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COMPREHENSIVE REVIEW

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Tooth autotransplantation: An umbrella review

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Abstract

Tooth autotransplantation is a versatile procedure with several clinical applications among patients across different age groups. The success of this procedure depends on multiple factors. Despite the wealth of studies available, no single primary study or systematic review is able to report on every factor affecting the outcomes of autotransplantation. The aims of this umbrella review were to evaluate treatment-related and patient-related outcomes of autotransplantation and to assess the pre-, peri- or post-operative factors that could affect these. An umbrella review was conducted according to the PRISMA statement. A literature search of five databases was performed up to 25 September 2022. Systematic Reviews (SR) with and without meta-analysis evaluating autotransplantation were included. Calibration among reviewers was carried out prior to study selection, data extraction and Risk of Bias (RoB) assessment. Study overlap was calculated using corrected covered area. Meta-meta-analysis (MMA) was performed for suitable SRs. The AMSTAR 2 critical appraisal tool was used to evaluate the quality of evidence. Seventeen SRs met the inclusion criteria. Only two SRs were suitable for conduct of MMA on autotransplantation of open apex teeth. The 5-year and 10-year survival rates were >95%. A narrative summary on factors that could affect autotransplantation outcomes and comparisons of autotransplantation to other treatment options were reported. Five SRs were rated as 'low quality' and 12 SRs were rated as 'critically low quality' in the AMSTAR 2 RoB assessment. In order to facilitate a more homogenous pool of data for subsequent meta-analysis, an Autotransplantation Outcome Index was also proposed to standardise the definition of outcomes. Autotransplantation of teeth with open apices have a high survival rate. Future studies should standardise the reporting of clinical and radiographic findings, as well as the definition of outcomes.

KEYWORDS
autologous transplantation, tooth autotransplantation, tooth auto-transplantation, umbrella review

1 | INTRODUCTION

The replacement of permanent teeth as a result of tooth agenesis, or tooth loss secondary to dental caries and dental trauma, remains one of the challenges of modern dentistry. Although multiple treatment options, such as fixed or removable prostheses, dental implants and tooth autotransplantation (AT), are available to address this clinical conundrum, the search for an ideal replacement technique that is aesthetically pleasing, simple, acceptable, biological and cost effective is still ongoing. The rapid development in the fields of dental implantology and AT in the past two decades has revolutionised and improved the dental outcomes for these patients.[1,2]

Autotransplantation offers a biological replacement option to patients. The procedure is versatile with various clinical applications among patients across different age groups. In children and adolescents, AT is primarily used to replace traumatised maxillary anterior teeth that have a poor prognosis.[3] Additional applications include redistribution of teeth into strategic locations as part of an interdisciplinary hypodontia management plan, and repositioning of ectopic maxillary canines as part of comprehensive orthodontic treatment.[4] In adults, AT of third molars has been used to replace other permanent molars lost due to dental caries, periodontal disease or endodontic infections.[5]

The success and survival of an AT tooth depends on multiple factors such as root development stage, bone management, type of surgical protocol, splinting technique, use of antibiotic cover and timing of endodontic treatment.[6,7] Despite the wealth of studies available on AT, no single primary study or systematic review (SR) has reported on every factor affecting AT outcomes.[8] Furthermore, to aid in clinical decision making, comparison among various replacement options (e.g. implants) is required. A comprehensive integration of the published evidence, such as collating systematic reviews on AT under an umbrella review,[8] is warranted to help clinicians decide on the most suitable treatment option to replace missing teeth, to determine clinical protocols to provide the best chance for a successful AT outcome and to identify gaps in the literature. Therefore, an umbrella review was planned with the following aims:

1. To identify and critically appraise the evidence for both treatment-related and patient-related outcomes of AT and
2. To assess the pre-, peri- or post-operative factors that could affect treatment-related outcomes.

2 | MATERIALS AND METHODS

The umbrella review was registered in PROSPERO (ref. CRD42022324471) and conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) statement.[9] The research questions were formulated with the PICOS framework (Table 1).[10,11] The primary research questions of this umbrella review were:

TABLE 1 PICOS Framework.

Criteria	Definition
Population	Patient receiving tooth autotransplantation No limitation to the patient's age, medical history and tooth type used for transplant
Intervention	Tooth autotransplantation of teeth No limitation to donor tooth type, root development status, reasons for autotransplantation, recipient site location and follow-up duration
Comparison	Comparison within tooth autotransplantation with respect to treatment protocols used, including (but were not limited to) any pre-, peri- or post-operative factors that could affect the prognosis or outcome of tooth autotransplantation, e.g. root development of donor teeth, clinician experience, surgical techniques and materials used, post-transplantation orthodontic treatment, etc. Comparison against other treatment options, that is fixed and removable prosthodontics, implants, orthodontic treatment and no treatment.
Outcome	Primary: • Success and survival rates • Pulp and periodontal outcomes • Factors affecting success and survival Secondary: • Aesthetic outcomes • Patient-reported outcomes, including acceptability towards treatment and impact on quality of life • Adverse effects/outcomes • Cost effectiveness
Study Design	Systematic review, with/without meta-analysis No restriction on language, publication year and follow-up timeframe

In patients receiving AT (Population),

a. What are the success and survival rates of AT (Outcome)?
b. What are the pre-, peri- or post-operative factors (Intervention and Comparison) that affect success and survival rates (Outcome)?
c. What are the pulp and periodontal outcomes associated (Outcome) with the procedure (Intervention)?
d. What are the success and survival rates (Outcome) of AT (Population/Intervention) compared to other treatment options (e.g. implants) (Comparison)?

The secondary research questions were:

1. What is the impact of AT on dentofacial aesthetics?
2. What is the impact of AT on quality of life (QoL)?
3. What is the level of acceptability towards AT compared to other treatment options?
4. Is tooth AT cost effective compared to other treatment options?

A systematic search was undertaken on 10 April 2022, and repeated on 25 September 2022, with no restrictions on publication year, language or follow-up timeframe. Five databases (PubMed, Embase, Scopus, Web of Science and The Cochrane Library) were searched. The top 10 journals with the highest impact factor in oral surgery, periodontology, endodontics, paediatric dentistry and dental traumatology were hand-searched for potentially suitable studies. The reference lists of included SRs were searched to identify additional studies. Searches for unpublished research and theses were carried out on the Open Grey and Google Scholar databases. Only SRs, which assessed the following but were not limited to: success, survival, aesthetics, acceptability towards treatment, QoL, were included. The search strategy can be found in Appendix S1: 1A. Reviewers were calibrated prior to study commencement.

Study selection was performed independently and in duplicate, followed by data extraction by two members (HN and BLT). This comprised title and abstract screening using Rayyan (https://www.rayyan.ai/),[12] followed by review of full-text manuscripts. The agreement between reviewers was evaluated using Cohen's kappa. A standardised pre-tested electronic data collection form was used to extract the necessary data from each eligible SR. Disagreements regarding study selection or data extraction were resolved through discussion with a third member (HJT) and biostatistician (SN) where relevant.

A narrative synthesis of the findings from the included studies, structured around pre-, peri- or post-operative factors that could affect the prognosis or outcome of AT was collated and tabulated. Mean values and range of success and survival rates were calculated from the values reported in all included studies. Pathological clinical and radiographic findings were also reported to support the aetiology of failed cases. Descriptive synthesis of the summary effect size and its 95% CI, heterogeneity between studies (I^2 or Cochran's Q) and small study effects (*p*-value of Egger's or Begg's test) from all the included meta-analyses were tabulated. Attempts were made to contact the authors of the SRs to clarify any missing or ambiguous data.

The degree of overlap in primary studies among all the included SRs was assessed and calculated using the corrected covered area (CCA) index. Citation matrices were developed in an Excel spreadsheet. CCAs were calculated using the GROOVE tool (Graphical Representation of Overlap for OVErviews).[13] The level of overlap was interpreted as follows: CCA values of 0–5 = slight; 6–10 = moderate; 11–15 = high; and >15 = very high.

Due to the variations in the research question among the included SRs and to avoid underestimating the degree of overlap, additional CCA analyses were calculated, specifically AT of:

1. open apex teeth
2. closed apex teeth
3. combination of teeth with both apex types and
4. canine teeth

If the overlap appeared to be high or very high among the reviews included in the MMA, data from the primary studies was extracted to minimise the overestimation of the results. If the CCA values were moderate or less, the estimates and its 95% CI reported in the included SRs were pooled together.

Identical meta-analyses were collated within each outcome measure. Meta-meta-analysis (MMA) was performed using a random-effects model and the restricted maximum likelihood (REML) method. Tests for overall effect were reported as *Z*-scores and $p < .05$ considered as statistically significant. The results were presented as forest plots, consisting of weighted compilation of all the survival rates and corresponding 95% CI reported by the included reviews. The degree of heterogeneity among the included meta-analyses was determined using Cochran's *Q* test ($p < .1$) and I^2 statistics. The 95% prediction interval (95% PI) for each MMA was planned to estimate whether they excluded null value, which further accounts for heterogeneity between the studies and specifies the uncertainty for the effect size that would be expected in future studies. If the number of included reviews in the MMA was >10, meta-bias assessment (publication bias) was planned using funnel plot and Egger's regression test. If needed, sensitivity analysis was also planned to provide unbiased estimate. All analyses were done using STATA version 17 (StataCorp, College Station).

For this umbrella review, the definition of success and survival (adapted from Kafourou et al. 2017)[3] were:

1. Success

i. Immature teeth: Pulp revascularisation following AT or successful endodontic treatment with good long-term prognosis.

ii. Mature teeth: Successful endodontic treatment in which the pulp was electively removed following AT.

iii. Favourable periodontal healing with either no evidence of external root resorption or where the resorption was effectively treated and controlled with endodontic treatment.

iv. Normal alveolar bone growth.

2. Survival: the presence of the tooth in its transplanted position at final follow-up visit regardless of the clinical and radiographic outcomes.

Two reviewers (HJT and ABH) independently assessed the quality of evidence using the AMSTAR 2 critical appraisal tool for SR.[14] The overall confidence in the AMSTAR 2 was rated through spotting of critical and non-critical weaknesses, where the overall rating was categorised as: high, moderate, low and critically low, respectively. Statistical input and any disagreements were resolved through discussion with a third author/biostatistician (SN). The overall score of each article was finally agreed upon by consensus.

3 | RESULTS

The electronic search yielded 1118 records after duplicate removal, of which 1100 articles were excluded after title and abstract evaluation. Eighteen articles were considered for full-text reading, following which two more were excluded.[15,16] The final search yielded one more SR, resulting in a total of 17 SRs.[2,4,6,7,17–29] These comprised 10 SRs with meta-analysis and seven without. Fifteen SRs[2,4,6,7,17,19–26,28,29] were published in international peer reviewed journals while two were Master's Thesis dissertations.[18,27] Sixteen SRs were published in the English language,[2,4,6,7,17,19–29] while one was published in Portuguese.[18] The search and screening process results, as well as reasons for exclusion of two articles are presented in detail in the PRISMA flowchart (Figure 1) and Appendix S1: 2A. The inter-examiner agreement (HN and BLT) was strong ($k = .72$).

