Accepted: 26 April 2018

DOI: 10.1111/clr.13276

REVIEW ARTICLE

WILEY CLINICAL ORAL IMPLANTS RESEARCH

Implant placement and loading protocols in partially edentulous patients: A systematic review

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Abstract

Objectives: To systematically review the evidence for the clinical outcome of fixed implant prostheses treated with different combinations of implant placement and loading protocols in partially edentulous patients.

Materials and methods: An electronic search was performed in Medline, Embase, and Central to identify studies investigating the outcome of implants subjected to immediate placement + immediate restoration/loading (Type 1A), immediate placement + early loading (Type 1B), immediate placement + conventional loading (Type 1C), early placement + immediate restoration/loading (Type 2-3A), early placement + early loading (Type 2-3B), early placement + conventional loading (Type 2-3C), late placement + immediate restoration/loading (Type 4A), late placement + early loading (Type 4B), late placement + conventional loading (Type 4C) with implant-supported fixed dental prostheses (IFDPs) in partially edentulous patients. Only human studies with at least 10 cases and a minimum follow-up time of 12 months, reporting on solid-screw-type implants with rough surfaces and an intra-osseous diameter between 3 and 6 mm, were included. A cumulative survival rate for each type of the implant placement and loading protocols was weighted by the duration of follow-up and number of implants.

Results: The search provided 5,248 titles from which 2,362 abstracts and 449 full-text articles were screened. A total of 69 publications that comprised 23 comparative studies (15 randomized controlled trials, 7 controlled clinical trials) and 47 noncomparative studies (34 prospective cohort studies, 13 retrospective cohort studies) were included for analysis. Considerable heterogeneity in study design was found, and therefore, a meta-analysis of controlled studies was not possible. The weighted cumulative survival rate of each type of placement and loading protocol was 98.4% (Type 1A), 98.2% (Type 1B), 96.0% (Type 1C), 100% (Type 2-3B), 96.3% (Type 2-3C), 97.9% (Type 4A), 98.3% (Type 4B), and 97.7% (Type 4C). Type 1C, Type 2-3C, Type 4B, and Type 4C were scientifically and clinically validated (SCV). Type 1A, Type 1B, and Type 4A were clinically documented (CD), and Type 2-3A and Type 2-3B were clinically insufficiently documented (CID).

Conclusions: Evaluating outcomes in oral implantology by combining the placement and loading protocols are paramount. The selected loading protocol appears to influence the outcome of immediate implant placement.

KEYWORDS

dental implants, early loading, early placement, immediate loading, immediate placement

1 | INTRODUCTION

Various surgical and prosthodontic protocols used in oral implantology are directly associated with the long-term outcome of implant prosthesis (Cochran et al., 2011; Moraschini, Poubel, Ferreira, & Barboza Edos, 2015; Ormianer et al., 2012; Payer et al., 2010; Polizzi et al., 2000; Zuffetti et al., 2016). In this context, implant placement protocols have been differentiated by the duration of the healing period following tooth extractions prior to implant placement. Likewise, implant loading protocols have been differentiated by the duration of the healing period following implant placement prior to the initial delivery of a provisional or definitive implant restoration.

Different implant placement options have been clinically applied as defined by the last three ITI Consensus Conferences in 2003, 2008, and 2013 (Chen & Buser, 2009; Chen, Wilson, & Hammerle, 2004; Hammerle, Chen, & Wilson, 2004). These options include the following: (a) *immediate implant placement* on the day of extraction (Type 1), (b) *early implant placement* after 4–8 weeks of soft tissue healing (Type 2), (c) *early implant placement* after 12–16 weeks of partial bone healing (Type 3), and (d) *late implant placement* after complete bone healing of at least 6 months (Type 4).

Each of the different implant placement protocols present unique clinical considerations (Buser, Chappuis, Belser, & Chen, 2017; Quirynen, Van Assche, Botticelli, & Berglundh, 2007). A reduction in overall treatment time with immediate and early implant placement protocols presents an attractive solution for patients and clinicians. However, immediate implant placement is thought to be significantly influenced by the local alveolar anatomy following tooth extraction (Levine et al., 2017). Dimensional changes following tooth extraction occur and are not mitigated by immediate implant placement (Araujo, Sukekava, Wennstrom, & Lindhe, 2005), which may lead to compromised long-term aesthetic outcomes (Chen & Buser, 2014; Hammerle, Araujo, Simion, & Osteology Consensus, 2012). The degree of dimensional changes may be influenced by the thickness of the labial buccal bone following tooth extraction (Chappuis, Araujo, & Buser, 2017; Chappuis et al., 2013; Matarasso et al., 2009). Thicker buccal bone leads to less dimensional ridge alterations and may provide more predictable results for immediate implant placement.

The reported ridge alterations following tooth extraction can be clearly visualized when performing early implant placement after 4–8 weeks of soft tissue healing (Belser et al., 2009; Buser, Bornstein, et al., 2008; Buser, Chappuis, Bornstein et al., 2013; Buser, Chappuis, Kuchler et al., 2013; Buser, Chen, Weber, & Belser, 2008; Buser et al.,

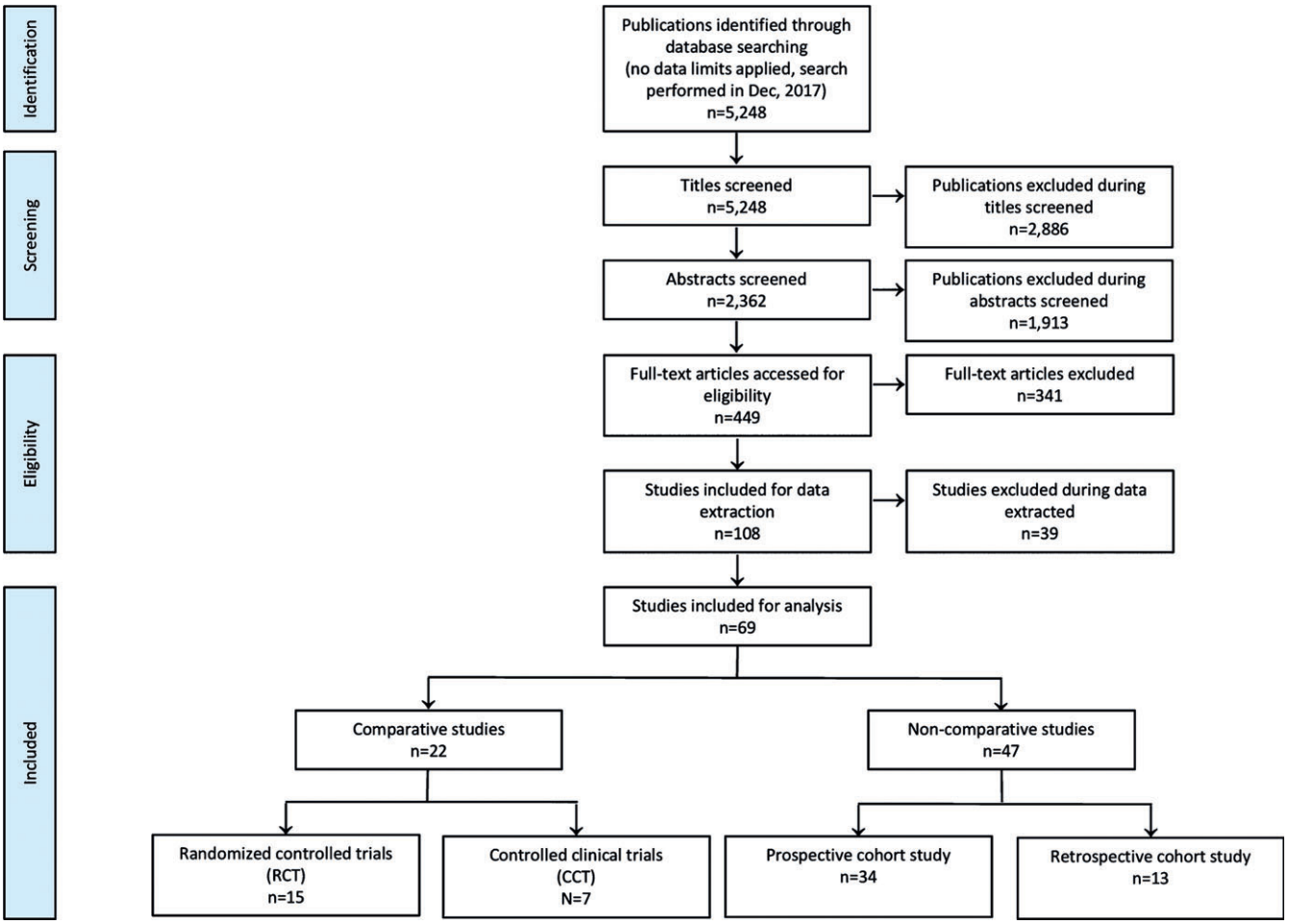

FIGURE 1 Search strategy and post-extraction dimensional changes

2009; Buser et al., 2011; Chappuis et al., 2018). At re-entry, there is often a bone defect at the facial aspect where the alveolar buccal bone wall is either thin or missing (Chen & Darby, 2017). This is more marked in the anterior maxilla than posterior sites and varies according to the initial thickness of the buccal plate at the time of tooth extraction. This approach is often associated with a local contour augmentation at the time of implant placement using guided bone regeneration (GBR) to compensate for these ridge alterations, and has been shown to provide long-term peri-implant tissue stability (Buser, Bornstein et al., 2008; Buser, Chappuis, Bornstein et al., 2013; Buser, Chappuis, Kuchler et al., 2013; Buser, Chen et al., 2008; Buser et al., 2009; Buser et al., 2011; Chappuis et al., 2017; Sanz et al., 2012; Schropp, Wenzel, Spin-Neto, & Stavropoulos, 2015; Schropp, Wenzel, & Stavropoulos, 2014; Soydan, Cubuk, Oguz, & Uckan, 2013).

