CLINICAL RESEARCH

The Global Periapical Health Study: A Big Data CBCT Analysis of Periapical Pathology across 54 Countries

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ABSTRACT

Introduction: Periapical pathology, a common outcome of pulpal infection or failed endodontic therapy, remains underexplored globally. Most studies are small-scale and based on two-dimensional radiographs. This study aimed to provide a standardized worldwide estimate of its prevalence using cone-beam computed tomography (CBCT). **Methods:** A cross-sectional, multicenter study was conducted across 54 countries, each represented by one calibrated examiner. Examiners consecutively assessed 3,500 roots from pre-existing CBCT scans, yielding data from 189,000 roots (138,536 teeth) of 6,688 patients. A standardized protocol was applied using the CBCT periapical index to record lesion presence, tooth type, previous root canal treatment, and demographic variables. Only scans with voxel size $\leq$200 μm were included. Data were analyzed through meta-analysis and logistic regression model to evaluate factors associated with periapical pathology, with meta-regression assessing voxel size and field-of-view effects. **Results:** At the patient level, periapical pathology affected 58.6% of individuals worldwide. Secondary tooth-level analysis showed a prevalence of 7.3%, ranging from 2.5% in Oceania to 9.6% in Africa. Maxillary teeth (9.3%) were more frequently affected than mandibular teeth (5.3%), with maxillary first molars showing the highest prevalence (18.6%). Prevalence increased with age, from 2.9% ($\leq$20 years) to 10.5% ($\geq$61 years). Endodontically treated teeth showed markedly higher prevalence of post-treatment periapical radiolucencies (44.3%) than untreated teeth (2.6%) (odds ratio = 21.6; confidence interval 19.1-23.1; $P < .001$). Voxel size and field-of-view did not influence outcomes. **Conclusion:** Periapical pathology is highly prevalent worldwide, with notable regional and age-related differences. Endodontically treated teeth showed a disproportionately high prevalence of periapical pathology. *(J Endod 2026;■:1–21.)*

KEY WORDS

Cone-beam computed tomography; endodontics; epidemiology; periapical pathology; prevalence; root canal treatment

SIGNIFICANCE

This global CBCT study demonstrates that periapical pathology remains highly prevalent worldwide, affecting 58.6% of individuals, highlighting the importance of standardized follow-up protocols, appropriate surveillance strategies, and preventive approaches to support long-term periapical health.

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Periapical pathology is a common and often asymptomatic consequence of pulpal necrosis and infection, typically arising from untreated dental caries, trauma, or failed endodontic therapy[1]. Radiographically characterized by a periapical radiolucency, it represents a microbially driven inflammatory process within the periapical tissues. If undiagnosed or inadequately managed, these lesions may remain silent for long periods or progress to cause pain, infection, and systemic complications[2]. Beyond its significance in clinical practice, periapical pathology carries substantial psychological and economic impacts, often requiring root canal treatment, surgical intervention, or tooth extraction to eradicate infection and to restore oral health and quality of life[3].

Persistent periapical lesions are frequently associated with previously treated teeth[4,5], mainly due to missed anatomy, residual infection, or suboptimal obturation[6]. Consequently, accurate diagnosis and long-term radiographic monitoring are essential for appropriate clinical management and outcome evaluation. Traditionally, periapical assessment relied on two-dimensional radiography[5,7], which suffers from limitations such as anatomical superimposition and underestimation of lesion size. Cone-beam computed tomography (CBCT) has since become the gold standard for detecting and characterizing periapical pathology, owing to its superior spatial resolution and three-dimensional capability[8]. CBCT

enables the detection of lesions undetectable on conventional radiographs and provides more accurate evaluations of their size, extent, and relationship to surrounding structures[9,10].

Despite advances in diagnostic imaging, the global epidemiology of periapical pathology remains poorly characterized. Most existing data are derived from small, region-specific studies with heterogeneous methodologies and inconsistent diagnostic criteria[5]. Large-scale CBCT-based epidemiologic analyses are rare, primarily due to the high cost and variability of imaging protocols, which constrain our understanding of disease distribution and its underlying factors. The *Global Periapical Health Study (GPHS)* was therefore established as part of a series of investigations designed to evaluate the periapical status of teeth under different conditions using big data CBCT analysis. In this first GPHS study, a large-scale, multicenter assessment was performed using pre-existing CBCT datasets from 54 countries across 5 continents. Through a standardized diagnostic protocol, unified training materials, and centralized coordination, this big-data framework ensured methodological consistency while generating a robust and globally representative epidemiological profile of periapical pathology.

MATERIAL AND METHODS

Research Protocol

The study protocol was approved by the Local Ethics Committee (Registration No. CE-FMDUL 202429) and followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines[11] for cross-sectional studies.

Study Outcomes and Sample Size Calculation

Data were obtained from existing CBCT datasets in accordance with the AAE/AAOMR joint position statement[12]. No additional scans were acquired, and patient identifiers were not accessed. Fifty-four field examiners from 54 countries across 5 continents (Table 1) evaluated the prevalence of periapical pathology (primary outcome) in all tooth groups. Each examiner received identical written instructions describing the study objectives, inclusion and exclusion criteria, definitions of periapical pathology, CBCT evaluation protocol, data recording procedures, timelines, and representative sagittal CBCT images. The same documentation and Ethics Committee correspondence were shared with all participants. A tutorial video demonstrating the 3D assessment protocol was distributed simultaneously to ensure methodological consistency. Questions and clarifications were shared openly with the entire group. All materials were prepared by the study coordinator (J.M.) and reviewed by 2 independent experts who did not participate as observers (M.A.V. and E.S.) before distribution and Ethics Committee submission, ensuring calibration of all examiners. Primary analyses were conducted at the tooth level. During a pilot phase, data were collected at the root level to standardize numbering and scoring. Based on 200 roots from the 54 regions, sample size was calculated using the 2 regions with the largest difference in primary outcomes (Italy vs Latvia). Assuming a 95% confidence level, 80% power, and an effect size of 24.5% for overall periapical pathology prevalence, a minimum of 36 roots was required (G*Power 3.1; Heinrich Heine University, Dusseldorf, Germany). To strengthen statistical power and enable inter-regional comparisons, the final target was increased to 3,500 roots per region, ensuring robust analyses at both root and tooth levels.

Data Collection and Screening Process

A convenience sample of patients attending health centers in the participating regions was included to ensure adequate population representation. One examiner was assigned per region. Different CBCT units were permitted, provided the voxel size was $\leq$ 200 μm. The field of view (FOV) could be large, medium, or obtained from stitched scans, provided that at least one complete dental arch was captured. Third molars were not required, and focused or restricted FOVs were excluded to avoid bias from scans acquired solely for endodontic purposes.

Each examiner consecutively analyzed pre-existing CBCT scans in alphabetical or numerical order until 3,500 roots had been assessed. Teeth were excluded if they were third molars, exhibited severe resorption, were root stumps or impacted, belonged to the primary dentition, presented numbering uncertainty, lacked demographic information, or showed image artefacts compromising interpretation. Exclusion counts and reasons per region are presented in Table 1. Tooth axes were aligned with the software reference planes in three dimensions before interpretation in coronal, sagittal, and axial views. Observers were allowed to adjust visualization parameters, including filters and noise-reduction tools, to optimize image quality. For each tooth, the following data were recorded: Universal tooth number, identification of individual roots (molars only), presence of fused roots (molars only), history of root canal treatment, and periapical status according to the CBCT periapical index[13]. In this index, a score 0 represents intact periapical bone (absence of pathology), while scores 1–5 indicate a periapical radiolucency exceeding 0.5 mm (presence of pathology).

Root identification was restricted to molars. In maxillary molars, the mesiobuccal, distobuccal, palatal, and any additional roots were scored. In mandibular molars, mesial, distal, and additional roots were scored. Root fusion was also documented: in maxillary molars, fused roots were recorded as such, and any remaining root was scored separately; in mandibular molars, fusion of both primary roots was recorded as a single fused root. When root canal treatment was present, it was recorded at both the tooth and root levels. Periapical pathology was assessed per root and considered present at the tooth level if any root exhibited pathology (worst-case scenario).

Demographic variables (sex and age) were also recorded. Ethnic group reflecting the population served by the health unit rather than the patient's country of origin was documented for group characterization. In cases of uncertainty, observers consulted the study coordinator until consensus was achieved. To minimize bias, all observers were blinded to the results of other participants. Data were entered into a standardized Excel spreadsheet (Microsoft Office v15.0.5537, Redmond, WA, USA) distributed simultaneously to all examiners. The template allowed cross-checking of critical variables and direct export to statistical software. Any inconsistencies were returned to regional examiners for correction. Results of data-quality checks are presented in Supplemental Tables S1 and S2. Two independent nonobserver experts monitored examiner progress, ensured adherence to the protocol, and verified that data collection proceeded uniformly across all regions.

