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Review article

CAD-CAM removable complete dentures: A systematic review and meta-analysis of trueness of fit, biocompatibility, mechanical properties, surface characteristics, color stability, time-cost analysis, clinical and patient-reported outcomes

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ABSTRACT

Objectives: This review compared Computer-aided designand Computer-aided manufactured (CAD-CAM) and conventionally constructed removable complete dentures (CDs).
Data: Seventy-three studies reporting on CAD-CAM (milled/3D-printed) CDs were included in this review. The most recent literature search was performed on 15/03/2021.
Sources: Two investigators searched electronic databases [PubMed (MEDLINE), Embase, CENTRAL], online search engines (Google) and research portals. Hand searches were performed to identify literature not available online.
Study selection: Studies on CAD-CAM CDs were included if they reported on trueness of fit, biocompatibility, mechanical, surface, chemical, color , microbiological properties, time-cost analysis, and clinical outcomes. Inter-investigator reliability was assessed using kappa scores. Meta-analyses were performed on the extracted data .
Results: The kappa score ranged between 0.897–1.000. Meta-analyses revealed that 3D-printed CDs were more true than conventional CDs ($p = 0.039$). Milled CDs had a higher flexural-strength than conventional and 3D-printed CDs ($p < 0.0001$). Milled CDs had a higher flexural-modulus than 3D-printed CDs ($p < 0.0001$). Milled CDs had a higher yield-strength than injection-molded ($p = 0.004$), and 3D-printed CDs ($p = 0.001$). Milled CDs had superior toughness ($p < 0.0001$) and surface roughness characteristics ($p < 0.0001$) than other CDs . Rapidly-prototyped CDs displayed poor color-stability compared to other CDs ($p = 0.029$). CAD-CAM CDs d displayed better retention than conventional CDs ($p = 0.015$). Conventional CDs had a higher strain at yield point than milled CDs ($p < 0.0001$), and had superior esthetics than 3D-printed ($p < 0.0001$). Fabrication of CAD-CAM CDs required less chairside time ($p = 0.037$) and lower overall costs ($p < 0.0001$) than conventional CDs.
Conclusions: This systematic review concludes that CAD-CAM CDs offer a number of improved mechanical/surface properties and are not inferior when compared to conventional CDs.
Clinical significance: CAD-CAM CDs should be considered for completely edentulous patients whenever possible, since this technique offers numerous advantages including better retention, mechanical and surface properties but most importantly preserves a digital record. This can be a great advantage for older adults with limited access to dental care.

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Table 1
PICO focused question, criteria for inclusion, sources of information, search terms, search strategy, search filters, and search dates.

Focus question	In completely edentulous patients, are CAD-CAM removable complete dentures (CDs) inferior to conventional CDs with respect to trueness of fit, biocompatibility, mechanical properties, surface characteristics, color stability, time-cost efficiency, clinical and patient-reported outcomes?		
Criteria		Inclusion criteria	Studies reporting on CDs manufactured by CAD-CAM (milled/3D-printed) and conventional processesAll study designs
		Exclusion criteria	Studies reporting on fixed dental prosthesis Studies reporting on partial removable dental prosthesis Reviews Studies reporting on software analysis, finite element analysis
Information sources		Electronic databases	MEDLINE PubMed (https://www.ncbi.nlm.nih.gov/pubmed/); Embase (https://www.embase.com/#search); Central Register of Controlled Trials CENTRAL in the Cochrane Library (https://www.cochranelibrary.com/advanced-search?q = *&t = 6)
		Others	Popular online internet search engines e.g. Google, Yahoo, research community websites on the internet https://www.researchgate.net/, reference crosschecks, personal communications and hand searches. Hand searches in dental journals were only performed for records not available electronically, or without an electronic abstract.
Search Terms	Population #1	#1.1: MeSH	jaw, edentulous, partially [MH] OR jaw, edentulous [MH] OR mouth, edentulous [MH] OR maxilla [MH] OR mandible [MH]
		#1.2: All Fields	complete edentulism OR completely edentulous OR fully edentulous OR partially edentulous OR partial edentulism OR edentulous ridge OR edentulous arch OR edentulous area OR edentulous OR edentulism OR edentulous maxilla OR edentulous mandible OR edentulous space OR edentulous region OR partially edentulous OR fully edentulous OR completely edentulous OR partially edentulous maxilla OR fully edentulous maxilla OR completely edentulous maxilla OR partially edentulous mandible OR fully edentulous mandible OR completely edentulous mandible OR denture OR clasp OR base OR framework
	Intervention or exposure #2	#2.1: MeSH	dental prosthesis [MH] OR denture, overlay [MH] OR denture bases [MH] OR denture, complete [MH] OR denture, complete, immediate [MH] OR denture, complete, lower [MH] OR denture, complete, upper [MH] OR denture, partial [MH] OR denture, partial, immediate [MH] OR denture, partial, removable [MH] OR denture, partial, temporary [MH] OR dental restoration, temporary [MH] OR dental prosthesis, implant-supported [MH] NOT Dental Implants [MH] NOT Denture, Partial, Fixed [MH]
		#2.2: All Fields	complete denture OR removable complete denture OR removable partial denture OR removable dental prosthesis OR complete denture prosthetic OR complete denture prosthodontics OR diagnostic denture OR immediate denture OR provisional denture OR transitional denture OR treatment denture OR trial denture OR full denture OR interim denture OR interim prosthesis OR overlay denture OR digital workflow OR implant supported removable dental prostheses OR implant supported complete removable dental prosthesis OR implant supported partial removable dental prosthesis OR implant supported overdenture OR implant assisted over dentures NOT implant fixed
	Comparison #3	#3.1: MeSH #3.2: All Fields:	Computer-Aided Design [MH] OR printing, three-Dimensional [MH] OR stereolithography [MH] CAD CAM denture OR Computer Aided Design denture OR Computer Aided Manufacturing denture OR Computer Assisted Machining denture OR CNC denture OR Computer Numerical Control denture OR digital denture OR digitally fabricated denture OR CAE denture OR Computer Aided Engineering denture OR Milling CAD CAM OR 3D printed denture OR Milled denture OR subtractive fabrication denture OR three dimensional printed denture OR Stereolithography denture OR SLA denture OR additive fabrication denture OR rapid prototyping denture OR selective laser sintering denture OR additive layer denture OR DMLS denture OR Direct metal laser sintering denture OR SLS denture OR selective laser sintering denture OR Photo solidification OR resin printing
	Outcome #4	#4.1: MeSH	quality of life [MH] OR patient satisfaction [MH] OR patient preference [MH] OR patient reported outcome measures [MH] OR patient outcome assessment [MH] OR treatment outcome [MH] OR dental prosthesis retention [MH] OR biomechanical phenomena [MH] OR dental prosthesis retention [MH] OR elastic modulus [MH] OR shear strength [MH] OR stress, mechanical [MH] OR hardness [MH] OR porosity [MH] OR shear strength [MH] OR color [MH] OR dental polishing [MH] OR cost-benefit analysis [MH] OR dental restoration wear [MH] OR dental restoration failure [MH] OR Mechanical Phenomena [MH]
		#4.2: All Fields	material properties OR surface roughness OR accuracy OR precision OR trueness OR color stability OR residual monomer content OR monomer release OR cost-effectiveness OR cost-minimization OR time OR OHRQoL OR fit OR case OR system OR experience OR stainability
Filters	No filters were applied		
Search queries run as performed in the various databases	Using search combination: (#1.1 OR #1.2) AND (#2.1 OR #2.2) AND (#3.1 OR #3.2) AND (#4.1 OR #4.2)		
Search dates	Final confirmatory online search was performed on 15/03/2021. No further online searches were performed after this date.		

Table 2
Studies reporting trueness of fit.

First author (Year)	Fabrication method	Brand/ Manufacturer	Surface deviation (mean ± SD in mm)	Sample size (n)	Samples and testing methods	Conclusion
Gao et al. (2021) [25]	3D-printing Orientation: 0°	VisJet M3 crystal, 3D systems	0.185 ± 0.060	9	Samples: Mandibular dentures were fabricated with different build orientation settings; 0°, 45°, 90°. Dentures were scanned and trueness was calculated by comparing against the original STL file using a 3D comparison software (Geomagic Control X software, 3D Systems)	Mandibular dentures: 3D-printed with a 45° build orientation displayed the best trueness of fit.
	3D-printing Orientation: 45°	VisJet M3 crystal, 3D systems	0.170 ± 0.043	9		
	3D-printing Orientation: 90°	VisJet M3 crystal, 3D systems	0.183 ± 0.044	9		
Katheng et al. (2021) [26]	3D-printing	Clear resin, Formlabs	NS	10	Samples: Geometric specimen that simulated maxillary complete denture were 3D-printed. Different polymerization time (15 mins, 30 mins) and temperature (40 °C, 60 °C, 80 °C) were evaluated The fabricated specimens were scanned and trueness was calculated by comparing against the original files using a 3D comparison software (CATIA V5, Dassault Systems)	The optimal post-polymerization time and temperature conditions for 3D-printing were found to be 30 mins and 40 °C, respectively
Tasaka et al. (2021) [27]	Injection-molding	SR Ivocap, Ivoclar Vivadent	NS	5	The fabricated dentures were scanned and the tooth displacement compared to the original tooth arrangement on the wax pattern was measured using a 3D comparison software (GOM Inspect, GOM)	3D-printed maxillary dentures displayed more tooth displacement when compared to heat-cured CDs.
	3D-printing	Vero Clear RGD835, Stratasys	NS	5		
You et al. (2021) [28]	3D-printing Layer thickness: 50 µm	ZMD-1000B, Dentis	0.152 ± 0.010	10	Samples: Maxillary complete dentures fabricated with different layer thickness setting; 50 µm, 100 µm. The trueness was measured by scanning the intaglio and cameo surfaces to find the best overlap with the reference model to obtain the root mean square (RMS) values using a 3D comparison software (Geomagic Verify 2015, Geomagic GmbH)	Setting the layer thickness to 100 µm produced more accuracy than 50 µm for the fabrication of trial dentures when using SLA
	3D-printing Layer thickness: 100 µm	ZMD-1000B, Dentis	0.132 ± 0.012	10		
Hada et al. (2020) [29]	3D-printing Orientation: 0°	Clear, Formlabs	0.129 ± 0.006	6	The mucosal surface of fabricated dentures was scanned. Precision and trueness were calculated by comparing the scans to the original STL file, using a 3D comparison software (CATIA V5, Dassault Systèmes)	The 45° build orientation displayed the highest trueness and precision.
	3D-printing Orientation: 45°	Clear, Formlabs	0.086 ± 0.004	6		
	3D-printing Orientation: 90°	Clear, Formlabs	0.109 ± 0.005 [Root mean square error values of trueness in mm]	6		
Hsu et al. (2020) [30]	Compression-molding	Lucitone 199, Dentsply Sirona	NS	10	Samples: Maxillary and mandibular complete dentures. The layer thickness of the	The milled groups illustrated the best denture adaptation. The compression and

