INTERNATIONAL
ENDODONTIC JOURNAL

doi:10.1111/iej.13169

REVIEW

Prevalence of C-shaped canal morphology using cone beam computed tomography – a systematic review with meta-analysis

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Abstract

Martins JNR, Marques D, Silva EJNL, Caramês J, Mata A, Versiani MA. Prevalence of C-shaped canal morphology using cone beam computed tomography – a systematic review with meta-analysis. *International Endodontic Journal*.

Background and aim To perform a systematic review of anatomical studies using cone beam computed tomography (CBCT) to assess the influence of demographic factors (age, gender and geographic region) on the prevalence of C-shaped canal anatomy in maxillary molars, mandibular premolars and molars.

Data sources A search was conducted between May and August 2018 in four electronic databases and five peer-reviewed journals. The authors of included articles were also contacted for additional studies and the bibliographic references hand-searched.

Study eligibility criteria, participants and interventions The research protocol was previously registered in the International Prospective Register of Ongoing Systematic Reviews (CRD42018095201) and included defined inclusion/exclusion criteria. Prevalence studies on C-shaped canal anatomy in maxillary molars, mandibular premolars and molars were searched.

Study appraisal and synthesis methods The selected studies were submitted to full-text analysis and critical appraisal by two evaluators using the Joanna Briggs Institute Critical Appraisal tool. The final group of papers ($n = 25$) were pooled and forest plots with proportions and odds ratio with a 95% confidence interval performed. Meta-regression was undertaken to evaluate possible sources of heterogeneity and funnel plot visual analysis to assess publication bias.

Results The included studies reported data on 25 445 teeth of 13 142 patients. A significant difference in the average prevalence proportion of C-shaped configuration was observed between mandibular first (0.3%; 0.1–0.6%) and second (12%; 10.3–13.7%) molars ($P < 0.05$). No significant difference in the prevalence of C-shaped configurations was observed comparing males (13.5%; 8.8–18.3%) and females (20.5%; 13.7–27.4%) in mandibular second molars ($P > 0.05$), although males were associated with significantly lower odds (0.573; 0.511–0.641) ($P < 0.05$). The pooled proportion of C-shaped anatomy in mandibular second molars in East Asian countries (39.6%; 36.0–43.1%) was significantly higher compared with other regions.

Limitations Because of the limited number of studies, no statistical analysis was performed for maxillary molars and mandibular premolars.

Conclusion Meta-analysis revealed that gender and geographic region may act as a confounding factor for the prevalence of C-shaped anatomy in mandibular second molars, whilst age did not influence the prevalence of C-shaped configurations in this tooth group. Knowing these preoperative factors would help to anticipate complex morphologies in clinics.

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Keywords: anatomy, C-shape, meta-analysis, prevalence studies, root canal, systematic review.

Received 17 December 2018; accepted 13 June 2019

Introduction

C-shaped canal morphology is based on the cross section of the root and canal which resembles the shape of a letter C. Its main anatomic feature is the presence of fins or isthmuses connecting the individual root canals, whereas the orifice may appear as a single ribbon-shaped opening with an arc of 180° or more, which makes the canal cross-sectional and 3D shape variable along the root (Fan *et al.* 2004). As it would be expected, this morphological complexity creates major challenges with respect to debridement, disinfection and canal filling procedures, which ultimately may influence the prognosis of the root canal treatment (Amoroso-Silva *et al.* 2015).

Historically, the existence of C-shaped canal anatomy in teeth was firstly recognized in the 18th century (Malpighi 1743, Hunter 1778) and described in details at the beginning of the 20th century (Keith & Knowles 1911, Keith 1913). However, it took several decades of technological advancements in endodontics until this information could be applied for the effective clinical management of C-shaped anatomy (Cooke & Cox 1979). Since then, several studies have addressed its morphological features reporting differences in the prevalence of this anatomical anomaly amongst various groups of teeth and populations (Fan *et al.* 2012, Ladeira *et al.* 2014, Martins *et al.* 2016b, Ordinola-Zapata *et al.* 2017, Shemesh *et al.* 2017). Interestingly, despite authors justifying these differences based on ethnicity (Kato *et al.* 2014, Martins *et al.* 2018a), geographic location (von Zuben *et al.* 2017) and gender (Kim *et al.* 2016a,b, Martins *et al.* 2016b, von Zuben *et al.* 2017), no anthropological approach has been employed to support these findings.

Although single epidemiological-type studies on C-shaped canal anatomy are common, a true systematic review allowing for a synthesis of evidence-based data with a clear, detailed and reproducible methodology, followed by a meta-analysis that specifically evaluates the influence of demographic characteristic factors on the prevalence of this anatomy, based on *in vivo* cross-sectional studies of different groups of teeth and populations, has not been published. Undoubtfully, association of this knowledge with a proper diagnostic tool would help clinicians to anticipate and treat this complex morphological variation of root canals in practice. Therefore, this systematic review with meta-analysis aimed to assess and explain the influence of demographic factors such as age, gender and geographic region on the prevalence of C-shaped anatomy in maxillary molars, mandibular premolars and mandibular molars, by combining the results of a large collection of data from individual epidemiological studies that used cone beam computed tomographic (CBCT) imaging as an analytical tool. The null hypotheses tested were that there was no difference between (I) age, (II) gender or (III) geographic regions regarding the prevalence of C-shaped canal morphology in maxillary molars, mandibular molars or mandibular premolars.

Review

This systematic review and meta-analysis protocol of anatomical studies using CBCT technology was registered in the International Prospective Register of Ongoing Systematic Reviews (PROSPERO) (CRD42018095201) and attempted to follow the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (Moher *et al.* 2009) and the Assessment of Multiple Systematic Reviews (AMSTAR 2) (Shea *et al.* 2017).

Literature search strategy

Four electronic databases were accessed (PubMed, Science Direct, Lilacs and Cochrane Collaboration), and a search was undertaken for prevalence studies on root/canal anatomy using CBCT imaging, according to specific terms and filters (Table S1). The reference list from the identified studies as well as five relevant peer-reviewed scientific journals (International Endodontic Journal, Journal of Endodontics, Australian Endodontic Journal, Evidence-Based Dentistry and Journal of Evidence-Based Dental Practice) was also hand-searched. Additionally, when available, authors from the included studies were contacted via email and asked for additional material from their research group, whether as a format of scientific articles or grey literature, or if they were aware of any ongoing project which could also be accessed. Selection of the studies followed a '3 stage assessment'. In the first stage, titles and abstracts of the papers were accessed and, according to a pre-defined inclusion/exclusion criteria (Table S2), were labelled as 'relevant' or 'irrelevant'. In the second stage, the full text of the relevant articles was analysed and re-labelled according to the same criteria, and in the last stage, they were submitted to a critical appraisal on the level of their scientific merit. Literature search was conducted between May 2018 and August 2018 without language restrictions for studies published since January 1990.

Scientific merit assessment

The quality assessment of the selected studies followed the checklist for prevalence studies from the Joanna Briggs Institute (JBI) Critical Appraisal tool for use in systematic reviews (Munn *et al.* 2015). Two evaluators (DM and JM) independently assessed the eligible studies and scored each JBI question (Table S2) as yes, no, unclear or not applicable. The assessment discrepancies were discussed until consensus was reached. Inter-rater reliability tests between both evaluators were undertaken with kappa above 0.61 which is considered as good agreement. The final score of each study applied to the JBI questions was calculated based on the percentage of positive answers ('yes') only. Then, the risk of bias (RoB) of each study was categorized according to the final score as 'high' (score equal or lower than 49%, which lead to article exclusion), 'moderate' (score ranging from 50% to 69%) or 'low' (score higher than 70%) (Saletta *et al.* 2019).