Table 2 summarises the characteristics of each included SR. The number of databases used in each SR differed, with two SRs utilising only one database (PubMed),[2,18] while the majority searched at least three databases, with one SR searching up to a maximum of 13 databases.[6] The publication years of the primary articles included in the SRs ranged from 1968 to 2021, with six SRs limiting their search to 1990 onwards.[17–19,23,26,27] Seven SRs restricted the language of publication to English,[2,7,22,24,25,27,28] one SR restricted articles to English and Spanish,[26] one SR restricted to English and Portugese,[18] and one SR restricted to English, Spanish and Portugese,[17] with the remaining seven placing no restrictions.[4,6,19–21,23,29]

The authors of 12 SRs declared no conflict of interest, and of the four SRs which did not declare,[18,20,25,27] two were theses.[18,27] One SR reported that the authors had received grants but did not specify if there was competing interest related to the SR.[17] Six SRs reported on funding, with one being funded by a dental association,[28] two from the authors' institutions,[7,29] and three were self-funded/ received no external funding.[4,22,23]

A total of 151 unique primary studies published between 1968 to 2021 (Appendix S1: 3A) were included. The majority were case reports/series or cohort studies, with only two SRs reporting inclusion of clinical trials.[6,26] The number of primary articles included in each SR ranged from 5[19,20] to 38.[6]

The overall CCA value was moderate (6.25%). Additional CCA analyses for the reviews that evaluated similar parameters are represented in Table 3. The CCA value for the reviews based on AT of open apex teeth and canine teeth were found to be very high (15.24%) and high (14.7%), respectively. The detailed CCA analysis and the graphical representations are presented in Appendix S1: 3B,C.

Table 4 summarises the characteristics of papers included in each SR. The evaluated population involved both paediatric and adult patients across a wide age range (4.8[27]–79[18]years). A range of 264[2]–3295[18] teeth were included in each SR, with each transplanted tooth being the unit of analysis.

Three SRs solely evaluated maxillary canines,[4,19,20] one SR included only premolars,[2] and the remaining SRs evaluated different types of donor teeth. Four SRs evaluated teeth with open apices,[17,24,26,27] four with closed apices[4,7,19,25]; seven SRs reported a combination of open and closed apices[6,18,21–23,28,29] and two SRs[2,20] did not report the stage of root development. Five SRs[4,6,22,28,29] included primary studies in which the stage of root development was not reported. The Moorrees et al. classification of root development stages[30] was the most used classification (6/11). The follow-up duration for SRs ranged from one month[6,24] to 41 years.[17,23,24]

Table 5 summarises the reported definitions, success rates, survival rates and main conclusions of each SR. The overall success and survival rates reported ranged from 31–100% and 30.4%–100%, respectively. The one-, five- and 10-year survival rates ranged from 87%–100%,[7,18] 30.4%–100%,[7,18,24,25] and 59.6%–100%,[18,24,25] respectively. The definitions of treatment success and survival, as well as failure, were not standardised across all SRs, with some SRs providing a partial definition while others did not provide any definition. Hence, the figures reported should be interpreted with caution.

Meta-meta-analyses for the 5-year and 10-year survival rates of AT with open apices were performed. Two SRs were included in the MMA.[24,26] The CCA values for the two SRs were either moderate (CCA = 6.67% for 5-year) or had no overlap (CCA = 0% for 10-year; Table 3). Hence, the pooled data (effect estimate and 95% CI) reported in the reviews were extracted. The obtained estimates (95% CI) from MMA of 5-year and 10-year survival rates (Figures 2A,B) were 97.3% (95.6, 99.07) and 96.63% (93.6, 99.6), respectively, which were statistically significant ($p < .001$) and without significant heterogeneity (I^2 and $Tau^2 = 0$). As the MMAs only included two SRs, publication bias assessment, sensitivity analysis and estimation of 95% PI were not carried out. Analysis was not carried out for success and failure rates as neither was sufficiently reported nor defined clearly.

The pre-, intra- and post-operative factors, which could potentially affect prognosis of AT is presented in Appendix S1: 4A.

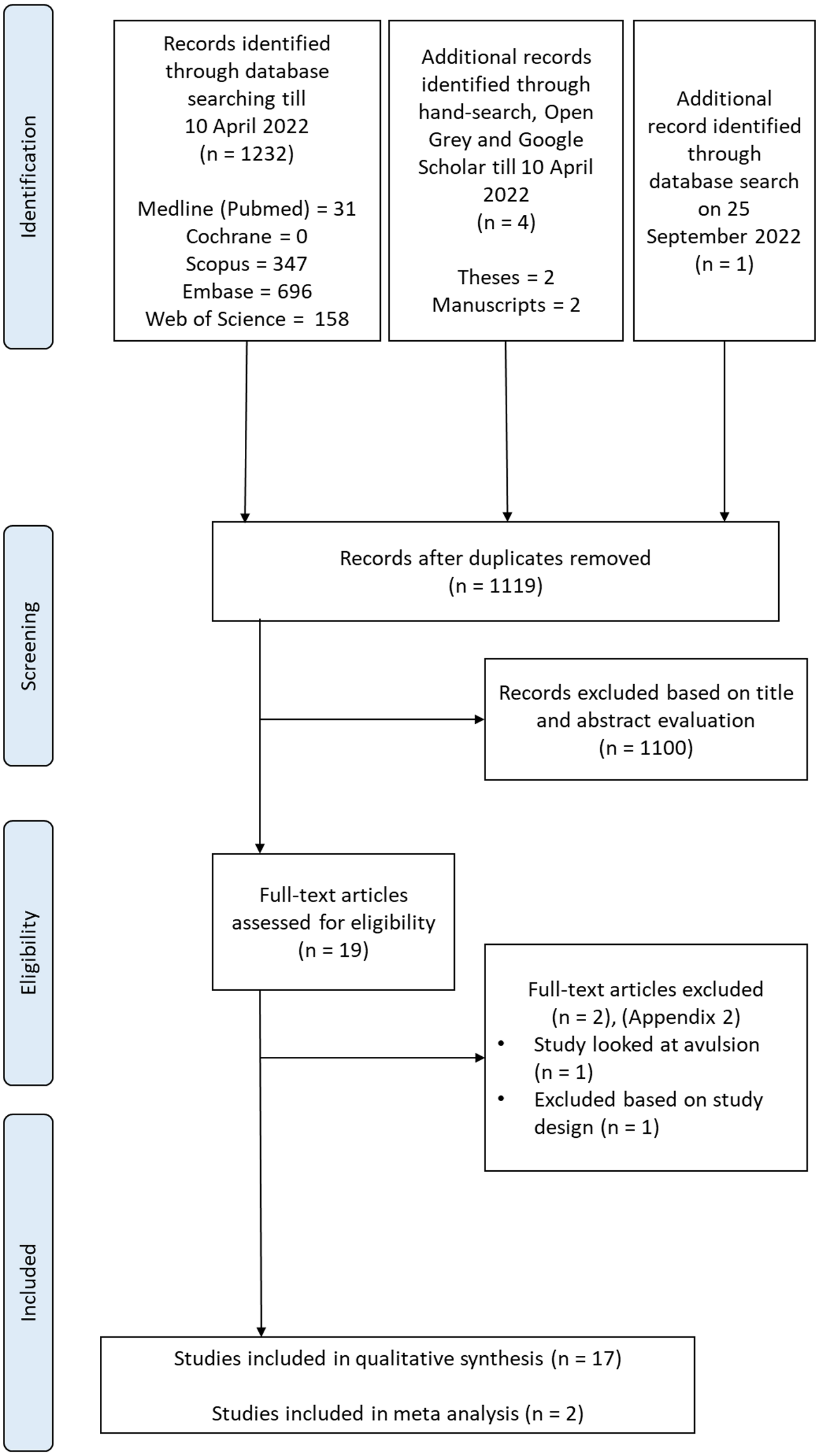

FIGURE 1 Preferred reporting items for systematic reviews and meta-analysis flowchart.

Analysis was not carried out as the data were neither sufficiently reported nor defined clearly in the included SRs. A narrative summary is presented below.

One SR evaluated the effects of patient-related factors (gender and age) on AT tooth extraction.[6] Females had more extractions of AT teeth than males (Relative Risk = 0.94, CI: 0.70–1.27, $p = .685$).

TABLE 2 Characteristics of Included Systematic Reviews.

Author/year/Country[a]	Study designs included in final analysis[b]	Included primary studies in systematic review: *N*	Included primary studies in systematic review: Publication range	Meta-analysis conducted	Risk of bias assessment tool used	Conflict of interest/ Funding source
Akhlef et al. 2017[2] Denmark	Case reports/ case series Cross-sectional Cohort studies	14	1978–2016	No	NR	Conflict of interest: None Funding: NR
Almpani et al. 2015[6] Greece	Case reports / case series Cohort studies Clinical trial	38	1978–2011	Yes Random-effects model (DerSimonian-Laird method) Risk ratios calculated to assess influence of factors on outcome of autotransplantation Subgroup analysis – mixed effect model	Downs and Black Scale[43]	Conflict of interest: None Funding: NR
Atala-Acevedo et al. 2017[17] Chile	Case reports / case series Cross-sectional Cohort studies	25	1990–2014	Yes Measure of effect: Odds ratio, 95% CI Random-effects model (DerSimonian-Laird method)	Effect Public Health Practice Project[47]	Conflict of interest: Yes, Contract research grant (Project no. CP15_00116, Instituto de Investigacion en Salud Carlos III, Spain) CONICYT/ MEC grant (Grant 800,140,042). Funding: NR
Barata 2020[18] Portugal	Case reports / case series Cohort studies	28	1990–2020	No	NR	Conflict of interest: NR Funding: NR
Bouchghel et al. 2022[19] Morocco	Case reports / case series Cohort studies	5	2011–2020	No	MINORS[39]	Conflict of interest: None Funding: NR
Chung et al. 2014[7] Taiwan	Case reports / case series Cohort studies	26	1968–2011	Yes Publication bias: regression asymmetry test (Egger et al 1997) Primary outcomes: multilevel Poisson regression Secondary outcomes: incidence rate ratio estimates calculated using the multilevel Poisson regression	Newcastle-Ottawa Scale[40]	Conflict of interest: None Funding: Support from the authors' institution
Grisar et al. 2018[4] Belgium	Case reports / case series Cohort studies	12	1983–2011	Yes Generalised linear mixed model for binary outcomes built using logit-link	MINORS[39]	Conflict of interest: None Funding: No external Funding
Grisar et al. 2021[20] Belgium	Case reports / case series	5	1983–2018	No	Murad RoB[44]	Conflict of interest: NR Funding: NR

TABLE 2 (Continued)