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Table 2 (*continued*)

First author (Year)	Fabrication method	Brand/ Manufacturer	Surface deviation (mean ± SD in mm)	Sample size (n)	Samples and testing methods	Conclusion
					indicator was measured. Additionally, the fabricated dentures were scanned and trueness was calculated using a 3D comparison software (Geomagic Control X 2018, 3D Systems Inc).	injection molding groups had similar features and produced greater denture adaptation in the maxilla. The 3D-printed groups recorded divergent results and the lowest trueness values.
	Injection-molding	Ivobase High Impact, Ivoclar Vivadent AG	NS	10		
	Milled	Polywax PMMA, BiLKiM	NS	10		
	Milled	Yamahachi PMMA, Yamahachi Dental Mfg	NS	10		
	3D-printing	MiiCraft BV-005 printable resin, Young Optics Inc	NS	10		
	3D-printing	NextDent Base printable resin, NextDent BV	NS Silicone thickness Digital superimposition analysis	10		
Jin et al. (2020) [31]	3D-printing Arch, Build angle setting: Maxillary, 90°	NextDent Base, NextDent	0.095 ± 0.008	10	Samples: Maxillary and mandibular complete dentures. Surface deviation data, including root-mean-square estimates (RMSE); positive average deviation, and negative average deviation values, were calculated to report the degree of tissue surface adaptation using a 3D comparison software (Geomagic Control X, 3D Systems) with different build angle settings: 90°, 100°, 135°, 150°	No statistically significant differences were found for root-mean-square estimate values amongst any build angle groups in either the maxillary or mandibular arch.
	3D-printing Arch, Build angle setting: Maxillary, 100°	NextDent Base, NextDent	0.079 ± 0.003	10		
	3D-printing Arch, Build angle setting: Maxillary, 135°	NextDent Base, NextDent	0.087 ± 0.007	10		
	3D-printing Arch, Build angle setting: Maxillary, 150°	NextDent Base, NextDent	0.088 ± 0.006	10		
	3D-printing Arch, Build angle setting: Mandibular, 90°	NextDent Base, NextDent	0.114 ± 0.005	10		
	3D-printing Arch, Build angle setting: Mandibular, 100°	NextDent Base, NextDent	0.103 ± 0.007	10		
	3D-printing Arch, Build angle setting: Mandibular, 135°	NextDent Base, NextDent	0.123 ± 0.008	10		
	3D-printing Arch, Build angle setting: Mandibular, 150°	NextDent Base, NextDent	0.136 ± 0.015 Root-mean-square estimates in mm	10		
Katheng et al. (2020) [32]	3D-printing Polymerization time: 15 min, Temperature: 40 °C	Clear resin, Formlabs	NS	10	Samples: Geometric specimen that simulated maxillary complete denture with different polymerization time and temperature; 15 min, 30 min, 40 °C, 60 °C, 80 °C. The fabricated specimens were	The recommended polymerization parameters were 15 mins and 40 °C. These conditions offered high dimensional accuracy, favorable surface tissue

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Table 2 (*continued*)

First author (Year)	Fabrication method	Brand/ Manufacturer	Surface deviation (mean ± SD in mm)	Sample size (n)	Samples and testing methods	Conclusion
					scanned and the calculated trueness were compared to the original STL files using a 3D comparison software (CATIA V5, Dassault Systems). Additionally, the gap between the fabricated specimens and the original cast was measured under a stereomicroscope. Fourier transform infrared spectrometry was used to determine the degree of conversion of all specimens.	adaptation, and a satisfactory degree of conversion.
	3D-printing Polymerization time: 15 min, Temperature: 60 °C	Clear resin, Formlabs	NS	10		
	3D-printing Polymerization time: 15 min, Temperature: 80 °C	Clear resin, Formlabs	0.10 ± 0.01	10		
	3D-printing Polymerization time: 30 min, Temperature: 40 °C	Clear resin, Formlabs	0.07 ± 0.02	10		
	3D-printing Polymerization time: 30 min, Temperature: 60 °C	Clear resin, Formlabs	0.09 ± 0.02	10		
	3D-printing Polymerization time: 30 min, Temperature: 80 °C	Clear resin, Formlabs	0.11 ± 0.02 Root-mean-square estimate in mm	10		
†Wemken et al. (2020) [33]	Injection-molding	PalaXpress, Kulzer	0.072 ± 0.011	16	Samples: Maxillary complete dentures. The fabricated dentures were hydrothermally aged and microwave sterilized. The trueness was measured before and after the aging process, using a 3D comparison software (Geomagic Control X, 3D Systems).	Before the aging process, the milled group demonstrated the lowest surface deviation, followed by the injection-molded and 3D-printed groups. Hydrothermal cycling did not affect the milled group's trueness in contrast to the injection-molded and 3D-printed groups. Microwave sterilization caused no effect on the 3D-printed group's dimensional trueness; but led to clinically critical deformations of the injection-molded and milled groups.
	Milled	IvoBase CAD, Ivoclar Vivadent	0.054 ± 0.016	16		
	3D-printing	Denture Base LP, Formlabs	0.096 ± 0.017 Root-mean-square estimates before the aging process in mm	16		
†Yoon et al. (2020) [34]	Compression molding (Maxillary)	SR Triplex Hot, Ivoclar Vivadent AG	0.428 ± 0.280	7	Samples: Maxillary and mandibular complete dentures. Silicone replica technique was used for the measurement of the adaptation. The layer thickness of the indicator was measured at each designated point under a stereomicroscope.	No statistically significant differences were found amongst the 3 denture base fabrication techniques.
	Milled (Maxillary)	VIPI Block GUM, VIPI	0.552 ± 0.216	7		
	3D-printing (Maxillary)	NextDent Base, NextDent B.V.	0.427 ± 0.191	7		
	Compression molding (Mandibular)	SR Triplex Hot, Ivoclar Vivadent AG	0.311 ± 0.163	5		
	Milled (Mandibular)	VIPI Block GUM, VIPI	0.263 ± 0.199	5		

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Table 2 (*continued*)

First author (Year)	Fabrication method	Brand/ Manufacturer	Surface deviation (mean ± SD in mm)	Sample size (n)	Samples and testing methods	Conclusion
	3D-printing (Mandibular)	NextDent Base, NextDent B.V.	0.268 ± 0.174 The value was calculated from the data in the original article in mm	5		
†You et al. (2020a) [35]	Milled	HUGE PMMA Block-Pink, Huge Dental Material	0.150 ± 0.006	5	Samples: Maxillary complete dentures. Root mean square values between the socketed surface of the denture base, comparing to the original maxillary edentulous model were reported, using a 3D comparison software (Verify, Geomagic)	The milling group demonstrated lower surface deviations than the 3D-printed groups.
	3D-printing Orientation: Horizontal	NextDent Base, NextDent	0.228 ± 0.010	5		
	3D-printing Orientation: Vertical	NextDent Base, NextDent	0.328 ± 0.004 Root-mean-square value in mm	5		
†You et al. (2020b) [36]	Milled	Milling machine DWX-50, Roland DG Corp	0.297 ± 0.011	10	Samples: Maxillary metal denture bases. CAD-CAM was used to fabricate wax or resin patterns. Maxillary metal base was then cast from these patterns. Silicone replica technique was used for the measurement procedure.	The SLA group was the most precise in the fabrication of complete denture metal bases. The fabricated metal bases' adaptation varied significantly across the techniques but fell within a clinically acceptable range.
	3D-printing (SLA)	SLA printer ZENITH U, Dentis	0.218 ± 0.033	10		
	3D-printing (DLP)	DLP printer ZENITH D, Dentis	0.099 ± 0.035	10		
†Einarsdottir et al. (2019) [37]	Compression molding	Lucitone 199 Denture Base Resin, Dentsply Sirona	0.521 ± 0.257	15	Samples: Mandibular complete dentures. Each base's intaglio surface was scanned and compared with the titanium master cast using a 3D comparison software (Geomagic Freeform, 3D Systems).	The milled group exhibited fewer dimensional changes than either the compression or injection-molded groups.
	Injection-molding	IvoBase Hybrid, Ivoclar Vivadent AG	0.545 ± 0.29	15		
	Milled	AvaDent, Global Dental Science	0.306 ± 0.231 The value was calculated from the data in the original article (mm)	15		
†Hwang et al. (2019) [38]	Compression-molding	SR Triplex Hot, Ivoclar Vivadent AG	0.165 ± 0.056	10	Samples: Maxillary complete dentures. The intaglio surfaces of the dentures were scanned and superimposed on the corresponding casts to compare the degree of tissue surface adaptation using a 3D comparison software (Geomagic Verify, 3D Systems)	The 3D-printed group revealed better trueness and tissue surface adaptation than the milled and compression-molded groups.
	Milled	VIPI Block GUM, VIPI	0.177 ± 0.003	10		
	3D-printing	NextDent Base, NextDent	0.074 ± 0.005 Root-mean-square estimates in mm	10		
†Kalberer et al. (2019) [39]	Milled	AvaDent Digital Dental Solutions	0.0349 ± 0.0047	10	Samples: Maxillary complete dentures.	The trueness of the milled group was superior to the 3D-