Reliability Measurements

Three reliability analyses were performed for each variable at both the individual and group levels. Before final data collection, intra- and inter-rater reliability were evaluated. For intra-rater reliability, each examiner re-evaluated the same regional dataset after 1 month. A total of 200 roots (5.7% of the sample) were assessed twice for the presence of periapical pathology (primary outcome) and previous root canal treatment. Agreement within examiners was quantified using Cohen's kappa. For inter-rater reliability, all 54

TABLE 1 - Summary of Regional Data: Geographic Location, CBCT Scanner Specifications, Imaging Parameters and Characteristics, and Dates of Imaging Assessments

Country	City	Continent	Field observer	CBCT model (Brand, City, Country)	Visualization software (Brand)	CBCT FOV	CBCT settings (μm, kV, mA)	Excluded CBCT images (reasons)	Date of CBCT assessment
Argentina	Salta	Americas	P.E.	CS 9600 (Carestream, Atlanta, USA)	CS 3D Imaging (Carestream)	M, L	75, 60-80, 2-15	142 (impaction, resorptions, root stumps, third molars)	Aug 2024 to Nov 2024
Armenia	Yerevan	Asia	N.H.	Promax 3D (Planmeca, Helsinki, Finland)	Romexis (Planmeca)	M	200, 90, 8-10	2 (artifacts)	Aug 2024 to Mar 2025
Australia	Melbourne	Oceania	F.C.	Accuitomo 80 (Morita, Kyoto, Japan)	InteleViewer (InteleRad, Montreal, Canada)	M, L	125-160, 86-90, 6-8	4 (artifacts, root stumps, unclassifiable tooth)	Aug 2024 to Dec 2024
Azerbaijan	Baku	Asia	N.B.	Promax 3D (Planmeca, Helsinki, Finland)	Romexis (Planmeca)	L	200, 90, 6	15 (root stumps/ trauma)	Aug 2024 to Mar 2025
Brazil	Campinas	Americas	L.B.	i-CAT FLX (i-CAT, Hatfield, England)	i-CAT Vision (i-CAT)	L	200, 90, 5	—	Aug 2024 to Mar 2025
Chile	Santiago do Chile	Americas	M.Ri.	CS 8100 (Carestream, Atlanta, USA)	CS 3D Imaging (Carestream)	M, St	150, 82, 5	23 (artifacts, root stumps)	Aug 2024 to Feb 2025
China	Suzhou	Asia	Y.G.	Kavo 3D eXam (Kavo Sybron, Munich, Germany)	eXam vision (Kavo)	L	125-200, 120, 3	—	Aug 2024 to Dec 2024
Colombia	Bogota	Americas	C.E.	Promax 3D (Planmeca, Helsinki, Finland)	Romexis (Planmeca)	M	150-200, 90, 3	20 (artifacts)	Aug 2024 to Mar 2025
Dominican Republic	Santo Domingo	Americas	S.G.	Promax 3D (Planmeca, Helsinki, Finland)	Romexis (Planmeca)	M, L	150, 110, 8	—	Aug 2024 to Mar 2025
Ecuador	Quito	Americas	J.C.	Newtom Giano (Newtom, Verona, Italy)	NNT (Newtom)	M, L	150, 110, 3	55 (artifacts)	Aug 2024 to Mar 2025
Egypt	Cairo	Africa	M.B.A.	Promax 3D (Planmeca, Helsinki, Finland)	Romexis (Planmeca)	L	150-200, 88, 11	—	Aug 2024 to Apr 2025

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TABLE 1 - Continued

Country	City	Continent	Field observer	CBCT model (Brand, City, Country)	Visualization software (Brand)	CBCT FOV	CBCT settings (μm, kV, mA)	Excluded CBCT images (reasons)	Date of CBCT assessment
England	London	Europe	T.P.	CS 8100 (Carestream, Atlanta, USA)	CS 3D Imaging (Carestream)	M/L	150, 90, 3-6	14 (artifacts)	Aug 2024 to Mar 2025
Estonia	Tallinn	Europe	A.E.	CS 8100 (Carestream, Atlanta, USA)	CS 3D Imaging (Carestream)	M	75, 60-90, 2-15	—	Aug 2024 to Mar 2025
Finland	Lappeenranta, Lahti, Kouvola	Europe	W.J.	Promax 3D (Planmeca, Helsinki, Finland)	Romexis (Planmeca)	M	75, 90, 6	3 (artifacts)	Aug 2024 to May 2025
Georgia	Tbilisi	Asia	T.N.	Orthophos XG (Dentsply, Ballaigues, Switzerland)	Sidexis (Dentsply)	M	160, 90, 12	—	Aug 2024 to Apr 2025
Greece	Kalithea	Europe	A.C.	Newtom VGI (Newtom, Verona, Italy)	NNT (Newtom)	L	150, 110, 8	—	Aug 2024 to Mar 2025
Hungary	Budapest	Europe	G.B.	Promax 3D (Planmeca, Helsinki, Finland) CS 8200 3D (Carestream, Atlanta, USA) Vatech Green X (Vatech, Gyeonggi-do, Korea)	Romexis (Planmeca) CS 3D Imaging (Carestream) Vatech MAR (Vatech)	L	200, 84, 15 200, 60-90, 2-15 200, 6-99, 4-16	—	Aug 2024 to Apr 2025
Iceland	Hafnarfjördur	Europe	M.Ra.	i-CAT FLX (i-CAT, Hatfield, England)	i-CAT Vision (i-CAT)	L	200, 120, 4	5 (artifacts)	Aug 2024 to Feb 2025
India	Palakkad	Asia	J.K.	Newtom Giano (Newtom, Verona, Italy)	NNT (Newtom)	M/L	150, 90, 4-9	142 (artifacts, impaction, root stumps, third molars)	Aug 2024 to Apr 2025
Iran	Tehran	Asia	M.Ne.	Promax 3D (Planmeca, Helsinki, Finland)	Romexis (Planmeca)	M	160, 70, 4	—	Aug 2024 to Mar 2025

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TABLE 1 - Continued

Country	City	Continent	Field observer	CBCT model (Brand, City, Country)	Visualization software (Brand)	CBCT FOV	CBCT settings (μm, kV, mA)	Excluded CBCT images (reasons)	Date of CBCT assessment
Ireland	Dublin	Europe	N.G.	CS 8100 3D (Carestream, Atlanta, USA)	CS 3D Imaging (Carestream)	St	75, 90, 15	—	Aug 2024 to Feb 2025
Israel	Ramat Gan	Asia	A.S.	Alioth (Asahi Roentgen, Kyoto, Japan)	RadiAnt Dicom Viewer (Medixant, Pozlan, Poland)	L	155, 85, 6	31 (artifacts)	Aug 2024 to Apr 2025
Italy	Rome	Europe	R.C.	Accuitomo 170 (Morita, Kyoto, Japan)	i-Dixel (Morita)	M, St	200, 88, 8	—	Aug 2024 to Mar 2025
Jamaica	Kingston	Americas	S.T.	OP 300 (Kavo, Charlotte, USA)	Invivo (Anatomage, Santa Clara, USA)	L	85, 57-90, 4-16	—	Aug 2024 to Dec 2024
Japan	Tokyo	Asia	S.M.	Accuitomo F17 (Morita, Kyoto, Japan)	Infinitt Pacs (Infinitt Medical, Phillipsburg, USA)	M	100, 90, 6	2 (artifacts)	Aug 2024 to Mar 2025
Jordan	Amman	Asia	M.H.	X Mind (Acteon, Merignac, France)	X Mind Trium (Acteon)	L	80, 90, 10	—	Aug 2024 to Mar 2025
Kazakhstan	Astana	Asia	M.O.	Promax 3D (Planmeca, Helsinki, Finland)	Romexis (Planmeca)	L	200, 90, 6	—	Aug 2024 to Apr 2025
Kuwait	Salmiya	Asia	H.O.	Promax 3D (Planmeca, Helsinki, Finland)	Romexis (Planmeca)	M	150, 90, 10	—	Aug 2024 to Dec 2024
Kyrgyzstan	Bishkek	Asia	A.Ma.	Promax 3D (Planmeca, Helsinki, Finland)	Romexis (Planmeca)	M	150, 90, 8	2 (artifacts)	Aug 2024 to Feb 2025
Latvia	Riga	Europe	M.S.	X800 (Morita, Kyoto, Japan)	i-Dixel (Morita)	St	125, 60-100, 2-10	1 (artifacts)	Aug 2024 to Apr 2025
Lebanon	Beirut	Asia	A.Kh.	CS 9000 (Carestream, Atlanta, USA)	CS 3D Imaging (Carestream)	M	200, 90, 7	—	Aug 2024 to Jan 2025
Malaysia	Kuala Lumpur	Asia	A.P.	Promax 3D (Planmeca, Helsinki, Finland)	Romexis (Planmeca)	L	200, 60-120, 1-4	—	Aug 2024 to Jan 2025