Statistical analysis

The pooled C-shaped prevalence was calculated based on the prevalence reported in the included studies. All data were processed using a random-effects model (Dersimonian-Laird test) using the OpenMeta [Analyst] v. 10.10 (http://www.cebm.brown.edu/openmeta/) software. Results were presented as forest plots displaying the odds ratio (OR) and untransformed proportions with a 95% confidence interval (CI). The heterogeneity amongst studies was assessed with τ^2 (estimate of between-study variance). Q-Cochran test with Dersimonian and Laird (occurrence of heterogeneity) and the I^2 statistic was used to measure the proportion of statistical heterogeneity of the proposed outcomes, quantified as low (25%), moderate (50%) and high (75%). Significant heterogeneity was considered to be present if I^2 was 50% or more (Higgins & Thompson 2002, Higgins 2011). Meta-regression was used to assess possible sources of heterogeneity (Higgins & Thompson 2002, Higgins 2011). A funnel plot visual analysis was undertaken to assess publication bias (RevMan v.5.3.5; Cochrane Collaboration, Denmark). Statistical significance was set at $P < 0.05$.

Results

The electronic and manual searches identified 126 relevant studies. Email contact return rate with authors was 29.1% (16 answers out of 55 contacts), and four studies were added. From a full textual analysis of these studies, 105 were excluded (Table S3). Cohen kappa inter-rater reliability results between evaluators for the selected studies ($n = 25$) submitted to the JBI critical assessment are summarized in Table S4. The average JBI score for the 25 included papers was 76.0%. Nine papers were classified as having moderate RoB (Zhang *et al.* 2011a,b, Yu *et al.* 2012, Silva *et al.* 2013, 2014, Arslan *et al.* 2015, Torres *et al.* 2015, Rogazkyn *et al.* 2016, Pedemonte *et al.* 2018), whilst the remaining studies ($n = 16$) were categorized as low RoB. According to the Joanna Briggs Institute levels of evidence, the present review was categorized as Level 4a (systematic review of descriptive studies). The search flow diagram is presented as Fig. 1.

The included studies ($n = 25$) reported data on 25 445 teeth from 13 142 patients including 2540 maxillary first molars, 3300 maxillary second molars, 5240 mandibular first molars, 11 308 mandibular second molars, 1656 mandibular first premolars and 1401 mandibular second premolars. Evaluation included at least 4110 males and 5559 females, once six studies reported incomplete data regarding gender ratio (Yu *et al.* 2012, Zhang *et al.* 2015, Rogazkyn *et al.* 2016, Pawar *et al.* 2017, von Zuben *et al.* 2017, Pedemonte *et al.* 2018). The average age of the patients was 42.3 years and was calculated based on 18 studies that reported this information. The publication year of the final poll of studies ranged from 2011 to 2018, including data from 17 countries (Belgium, Brazil, Chile, China, England, India, Israel, Korea, Mexico, Poland, Portugal, Russia, Spain, South Africa, Thailand, Turkey and USA).

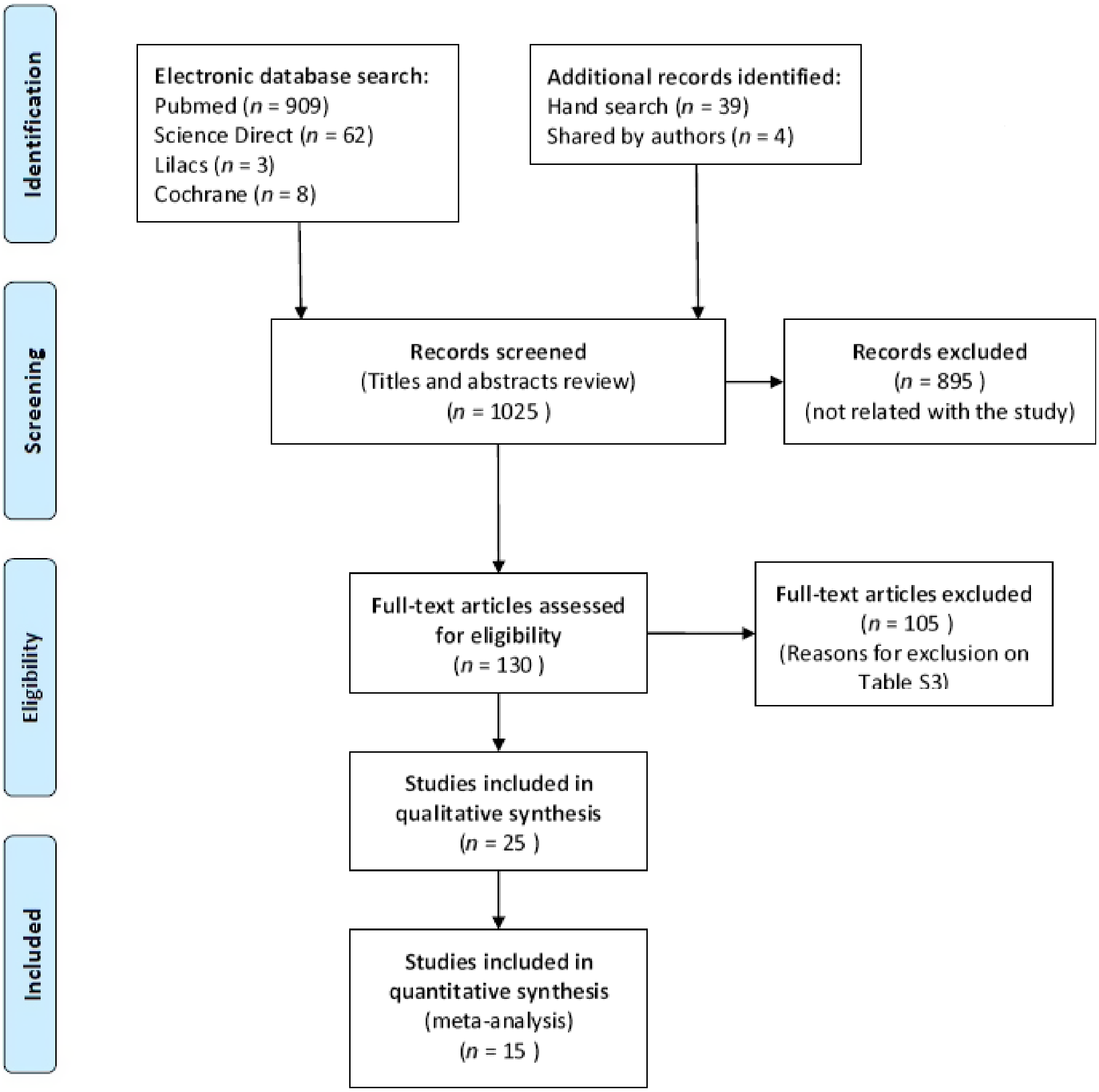

Figure 1 Flow diagram of the search strategy.

Prevalence of C-shaped canal morphology

Table 1 summarizes the overall results on the prevalence of C-shaped canal morphology according to tooth group, age, gender and geographic region. All papers present on Table 1 were submitted to a qualitative synthesis (n = 25) (systematic review); however, only the studies on mandibular first and second molars (n = 15) were submitted to a quantitative synthesis (meta-analysis).

In maxillary molars, C-shaped canal morphology was a rare finding, with the highest prevalence reported being 1.1% and 3.4% of first and second molar teeth (Martins *et al.* 2016a), respectively. C-shaped canal configuration in mandibular premolars was reported in only four papers. Although uncommon, results suggest that its prevalence might be greater in mandibular first premolars. Because of limited number of selected papers on the anatomy of maxillary molars and mandibular premolars, no further statistical analysis regarding gender, age or geographic region could be performed.

