	P=0.24
Female	2.13 (1.73, 2.65)	1.97 (1.56, 2.51)	2.13(1.85,2.47)	1.96(1.67,2.30)	2.33(1.70,3.26)	2.30(1.62,3.35)	1.42(1.12,1.82)	1.54(1.17,2.06)
IMD	P = 0.58	P = 0.68	P=0.78	P=0.92	P=0.72	P=0.76	P=0.16	P=0.13
IMD 1	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
IMD 2	1.06 (0.82, 1.37)	1.04 (0.80, 1.35)	1.01(0.84,1.23)	1.00(0.82,1.2)	1.21(0.85,1.75)	1.20(0.84,1.74)	0.67(0.48,0.93)	0.66(0.47,0.92)
IMD 3	1.21 (0.91, 1.61)	1.18 (0.89, 1.58)	0.95(0.77,1.18)	0.93(0.74,1.20)	1.13(0.74,1.70)	1.12(0.73,1.69)	1.00(0.70,1.40)	0.99(0.70,1.39)
IMD 4	1.00 (0.70, 1.39)	0.94 (0.66, 1.32)	1.04(0.81,1.33)	1.00(0.77,1.28)	0.94(0.56,1.53)	0.90(0.53,1.47)	0.87(0.57,1.30)	0.86(0.56,1.29)
IMD 5	1.28 (0.84, 1.91)	1.18 (0.77, 1.77)	1.20(0.87,1.67	1.09(0.78,1.52)	1.31(0.71,2.29)	1.20(0.65,2.10)	0.80(0.45,1.40)	0.77(0.43,1.29)
Dental attendance	P = 7.00 ×10-5	P = 5.00 ×10-4	P=2.03x10-7	P=1.02x10-6	P=5.00x10-4	P=9x10-3	P=1.27x10-9	P=1.98×10-6
Regular attendance	0.58 (0.44, 0.75)	0.57(0.41,0.78)	0.63(0.52,0.75)	0.60(0.49,0.74)	0.46(0.29,0.70)	0.52(0.31,0.83)	0.22(0.13,0.35)	0.28(0.16,0.45)
Dental anxiety	P = 0.09	P = 0.29	P=0.003	P=0.32	P=0.32	P=0.83	P=2x10-3	P=0.02
Dental anxiety	1.38 (0.94, 2.00)	1.24 (0.82, 1.90)	1.63(1.20,2.26)	1.45(1.03,1.00)	1.33(0.73,2.26)	1.07(0.53,1.92)	1.91(1.25,2.87)	1.70(1.05,2.66)
Filled teeth	P = 0.34	P = 0.04	P=0.02	P=0.10	P=0.78	P=0.96	P=4.4x10-5	P=6.1×10-4
No filled teeth	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Filled teeth 1–4	1.06 (0.88, 1.28)	1.01 (0.82, 1.26)	1.14(0.99,1.31)	1.09(0.92,1.25)	1.13(0.87,1.48)	1.07(0.79,1.46)	0.96(0.75,1.21)	1.05(0.80,1.38)
Filled teeth 5–9	1.33 (0.97, 1.82)	1.27 (0.86, 1.26)	1.44(1.12,1.87)	1.45(1.08,1.96)	0.94(0.55,1.52)	0.99(0.55,1.69)	1.79(1.25,2.52)	1.98(1.30,2.95)
Filled teeth >9	1.21 (0.64, 2.12)	1.07 (0.50, 2.10)	1.19(0.75,1.92)	1.00(0.57,1.73)	1.08(0.41,2.34)	1.13(0.39,2.65)	2.73(1.56,4.58)	2.78(1.41,5.14)
Previous extractions due to decay	P = 0.75	P = 0.70	P=0.75	P=0.45	P=0.7	P=0.70	P=0.46	P=0.30
0	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
1-3	0.59 (0.32, 1.01)	0.54 (0.27, 0.96)	1.00(0.70,1.44)	0.96(0.66,1.42)	0.77(0.32,1.60)	0.74(0.28,1.60)	0.75(0.37,1.36)	0.72(0.33,1.40)
>=4	0.74 (0.35, 1.39)	0.59 (0.26, 1.19)	0.84(0.54,1.33)	0.73(0.45,1.20)	0.75(0.22,1.86)	0.78(0.23,2.1.95)	1.30(0.64,2.41)	1.52(0.74,2.86)
Sugar Intake	P = 0.20	P = 0.53	P=0.04	P=0.32	P=0.32	P=0.52	P=0.09	P=0.09
Per 100 g	0.99 (0.96, 1.00)	1.01 (0.98, 1.03)	0.98(0.97,1.00	0.99(0.97,1.00)	0.98(0.951,1.01)	1.01(0.97,1.04)	1.02(0.99,1.04)	1.02(1.00,1.06)

If present, a biomechanical reason for sex differences in third molar symptoms might suggest a need for sex-specific protocols in clinical management. The interplay between sex, third molar biomechanics and health-seeking behaviour cannot be fully explored in this study but is suggested as a topic for future research.

In this study irregular dental attenders had lower odds of reporting either pain or swelling from their third molars and had lower odds of receiving treatment. Interpretation of this finding is complex. While historically it was believed that prevention at regular dental attendance should associate with lower levels of dental pathology<sup>33</sup>, there is now a drive in the UK for targeted recall intervals where patients deemed at highest risk of dental problems are seen most frequently, and patients with acute dental problems may attend more frequently for management of those problems. This complicates interpretation in the context of an observational study. There is a disparity between the number of participants reporting pain and those that receive any form of treatment suggesting most cases go untreated. Other UK studies have demonstrated the impact of NICE guidelines on increasing the modal age of patients receiving third molar treatment, from 26 to 29 years, which may add to the complexity of surgery and risk of complications<sup>34</sup>.