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TABLE 1 - Continued

Country	City	Continent	Field observer	CBCT model (Brand, City, Country)	Visualization software (Brand)	CBCT FOV	CBCT settings (μm, kV, mA)	Excluded CBCT images (reasons)	Date of CBCT assessment
Mexico	León	Americas	R.R.A.	OP 300 (Kavo, Charlotte, USA)	OnDemand 3D (Kavo)	M	200, 90, 8	—	Aug 2024 to May 2025
New Zealand	Hastings	Oceania	I.C.	Orthophos SL (Dentsply, Ballaigues, Switzerland)	Sidexis (Dentsply)	L	80, 85, 6	2 (artifacts)	Aug 2024 to Jan 2025
Nigeria	Lagos	Africa	O.O.	CS 8100 (Carestream, Atlanta, USA)	CS 3D Imaging (Carestream)	St	150, 90, 3	60 (artifacts, no demographic data, root stumps)	Aug 2024 to Mar 2025
Pakistan	Karachi	Asia	M.Na.	Promax 3D (Planmeca, Helsinki, Finland) CS 9600 (Carestream, Atlanta, USA)	Romexis (Planmeca) CS 3D Imaging (Carestream)	L	180-200, 85-90, 4-6	19 (artifacts)	Aug 2024 to Apr 2025
Paraguay	Asunción	Americas	C.H.	Evo 3D (Villa Sistemi Medicali, Milan, Italy) Imax 3D (Owandy, Beaubourg, France)	CS 3D Imaging (Carestream)	M	170, 82-84, 5-10	4 (artifacts)	Aug 2024 to Mar 2025
Peru	Lima	Americas	C.N.	OP 300 (Kavo, Charlotte, USA)	OnDemand 3D (Kavo)	L	200, 57-90, 4-16	12 (artifacts, unclear anatomy)	Aug 2024 to Mar 2025
Poland	Wroclaw	Europe	B.K.	CS 8200 (Carestream, Atlanta, USA)	CS 3D Imaging (Carestream)	M, L	75-150, 90, 4	—	Aug 2024 to Mar 2025
Portugal	Lisbon	Europe	J.M.	Promax 3D (Planmeca, Helsinki, Finland)	Romexis (Planmeca)	L	200, 84, 15	34 (artifacts, root stumps, unclassifiable tooth)	Aug 2024 to Dec 2024
Romania	Bucharest	Europe	S.N.	Promax 3D (Planmeca, Helsinki, Finland)	Romexis (Planmeca)	M	160-200, 87-90, 5-8	—	Aug 2024 to Apr 2025

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TABLE 1 - Continued

Country	City	Continent	Field observer	CBCT model (Brand, City, Country)	Visualization software (Brand)	CBCT FOV	CBCT settings (μm, kV, mA)	Excluded CBCT images (reasons)	Date of CBCT assessment
Russia	Yekaterinburg	Asia	E.L.	CB 500 (Gendex, Hatfield, England)	i-CAT Vision (i-CAT)	M/L	200, 120, 3-8	22 (artifacts, unclear anatomy)	Aug 2024 to Jan 2025
Saudi Arabia	Riyadh	Asia	H.A.	Promax 3D (Planmeca, Helsinki, Finland)	Romexis (Planmeca)	M	200, 60-90, 14	52 (artifacts, low image quality)	Aug 2024 to Apr 2025
South Africa	Durban	Africa	H.S.	CS 8100 (Carestream, Atlanta, USA)	CS 3D Imaging (Carestream)	M	150, 90, 3	—	Aug 2024 to Apr 2025
South Korea	Seoul	Asia	S.C.	Alphard 300 (Asahi Roentgen Ind, Kyoto, Japan)	Zetta PACS Viewer (Asahi)	L	200, 60-100, 2-15	—	Aug 2024 to May 2025
Spain	Barcelona	Europe	J.G.	CS 8100 (Carestream, Atlanta, USA) Promax 3D (Planmeca, Helsinki, Finland)	CS 3D Imaging (Carestream) Romexis (Planmeca)	L	150-200, 90, 3-6	—	Aug 2024 to Mar 2025
Switzerland	Bern	Europe	T.W.	3D Accuitomo (Morita, Kyoto, Japan)	i-Dixel (Morita)	M	125, 85, 4	3 (artifacts)	Aug 2024 to Apr 2025
Syria	Damascus	Asia	Z.A.	Viso G5 (Planmeca, Helsinki, Finland)	Romexis (Planmeca)	L	200, 60-120, 1-16	—	Aug 2024 to Mar 2025
Thailand	Bangkok	Asia	R.A.	3D Accuitomo (Morita, Kyoto, Japan)	OneVolumeViewer (Morita)	M	160, 90, 5	—	Sep 2024 to Mar 2025
Turkey	Bolu	Europe	A.Ke.	5 G XL (Newtom, Verona, Italy)	NNT (Newtom)	M/L	150-200, 110, 3-5	29 (artifacts, resorption, unclear anatomy)	Aug 2024 to Feb 2025
Uruguay	Montevideo	Americas	I.M.	Orthophos XG (Dentsply, Ballaigues, Switzerland)	CS 3D Imaging (Carestream)	L	75, 85, 6	6 (artifacts)	Aug 2024 to Feb 2025

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TABLE 1 - Continued

Country	City	Continent	Field observer	CBCT model (Brand, City, Country)	Visualization software (Brand)	CBCT FOV	CBCT settings (μm, kV, mA)	Excluded CBCT images (reasons)	Date of CBCT assessment
USA	Vista	Americas	A.Mo.	Dexis OP 3D (Dexis, Quakertown, USA)	DTX Studio (Dexis)	L	100, 80-90, 14-16	—	Aug 2024 to Mar 2025
Uzbekistan	Tashkent	Asia	S.R.	3D Accuitomo (Morita, Kyoto, Japan)	OneVolumeViewer (Morita)	M	80, 100, 8	—	Aug 2024 to Mar 2025
Venezuela	Caracas	Americas	C.B.	CS 9300 (Carestream, Atlanta, USA)	CS 3D Imaging (Carestream)	M, L	180, 60-90, 2-15	23 (artifacts, resorptions, root stumps, unclear anatomy)	Aug 2024 to Mar 2025

CBCT, cone-beam computed tomography; FOV, field of view; L, large FOV; M, medium FOV; St, Stitched FOV.

examiners assessed the same 161 roots obtained from 6 CBCT scans excluded from the regional datasets. The same parameters were evaluated, and overall agreement was determined using the intraclass correlation coefficient. Each examiner's results were also compared with a consensus classification established by 2 independent experts (E.J.N.L.S. and M.Sol.), and the percentage of agreement was calculated. A minimum threshold of 0.61 (substantial agreement) was required for both Cohen's kappa and the intraclass correlation coefficient. Examiners not meeting this criterion were instructed to review the protocol and repeat the evaluation. All reliability testing followed the standardized CBCT screening protocol and was conducted concurrently by all examiners.

Statistical Analysis

Given the multicenter design, data were analyzed using a random-effects meta-analysis model (OpenMeta[Analyst], version 10.10; www.cebm.brown.edu/openmeta). The primary outcome was stablished as the presence of periapical pathology at patient-level. The teeth-level secondary outcome (presence of periapical pathology) was assessed across groups and subgroups defined by tooth category, age, sex, geographical region, and history of root canal treatment. Results were expressed as raw proportions and, when appropriate, as untransformed proportions with 95% confidence interval forest plots. Meta-regression was used to explore potential heterogeneity related to voxel size and FOV. Statistical significance was set at $P < .05$. To account for intra-patient correlations with predictors, a logistic regression model that include patient identification as a cluster (General Estimating Equations, GEE; SPSS for Windows, version 24.0) was applied. Predictors included prior root canal treatment (yes/no), sex, age group, world region (Americas, South Asia & Middle East, Oceania, Asia, Africa, and Europe), and tooth/root category. Odds ratios were calculated and reported when significant. Model validity was confirmed by the Omnibus Test of Model Coefficients ($P < .05$) and good fit by the Hosmer–Lemeshow test ($P > .05$).

RESULTS

Assessment and Data Scoring

Reliability

Intra-rater reliability showed substantial to almost perfect agreement for both periapical pathology ($\kappa = 0.654–1.000$; Supplemental Table S1) and previous root canal treatment ($\kappa = 0.694–1.000$; Supplemental Table S2).

Inter-rater reliability was nearly perfect, with coefficients of 0.988 and 0.999, respectively. Agreement with external observers ranged from 84.47% to 98.76% for periapical pathology and from 96.27% to 100% for root canal treatment. Datasheet inconsistencies were minimal, ranging from 0% to 0.43% and 0% to 3.57% (Supplemental Tables S1 and S2).

Patient-level Prevalence of Periapical Pathology

A total of 189,000 roots representing 138,536 teeth were assessed: 46.8% anterior, 28.0% premolars, and 25.2% molars. Data referred to 6,688 patients (41.7% male, 58.3% female; mean age, 45 ± 17 years; Table 2). The overall prevalence of periapical pathology at the patient level was 58.6%, ranging from 10.6% in Italy to 100% in Uzbekistan (Fig. 1).

Teeth-level Prevalence of Periapical Pathology

At the tooth level, the global prevalence was 7.3% (6.3%–8.4%), ranging from 0.5% (0.2%–0.8%) in Jamaica to 19.3% (17.7%–20.9%) in Uzbekistan (Fig. 2; Supplemental Fig. S1). Maxillary teeth showed higher prevalence than mandibular teeth (9.3% vs 5.3%). Outcomes for all 54 regions are presented in Supplemental Tables S3–S56.