Author/year/Country[a]	Study designs included in final analysis[b]	Included primary studies in systematic review: N	Included primary studies in systematic review: Publication range	Meta-analysis conducted	Risk of bias assessment tool used	Conflict of interest/ Funding source
Larcerda-Santos et al. 2020[21] Brazil	Case reports / case series Cohort studies	10	1986–2019	No	MINORS[39]	Conflict of interest: None Funding: NR
Lucas-Taulé et al. 2022[22] Spain	Case reports / case series Case-controlled Cohort studies	24	1978–2019	Yes Meta-analysis of random-effects meta-regression model with a moderating variable of apex type and under random-effects approach	ROBINS-I (Risk Of Bias In Non-randomised Studies - of Interventions) [42]	Conflict of interest: None Funding: No external Funding
Machado et al. 2016[23] Brazil	Case reports / case series Cohort studies	6	1995–2012	Yes Events and total sample were collected to achieve a combined effect size of proportion for evaluation Fixed effect model	MINORS[39]	Conflict of interest: None Funding: provided by the authors
Rohof et al. 2018[24] the Netherlands	Case reports / case series Cross-sectional Case-controlled Cohort studies	32	1974–2014	Yes Weighted average rates per year Weighted average 1-, 5-, 10-year survival Random-effects model (DerSimonian-Laird method)	Newcastle-Ottawa Scale[40]	Conflict of interest: None Funding: NR
Ruano et al. 2016[25] United States of America	Cohort studies	7	1985–2012	Yes Random-effects meta-analysis (methods NR)	Newcastle-Ottawa Scale[40]	Conflict of interest: NR Funding: NR
Sicilia-Pasos et al. 2022[26] Spain/United States of America	Case reports / case series Cohort studies Clinical Trial	17	2010–2021	Yes Fixed effects method due to homogeneity obtained between studies, through Cochran's Q statistic	Joanna Briggs Institute[41]	Conflict of interest: None Funding: NR
Taimour 2018[27] Lithuania	Case reports / case series Case-controlled Cohort studies	28	2007–2017	No	NR	Conflict of interest: NR Funding: NR
Terheyden and Wüsthoff 2015[28] Germany	Case reports / case series Cohort studies	Total: 42; Specific to Autotransplantation: 11	Total: 1989–2014 Specific to Autotransplantation: 1991–2013	No	Modified US Agency for Healthcare Research and Quality Methods Guide[45]	Conflict of interest: Lecture fees and/or unrestricted research grants. No competing interests related to this systematic review Funding: German Association of Dental Implantology

(Continues)

TABLE 2 (Continued)

Author/year/Country[a]	Study designs included in final analysis[b]	Included primary studies in systematic review: N	Publication range	Meta-analysis conducted	Risk of bias assessment tool used	Conflict of interest/ Funding source
Verweij et al. 2017[29] the Netherlands	Case reports / case series Case-controlled Cohort studies	15	2001–2016	No	Case Report (CARE) checklist[46] MINORS[39] Cochrane handbook for systematic reviews of intervention	Conflict of interest: None Funding: Authors' institution

Abbreviations: MINORS, Methodological Index for Nnon-Randomized Randomised Studies; NR, not reported.

[a]Country of corresponding author.

[b]Refer to Appendix S1: 3A for list of primary studies.

Patients aged ≥20 years had more extraction of AT teeth than those aged <20 years (Relative Risk = 0.94, CI:0.68–1.28, p = .676).

Donor tooth-related factors evaluated included the type of donor tooth, donor tooth location and stage of root development. Three SRs evaluated the effect of donor tooth type.[6,17,22] Almpani et al. found more extractions in the canines than molar donor teeth (Relative Risk = 1.29, CI: 0.63–2.62; p = .482).[6] Atala-Acevedo et al. found more extraction in the molars than premolar donor teeth (Odds Ratio = 0.46; 95% CI:0.25–0.84; p = .790).[17] Lucas-Taulé et al. found among donor teeth with open apices, third molars had higher success (90.6 ± 3.5% >87.5 ± 3.2%, p = .534) and survival (99.7 ± 0.8% >95.5 ± 1.2%, p = .008) rates than premolars whilst for teeth with closed apices, there were no significant differences (p = .137) between canine (91.6 ± 3.3%), premolar (90.2 ± 9.8%) and molar (88.4 ± 2.6%) survival rates.[22] Two SRs assessed donor tooth location. Almpani et al. reported more extractions when the donor tooth was from the mandible than the maxilla (Relative Risk = 1.06, CI:0.18–6.23, p = .947).[6] Chung et al. reported both the 1-year and 5-year survival rates of anterior, premolar and molar donor teeth. The anterior donor teeth (1-year: 99.4%; 5-year: 96.9%) had the highest survival rate, while molars (1-year: 96.7%; 5-year: 84.3%) had the lowest survival rate.[7] No statistical comparison among groups was carried out. Three SRs reported better outcomes (i.e. better survival rates, fewer failures and extractions) for donor teeth with open apices than closed apices.[6,17,22] Regarding AT recipient site location, Almpani et al. found that there were more extractions after autologous transplantations compared to allogenic transplantations (Relative Risk = 1.32, CI:0.55–3.12; p = .533).[6] Atala-Acevedo et al. noted fewer failures in AT to maxillary sites than mandibular sites in the same patient (Odds Ratio = 0.38, CI:0.09–1.60; p = .780).[17]

The intra-operative factors evaluated include the use of a donor tooth replica, bone graft use, splint protocol (type and duration), antibiotic regimen, time of endodontic treatment post-AT. The use of a donor tooth replica enabled accurate positional planning, decreased surgical difficulty, extraoral time and risk of iatrogenic damage to the PDL of the donor tooth, potentially increasing success and survival rates.[29] One SR found that there were more extractions amongst AT teeth that had a bone graft (Relative Risk = 2.61, CI:0.48–14.23, p = .269).[6] Three SRs evaluated the type of splint and splinting duration.[6,7,24] Almpani et al. found that AT with wire-composite splints had more extractions than those with suture 'splints' (Relative Risk = 3.79, CI:1.09–12.63; p = .036).[6] This was based on one study in which the wire-composite splint was deemed as a rigid splint.[31] Conversely, in AT of teeth with complete root formation, Chung et al. found that those with wire splints had fewer teeth extracted than those with suture 'splints' (Incidence Risk Ratio = 0.8, CI:0.1–5.5).[7] The authors also found that for wire splints, longer splinting duration of >14 days had a lower failure rate than that of ≤14 days (Incidence Risk Ratio = 0.4, CI:0.1–2). The final study[24] reported that there were conflicting outcomes regarding the stabilisation techniques and also a lack of information regarding the splinting duration in the primary studies. Regarding the use of antibiotics, Chung et al.

TABLE 3 Corrected covered area analyses.

Category	No. of systematic reviews-(c)	No. of index publications (r)	Number of included primary studies (including double counting) –(N)	CCA value = (N-r)/(rc-r)	Interpretation of overlap
All the included reviews on AT	17[2,4,6,7,17–29]	151	302	6.25%	Moderate Overlap
Reviews on AT of Open apex teeth	4[17,24,26,27]	70	102	15.24%	Very high Overlap
Reviews on AT of Closed apex teeth	4[4,7,19,25]	42	50	6.35%	Moderate Overlap
Reviews combining both closed and open apex teeth	7[6,18,21–23,28,29]	95	131	6.32%	Moderate Overlap
Reviews on AT of Canine teeth	3[4,19,20]	17	22	14.71%	High Overlap
Reviews included in the meta-analysis of 5-year survival rate in AT of open apex teeth	2[24,26]	15	16	6.67%	Moderate Overlap
Reviews included in the meta-analysis of 10-year survival rate in AT of open apex teeth AT in open apex	2[24,26]	9	9	0%	No Overlap

Abbreviation: AT, autotransplantation.

found that patients who were not prescribed antibiotics had a higher rate of failure (Incidence Risk Ratio = 2.5, CI:0.9–7.2) than those who were prescribed antibiotics (regardless of whether pre- or post-operatively).[7] Conversely, Rohof et al. reported that there was insufficient information on the antibiotic regimen for a meta-analysis.[24] Regarding the timing of endodontic treatment (pre- or within 14 days post-transplant and >14 days post-transplant), Chung et al. reported comparable failure rates (Incidence Risk Ratio = 1, CI:0.2–5.2).[7]

None of the studies were able to evaluate the impact of the following factors on prognosis: operator experience, socket type (e.g. extraction socket or surgically prepared socket), ease of extraction of donor tooth, extra-alveolar time of donor tooth, management of donor tooth (e.g. storage medium, root surface treatment).

Regarding post-AT factors, one SR found that the presence of ankylosis was related to higher tendency for tooth loss (Odds Ratio = 10.97, CI:0.73–165.2, $p = .185$).[17] None of the studies were able to evaluate if the type of orthodontic intervention (e.g. extrusion vs. rotation), and time lapse between AT and orthodontic intervention affected success and survival outcomes.

Appendix S1: 4B summarises the definitions, pulp and periodontal outcomes of each SR. Three SRs[4,6,24] reported both pulp and periodontal outcomes, and three SRs[7,22,23] reported periodontal outcomes only. The remaining SRs[2,18–21,25–29] did not report pulp and periodontal outcomes. Due to different methods of reporting pulp and periodontal outcomes among the SRs, MMA could not be carried out. The factors which could affect pulp and periodontal outcomes are presented in Appendix S1: 4C. Analyses for various factors affecting the outcomes were not carried out as the data were presented differently among the SRs. A narrative summary is presented below.

The pulp outcomes evaluated were pulp canal obliteration (PCO) and pulp necrosis (PN).[6] Two factors were associated with PCO:

1. Suture 'splint' rather than rigid splint (Relative Risk = 0.8, CI:0.7–1.0, $p = .04$) and
2. Absence of orthodontic treatment (Relative Risk = 0.8, CI:0.7–1.0, $p = .007$)

Five patient-related factors were associated with PN:

1. Second premolars compared to first premolars (Relative Risk = 2.6, CI:1.5–4.4; $p < .001$).
2. Canines compared to molars (Relative Risk = 1.9, CI: 1.1–3.4; $p = .028$).
3. AT of teeth with closed apices compared to open apices (Relative Risk = 0.1, CI:0.1–0.2; $p < .001$).
4. Allogenic transplantation compared to autogenous transplantation (Relative Risk = 0.4, CI:0.3–0.7; $p = .001$) and
5. Female patients compared to male patients (Relative Risk = 1.5, CI:1.0–2.1; $p = .037$).

The periodontal outcomes reported were external inflammatory (infection-related) resorption (EIR) and external replacement (ankylosis-related) resorption (ERR). Two SR reported on

TABLE 4 Characteristics of primary studies included into systematic reviews.

	Patient characteristics (primary studies, *n*=)		Age in years			Donor teeth			Root development reported		Follow-up duration (months)	
Author/year	Sample	Gender	Mean Age/ Range of Mean Age	Age Range	Total teeth (primary studies, *n*=)	Type	Sample	Primary studies, *n*=	Stage (Open/ Closed/ Combination[b])	Classification	Mean/Range of mean (primary studies, *n*=)	Range (primary studies, *n*=)
Akhlef et al. 2017[2]	NR	NR	NR	NR	264 (*n*=11/14)	Premolar	264	11/14	NR	NR	18 – 194.4 (*n*=7/14)	6 – 264 (*n*=6/14)
Almpani et al. 2015[6]	2518 (*n*=37/38)	Male 979[a] (*n*=27/38) Female 1387[a] (*n*=27/38)	17.3 – 39.8 (*n*=32/38)	10 – 75 (*n*=24/38)	2953 (*n*=38)	Canine	161	5/38	Open (*n*=8/38)	Moorees	1 – 6.3 (*n*=22/38)	1 – 216 (*n*=28/38)
						Premolar	529	6/38	Closed (*n*=8/38)			
						Molar	907	14/38				
						Mixed[c]	1356	13/38	Combination (*n*=18/38)			
									NR (*n*=4/38)			
Atala-Acevedo et al. 2017[17]	NR	NR	NR	6.6 - 39 (*n*=24/25)	1752 (*n*=25/25)	Incisor	14	3/25	Open	Moorees	75	12 – 492
						Canine	67	2/25				
						Premolar	562	10/25				
						Molar	463	10/25				
						Supernumerary	2	1/25				
						Mixed[c]	644	6/25				
Barata 2020[18]	2725 (*n*=28/28)	NR	10 – 44.1 (*n*=25/28)	7 – 79 (*n*=27/28)	3295[a] (*n*=28/28)	Incisor	49	7/28	Open (*n*=8/28)	NR	99.48	15.6 – 316.8
						Canine	529	8/28	Closed (*n*=8/28)			
						Premolar	1172	21/28				
						Molar	1176	14/28	Combination (*n*=12/28)			
						Supernumerary	2	1/28				
						Mixed[c]	366	1/28				
Bouchghel et al. 2022[19]	417 (*n*=5/5)	NR	13 – 42.1 (*n*=4/5)	9 – 51 (*n*=5/5)	455 (*n*=5/5)	Canine	455	5/5	Closed	NR	28 – 318 (*n*=5/5)	NR
Chung et al. 2014[7]	NR	NR	NR	NR	1264 (*n*=26)	Incisor	9	3	Closed	NR	12 – 120 (*n*=20)	0 – 333.6 (*n*=18)
						Canine	475	16				
						Premolar	102	7				
						Molar	469	10				
						Tooth type not reported	210	3				
Grisar et al. 2018[4]	370 (*n*=8)	Male 94 (*n*=5/12) Female 181 (*n*=5/12)	19.8 – 36.5 (*n*=9)	11 – 76 (*n*=8)	783 (*n*=12)	Canine	783	12/12	Closed (*n*=3)	NR	24–174 (*n*=12)	NR
									NR (*n*=9)			

