Empirical evidence on impact by accounting for cluster effect within patients in cohort studies evaluating comparative effectiveness of dental treatments: a meta-epidemiological study

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Background

- In dental research, clustering naturally occurs when multiple teeth are treated within the same patient. However, this is rarely considered in the design or analysis of studies.

Objective

- The primary objective of this meta-epidemiological study is to examine the proportion of studies that accounted for patient clusters in their design or analysis, and to compare these studies with those that did not account for clusters, in terms of their characteristics and outcome significance.
- We also identified the methods currently used to consider clusters in dental cohort studies and discussed appropriate approaches applicable.

Methods

- Comparative effectiveness studies of dental treatments using a cohort design from major dental journals were included. We collected study characteristics relating to design, cohort information, and analytic approaches; and assessed the quality of studies based on their descriptions for design, outcome and analysis.
- Studies that accounted for patient clusters in design or analysis were categorized as 'clustering-considered' (CC); otherwise, 'clustering-not-considered' (CNC). We then compared the characteristics of the CC and CNC studies after categorizing the following: study design (Retrospective, Prospective); publication period (<2015, ≥2015); Intervention criteria (Endodontic, Prosthodontic, Orthodontic); data source (Hospital, Clinic); cohort size (<200, ≥200); the number of clusters (<100, ≥100); and cluster size (<2, ≥2).
- We explored the methods used to account for clustering within patients in the cohort design and/or statistical analysis and examined the difference in the statistical significance of the primary outcome result between the CC and CNC groups using chi-squared tests.
- Multiple logistic regression model was used to evaluate the impact of the consideration of clustering on the significance of the results and its potential interaction with other study characteristics. These interactions were also examined after adjusting for other correlated variables. Correlations between factors were calculated using Cramer's V coefficient.

Results

- Of the 97 cohort studies included, 45 studies (46%) were categorized as CC, of which 26 (58%) considered clustering within patients when designing the cohort (Figure 1).

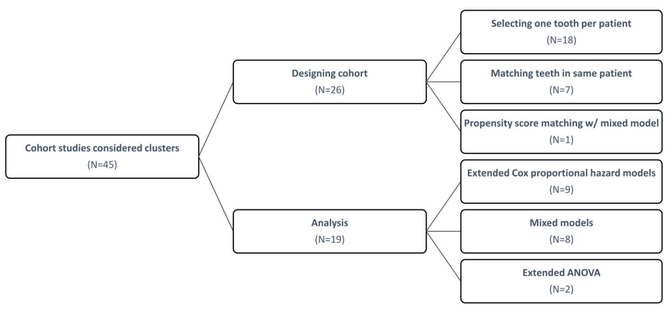

Figure 1. Cluster consideration in the study design and the analysis.

Variable		Category	Total N (%)	CNC (%)	CC (%)	p-value
Cohort study design		Prospective	37 (38.1)	23 (44.2)	14 (31.1)	0.18
		Retrospective	60 (61.9)	29 (55.8)	31 (68.9)	
Publication period		< 2015	67 (69.1)	41 (78.8)	26 (57.8)	0.03
		≥ 2015	30 (30.9)	11 (21.2)	19 (42.2)	
Intervention type		Endodontic	41 (42.3)	23 (44.2)	18 (40.0)	0.57
		Prosthodontic	55 (56.7)	28 (53.8)	27 (60.0)	
		Orthodontic	1 (1.0)	1 (1.9)	0 (0.0)	
Data Source		Hospital	48 (49.5)	23 (44.2)	25 (55.6)	0.40
		Clinic	46 (47.4)	26 (50.0)	20 (44.4)	
		NR	3 (3.1)	3 (5.8)	0 (0.0)	
Cohort size	Tooth	< 200	44 (45.4)	21 (40.4)	23 (51.1)	0.29
		≥ 200	53 (54.6)	31 (59.6)	22 (48.9)	
	Patient	< 100	48 (49.5)	24 (46.2)	24 (53.3)	0.50
		≥ 100	42 (43.3)	24 (46.2)	18 (40.0)	
		NR	7 (7.2)	4 (7.6)	3 (6.7)	
Cluster size		< 2	47 (48.5)	25 (48.1)	22 (48.9)	0.98
		≥ 2	43 (44.3)	23 (44.2)	20 (44.4)	
		NR	7 (7.2)	4 (7.6)	3 (6.7)	
Results of analysis		Significant	40 (41.2)	24 (46.2)	16 (35.5)	0.22
		NS	55 (56.7)	26 (50.0)	29 (64.5)	
		NR	2 (2.1)	2 (3.8)	0 (0.0)	