Tooth and Root Assessments

Among tooth groups, mandibular canines showed the lowest prevalence of periapical pathology (2.0%), whereas maxillary first molars exhibited the highest (18.6%) (Tables 3 and 4). The logistic regression model identified several teeth with a significantly lower odds of apical periodontitis (AP).

The greatest reduction in the likelihood of AP was observed for the mandibular canines (tooth 27: 79.0% reduced odds, odds ratio (OR) = 0.22; 95% confidence interval (CI): 0.07–0.70; $P = .01$; and tooth 22: 78.3%, OR = 0.21; 95% CI: 0.07–0.70; $P = .009$), followed by the mandibular first premolars (tooth 28: 78.4%, OR = 0.22; 95% CI: 0.07–0.70; $P = .01$; and tooth 21: 69.8%, OR = 0.31; 95% CI: 0.09–0.97; $P = .045$), maxillary canines (tooth 6: 73.7%, OR = 0.27; 95% CI: 0.09–0.86; $P = .026$; and tooth 11: 70.4%, OR = 0.30; 95% CI: 0.10–0.95; $P = .041$), mandibular second premolars (tooth 20: 71.5%, OR = 0.29; 95% CI: 0.09–0.92; $P = .035$; and tooth 29: 69.0%, OR = 0.32; 95% CI: 0.10–0.99; $P = .049$) and mandibular lateral incisors (tooth 26: 71.7%, OR = 0.30; 95% CI: 0.09–0.95; $P = .040$; and tooth 23: 70.7%, OR = 0.29; 95% CI: 0.09–0.918; $P = .035$).

Among molar roots, the mesiobuccal roots of maxillary molars showed the highest prevalence of AP, with the mesiobuccal root of the maxillary first molar reaching 16.3%. In mandibular molars, mesial roots exhibited higher prevalence than distal roots (Table 5). Additional roots generally showed lower prevalence than other roots of the same tooth, whereas fused roots presented rates of 10.7% and 13.8% in maxillary second and first molars, respectively, and ≤7.8% in mandibular molars (Table 5).

Geographic Region

The meta-analysis revealed a significantly lower prevalence of periapical pathology in Oceania (2.5% [2.0%–4.0%], $P < .05$) compared with all other regions, which showed no significant differences among themselves ($P > .05$). Africa had the highest prevalence (9.6% [6.5%–12.7%]) (Supplemental Fig. S1). The logistic regression confirmed a protective effect for Oceania, with a 34% lower likelihood of periapical pathology (OR = 0.66; 95% CI: 0.52–0.84; $P = .001$), whereas Africa showed 1.52-fold higher odds (OR = 1.52; 95% CI: 1.24–1.86; $P < .001$). Asia also demonstrated a modestly increased odds (OR = 1.36; 95% CI: 1.19–1.55; $P < .001$).

Sex and Age

The meta-analysis found no significant difference in periapical pathology prevalence between sexes ($P > .05$) (Supplemental Fig. S2). Prevalence was 7.5% (6.5%–8.6%) in males and 7.2% (6.1%–8.2%) in females. However, the logistic regression indicated that males had 1.22-fold higher odds of periapical pathology worldwide (OR = 1.22; 95% CI: 1.12–1.32; $P < .001$). The age-group analysis revealed significant differences across all categories ($P < .05$) (Fig. 3). The lowest prevalence occurred in patients ≤20 years (2.9% [2.5%–3.2%]), increasing progressively to 10.5% (10.1%–10.9%) in those ≥61 years. However, regression analysis showed no statistically significant association between age group and apical periodontitis (all $P > .05$), with odds ratios ranging from 0.90 (95% CI: 0.72–1.12) to 1.11 (95% CI: 0.99–1.23).

Previous Root Canal Treatment and Post-treatment Periapical Radiolucencies

The forest plots showed a significantly higher prevalence of post-treatment periapical radiolucencies in teeth with previous root canal treatment (44.3% [40.2%–48.4%]) compared with untreated teeth (2.6% [2.2%–2.9%]; $P < .05$) (Supplemental Fig. S3). These findings reflect a single time point, as no information was available regarding the time elapsed since root canal treatment or the stage of periapical healing. The GEE logistic regression confirmed this association, indicating 22-fold higher odds of periapical pathology in endodontically treated teeth (OR = 21.6; 95% CI: 19.1–23.1; $P = .001$).

Voxel Size and FOV

Meta-regression analysis showed that neither voxel size nor FOV significantly influenced the results (omnibus $P = .745$ and .082, respectively) (Supplemental Fig. S4)

DISCUSSION

The digitization of health care has initiated the era of big data, marked by vast, heterogeneous information drawn from clinical practice, ranging from imaging and electronic health records to laboratory diagnostics and patient registries[14]. In dentistry, and particularly in endodontics, the routine use of advanced imaging techniques such as CBCT generates large datasets with unprecedented diagnostic precision and anatomical detail[8]. Beyond simple volume, the value of big data lies in its capacity to integrate and analyze information at a scale that transcends the limitations of traditional, small-sample studies[15,16]. This first GPHS study used this potential by analyzing 189,000 roots from 54 countries under a standardized CBCT protocol, exemplifying the application of real-world data, that is information collected in everyday clinical settings rather than controlled trial environments. Although randomized controlled trials remain essential for establishing efficacy, they often sacrifice external validity for control. In contrast, big data and real-world evidence expand the evidence base by providing globally relevant insights that reflect clinical reality across diverse patient populations, health care access, and regional practices[17-19]. This perspective not only supports more effective and equitable approaches to diagnosis, treatment, and long-term endodontic care but also increasingly guides clinical decisions, institutional protocols, and public health policies.

Global organizations, including the World Health Organization[20], recognize real-world evidence as a critical tool for assessing treatment effectiveness, surveillance, and health system planning. Particularly where large-scale or long-term controlled trials are impractical, real-world evidence provides practical insights grounded in authentic clinical experience, complementing traditional

TABLE 2 - Demographic Information of Patients and Characteristics of the Evaluated Tooth Samples

	Demographics					Overall sample characteristics					
Region	Sample size (patients)	Ethnic groups*	Age in y (mean ± SD) [range]	Proportion of males	Proportion of females	Sample size (teeth/ roots)	Anterior teeth	Premolar teeth	Molar teeth	Maxillary teeth	Mandibular teeth
Argentina	124	Mixed (Hispanic and American Natives)	47 ± 14 [14-79]	52 (41.9%)	72 (58.1%)	2649/3500	1326 (50.1%)	737 (27.8%)	586 (22.1%)	1303 (49.2%)	1346 (50.8%)
Armenia	115	Asians (Armenians)	44 ± 16 [17-75]	49 (42.6%)	66 (57.4%)	2626/3500	1303 (49.6%)	715 (27.2%)	608 (23.2%)	1307 (49.8%)	1319 (50.2%)
Australia	139	Mixed (Asians and Caucasians)	36 ± 19 [12-89]	49 (35.3%)	90 (64.7%)	2605/3500	1192 (45.7%)	733 (28.2%)	680 (26.1%)	1095 (42.0%)	1510 (58.0%)
Azerbaijan	112	Mostly Caucasians	37 ± 13 [16-74]	40 (35.7%)	72 (64.3%)	2491/3500	1154 (46.3%)	692 (27.8%)	645 (25.9%)	1398 (56.1%)	1093 (43.9%)
Brazil	103	Mixed (Caucasians (non-Hispanic) with Africans, American Natives and Asians)	50 ± 20 [14-92]	48 (46.6%)	55 (53.4%)	2604/3500	1168 (44.9%)	745 (28.6%)	691 (26.5%)	1298 (49.8%)	1306 (50.2%)
Chile	146	Mostly Caucasians (Hispanic origin)	42 ± 19 [11-80]	54 (37.0%)	92 (63.0%)	2593/3500	1255 (48.4%)	653 (25.2%)	685 (26.4%)	1433 (55.3%)	1160 (44.7%)
China	88	Asians	35 ± 12 [20-79]	33 (37.5%)	55 (62.5%)	2450/3500	1051 (42.9%)	700 (28.6%)	699 (28.5%)	1228 (50.1%)	1222 (49.9%)
Colombia	196	Caucasians (Hispanic origin)	57 ± 14 [18-86]	88 (44.9%)	108 (55.1%)	2770/3500	1397 (50.4%)	767 (27.7%)	606 (21.9%)	1577 (56.9%)	1193 (43.1%)
Dominican Republic	112	Mixed	47 ± 16 [15-77]	49 (43.8%)	63 (56.2%)	2522/3500	1151 (45.6%)	740 (29.3%)	631 (25.0%)	1342 (53.2%)	1180 (46.8%)
Ecuador	107	Mostly Caucasians (Hispanic origin)	54 ± 14 [14-90]	41 (38.3%)	66 (61.7%)	2602/3500	1207 (46.4%)	713 (27.4%)	682 (26.2%)	1276 (49.0%)	1326 (51.0%)
Egypt	112	Mostly Africans (Egyptians)	44 ± 16 [17-81]	57 (50.9%)	55 (49.1%)	2550/3500	1201 (47.1%)	733 (28.7%)	616 (24.2%)	1360 (53.3%)	1190 (46.7%)
England	180	Mostly Caucasians	62 ± 15 [14-95]	83 (46.1%)	97 (53.9%)	2597/3500	1272 (49.0%)	705 (27.1%)	620 (23.9%)	1454 (56.0%)	1143 (44.0%)
Estonia	104	Caucasians	44 ± 12 [18-83]	47 (45.2%)	57 (54.8%)	2604/3500	1224 (47.0%)	740 (28.5%)	640 (24.5%)	1296 (49.8%)	1308 (50.2%)
Finland	129	Mostly Caucasians	55 ± 17 [14-92]	44 (34.1%)	85 (65.9%)	2570/3500	1215 (47.3%)	744 (28.9%)	611 (23.8%)	1382 (53.8%)	1188 (46.2%)
Georgia	110	Caucasians (Georgians)	40 ± 12 [21-75]	38 (34.5%)	72 (65.5%)	2633/3500	1254 (47.6%)	743 (28.2%)	636 (24.2%)	1322 (50.2%)	1311 (49.8%)
Greece	176	Caucasians	53 ± 15 [14-81]	89 (50.6%)	87 (49.4%)	2613/3500	1245 (47.6%)	723 (27.7%)	645 (24.7%)	1419 (54.3%)	1194 (45.7%)
Hungary	101	Mostly Caucasians	48 ± 14 [18-78]	45 (44.6%)	56 (55.4%)	2525/3500	1193 (47.2%)	690 (27.3%)	642 (25.4%)	1254 (49.7%)	1271 (50.3%)
Iceland	104	Mostly Caucasians	40 ± 17 [17-75]	40 (38.5%)	64 (61.5%)	2537/3500	1147 (45.2%)	726 (28.6%)	664 (26.2%)	1237 (48.7%)	1300 (51.3%)
India	111	Indians	41 ± 16 [13-78]	44 (39.6%)	67 (60.4%)	2497/3500	1154 (46.2%)	661 (26.5%)	682 (27.3%)	1323 (53.0%)	1174 (47.0%)
Iran	123	Asians (Iranian/ Persian origins)	44 ± 13 [13-76]	58 (47.2%)	65 (52.8%)	2462/3500	1068 (43.4%)	704 (28.6%)	690 (28.0%)	1232 (50.0%)	1230 (50.0%)
Ireland	138	Mixed	49 ± 18 [13-88]	60 (43.5%)	78 (56.5%)	2650/3500	1264 (47.7%)	733 (27.7%)	653 (24.6%)	1438 (54.3%)	1212 (45.7%)
Israel	103	Mixed (Jewish, Arabs, and Africans)	44 ± 14 [14-81]	55 (53.4%)	48 (46.6%)	2559/3500	1219 (47.6%)	732 (28.6%)	608 (23.8%)	1340 (52.4%)	1219 (47.6%)
Italy	151	Mostly Caucasians	28 ± 9 [18-55]	60 (39.7%)	91 (60.3%)	2581/3500	1110 (43.0%)	736 (28.5%)	735 (28.5%)	784 (30.4%)	1797 (69.6%)