TABLE 4 (Continued)

Author/year	Patient characteristics (primary studies, n=): Sample	Gender	Age in years: Mean Age/Range of Mean Age	Age Range	Total teeth (primary studies, n=)	Donor teeth: Type	Sample	Primary studies, n=	Root development reported: Stage (Open/Closed/Combination[b])	Classification	Follow-up duration (months): Mean/Range of mean (primary studies, n=)	Range (primary studies, n=)
Grisar et al. 2021[20]	302 (n=5/5)	Male 112 (n=5/5) Female 190 (n=5/5)	22.5 (n=5/5)	11 – 76 (n=5/5)	346 (n=5/5)	Canine	346	5/5	NR	NR	18 – >240 (n=5/5)	NR
Larcerda-Santos et al. 2020[21]	715 (n=10/10)	Male 340[a] (n=10/10) Female 493[a] (n=10/10)	12.3 – 29.1 (n=10/10)	9 – 58.1 (n=10/10)	934[a] (n=10/10)	Incisor	43	3/10	Open (n=2/10)	Moorrees	19.2 – >108	NR
						Premolar	579	8/10	Closed (n=2/10)			
						Molar	282	5/10				
									Combination (n=6/10)			
Lucas-Taulé et al. 2022[22]	Open Apex 394 (n=8/24)	NR	Overall: 25.2 ± 12.3	7 – 75 (n=22/24)	Overall 1516 (n=24/24)	Open Apex			Open (n=10/24)	NR	Open 41.52 ± 19.44	Open 6 – 216
	Closed Apex 338 (n=7/24)		Open: 15.7 ± 4.6		Open 987 (n=15/24)	Premolar	752	10/24	Closed (n=7/24)			
			Closed: 36.9 ± 8.3			Molar	235	6/24			Closed 68.04 ± 25.44	Closed 12-216
						Closed Apex			Combination (n=5/24)			NR 15 – 24 (n=2/24)
	NR 72 (n=2/24)				Closed 453 (n=12/24)[a]	Incisor	1	1/24				
						Canine	70	3/24	NR (n=2/24)			
					NR 76 (n=2/24)	Premolar	99	6/24				
						Molar	242	6/24				
						Root Development NR						
						Molar	76	2/24				
Machado et al. 2016[23]	131 (n=4/6)	NR	NR	8 – 46 (n=4/6)	274 (n=6/6)	Incisor[d]	7	2/6	Open (n=3/6)	Reported as 1/2, 3/4, complete root formation	110.4 – 316.8 (n=3/6)	72 – 492 (n=6/6)
						Canine	69	1/6	Closed (n=1/6)			
						Premolar[d]	178	6/6	Combination (n=2/6)			
						Molar[d]	8	2/6				
						Supernumerary	2	1/6				

(Continues)

TABLE 4 (Continued)

	Patient characteristics (primary studies, n=)				Donor teeth				Root development reported		Follow-up duration (months)	
			Age in years									
Author/year	Sample	Gender	Mean Age/ Range of Mean Age	Age Range	Total teeth (primary studies, n=)	Type	Sample	Primary studies, n=	Stage (Open/ Closed/ Combination[b])	Classification	Mean/Range of mean (primary studies, n=)	Range (primary studies, n=)
Rohof et al. 2018[24]	NR	NR	10 – 18[e] (n=14/32)	8 – 29 (n=14/32)	1891[a] (n=32/32)	Incisor	3	2/32	Open	Moorrees	12 – 317 (n=26/32)	1 – 492 (n=30/32)
						Canine	9	2/32				
						Premolar	1266	18/32				
						Molar	425	14/32				
						Supernumerary	2	1/32				
						Mixed[c]	186	5/32				
Ruano et al. 2016[25]	1187 (n=7/7)	Male 494[a] (n=6/7) Female 621[a] (n=6/7)	15.2 – 40[e] (n=7/7)	NR	1185 (n=7/7)	Incisor	3	2/7	Closed	NR	NR	2 – 132 (n=7/7)
						Canine	155	5/7				
						Premolar	235	4/7				
						Molar	533	6/7				
Sicilia-Pasos et al. 2022[26]	165 (n=5/17)	NR	NR	NR	610 (n=17/17)	Premolar	158	4/17	Open	Moorrees	NR	NR
						Molar	195	5/17				
						Mixed[c]	116	3/17				
						Tooth type not reported	141	5/17				
Taimour 2018[27]	321 (n=28/28)	NR	11.6	4.8[a] – 18	401 (n=28/28)	Incisor	10	5/28	Open	Moorrees et al 1963, modified by Kristerson 1985	51.12	6 – 252
						Canine	3	2/28				
						Premolar	338	19/28				
						Molar	47	9/28				
Terheyden and Wüsthoff 2015[28]	787 (n=11)	NR	NR	NR	917 (n=11)	Premolar	162	1/11	Combination (n=3)	NR	NR	1 – 316.8 (n=11)
						Molar	49	1/11				
						Tooth type not reported	706	10/11	NR (n=8)			

TABLE 4 (Continued)

Author/year	Patient characteristics (primary studies, n=) Sample	Gender	Age in years: Mean Age/ Range of Mean Age	Age in years: Age Range	Total teeth (primary studies, n=)	Donor teeth: Type	Donor teeth: Sample	Donor teeth: Primary studies, n=	Root development reported: Stage (Open/ Closed/ Combination[b])	Root development reported: Classification	Follow-up duration (months): Mean/Range of mean (primary studies, n=)	Follow-up duration (months): Range (primary studies, n=)
Verweij et al. 2017[29]	NR	NR	NR	NR	Case Reports 10 (n=9)	Case Reports			Case Report	NR	NR	Case report 6-48 (n=9)
						Incisor	1	1	Open (n=4)			
						Premolar	5	5	Closed (n=5)			
						Molar	3	2				
						Mesiodens	1	1				
					Clinical studies[f] 444 (n=6)	Clinical Studies[f]			Clinical studies[f]			Clinical studies[f] 2–90 (n=3)
						Incisor	1	1	Open (n=2)			
						Canine	1	1	Combination (n=1)			
						Premolar	65	3	NR (n=3)			
						Molar	355	3				
						Tooth type not reported	22	1				

Abbreviations: NR, Not Reported.

[a]Discrepancy in values reported in this study.

[b]Combination refers to teeth with both closed and open root apices.

[c]The studies report the types of donor tooth used for autotransplantation, for example incisors, canines and/or premolars. However, they do not provide a breakdown of the sample for each tooth type.

[d]Calculated with reference to original primary studies.

[e]Study did not report whether the age presented here is mean or median.

[f]Clinical studies refer to case series and cohort studies.

TABLE 5 Success and Survival of Autotransplantation.

Author/year	Outcome measured and definition (if applicable)	Main result (primary studies, *n*=)	Meta-analysis (primary studies, *n*=)	Main conclusion	Adverse events
Akhlef et al. 2017[2]	Success: not defined Survival: not defined	Reported success ($n = 9/14$): • 70%–100% Reported survival ($n = 11/14$): • 93–100% • weighted mean: 96.7% • median: 100%	Not carried out	Premolars AT to the anterior maxilla have a high survival rate. Adequate aesthetic results and patient satisfaction have been reported but the level of evidence is low and additional studies is required.	NR
Almpani et al. 2015[6]	Success: not defined Survival failure: The need to extract the tooth, due to untreatable clinical complications	Reported success ($n = 18/38$): • 62%–100% Reported survival ($n = 34/38$): • 62%–100%	Success ($n = 17$): • 85.4% (CI: 80.9–89.9), $I_2 = 86\%$ Survival ($n = 15$): • 92.2% (CI: 89.1–95.3), $I_2 = 88\%$	The need to extract an AT is smaller than 10%, although existing evidence precludes accurate estimation. The stage of root development of the donor teeth influence negative outcomes like ankylosis, pulp necrosis, root resorption, and therefore, the success of AT. The small number of the contributing studies, their methodological limitations and the heterogeneous results reported prevent drawing of conclusions.	NR
Atala-Acevedo et al. 2017[17]	Success: Presence of tooth in the mouth without ankylosis or inflammatory root resorption, normal mobility and continuation of root development in the period reported in the included studies, minimum of a 12-month follow-up Survival: permanence of the tooth in the mouth in the duration reported in the included studies	Reported success ($n = 25/25$): • 61.9%–100% Reported survival ($n = 20/25$): • 88%–100%	Success ($n = 17$): • 89.68% (CI: 86.77–92.59), $I_2 = 64.6\%$ Survival (n = 15): • 98.21% (CI: 96.99–99.44), $I_2 = 25.3\%$	The overall success rate and survival were high, despite the methodologic limitations of the included studies. Further study is needed of the prognostic factors that influence the success of AT with an open apex (e.g. degree of root formation, influence of anatomy and number of roots, and surgical protocol).	NR
Barata 2020[18]	Success: not defined Survival: not defined	Reported success: Overall ($n = 15/28$): • 57.2%–92.5% • Mean: 79.24% Reported survival: Overall ($n = 27/28$): • 67.9%–100% • Mean: 91.48%. 1-year ($n = 19/28$): • 87%–100% • Mean: 98.33%. 5-year ($n = 13/28$): • 81.4%–100% • Mean: 91.94%. 10-year ($n = 8/28$): • 70.5%–97.5% • Mean: 88.95%	Not carried out	AT have success and survival rates and can be considered a treatment option for tooth replacement, especially for growing patients.	NR

TABLE 5 (Continued)