Table 1. Descriptive statistics of eligible studies between CNC group and CC group. CNC, Clustering-not-considered; CC, Clustering-considered; NR, None reported; NS, Not significant.

- The CC and CNC groups differed in terms of data source, cohort size, and publication period (Table 1).
- The yearly proportion also increased significantly by the publication year (p=0.02; Figure 2).

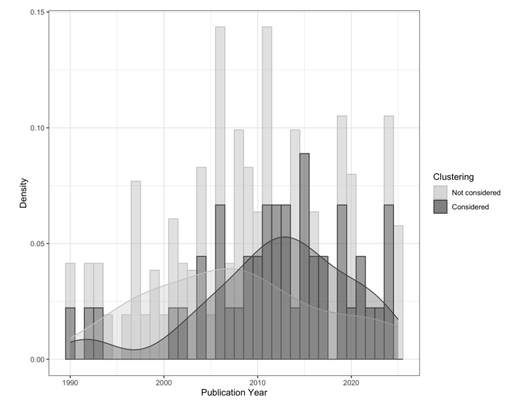

Figure 2. Publication year distribution by considering clustering within patients.

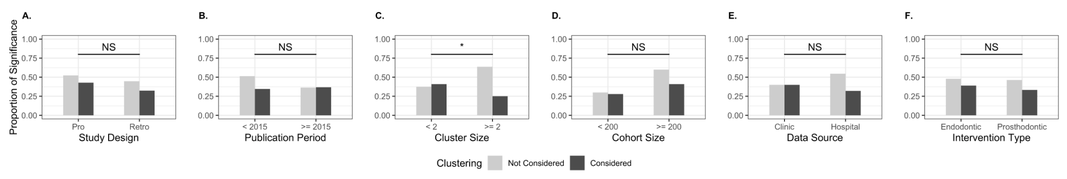

Figure 3. Impact of the consideration of clustering on the significance of the results and its potential interaction with other study characteristics (n=97).
NS, Not significant. *, p<0.05.

- More recent studies, or those conducted in hospitals, of greater cluster size, or of large cohort size, presented positive results more in the CNC group (Figure 3).
- The interaction on the significance of the results between cluster size and consideration of clustering was statistically significant (p=0.05), and this remained significant after adjusting for correlated factors.

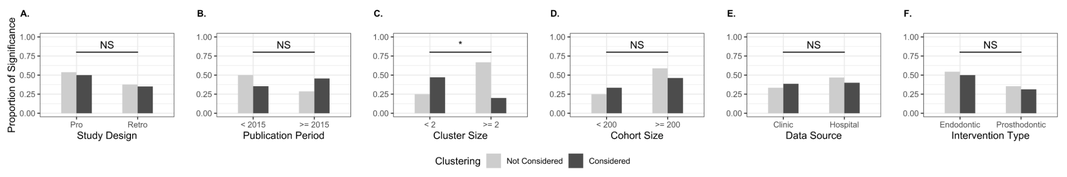

Figure 4. Impact of the consideration of clustering on the significance of the results and its potential interaction with other study characteristics (n=57).
NS, Not significant. *, p<0.05.

- Out of 97 studies, 57 (58.8%) satisfied all the assessment criteria. While all the studies provided sufficient information on their aims, 36 studies (37.1%) did not explicitly designate their primary outcome.
- The same result was confirmed when the same analysis was repeated using only the 57 studies (Figure 4).

Conclusions

- Our meta-epidemiological study demonstrated that statistically significant treatment effects were more frequently observed in studies that did not account for within-patient clustering when more than two teeth were clustered within a patient.

Author Profile:

Conflict of Interest

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