Different implant loading options, as defined by the last three ITI Consensus Conferences in 2003, 2008, and 2013, have also been clinically applied (Benic, Mir-Mari, & Hammerle, 2014; Chiapasco, 2004; Cochran, Morton, & Weber, 2004; Gallucci, Morton, & Weber, 2009; Gallucci et al., 2014; Ganeles & Wismeijer, 2004; Grutter & Belser, 2009; Morton, Jaffin, & Weber, 2004; Papaspyridakos, Chen, Chuang, & Weber, 2014; Roccuzzo, Aglietta, & Cordaro, 2009; Schimmel, Srinivasan, Herrmann, & Muller, 2014; Schrott, Riggi-Heiniger, Maruo, & Gallucci, 2014; Weber et al., 2009). The definition of loading protocols has been slightly modified over the years and is currently accepted as follows: (a) *Immediate loading* of dental implants is defined as being earlier than 1 week after implant placement, (b) *Early loading* of dental implants between 1 week and 2 months after implant placement, and (c) *Conventional loading* of dental implants >2 months after implant placement (Gallucci et al., 2014; Weber et al., 2009).

Likewise, reduced overall treatment times with immediate and early loading protocols, together with the potential to avoid a removable provisional prosthesis, present attractive solutions for clinicians and patients. Surface modification of dental implants has accelerated the bone response during implant healing (Buser et al., 2004). High survival rates for each of the various loading protocols have been reported (Benic et al., 2014; Gallucci et al., 2014; Sanz-Sanchez, Sanz-Martin, Figuero, & Sanz, 2015; Schrott et al., 2014). However, bone turnover during the healing period may compromise implant stability and reduce the ability of an implant to resist significant lateral forces prior to adequate osseointegration (Neugebauer, Traini, Thams, Piattelli, & Zoller, 2006).

Throughout history, implant placement and loading protocols have been analyzed separately from one another. However, the implant placement technique and its related surgical outcome at the time of placement are determinant factors for selecting the loading protocol. For instance, primary implant stability is known to be one of the key factors for success associated with placement and loading protocols (Schrott et al., 2014). Hence, it appears that many treatment factors need to align with careful patient and site assessment to select the ideal placement/loading option.

TABLE 1 Studies excluded during data extraction

Reason for exclusion	Number	Studies
Insufficient information to separate partially and completely edentulous patients	6	Degidi, Nardi, and Piattelli (2012), Horwitz and Machtei (2012), Malchiodi, Ghensi, Cucchi, and Corrocher (2011), Malchiodi et al. (2010), Siebers, Gehrke, and Schliephake (2010), Vandeweghe et al. (2012)
Insufficient information to separate implant failure from partially and completely edentulous patients	5	Bekcioglu, Sagirkaya, Karasoy, and Cehreli (2012), Danza, Guidi, and Carinci (2009), Glauser et al. (2001), Kopp et al. (2013), Penarrocha-Diago, Carrillo-Garcia, Boronat-Lopez, and Garcia-Mira (2008)
Less than 10 partially edentulous patients	1	Polizzi and Cantoni (2015)
Not screw-type implant	2	Kopp et al. (2013), Mangano et al. (2014)
Intra-osseous Implant diameter more than 6.0 mm	1	Atieh et al. (2013)
Insufficient information to separate machined surface implants and rough surface implants	1	Wagenberg, Froum, and Eckert (2013)
Insufficient information of failed implants in different placement protocol	3	Glauser et al. (2003), Glauser (2013), Ostman, Hellman, Albrektsson, and Sennerby (2007)
Insufficient information of failed implants in different loading protocol	2	Felice, Grusovin, Barausse, Grandi, and Esposito (2015), Wilson, Roccuzzo, Ucer, and Beagle (2013)
Study scope focusing on grafting techniques	3	Lang et al. (2015), Siormpas, Mitsias, Kontsiotou-Siormpa, Garber, and Kotsakis (2014), Urban, Kostopoulos, and Wenzel (2012)
Data retrieved from chart reviews	6	Al Amri et al. (2017), Bell and Bell (2014), El-Chaar (2011), Harel, Moses, Palti, and Ormianer (2013), Ormianer and Palti (2008), Pozzi, Tallarico, Marchetti, Scarfo, and Esposito (2014)
Multiple studies on the same population	9	Buser, Bornstein et al. (2008), Buser, Chappuis, Kuchler et al. (2013), Buser et al. (2009, 2011), Kan, Rungcharassaeng, and Lozada (2003), Mangano et al. (2012), Schropp, Kostopoulos, Wenzel, and Isidor (2005), Shibly, Kutkut, Patel, and Albandar (2012)
Total	39	

TABLE 2 Quality assessment and risk of bias of included CCTs

Study	Representative of the exposed cohort	Selection of the nonexposed cohort	Ascertainment of exposure	Outcome of risk not present at commencement of study	Comparability of cases and controls	Assessment of outcome	Sufficient follow-up time for outcomes to occur	Adequacy of follow-up	Total
Achilli et al. (2007)	*	*	*	*	*	*	*	*	8
De Bruyn et al. (2013)	*	*	*	*	*	*	*	*	8
Heinemann, Biffar, Schwahn, and Mundt (2013)	*	*	*	*	*	*	*		7
Meizi, Meir and Laster (2014)	*	*	*	*		*	*		6
Mertens and Steveling (2011)	*	*	*	*		*	*	*	7
Schropp and Isidor (2008)	*	*	*	*	*	*	*	*	8
Vandeweghe et al. (2013)	*		*	*	*	*	*		6

FIGURE 2 Risk of bias summary: review authors' judgements about each risk of bias item for each included RCTs

Despite the vast scientific evidence on implant placement and implant loading protocols, treatment outcomes assessing the timing of implant placement and loading as treatment co-variables have not been systematically reviewed. The aim of this systematic review is to answer the PICO question: "In partially edentulous patients with immediate or early placement and loading protocols, do the implant-prosthodontic survival and success differ when compared to conventional protocols?"

2 | MATERIAL AND METHODS

This systematic review was conducted consulting the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (Liberati et al., 2009), the Standards for Developing Trustworthy Clinical Practice Guidelines published by the Institute of Medicine (IOM) (Institute of Medicine Committee on Standards for Developing Trustworthy Clinical Practice, 2011), and the Cochrane Handbook for Systematic Reviews of Interventions (Higgins and Green 2017). The review was registered with the PROSPERO database (CRD42017080776).

2.1 | Focus question

The focus PICO question (population, intervention, comparison, outcome) was formulated with partially edentulous patients as the population; immediate/early placement and loading protocols as the intervention of interest; late placement and conventional loading protocols as the intervention of comparison; and implant-prosthodontic survival and success as the primary outcome. Thus, the PICO question was formulated as follows: "In partially edentulous patients with immediate or early placement and loading protocols, do the implant-prosthodontic survival and success differ when compared to conventional protocols?"

The placement protocols were defined as follow:

- Late implant placement: Dental implants are placed after completely bone healing, more than 6 months after tooth extraction.
- Early implant placement: Dental implants are placed with soft tissue healing or with partial bone healing, 4–8 weeks or 12–16 weeks after tooth extraction.
- Immediate implant placement: Dental implants are placed in the fresh socket on the same day of tooth extraction (Chen & Buser, 2009; Chen et al., 2004; Hammerle et al., 2004).

The loading protocols were defined as follows:

TABLE 3 RCT included for analysis [In PDF format, this table is best viewed in two-page mode]

Study	Comparison	Timing of placement	Timing of restoration/loading	Mean follow-up (mo)	No. of patients	No. of patients drop-out
Bömicke, Gabbert, Koob, Krisam, and Rammelsberg (2017)	Type 4A	>6 weeks	≤1 day	36	19	0
	Type 4C	>6 weeks	3 months		19	3
Cucchi et al. (2017)	Type 1C	≤1 day	3 months	24.4	48	3
	Type 4C	>3 months	3 months		44	4
Felice et al. (2015)	Type 1A	≤1 day	≤1 day	12	16	0
	Type 1C	≤1 day	4 months		9	0
	Type 4A	4 months	≤1 day		6	2
	Type 4C	4 months	4 months		19	
Ganeles et al. (2008)	Type 4A	≥4 months	≤1 day	12	138	NR
	Type 4B	≥4 months	28–34 days		128	NR
Gjelvold, Kisch, Chrcanovic, Albrektsson, and Wennerberg (2017)	Type 4A	≥4 months	≤1 day	12	25	0
	Type 4C	≥4 months	≥4 months		25	0
Göthberg, Andre, Grondahl, Thomsen, and Slotte (2016)	Type 4A	>3 months	<2 days	12	26	0
	Type 4C	>3 months	3 months		24	0
Hall et al. (2007)	Type 4A	NR	≤1 day	12	14	0
	Type 4C	NR	6 months		14	2
Kim et al. (2015)	Type 4A	≥6 months	≤1 day	12	21	0
	Type 4C	≥6 months	20–23 weeks			0
Malchiodi, Balzani, Cucchi, Ghensi, and Nocini (2016)	Type 1C	≤1 day	3 months	12	20	0
	Type 2-3C	>12 weeks	3 months		20	0
Margossian et al. (2012)	Type 4A	≥4 months	≤1 day	24	80	0
	Type 4C	≥4 months	NR		37	0
Schincaglia, Marzola, Giovanni, Chiara, and Scotti (2008)	Type 4A	≥4 months	≤1 day	12	15	0
	Type 4C	≥4 months	3–4 months		15	0
Schropp et al. (2014)	Type 2-3C	10 days	3 months	120	22	4
	Type 4C	>3 months	3 months		22	1
	Type 4C	17 months	3 months		19	2
Shibly et al. (2010)	Type 1A	≤1 day	≤1 day	24	30	2
	Type 1C	≤1 day	3 months		30	
Slagter et al. (2016)	Type 1C	≤1 day	3 months	12	20	0
	Type 4C	>3 months	3 months		20	0
Van de Velde, Sennerby, and De Bruyn (2010)	Type 4A	≥4 months	≤1 day	18	13	1
	Type 34B	≥4 months	6 weeks		13	

BL: bone level implant; NR: not reported; RBM: resorbable blast media; SLActive: hydrophilic and chemically active sandblasted, large grit, acid etched; TL: tissue level implant.