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TABLE 2 - Continued

	Demographics					Overall sample characteristics					
Region	Sample size (patients)	Ethnic groups*	Age in y (mean ± SD) [range]	Proportion of males	Proportion of females	Sample size (teeth/ roots)	Anterior teeth	Premolar teeth	Molar teeth	Maxillary teeth	Mandibular teeth
Jamaica	94	Mixed (Africans, Asians, and Caucasians)	31 ± 10 [16-61]	23 (24.5%)	71 (75.5%)	2489/3500	1089 (43.8%)	714 (28.7%)	686 (27.6%)	1228 (49.3%)	1261 (50.7%)
Japan	103	Asians	54 ± 15 [23-87]	41 (39.8%)	62 (60.2%)	2516/3500	1158 (46.0%)	726 (28.9%)	632 (25.1%)	1287 (51.2%)	1229 (48.8%)
Jordan	102	Arabs	47 ± 11 [15-68]	45 (44.1%)	57 (55.9%)	2480/3500	1129 (45.6%)	700 (28.2%)	651 (26.2%)	1303 (52.5%)	1177 (47.5%)
Kazakhstan	100	Mostly Asians	37 ± 15 [12-68]	26 (26.0%)	74 (74.0%)	2542/3500	1175 (46.2%)	717 (28.2%)	650 (25.6%)	1261 (49.6%)	1281 (50.4%)
Kuwait	103	Mixed (Asians and Caucasians)	45 ± 15 [13-78]	37 (35.9%)	66 (64.1%)	2573/3500	1179 (45.8%)	725 (28.2%)	669 (26.0%)	1291 (50.2%)	1282 (49.8%)
Kyrgyzstan	120	Mostly Asians	42 ± 16 [12-76]	36 (30.0%)	84 (70.0%)	2656/3500	1313 (49.4%)	728 (27.4%)	615 (23.2%)	1285 (48.4%)	1371 (51.6%)
Latvia	212	Caucasians	46 ± 15 [11-83]	71 (33.5%)	141 (66.5%)	2601/3500	1320 (50.7%)	696 (26.8%)	585 (22.5%)	1652 (63.5%)	949 (36.5%)
Lebanon	185	Asians (Lebanese)	49 ± 15 [18-89]	85 (45.9%)	100 (54.1%)	2666/3500	1396 (52.4%)	761 (28.5%)	509 (19.1%)	1412 (53.0%)	1254 (47.0%)
Malaysia	104	Asians	41 ± 15 [16-77]	40 (38.5%)	64 (61.5%)	2545/3500	1174 (46.2%)	726 (28.5%)	645 (25.3%)	1273 (50.0%)	1272 (50.0%)
Mexico	117	Mixed	48 ± 19 [19-88]	57 (48.7%)	60 (51.3%)	2422/3500	1102 (45.5%)	693 (28.6%)	627 (25.9%)	1304 (53.8%)	1118 (46.2%)
New Zealand	97	Mixed	44 ± 15 [21-76]	39 (40.2%)	58 (59.8%)	2559/3500	1151 (45.0%)	712 (27.8%)	696 (27.2%)	1271 (49.7%)	1288 (50.3%)
Nigeria	103	Africans	41 ± 17 [11-83]	47 (45.6%)	56 (54.4%)	2506/3500	1105 (44.1%)	723 (28.9%)	678 (27.1%)	1241 (49.5%)	1265 (50.5%)
Pakistan	137	Asians	43 ± 14 [18-75]	55 (40.1%)	82 (59.9%)	2651/3500	1276 (48.1%)	781 (29.5%)	594 (22.4%)	1371 (51.7%)	1280 (48.3%)
Paraguay	200	Mostly Caucasians (Hispanic origin)	45 ± 17 [14-81]	86 (43.0%)	114 (57.0%)	2570/3500	1222 (47.5%)	698 (27.2%)	650 (25.3%)	1582 (61.6%)	988 (38.4%)
Peru	103	Mixed (Hispanic origin and American Natives)	38 ± 17 [16-77]	44 (42.7%)	59 (57.3%)	2535/3500	1169 (46.1%)	689 (27.2%)	677 (26.7%)	1270 (50.1%)	1265 (49.9%)
Poland	94	Mostly Caucasians	41 ± 14 [16-78]	41 (43.6%)	53 (56.4%)	2538/3500	1151 (45.4%)	716 (28.2%)	671 (26.4%)	1261 (49.7%)	1277 (50.3%)
Portugal	153	Mostly Caucasians	48 ± 15 [13-83]	70 (45.8%)	83 (54.2%)	2674/3500	1327 (49.6%)	760 (28.4%)	587 (22.0%)	1362 (50.9%)	1312 (49.1%)
Romania	168	Mostly Caucasians	48 ± 13 [14-81]	65 (38.7%)	103 (61.3%)	2718/3500	1419 (52.2%)	766 (28.2%)	533 (19.6%)	1575 (57.9%)	1143 (42.1%)
Russia	93	Mixed (Russians, Ukrainians, Tatars, Bashkirs, and Kazakh)	36 ± 10 [13-61]	41 (44.1%)	52 (55.9%)	2497/3500	1100 (44.1%)	714 (28.5%)	683 (27.4%)	1253 (50.2%)	1244 (49.8%)
Saudi Arabia	139	Mostly Arabs	39 ± 13 [20-74]	59 (42.2%)	80 (57.6%)	2545/3500	1192 (46.8%)	727 (28.6%)	626 (24.6%)	1316 (51.7%)	1229 (48.3%)
South Africa	108	Mixed (Asians, Caucasians and Africans)	51 ± 17 [15-86]	48 (44.4%)	60 (55.6%)	2534/3500	1175 (46.4%)	686 (27.1%)	673 (26.6%)	1287 (50.8%)	1247 (49.2%)
South Korea	103	Asians	36 ± 18 [17-88]	51 (49.5%)	52 (50.5%)	2568/3500	1148 (44.7%)	714 (27.8%)	706 (27.5%)	1278 (49.8%)	1290 (50.2%)
Spain	93	Mostly Caucasians	42 ± 17 [16-80]	53 (57.0%)	40 (43.0%)	2468/3500	1069 (43.3%)	715 (29.0%)	684 (27.7%)	1237 (50.1%)	1231 (49.9%)
Switzerland	174	Caucasians	52 ± 20 [11-100]	78 (44.8%)	96 (55.2%)	2676/3500	1332 (49.8%)	761 (28.4%)	583 (21.8%)	1300 (48.6%)	1376 (51.4%)