In this study, participants who reported having filled teeth had greater odds of reporting third molar removal and there were directionally consistent but weak associations with third molar swelling and pain. This might reflect shared risk factors for dental caries and symptomatic third molars, for example poor oral hygiene is an established risk factor for both caries<sup>35</sup> and pericoronitis<sup>36</sup>. Associations between previous dental extractions due to decay and third molar symptoms or treatment were imprecisely estimated, probably reflecting the small number of people with previous dental extractions in this cohort.

In this study IMD was not strongly associated with third molar pathology, which is in keeping with another UK third molar study<sup>37</sup>, while previous publications in the same cohort show strong associations between socio-demographic variables and caries<sup>38,39</sup>. This suggests deprivation is less strongly associated with third molar symptoms than other dental diseases, although power to detect an association may have been limited as the ALSPAC study cohort who were still active at the time of this questionnaire was biased towards people from less deprived backgrounds. In addition, there was relatively little variance in deprivation since all the participants were originally recruited from three District Health Authorities (Southmead, Frenchay and Bristol and Weston). Thus, the quintiles of deprivation scores (assigned within the study population) do not represent the full range of deprivation seen in the UK. Sugar intake was not associated with self-reported third molar problems or treatment in this study. This may suggest the third molar problems experience by participants in this study

are not due to caries (where sugar is a risk factor<sup>40</sup>), or might reflect changes in dietary habit between completing the diet diaries at age 13 and participating in the oral health questionnaire at age 23.

Host genetic factors are known to influence dento-maxillofacial morphology<sup>41,42</sup> and govern events leading to tooth eruption. It seems plausible that host genetic factors could therefore predispose to unfavorable third molar position, morphology or available space for eruption, and could therefore be risk factors for third molar symptoms<sup>43</sup>. In this study, heritability estimates using the GREML method produced wide confidence intervals. While there was weak evidence for a genetic contribution to third molar pain, larger sample sizes or other designs such as twin-based studies<sup>44,45</sup> will be required to confirm this.

This study has the advantage of using an unascertained population so includes those who do not, or are unable to, access dental care. This should give a more representative estimate of prevalence than studies in clinical settings such as oral surgery or primary care units. While using a population-based rather than clinical design has natural advantages, it also has the disadvantage that the data were self-reported and will include both over- and under-reporting of outcomes. To try and reduce error from recall bias, data was collected at age 23, which is likely to be near the peak age for wisdom tooth problems<sup>46</sup>. To minimize error, the question stems needed to be simple, and this means the questions did not attempt to distinguish between different types of non-surgical treatment such as analgesic advice, mechanical cleaning of the operculum or removal of the operculum. It is not possible to comment on the risk factors for different types of non-surgical treatment or make any comments of what forms of treatment are more common in particular patient groups. In general, the risk factor profiles were similar for pain, swelling, surgical and nonsurgical treatment, suggesting the available questions acted as proxies for a similar underlying condition, and detailed dissection of any one of these questions may not change the overall interpretation of results.

In summary, the study highlighted that third molar problems are common in young adults. The risk factors for third molar symptoms appear different from the risk factors for caries, given that the expected risk factors for caries such as socioeconomic status, sugar intake and irregular attendance were not strongly associated with third molar symptoms. By contrast, female sex was strongly associated with both self-reported third molar symptoms and self-reported treatment. It may be useful to investigate sex differences in third molar biomechanics and care-seeking behaviour to understand whether sex-specific third molar protocols would be useful in clinical practice.

#### Data availability

#### Underlying data

ALSPAC data access is through a system of managed open access. The steps below highlight how to apply for access to

the data included in this research article and all other ALSPAC data. The datasets presented in this article are linked to ALSPAC project number B3482, please quote this project number during your application. The ALSPAC variable codes highlighted in the dataset descriptions can be used to specify required variables.

- 1. Please read the ALSPAC access policy which describes the process of accessing the data and samples in detail, and outlines the costs associated with doing so.
- 2. You may also find it useful to browse our fully searchable research proposals database, which lists all research projects that have been approved since April 2011.
- 3. Please submit your research proposal for consideration by the ALSPAC Executive Committee. You will receive a response within 10 working days to advise you whether your proposal has been approved.

If you have any questions about accessing data, please email alspac-data@bristol.ac.uk.

The study website also contains details of all the data that is available through a fully searchable data dictionary.

#### Extended data

figshare: Extended\_data\_17\_02\_2022.pdf. https://doi.org/10.6084/ m9.figshare.19188224.v1<sup>24</sup>

Data are available under the terms of the Creative Commons Attribution 4.0 International license (CC-BY 4.0).

#### Author contributions

D. Bruce was involved in conceptualization, formal analysis, writing the original draft and review and editing. T. Dudding was involved in conceptualization, formal analysis, supervision, writing the original draft, review and editing. M. Gormley was involved in conceptualization, data curation, formal analysis, supervision, writing the original draft, review and editing. R. C. Richmond was involved in data curation, formal analysis, supervision, review and editing. S Haworth was involved in conceptualization, review and editing.

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