- Conventional loading: Dental implants are allowed a healing period more than 2 months after implant placement with no connection to the prosthesis.
- Early loading: Dental implants are connected to the prosthesis between 1 week and 2 months after implant placement.
- Immediate loading: Dental implants are connected to the prosthesis within 1 week subsequent to implant placement.

This is in line with the publications of the previous ITI Consensus Conferences (Benic et al., 2014; Chiapasco, 2004; Cochran et al., 2004; Gallucci et al., 2009, 2014; Ganeles & Wismeijer, 2004; Grutter & Belser, 2009; Morton et al., 2004; Papaspyridakos et al., 2014; Roccuzzo et al., 2009; Schimmel et al., 2014; Schrott et al., 2014; Weber et al., 2009).

2.2 | Search strategy

The search strategy was developed in close collaboration with a trials search coordinator, who also serves as the Reference and Education Services Librarian at the Countway Library of Medicine of the Harvard Medical School, Boston, Massachusetts. The electronic search was performed utilizing the databases of PubMed/Medline,

TABLE 3 (additional columns)

No. of implants	Implant type	Implant surface	No. of implant failed	Implant survival rate (%)	Implant success rate (%)	Prosthetic success rate (%)
19	Nobel BL tapered	TiUnite	1	94.8	NR	84.2
16			0	100	NR	68.8
49	BTK BL tapered	Dual acid etched	2	95.5	NR	100
48			0	100	NR	100
16	Dentsply XiVE	NR	2	87.5	NR	100
9			0	100	NR	100
6			0	100	NR	100
19			0	100	NR	100
197	Straumann TL parallel	SLActive	4	98	NR	NR
186			6	97	NR	NR
25	BioHorizons tapered	NR	0	100	96	100
25			1	96	88	100
78	Nobel BL	TiUnite	4	94.9	NR	NR
72			2	97.2	NR	NR
14	Southern tapered	Roughened	1	92.9	NR	92.3
14			0	100	NR	85.7
22	Straumann TL parallel	SLActive	3	86.4	NR	NR
24			0	100	NR	NR
20	SybronPRO XRT parallel	RBM	0	100	100	NR
20			0	100	100	NR
209	Biomet 3i	Osseotite	7	96.7	96.7	NR
98			0	100	100	NR
15	Nobel	TiUnite	1	93.3	NR	NR
15	BL parallel		0	100	NR	NR
22	Biomet 3i parallel	Osseotite	2	90.9	NR	NR
22			1	95	NR	NR
19			0	100	NR	NR
30	Nobel BL parallel	TiUnite	1	96.7	NR	NR
30			2	93.3	NR	NR
20	NR	NR	0	100	NR	NR
20	NR	NR	0	100	NR	NR
36	Straumann TL tapered	SLA	1	97.3	72.2	100
34			0	100	82.35	100

TABLE 4 CCT included for analysis [In PDF format, this table is best viewed in two-page mode]

Study	Comparison	Timing of placement	Timing of restoration/ loading	Mean follow-up (mo)	No. of patients	No. of patients drop-out
Achilli et al. (2007)	Type 4A	≥3 months	≤1 day	12	21	0
	Type 4B	≥3 months	6 weeks		33	0
De Bruyn et al. (2013)	Type 1A	≤1 day	≤1 day	36	55	0
	Type 4A	NR	≤1 day		58	0
Heinemann et al. (2013)	Type 1C	≤1 day	5–6 months	4–45.6	35	NR
	Type 4C	≥6 months	5–6 months		23	NR
Meizi et al. (2014)	Type 1A	≤1 day	≤3 days	12	155	NR
	Type 4A	≥3 months	≤3 days			
	Type 1C	≤1 day	Max: 6 months; mand: 3 months			
	Type 4C	≥3 months	Max: 6 months; mand: 3 months			
Mertens and Steveling (2011)	Type 1A	≤1 day	≤1 day	60	17	2
	Type 4A	NR	≤1 day			
	Type 1B	≤1 day	9.56 weeks			
	Type 4B	NR	9.56 weeks			
Schropp and Isidor (2008)	Type 2-3C	10 days	4–5 months	60	23	2
	Type 4C	>3 months	4–5 months		22	
Vandeweghe et al. (2013)	Type 1A	≤1 day	≤1 day	26	38	NR
	Type 4A	NR	≤1 day			NR

BL: bone level implant; NR: not reported; Mand: mandible; Max: maxilla.

Embase, and the Cochrane Central Register of Controlled Trials (CENTRAL) to identify publications in English up to December 2017.

For the PubMed/MEDLINE screening, combinations of controlled terms (MeSH) and keywords were used whenever possible. The search terms used for the PubMed search were as follows: (dental implantation, endosseous[MeSH] OR dental implants[MeSH] OR implantation OR implant OR implants) AND (denture, partial, fixed[MeSH] OR dental prostheses, implant supported [MeSH] OR fixed partial denture OR FPD OR FPDs OR fixed dental prosthesis OR fixed dental prostheses OR bridge OR crown) AND (immediate implant OR immediate implantation OR immediate implant placement OR immediate placement OR immediate OR early OR placement OR time OR timing OR fresh extraction sockets OR immediate extraction sockets OR post-extraction implant placement OR post-extractive OR early implantation OR early implant placement) AND (immediate dental implant loading[MeSH] OR function OR time OR immediate OR early OR load) AND (English[Language]). The references were managed with a specific bibliographic software (EndNote X8, Version 8.1, Thomson Reuters®, New York, NY, USA).

2.3 | Selection criteria

All types of study designs were included provided they met the following criteria:

- Human studies;
- At least 10 participants;
- Partially edentulous patients receiving Implant Fixed Dental Prostheses (IFDPs);
- Implant placement and implant loading protocols were specifically reported;
- Implant success criteria were reported;
- Minimum follow-up period of 1 year;
- Root-form or cylindrical implant with a rough surface;
- Intra-osseous implant diameter between 3 and 6 mm.

The exclusion criteria were as follows:

- Animal or in vitro studies;
- Zirconia implants;
- Implants with machined surfaces or hydroxyapatite (HA) coatings;
- Implants supporting full-arch restorations or removable appliances;
- Implants placed in irradiated bone or alveolar clefts;
- Data retrieved from chart reviews or questionnaires;
- Insufficient information provided on implant placement protocol;
- Insufficient information provided on loading protocol or type of implant superstructures;
- Insufficient information provided to determine implant survival rate or success rate;

TABLE 4 (additional columns)

No. of implants	Implant type	Implant surface	No. of implant failed	Implant survival rate (%)	Implant success rate (%)	Prosthetic success rate (%)
43	Nobel BL tapered	TiUnite	0	100	100	NR
69			0	100	100	NR
55	Dentsply	OsseoSpeed	3	94.6	87	NR
58			1	98.3	92	NR
83	Dentaurum BL tapered	Rough ceramic blasted	0	100	100	NR
53			0	100	100	NR
161	Saturn	NR	7	95.65	NR	NR
23			0	100	NR	NR
54			3	98.2	NR	NR
106					NR	NR
10	Dentsply	OsseoSpeed	0	100	100	100
4			0	100	100	100
3			1	97.14	97.14	100
32						100
23	Biomet 3i parallel	Osseotite	2	91.3	NR	95.24
22			1	95.45	NR	
23	Southern tapered	Moderately rough	0	100	NR	97.7
20			0	100	NR	

- Insufficient information provided to identify success criteria.

In case of multiple publications on the same study population, only the study with the longest follow-up was included for reporting of results, whilst previous studies were consulted only to retrieve information not provided in the most recent publication.

Studies pertaining to implant rehabilitation in both completely edentulous and fully edentulous patients will only be included where success/survival data are clearly separated between these two different population groups.

2.4 | Screening of studies

Screening and data extraction were performed independently by two reviewers (WZ and AH). Disagreements were resolved by discussion between reviewers and consultation with a third reviewer (GO) where required.

2.5 | Data collection

Data on study design, timing of implant placement postextraction, timing of functional loading, mean follow-up period, number of patients, number of implants, location, implant characteristics (i.e., diameter, length, type and surface), flap design, bone graft, surgical guide, implant stability assessment, intention to treat (ITT), occlusion contact of provisional prosthesis, final prosthesis design, success criteria, time of failure, implant survival rate, implant success rate, and prosthesis success rate were extracted from the included studies and recorded on standardized forms.

Authors were contacted directly via email as needed for clarification or missing information. Authors were contacted if further clarification on the extracted data was necessary.

2.6 | Quality assessment

Two independent reviewers (WZ and AH) assessed the methodological quality of all included comparative studies. Randomized controlled trials (RCTs) were rated per their risk of bias using the Cochrane quality assessment tool for RCTs. The Newcastle–Ottawa scale (NOS) was used to assess the quality of controlled clinical trials (CCTs).

Some RCT studies which reported detailed information on timing of implant placement and loading were included but analyzed as CCTs (Cannizzaro, Torchio, Felice, Leone, & Esposito, 2010; Schropp & Isidor, 2008) or prospective cohort studies (Barone et al., 2016; Bianchi & Sanfilippo, 2004; De Angelis et al., 2011; Fung, Marzola, Scotti, Tadinada, & Schincaglia, 2011; Meloni, Jovanovic, Pisano, & Tallarico, 2016; Migliorati, Amorfini, Signori, Biavati, & Benedicenti, 2015; Prosper, Gherlone, Redaelli, & Quaranta, 2003) as the comparison was not between different placement or loading protocols. For prospective and retrospective cohort study, no quality assessment was performed.