In mandibular first molars, the prevalence of C-shaped canals ranged from 0% (Martins *et al.* 2018a)

Table 1 Prevalence (%) of C-shaped canal morphology according to gender in different groups of teeth

Author	Country	CBCT device	Voxel size (μm)	Number of Subjects	Males/ Females	Age average	Number of Teeth	Overall Prevalence of the C-shape (%)	Number of Teeth in Males	C-shaped Prevalence in males (%)	Number of Teeth in Females	C-Shaped Prevalence in Females (%)
Mandibular first premolar												
Arslan *et al.* (2015)	Turkey	NewTom	150	88	41/47	35.5	154	2.5 (4)	n/a	n/a	n/a	n/a
Martins *et al.* (2017a)[a]	Portugal	Planmeca	200	634	232/402	50.0	1123	2.3 (26)	420[a]	3.8 (16)[a]	703[a]	1.4 (10)[a]
Pedemonte *et al.* (2018)	Belgium	Accuitomo	250	73	n/a	n/a	101	10.9 (11)	n/a	n/a	n/a	n/a
Pedemonte *et al.* (2018)	Chile	Accuitomo	250	114	n/a	n/a	100	7.0 (7)	n/a	n/a	n/a	n/a
Yu *et al.* (2012)	China	Accuitomo	125	149	n/a	n/a	178	1.1 (2)	n/a	n/a	n/a	n/a
Mandibular second premolar												
Arslan *et al.* (2015)	Turkey	NewTom	150	88	41/47	35.5	133	1.5 (2)	n/a	n/a	n/a	n/a
Martins *et al.* (2017a)[a]	Portugal	Planmeca	200	634	232/402	50.0	889	0.6 (5)	341[a]	1.2 (4)[a]	548[a]	0.3(1)[a]
Pedemonte *et al.* (2018)	Belgium	Accuitomo	250	73	n/a	n/a	101	1.0 (1)	n/a	n/a	n/a	n/a
Pedemonte *et al.* (2018)[b]	Chile	Accuitomo	250	114	n/a	n/a	100	0[b]	n/a	0[b]	n/a	0[b]
Yu *et al.* (2012)	China	Accuitomo	125	149	n/a	n/a	178	0.6 (1)	n/a	n/a	n/a	n/a
Maxillary first molar												
Kim *et al.* (2012)[b]	Korea	Dinnova	167	415	198/217	28.5	814	0[b]	n/a	0[b]	n/a	0[b]
Martins *et al.* (2016a)[a]	Portugal	Planmeca	200	895	310/585	52.0	928	1.1 (10)	343[a]	0.6 (2)[a]	585[a]	1.4 (8)[a]
Olczak & Pawlicka (2017)[b]	Poland	Gendex	125	112	38/74	34.8	185	0[b]	n/a	0[b]	n/a	0[b]
Silva *et al.* (2014)[a,b]	Brazil	i-Cat	200	294	108/186	n/a	314	0[b]	140[a]	0[b]	174[a]	0[b]
Zhang *et al.* (2011b)[b]	China	Accuitomo	125	269	129/140	35.0	299	0[b]	n/a	0[b]	n/a	0[b]
Maxillary second molar												
Kim *et al.* (2012)[b]	Korea	Dinnova	167	415	198/217	28.5	821	0[b]	n/a	0[b]	n/a	0[b]
Martins *et al.* (2016a)[a]	Portugal	Planmeca	200	895	310/585	52.0	1299	3.8 (49)	431[a]	1.4 (6)[a]	868[a]	5.0 (43)[a]
Olczak & Pawlicka (2017)	Poland	Gendex	125	112	38/74	34.8	207	1.9 (4)	n/a	n/a	n/a	n/a
Ratanajirasut *et al.* (2018)	Thailand	Accuitomo	250	266	107/159	n/a	457	0.9 (4)	n/a	n/a	n/a	n/a
Silva *et al.* (2014)[a,b]	Brazil	i-Cat	200	294	108/186	n/a	306	0[b]	152[a]	0[b]	154[a]	0[b]
Zhang *et al.* (2011b)[b]	China	Accuitomo	125	269	129/140	35.0	210	0[b]	n/a	0[b]	n/a	0[b]
Mandibular first molar												
Kim *et al.* (2013b)	Korea	Dinnova	167	976	460/516	28.8	1952	0.61 (12)	920	0.8 (7)	1032	0.5 (5)
Martins *et al.* (2018a)[a,b]	China	Carestream	200	120	54/66	28.0	220	0[b]	104[a]	0[b]	116[a]	0[b]
Martins *et al.* (2016b)[a,b]	Portugal	Planmeca	200	792	303/489	51.0	695	0.6 (4)	276[a]	0[a,b]	419[a]	1.0 (4)[a]
Shemesh *et al.* (2017)	Israel	Alioth	155	1020	447/573	43.1	1229	0.2 (2)	n/a	n/a	n/a	n/a
Silva *et al.* (2013)[a,b]	Brazil	i-Cat	200	154	70/84	n/a	234	1.7 (4)	112[a]	0[a,b]	122[a]	3.3 (4)[a]
Zhang *et al.* (2015)	China	Galileos	125	455	n/a	n/a	910	0.1 (1)	514	n/a	396	n/a
Mandibular second molar												
Helvacioglu-Yigit & Sinanoglu (2013)	Turkey	i-Cat	250	251	111/140	40.7	271	8.9 (24)	n/a	n/a	n/a	n/a
Kim *et al.* (2016a)	Korea	Dinnova	167	960	441/519	28.7	1920	40.1 (770)	882	32.1 (283)	1038	45.1 (487)

Table 1 Continued

Author	Country	CBCT device	Voxel size (μm)	Number of Subjects	Males/ Females	Age average	Number of Teeth	Overall Prevalence of the C-shape (%)	Number of Teeth in Males	C-shaped Prevalence in males (%)	Number of Teeth in Females	C-Shaped Prevalence in Females (%)
Ladeira *et al*. (2014)	Brazil	i-Cat	250	214	84/130	29.9	406	15.3 (62)	158	4.7 (19)	248	10.6 (43)
Martins *et al*. (2018a)[a]	China	Carestream	200	120	54/66	28.0	240	43.3 (104)	108[a]	36.1 (39)[a]	132[a]	49.2 (65)[a]
Martins *et al*. (2016b)	Portugal	Planmeca	200	792	303/489	51.0	1088	8.5 (93)	398	4.0 (16)	690	11.2 (77)
Pawar *et al*. (2017)	India	Planmeca	100	1120	n/a	26.8	983	13.1 (129)	489	10.8 (53)	494	15.4 (76)
Rogazkyn *et al*. (2016)	Russia	Vatech	200	300	n/a	n/a	600	10.8 (65)	n/a	n/a	n/a	n/a
Shemesh *et al*. (2017),	Israel	Alioth	155	1020	447/573	43.1	1465	4.6 (68)	647	4.0 (26)	818	5.1 (42)
Silva *et al*. (2013)[a]	Brazil	i-Cat	200	154	70/84	n/a	226	3.5 (8)	94[a]	2.1 (2)[a]	132[a]	4.5 (6)[a]
Torres *et al*. (2015)	Belgium	Accuitomo	250	100	52/48	19.5	112	10.7 (12)	n/a	n/a	n/a	n/a
Torres *et al*. (2015)	Chile	Accuitomo	250	170	75/95	19.0	112	8.9 (10)	n/a	n/a	n/a	n/a
von Zuben *et al*. (2017)	Brazil	i-Cat	200	237	n/a	42.0	400	6.8 (27)	169	5.3 (9)	231	7.8 (18)
von Zuben *et al*. (2017)	China	Kodak	200	214	n/a	33.0	400	44.0 (176)	190	35.8 (68)	210	51.4 (108)
von Zuben *et al*. (2017)	England	Accuitomo	80	400	159/241	44.0	400	7.8 (31)	159	5.7 (9)	241	9.1 (22)
von Zuben *et al*. (2017)	India	Newtom	150	232	n/a	33.0	400	12.3 (49)	248	9.3 (23)	152	17.1 (26)
von Zuben *et al*. (2017)	Mexico	OP300Maxio	250	400	130/270	44.0	400	14.2 (57)	130	7.7 (10)	270	17.4 (47)
von Zuben *et al*. (2017)	South Africa	Galileos	200	217	n/a	43.0	400	9.3 (37)	172	8.1 (14)	228	10.1 (23)
von Zuben *et al*. (2017)	Spain	Planmeca	200	362	n/a	43.0	400	11.0 (44)	181	6.1 (11)	219	15.1 (33)
von Zuben *et al*. (2017)	USA	Kodak	76	400	163/237	57.0	400	11.3 (45)	163	8.0 (13)	237	13.5 (32)
Zhang *et al*. (2011a)	China	Accuitomo	125	211	101/110	37.0	157	29.0 (46)	n/a	n/a	n/a	n/a
Zheng *et al*. (2011)	China	Accuitomo	125	528	297/231	40.1	528	38.6 (204)	297	36.4 (108)	231	41.6 (96)

n/a, Not available.
[a]Information not available in the original manuscript, but provided by the author after contact.
[b]Studies that clearly stated that no C-shaped morphology was found.