(*continued on next page*)

TABLE 2 - Continued

	Demographics					Overall sample characteristics					
Region	Sample size (patients)	Ethnic groups*	Age in y (mean ± SD) [range]	Proportion of males	Proportion of females	Sample size (teeth/ roots)	Anterior teeth	Premolar teeth	Molar teeth	Maxillary teeth	Mandibular teeth
Syria	107	Arabs	35 ± 14 [13-69]	32 (29.9%)	75 (70.1%)	2556/3500	1158 (45.3%)	731 (28.6%)	667 (26.1%)	1378 (53.9%)	1178 (46.1%)
Thailand	153	Asians (Thai)	45 ± 17 [15-75]	66 (43.1%)	87 (56.9%)	2436/3500	1073 (44.0%)	709 (29.1%)	654 (26.9%)	1515 (62.2%)	921 (37.8%)
Turkey	126	Mostly Caucasians	39 ± 15 [17-77]	45 (35.7%)	81 (64.3%)	2626/3500	1260 (48.0%)	722 (27.5%)	644 (24.5%)	1280 (48.7%)	1346 (51.3%)
Uruguay	102	Mixed (Hispanic origin and Africans)	45 ± 15 [17-82]	40 (39.2%)	62 (60.8%)	2500/3500	1148 (45.9%)	693 (27.7%)	659 (26.4%)	1270 (50.8%)	1230 (49.2%)
USA	106	Mostly Caucasians	59 ± 17 [18-89]	47 (44.3%)	59 (55.7%)	2579/3500	1196 (46.4%)	725 (28.1%)	658 (25.5%)	1290 (50.0%)	1289 (50.0%)
Uzbekistan	91	Mostly Asians	44 ± 13 [18-70]	46 (50.5%)	45 (49.5%)	2426/3500	1078 (44.4%)	634 (26.1%)	714 (29.4%)	1177 (48.5%)	1249 (51.5%)
Venezuela	114	Caucasians (Hispanic origin)	42 ± 12 [13-58]	51 (44.7%)	63 (55.3%)	2594/3500	1240 (47.8%)	716 (27.6%)	638 (24.6%)	1269 (48.9%)	1325 (51.1%)
Total	6688	—	45 ± 17 [11-100]	2788 (41.7%)	3900 (58.3%)	138536/ 189000	64794 (46.8%)	38843 (28.0%)	34899 (25.2%)	71177 (51.4%)	67359 (48.6%)

SD, standard deviation.

*Ethnic group reflecting the population served by the health unit rather than the patient's country of origin.

evidence and strengthening evidence-based health care. In epidemiology, this realistic approach bridges the gap between idealized research conditions and the complexity of real-world clinical environments. Whereas explanatory trials determine whether an intervention can work under ideal circumstances, pragmatic studies reveal how it performs in everyday care[17]. This distinction is especially relevant to global disease prevalence studies, where disparities in health care infrastructure, education, and access profoundly influence outcomes.

Within this real-world big data framework, careful consideration of the unit of analysis is essential to ensure clinically meaningful interpretation. Although root-level assessment enabled detailed anatomical characterization of periapical pathology, patient-level prevalence was prioritized for epidemiological interpretation, as multiple roots within the same individual are not independent observations. To minimize potential inflation effects associated with root-based analyses, clustered regression models (GEE) were applied, and patient-level prevalence was emphasized as the primary outcome reflecting global disease burden. Tooth- and root-level results are therefore presented as secondary analyses intended to describe anatomical distribution patterns rather than population prevalence.

In this large multicenter study, the markedly higher prevalence of AP in endodontically treated teeth (post-treatment periapical radiolucencies) (44.3%) compared with untreated teeth (2.6%) underscores the clinical value of real-world data in revealing associations often missed in controlled studies. This global assessment of AP both aligns with and extends previous findings, particularly those of the systematic review and meta-analysis by Tiburcio–Machado et al.[21], which included 114 studies encompassing 34,668 individuals and 639,357 teeth. Both studies demonstrate a strong association between previous root canal treatment and AP prevalence. Our results (44.3% in root-filled teeth versus 2.6% in untreated teeth, corresponding to a 21-fold higher odds; OR = 21.6) closely match those of Tiburcio–Machado et al.[21] (39% and 3%, respectively). This shared conclusion reinforces the public health relevance of persistent or secondary AP. Both studies also identify age as an important factor influencing the prevalence of AP. In the present investigation, teeth AP prevalence increased progressively from 2.9% in patients ≤20 years to 10.5% in those ≥61 years. Tiburcio-Machado et al.[21] similarly reported age as a modifier of AP

FIGURE 1 – Worldwide prevalence of periapical pathology at the patient level. The color scale represents the proportion of affected patients. The lowest prevalence was observed in Italy, and the highest in Uzbekistan.

prevalence, reflecting the cumulative impact of caries, trauma, and restorative procedures over time.

Despite these agreements, differences emerged in overall prevalence rates and the influence of sex. In the present study, the patient-level prevalence of AP was 58.6%, higher than the 52% reported by Tiburcio-Machado et al.[21]. Similarly, our tooth-level prevalence (7.3%) exceeded their 5%. These discrepancies likely reflect methodological and scope differences between the two investigations. Tiburcio-Machado et al.[21] conducted a systematic review and meta-analysis pooling data from 114 studies, introducing heterogeneity due to variations in diagnostic criteria, imaging methods (periapical, panoramic, or CBCT), and study populations. In contrast, our analysis of 189,000 roots from 6,688 patients was based on standardized CBCT datasets, minimizing methodological variability. The exclusive use of CBCT, combined with a uniform diagnostic protocol, likely contributed to the higher prevalence observed. Additionally, the inclusion of regions with exceptionally high rates, such as Uzbekistan, where patient-level prevalence reached 100%, may have further elevated the global average compared with the pooled estimates of the prior meta-analysis.

Our logistic regression revealed that males had 1.22-fold higher odds of AP globally, while the meta-analysis by Tiburcio–Machado et al.[21] found no significant sex-related difference. This discrepancy likely arises from methodological differences: their meta-analysis reported pooled prevalence averages, while our logistic regression model accounted for clustering effects (within patients and regions) and adjusted for confounders such as age and tooth type. Consequently, our analysis identified male sex as a small but statistically significant independent associated factor. This association may reflect behavioral influences, including higher rates of dental trauma or less frequent dental visits among men, which are often overlooked in prevalence-based analyses. Overall, our findings reinforce that previous endodontic treatment remains the strongest predictor of AP, while also indicating a higher global burden of disease and a modest sex-related association that merits further investigation.

In the present study, the prevalence of 7.3% of AP at the tooth level underscores the epidemiologic relevance of periapical disease. Regional variation was evident, with Africa showing the highest prevalence (9.6%) and Oceania the lowest (2.5%), likely reflecting disparities in health care infrastructure and endodontic care quality. Strengthening diagnostic standards, treatment quality, and follow-up care in high-prevalence regions may help reduce these rates. Although direct global comparisons are unavailable, previous country-level CBCT studies provide context. The European prevalence (7.0%) in the present study (Supplemental Fig. S1) aligns with findings from Poland (6.0%)[22], Belgium (5.9%)[23], and Scotland (5.8%)[4], but is slightly lower than that of Portugal (10.0%)[5]. In South Asia and the Middle East, the prevalence (8.7%) was lower than reported in Iraq (20.0%)[24] and Saudi Arabia (18.2% in posterior teeth)[25]. In South America, the prevalence observed in the present study

FIGURE 2 – Worldwide prevalence of periapical pathology at the tooth level. The color scale represents the proportion of affected teeth. The lowest prevalence was recorded in Jamaica, and the highest in Uzbekistan.

(7.1%; Supplemental Fig. S1) is higher than the 3.4% previously reported in Brazil[26]. This difference, with Brazil showing 7.3% in the current dataset (Fig. 2), is likely attributable to sampling variability. In Eastern Europe, the Bulgarian rate (23.1%)[27] exceeded the present regional average (Supplemental Fig. S1). Overall, the multicontinental prevalence observed here falls within the range of previous single-country reports, with residual heterogeneity likely reflecting differences in sampling, patient demographics, and diagnostic or health care protocols.

No significant difference in periapical pathology prevalence between sexes was found at the tooth level in the meta-analysis, although logistic regression showed a slightly higher odds for males. This difference is likely statistical rather than clinical, given the nearly identical proportions observed between males (7.5%) and females (7.2%) (Supplemental Fig. S2). These findings align with previous CBCT-based studies from Portugal[5], Belgium[23], and Scotland[4], which also reported similar results. In contrast, a Saudi Arabian study observed a male predilection for posterior tooth pathology[25]. Prevalence increased steadily with age, from 2.9% in patients ≤20 years to 10.5% in those ≥61 years (Fig. 3). Similar trends have been reported in Brazil, where prevalence rose from 15.0% in patients aged 12–19 to 73.1% in those aged 60–69[26], and in Belgium, where lesions increased from 1.7% in patients <20 years to 7.3% in those >60[23]. Conversely, Dutta et al.[4] found a higher prevalence among middle-aged Scottish patients (46–55 years). Overall, sex does not appear to be a strong determinant of periapical pathology, whereas age exerts a consistent influence, likely reflecting the cumulative effects of restorative procedures, endodontic treatments, and long-term exposure to associated factors.