Author/year	Outcome measured and definition (if applicable)	Main result (primary studies, *n*=)	Meta-analysis (primary studies, *n*=)	Main conclusion	Adverse events
Bouchghel et al. 2022[19]	Success: Percentage of transplanted teeth still present and functioning well at the time of recall Survival: Percentage of transplanted maxillary canine present during the observation period	Reported success and survival with mean follow-up <5 years ($n = 2/5$) • Success: 68%, 74% • Survival: 100%, 96% Reported success and survival with mean follow-up >5 years ($n = 3/5$) • Success ($n = 1$): 38% • Survival ($n = 3$): 83%, 67%, 97%	Not carried out	With proper indication, AT of maxillary canines, with closed apices, as a suitable treatment option. The literature is deficient in high-quality clinical studies. Standardisation is needed for clinical assessment parameters, clinical benefits, aesthetic outcomes, risks of orthodontic movement and quality of life of patients with AT.	NR
Chung et al. 2014[7]	Survival: not defined Failure: loss of the AT during the observation period	Survival rate with mean follow-up of: • ≥1-year ($n = 2/26$): 88.9%, 100% • ≥2-year ($n = 6/26$): 89.3%–100% • ≥3-year ($n = 5/26$): 50%–95.7% • ≥4-year ($n = 4/26$): 85.1%–100% • ≥5-year ($n = 9/26$): 30.4%–96.9%	Survival (25 studies) 1-year: • Total: 98% (CI: 96.8–98.8) 5-year: • Total: 90.5% (CI: 84.9–94.1)	AT with complete root formation has rare failure, infection-related root resorption and ankylosis rate. The absence of systemic antibiotic therapy, suture splinting method, wire splinting for ≤14 days and posterior donor tooth were influencing factors, which aggravated failure such as external inflammatory resorption and ankylosis. More research is required based on a greater amount of RCTs.	NR
Grisar et al. 2018[4]	Success: Percentage of AT still present and functioning well at the time of recall Failure: Loss of the transplanted maxillary canine during the observation period	Reported success: • 2–5 years ($n = 8/12$): 62%–100% • 5 years ($n = 4/12$): 83%–96.7%	Success: • 2–5 years ($n = 8$): 87.5% (CI: 77.2–93.6) • 5 years ($n = 4$): 88.2% (CI: 81.4–92.7)	AT of maxillary canines is a legitimate treatment option with proper indication with good overall long-term outcome. Future studies should be based on larger samples and RCTs, and focus on indications for AT of maxillary canines, long-term clinical success parameters, revisit surgical techniques, 3D planning, aesthetic results, and patient satisfaction.	NR
Grisar et al. 2021[20]	Success: Presence of the canine in the tooth-arch	Reported success: • Autotransplantation ($n = 4/5$): 89.5%, 280/313 • Apicoectomy ($n = 1/5$): 90.9%, 30/33	Not carried out	Apicoectomy and AT may be considered as alternative treatment modalities for maxillary canine impaction even though there is insufficient evidence for conclusions on the efficiency of both techniques.	NR

(Continues)

TABLE 5 (Continued)

Author/year	Outcome measured and definition (if applicable)	Main result (primary studies, *n*=)	Meta-analysis (primary studies, *n*=)	Main conclusion	Adverse events
Larcerda-Santos et al. 2020[21]	Success: not defined Survival: not defined	Reported success (n = 10/10): • 31%–100% Reported survival (n = 10/10): • 60%–100%	Not carried out	AT is suitable in patients who needed orthodontic movement. There was an increase in root resorption influenced by orthodontics, but without impacting on the general long-term results. Bone and periodontal tissue are not affected by orthodontics. The patient's aesthetic satisfaction was not evaluated. The quality evidence was medium due to the methodological problems, risk of bias, and significant heterogeneity in the evaluated studies.	NR
Lucas-Taulé et al. 2022[22]	Success: not defined Survival: not defined	Reported success: • Open (n = 8/24): 82%–100% • Closed (n = 3/24): 83.33%, 88%, 95.85% • Not defined (n = 2/24): 86%, 94.73% Reported Survival: • Open (n = 12/24): 88%–100% • Closed (n = 10/24): 81.4%–98% • Not defined (n = 2/24): 94.73%, 98.24%	Success: • Overall (n = 13): 89.4 ± 1.55%, CI 0.864–0.925, I^2 = 42.5% • Open (n = 8): 88.6 ± 2.1%, I^2 = 46.5% • Closed (n = 3): 90.9 ± 3.5%, I^2 = 55% • Difference between closed and open apex group was not significant (p = .564) Survival: • Overall (n = 22): 95.9 ± 0.8%, CI 0.945–0.975, I^2 = 52.7% • Open (n = 12): 96.9 ± 1%, CI: 0.95–0.989, I^2 = 61.8% • Closed (n = 10): 93 ± 1.7%, CI: 0.898–0.962, I^2 = 46.1% • Difference between closed and open apex group was not significant (p = .052)	AT is a viable treatment option with high survival and success rates after a mean follow-up of 4 years. In general, open apex teeth have higher survival rate and lower complication rates (e.g. ankylosis) compared to closed apex teeth. However, similar outcomes were observed in premolars regardless of apex type.	
Machado et al. 2016[23]	Survival Rate: Percentage of AT still present at the time of examination over the total number of AT	Reported survival (n = 4/6): • 75.3%–91%	Survival, effect size (n = 4): • 81% (CI: 73.8–86.6) I_2 = 31%	An excellent survival rate (81%), after a follow-up period of at least 6 years, was observed. Ankylosis (4%) and root resorption (4%) affected the prognosis of the transplant. The absence of RCTs may have limited the power of this investigation.	NR

TABLE 5 (Continued)

Author/year	Outcome measured and definition (if applicable)	Main result (primary studies, *n*=)	Meta-analysis (primary studies, *n*=)	Main conclusion	Adverse events
Rohof et al. 2018[24]	Success: Presence of AT without ankylosis or inflammatory root resorption, normal mobility and continuation of root development during the follow-up period Survival: Tooth presence during the follow-up	Success ($n = 23/32$): • 61.1%–100% Survival: • Overall ($n = 28/32$): 75%–100% • 5-year ($n = 11/32$): 88.9%–100% • 10-year ($n = 6/32$): 83.3%–100%	Weighted estimated yearly success rate (n = 23): 96.6% (CI: 94.8–97.8), $I_2 = 0\%$ Weighted survival rate: • Overall survival per year ($n = 24$): 98.2% (CI: 96.4–99.1), $I_2 = 56.8\%$ • 1-year ($n = 26$): 97.4% (CI: 96.2–98.2), $I_2 = 0\%$ • 5-year ($n = 11$): 97.8% (CI: 95–99), $I_2 = 19.6\%$ • 10-year ($n = 6$): 96.3% (CI: 89.8–98.7), $I_2 = 56.8\%$	AT with immature root could be considered as an option for tooth replacement. The survival and success rates were high and complications (ankylosis, root resorption and pulp necrosis) were low. Premolars were slightly preferred over molars as donor teeth. Existing evidence on prognostic factors such as stage of root formation, postsurgical stabilisation methods, and orthodontic treatment is insubstantial to merit a firm conclusion.	NR
Ruano et al. 2016[25]	Success: not defined Survival: not defined	Reported success ($n = 4/7$): • 57.5%–88% Reported survival ($n = 7/7$): • 5-year: 76.2%–88.3% ($n = 5$) • 10-year: 59.6%, 75.3% ($n = 2$)	Weighted mean of success and survival rate with ≥5 years follow- up: • Success ($n = 5$): 75.6% (CI: 60.4–86.3), $p = .36$ • Survival: ($n = 6$): 82.1% (CI: 77.1–86.2), $p = .51$	A 5-year survival rate and success rate of this procedure was 82.1% and 75.6%, respectively.	NR
Sicilia-Pasos et al. 2022[26]	Success: not defined Survival: not defined	Reported success ($n = 9/17$): • 70.6%–100% Reported survival ($n = 10/17$): • 89.4%–100%	Survival: • Overall ($n = 14$): 97.9% (CI: 96.2–99.6), $I_2 = 0\%$ • 1-year (n = 11): 98% (CI: 96.1–99.9), $I_2 = 0\%$ • 2-year ($n = 9$): 97% (CI: 94.4–95.5), $I_2 = 0\%$ • 5-year ($n = 5$): 95.9% (CI: 92–99), $I_2 = 0\%$ • 10-year ($n = 3$): 96.9% (CI: 93–101), $I_2 = 0\%$	AT is an option for the rehabilitation of tooth loss in patients, especially in those who are still in a growth period. It is a safe and reliable procedure due to a low complication rate and high 10-year survival rate	NR

(Continues)

TABLE 5 (Continued)

Author/year	Outcome measured and definition (if applicable)	Main result (primary studies, *n*=)	Meta-analysis (primary studies, *n*=)	Main conclusion	Adverse events
Taimour 2018[27]	Success: (1) Pain-free transplant (2) No percussion sensitivity (3) Positive cold test (6 months post-surgery) (4) Normal chewing, (5) Grade-I tooth mobility (6) Radiographs: continuous root development (crown:root ratio <1, normal lamina dura), pulp canal obliteration, no progressive root resorption, no pathologies (6-9 month post-surgery): ankylosis or any type of root resorption, new bone regeneration around transplant, normal healing of recipient alveolus (3 month post-surg.) during oral examination- normal periodontal tissues: depth of sulcus<3 mm, gingival contour and gingival colour Survival: presence of the AT during the follow-up period (>0.5 year) with any complication that could be treated without leading to loss.	Reported success rate: 100% ($n = 18/28$) 80%–96% ($n = 8/28$) 60%, 73% ($n = 2/28$) Reported survival rate: 100% ($n = 25/28$) 87%–97.2% ($n = 3/28$)	Not carried out	AT has a high success and survival rates and is predictable as any other conventional treatments. If failure occurs, AT could serve as a temporary solution preserving bone and soft tissue dimensions until skeletal maturity for implant placement.	NR
Terheyden and Wüsthoff 2015[28]	Success: No reports of ankylosis or severe root resorption, infection or mobility Survival: Tooth/implant/prosthesis was present in the oral cavity	Reported success ($n = 7/11$): 44%–96% Reported survival ($n = 11/11$): 87%–100%	Not carried out	Implants yielded the best results, however, not in children younger than 13 years. AT and deciduous teeth have low annual failure rates and are appropriate treatments in children and adolescents at low cost. Conventional prosthetics had lower survival/success rates than the other options. Due to heterogeneity and low number of studies, patient-reported outcomes in this review have to be interpreted with caution.	NR
Verweij et al. 2017[29]	Success: not defined Survival: not defined	Case Reports ($n = 9/9$): 10/10 AT survived Reported success and survival rates of 3D AT in clinical studies (case series and cohort studies; $n = 6$)[a]: • Success: 80%–91.1% • Survival: 95.5%–100%	Not carried out	3D AT is an effective treatment option for tooth replacement. Producing individualised tooth models by cone beam computed tomography and rapid prototyping can minimise the risk of iatrogenic damage to the periodontal ligament of the donor tooth. This could contribute to an increase in success and survival rates. The studies in this review have a low level of evidence and high risk of bias.	NR

Abbreviations: 3D, Three-dimensional, AT, Autotransplantation; CI, 95% confidence interval; NR, Not reported; RCTs, Randomised Clinical Trials.

[a]Discrepancies noted between main text and tables in systematic reviews.