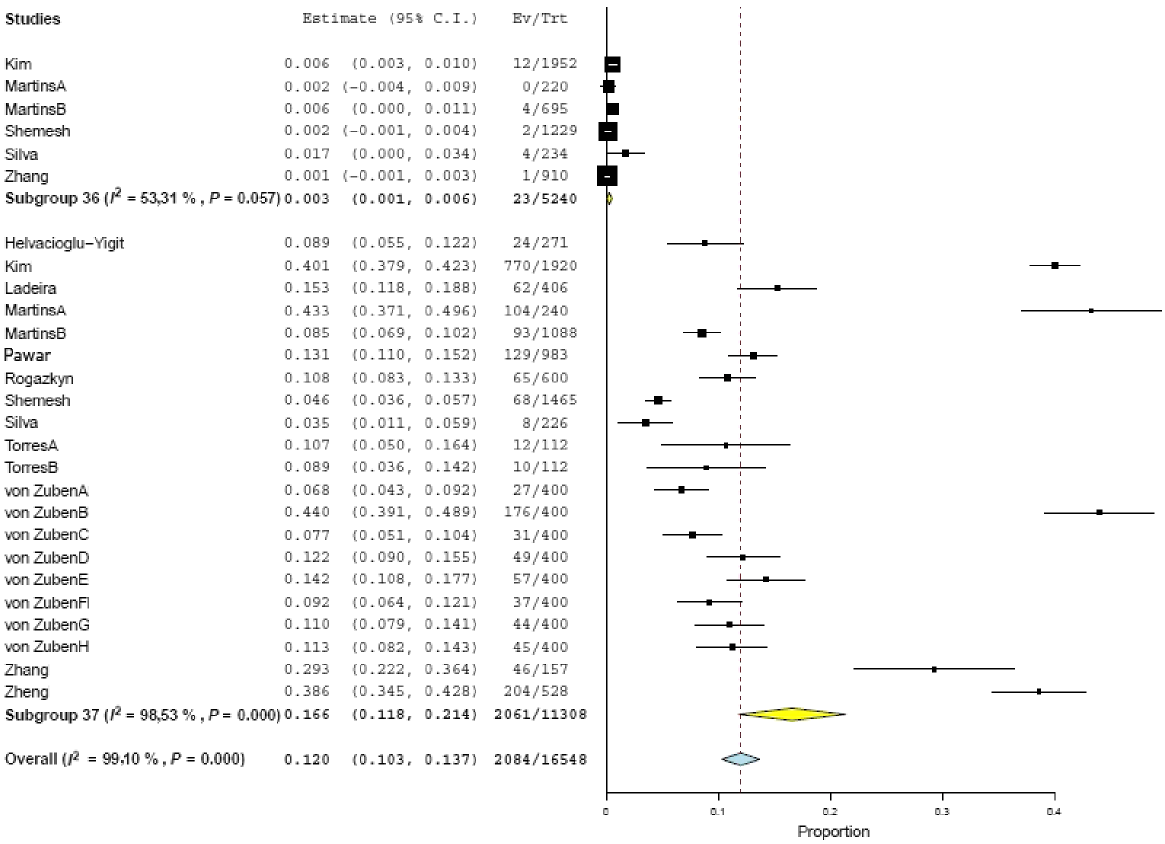

Figure 2 Forest plot of C-shaped proportions between mandibular molars in the studies included. Subgroup 36 refers to the mandibular first molar (both sides included), and Subgroup 37 refers to the mandibular second molar (both sides included).

to 1.7% (Silva *et al.* 2013), whilst 12 studies reported C-shaped morphology ranging from 3.5% (Silva *et al.* 2014) to 44.0% (von Zuben *et al.* 2017) in mandibular second molars. A significant difference in the average prevalence proportion of C-shaped configuration was observed between mandibular first (0.3%; 0.1–0.6%) and second (12%; 10.3–13.7%) molars ($P < 0.05$) (Fig. 2). The I^2 analysis revealed moderate heterogeneity ($I^2 = 53.31\%$) for the first molars and high heterogeneity for second molars ($I^2 = 98.53\%$).

C-shaped canal and gender

Three studies (four populations) described the influence of gender on the prevalence of C-shaped configuration in mandibular first molars and were pooled in the meta-analysis (Fig. 3). Because of a low number of studies, a funnel plot for publication bias assessment was not possible. Comparing the prevalence of C-shaped canals in males (0.4%; 0.1–0.8%) and females (0.6%; 0.2–1.1%), as well as odds ratio (0.647; 0.163–2.562) with heterogeneity of τ^2 (0.57), χ^2 (4.05; df = 3) and I^2 (25.94%), no significant difference was observed between gender in this group of teeth ($P > 0.05$).

Meta-analysis calculation of eight studies (16 populations) on C-shaped canal in mandibular second molar revealed no significant difference in its prevalence when comparing males (13.5%; 8.8–18.3%) and females (20.5%; 13.7–27.4%) ($P > 0.05$) (Fig. 4). However, the odds ratio significantly favoured males (0.573; 0.511–0.641) (lower odds of presenting C-shape) with a heterogeneity of τ^2 (0.00), χ^2 (13.96, df = 15) and I^2 (0%) ($P < 0.05$) (Fig. 5). No bias was demonstrated in the funnel plot for publication bias assessment (Fig. 6), and the meta-regression conducted to assess geographic region as a possible confounding factor revealed an omnibus P-value of 0.342, which excluded region as a factor in the heterogeneity when comparing gender.