TABLE 5 Noncomparative studies included for analysis [In PDF format, this table is best viewed in two-page mode]

Study	Study design	Placement and loading protocol	Timing of placement	Timing of restoration/loading	Mean follow-up (mo)	No. of patients	No. of patients drop-out
Becker et al. (2011)	RC	Type 1A	≤1 day	≤3 days	12	100	NR
Belser et al. (2009)	RC	Type 2-3B	4–8 weeks	6–12 weeks	31.44	45	4
Blus and Szmukler-Moncler (2010)	RC	Type 1A	≤1 day	≤1 day	12	23	NR
		Type 1B	≤1 day	1 week to 3 months	12		
		Type 1C	≤1 day	3–6 months	12		
Boronat, Penarrocha, Carrillo, and Marti (2008)	RC	Type 1B	≤1 day	8 weeks (max); 6 weeks (mand)	12	30	12
		Type 4B	NR	8 weeks (max); 6 weeks (mand)	12		
Brown and Payne (2011)	RC	Type 1A	≤1 day	≤1 day	12	25	0
Fugazzotto (2012)	RC	Type 1C	≤1 day	3–7 months	62	64	NR
Hartlev et al. (2013)	RC	Type 1A	≤1 day	≤1 day	33	55	13
Kolerman et al. (2016)	RC	Type 1A	≤1 day	≤1 day	29	34	NR
Mangano et al. (2013)	RC	Type 1A	≤1 day	≤1 day	31.09	22	0
		Type 4A	≥6 months	≤1 day	34.4	18	0
Mura (2012)	RC	Type 1A	≤1 day	≤1 day	60	48	8
Paul and Held (2013)	RC	Type 1A	≤1 day	≤1 day	40.8	26	2
Sener-Yamaner, Yamaner, Sertgoz, Canakci, and Ozcan (2017)	RC	Type 4B	≥4 months	3–8 weeks	81	55	NR
Van Nimwegen et al. (2016)	RC	Type 1A	≤1 day	≤1 day	48	51	NR
Akca, Cavusoglu, Uysal, and Cehreli (2013)	PC	Type 4B	NR	5–6 weeks	14	22	0
Barone et al. (2016)	PC	Type 4C	≥3 months	3 months	12	116	0
Bianchi and Sanfilippo (2004)	PC	Type 1C	≤1 day	3–4 months	108	116	3
Bornstein et al. (2010)	PC	Type 4B	≥4 months	3 weeks	36	39	0
Buser, Chappuis, Bornstein et al. (2013), Buser, Chappuis, Kuchler et al. (2013)	PC	Type 2-3C	4–8 weeks	8–12 weeks	84	41	8
Calandriello and Tomatis (2011)	PC	Type 4A	≥4 months	≤1 day	60	33	NR
Calvo-Guirado et al. (2015)	PC	Type 1A	≤1 day	≤1 day	36	53	NR
Chappuis et al. (2013)	PC	Type 2-3C	4–8 weeks	8–12 weeks	120	20	0
Covani et al. (2012)	PC	Type 1C	≤1 day	6 months	120	91	7
Covani, Canullo, Toti, Alfonsi, and Barone (2014)	PC	Type 1C	≤1 day	4 months	60	47	NR
Cristalli et al. (2015)	PC	Type 1A	≤1 day	≤1 day	12	24	0
Degidi et al. (2011)	PC	Type 4A	NR	≤1 day	36	24	0
Del Fabbro, Boggian, and Taschieri (2009)	PC	Type 1C	≤1 day	3–4 months	18.5	30	2 implants
De Angelis et al. (2011)	PC	Type 1C	≤1 day	3–4 months	12	80	1
De Rouck, Collys, and Cosyn (2008)	PC	Type 1A	≤1 day	≤1 day	12	30	1
Fugl et al. (2017)	PC	Type 4A	≥2 months	≤1 day	12	91	6
Fung et al. (2011)	PC	Type 4A	≥4 months	≤1 day	36	10	0

(Continues)

TABLE 5 (additional columns)

No. of implants	Implant type	Implant surface	No. of implant failed	Implant survival rate (%)	Implant success rate (%)	Prosthetic success rate (%)
100	Straumann TL parallel	SLActive	1	99	99	100
45	Straumann TL parallel	SLA	0	100	100	NR
6	NR	NR	0	100	NR	NR
24			0	100	NR	NR
10			0	100	NR	NR
16	DEFCON TSA	Avantblast	1	93.75	93.75	NR
90			2	97.78	97.78	NR
26	Co-Axis TL tapered	Roughened surfaces of Sa	0	100	NR	92.31
128	NR	NR	0	100	98.2	NR
55	Nobel BL tapered	TiUnite	1	98	NR	100
34	MIS BL	NR	0	100	88	NR
22	Leone Ortodonzia	NR	0	100	100	100
18			0	100	100	100
66	Nobel BL tapered	TiUnite	0	100	NR	98.5
31	Nobel	NR	0	100	100	NR
175	Straumann TL	SLA *n* = 48; SLActive *n* = 48	3	98.2	NR	NR
64	Biomet 3i	Osseotite	2	96.9	NR	NR
52	Straumann BL parallel	NR	0	100	100	100
112	Blossom BL tapered	NR	3	97.4	93.1	NR
116	Straumann TL parallel	TPS	0	100	100	NR
56	Straumann TL parallel	SLActive	0	100	100	NR
41	Straumann TL parallel& tapered	SLA	0	100	NR	NR
40	Nobel BL tapered	TiUnite	2	95	95	NR
71	MIS	Rough	0	100	NR	NR
20	Straumann BL	SLActive	0	100	95	NR
159	Sweden & Martina	SLA	13	91.8	91.8	98.7
47	Sweden & Martina	NR	2	95.7	NR	NR
25	Nobel BL tapered	TiUnite	2	91.67	91.67	NR
48	Ankylos Dentsply	SLA	0	100	100	100
61	BTI Biotechnology Institute	Acid etched	1	98.4	98.4	100
80	Biomet 3i BL tapered	Dual acid etched	7	91.25	NR	NR
30	Nobel BL tapered	TiUnite	1	97	NR	100
93	NR	NR	1	99	97	NR
20	Nobel BL	ADZ	0	100	100	85

(Continues)

TABLE 5 (Continued) [In PDF format, this table is best viewed in two-page mode]

Study	Study design	Placement and loading protocol	Timing of placement	Timing of restoration/loading	Mean follow-up (mo)	No. of patients	No. of patients drop-out
Grandi, Guazzi, Samarani, Maghaireh, and Grandi (2014)	PC	Type 1A	≤1 day	≤1 day	12	25	0
Kan, Rungcharassaeng, Lozada, and Zimmerman (2011)	PC	Type 1A	≤1 day	≤1 day	48	35	0
Karabuda, Abdel-Haq, and Arisan (2011)	PC	Type 4B	≥3 months	12 weeks (max); 8 weeks (mand)	15	22	0
Lang, Turkyilmaz, Edgin, Verrett, and Garcia (2014)	PC	Type 4A	NR	≤1 day	60	20	5
Luongo, Di Raimondo, Filippini, Gualini, and Paoleschi (2005)	PC	Type 4A	NR	≤1 day *n* = 10; 2–11 days *n* = 30	12	40	0
Malchiodi, Cucchi, Ghensi, and Nocini (2013)	PC	Type 1A	≤1 day	≤1 day	36	58	0
Mayer, Hawley, Gunsolley, and Feldman (2002)	PC	Type 4C	NR	6 months (max); 4 months (mand)	45.9	57	2 implants
		Type 1C	≤1 day	6 months (max); 4 months (mand)	45.9	2	
Meloni et al. (2016)	PC	Type 4C	NR	3 months	36	18	0
Migliorati et al. (2015)	PC	Type 1A	≤1 day	≤1 day	24	47	1
Montoya-Salazar et al. (2014)	PC	Type 1C	≤1 day	4.5 months	36	NR	NR
Noelken, Neffe, Kunkel, and Wagner (2014)	PC	Type 1A	≤1 day	≤1 day	27	19	1
Ostman et al. (2008)	PC	Type 4A	≥4 months	≤1 day	48	NR	0
Oyama, Kan, Rungcharassaeng, and Lozada (2012)	PC	Type 4A	≥2 months	≤1 day	12	13	NR
Prosper et al. (2003)	PC	Type 1C	≤1 day	4–6 months	48	83	0
Romeo, Chiapasco, Ghisolfi, and Vogel (2002)	PC	Type 4C	>6 months	3–6 months	84	109	6
Siddiqui et al. (2008)	PC	Type 4A	>6 months	≤1 day	12	44	NR
Valentini, Abensur, Albertini, and Rocchesani (2010)	PC	Type 1A	<1 week	<1 week	33.6	40	NR

ADZ: oxide-anodized; BL: bone level implant; FBR: fast bone regeneration; HA: hydroxyapatite; Mand: mandible; Max: maxilla; NR: not reported; PC: prospective cohort study; RC: retrospective cohort study; SLA: sandblasted, large grit, acid etched; SLActive: hydrophilic and chemically active sandblasted, large grit, acid etched; TL: tissue level implant; TPS: titanium-sprayed surface.