(continued on next page)

Table 2 (*continued*)

First author (Year)	Fabrication method	Brand/ Manufacturer	Surface deviation (mean ± SD in mm)	Sample size (n)	Samples and testing methods	Conclusion
		Europe, Global Dental Science Europe BV			The intaglio surfaces of the fabricated complete dentures were scanned at baseline using a laboratory scanner. A purpose-built 3D comparison software program (Oracheck version 2.10, Cyfex) was used to analyze the complete dentures' trueness.	printed complete dentures in terms of the trueness of the intaglio surface
	3D-printing	NextDent Denture 3+, Next- Dent B. V.	0.0953 ± 0.0075	10		
†Lee et al. (2019) [40]	Injection molding	SR-Ivocap high impact, Ivoclar Vivadent AG	0.149 ± 0.011	10	Samples: Maxillary complete dentures. Intaglio surfaces were analyzed using a surface matching software (Geomagic control X, 3D systems).	The denture base's overall accuracy was higher in the milled and 3D-printed methods than the injection-molding method.
	Milled	Vipi block GUM, Vipi	0.081 ± 0.018	10		
	3D-printing	NextDent Base, NextDent	0.066 ± 0.014 The value was calculated from the data in the original article in mm	10		
McLaughlin et al. (2019) [41]	Compression-molding	Lucitone 199 Denture Base Resin, Dentsply Sirona	0.404 ± 0.095	27	Samples: Maxillary denture fabrication. The space between the denture and the master cast, was quantified using a silicone duplicating material.	Overall, the injection-molding and milled fabrication methods produced equally well-fitting dentures, and both produced a better fit than compression-molding.
	Injection-molding	IvoBase Hybrid, Ivoclar Vivadent AG	0.283 ± 0.073	27		
	Milled	AvaDent, Global Dental Science	0.278 ± 0.053 Weight per area of ovoid and medium arch palate from duplicated silicone (mg/mm^2)	27		
Tasaka et al. (2019) [42]	Compression-molding	Acron No.5, GC	0.02 ± 0.08	1	Samples: Maxillary complete denture base. The working casts and the fabricated denture bases were compared for accuracy using a 3D-comparison software (GOM Inspect 3D data test software, GOM).	In this study, the experimental denture base fabricated using additive manufacturing was more accurate and obtained greater retentive force than the experimental heat-cured denture base.
	3D-printing	Vero Clear RGD835, Stratasys	0.03 ± 0.01	1		
†Deng et al. (2018) [43]	3D-printing (Polylactic acid)	FDM 3D printer, Lingtong-II	0.277 ± 0.021	5	A light-body silicone film was made after each denture pattern had been seated on the plaster model and was scanned to determine its thickness, which reflected the 3D space between the plaster model and the tissue surface of the denture pattern.	The adaptation of the polylactic acid pattern of maxillary complete denture printed by fused deposition modeling technology was comparable to that prepared by a wax printer and satisfied the accuracy requirements.
	3D-printing (Wax)	3D wax printer ProJet CPX 3500, 3D Systems	0.279 ± 0.045	5		
Goodacre et al. (2018) [44]	Compression-molding	Lucitone 199 Denture Base Resin, Dentsply Sirona	NS	10	Samples: Maxillary complete dentures. The pre-processing and post-processing scan files of each denture were superimposed using surface-matching software	In terms of tooth movement's accuracy, the CAD-CAM monolithic (fully-milled) technique was the most accurate, followed by fluid resin, CAD- CAM-bonded,

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Table 2 (*continued*)

First author (Year)	Fabrication method	Brand/ Manufacturer	Surface deviation (mean ± SD in mm)	Sample size (n)	Samples and testing methods	Conclusion
					(Geo- magic Control 2014, 3D Systems Inc).	pack-and-press, and then injection-molding.
	Autopolymerization	Lucitone Fas-Por, Dentsply Sirona	NS	10		
	Injection-molding	IvoBase Hybrid, Ivoclar Vivadent AG	NS	10		
	Milled (Bonded teeth)	AvaDent, Global Dental Science	NS	10		
	Milled (fully-milled teeth)	AvaDent, Global Dental Science	NS	10		
			Tooth movement			
†Steinmassl et al. (2018) [45]	Compression-molding	AESTHETIC RED, CANDULOR AG	0.105 ± 0.019	5	Samples: Maxillary complete dentures The master casts and all denture bases were scanned and matched digitally using a 3D comparison software (GOM Inspect 2016, GOM).	The milled group showed a better fit than the compression-molding group.
	Milled	Baltic Denture System, Merz Dental GmbH	0.086 ± 0.012	5		
	Milled	Whole You Nexteeth, Whole You Inc.	0.074 ± 0.011	5		
	Milled	Wieland Digital Dentures, Wieland Dental + Technik GmbH & Co. KG	0.068 ± 0.005	5		
	Milled	AvaDent Digital Dentures, Global Dental Science Europe BV	0.058 ± 0.005	5		
†Yoon et al. (2018) [46]	Compression-molding	SR Triplex Hot, Ivoclar Vivadent AG	0.118 ± 0.053	10	Samples: Mandibular complete dentures. The dentures' intaglio surfaces were scanned and superimposed on the corresponding casts to compare the degree of tissue surface adaptation using a 3D comparison software (Geomagic Verify, 3D Systems).	For trueness, the milled group was better than the 3D-printed group. However, no statistically significant difference was detected concerning tissue surface adaptation.
	Milled	VIPI BLOCK gum, VIPI	0.104 ± 0.015	10		
	3D-printing	NextDent Base, NextDent BV	0.101 ± 0.011	10		
			Root-mean-square estimate in mm			
†Davda et al. (2017) [47]	Autopolymerization (W/Tray)	NS	0.168 ± 0.047	6	Samples: Maxillary complete dentures. Dentures produced by each construction method were investigated by comparing scans of the templates to the original denture scan. The analyses of the trueness and precision were restricted to the teeth and polished surfaces. The fitting surface was ignored.	The 3D-printed group showed better trueness and precision than the compression-molding group.
	3D-printing	Resin printer DWS 020D, DWS System	0.103 ± 0.021	6		
†Srinivasan et al. (2017) [48]	Compression-molding	Ivoclar ProBase, Ivoclar Vivadent AG	0.048 ± 0.05	11	Samples: Maxillary denture fabrication. The dentures' intaglio surfaces were scanned and superimposed using a 3D-software (Oracheck version 2.10, Cyfex).	Trueness of the intaglio surface of the three techniques seemed to remain in an acceptable clinical range.

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Table 2 (*continued*)

First author (Year)	Fabrication method	Brand/ Manufacturer	Surface deviation (mean ± SD in mm)	Sample size (n)	Samples and testing methods	Conclusion
	Injection-molding	Ivobase High Impact, Ivoclar Vivadent AG	0.031 ± 0.005	11		
	Milled	AvaDentTM, Global Dental Science Europe BV	0.065 ± 0.01	11		
†Goodacre et al. (2016) [49]	Compression molding	Lucitone 199 Denture Base Resin, Dentsply Sirona	0.0007 ± 0.08077	10	Samples: Maxillary complete dentures. The intaglio surface was laser scanned. Each denture's scan file was superimposed on the scan file of the corresponding cast using surface matching software (Geomagic Control 2014, 3D Systems).	The CAD-CAM fabrication process was the most accurate and reproducible technique compared to the other investigated techniques.
	Autopolymerization	Lucitone Fas-Por, Dentsply Sirona	0.00467 ± 0.05719	10		
	Injection-molding	IvoBase Hybrid, Ivoclar Vivadent AG	0.00254 ± 0.05759	10		
	Milled	AvaDent, Global Dental Science	0.00474 ± 0.03472	10		
Yamamoto et al. (2016) [50]	Milled (Bonded teeth) Comparison among different artificial teeth types, combined with offset values and shape of artificial teeth's basal areas.	Aadva PMMA disc, GC Corp.	NS	3	Samples: Artificial teeth were bonded to custom-fabricated resin blocks. After bonding artificial teeth to custom-fabricated resin blocks, the samples were scanned by a 3D scanner and compared to the original data using a 3D comparison software (Mimics, Materialise).	Both the offset values and the shapes of the basal areas of artificial teeth can be optimized to improve the accuracy of positioning of bonded artificial teeth in a milled denture. The optimal offset values were 0.20 mm for mandibular left first premolar and mandibular left first molar.
Chen et al. (2015) [51]	Conventional method (Wax)	NS	0.3 ± 0.17	2	Samples: Wax patterns. The scanned tissue surface deviations were compared using a 3D comparison software (Geomagic Studio/Qualify 2013, Geomagic).	For both wax patterns produced by the 3D-printing method and the conventional method, scan data of the tissue surfaces and cast surfaces revealed a good fit in the majority. No statistically significant difference was observed between the two techniques.
	3D-printing (Wax)	3D wax printer ProJet CPX 3500, 3D Systems	0.29 ± 0.14	2		
Yamamoto et al. (2014) [52]	Milled (offset: 0.00 mm)	ACRON, GC	0.15 ± 0.02	3	Samples: Artificial teeth were bonded to custom-fabricated resin blocks with different offset values; 0.00, 0.10, 0.15, 0.20, 0.25 mm and different types of artificial teeth. After bonding artificial teeth to custom-fabricated resin blocks, the samples were scanned by a cone-beam computed tomography (CBCT) and then compared to the original data using a 3D comparison software (Mimics, Materialise).	Optimal offset values were 0.15–0.25 mm for maxillary left incisor, 0.15 and 0.25 mm for maxillary left canine, 0.25 mm for maxillary left first premolar, and 0.10–0.25 mm for maxillary left molar.
	Milled (offset: 0.10 mm)	ACRON, GC	0.06 ± 0.01	3		
	Milled (offset: 0.15 mm)	ACRON, GC	0.05 ± 0.01	3		
	Milled (offset: 0.20 mm)	ACRON, GC	0.06 ± 0.00	3		
	Milled (offset: 0.25 mm)	ACRON, GC	0.08 ± 0.00	3		