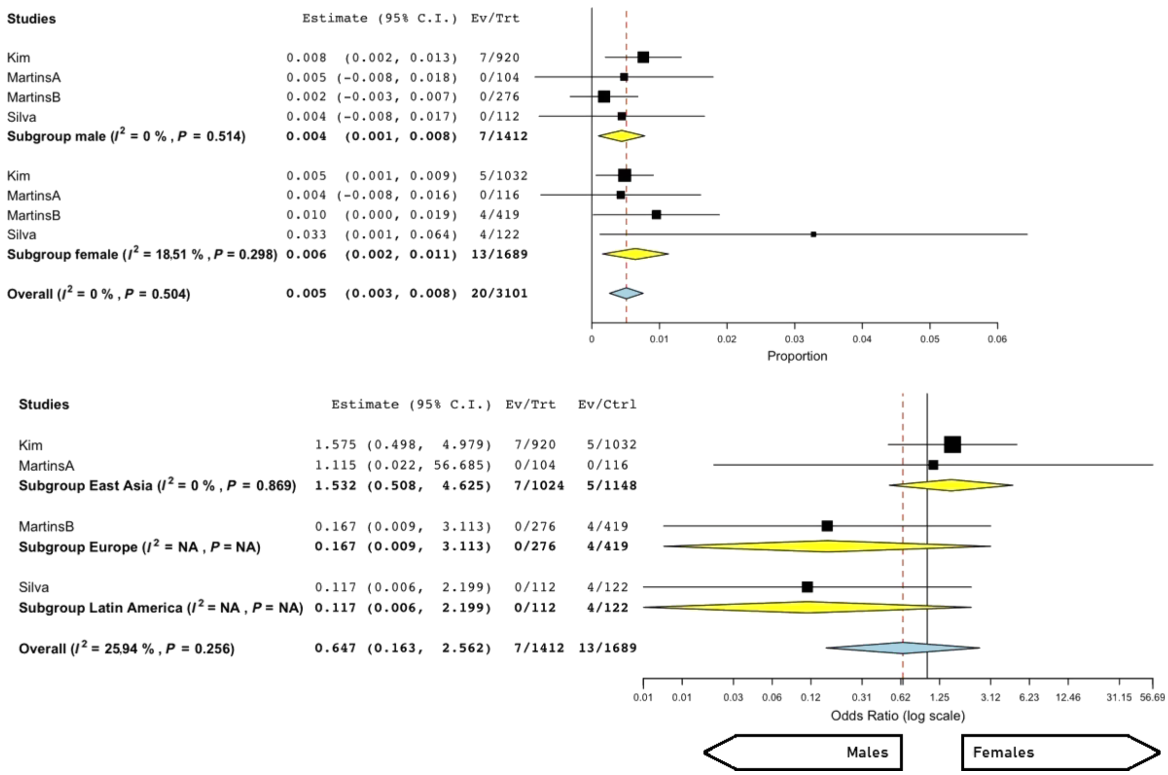

Figure 3 Forest plot for C-shaped prevalence comparison between genders in mandibular first molars. Proportions on the top and odds ratio on the bottom.

C-shaped canal and age

The influence of age on the prevalence of the C-shaped morphology in mandibular second molars was possible to assess in six studies (seven populations). However, because authors reported 38 different age intervals, the middle age value calculated to each one of these age intervals was used as a variable for meta-regression calculation.

Considering the average ages and geographic regions, the forest plot revealed a small decrease of the C-shaped configuration prevalence in every region as age increased. Even though it was also reflected in the age meta-regression chart (Fig. 7), the omnibus *P*-value (0.384) excluded age as a factor that could have influenced the heterogeneity of C-shaped morphology. In contrast, the meta-regression omnibus *P*-value of geographic region (<0.001) revealed it as an influencing factor of the heterogeneity of C-shaped morphology. Moreover, the age forest plot revealed a high heterogeneity value ($I^2 = 96.0\%$) which decreased to lower values (I^2: 0.0%, 16.3%, 22.7% and 77.6%) when splitting the overall age analysis into geographic region subgroups.

C-shaped canal and geographic region

Forest plot sub-grouped per geographic region revealed no significant difference in the prevalence of C-shaped canals in mandibular first molars ($P > 0.05$) (Fig. 8). On the other hand, the pooled proportion of C-shaped anatomy in mandibular second molars in East Asian countries (39.6%; 36.0–43.1%) was significantly higher than in Europe (8.9%), Africa (9.2%), Latin America (9.7%), West Asia (9.9%) and North America (11.3%) (Fig. 8) ($P < 0.05$). The meta-regression omnibus *P*-value was <0.001, confirming geographic region as a heterogeneity factor influencing the prevalence of C-shaped morphology.

Discussion

In the health field, demographic characteristics are widely accepted as factors that may impact on

Studies	Estimate (95% C.I.)	Ev/Trt
Kim	0.321 (0.290, 0.352)	283/882
Ladeira	0.120 (0.070, 0.171)	19/158
MartinsA	0.361 (0.271, 0.452)	39/108
MartinsB	0.040 (0.021, 0.059)	16/398
Pawar	0.108 (0.081, 0.136)	53/489
Shemesh	0.040 (0.025, 0.055)	26/647
Silva	0.021 (−0.008, 0.050)	2/94
von ZubenA	0.053 (0.019, 0.087)	9/169
von ZubenB	0.358 (0.290, 0.426)	68/190
von ZubenC	0.057 (0.021, 0.093)	9/159
von ZubenD	0.093 (0.057, 0.129)	23/248
von ZubenE	0.077 (0.031, 0.123)	10/130
von ZubenF	0.081 (0.041, 0.122)	14/172
von ZubenG	0.061 (0.026, 0.096)	11/181
von ZubenH	0.080 (0.038, 0.121)	13/163
Zheng	0.364 (0.309, 0.418)	108/297
Subgroup male (I^2 = 97,04 % , P = 0.000)	**0.135 (0.088, 0.183)**	**703/4485**
Kim	0.469 (0.439, 0.500)	487/1038
Ladeira	0.173 (0.126, 0.221)	43/248
MartinsA	0.492 (0.407, 0.578)	65/132
MartinsB	0.112 (0.088, 0.135)	77/690
Pawar	0.154 (0.122, 0.186)	76/494
Shemesh	0.051 (0.036, 0.066)	42/818
Silva	0.045 (0.010, 0.081)	6/132
von ZubenA	0.078 (0.043, 0.112)	18/231
von ZubenB	0.514 (0.447, 0.582)	108/210
von ZubenC	0.091 (0.055, 0.128)	22/241
von ZubenD	0.171 (0.111, 0.231)	26/152
von ZubenE	0.174 (0.129, 0.219)	47/270
von ZubenF	0.101 (0.062, 0.140)	23/228
von ZubenG	0.151 (0.103, 0.198)	33/219
von ZubenH	0.135 (0.092, 0.179)	32/237
Zheng	0.416 (0.352, 0.479)	96/231
Subgroup female (I^2 = 98,34 % , P = 0.000)	**0.205 (0.137, 0.274)**	**1201/5571**
Overall (I^2 = 97,92 % , P = 0.000)	**0.170 (0.130, 0.211)**	**1904/10056**

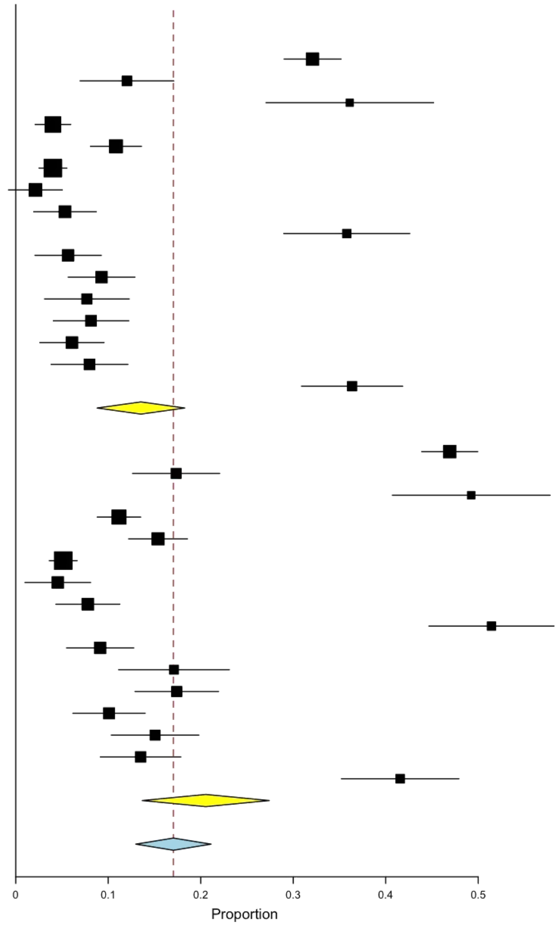

Figure 4 Proportion forest plot for C-shaped prevalence between genders in mandibular second molars.