2.7 | Validation criteria

To formulate conclusions and propose clinical recommendations for all types of placement and loading protocols, the included studies were ranked per their design, sample size, and outcome homogeneity (OH). The outcome homogeneity was considered positive (OH+) when the variation of implant survival rates for the same treatment protocol was 10% or less, and negative (OH–) when the variation was >10% (Gallucci et al., 2009). Using these criteria, scientific and/or clinical validation was determined as follows:

Scientifically and clinically validated (SCV):

- Systematic reviews of RCTs; or
- Two or more RCTs + ≥100 patients + OH+; or
- One RCT and two or more prospective studies + ≥150 patients + OH+

Clinically well documented (CWD):

- One RCT and two or more prospective studies + ≥40 patients + OH+; or

TABLE 5 (additional columns - continued)

No. of implants	Implant type	Implant surface	No. of implant failed	Implant survival rate (%)	Implant success rate (%)	Prosthetic success rate (%)
25	JDentalCare tapered	Dual acid etched	0	100	NR	100
35	Nobel BL tapered	HA	0	100	100	NR
96	Straumann TL parallel	SLA *n* = 48; SLActive *n* = 48	1	NR	98.96	NR
20	Zimmer tapered	NR	1	95	NR	NR
82	Straumann TL parallel	SLA	1	98.8	97.5	NR
64	NR	FBR	0	100	100	NR
67	Biomet 3i	Osseotite Dual acid etched	1	98.51	98.51	NR
4			0	100	NR	NR
36	Nobel BL tapered	TiUnite	0	100	NR	100
47	Straumann BL tapered	SLActive	0	100	NR	NR
36	MIS	NR	1	97.22	NR	NR
34	NR	OsseoSpeed	0	100	100	NR
180	Nobel	TiUnite	1	99.44	NR	NR
17	Dentsply Xives	Grit-blasted thermal acid etched	0	100	100	NR
111	NR	Sand blasted	3	NR	97.3	NR
187	Straumann TL parallel	TPS	9	96.7	93.6	NR
51	Zimmer tapered	Microtextured	1	98.04	98.04	NR
43	Dentsply	TiOblast	2	95.3	NR	NR

- No RCTs but at least three prospective studies + ≥60 patients + OH+; or
- No RCTs but two or fewer prospective studies + ≥100 patients + OH+

Clinically documented (CD):

- No RCTs, at least two prospective + any retrospective studies + ≤40 patients + OH−; or
- No RCTs, retrospective studies + ≥60 patients + OH−/+

Clinically insufficiently documented (CID):

- None of the above, expert opinion only, case report only.

2.8 | Statistical analysis

Agreement between the reviewers was calculated by Cohen's kappa statistical analysis. Descriptive analysis was used to report the success and survival rates for the various implant placement protocols and loading protocols. A mean cumulative survival rate for each of the implant placement and loading protocols was calculated and weighted by the duration of patient follow-up and number

TABLE 6 Classification according to the implant placement and loading protocol [In PDF format, this table is best viewed in two-page mode]

	Loading protocol							
	Immediate restoration/loading (type A)					Early loading (type B)		
	Type	Weighted mean survival (%)	Mean follow-up (mo)	N° of included implants	N° of studies	Type	Weighted mean survival (%)	Mean follow-up (mo)
Implant placement protocol								
Immediate placement (Type 1)	1A	98.4 (87.5–100)	28.9 (12–60)	1,067	6[a] 18[b]	1B	98.2 (93.8–100)	28.0 (12–60)
Early placement (Type 2-3)	2-3A	NA	NA	NA	0[a] 0[b]	2–3B	100	31.4
Conventional placement (Type 4)	4A	97.9 (83.3–100)	24.3 (12–60)	1,356	16[a] 10[b]	4B	98.3 (97–100)	29 (12–81)

Note.. Range of results indicated in brackets.
Type 1A: Immediate Placement + Immediate Restoration/Loading; Type 1B: Immediate Placement + Early Loading; Type 1C: Immediate Placement + Conventional Loading; Type 2-3A: Early Placement + Immediate Restoration/Loading; Type 2-3B: Early placement + Early Loading; Type 2-3C: Early Placement + Conventional Loading; Type 4A: Late Placement + Immediate Restoration/Loading; Type 4B: Late Placement + Early Loading; Type 4C: Late Placement + Conventional Loading.
[a]No. of comparative studies.
[b]No. of noncomparative studies.

of implants. The weighted average of survival rate is calculated as followed:

$$\bar{x} = \frac{X_1 t_1 n_1 + X_2 t_2 n_2 + \ldots + X_k t_k n_k}{t_1 n_1 + t_2 n_2 + \ldots + t_k n_k} \times 100\%$$

X = survival rate reported in the included study; t = follow-up period; n = number of implants. All studies included in this SR were carefully selected according to their described research variables. For each study, we looked for a clear information on the placement and loading protocols to be one of the variables studied/reported.

3 | RESULTS

A total number of 5,248 titles publications were identified by the search. Following the title screening, 2,362 abstracts and 449 full-text articles were evaluated for inclusion (Figure 1). The interrater reliability Kappa score was 0.97. A total of 108 articles were included for data extraction. Thirty-nine articles had to be excluded from the final analysis for not meeting the inclusion criteria (Table 1). A total of 69 studies met the including criteria and were finally included in this systematic review, which were comprised of 15 RCTs, 7 CCTs, 34 prospective cohort studies, and 13 retrospective cohort studies. The excluded studies and the reasons for exclusion were listed in Table 1.

Several follow-up studies reporting on the same patient population previously published were each combined to one line with the most comprehensive results from each reported. Data were extracted from the most recent publications and tabulated. Any missing data were obtained from the earlier publications.

Although all included studies defined specific survival/success criteria, the definitions of survival/success varied between the studies making standardization of the criteria not possible. Furthermore, despite reporting success criteria, many of the studies still only reported survival rates as an outcome measure.

Considerable heterogeneity in study design was found, with a lack of RCTs and comparative studies which compared across the same implant placement and loading protocol combinations. Therefore, a meta-analysis of controlled studies was not possible.

3.1 | Quality assessment for including comparative studies

Table 2 demonstrated the risk of bias for included RCTs. Twelve studies were well conducted with respect to randomization by reporting the methods to generate randomized sequences. Ten studies reported the concealment of allocation. However, regarding of blinding of participants/operators (performance bias), all the studies had a high risk of bias, as the operators would know the randomized type of treatment and the patients had the right to know which treatment was used. For the CCTs, the Newcastle–Ottawa scale (NOS) results are presented in Figure 2.

3.2 | Outcome analysis of each placement and loading protocol

The data extraction is summarized in Tables 3 and 4 for comparative data (RCT and CCT studies) and Table 5 for noncomparative data (prospective and retrospective cohort studies).

TABLE 6 (additional columns)

		Conventional loading (type C)				
N° of included implants	N° of studies	Type	Weighted mean survival (%)	Mean follow-up (mo)	N° of included implants	N° of studies
43	1[a] 2[b]	1C	96.0 (91.3–100)	38.4 (12–120)	963	6[a] 10[b]
45	0[a] 1[b]	2–3C	96.3 (90.9–100)	96.0 (60–120)	106	2[a] 2[b]
789	4[a] 5[b]	4C	97.7 (95.5–100)	30.6 (12–120)	898	14[a] 4[b]

Placement and loading protocols were used to group the data set in 12 well-differentiated treatment protocols (Table 6). This resulted in a novel classification combining placement and loading protocols in oral implantology as follows:

Type 1A: Immediate Placement + Immediate Restoration/Loading
Type 1B: Immediate Placement + Early Loading
Type 1C: Immediate Placement + Conventional Loading
Type 2A: Early Placement with Soft Tissue Healing + Immediate Restoration/Loading
Type 2B: Early placement with Soft Tissue Healing + Early Loading
Type 2C: Early Placement with Soft Tissue Healing + Conventional Loading
Type 3A: Early Placement with Partial Bone Healing + Immediate Restoration/Loading
Type 3B: Early placement with Partial Bone Healing + Early Loading
Type 3C: Early Placement with Partial Bone Healing + Conventional Loading
Type 4A: Late Placement + Immediate Restoration/Loading
Type 4B: Late Placement + Early Loading
Type 4C: Late Placement + Conventional Loading.

Due to the limitations in distinct specification of the implant placement time in many clinical studies reports, the implant paced with both early loading protocols (types 2 and 3) were combined for this review.

3.2.1 | Type 1A—Immediate Placement + Immediate Restoration/Loading

Two RCTs, 4 CCTs, and 18 noncomparative studies provided the data on the outcomes of implants following Type 1A protocol. In total, 35 of 1,079 Type 1A implants failed. The weighted cumulative survival rate was of 98.4% (median 100%; range 87.5%–100%) with a mean follow-up of 28.9 (*SD* = 15.2; range 12–60) months. The success rates ranged from 87% to 100%.

3.2.2 | Type 1B—Immediate Placement + Early Loading

One CCT and two noncomparative studies reported on the outcome of implants following Type 1B protocol. One of the 43 Type 1B implants failed. The weighted cumulative survival rate was of 98.2% (median 100%; range 93.75%–100%) with a mean follow-up of 28.0 (*SD* = 27.7; range 12–60) months. Implant success rates ranged from 93.75% to 100%.

3.2.3 | Type 1C Immediate Placement + Conventional Loading

Five RCTs, 1 CCT, and 10 noncomparative studies provided data on outcomes of implants following Type 1C protocol. In total, 24 of 963 Type 1C implants failed. The weighted cumulative survival rate was 96% (median 99.2%; 91.3%–100%) with a follow-up of 38.7 (*SD* = 34.3; range 12–120) months. The success rates ranged from 91.8% to 100%.

3.2.4 | Type 2-3A—Early Placement + Immediate Restoration/Loading

None of the included study reported on this protocol.