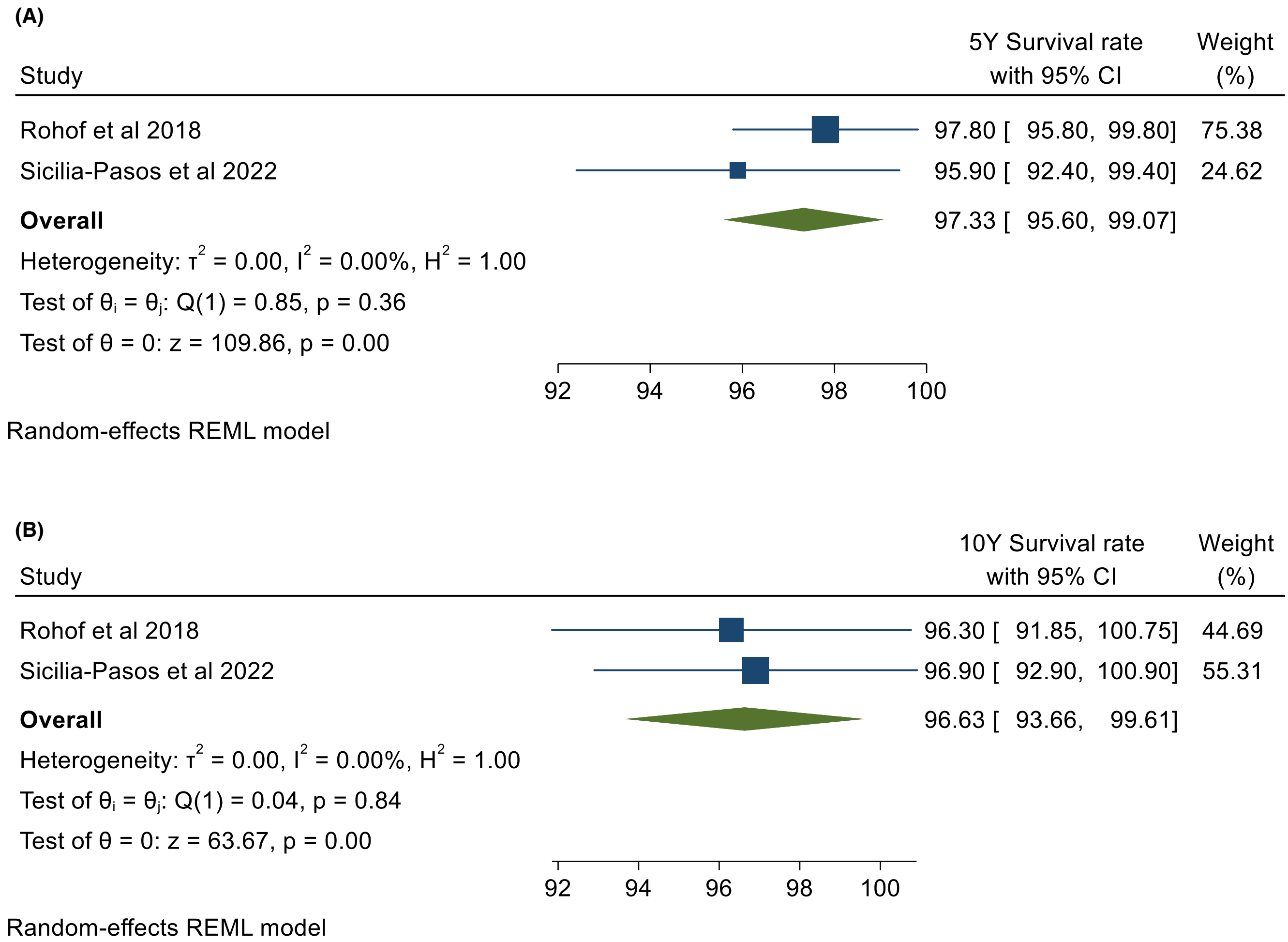

FIGURE 2 (A) Forest plot for 5-year survival rate of autotransplanted teeth with open apex. (B) Forest plot for 10-year survival rate of autotransplanted teeth with open apex.

pre-operative factors associated with EIR.[6,22] Almpani et al. identified two factors:

1. Teeth with closed apices compared to open apices (Relative Risk = 0.2, CI:0.1–0.3; $p < .001$) and
2. Second premolars compared to first premolars (Relative Risk = 2.0, CI:1.1–3.7; $p < .024$).[6]

Lucas-Taulé et al. noted higher rates of EIR in premolar than in third molars for both open ($2.9 \pm 0.7\% > 2.6 \pm 2.5\%$, $p = .714$) and closed apices ($20.7 \pm 4.8\% > 6.8 \pm 3.9\%$, $p = .0035$).[22] In terms of treatment-related factors, Chung et al. found that endodontic treatment after post-operative day 14 (Incidence Risk Ratio = 2, CI:0.2–9.3) and patients who were not prescribed antibiotics (Incidence Risk Ratio = 1.4, CI:0.2–8.9) were associated with a higher rate of EIR than when endodontic treatment was done either pre-operatively, within 14 days post-operatively or extra-orally or when patients prescribed antibiotics, respectively.[7]

Two SRs looked at pre-operative factors and found that ERR was more common in teeth with closed apices than open apices.[6,22] Lucas-Taulé et al. further analysed their data based on tooth type and found significantly different ERR rates between premolars with closed and open apices ($22.1 \pm 0.7\% > 4.3 \pm 0.8\%$, $p = .001$) but not between molars ($3.8 \pm 2\% > 2.7 \pm 1.5\%$, $p = .660$).[22] One SR assessed splint type and found that those with wire splints had higher ankylosis rates than those with suture 'splint' (Incidence Risk Ratio = 3, CI: 0–607.9).[7]

Two SRs compared AT against other treatment options (Appendix S1: 4D).[20,28] Grisar et al. compared AT and apicoectomy for the management of impacted maxillary canines.[20] Based on five case series, the number of successful outcomes versus teeth that were extracted were similar. Terheyden and Wüsthoff compared outcomes (success and survival) of AT against implants, conventional prosthetics and preservation of deciduous teeth at tooth/implant- and patient-level.[28] Implants had the highest level of success at both levels, followed by AT, conventional prosthetics and preservation of deciduous teeth. Autotransplantation had slightly higher survival rates than implants, followed by preservation of deciduous teeth and conventional prosthetics at the tooth/implant-level. However, at the patient-level, implants had the highest survival, followed by AT, preservation of deciduous teeth and conventional prosthetics.

TABLE 6 Risk of Bias Assessment.

	AMSTAR 2								
Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9 RCT
Akhlef et al. 2017[2]	Yes	No	No	No	No	No	No	No	Includes only NRSI
Almpani et al. 2015[6]	Yes	Partial Yes	No	Partial Yes	No	Yes	No	Partial Yes	Partial Yes
Atala-Acevedo et al. 2017[17]	Yes	Partial Yes	No	Partial Yes	Yes	Yes	Yes	Partial Yes	Includes only NRSI
Barata 2020[18]	Yes	No	No	No	No	No	No	No	Includes only NRSI
Bouchghel et al. 2022[19]	Yes	Yes	No	Partial Yes	Yes	Yes	No	Partial Yes	Includes only NRSI
Chung et al. 2014[7]	Yes	Partial Yes	No	Partial Yes	Yes	Yes	No	Partial Yes	Includes only NRSI
Grisar et al. 2018[4]	Yes	Yes	No	Partial Yes	Yes	Yes	No	Partial Yes	Includes only NRSI
Grisar et al. 2021[20]	Yes	Yes	No	Partial Yes	Yes	Yes	No	Partial Yes	Includes only NRSI
Larcerda-Santos et al. 2020[21]	Yes	Yes	Yes	Partial Yes	Yes	Yes	No	Partial Yes	Includes only NRSI
Lucas-Taulé et al. 2022[22]	Yes	Partial Yes	No	Partial Yes	Yes	Yes	No	Partial Yes	Includes only NRSI
Machado et al. 2016[23]	Yes	Yes	No	Partial Yes	Yes	Yes	No	Partial Yes	Includes only NRSI
Rohof et al. 2018[24]	Yes	Partial Yes	Yes	Partial Yes	Yes	Yes	No	Partial Yes	Includes only NRSI
Ruano et al. 2016[25]	Yes	Partial Yes	No	Partial Yes	No	No	No	Partial Yes	Includes only NRSI
Sicilia-Pasos et al. 2022[26]	Yes	Partial Yes	No	Partial Yes	No	Yes	No	Partial Yes	Includes only NRSI
Taimour 2018[27]	Yes	No	No	No	No	No	No	Partial Yes	Includes only NRSI
Terheyden and Wüsthoff 2015[28]	Yes	Partial Yes	No	Partial Yes	Yes	No	No	Partial Yes	No
Verweij et al. 2017[29]	Yes	Partial Yes	No	Partial Yes	Yes	No	No	Partial Yes	Includes only NRSI

Abbreviations: MA, meta-analysis; NRSI, non-randomized randomised studies of interventions; RCT, randomizeised controlled trials.

The secondary outcomes reported were aesthetic outcomes and patient satisfaction. Only one SR evaluated aesthetic outcomes.[2] This was based on four primary studies.[32–35] A favourable aesthetic outcome (e.g. colour, anatomy, position) was reported objectively[32,33] and subjectively (patients' and parents' opinion).[32–35] One SR reported on patient satisfaction towards various treatment options.[28] The weighted mean percentage were: orthodontic closure (66.5%), AT (75%), conventional prosthetics (76.6%) and implants (93.4%). None of the SRs reported on 1. cost analyses of AT compared to other treatment modalities or long-term expenditure related to prior AT treatment, 2. patient's experience 3. QoL or 4. adverse outcomes of AT.

The various Risk of Bias Assessment tools used in the included SRs are presented in Table 2. Only three SRs[2,18,27] did not include a quality assessment. The GRADE approach for evidence certainty and clinical recommendation was performed in only one SR.[6]

Excellent inter-examiner reliability at the RoB screening was recorded (kappa score = 0.942). None of the SRs fully satisfied the AMSTAR 2 Criteria (Table 6). Five SRs were rated as 'low quality',[7,17,23,29] and 12 SRs were rated as 'critically low quality'.[2,4,6,18–22,24–28] The critical domains that were not addressed by most SRs were: Item 7 (16/17 SRs) and Item 15 (6/9 eligible SRs). Similarly, the following non-critical domains that were not addressed were: Item 3 (15/17 SRs), Item 9 (9/9 eligible SRs) and Item 10 (17/17 SRs).

Seven SRs only included primary studies published in English,[2,7,22,24,25,27,28] therefore, increasing the possibility of leaving out eligible studies and thus selection bias cannot be ruled out. In two SRs,[2,18] concerns were raised regarding identification and selection, with their search being restricted to only a single strategy/database. Data collection and risk of bias assessment/study appraisal were adequate in most SRs.

Nine SRs carried out meta-analyses.[4,6,7,17,22–26] However, critical concerns were raised regarding the quantitative synthesis of results, where there were often inadequate justifications for combining data for meta-analysis. This included concerns regarding the assessment of clinical and methodological heterogeneity of the included studies being either inaccurate, inadequate or absent, or confounders adjusted effect size from individual studies were not considered. In some studies, the event rates (success or survival) from the included studies at varying time-points were pooled to obtain the overall estimate. Others failed to conduct subgroup or regression analysis

Q9 NSRI	Q10	Q11 RCT	Q11 NRSI	Q12	Q13	Q14	Q15	Q16	OVERALL
No	No	No MA	No MA	No MA	No	No	No MA	Yes	Critically Low
Partial Yes	No	No	Yes	Yes	Partial Yes	Yes	Yes	Yes	Critically Low
Partial Yes	No	No MA	Yes	Yes	Yes	Yes	No	Yes	Low
No	No	No MA	No MA	No MA	No	No	No MA	No	Critically Low
Partial Yes	No	No MA	No MA	No MA	No	No	No MA	Yes	Critically Low
Partial Yes	No	No MA	Yes	No	Yes	Yes	Yes	Yes	Low
Partial Yes	No	No MA	Yes	No	Yes	No	No	Yes	Critically Low
No	No	No MA	No MA	No MA	No	No	No MA	No	Critically Low
Partial Yes	No	No MA	Yes	No	No	Yes	No	Yes	Critically Low
Partial Yes	No	No MA	Yes	Yes	No	Yes	No	Yes	Critically Low
Partial Yes	No	No MA	No	No	Yes	Yes	Yes	Yes	Low
Partial Yes	No	No MA	Yes	No	Yes	Yes	No	Yes	Critically Low
Partial Yes	No	No MA	Yes	No	No	Yes	No	No	Critically Low
Partial Yes	No	No MA	Yes	No	No	Yes	No	Yes	Critically Low
No	No	No MA	No MA	No MA	No	No	No MA	No	Critically Low
Partial Yes	No	No MA	No MA	No MA	Yes	Yes	No MA	Yes	Critically Low
Partial Yes	No	No MA	No MA	No MA	Yes	Yes	No MA	Yes	Low

based on the time-period to explore the heterogeneity secondary to variability in the follow-up periods. In addition, the potential impact of risk of bias within the individual studies and across the studies was not considered by conducting appropriate sensitivity analyses.