Bonded, the denture teeth were bonded into the milled base; *DLP*, digital light processing; *FDM*, fused deposition modeling; *Monolithic*, the denture teeth were milled as part of the denture base; *n*, sample size; *NS*, not specified; *PLA*, polylactic acid; *W/Tray*, copy denture technique with tray; *SD*, standard deviation; *SLA*, stereolithography; †, study used for meta-analysis.

Table 3
Studies reporting flexural strength of denture bases.

First author (Year)	Fabrication method	Brand/ Manufacturer	Flexural strength (mean ± SD in MPa)	n	Testing method(Sample dimension)	Conclusion
†Becerra et al. (2021) [58]	Compression-molding	Probase Hot, Ivoclar Vivadent Inc.	73.6 ± 11.9	30	Three-point bending test (65 × 10 × 3.3 mm)	The milled group had the highest flexural strength while there was no difference between the other two groups.
	Injection-molding	Probase Hot, Ivoclar Vivadent Inc.	78.2 ± 11.1	30		
	Milled	Ivobase CAD, Ivoclar Vivadent Inc.	93.1 ± 3.4	30		
Iwaki et al. (2020) [59]	Compression-molding	Acron, GC	111.40 ± 7.3	5	Three-point bending test (65 × 10 × 3.3 mm)	The custom-made milled group demonstrated a higher flexural strength than the conventional compression-molding group.
	Milled * (fabricated by high-pressure molding of heat-curing denture base resin)	Acron, GC	124.08 ± 5.16	5		
Perea-Lowery et al. (2020) [60]	Compression-molding	Paladon 65, Kulzer GmbH	NS	8	A static 3-point bending test on dry-stored, water-stored and repaired specimen was performed. (65 × 10 × 3.2 mm)	The CAD-CAM group did not generally demonstrate a flexural strength greater than the conventional group.
	Autopolymerization	Palapress, Kulzer GmbH	NS	8		
	Milled	Degos Dental L-Temp, Degos Dental GmbH	NS	8		
	Milled	IvoBase CAD, Ivoclar Vivadent AG	NS	8		
	Milled	Zirkonzahn Temp Basic Tissue, Zirkonzahn SRL	NS	8		
†Aguirre et al. (2019) [61]	Compression-molding	Lucitone 199 Denture Base Resin, Dentsply Sirona	116.6 ± 3.1	10	Three-point bending test (64 × 10 × 3.3 mm)	The flexural strength of the CAD-CAM milled group was significantly higher than that of the other groups.
	Injection-molding	SR Ivocap High Impact, Ivoclar Vivadent AG	86.7 ± 7.1	10		
	Milled	Vertex PMMA, AvaDent Original shade, Global Dental Science	146.6 ± 6.6	10		
†Alp et al. (2019) [62]	Compression-molding	Art Concept Artegral Dentine, Merz Dental GmbH	66.1 ± 13.1	15	Three-point flexural strength after thermocycling (25 × 2 × 2 mm)	Flexural strength was highest in CAD-CAM resins, followed by bis-acrylate resin.
	Autopolymerization	Protemp 4, 3M ESPE	85.2 ± 20.4	15		
	Milled//	M-PM Disc A3, Merz Dental GmbH	131.9 ± 19.8	15		
	Milled	PINK CAD-CAM DISC, Polident d.o.o.	113.0 ± 16.9	15		
	Milleded	Telio CAD, Ivoclar Vivadent AG	106.2 ± 20.2	15		
†Müller et al. (2019) [63]	Milled	Avadent Extreme CAD-CAM shaded puck YW10, AvaDent Global Dental Science Europe	114.508 ± 4.63	5	Three-point bending test (65 × 10 × 3 mm)	Milling groups revealed a significantly higher flexural strength than 3D-printed groups. 3D-printing with the recommended 3D printer demonstrated a higher flexural strength than third-party 3D-printer.
	Milled	AvaDent Denture base puck, AvaDent Global Dental Science Europe	114.108 ± 3.03	5		
	3D-printing	NextDent C&B, Vertex-Dental B.V.	99.684 ± 1.61	5		
	3D-printing *i*	NextDent Base, Vertex-Dental B.V.	90.756 ± 16.29	5		
	3D-printing *ii*	NextDent Base, Vertex-Dental B.V.	67.348 ± 11.39	5		
	3D-printing *iii*	NextDent Base, Vertex-Dental B.V.	71.512 ± 10.77	5		
†Pacquet et al. (2019) [64]	Compression-molding	ProBase Hot, Ivoclar Vivadent AG	97.31 ± 4.96	25	Three-point bending test (65 × 10 × 2.5 mm for compression-molding and CAD-CAM group) (40 × 4 × 2 mm for injection-molding)	CAD-CAM group had greater flexural strength than injection-molding group, but less than the compression-molding group.
	Injection-molding	Ivocap, Ivoclar Vivadent AG	79.35 ± 10.01	25		

(*continued on next page*)

Table 3 (*continued*)

First author (Year)	Fabrication method	Brand/ Manufacturer	Flexural strength (mean ± SD in MPa)	n	Testing method(Sample dimension)	Conclusion
	Milled	IvoBase CAD, Ivoclar Vivadent AG	87.98 ± 7.37	25		
†Al-Dwairi et al. (2018) [65]	Compression-molding	Meliodent, Kulzer GmbH	93.33 ± 8.64	15	Three-point bending test (65 × 10 × 3 mm)	CAD-CAM demonstrated improved flexural strength.
	Milled	Tizian, Schütz Dental	130.67 ± 10.48	15		
	Milled	Avadent, Global Dental Science	123.11 ± 9.47	15		
†Arslan et al. (2018) [66]	Compression-molding	Promolux, Merz Dental GmbH	108.95 ± 5.36α	10	A three-point bending test was performed before and after thermocycling (64 × 10 × 3.3 mm)	CAD-CAM group demonstrated a higher flexural strength than the compression-molding group.
	Milled	PINK CAD-CAM DISC, Polident d.o.o.	133.43 ± 5.9α	10		
	Milled	M-PM Disc, Merz Dental GmbH	122.47 ± 5.54α	10		
	Milled	AvaDent Puck Disc, Avadent Global Dental Science LLC	118.32 ± 4.66α	10		
†Srinivasan et al. (2018) [67]	Compression-molding	AESTHETIC RED, CANDULOR AG	96 ± 4	5	Three-point bending test (65 × 10 × 3 mm)	Higher flexural strength for CAD-CAM group.
	Milled	AvaDent Digital Dentures, Global Dental Science Europe BV	121 ± 2	5		
†Ayman et al. (2017) [68]	Compression-molding	Vertex Rapid Simplified, Vertex-Dental B.V.	62.38 ± 1.73	10	Three-point testing design (65 × 10 × 3 mm)	Higher flexural strength and modulus for compression molding.
	Milled	PINK CAD-CAM DISC, Polident d.o.o.	34.05 ± 2.32	10		

α, this value is before thermocycling; *i*, manufacturer-recommended 3D-printer; *ii*, third-party 3D-printer; *iii*, printed in a vertical orientation; *n*, sample size; *NS*, not specified; *SD*, standard deviation; †, study used for meta-analysis.

1. Introduction

Epidemiological surveys indicate that people are both living longer and retaining more of their natural teeth into old age. [1–3]. Rehabilitation of completely edentulous jaws with conventional removable complete dentures (CDs) is a well-established treatment protocol. Traditionally, CDs are fabricated either as a completely new CD or by using copy techniques [4–6]. Whilst some clinical aspects of these techniques differ, they both include intra-oral impressions taken of the denture bearing areas with occlusal information provided using wax rims. However, the use of computer-aided design and computer-aided manufacturing (CAD-CAM) techniques in the construction of CDs has recently gained popularity [7]. CAD-CAM CDs can be constructed in as few as two clinical visits. At the first visit, all clinical records are captured, which can take the form of traditional impressions or digital records produced using intra-oral scanning technology. The records are transferred to the digital dental laboratory, where the entire denture is designed virtually. A design preview for the clinician to approve is possible for some techniques, before the digital dental laboratory completes the denture. At the second clinical visit, the dentures are ready for insertion. Whilst this technology is still in its infancy, it may offer significant benefits to older patients, including fewer clinical appointments alongside some reports of improved fit and better material properties compared to traditionally manufactured dentures [8].