TABLE 7 Criteria for placement and loading protocol and intention to treat (ITT) analysis

Study	Placement and loading protocol	Criteria for placement protocol (Type 1 or Type 2)	Criteria for loading protocol (immediate or early loading)	No. of patients intended to treat	No. of patients failed to treat	ITT (%)	Reason for exclusion
RCT							
Bömicke et al. (2017)	Type 4A vs. Type 4C	Bone height ≥12 mm and bone width of 6 mm; Enabling implant placement without grafting; Attached gingiva ≥4 mm	IT ≥35 Ncm	38	38	100	–
Cucchi et al. (2017)	Type 1C vs. Type 4C	Adequate bone to place a 3.7 × 10 mm or larger implant without bone augmentation procedures	NR	102	3	97.1	Three patients decided not to restore implant with a definitive crown
Felice et al. (2015)	Type 1A vs. Type 1C vs. Type 4A vs. Type 4C	<4 mm of the buccal wall missing after tooth extraction	IT ≥35 Ncm	55	5	90.9	>4 mm of buccal bone loss when compared to the palatal wall after extraction
Ganeles et al. (2008)	Type 4A vs. Type 4B	Adequate bone quality and quantity	NR	NR	NR	NR	NR
Gjelvold et al. (2017)	Type 4A vs. Type 4C	No need for bone grafting or ridge augmentation at the implant site	IT ≥30 Ncm	62	12	80.6	Four patients did not want treatment for economic reasons; three patients presented extensive osseous defects that would require a bone graft to make the insertion of an implant possible; one patient desired a tooth supported bridge instead of an implant; three patients decided to leave the study before surgery
Gothberg et al. (2016)	Type 4A vs. Type 4C	NR	Good primary stability with ≥1 mm coverage of surrounding bone	NR	NR	NR	NR
Hall et al. (2007)	Type 4A vs. Type 4C	No need for bone grafting or ridge augmentation prior to implant surgery	Primary implant stability could be achieved following placement	28	0	100	–
Kim et al. (2015)	Type 4A vs. Type 4C	Adequate bone to place 4.1/4.8 × 10/12 mm implants without bone augmentation; ≥2 mm attached (keratinized) gingiva	NR	21	0	100	–
Malchiodi et al. (2016)	Type 1C vs. Type 4C	Extraction socket with a containing alveolus (4 bone-wall defect); Bone height ≥9 mm in the maxilla and ≥11 mm in the mandible; ≥3 mm of bone beyond the root apex	NR	40	0	100	–
Margossian et al. (2012)	Type 4A vs. Type 4C	Adequate bone height to place a 10 mm or longer implant	IT ≥30 Ncm ISQ ≥60	117	0	100	–
Schincaglia et al. (2008)	Type 4A vs. Type 4C	Adequate bone to place a 5 × 8.5 mm or larger implant	IT ≥20 Ncm	NR	NR	NR	NR

(Continues)

TABLE 7 (continued)

Study	Placement and loading protocol	Criteria for placement protocol (Type 1 or Type 2)	Criteria for loading protocol (immediate or early loading)	No. of patients intended to treat	No. of patients failed to treat	ITT (%)	Reason for exclusion
Schropp et al. (2014)	Type 2-3C vs. Type 4C	NR	NR	72	9	87.5	Four patients were judged not suitable for single implant therapy; five patients withdrew during the period from tooth extraction to commencement of implant treatment
Shibly et al. (2010)	Type 1A vs. Type 1C	Extraction sockets with an open defect, lacking ≥1 bone walls	IT ≥35 Ncm	72	12	83.3	The placement of immediate implants after extraction was not possible
Slagter et al. (2016)	Type 1C vs. Type 4C	Labial bony defect of ≥5 mm after tooth removal; sufficient bone on the palatal side	NR	40	0	100	–
Van de Velde et al. (2010)	Type 4A vs. Type 4B	Adequate bone to place 2–3 4.1 × 8–12 mm implants	NR	14	2	85.7	One patient needed bone regeneration; one patient died during the course of study
CCT							
Achilli et al. (2007)	Type 4A vs. Type 4B	NR	Reverse IT of 30 Ncm	NR	NR	NR	NR
De Bruyn et al. (2013)	Type 1A vs. Type 4A	No need for bone grafting	IT 15–20 Ncm	157	44	72.0	25 implants need bone regenerative procedures; nine implants insufficiently stable for immediate loading
Heinemann et al. (2013)	Type 1C vs. Type 4C	NR	NR	NR	NR	NR	NR
Meizi et al. (2014)	Type 1A vs. Type 4A vs. Type 1C vs. Type 4C	Adequate bone height ≥8 mm; Adequate bone width to retain ≥1 mm of cortical bone on the buccal and lingual/palatal after osteotomy preparation	IT ≥30 Ncm	NR	NR	NR	NR
Mertens and Steveling (2011)	Type 1A vs. Type 4A vs. Type 1B vs. Type 4B	No signs of inflammation; adequate vertical bone height to retain an implant	Good bone quantity and quality; high primary stability could be achieved during implant placement	NR	NR	NR	NR
Schropp and Isidor (2008)	Type 2-3C vs. Type 4C	NR	NR	NR	NR	NR	NR
Vandeweghe et al. (2013)	Type 1A vs. Type 4A	No signs of peri-apical inflammation	IT ≥40 Ncm	NR	NR	NR	NR
Retrospective cohort study							
Becker et al. (2011)	Type 1A	≥3 mm of apical circumferential bone to place a 5.8 mm or longer implant; ≥1 mm inside facial plate	IT ≥15 Ncm ISQ ≥50	NR	NR	NR	NR

(Continues)

TABLE 7 (continued)

Study	Placement and loading protocol	Criteria for placement protocol (Type 1 or Type 2)	Criteria for loading protocol (immediate or early loading)	No. of patients intended to treat	No. of patients failed to treat	ITT (%)	Reason for exclusion
Belser et al. (2009)	Type 2-3B	NR	NR	NR	NR	NR	NR
Blus and Szmukler-Moncler (2010)	Type 1A vs. Type 1B vs. Type 1C	No signs of periodontal disease or infection at the apex; nonresorbed buccal wall	NR	NR	NR	NR	NR
Boronat et al. (2008)	Type 1B vs. Type 4B	NR	NR	NR	NR	NR	NR
Brown and Payne (2011)	Type 1A	Presence of 4 mm bone apical to the socket; stable socket walls postextraction with three-wall dehiscence of <4 mm; sockets allowing to place a 4 × 13 mm or larger implant; Mesial distal proximal distance ≥6 mm; adequate bone quality and quantity (Types I–III)	IT 35–40 Ncm	27	2	92.6	Low IT
Fugazzotto (2012)	Type 1C	Buccal alveolar wall was intact, or a fenestration was present that was ≥5 mm apical to the alveolar crest	NR	NR	NR	NR	NR
Hartlev et al. (2013)	Type 1A	Marginal bone loss <1 mm buccally after tooth extraction; no acute infection	IT >30 Ncm	NR	NR	NR	NR
Kolerman et al. (2016)	Type 1A	Compromised buccal plate (<1 mm, dehiscenced or fenestrated); augmentation procedure needed; ≥5 mm of apical or palatal bone	IT ≥32 Ncm	NR	NR	NR	NR
Mangano et al. (2013)	Type 1A vs. Type 4A	Intact socket walls; thick gingival biotype; no active periodontal infections; no need for hard/soft tissue grafting before implant placement	NR	NR	NR	NR	NR
Mura (2012)	Type 1 A	No signs of active periodontal disease	IT ≥45 Ncm for single implant; IT ≥35 Ncm for multiple splinted implants	NR	NR	NR	NR
Paul and Held (2013)	Type 1A	NR	NR	NR	NR	NR	NR
Sener-Yamaner et al. (2017)	Type 4B	NR	NR	NR	NR	NR	NR
Van Nimwegen et al. (2016)	Type 1A	No significant soft tissue loss; distance of the contact point to bone level at the adjacent teeth ntct; mid-buccal vertical bone loss ≤3 mm	IT >35 Ncm	NR	NR	NR	NR
Prospective cohort study							
Akca et al. (2013)	Type 4B	Adequate bone height to place a 10 mm or longer implant; reduced bone (<6 mm) width that need augmentation to place a regular diameter implant	NR	NR	NR	NR	NR

(Continues)

TABLE 7 (continued)

Study	Placement and loading protocol	Criteria for placement protocol (Type 1 or Type 2)	Criteria for loading protocol (immediate or early loading)	No. of patients intended to treat	No. of patients failed to treat	ITT (%)	Reason for exclusion
Barone et al. (2016)	Type 4C	No bone augmentation needed	NR	120	4	96.7	Two patients required bone augmentation simultaneously with placement, one patient did not accept to undergo the follow-up, one patient showed an excessive insertion torque during surgery
Bianchi and Sanfilippo (2004)	Type 1C	Adequate width and height to place an immediate implant	NR	NR	NR	NR	NR
Bornstein et al. (2010)	Type 4B	NR	Bone densities of Class I to III	56	2	96.4	Two implants rotated slightly during healing cap removal were considered to be "spinners" after the initial healing phase
Buser, Chappuis, Bornstein et al. (2013), Buser, Chappuis, Kuchler et al. (2013)	Type 2-3C	NR	NR	NR	NR	NR	NR
Calandriello and Tomatis (2011)	Type 4A	Adequate bone height to place a 8.5 mm or longer implant; implant to crown length ratio ≥1:1	IT ≥35 Ncm	NR	NR	NR	NR
Calvo-Guirado et al. (2015)	Type 1A	Adequate bone to place a 4.1 × 10 mm or larger implant; ≥3 mm width of soft tissue	ISQ <60	71	0	100	–
Chappuis et al. (2013)	Type 2-3C	NR	NR	20	0	100	–
Covani et al. (2012)	Type 1C	≥4 mm native bone apical to the root apex; adequate quality	NR	115	17	85.2	Seven patients declined to participate; postextraction socket of 10 patients did not allow for the insertion of an immediate implant.
Covani et al. (2014)	Type 1C	Extraction sites with no deficiency of buccal bone plate	NR	NR	NR	NR	NR
Cristalli et al. (2015)	Type 1A	Absence of active infection around the surgical site; adequate bone (≥4 mm beyond the root apex); keratinized tissue ≥2 mm	IT ≥35 Ncm	28	4	85.7	Presence of fenestrations or dehiscences on buccal plate of extraction socket
Degidi et al. (2011)	Type 4A	Adequate quantity of bone in the surgery site	IT ≥25 Ncm ISQ ≥60	NR	NR	NR	NR
Del Fabbro et al. (2009)	Type 1C	Adequate quality and quantity of native bone to achieve primary stability	NR	NR	NR	NR	NR