One of the most relevant findings of this study was the marked difference in AP prevalence between untreated teeth (2.6%) and endodontically treated teeth (44.3%), a pattern consistent across regions. This gradient aligns with previous CBCT-based investigations, although absolute values vary. In Belgium, 2.2% of untreated and 32.7% of root-filled teeth were affected[23], while in Scotland the values were 3.7% and 47.4%, respectively[4]. Similar trends were reported in Portugal (4.6% vs 54.0%)[5] and Iraq (17.7% vs 80.2%)[24], as well as in studies from Bulgaria[27], Turkey[28], and Brazil[26]. Collectively, these findings confirm that endodontically treated teeth exhibit a substantially higher prevalence of apical hypodense areas than untreated teeth, emphasizing the importance of treatment quality and long-term follow-up. This outcome, however, is not unexpected, as endodontically treated teeth inherently represent cases with previous pulpal necrosis or irreversible pulpitis, conditions predisposing them to apical inflammation[29]. Consequently, periapical changes may reflect either residual lesions from preoperative infection or persistent inflammation due to treatment-related factors. The global dataset of the present study reinforces this pattern across diverse health care systems and populations, underscoring the need for

TABLE 3 - Overall Outcomes for Maxillary Teeth Assessments

Assessed variables	Maxillary teeth groups							Overall
	Central incisor	Lateral incisor	Canine	First premolar	Second premolar	First molar	Second molar	
Presence of periapical pathology								
With periapical pathology	805/11002 (7.3%)	710/10951 (6.5%)	452/11078 (4.1%)	952/9780 (9.7%)	962/9555 (10.1%)	1700/9160 (18.6%)	1062/9651 (11.0%)	6643/71177 (9.3%)
Previous root canal treatment								
No root canal treatment	251/9514 (2.6%)	238/9660 (2.5%)	187/10134 (1.9%)	308/8258 (3.7%)	251/7692 (3.7%)	436/7123 (6.1%)	358/8388 (4.3%)	2029/60769 (3.3%)
With root canal treatment	554/1488 (37.2%)	472/1291 (36.6%)	265/944 (28.1%)	644/1522 (42.3%)	711/1863 (38.2%)	1264/2037 (62.1%)	704/1263 (55.7%)	4614/10408 (44.3%)
Geographic location								
Africa	61/569 (10.7%)	55/573 (9.6%)	47/593 (7.9%)	110/545 (20.2%)	77/522 (14.7%)	108/543 (19.9%)	65/543 (11.9%)	523/3888 (13.5%)
Americas	202/2678 (7.5%)	175/2707 (6.5%)	109/2771 (3.9%)	228/2342 (9.7%)	232/2353 (9.8%)	375/2214 (16.9%)	258/2377 (10.8%)	1579/17442 (9.1%)
Asia	104/1722 (6.0%)	90/1724 (5.2%)	53/1736 (3.1%)	120/1571 (7.6%)	115/1572 (7.3%)	286/1590 (17.9%)	176/1642 (10.7%)	944/11557 (8.2%)
Europe	239/3198 (7.5%)	189/3120 (6.1%)	126/3157 (3.9%)	227/2767 (8.2%)	273/2622 (10.4%)	483/2444 (19.7%)	309/2623 (11.8%)	1846/19931 (9.3%)
Oceania	9/354 (2.5%)	12/352 (3.4%)	2/351 (0.6%)	8/331 (2.4%)	11/330 (3.3%)	12/317 (3.8%)	11/331 (3.3%)	65/2366 (2.7%)
South Asia and Middle East	190/2481 (7.7%)	189/2475 (7.6%)	115/2470 (4.6%)	259/2224 (11.6%)	254/2156 (11.8%)	436/2052 (21.2%)	243/2135 (11.4%)	1686/15993 (9.8%)
Sex								
Male	363/4557 (7.9%)	343/4553 (7.5%)	207/4642 (4.5%)	398/4074 (9.8%)	412/4031 (10.2%)	703/3774 (18.6%)	487/3999 (12.2%)	2913/29630 (9.8%)
Female	442/6445 (6.8%)	367/6398 (5.7%)	245/6436 (3.8%)	554/5706 (9.7%)	550/5524 (9.9%)	997/5386 (18.5%)	575/5652 (10.2%)	3730/41547 (9.0%)
Age groups								
$\leq$ 20 y	34/718 (4.7%)	29/714 (4.1%)	4/669 (0.6%)	21/696 (3.0%)	19/696 (2.7%)	66/707 (9.3%)	18/677 (2.7%)	191/4877 (3.9%)
21-40 y	263/4207 (6.2%)	213/4172 (5.1%)	108/4184 (2.6%)	257/3966 (6.5%)	258/3961 (6.5%)	525/3934 (13.4%)	283/4036 (7.0%)	1907/28460 (6.7%)
41-60 y	313 4102 (7.6%)	279/4110 (6.8%)	207/4169 (4.9%)	446/3530 (12.6%)	457/3408 (13.4%)	782/3219 (24.3%)	506/3495 (14.5%)	2990/26033 (11.5%)
$\geq$ 61 y	195/1975 (9.9%)	189/1955 (9.7%)	133/2056 (6.5%)	228/1588 (14.4%)	228/1490 (15.3%)	327/1300 (25.1%)	255/1443 (17.7%)	1555/11807 (13.2%)

TABLE 4 - Overall Outcomes for Mandibular Teeth Assessments

Assessed variables	Mandibular teeth groups							Overall
	Central incisor	Lateral incisor	Canine	First premolar	Second premolar	First molar	Second molar	
Presence of periapical pathology								
With periapical pathology	359/10527 (3.4%)	267/10576 (2.5%)	212/10660 (2.0%)	332/10019 (3.3%)	506/9489 (5.3%)	1105/7579 (14.6%)	798/8509 (9.4%)	3579/67359 (5.3%)
Previous root canal treatment								
No root canal treatment	211/10237 (2.1%)	147/10299 (1.4%)	104/10354 (1.0%)	115/9351 (1.2%)	168/8290 (2.0%)	221/5896 (3.7%)	255/7349 (3.5%)	1221/61776 (1.9%)
With root canal treatment	148/290 (51.0%)	120/277 (43.3%)	108/306 (35.3%)	217/668 (32.5%)	338/1199 (28.2%)	884/1683 (52.5%)	543/1160 (46.8%)	2358/5583 (42.2%)
Geographic location								
Africa	26/585 (4.4%)	27/582 (4.6%)	12/579 (2.1%)	23/534 (4.3%)	28/541 (5.2%)	49/428 (11.4%)	40/453 (8.8%)	205/3702 (5.5%)
Americas	78/2486 (3.1%)	55/2493 (2.2%)	49/2535 (1.9%)	65/2311 (2.8%)	115/2277 (5.0%)	233/1849 (12.6%)	193/2036 (9.5%)	788/15987 (4.9%)
Asia	50/1686 (2.9%)	48/1694 (2.8%)	43/1708 (2.5%)	52/1664 (3.1%)	82/1561 (5.3%)	206/1323 (15.6%)	157/1443 (10.9%)	638/11079 (5.8%)
Europe	106/3007 (3.5%)	74/3016 (2.4%)	53/3050 (1.7%)	75/2910 (2.6%)	121/2634 (4.6%)	270/2064 (13.1%)	195/2366 (8.2%)	894/19047 (4.7%)
Oceania	11/432 (2.6%)	5/428 (1.2%)	3/426 (0.7%)	3/397 (0.8%)	6/387 (1.6%)	20/361 (5.5%)	15/367 (4.1%)	63/2798 (2.3%)
South Asia and Middle East	88/2331 (3.8%)	58/2363 (2.5%)	52/2362 (2.2%)	114/2203 (5.2%)	154/2089 (7.4%)	327/1554 (21.0%)	198/1844 (10.7%)	991/14746 (6.7%)
Sex								
Male	153/4371 (3.5%)	112/4385 (2.6%)	83/4429 (1.9%)	147/4209 (3.5%)	209/3998 (5.2%)	463/3198 (14.5%)	335/3573 (9.4%)	1502/28163 (5.3%)
Female	206/6156 (3.3%)	155/6191 (2.5%)	129/6231 (2.1%)	185/5810 (3.2%)	297/5491 (5.4%)	642/4381 (14.7%)	463/4936 (9.4%)	2077/39196 (5.3%)
Age groups								
$\leq$ 20 y	8/678 (1.2%)	9/675 (1.3%)	12/671 (1.8%)	7/660 (1.1%)	6/654 (0.9%)	26/660 (3.9%)	14/635 (2.2%)	82/4633 (1.8%)
21-40 y	87/4101 (2.1%)	59/4094 (1.4%)	45/4097 (1.1%)	71/3966 (1.8%)	128/3912 (3.3%)	408/3576 (11.4%)	243/3802 (6.4%)	1041/27548 (3.8%)
41-60 y	150/3872 (3.9%)	108/3893 (2.8%)	85/3929 (2.2%)	149/3662 (4.1%)	245/3427 (7.1%)	476/2399 (19.8%)	394/2946 (13.4%)	1607/24128 (6.7%)
$\geq$ 61 y	114/1876 (6.1%)	91/1914 (4.8%)	70/1963 (3.6%)	105/1731 (6.1%)	127/1496 (8.5%)	195/944 (20.7%)	147/1126 (13.1%)	849/11050 (7.7%)