Despite the increasing availability of CAD-CAM CDs, the majority of edentulous patients still receive dentures constructed using more traditional techniques. In this review, conventional techniques employed to fabricate CDs include flask-pack-press (FPP) or injection-molding using polymethylmethacrylate (PMMA) resin materials that may be either heat-polymerized or auto-polymerized, polyamides, or composite resin materials. In comparison, the CAD-CAM methods referred to are either additive [rapidly-prototyped (RP)/3D-printed] or subtractive (milled) processes. The 3D-printing techniques include stereolithography, digital light processing or fused deposition modeling. This aim of this systematic review was to evaluate and compare CAD-CAM CDs with conventionally manufactured CDs in terms of trueness of fit, biocompatibility, mechanical properties, surface characteristics, color stability, time-cost analysis, clinical and patient-reported outcomes. The PICO (Population Intervention/exposure Comparison Outcome) focused research question set for this systematic review was: "In completely edentulous patients, are CAD-CAM removable complete dentures (CDs) inferior to conventional CDs with respect to trueness of fit, biocompatibility, mechanical properties, surface characteristics, color stability, time-cost efficiency, clinical and patient-reported outcomes?"

2. Materials and methods

2.1. Protocol and registration

This systematic review was conducted and reported according to the PRISMA (preferred reporting items for systematic reviews and meta-

Table 4
Studies reporting flexural modulus for denture bases.

First author (Year)	Fabrication method	Brand/ Manufacturer	Flexural modulus (mean ± SD in MPa)	n	Testing method (Sample dimension)	Conclusion
†Becerra et al. (2021) [58]	Compression-molding	Probase Hot, Ivoclar Vivadent Inc.	2990 ± 130	30	Three-point bending test (65 × 10 × 3.3 mm)	The injection-molding group had the highest flexural modulus, while the milled group demonstrated the lowest flexural modulus.
	Injection-molding	Probase Hot, Ivoclar Vivadent Inc.	3320 ± 230	30		
	Milled	Ivobase CAD, Ivoclar Vivadent Inc.	2600 ± 110	30		
Iwaki et al. (2020) [59]	Compression-molding	Acron, GC	3660 ± 50	5	Three-point bending test (65 × 10 × 3.3 mm)	The custom-made milled group demonstrated higher flexural modulus than the conventional compression-molding group.
	Milled* (fabricated by high-pressure molding of heat-curing denture base resin)	Acron, GC	3790 ± 30	5		
†Aguirre et al. (2019) [61]	Compression-molding	Lucitone 199 Denture Base Resin, Dentsply Sirona	2918.4 ± 106.3	10	Three-point bending test (64 × 10 × 3.3 mm)	The flexural modulus of the CAD-CAM milled group was significantly higher than that of the other tested groups.
	Injection-molding	SR Ivocap High Impact, Ivoclar Vivadent AG	2121.3 ± 176.6	10		
	Milled	Vertex PMMA, AvaDent Original shade, Global Dental Science	3816.7 ± 44.3	10		
†Müller et al. (2019) [63]	Milled	Avadent Extreme CAD-CAM shaded puck YW10, AvaDent Global Dental Science Europe	3.064 ± 0.05	5	Three-point bending test (65 × 10 × 3 mm)	Milled groups had a significantly higher flexural modulus than the printed group. Printing with the recommended 3D printer demonstrated a higher flexural modulus than a third-party 3D printer. Printing in horizontal orientation showed a higher flexural modulus than printing in a vertical orientation.
	Milled	AvaDent Denture base puck, AvaDent Global Dental Science Europe	3.038 ± 0.08	5		
	3D-printing	NextDent C&B, Vertex-Dental B.V.	2.624 ± 0.04	5		
	3D-printing *i*	NextDent Base, Vertex-Dental B.V.	2.716 ± 0.14	5		
	3D-printing *ii*	NextDent Base, Vertex-Dental B.V.	2.108 ± 0.04	5		
	3D-printing *iii*	NextDent Base, Vertex-Dental B.V.	1.832 ± 0.22	5		
†Al-Dwairi et al. (2018) [65]	Compression-molding	Meliodent, Kulzer GmbH	2117.2 ± 154.3	15	Three-point bending test (65 × 10 × 3 mm)	Milled groups demonstrated improved flexural modulus.
	Milled	Tizian, Schütz Dental	2474.7 ± 249.0	15		
	Milled	Avadent, Global Dental Science	2519.6 ± 245.4	15		
†Srinivasan et al. (2018) [67]	Compression-molding	AESTHETIC RED, CANDULOR AG	2.7 ± 0.1	5	Three-point bending test (65 × 10 × 3 mm)	The flexural modulus was the same.
	Milled	AvaDent Digital Dentures, Global Dental Science Europe BV	2.7 ± 0.2	5		
Ayman et al. (2017) [68]	Compression-molding	Vertex Rapid Simplified, Vertex-Dental B.V.	1.55 ± 0.06	10	Three-point testing design (65 × 10 × 3 mm)	Higher flexural modulus for the milled group
	Milled	PINK CAD-CAM DISC, Polident d.o.o.	2.85 ± 0.01	10		

i, manufacturer-recommended 3D-printer; *ii*, third-party 3D-printer; *iii*, printed in a vertical orientation; *n*, sample size; *NS*, not specified; *SD*, standard deviation; †, study used for meta-analysis.

Table 5
Studies reporting on the yield strength of denture bases.

First author (Year)	Fabrication method	Brand/ Manufacturer	Yield strength (mean ± SD in MPa)	n	Testing method (Sample dimension)	Conclusion
†Müller et al. (2019) [63]	Milled	Avadent Extreme CAD-CAM shaded puck YW10, AvaDent Global Dental Science Europe	5.538 ± 0.87	5	Three-point bending test (65 × 10 × 3 mm)	The milled group revealed the same yield strength compared to the 3D-printed groups.
	Milled	AvaDent Denture base puck, AvaDent Global Dental Science Europe	8.134 ± 3.05	5		
	3D-printing	NextDent C&B, Vertex-Dental B.V.	5.658 ± 1.21	5		
	3D-printing *i*	NextDent Base, Vertex-Dental B.V.	5.818 ± 1.73	5		
	3D-printing *ii*	NextDent Base, Vertex-Dental B.V.	4.346 ± 0.11	5		
	3D-printing *iii*	NextDent Base, Vertex-Dental B.V.	4.16 ± 0.07	5		
†Pacquet et al. (2019) [64]	Compression-molding	ProBase Hot, Ivoclar Vivadent AG	81.45 ± 2.34	25	Three-point bending test (65 × 10 × 2.5 mm for compression molding and CAD-CAM group) (40 × 4 × 2 mm for injection molding)	The compression-molded group demonstrated a higher yield strength than the milled group. The milled group demonstrated a higher yield strength than the injection-molding group.
	Injection-molding	Ivocap, Ivoclar Vivadent AG	61.06 ± 7.45	25		
	Milled	IvoBase CAD, Ivoclar Vivadent AG	65.98 ± 3.40	25		
†Srinivasan et al. (2018) [67]	Compression-molding	AESTHETIC RED, CANDULOR AG	54 ± 11	5	Three-point bending test (65 × 10 × 3 mm)	The milled group had a higher yield strength than the compression-molding group.
	Milled	AvaDent Digital Dentures, Global Dental Science Europe BV	71 ± 6	5		

i, manufacturer-recommended 3D-printer; *ii*, third-party 3D-printer; *iii*, printed in a vertical orientation; *n*, sample size; *NS*, not specified; *SD*, standard deviation; †, study used for meta-analysis.

Table 6
Studies reporting strain at yield-point of denture bases.

First author (Year)	Fabrication method	Brand/ Manufacturer	Strain at yield-point(mean ± SD)	n	Testing method (Sample dimension)	Conclusion
†Müller et al. (2019) [63]	Milleded	Avadent Extreme CAD-CAM shaded puck YW10, AvaDent Global Dental Science Europe	0.175 ± 0.03	5	Three-point bending test (65 × 10 × 3 mm)	No significant differences between the groups were detected
	Milled	AvaDent Denture base puck, AvaDent Global Dental Science Europe	0.271 ± 0.11	5		
	3D-printing	NextDent C&B, Vertex-Dental B.V.	0.205 ± 0.05	5		
	3D-printing *i*	NextDent Base, Vertex-Dental B.V.	0.212 ± 0.06	5		
	3D-printing *ii*	NextDent Base, Vertex-Dental B.V.	0.203 ± 0.01	5		
	3D-printing *iii*	NextDent Base, Vertex-Dental B.V.	0.211 ± 0.06	5		
†Srinivasan et al. (2018) [67]	Compression-molding	AESTHETIC RED, CANDULOR AG	0.020 ± 0.005	5	Three-point bending test (65 × 10 × 3 mm)	The milled group had a higher strain at yield-point than the compression-molding group.
	Milled	AvaDent Digital Dentures, Global Dental Science Europe BV	0.003 ± 0.002	5		

i, manufacturer-recommended 3D-printer; *ii*, third-party 3D-printer; *iii*, printed in a vertical orientation; *n*, sample size; *NS*, not specified; *SD*, standard deviation; †, study used for meta-analysis.

analysis) guidelines [9]. The protocol used in this systematic review is similar to the design used in previously published systematic reviews [10,11]. The review protocol was registered with PROSPERO: International prospective register of systematic reviews (CRD42020175673).

2.2. Eligibility criteria and information sources

The predefined list of inclusion and exclusion criteria used for this systematic review are detailed in Table 1. All studies reporting on CDs manufactured using CAD-CAM and conventional processes in completely edentulous patients were searched using online electronic databases (PubMed, Embase and CENTRAL). Relevant publications identified but which were not accessible online were hand-searched. Other sources such as online search engines (including Google Scholar and Yahoo), online research community websites (https://www.researchgate.net/), and reference cross-checks were all accessed to ensure the maximum pool of relevant studies was generated. No further searches were performed after the last update, which was on March 15th, 2021.

Table 7
Studies reporting toughness of denture bases.