Analysis of publication bias was performed in only three of nine SRs, which carried out a meta-analysis.[6,7,23] Machado et al. demonstrated a tendency toward the publication of studies with high survival rates.[23] However, only four SRs were included in the funnel plot, thereby compromising the power of this test in determining the real asymmetry. Similarly, funnel plot asymmetry for all outcomes was reported by Almpani et al.,[6] with the Eggers test being significant for failure rates, EIR and PN outcomes. Likewise, Chung et al. reported moderate study heterogeneity, with similar funnel plot asymmetry noted for the outcome of estimated failure rates.[7] This was attributed to the inclusion of mainly observational studies in their review.

4 | DISCUSSION

The aim of this review was to understand the pre-, peri- and post-operative factors that affect success and survival rates in patients having AT. Additionally, the authors sought to evaluate the success and survival rates of AT in comparison with other treatment options. Secondary outcomes, such as aesthetics and patient satisfaction, were also assessed. To bring about greater inclusivity and breadth of information available on the topic, multiple databases and grey literature were searched, and all eligible SRs were included. Detailed assessment of CCA between every possible pair of SRs allowed better prediction of the overlap of the primary studies among SRs, thereby strengthening and allowing more meaningful interpretation of the evidence synthesised. As such, this umbrella review presents the most comprehensive critical appraisal of published data on AT, with a high ratio of studies to SRs.

Only one SR evaluated the success and survival of various treatment options to replace congenitally missing teeth.[28] The overall success and survival of each option was calculated using a weighted mean method, thus giving an overview of the outcomes of various treatment options. Future studies of a similar nature can consider additional subgroup analysis by age group (i.e. adolescence vs. adulthood) and transplant location (e.g. anterior vs. posterior; maxilla vs. mandible) to indicate the more appropriate treatment option.

Compared to other restorative options, AT provides additional advantages such as preservation and growth of alveolar bone dimensions,[36] and potential for regeneration of normal PDL, which facilitates proprioception, allows orthodontic tooth movement,[37] and concurrently confers a satisfactory gingival outcome. Given that implants are not suitable for those who have yet to attain skeletal maturity,[38] AT should rank high on the considerations as a treatment option. Even in the event of ERR, AT remains a viable interim option for patients. Together with protocols such as decoronation, preservation of both the bucco-palatal width and the vertical bone height can still occur to facilitate future implant placement without requiring further bone augmentation.[39,40]

For adults, prosthodontic replacement or dental implants are the conventional treatment of choice for the replacement of missing teeth.[41] However, obtaining an aesthetic result for single[42] or two adjacent[43] implants or prostheses[44] is difficult and unpredictable, especially in patients with a high smile line. This may be overcome through AT. With respect to direct cost effectiveness (i.e. clinical and laboratory costs), AT was more cost effective than implants and fixed partial dentures to replace congenitally missing lateral incisors.[45] The actual difference in cost effectiveness between dental implants or prostheses and AT may be even greater, since prostheses often require additional fees for follow-up and maintenance. More primary studies evaluating cost effectiveness of various treatment options are warranted. Nonetheless, given the high success and survival rates of AT of closed apex teeth alongside the biological advantages it confers, with proper planning and execution, AT can still be considered as an alternative treatment option for adult patients if there is a suitable donor tooth.

Autotransplantation of teeth with open apices consistently demonstrated better success and survival outcomes, and lower risk of PN and external root resorption than for teeth with closed apices. During AT, severance of the neurovascular bundle to the pulp occurs, risking irreversible damage to the pulp. Teeth with open apices have increased vascularity and hence a better chance for pulp healing.[46] Since children or adolescents are more likely to have teeth with open apices, AT is a good treatment option as part of an interdisciplinary treatment plan to replace missing teeth or teeth with poor prognosis.

The quality and quantity of recipient site alveolar bone might be associated with periodontal healing of the transplant. Whilst transplanted teeth placed in areas with no deficiency demonstrated better PDL healing,[3] other studies have shown that with proper socket management and atraumatic handling of the donor tooth, PDL healing and resolution of periapical pathosis at the transplant site, or even vertical bone growth can be obtained.[5,47–49] It should be noted that none of the SRs specifically evaluated the quality and quantity of bone volume at baseline and investigated its relationship as a prognostic factor for successful AT. This should be evaluated in future studies.

In terms of treatment protocols, studies have shown that operator experience levels may influence the ease of graft placement and the degree of injury to PDL, which may consequently affect AT pulp and periodontal outcomes.[46,50] This factor was not evaluated in any of the SRs included in this umbrella review. During extraction and handling of the donor tooth, care must be taken to avoid compression and to minimise injury to the PDL, as iatrogenic cemental damage increases its vulnerability to resorptive osteoclastic activity. Extraoral time is also significant for PDL healing, where normal healing was observed when the extraoral time was <18 minutes.[51] Intra-operative iatrogenic procedural PDL injury has been reported as the main factor associated with non-favourable healing of transplanted teeth,[46] with every fitting attempt further increasing extraoral time and the risk of trauma to the PDL.[52]

Recent improvements in AT surgical methods aim to circumvent problems related to operator factors, in order to preserve donor tooth PDL cells, and increase success and survival rates. This includes using cone beam computed tomographic scans to assess the feasibility of transplantation using virtual reality platforms,[53] and developing highly accurate three-dimensional (3D)-printed replicas of the donor teeth[54,55] to aid in socket preparation prior to transplantation of the donor tooth. Additional benefits of immediate good fit and significant reduction in donor tooth extraoral time plus overall surgery time with this method, has resulted in high success and survival rates compared to the conventional method.[56] Only one SR evaluated AT using computer-aided rapid prototyping of 3D replicas of donor teeth.[29] Several printing techniques were used in the studies included, and all produced accurate models that had a clinically acceptable level of accuracy, suggestive of future potential for more widespread adoption of this method. However, there remains much room for well-conducted randomised controlled clinical studies in order to conclusively determine the advantages, cost considerations and long-term clinical outcomes of AT using these techniques.

Although AT has shown potential for bone induction and re-establishing normal alveolar bone process, bone grafts have been used in alveolar augmentation of atrophic ridges,[57] or guided bone regeneration techniques to cover roots of transplanted teeth exposed by bony dehiscence to create space for bone regeneration.[5,58] However, more extractions among transplanted teeth that had a bone graft was found, albeit in one single study with a small sample size.[59] Given that there are varied alveolar bone volumes at baseline and different techniques and timing of bone graft placement (i.e. a few months before autotransplantation[60] vs. concurrently with AT), more studies are required before recommending a bone graft as part of a standard AT protocol.

Autotransplantations, which had suture 'splints' compared with wire splints, and those without post-transplantation orthodontic treatment, were associated with higher levels of PCO indicative of physiological healing.[6] However, the evidence was based on a single primary study and thus the findings should be taken with caution. Although wire splinting provides greater stability to the transplanted tooth, it may reduce physiological stimuli and thus compromise adaptation of the PDL of the transplanted tooth at its recipient site. Furthermore, rigid wire splinting also runs the risks of higher ankylosis rates[7] and is discouraged. Similarly, orthodontic forces that are not well controlled, may lead to strangulation of the pulp's vasculature or avascular necrosis secondary to pressure applied through the wires. Presently, there remains inadequate evidence with respect to the splinting regimen and orthodontic protocol, which support the most optimal healing outcomes. More well-designed controlled clinical studies are required to investigate the effect of the splinting regimen or orthodontic protocol relative to periodontal and pulp healing.

EIR was more common in closed apex teeth that underwent pulp extirpation >14 days post-AT, compared to those where endodontic treatment was initiated within 14 days after AT.[7] For transplanted teeth with closed apices, prompt initiation of endodontic treatment is strongly recommended to help prevent pulp necrosis and infection, which leads to EIR.[5] Conversely, frequent reviews are suggested for monitoring of root development and early detection of pulp and periapical pathosis in transplanted teeth with open apices.

Treatment failure was also found to be greater in cases without antibiotic cover.[7] The prescription of antibiotics could possibly help reduce bacterial contamination and infection-related reactions in the periodontium, thereby protecting the transplanted tooth. However, there is currently insufficient information regarding the specifics of antibiotic cover (i.e. pre- vs. post-operative prescription, antibiotic type, dose, duration) to provide definitive recommendations.[7,24] As such, future studies are required to evaluate the effect of different antibiotic regimens on treatment outcomes of transplanted teeth.

Beyond disease and treatment-oriented outcomes, there is now increasing emphasis on patient-related outcomes.[61,62] Only two SRs reported on the secondary outcomes intended for this study.[2,28] This stems from a lack of well-conducted primary studies which have included these outcomes in their evaluation. In addition, attempts should be made to compare patient perspectives on the acceptability of AT with other treatment options (e.g. prosthetic replacement or orthodontic space closure). It should be noted that patient-reported outcomes are highly subjective by nature and careful consideration using validated measures and robust research methodology is needed to accurately capture the necessary data so that these measures can be meaningfully analysed.

There are a few limitations among the included SRs in this umbrella review. Firstly, more than a third of the SRs did not provide a definition for both success and survival with respect to pulp and periodontal outcomes, and five SRs only provided partial definitions for either outcomes. The lack of standardised definitions of success and survival of AT among the SRs resulted in the report of a wide range of success and survival rates. Additionally, follow-up periods also differed among the studies. As a result, only two SRs fulfilled the criteria for MMA.

Some of the other marked limitations which have arisen during the data analysis include failure of some SRs to distinguish between outcomes of open versus closed apex teeth. Additionally, failure of standardisation of reporting of outcomes, with distinct lack of information on surgical conditions and techniques used (e.g. transplant conditions, socket preparation needs and technique), information on tooth-related factors (e.g. tooth type, allogenic vs. autogenous graft), and long-term survival information (>5 years) was noted.

Therefore, within the context of the conduct of a SR and more so an umbrella review, it should be noted that there are limitations for adequate evaluation of the differences in peri-operative conditions, clinician experience levels and surgical protocols used, thus rendering the data or assessments as being 'discrepant' across the included SRs. These factors likely bring about great inconsistencies, and it should be recognised that data analyses are being carried out with the understanding that high variability at the procedural level exists and are to be expected.[63] These problems are present not only at SR level, but stem fundamentally from non-standardisation in reporting outcomes and differences in evaluation of success/survival at the primary study level.