prevalence outcomes for either anatomical traits (Guo *et al.* 2014, Verkicharla *et al.* 2017, Shao *et al.* 2018) or diseases (Vitalis *et al.* 2017). In dentistry, variations in tooth, root or root canal morphologies have also been strongly associated with ethnicity (Kato *et al.* 2014, Martins *et al.* 2018a). In this systematic review, prevalence outcomes of C-shaped canal morphology in maxillary and mandibular first and second premolars and molars were assessed. Results revealed this anatomic variant to be an uncommon canal configuration in maxillary molars (<4% in all studies) and mandibular first (between 1.1% and 10.9%) and second (up to 1.5%) premolars. Unfortunately, for these groups of teeth, meta-analysis calculations on the prevalence of C-shaped anatomy regarding gender, age or geographic factors were not accomplished considering the small number of studies selected after critical appraisal based on well-defined criteria. Notwithstanding, in some studies, a significantly higher prevalence of C-shaped morphology was reported in maxillary molars of females (Martins *et al.* 2016a) and mandibular premolars of males (Martins *et al.* 2017a). The prevalence of C-shaped canal morphology in mandibular premolars diagnosed by CBCT (Table 1) was much lower (0% to 10.9%) when compared to the proportion of 66.2% (Fan *et al.* 2012) and 67.5% (Ordinola-Zapata *et al.* 2015) reported in *ex vivo* studies using micro-CT technology. Such differences can be explained by the higher spatial resolution of the micro-CT scan, and because of specimen selection, the use of mandibular premolars with radicular grooves has been associated with a high incidence of C-shaped canal anatomy (Fan *et al.* 2012).

On the other hand, the influence of various demographic characteristics on the prevalence of C-shaped canal configuration in mandibular first and second molars was possible to assess by the meta-analysis of 5 and 12 anatomical studies, respectively. According

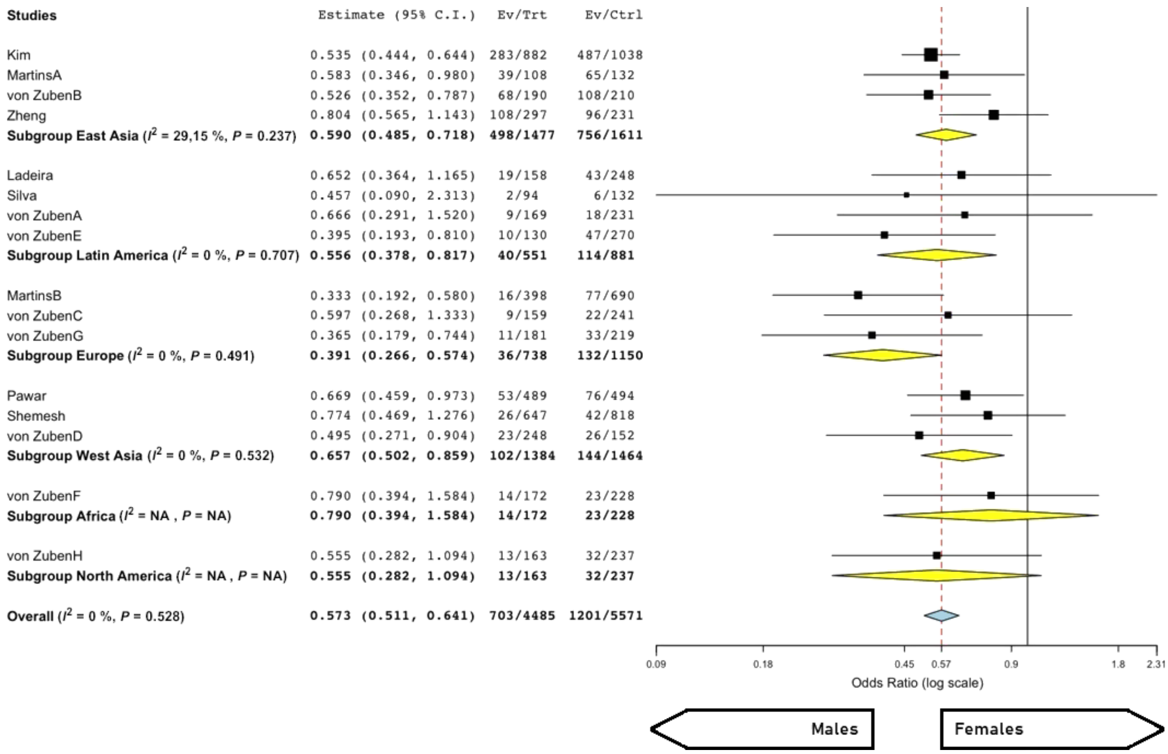

Figure 5 Odds ratio forest plot for C-shaped prevalence comparison between genders in mandibular second molars.

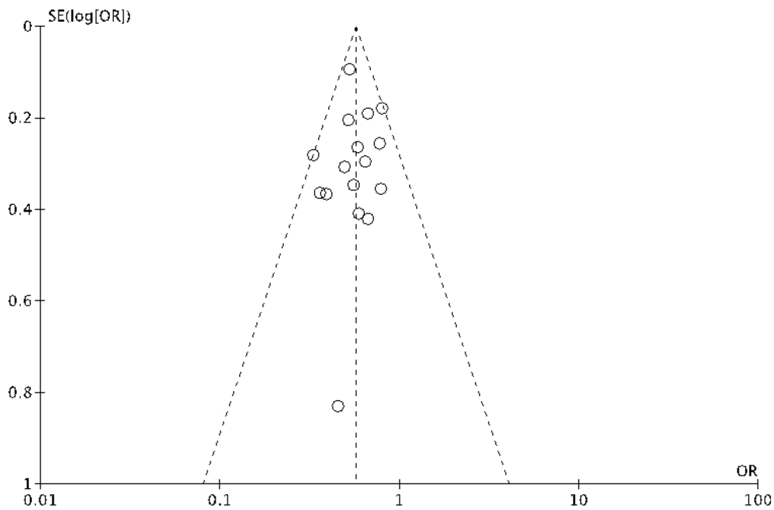

Figure 6 Funnel plot for assessment of publication bias on mandibular second molar studies.

to the meta-analysis of selected studies (Table 1, Figs 3 and 8), C-shaped canal configuration in mandibular first molars was not affected by gender, age or geographic regions. Consequently, the null hypotheses tested for this tooth group were accepted, although caution should be exercised regarding external validity of these results due to the small number of included studies.

Considering that in the mandibular second molar group a larger sample size could be analysed and the JBI score excluded studies with a high risk of bias, the funnel plot assessment could be performed, increasing