First author (Year)	Fabrication method	Brand/ Manufacturer	Toughness(mean ± SD in N•mm)	n	Testing methods (Sample dimension)	Conclusion
†Müller et al. (2019) [63]	Milled	Avadent Extreme CAD-CAM shaded puck YW10, AvaDent Global Dental Science Europe	678.984 ± 137.27	5	Three-point bending test (65 × 10 × 3 mm)	The milled denture base group demonstrated a higher toughness than the 3D-printed denture base group.
	Milled	AvaDent Denture base puck, AvaDent Global Dental Science Europe	794.322 ± 65.17	5		
	3D-printing	NextDent C&B, Vertex-Dental B.V.	586.086 ± 105.69	5		
	3D-printing *i*	NextDent Base, Vertex-Dental B.V.	408.038 ± 262.94	5		
	3D-printing *ii*	NextDent Base, Vertex-Dental B.V.	271.334 ± 192.55	5		
	3D-printing *iii*	NextDent Base, Vertex-Dental B.V.	414.050 ± 161.85	5		
†Srinivasan et al. (2018) [67]	Compression-molding	AESTHETIC RED, CANDULOR AG	436 ± 46	5	Three-point bending test (65 × 10 × 3 mm)	The milled group had a higher toughness than the compression-molding group.
	Milled	AvaDent Digital Dentures, Global Dental Science Europe BV	956 ± 85	5		

i, manufacturer-recommended 3D-printer; *ii*, third-party 3D-printer; *iii*, printed in a vertical orientation; *n*, sample size; *NS*, not specified; *SD*, standard deviation; †, study used for meta-analysis.

Table 8
Studies reporting fracture toughness of denture bases.

First author (Year)	Fabrication method	Brand/ Manufacturer	Fracture toughness KIc (mean ± SD in MPa•m1/2)	n	Testing methods (Sample dimension)	Conclusion
†Pacquet al. (2019) [64]	Compression-molding	ProBase Hot, Ivoclar Vivadent AG	1.41 ± 0.16	6	Three-point bending test (39 × 8 × 4 mm)	CAD-CAM milled group had greater fracture toughness than compression-molded group. No difference in fracture toughness was reported between CAD-CAM milled and injection-molded groups.
	Injection-molding	Ivocap, Ivoclar Vivadent AG	1.87 ± 0.10	6		
	Milled	IvoBase CAD, Ivoclar Vivadent AG	2.11 ± 0.29	6		
†Steinmassl et al. (2018) [69]	Compression-molding	AESTHETIC RED, CANDULOR AG	1.25 ± 0.11	10	Three-point bending test (39 × 8 × 4 mm)	CAD-CAM was not generally found to be better in fracture toughness than the conventionally manufactured groups. One of the six milled groups had a higher fracture toughness than the compression-molded group, while three of the six milled groups had a lower fracture toughness than the compression-molded group. Three milled groups had a higher fracture toughness than the auto-polymerization group, while one of six milling groups had a lower fracture toughness than the auto-polymerization group.
	Autopolymerization	AESTHETIC BLUE, CANDULOR AG	1.11 ± 0.08	10		
	Milled	Wieland Digital Dentures, Wieland Dental + TechnikGmbH & Co. KG	1.73 ± 0.19	10		
	Milled *ii*	Whole You Nexteeth, Whole You Inc.	1.31 ± 0.09	10		
	Milled *i*	Whole You Nexteeth, Whole You Inc.	1.29 ± 0.6	10		
	Milled	AvaDent Digital Dentures, Global Dental Science Europe BV	1.04 ± 0.10	10		
	Milled	Baltic Denture System, Merz Dental GmbH	1.02 ± 0.07	10		
	Milled	Vita VIONIC, Vita Zahnfabrik	0.80 ± 0.07	10		

i, without light-curing topcoat; *ii*, with light-curing topcoat; *KIc*, plane strain fracture toughness; *n*, sample size; *NS*, not specified; *SD*, standard deviation; †, study used for meta-analysis.

Table 9
Studies reporting hardness of denture bases.

First author (Year)	Fabrication method	Brand/ Manufacturer	Surface hardness (mean ± SD in MPa)	n	Testing methods (Sample dimension)	Conclusion
†Becerra et al. (2021) [58]	Compression-molding	Probase Hot, Ivoclar Vivadent Inc.	234.4 ± 20.59 α [23.9 ± 2.1 VHN]	30	Vickers hardness testing (NS)	The milled group demonstrated the lowest hardness while the other tested groups had the same hardness.
	Injection-molding	Probase Hot, Ivoclar Vivadent Inc.	226.50 ± 18.63 α [23.1 ± 1.9 VHN]	30		
	Milled	Ivobase CAD, Ivoclar Vivadent Inc.	183.40 ± 16.67 α [18.7 ± 1.7 VHN]	30		
Chang et al. (2021) [70]	Autopolymerization	Triplex Cold Polymer, Ivoclar Vivadent	NS	3	Vickers hardness testing (25 × 25 × 2.5 mm)	The milled group had higher hardness than the polyamide group but not generally higher than the autopolymerization group.
	Autopolymerization	Palapress vario, Heraeus Kulzer	NS	3		
	Polyamide	ThermoSens, Vertex-Dental	NS	3		
	Milled	IvoBase CAD, Ivoclar Vivadent	NS	3		
Perea-Lowery et al. (2020) [60]	Compression-molding	Paladon 65, Kulzer GmbH	NS	8	Vickers hardness testing and nanoindentation (10 × 10 × 2 mm)	CAD-CAM denture base resins did not generally have better mechanical properties than conventional denture base polymers.
	Autopolymerization	Palapress, Kulzer GmbH	NS	8		
	Milled	Degos Dental L-Temp, Degos Dental GmbH	NS	8		
	Milled	IvoBase CAD, Ivoclar Vivadent AG	NS	8		
	Milled	Zirkonzahn Temp Basic Tissue, Zirkonzahn SRL	NS	8		
Prpić et al. (2020) [71]	Compression-molding	ProBase Hot, Ivoclar Vivadent AG	NS	10	Brinell's method (64 × 10 × 3.3 mm)	The injection-molding group demonstrated the lowest surface hardness. Materials with the same polymerization type can have different mechanical properties and 3D-printed acrylics had lower mechanical properties than most other denture base materials.
	Compression-molding	Paladon 65, Kulzer GmbH	NS	10		
	Compression-molding	Interacryl Hot, Interdent d.o.o.	NS	10		
	Injection molding	Vertex ThersmoSens, Vertex-Dental B.V.	NS	10		
	Milled	IvoBase CAD, Ivoclar Vivadent AG	NS	10		
	Milled	Interdent CC disc PMMA, Interdent d.o.o.	NS	10		
	Milled	PINK CAD-CAM DISC, Polident d.o.o.	NS	10		
	3D-printing	NextDent Base, Vertex-Dental B.V.	NS	10		
†Al-Dwairi et al. (2019) [72]	Compression-molding	Meliodent, Kulzer GmbH	177.4 ± 3.04α [18.09 ± 0.31 VHN]	15	Vickers hardness number (25 × 25 × 3 mm)	The milled group was the hardest.
	Milled	Avadent, Global Dental Science	202 ± 3.236α [20.60 ± 0.33 VHN]	15		
	Milled	Tizian, Schütz Dental	194.2 ± 10.59α [19.80 ± 1.08 VHN]	15		
†Müller et al. (2019) [63]	Milled	Avadent Extreme CAD CAM shaded puck YW10, AvaDent Global Dental Science Europe	180.8 ± 9.709α [18.440 ± 0.99 VHN]	5	Nanoindentation test (11 × 11 × 2 mm)	The milled group demonstrated the same surface hardness as the 3D-printed group. 3D-printed group manufactured using the manufacturer recommended 3D printer revealed higher surface hardness than the group manufactured with a third-party 3D printer.
	Milled	AvaDent Denture base puck, AvaDent Global Dental Science Europe	156.3 ± 3.531α [15.940 ± 0.36 VHN]	5		

(continued on next page)

Table 9 (*continued*)

First author (Year)	Fabrication method	Brand/ Manufacturer	Surface hardness (mean ± SD in MPa)	n	Testing methods (Sample dimension)	Conclusion
	3D-printing	NextDent C&B, Vertex-Dental B.V.	181.8 ± 12.85α [18.540 ± 1.31 VHN]	5		
	3D-printing *i*	NextDent Base, Vertex-Dental B.V.	166.7 ± 12.36α [17.000 ± 1.26 VHN]	5		
	3D-printing *ii*	NextDent Base, Vertex-Dental B.V.	65.51 ± 22.16α [6.680 ± 2.26 VHN]	5		
†Pacquet et al. (2019) [64]	Compression-molding	ProBase Hot, Ivoclar Vivadent AG	190.799 ± 3.923α [19.46 ± 0.40 VHN]	10	Vickers hardness (NS)	The milled group had greater surface hardness than injection-molding. No differences were observed between milled and compression-molded groups.
	Injection-molding	Ivocap, Ivoclar Vivadent AG	165.2 ± 4.315α [16.85 ± 0.44 VHN]	10		
	Milled	IvoBase CAD, Ivoclar Vivadent AG	189.399 ± 14.5α [19.31 ± 1.48 VHN]	10		
†Srinivasan et al. (2018) [67]	Compression-molding	AESTHETIC RED, CANDULOR AG	232 ± 15	2	Nanoindentation test (11 × 11 × 2 mm)	Similar hardness.
	Milled	AvaDent Digital Dentures, Global Dental Science Europe BV	221 ± 14	2		
†Ayman et al. (2017) [68]	Compression-molding	Vertex Rapid Simplified, Vertex-Dental B.V.	13.22 ± 0.88	10	A digital Micromet hardness tester (65 × 10 × 3 mm)	Milled group was harder.
	Milled	PINK CAD-CAM DISC, Polident d.o.o.	22.41 ± 1.50	10		

α, this value is converted from the original value VHN to MPa; *i*, manufacturer-recommended 3D-printer; *ii*, third-party 3D-printer; *n*, sample size; *NS*, not specified; *SD*, standard deviation; *VHN*, Vickers hardness number; †, study used for meta-analysis.