The inclusion of case reports/series and uncontrolled longitudinal studies in SRs is often debatable as they rank low on the hierarchy of evidence and risks compromising the integrity of the results, be it narrative or meta-analytical estimates. The inclusion of uncontrolled clinical cases due to a lack of controlled clinical trials places the SR conclusions at risk of bias, and this is a known limitation acknowledged in many of the included SRs. However, within the context of AT, depending on the outcome measure of concern, comparative and especially controlled clinical trials are not always feasible nor ethical to conduct, particularly when one treatment is evidently superior to non-treatment (e.g. AT vs. non-treatment or extraction), or options for other treatment modalities are not suitable for patients of a certain age group (e.g. implants in children). As such, findings should be judiciously interpreted while bearing in mind the limitations of how the data were accrued and assessed.

During quality assessment of the SR, fundamental issues in the risk bias analyses were noted, including variability in the categorisation of study designs, with failure to clearly distinguish between controlled versus non-controlled studies and comparative versus observational studies. One of the major concerns, which surfaced was the appropriateness of the risk of bias tool used in each SR to assess the primary studies. This was specifically noted in SRs, which included papers with multiple study designs, where some used only a single risk of bias tool and adapted it for use across all types of study designs, thus rendering it not fit for purpose.

Other concerns in the quantitative synthesis among the included reviews, such as pooling the event rates at varying time-points, inadequate justifications while combining the heterogenous data and failing to conduct appropriate analyses to explore or overcome the bias altogether, increased the suspicion of biased estimates. As such, the quality of the data presented and the accuracy of the conclusions drawn, especially with respect to success rates, should be interpreted with extreme caution.

Although this umbrella review was carried out rigorously, the abovementioned limitations in the included SRs results in the inability to pool data for meaningful synthesis and MMA. In addition, the AMSTAR 2 risk of bias assessment rendered most SRs as being at high risk, thus decreasing the overall quality of evidence. Finally, this umbrella review was unable to provide success and survival rates beyond 10 years based on the stage of root development (open vs. closed apices) and the tooth type (premolars vs. molars), thus leaving uncertainty on its applicability as a life-long natural replacement option.

TABLE 7 Autotransplantation Outcome Index.

Outcome	Autotransplant-specific criteria: Pulp	Autotransplant-specific criteria: Periodontal	Patient-specific criteria
Level 1: Complete success	1. Pulp healing Clinical: • No abscess, swelling, sinus tract • No complaints of pain • Absence of tenderness to percussion and palpation • Positive response to sensibility test (electric pulp test, cold/thermal stimuli)[b] Radiographic: • Pulp canal obliteration (if evident).	1. Periodontal healing Clinical: • Normal gingival architecture • No metallic percussion sound • Periodontal probing depth of ≤3 mm • No clinical attachment loss • Bleeding on probing of <10% • No tooth mobility beyond physiologic limits Radiographic: • Normal periodontal ligament space and intact lamina dura • Continued root development (increased root length and thickening of dentinal wall and apical foramen closure) • No detectible alveolar bone loss 2. Successful elective endodontic treatment[A1] • Endodontic Outcome[A3]: Favourable	1. Aesthetics[A4]: Acceptable 2. Quality of life[A5]: Significant improvement
Level 2: Partial Success Level 2a: Complications that are self-limiting and/or successfully treated with fair long-term prognosis	1. Successful non-elective endodontic treatment[A2] • Endodontic Outcome[A3]: Favourable or Healed • Regenerative endodontic therapy[a]: Fulfil ESE success criteria (Galler et al. 2016)[71]	1. Signs of loss of periodontal support • Periodontal probing depth of ≤4 mm • Clinical attachment loss of 1-2 mm • Alveolar radiographic bone loss of ≤15% of the root length 2. Arrested root development with signs of thickening of dentinal wall and/or apical foramen closure and no signs of pulp pathosis 3. Root surface resorption 4. Successfully treated root resorption[A6] 5. Crown:root ratio ≤ 1	1. Aesthetics[A4]: Acceptable 2. Quality of life[A5]: Acceptable or slight improvement

Level 2: Partial Success
Level 2b
Tooth is likely to survive, fair short-term prognosis but uncertain long-term prognosis.
	1. Failed endodontic treatment or regenerative endodontic therapy requiring retreatment whereby retreatment offers good prognosis.
	2. Uncertain endodontic treatment
	• Endodontic Outcome[A3]: Uncertain or Healing or Functional
	• Regenerative endodontic therapy[a]:
	  • No signs/symptoms of pulp pathosis
	  • No increase in root length radiographically
	  • Presence of thickening of dentinal wall and/or apical foramen closure radiographically
		1. Signs of loss of periodontal support
		• Periodontal probing depth of ≤5 mm
		• Clinical attachment loss of 3–4 mm
		• Tooth mobility beyond physiologic limits but less than 1 mm in buccolingual direction
		• Alveolar radiographic bone loss of 15%–33% of the root length
		2. Arrested root development without signs of pathology[a]
		3. Successfully treated non-progressive root resorption[A6]
		4. Crown:root ratio ≥ 1 (with abovementioned tooth mobility)
			1. Aesthetics[A4]: Unacceptable (can be rectified)
			2. Quality of life[A5]: Acceptable or slight decrease

TABLE 7 (Continued)

	Autotransplant-specific criteria		
Outcome	Pulp	Periodontal	Patient-specific criteria
Level 3: Failure Irreversible complications that result in hopeless long-term prognosis and loss of tooth	1. Internal root resorption: Uncontrolled 2. Failed endodontic or regenerative endodontic treatment requiring tooth extraction. • Endodontic Outcome[A3]: Unfavourable or Non-healed	1. Signs of loss of periodontal support • Periodontal probing depth of more than 5 mm • Clinical attachment loss of more than 4 mm • Tooth mobility in vertical direction and/or exceeding 1 mm in buccolingual direction. • Signs of loss of periodontal support: Alveolar radiographic bone loss exceeding 33% of root length 2. External replacement (ankylosis-related) resorption 3. Root resorption[A6]: Uncontrolled 4. Crown:root ratio ≥ 1 (with abovementioned tooth mobility)	1. Aesthetics[A4]: Unacceptable (cannot be rectified) 2. Quality of life[A5]: Significant decrease (cannot be rectified)

Outcomes:
At final follow-up visit,
1. Complete Success: Tooth that fulfils level 1
2. Partial Success: Tooth that fulfils level 2a, 2b
3. Failure: Tooth that fulfils level 3
4. Survival: Tooth still present in its transplanted position.

	Terms	Elaboration
A1	Successful elective endodontic treatment	Endodontic treatment carried out pre- or post-autotransplantation as part of treatment protocol for autotransplanted teeth with closed apex
A2	Successful non-elective endodontic treatment	• Endodontic treatment carried out successfully due to clinical (e.g. pain/abscess) and/or radiographic (e.g. periapical radiolucency/lack of continued root development/internal root resorption) signs and symptoms of pulp and/or periapical pathology. • Endodontic treatment rendered includes but not limited to conventional root canal therapy, MTA apical plug, regenerative endodontic therapy
A3	Endodontic outcome	Endodontic outcomes defined by the European Society of Endodontology or the American Association of Endodontists

A4	Aesthetic	Aesthetic outcomes of autotransplanted tooth. Can be broken into objective and subjective findings.
		• Objective:
		  • Tooth related: colour match, anatomical contour, position, restoration quality (e.g. Ryge criteria)[72]
		  • Soft tissue related: gingival contour and morphology
		• Subjective question:
		  • e.g. 'On a 5-point Likert scale, are you happy with the aesthetic outcome of the (autotransplanted) tooth?' (1): very unhappy, (2): unhappy, (3): neither unhappy nor happy, (4): happy, (5): very happy

A5	Quality of life	Should be compared from baseline/pre-treatment, immediate post-treatment and at last follow-up • To involve patient and, if applicable, care-givers • Measured using any age appropriate validated quality of life measurement scale/questionnaire e.g. FIS, CPQ, OHIP-14, global questions
A6	Root resorption	Comprises of external inflammatory (infection-related) resorption and invasive cervical resorption (Heithersay 2004)[73]

[a]Findings specific to autotransplanted teeth with open apices only.

[b]Response to sensibility tests are desirable but not always achievable. Nonetheless, clinicians should still carry out these tests during review appointments.

Therefore, more well-conducted primary clinical trials utilising standardised criteria to report results, specifically those evaluating various prognostic indicators to obtain accurate protocols for AT, are required. Since data collection is typically limited by what is reported in the published manuscripts, authors are also strongly advised to adhere to existing research reporting guidelines (https://www.nlm.nih.gov/services/research_report_guide.html) when drafting their manuscripts. In addition, data on patient-reported outcomes (e.g.

QoL and cost effectiveness) and adverse outcomes of treatment are severely lacking in the current literature. This would be interesting to evaluate in a future systematic review.

To standardise reporting of clinical findings for future studies, a core outcome set, comprising of both treatment- and patient-related outcomes, for AT is recommended, given the numerous factors impacting success and survival. With a standardised data set available, the authors propose an Autotransplantation Outcome Index (AOI) to help standardise the definition and classification of outcomes (i.e. success and survival) for AT (Table 7). The AOI is divided into AT-specific criteria (pulp, periodontal, clinical and radiographic findings) and patient-specific criteria (aesthetics and QoL). Based on these criteria, the autotransplant procedure can then be assigned an outcome.

The strength of the AOI is the adoption of commonly used prognostication tools and definitions, such as the definitions approved by the European Society of Endodontology[64] or the American Association of Endodontists[65] to report endodontic treatment outcomes, to facilitate standardisation. Regarding the reporting of clinical findings, the authors encourage the use of commonly used indices for ease of comparison, such as using the Moorrees[30] and Millers classifications[66] to record the stage of root development and tooth mobility, respectively. As there is currently no validated objective and subjective index for aesthetic outcomes of AT, the authors suggest that certain tooth- and soft tissue-related variables be evaluated. Future development of any such indices can consider inclusion of these variables or draw reference from studies on smile/implant aesthetics,[67,68] which can subsequently be incorporated into the AOI. Similarly, there are no studies evaluating the effect of periodontal disease and long-term outcomes of AT teeth. As such, the authors can only propose a possible classification based on commonly recorded periodontal findings (e.g. probing depths and attachment loss) as described in published literature on periodontal prognosis.[69,70] Further development of the AOI can be carried out through consensus building with an expert group using the Delphi technique, followed by validation. Having standardised reporting utilising both the core outcome set and the AOI will ensure clarity in both primary and secondary outcomes and will facilitate a more homogeneous data pool that will facilitate future meta-analysis and more meaningful interpretation of data.

5 | CONCLUSIONS

Autotransplantation of teeth with open apices have >95% 5-year and 10-year survival rates. The overall evidence is of low certainty, with the majority of included SRs basing results mainly on single-arm (uncontrolled) prospective or retrospective studies. Further well-designed studies using standardised reporting outcomes on the evaluation of prognostic indicators and factors that affect the success of AT, and patient-reported outcomes are strongly recommended.

AUTHOR CONTRIBUTIONS

BLT and HJT should be considered as joint first author. ABH, BLT, HN and HJT participated in data collection; ABH, BLT, HJT, HN and SN analysed the data; BLT and HJT led the writing; ABH, BLT, HJT, HN, MD and SN revised the manuscript for important intellectual content.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest. All authors have made substantive contribution to this study and/or manuscript, and all have reviewed the final paper prior to its submission. The authors declare no financial conflict of interest.

DATA AVAILABILITY STATEMENT

The data that supports the findings of this study are available in the supplementary material of this article.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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