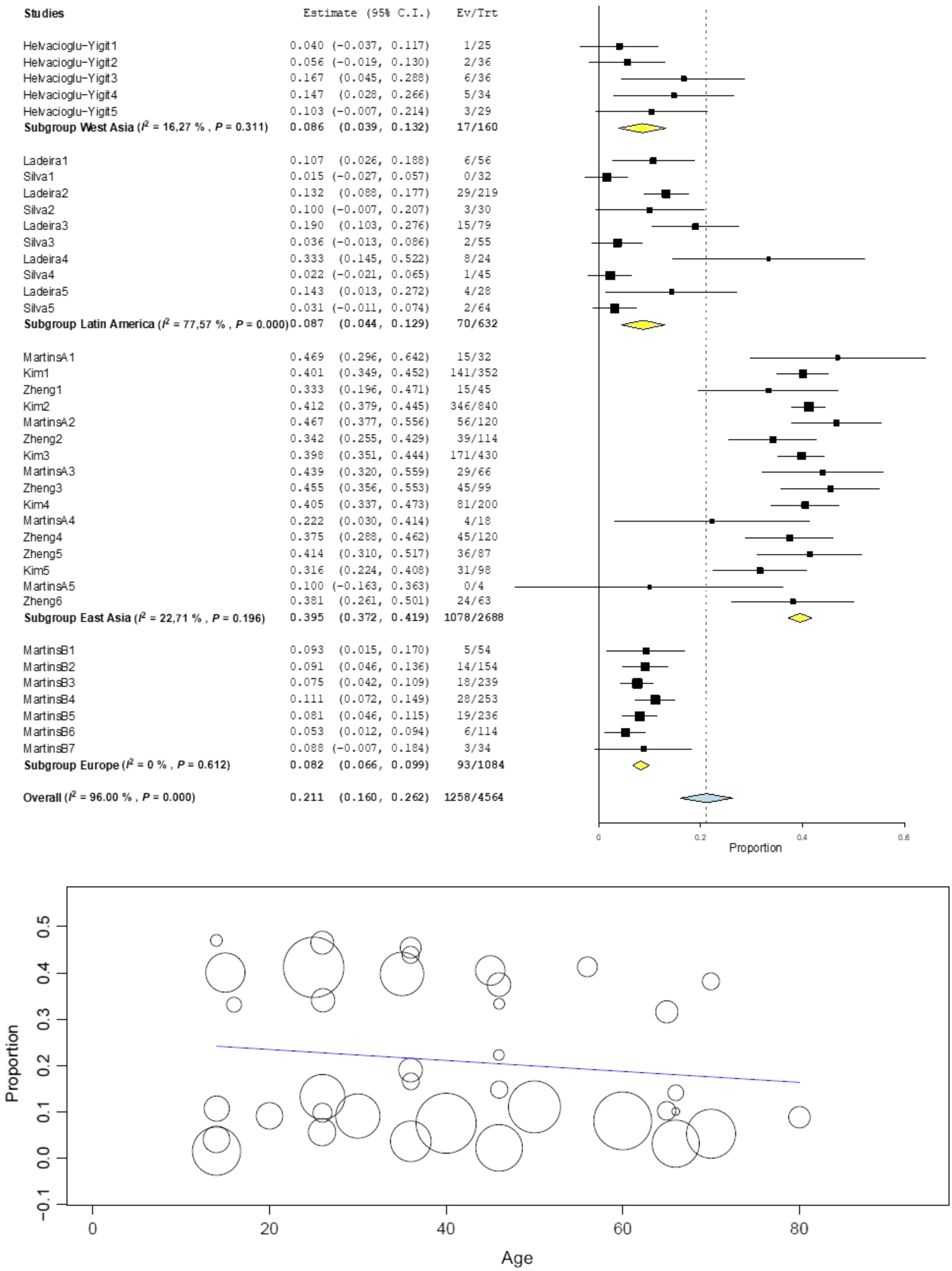

Figure 7 Meta-analysis calculations regarding the influence of ageing in the prevalence of the C-shape in mandibular second molars. Top: forest plot with studies ordered by age increase in different geographic regions, Bottom: age meta-regression.

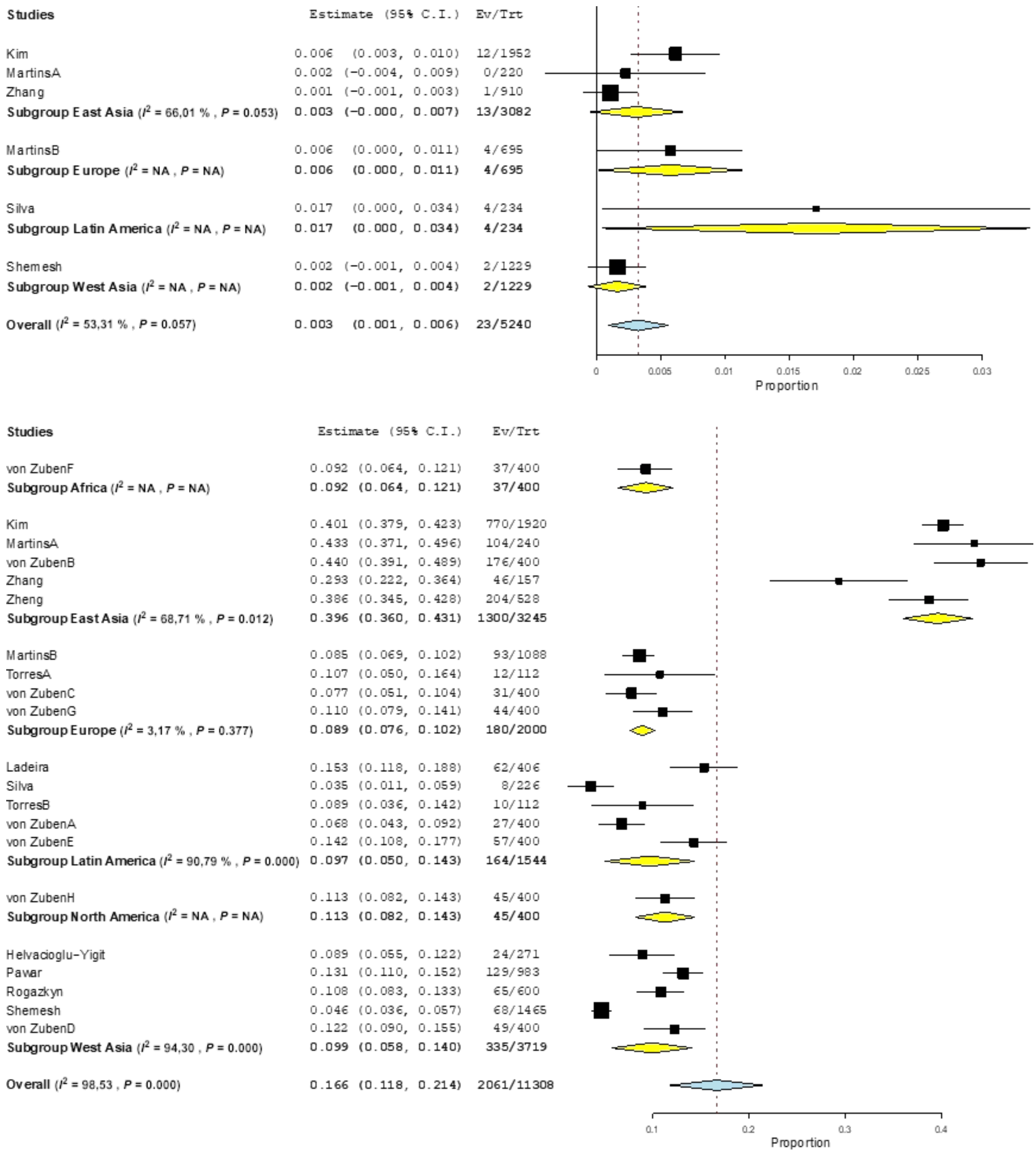

Figure 8 Forest plot for geographic regions. Top: mandibular first molar, Bottom: mandibular second molar.

the quality of the results. No significant difference regarding proportion of C-shaped morphologies between male (8.8–18.3%) and female (13.7–27.4%) was observed, but the high heterogeneity value (I^2) suggested that this result could be influenced by differences amongst geographic regions (Fig. 4). However, additional analysis detected a significant difference between gender with smaller odds for males, with no evident bias in the funnel plot (Fig. 6) and heterogeneity value of zero (Fig. 5), which means that the results were not influenced by the geographic region. Therefore, the second null hypothesis was rejected for this tooth.

Results from forest plot and meta-regression revealed an almost constant prevalence of C-shaped canals in the mandibular second molars over the years, with the meta-regression analysis excluding age as a possible confounding variable. Thus, the first null hypothesis for this tooth was accepted. The overall high heterogeneity of the age forest plot was clearly due to geographic region since the splitting in region decreased the heterogeneity value. However, differences in the age intervals reported in the studies hampered the analysis and the middle age value of each interval had to be calculated for meta-regression evaluation. Even though the middle interval value may not represent the average of the ages in a specific age interval, forest plot and meta-regression analysis confirmed that C-shaped canal prevalence remained constant over the years in this tooth (Fig. 7). Besides, the omnibus p-value excluded age as a heterogeneity source and the splitting of the age data amongst geographic regions decreased the I^2 value. Therefore, it may be inferred that geographic region might be the real heterogeneity source, not age. A further analysis of this factor identified East Asian countries with a significantly higher prevalence of C-shaped canals in mandibular second molars when compared to the other regions, and the third null hypothesis was also rejected for this tooth. Even though the results of this systematic review regarding the highest prevalence of C-shaped canals in mandibular second molars observed in the female gender and East Asian countries are supported by the literature (Zhang *et al.* 2011a, Zheng *et al.* 2011, Kim *et al.* 2016a, von Zuben *et al.* 2017, Martins *et al.* 2018a), proper explanations can only be found by tracing the genetic ancestry of human mankind 200 000 years ago (Hanihara 2013).