(Continues)

TABLE 7 (continued)

Study	Placement and loading protocol	Criteria for placement protocol (Type 1 or Type 2)	Criteria for loading protocol (immediate or early loading)	No. of patients intended to treat	No. of patients failed to treat	ITT (%)	Reason for exclusion
De Angelis et al. (2011)	Type 1C	Residual buccal bone-to-implant gap ≥1 mm	NR	95	15	84.2	Six patients refused to participate, five patients had an acute abscess and were treated with delayed implants; two patients would have had the implant inserted near another implant; two patients required a sinus lift procedure
De Rouck et al. (2008)	Type 1A	Ideal soft tissue contour at the facial; normal to thick-flat gingival biotype; adequate bone height apical to the alveolus of the failing tooth (≥5 mm)	IT ≥35 Ncm	32	2	93.75	Loss of the labial crest after extraction of the failing tooth
Fugl et al. (2017)	Type 4A	Adequate bone to place a 3.5 × 8 mm or larger implant; no need for major bone augmentation					
Fung et al. (2011)	Type 4A	Adequate bone height to place a 8.5 mm or longer implant; adequate bone width, no need for bone augmentation	IT ≥20 Ncm ISQ ≥60	NR	NR	NR	NR
Grandi et al. (2014)	Type 1A	Adequate bone to place a 3.7 × 11.5 mm or longer implant	IT ≥45 Ncm	28	3	89.3	Three patients had buccal wall fracture after tooth extraction
Kan et al. (2011)	Type 1A	Intact labial bony plate; adequate bone to place a 3.5 × 13.0 mm or larger implant without bone grafting; adequate and harmonious gingival architecture	Adequate primary implant stability	NR	NR	NR	NR
Karabuda et al. (2011)	Type 4B	NR	NR	22	0	100	–
Lang et al. (2014)	Type 4A	Adequate bone to place a 3.7 to 4.7 × 13 mm or larger implant without grafting; ≥2 mm attached keratinized tissue	IT ≥35 Ncm	NR	NR	NR	NR
Luongo et al. (2005)	Type 4A	Adequate bone volume	IT ≥15 Ncm	45	5	88.9	One patient withdrew from the study prior to implant surgery. 3 patients did not achieve primary stability and a torque of 15 Ncm; nine implants placed in one patient which violate the protocol.
Malchiodi et al. (2013)	Type 1A	Normal or thick soft tissue biotype; ≥2 mm attached keratinized tissue	NR	NR	NR	NR	NR
Mayer et al. (2002)	Type 1C vs. Type 4C	≥1 mm of bone available at the buccal and lingual aspects of the implant and below the apex	NR	NR	NR	NR	NR
Meloni et al. (2016)	Type 4C	Residual bone height ≥10 mm; Residual bone width ≥6 mm; ≥2 mm keratinized gingiva crestally	IT 35–45 Ncm	18	0	100	–
Migliorati et al. (2015)	Type 1A	Adequate native bone; ≥2 mm facial keratinized gingiva; Intact facial socket walls or only small dehiscence defects affecting the crestal bone <3 mm in height	Primary stability achieved	48	0	100	–

(Continues)

TABLE 7 (continued)

Study	Placement and loading protocol	Criteria for placement protocol (Type 1 or Type 2)	Criteria for loading protocol (immediate or early loading)	No. of patients intended to treat	No. of patients failed to treat	ITT (%)	Reason for exclusion
Noelken et al. (2014)	Type 1A	NR	IT ≥15 Ncm	NR	NR	NR	NR
Montoya-Salazar et al. (2014)	Type 1C	Adequate quality and quantity of native bone; adequate mesio-distal space (>7 mm)	Primary stability achieved	NR	NR	NR	NR
Ostman et al. (2008)	Type 4A	Adequate bone to place two 7-mm or longer implants or one 15-mm-long implant; no sigh of infection	IT ≥30 Ncm ISQ ≥60	91	14	84.6	Low primary stability
Oyama et al. (2012)	Type 4A	Adequate bone to place a 3.0 × 11 mm or larger implant	IT ≥25 Ncm	NR	NR	NR	NR
Prosper et al. (2003)	Type 1C	Postextraction pocket with 4 walls and minimal bone resorption; 3-5 mm of bone below the implant apex	NR	NR	NR	NR	NR
Romeo et al. (2002)	Type 4C	Adequate bone volume	No signs of peri-implant inflammation	NR	NR	NR	NR
Siddiqui et al. (2008)	Type 4A	Adequate bone to place a 3.7 mm × 10 mm or larger implant; adequate bone width to preserve ≥1.0 mm of buccal and lingual plate thickness after osteotomy preparation	IT ≥30 Ncm; Resist rotation of 30 Ncm when abutment screw tightening	73	29	60.3	Three for inadequate bone; three for personal reasons; two for previously undetected medical conditions that precluded implant placement; one patient required bone grafting; four patients failed to achieve primary implant stability (IT <30 Ncm); final restoration not performed within the required 2-week timeframe; insufficient bone remaining after implant placement; implant placement inadvertently performed using a straight rather than a tapered implant design from the same manufacture
Valentini et al. (2010)	Type 1A	NR	IT ≥40 Ncm	94	51	45.7	IT <40 Ncm

ISQ: implant stability quotient; IT: insertion torque; NR: not reported.

TABLE 8 Classification according to the implant placement and loading protocol

	Loading Protocol		
	Immediate restoration/loading (type A)	Early loading (type B)	Conventional loading (type C)
Implant placement protocol			
Immediate placement (Type 1)	Type 1A CD	Type 1B CD	Type 1C SCV
Early placement (Type 2-3)	Type 2-3A CID	Type 2-3B CID	Type 2-3C SCV
Late placement (Type 4)	Type 4A CD	Type 4B SCV	Type 4C SCV

Note. Type 1A: Immediate Placement + Immediate Restoration/Loading; Type 1B: Immediate Placement + Early Loading; Type 1C: Immediate Placement + Conventional Loading; Type 2-3A: Early Placement + Immediate Restoration/Loading; Type 2-3B: Early placement + Early Loading; Type 2-3C: Early Placement + Conventional Loading; Type 4A: Late Placement + Immediate Loading; Type 4B: Late Placement + Early Loading; Type 4C: Late Placement + Conventional Loading.
CD (yellow): clinically documented; CID (red): clinically insufficiently documented (includes loading protocols that are not documented); CWD (green): clinically well documented; SCV: scientifically and clinically validated.

3.2.5 | Type 2-3B—Early Placement + Early Loading

Only one retrospective cohort study reported the outcome of implants following Type 2-3B protocol. None of the 45 implants failed with a mean follow-up of 31.4 months. The success rate was 100%.

3.2.6 | Type 2-3C—Early Placement + Conventional Loading

One RCT, one CCT, and two noncomparative studies provided the data on the outcomes of implants following Type 2-3C protocol. In total, 5 of 106 Type 2-3C implants failed. The weighted cumulative survival rate was 96.3% (median 95.65; range 90.9%–100%) with a mean follow-up of 96.0 (*SD* = 29.4; range 60–120) months. The success rates reported by noncomparative studies were 100%.

3.2.7 | Type 4A—Late Placement + Immediate Restoration/Loading

Ten RCTs, 6 CCTs, and 10 noncomparative studies provided the data on the outcomes of implants following Type 4A protocol. In total, 42 of 1,338 Type 4A implants failed. The weighted cumulative survival rate was 97.90% (median 98.55; range 83.3%–100%) with a mean follow-up of 24.3 (*SD* = 17.0; range 12–60) month. The success rates ranged from 72.2% to 100%.

3.2.8 | Type 4B—Late Placement + Early Loading

Two RCTs, two CCTs, and five noncomparative studies reported data on the outcomes of implants following Type 4B protocol. In total, 9 of 789 Type 4B implants failed. The weighted cumulative survival rate of 98.3% (median 98.96%; 97.1%–100%) with a mean follow-up of 28.9 (*SD* = 25.3; range 12–60) months. The success rates ranged from 82.4% to 100%.

3.2.9 | Type 4C—Late Placement + Conventional Loading

Twelve RCTs, two CCTs, and four noncomparative studies provided the data on the outcomes of implants following Type 4C protocol. In total, 11 of 898 Type 4C implants failed. The weighted cumulative survival rate was 97.7% (median 100%; range 95.5%–100%) with a mean follow-up of 30.6 (*SD* = 30.2, range 12–120) months. The success rates ranged from 88% to 100%.

3.3 | Criteria for implant placement and loading protocol

Table 7 showed the criteria for selection of specific placement/loading protocols. These were generally presented separately for placement and loading protocols as follows:

3.3.1 | Anatomic criteria for implant placement protocol

An adequate bone height and width for implant placement was a requirement for inclusion in most studies; however, the specific criteria of what is considered adequate vary and are not always well reported. Bone grafting was not performed in most studies. Two studies required adequate bone volume for multiple implant placement.

Extraction sockets with an intact alveolus (four bone-wall defects) were required by 10 studies, three of which required a facial plate width ≥1 mm after the removal of tooth.

Socket wall with dehiscence or fenestration was acceptable by seven studies, but each of them gave a limitation of the defect size. For example, the range of dehiscence was limited to <4 mm (Brown & Payne, 2011) and the fenestration was required to be ≥5 mm apical to the alveolar crest (Fugazzotto, 2012).

Extraction socket with an open defect which lacks at least one bone wall was required by Shibly, Patel, Albandar, and Kutkut (2010) and Slagter, Meijer, Bakker, Vissink, and Raghoebar (2016) to evaluate the effect of bone augmentation along with immediate placement and immediate restoration/loading.

Adequate bone quality was another criterion in six studies. No signs of periodontal disease or infection at the apex were required by eight studies. Nine studies required adequate width of keratinized tissue and three studies required a thick biotype at the implant site.