2.3. Search strategy and study selection

An initial search strategy was designed and set up by the investigators. Two investigators performed the searches based on the identified medical subject headings (MeSH) search terms as dictated by the search design and strategy. The terms were then applied using the appropriate Boolean operators, "OR" or "AND," or "NOT" to perform the search in the databases. The full set of search terms used and the filters set when performing the search in the above databases are described in Table 1. No restrictions were applied to the type of studies included. The investigators (PK and MS) initially swept through the search results using a thorough title and abstract screening. After the initial sweep, the shortlisted studies were included for a full-text analysis only after a mutual agreement between the two investigators. Disagreements, if present, were resolved through a consensus meeting. If multiple publications existed on the same cohort by the same author, only the most recent publication was included in the review.

2.4. Data collection process and missing data

Data extraction was performed independently by two investigators (PK and MS), who were reciprocally blinded to the each other's data extraction. The corresponding authors of the included publications were contacted by email for any clarification of extracted data from their studies. The parameters extracted from the included studies are detailed in Tables 2–20. For any missing information from the included studies relevant to this systematic review, direct email contact was made with the corresponding author. Email reminders were sent to the authors in case of a non response. Follow-up emails were sent if the received information was inadequate or required further clarity. A non response from the author ultimately lead to the exclusion of the study, when necessary information was lacking.

2.5. Summary measures and synthesis of results

Inter-investigator reliability was assessed using kappa (κ) statistics. The meta-analysis was performed comparing CDs manufactured using CAD-CAM and traditional processes with regard to trueness of fit, biocompatibility, retention, flexural strength, flexural modulus, yield strength, strain at yield point, toughness, fracture toughness, hardness, surface wettability, surface roughness, color stability, residual monomer content, clinical and patient reported outcomes. In this review individual subgroups in the studies were considered independent. For each of the studied parameters, means, standard deviations along with sample sizes were extracted. Confidence intervals (CI) were set to 95%, and standardized mean differences were calculated for each outcome parameter using comprehensive meta-analysis software, version 3.0 (Biostat, Englewood, NJ, USA). Random-effects or fixed-effects models were used to calculate the weighted means across the studies [12] and I-squared statistics (I^2-statistics) was used to assess the heterogeneity

Table 10
Studies reporting surface wettability of denture bases.

First author (Year)	Fabrication method	Brand/ Manufacturer	Contact angle (mean ± SD in degrees)	n	Testing methods(Sample dimension)	Conclusion
†Al-Dwairi et al. (2019) [72]	Compression-molding	Meliodent, Kulzer GmbH	65.97 ± 4.67	15	Sessile drop method by distilled water (25 × 25 × 3 mm)	The milled groups were more hydrophobic than the compression-molding group.
	Milled	Avadent, Global Dental Science	72.87 ± 4.83	15		
	Milled	Tizian, Schütz Dental	69.53 ± 3.87	15		
†Murat et al. (2019) [73]	Compression-molding	Promolux, Merz Dental GmbH	73.43 ± 17.82	10	AAA An automated contact angle measurement device equipped with a video camera and an image analyzer (OCA 15 plus; Dataphysics Instruments GmbH, Filderstadt, Germany) (disc-shaped; 10(⌀) × 2 mm)	The milled groups were less hydrophobic when compared to conventional compression-molded heat-polymerized PMMA
	Milled	PINK CAD-CAM DISC, Polident d.o.o.	71.31 ± 6.94	10		
	Milled	AvaDent Puck Disc, Avadent Global Dental Science LLC	69.63 ± 4.85	10		
	Milled	M-PM Disc, Merz Dental GmbH	69.72 ± 10.57	10		
†Arslan et al. (2018) [66]	Compression-molding	Promolux, Merz Dental GmbH	73.97 ± 3.53	10	Water contact angle (64 × 10 × 3.3 mm)	Milled groups demonstrated increased hydrophobicity and low-wetting
	Milled	M-PM Disc, Merz Dental GmbH	81.03 ± 3.29	10		
	Milled	PINK CAD-CAM DISC, Polident d.o.o.	82.39 ± 3	10		
	Milled	AvaDent Puck Disc, Global Dental Science LLC	92.95 ± 2.65	10		
†Steinmassl et al. (2018) [74]	Compression-molding	AESTHETIC RED, CANDULOR AG	82.50 ± 3.44	10	Water contact angle (39 × 8 × 4 mm)	CAD-CAM milled groups were more hydrophilic than conventional groups, but no differences were observed in the free surface energy
	Milled *i*	Whole You Nexteeth, Whole You Inc.	77.70 ± 9.87	10		
	Milled	Wieland Digital Dentures, Wieland Dental + TechnikGmbH & Co. KG	77.50 ± 3.34	10		
	Milled	Baltic Denture System, Merz Dental GmbH	75.00 ± 5.42	10		
	Milled	Vita VIONIC, Vita Zahnfabrik	74.40 ± 2.32	10		
	Milled	AvaDent Digital Dentures, Global Dental Science Europe BV	70.35 ± 8.99	10		
	Milled *ii*	Whole You Nexteeth, Whole You Inc.	26.50 ± 5.58	10		
†Almamari et al. (2017) [68]	Compression-molding	Vertex Rapid Simplified, Vertex-Dental B.V.	70.41 ± 4.18	10	Water contact angle (30 × 15 × 3 mm)	The conventional group was more hydrophobic.
	Injection molding	bre.flex polyamide, Bredent GmbH & Co. KG	67.90 ± 2.56	10		
	Milled	PINK CAD-CAM DISC, Polident d.o.o.	66.86 ± 1.38	10		

⌀, diameter; *i*, without light-curing topcoat; *ii*, with light-curing topcoat; *n*, sample size; *NS*, not specified; *SD*, standard deviation; †, study used for meta-analysis.

across the included studies.

2.6. Risk of publication bias and additional analyses

Risk of publication bias was assessed across the studies using funnel plots [13]. Descriptive analysis was performed on all studies to report their outcomes, sample sizes, methods, conclusions as well as the fabrication techniques including brand and manufacturer names of sample materials used in each study.

3. Results

3.1. Study selection, study characteristics, and inter-investigator agreement

The initial search identified 2259 studies (PubMed: n = 1712; Embase: n = 360; CENTRAL: n = 187). An initial sweep of these articles removed duplicates and articles not relevant to the focus of this systematic review. This was followed by a title and abstract screening to leave a total of 68 [8,14,15,17–30,32,33,35–62,64–81,83–85] articles identified for full text analysis. An additional 5 articles [16,31,34,63,82]

Table 11
Studies reporting surface roughness of denture bases.

First author (Year)	Fabrication method	Brand/ Manufacturer	Surface roughnessRa value (mean ± SD in μm)	n	Testing methods(Sample dimension)	Conclusion
†Chang et al. (2021) [70]	Autopolymerization	Triplex Cold Polymer, Ivoclar Vivadent	0.0241 ± 0.0020	5	Surface roughness tester (Surftest SJ-410, Mitutoyo, Japan) (25 × 25 × 3 mm)	The milled group demonstrated the highest surface roughness, while the autopolymerization groups had the lowest surface roughness
	Autopolymerization	Palapress vario, Heraeus Kulzer	0.0256 ± 0.0020	5		
	Polyamide	ThermoSens, Vertex-Dental	0.1436 ± 0.0036	5		
	Milled	IvoBase CAD, Ivoclar Vivadent	0.3387 ± 0.0041	5		
†Kraemer-Fernandez et al. (2020) [75]	Autopolymerization	Aesthetic Blue, Candulor AG	0.05 ± 0.02	10	Profilometer testing (Mahr SP6, Mahr GmbH, Goettingen, Germany) (50 × 25 × 20 mm)	The milled group revealed the lowest surface roughness, while the autopolymerization group showed the highest surface roughness.
	Milled	Vita Vionic Base Deep-Pink, Vita	0.02 ± 0.00	10		
	3D-printing	Freeprint denture, Detax	0.03 ± 0.01	10		
†Al-Dwairi et al. (2019) [72]	Compression-molding	Meliodent, Kulzer GmbH	0.22 ± 0.07	15	A digital contact profilometer (RT-10, SM S.R.L, Italy) with a resolution of 0.001 μm and a total measurement length of 0.8 mm . (25 × 25 × 3 mm)	The compression-molded heat-polymerized specimens demonstrated the highest surface roughness.
	Milled	Avadent, Global Dental Science LLC	0.16 ± 0.03	15		
	Milled	Tizian, Schütz Dental GmbH	0.12 ± 0.02	15		
†Alp et al. (2019) [76]	Compression-molding	Vynacron, Vynacron Dental Resins Inc	0.08 ± 0.02	6	C CContact profilometer (Surftest SV-3100, Mitutoyo Corp) . The tracing length was 5.5 mm, the cut-off length was 0.8 mm, and the stylus speed was 1 mm/s (disk-shaped; 10(⌀) × 2 mm)	The milled groups had the same surface roughness as the compression-molded group. All were below the plaque accumulation threshold (0.2 μm). Coffee thermocycling increased surface roughness of all groups.
	Milled	AvaDent Puck Disc, Global Dental Science LLC	0.09 ± 0.03	6		
	Milled	M-PM Disc, Merz Dental GmbH	0.08 ± 0.02	6		
	Milled	PINK CAD-CAM DISC, Polident d.o.o.	0.07 ± 0.01	6		
†Müller et al. (2019) [63]	Milled	Avadent Extreme CAD CAM shaded puck YW10, AvaDent Global Dental Science Europe	0.078 ± 0.02	5	High-resolution white light non-contact laser profilometry (CyberSCAN CT 100, Cyber technologies, Eching-Dietersheim, Germany) with a z-resolution of 20 nm and a lateral resolution of 1 μm . (20 × 20 × 1.5 mm)	The milled group had the same surface roughness as the 3D-printing group. Printing with recommended 3D printer demonstrated a reduced surface roughness.
	Milled	AvaDent Denture base puck, AvaDent Global Dental Science Europe	0.086 ± 0.03	5		
	3D-printing	NextDent C&B, Vertex-Dental B.V.	0.088 ± 0.02	5		
	3D-printing *i*	NextDent Base, Vertex-Dental B.V.	0.118 ± 0.03	5		
	3D-printing *ii*	NextDent Base, Vertex-Dental B.V.	0.426 ± 0.28	5		
†Murat et al. (2019) [73]	Compression-molding	Promolux, Merz Dental GmbH	0.34 ± 0.06	10	A profilometric contact surface measurement device (Perthometer M2, Mahr, Gottingen, Germany) (disk-shaped; 10(⌀) × 2 mm)	CAD-CAM milled PMMA-based polymers showed less surface roughness when compared to conventional compression molded heat-polymerized PMMA
	Milled	PINK CAD-CAM DISC, Polident d.o.o.	0.21 ± 0.04	10		
	Milled		0.20 ± 0.05	10		