Currently, anthropological research indicates that the origin point of modern humans might be set in Nairobi, Kenya (Hanihara 2013). From there, world colonization is presumed to have occurred by two main pathways: the Levant corridor (the northern route), bordering the Mediterranean Sea, or the Horn of Africa (the southern route), along the Indian Ocean coastline. Then, pre-historic human dispersal out of Africa continued mostly to south-east and north-west directions, including Euroasia and Siberian routes (Hanihara 2013). This earlier pre-historic human migration has been considered the main reason for the different features observed amongst Caucasians (from Euroasia), Africans and Asians, since their evolutions were made independently from each other during world colonization (Hanihara 2013). Considering that human genome is the evolutionary result of genetic heritability and environment influences (Yaacob *et al.* 1996), and based on experimental evidences that size and shape of molar teeth might be changed by factors such as dietary modification, especially on mineral, vitamin or protein content on maternal diet (Potter *et al.* 1968), pre-historic colonization possibly submitted human species to environmental variability and shifting selection pressures (variability selection) (Mizoguchi 2013), which ultimately impacted the morphology of jaws and teeth. Somewhere along the way of the Asian expansion route, some type of body adaptation might have occurred due to the environment conditions leading those populations to develop a mandible bone morphology distinct from Caucasians in several anatomic landmarks, including its smaller size (Metzger *et al.* 2011). Therefore, based on the evidence that tooth phenotype is the sum of the effects of inherited genetics, developmental process, and interactions with neighbouring teeth and jaw (Yaacob *et al.* 1996), it may be suggested that fused roots on mandibular second molars, which is correlated with the presence of C-shaped canal morphology (Fan *et al.* 2004), can be seen as an adaptation to fit smaller sized teeth in smaller jaws. Interestingly, since human expansion to the American continent apparently was performed by a north route via Alaska by northern Asian populations (Hanihara 2013), a high prevalence of C-shaped canal morphology in American population would be expected, which is actually more likely than Caucasians and Africans. In fact, American populations have a strong influence of the migratory movement from European and African populations after the 16th century, which might have changed the local genome originally belonged to the American indigenous natives. Initially, before the 16th-century migratory movement, the genetic contribution from Euro-Americans might have been as low as 1% and 6% as reported for Papago and Pima American indigenous natives, respectively (Scott *et al.* 1983).

The hypothesis of a morphological genetic adaptation in the Asian populations to fit small-sized teeth into smaller jaws is also supported by several systematic studies reporting morphological differences between individuals of different gender in the same species (Karaman 2006, Macaluso 2011, Alvesalo 2013, Lakhanpal *et al.* 2013) and helped to enlighten the high prevalence of C-shaped canal morphology in mandibular second molars of females (20.5%; 13.7–27.4%) observed in this study.

One of the main strengths of the present review was the assessment of only epidemiological *in vivo* studies (cross-sectional studies), which tends to approach the present outcomes to the real clinical conditions. Considering that a rigorous quality assessment of studies being considered for inclusion is an essential part of the systematic review process, the critical appraisal performed herein examines the methodology of each study based on strictly pre-defined criteria independently by two evaluators taken into account the individual sources of risk of bias using the JBI assessment. The objective of this appraisal was to assess the methodological quality of each study and understand whether a possibility of bias exists in its study design, conduct and analysis. This approach allowed the identification and exclusion papers associated with high RoB (low JBI score), and aim for a higher homogeneity of the pooled studies and guaranteed the reliability and reproducibility of the methodology. However, the external validity of the present review should be interpreted with caution since the outcome could be directly associated with the demographic factors. According to the patient characteristics, the probability of presenting C-shaped morphology may vary which in turn could be a relevant preoperative information in clinical practice. In this review, all C-shape outcomes were investigated without excluding any participant. However, the outcomes on premolars and maxillary molars were not sufficient to be pooled in meta-analysis calculations due to the limited number of articles. A more robust analysis was performed for the mandibular molars, which are the group of teeth more prone to present this morphology, especially the second molars, which increase the relevance of the present outcomes.

In dentistry, CBCT imaging technology has been widely used to investigate root and root canal morphologies in various populations (Torres *et al.* 2015, von Zuben *et al.* 2017). CBCT has been validated by several authors as an accurate imaging technique for specific root canal anatomical variations based on micro-CT gold standard method (Vizzotto *et al.* 2013, Maret *et al.* 2014, Zhang *et al.* 2017a). Even though C-shaped morphology has never been previously validated using this same methodological approach, combination of root shape evaluation associated with an uncommonly larger root canal allowed this anatomy to be detected in a reliable manner using CBCT imaging, even when using larger voxel sizes (Torres *et al.* 2015, von Zuben *et al.* 2017). In the present study, however, a CBCT voxel size equal or lower than 250 μm was established as an inclusion criteria, based on the intra-rater reliability tests reported by von Zuben *et al.* (2017). Therefore, the limitations of this systematic review were mostly related to the small number of available studies, except for the mandibular second molar, which did not allow an analysis of the impact of demographic characteristics on the prevalence of C-shaped morphology in the other groups of teeth. Another limitation of this review is related to the impossibility to address the ethnic or racial variable, which seems to be related to the C-shape morphology prevalence (Jafarzadeh & Wu 2007). Except for one study (Martins *et al.* 2018a), which clearly stated that an effort was made to work with two specific ethnic groups, the other studies report the results from patients with available CBCT examinations in local health centres not clearly stating a specific ethnic group. For that reason, a geographic region variable was addressed instead of an ethnic variable. However, according to the Joanna Briggs Institute levels of evidence, systematic review of cross-sectional studies is categorized as Level 4a, which means a low level of evidence. This can be explained because in this type of review, it always expected some degree of heterogeneity amongst the pooled studies. At the same time, the number of included studies was reduced because of the strict inclusion criteria, which may influence the robustness of the outcomes.

A logical step for future research would be the development of guidelines for conducting cross-sectional studies on root canal anatomy using CBCT technology. For instance, the use of a study checklist would allow authors to provide readers with a more reliable and reproducible methodology, reducing the risk of bias. Taking into consideration the outcomes of the present review, a detailed description of the patients' demographic factors is recommended. Studies on unaddressed geographic regions, mainly countries with a low genetic variability such as some of Central and South America countries or indigenous populations in North America, South America or Oceania, would help to understand better how the roll of the human pre-historic migration and colonization interfered with the proportion and distribution of root canal morphologies observed nowadays.

Conclusions

C-shaped canal morphology is an uncommon anatomical finding in maxillary molars, mandibular premolars and mandibular first molars. This meta-analysis revealed that gender and geographic region may act as a confounding factor for the prevalence of the C-shaped anatomy in mandibular second molars, whilst age did not influence the prevalence of C-shaped configuration in this tooth group. The knowledge of these preoperative factors associated with a proper diagnostic tool would help clinicians to anticipate and treat this complex morphological variation of root canals in practice.

Conflict of interest

The authors have stated explicitly that there are no conflicts of interest in connection with this article.

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Table S1. Terms and filters used in each electronic database.

Table S2. Inclusion and exclusion criteria.

Table S3. List of the studies excluded from the review.

Table S4. Joanna Briggs Institute (JBI) Critical Appraisal tool for systematic reviews of prevalence studies questions.