3.3.2 | Procedural criteria for implant loading protocol

Adequate implant primary stability was required by most of the studies when attempting to conduct an immediate or early loading. Implant insertion torque (IT) judged by the surgeon intraoperatively was the most common evaluation indicator; however, the specific value may vary among studies. IT ≥45 Ncm was proposed by 1 study, IT ≥40 Ncm by 2 studies, IT ≥35 Ncm by 12 studies, IT ≥30 Ncm by 5 studies, IT ≥20 Ncm by 1 study, and IT ≥15 Ncm by 3 studies. Reverse torque of 30 Ncm at insertion was proposed by Achilli, Tura, and Euwe (2007).

Resonance frequency analysis (RFA) in conjunction with insertion torque was another significant evaluation indicator for immediate/early loading. IT ≥30 Ncm with ISQ ≥60 was proposed by Margossian, Mariani, Stephan, Margerit, and Jorgensen (2012) and Ostman, Hellman, and Sennerby (2008); IT ≥25 Ncm with ISQ ≥60 by Degidi, Nardi, and Piattelli (2011); IT ≥20 Ncm with ISQ ≥60 by Fung et al. (2011); and IT ≥15 Ncm with ISQ ≥50 by Becker, Wilson, and Jensen (2011). Bone density of Class I to III was required by Bornstein, Wittneben, Bragger, and Buser (2010) for an early loading.

3.3.3 | Intention to treat analysis (ITT)

Table 7 summarizes how many implants were originally intended for immediate/early placement and loading, and how many of those implants were ultimately not immediately/early placed and loaded because they did not fulfill certain criteria established by the respective authors. In addition, the calculated ITT percentage and detailed reasons for exclusion were listed in the Table 7.

A 100% ITT percentage was reported by 11 studies, which means there was no bias between the planning and treatment, and all implants achieved the required criteria for each type of placement and loading protocol. However, more than half of the studies (39/69) analyzed in this systematic review did not provide information on ITT.

Reasons for exclusion can be generalize into four categories: patient-related factors (28%), low primary stability (32%), need for bone augmentation (32%), and alteration of the study design (8%).

Using the validation tool for the 12 types of placement and loading protocols, Type 1C, Type 2-3C, Type 4B, and Type 4C were scientifically and clinically validated (SCV). Type 1A, Type 1B, and Type 4A were clinically documented (CD) and Type 2-3A and Type 2-3B were clinically insufficiently documented (CID) (Table 8).

4 | DISCUSSION

Implant placement and loading protocols have been widely presented as key elements of implant treatment planning. However, their assessment has mainly been by separating the surgical parameters pertaining to the implant placement technique from the loading aspects related to the restorative phase. Previous systematic reviews on implant placement/loading protocols only compared the various implant loading and placement protocols as entirely unrelated variables (Buser et al., 2017; Papaspyridakos et al., 2014; Schrott et al., 2014). In these reviews, the effects of the interrelated variables based on differing implant loading and implant placement protocols are not accounted for. Papaspyridakos, Chen, Singh, Weber, and Gallucci (2012) emphasized on the importance of assessing outcomes in oral implantology by considering the implant-prosthetics complex as a single variable. Hence, a broad PICO question and search strategy was used in this study, relating to all combinations of implant placement and loading protocols. Using this approach, this systematic review describes nine possible combinations of placement and loading protocols resulting in a proposed new classification and allowing for individual outcome assessment for each treatment protocol (Table 6).

Inconsistencies in outcome reporting and a lack of comparative studies which compare across the same implant placement/loading protocols combinations made meta-analysis of the results not possible. For prospective and retrospective cohort study, no quality assessment was performed. Despite these limitation, the broad search defined by this systematic review identifies the current basis of scientific evidence for the various combinations of implant placement and loading protocols (Table 8). It must be recognized that inclusion of study designs other than RCTs increases the risk of biases incorporated in this review.

The literature clearly shows that specific patient inclusion criteria have been outlined in most studies included in this systematic review (Table 7). These include specific anatomical criteria which were applied to select for suitability for immediate implant placement, as well as procedural criteria in determining suitability for immediate restoration/loading such as adequate primary stability. For instance, this indicates that survival rates may only be applicable in a select group of patients with specific anatomical conditions. It is interesting that the magnitude of individuals who have not met the inclusion criteria was generally not well reported. Thus, intention to treat analysis (ITT) seems to be a very important variable that allows for a comprehensive clinical translation of the available evidence. More than half of the studies (39/69) analyzed in this systematic review did not provide information on ITT.

Type 1A was deemed according the validation tool as presenting clinical documentation. Although there were six comparative studies and 18 noncomparative studies in this group, the validation of this protocol was influenced by a negative outcome homogeneity (OH) ranging from 87.5% to 100% survival rate. The studies that reported on the success criteria showed a range of 87% to 100%. From the studies assessing Type 1A, carefully case selection criteria were described.

Here, the presence of sufficient apical bone, intact buccal plate, and absence of infection at the extraction site was predominant. For Type 1A, the negative OH should be considered as clinical relevant particularly when careful patient selection criteria are recommended. Type 1B was deemed to be CD as only three studies reported on this group with a small cohort and a very short-term follow-up. Given the lack of evidence, the clinical indication for Type 1B compared to Type 1A needs to be carefully considered with limited potential patient benefits for the Type 1B protocol. Conversely to Type 1A and 1B, Type 1C was deemed to be SCV. Survival rates and success rates for Type 1C ranged from 91.3% to 100%. Here again, very strict case selection criteria were used. From the data pulled for Type 1—immediate placement, it appears evident that the loading protocol is the influential factor driving the variation in outcome observed for this group.

Considerable variation in surgical treatment protocols was reported with additional confounding factors being present; flapless vs. flapped, bone graft vs. no bone graft, connective tissue graft vs. no connective tissue graft. The studies on immediate implants (Type 1A, 1B, 1C) use a variation of these four interventions which make it difficult to interpret their influence on outcomes. Therefore, this systematic review is not able to make any conclusions on surgical, hard, and soft tissue grafting protocols utilized in conjunction with the loading protocols.

Type 2-3A was deemed as CID, as there were no articles reporting on this protocol. Type 2-3B presented favorable clinical documentation from only one article (Belser et al., 2009) with a large cohort of patients in a medium-term follow-up. This protocol showed the best outcome-benefit ratio for the patient in term of treatment duration and survival/success rate. It can be argued that identifying case selection criteria for Type 2-3A and 2-3B may result in potential benefits for the patient, particularly in reducing the overall treatment time and an early re-shaping of peri-implant soft tissues. Type 2-3C was scientifically and clinically validated showing excellent survival and success results in a long-term follow-up. Type 2C has been presented as the standard, in the anterior zone when predictable aesthetics outcomes are required.

Type 4A resulted in the category of CD. The validation of this protocol was influenced by a negative outcome homogeneity (OH) ranging from 83.3% to 100% survival rate. One study showed inferior results for Type 4A implants placed in the posterior maxilla. Further interpretation of this data should ideally separate the results based on implant location in the oral cavity and the type of implant reconstruction. Type 4B and Type 4C were all deemed to be SCV. In these groups, when implants were placed in healed sites, the loading protocols have not influenced the survival or success rate. Type 4C was the most documented study protocol and remains the standard of care, particularly when treatment modifiers such as bone augmentation, low insertion torque, reduced diameter implants, and patient local and systemic factors are present (Gallucci et al., 2014).

The criteria for selection of the placement protocols require attention when selecting among the 12 treatment protocols presented in this review. Although case selection criteria presented in this review have several commonalities, there are significant variations on the quantification of these criteria. More important, the implications of these case selection criteria for implant placement on long-term survival and success rate are at the present are not fully understood.

For loading protocols, primary stability, RFA in conjunction with insertion torque values was the most commonly used criterion for selecting the loading protocols. It was observed that the loading protocol was an influential outcome variable for Type 1 placement protocols. Otherwise, the loading protocol appears not having an influence on the outcome of Type 2-3 and Type 4 implant placement.

5 | CONCLUSION

Data assessed in this systematic review highlight the importance of evaluating outcomes in oral implantology by combining the placement and loading protocols variables as a single denominator for survival/success.

For Type 1 placement, the loading protocol appears influential in the treatment outcome, with Type 1C being the only approach scientifically and clinically validated. For Type 1A, Type B, and Type C, specific placement and loading criteria are required to ensure the clinical efficacy of these treatment modalities.

Type 2-3C was scientifically and clinically validated and should be considered routine when. Type 2-3B showed very promising results and more evidence is needed to validate this approach. Type 2-3A was not reported yet.

The selection among the 12 placement/loading types presented in this SR should be based on the consideration of specific procedural criteria for implant placement and loading protocol.

ACKNOWLEDGEMENTS

This study was supported by the Department of Restorative Dentistry and Biomaterial Sciences at Harvard School of Dental Medicine, Boston, Massachussets, USA, and the ITI Foundation, Basel, Switzerland. The authors would like to thank Dr. Faris Jamjoom, Dr. Mahmoud Qabazard, and Dr. Muhsen Alnasser for their help in data extraction, AGE resident, Department of Restorative Dentistry and Biomaterials Sciences, Harvard School of Dental Medicine, Boston, Massachusetts, for the statistical analysis and Dr. Paul Bain, Reference and Education Services Librarian, Countway Library of Medicine, Boston, Massachusetts, for his expertise in developing the search strategy.

CONFLICT OF INTERESTS

The authors wish to declare no conflict of interests and that no external funding was received for the completion of this systematic review.

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SUPPORTING INFORMATION

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

How to cite this article: Gallucci GO, Hamilton A, Zhou W, Buser D, Chen S. Implant placement and loading protocols in partially edentulous patients: A systematic review. *Clin Oral Impl Res*. 2018;29(Suppl. 16):106–134. https://doi.org/10.1111/clr.13276