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TABLE 5 - Overall Outcomes for Maxillary and Mandibular Roots Assessments

	Maxillary molars roots				
	Mesiobuccal root	**Distobuccal root**	**Palatal root**	**Extra root**	**Fused root**
Maxillary first molar	1477/9035 (16.3%)	1155/8815 (13.1%)	1054/8899 (11.8%)	0/10 (0.0%)	52/376 (13.8%)
Maxillary second molar	702/7961 (8.8%)	661/8214 (8.0%)	636/8469 (7.5%)	0/15 (0.0%)	193/1811 (10.7%)
	Mandibular molars roots				
	Mesial root	Distal root	Extra root		Fused root
Mandibular first molar	978/7563 (12.9%)	900/7563 (11.9%)	15/191 (7.9%)		1/25 (4.0%)
Mandibular second molar	661/7715 (8.6%)	606/7715 (7.9%)	6/83 (7.2%)		63/806 (7.8%)

preventive strategies, higher technical standards, and rigorous post-treatment monitoring. Nonetheless, as this cross-sectional study captures only a single time point, it cannot determine whether the detected lesions, particularly in previously endodontically treated teeth, represent healing, persistent, or progressing periapical pathology, nor does it provide information on the time elapsed since treatment. Therefore, the presence of a periapical radiolucency should not be interpreted as an indicator of endodontic treatment failure. This distinction likely inflates apparent prevalence in treated teeth, as radiolucencies may represent healing or scar tissue rather than active disease.

An important methodological aspect to consider in CBCT-based epidemiologic research relates to the clinical indications for image acquisition. Unlike conventional two-dimensional radiographs obtained routinely, CBCT examinations are generally prescribed to address specific diagnostic questions, including complex endodontic assessment, treatment planning, or the evaluation of suspected pathology. As a result, CBCT datasets may include a higher proportion of teeth with complex clinical histories. The exclusion of focused or restricted FOVs from the present study aimed to minimize this issue. Nevertheless, this characteristic also represents a key strength of CBCT-based assessment, as it allows for a more accurate and sensitive detection of periapical pathology compared with conventional two-dimensional radiographs, thereby reducing the chance of underdiagnosis.

Variability in international recommendations and position statements regarding CBCT use reflects differences in health care systems, access to technology, and radiation protection policies, which may influence the clinical contexts in which CBCT is prescribed across regions. In the present study, this potential heterogeneity was addressed through the application of standardized inclusion criteria, calibrated examiner training, and the exclusion of focused or endodontically driven FOVs, ensuring that only scans capturing at least one complete dental arch were analyzed. These measures were implemented to enhance interregional comparability and to support the validity of large-scale comparisons. Importantly, while absolute prevalence estimates should be interpreted in light of these considerations, the use of CBCT provides a robust and clinically meaningful assessment of periapical status, strengthening the reliability of associations observed across age groups, tooth types, and treatment status.

The main strength of this study lies in its unprecedented global scope, providing the first standardized worldwide estimate of periapical pathology prevalence based on CBCT data. By integrating information from multiple regions (many previously unreported) and diverse ethnic groups, it overcomes the geographical constraints of earlier single-country studies, enabling meaningful cross-continental comparisons. Another strength is the use of CBCT, a diagnostic method proven more sensitive than conventional periapical radiography for detecting periapical pathology[30], thereby reducing the likelihood of underestimating true prevalence. Some limitations must, however, be acknowledged. Although high intra- and inter-examiner agreement was achieved, CBCT-based identification of small periapical radiolucencies remains inherently sensitive, particularly near the 0.5-mm CBCT periapical index threshold, where anatomical structures or healing tissues may mimic pathology. Despite standardized calibration, multiplanar assessment, and

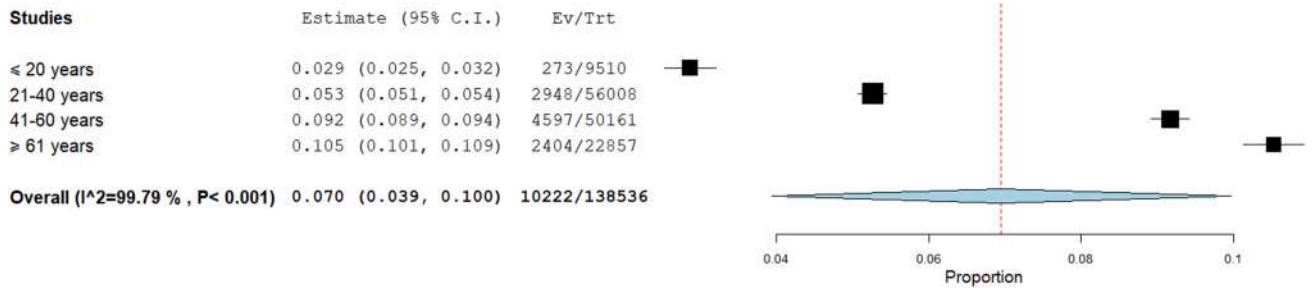

FIGURE 3 – Forest plot showing the prevalence of periapical pathology at the tooth level across age groups. The lowest prevalence occurred in patients aged ≤20 years (2.9%), increasing progressively with age to 10.5% in those aged ≥61 years. CI, confidence interval.

external validation, some degree of diagnostic misclassification cannot be entirely excluded. This limitation is intrinsic to CBCT-based epidemiologic studies and should be considered when interpreting prevalence estimates, especially in previously treated teeth. Additionally, variations in imaging devices and acquisition protocols across centers may have influenced lesion detection, although strict inclusion criteria helped minimize this effect. Importantly, this study analyzed 6,688 patients, 138,536 teeth, and 189,000 roots, far exceeding the scale of previous CBCT-based epidemiologic investigations. For comparison, the largest national study to date included 1,249 patients and 22,899 teeth in Portugal[5], while others ranged from 245 patients with 3,595 teeth in Scotland[4] to 631 patients with 11,117 teeth in Belgium[23]. This large sample enhances the robustness and external validity of the present findings. Although exact prevalence rates should be interpreted cautiously, the overall trends, particularly the differences between untreated and treated teeth, the age-related increase in prevalence, and regional variability, are likely generalizable at a population level. Although CBCT datasets were derived from convenience samples, standardized consecutive inclusion, high examiner agreement, and logistic regression modeling were used to enhance data reliability and reduce the impact of sampling-related bias.

The CBCT periapical index[13] and its 0.5-mm threshold were applied in accordance with the original validation study and established CBCT-based epidemiologic methodology. Although small radiolucencies may overlap with normal anatomical structures such as a widened periodontal ligament space or adjacent anatomical canals, this limitation is inherent to CBCT-based periapical indices. In the present study, standardized multiplanar evaluation, strict exclusion criteria, and high inter- and intraexaminer agreement were used to minimize potential diagnostic misclassification while preserving comparability with previously published CBCT studies. Given the high prevalence of AP and the clear association with endodontically treated teeth, standardized follow-up and surveillance protocols are essential. Periodic clinical and radiographic evaluations, preferably with CBCT when indicated, can enable early detection of persistent or recurrent apical pathology and guide retreatment decisions. Incorporating periapical healing assessment into long-term outcome evaluations would also enhance monitoring of endodontic treatment success. International collaboration to determine ideal CBCT acquisition parameters and diagnostic criteria would reduce methodological variability and improve comparability across studies. Future research should prioritize longitudinal cohort designs to clarify the natural history of periapical lesions in treated teeth, determining whether they progress, remain stable, or heal over time. Additionally, technical treatment parameters (such as obturation characteristics and coronal restoration), along with region-specific factors such as operator expertise, access to follow-up care, and local treatment standards should be investigated to better understand determinants of post-treatment outcomes. Addressing these aspects will be crucial to advance from prevalence assessment toward preventive and therapeutic strategies that reduce the global burden of periapical disease.

CONCLUSIONS

This global multicenter CBCT study, encompassing 189,000 roots from 138,536 teeth across 54 countries, revealed that periapical pathology is highly prevalent worldwide, affecting 58.6% of patients. At teeth level, the prevalence was 7.3%. Maxillary teeth, particularly first molars, were most frequently involved, and prevalence increased progressively with age. While no sex-related differences were found, marked regional variability emerged, with the highest rates in Africa and the lowest in Oceania. Endodontically treated teeth exhibited a substantially higher prevalence of post-treatment periapical radiolucencies.

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SUPPLEMENTARY MATERIAL

Supplementary material associated with this article can be found in the online version at www.jendodon.com (https://doi.org/10.1016/j.joen.2026.01.021).

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