(continued on next page)

Table 11 (*continued*)

First author (Year)	Fabrication method	Brand/ Manufacturer	Surface roughnessRa value (mean ± SD in μm)	n	Testing methods(Sample dimension)	Conclusion
		AvaDent Puck Disc, Avadent Global Dental Science LLC				
	Milled	M-PM Disc, Merz Dental GmbH	0.18 ± 0.04	10		
†Arslan et al. (2018) [66]	Compression-molding	Promolux, Merz Dental GmbH	0.22 ± 0.07	10	Profilometric contact surface measurement device (Perthometer M2; Mahr GmbH, Gottingen, Germany) (with a measurement length of 5.5 mm and 0.5 mm/s) (64 × 10 × 3.3 mm)	No difference between the groups.
	Milled	PINK CAD-CAM DISC, Polident d.o.o.	0.26 ± 0.09	10		
	Milled	AvaDent Puck Disc, Avadent Global Dental Science LLC	0.22 ± 0.06	10		
	Milled	M-PM Disc, Merz Dental GmbH	0.21 ± 0.07	10		
†Srinivasan et al. (2018) [67]	Compression-molding	AESTHETIC RED, CANDULOR AG	0.12 ± 0.29	5	High-resolution white light non-contact laser profilometry (CyberSCAN CT 100, Cyber technologies, Eching-Dietersheim, Germany) with a z-resolution of 20 nm and a lateral resolution of 1 μm . (20 × 20 × 1.5 mm)	CAD-CAM milled group was rougher than the conventional group
	Milled	AvaDent Digital Dentures, Global Dental Science Europe BV	0.37 ± 0.03	5		
†Steinmassl et al. (2018) [74]	Compression-molding	AESTHETIC RED, CANDULOR AG	0.55 ± 0.14	10	Contact profilometry (Taylor Hobson, Leicester, UK) (fabricated dentures)	The CAD-CAM milled group had lower surface roughness than the conventional compression-molded group.
	Milleded	Baltic Denture System, Merz Dental GmbH	0.44 ± 0.13	10		
	Milled	Wieland Digital Dentures, Wieland Dental + TechnikGmbH & Co. KG	0.30 ± 0.10	10		
	Milled	AvaDent Digital Dentures, Global Dental Science Europe BV	0.28 ± 0.16	10		
	Milled	Vita VIONIC, Vita Zahnfabrik	0.28 ± 0.07	4		
	Milled	Whole You Nexteeth, Whole You Inc.	0.04 ± 0.01	10		
†Almamari et al. (2017) [68]	Compression-molding	Vertex Rapid Simplified, Vertex-Dental B.V.	2.44 ± 0.07	10	Surface profilometry (Surftest SJ-201P, Mitutoyo; America Corporation) (30 × 15 × 3 mm)	The milled group had lower surface roughness than the conventional group.
	Injection-molding	bre.flex polyamide, Bredent GmbH & Co. KG	1.77 ± 0.06	10		
	Milled	PINK CAD-CAM DISC, Polident d.o.o.	1.08 ± 0.23	10		
Al-Fouzan et al. (2017) [77]	Compression-molding	MAJOR.BASE 20, MAJOR PRODOTTI DENTARI S.P.A	NS	10	Non-contact optical three-dimensional profilometry (Contour GT-I, Bruker) (disk-shaped; 10(⌀) × 3 mm)	CAD-CAM milled group demonstrated lower surface roughness than the conventional compression-molded group
	Milled	Wieland Digital Denture, Ivoclar Vivadent	NS	10		
Shinawi et al. (2017) [78]	Milled	PINK CAD-CAM DISC, Polident d.o.o.	0.30 ± 0.07	40	Surface Profilometry (Surftest SJ-201P, Mitutoyo America Corporation) (65 × 10 × 3 mm)	CAD-CAM milled resins displayed a homogenous surface initially with a low surface roughness that was significantly affected following simulating three years of manual brushing. However, despite the significant weight loss, the findings were within clinically acceptable limits.

⌀, diameter; *i*, manufacturer-recommended 3D-printer; *ii*, third-party 3D-printer; *n*, sample size; *NS*, not specified; *Ra*, arithmetical mean deviation of the assessed profile; *SD*, standard deviation; †, study used for meta-analysis.

Table 12
Studies reporting color stability of denture material.

First author (Year)	Fabrication methods	Brand/ Manufacturer	Color differenceΔE (mean ± SD)	n	Testing methods(Sample dimension)	Conclusion
Iwaki et al. (2020) [59]	Compression-molding *PS*	Acron, GC	2.46 ± 0.28	3	Immersed in 0.05% curry solution for 7 days. (disc-shaped; 20(⌀) × 1 mm)	The custom-made milled group demonstrated higher color stability than the conventional compression-molding group.
	Milled * *PS* (fabricated by high-pressure molding of heat-curing denture base resin)	Acron, GC	1.61 ± 0.03	3		
†Gruber et al. (2020) [79]	Compression-molding *PS*	ProBase Hot, Ivoclar Vivadent AG	0.39 ± 0.22 †	4	Thermocycling (as one of the study groups), immersion with distilled water, red wine and coffee for 7 days and 30 days (15 × 15 × 3 mm)	3D-printed denture resins demonstrated the maximum color change compared to conventional heat-polymerized compression-molded and CAD-CAM milled denture resins. Furthermore, CAD-CAM milled denture resins were not inferior to conventional resins in terms of color stability.
	Compression-molding *TS*	Ivocron Dentin Body, Ivoclar Vivadent AG	1.42 ± 0.30α	4		
	Milled *PS*	IvoBase CAD, Wieland Dental + Technik GmbH & Co. KG	0.91 ± 0.13α	4		
	Milled *PS*	M-PM Disc, Merz Dental GmbH	0.57 ± 0.16α	4		
	Milled *PS*	PINK CAD-CAM DISC, Polident d.o.o.	0.51 ± 0.02α	4		
	Milled *PS*	AvaDent Denture base puck, AvaDent Global Dental Science Europe	0.46 ± 0.18α	4		
	Milled *TS*	Avadent Extreme CAD CAM shaded puck YW10, AvaDent Global Dental Science Europe	1.63 ± 0.90α	4		
	Milled *TS*	M-PM Disc A3, Merz Dental GmbH	0.53 ± 0.26α	4		
	Milled *TS*	PMMA CAD-CAM DISC multilayer A3, Polident d.o.o.	0.22 ± 0.13α	4		
	3D-printing*PS*	NextDent Base, Vertex-Dental B.V.	0.90 ± 0.23α	4		
	3D-printing*TS*	NextDent C&B, Vertex-Dental B.V.	1.00 ± 0.34α	4		
†Alp et al. (2019) [76]	Compression-molding *PS*	Vynacron, Vynacron Dental Resins Inc	1.19 ± 0.53	6	5000 cycles of thermocycling in coffee solution (disk-shaped; 10(⌀) × 2 mm)	The material was not found to affect the color change due to coffee thermocycling (CTC) after 5000 cycles. All tested materials had imperceivable color changes after this CTC.
	Milled *PS*	AvaDent Puck Disc, Global Dental Science LLC	1.52 ± 0.71	6		
	Milled *PS*	PINK CAD-CAM DISC, Polident d.o.o.	1.10 ± 0.38	6		
	Milled *PS*	M-PM Disc, Merz Dental GmbH	0.95 ± 0.67	6		
†Al-Qarni et al. (2019) [80]	Compression-molding *PS*	Lucitone 199 Denture Base Resin, Dentsply Sirona	2.30 ± 0.30α	5	Immersion in coffee, water and red wine for 7 days (10 × 10 × 2 mm for pink shade; tooth shade is measured as tooth form)	All evaluated acrylic resin specimens demonstrated significant color change when immersed in coffee or red wine. Coffee produced the most color difference. Monolithic teeth and base acrylic resin materials used in CAD-CAM dentures had a similar color change to conventionally processed acrylic resin.
	Injection-molding *PS*	IvoBase Hybrid, Ivoclar Vivadent AG	1.80 ± 0.20α	5		
	Acrylic denture tooth	SR Vivodent DCL A1/ A24B, Ivoclar Vivadent AG	3.80 ± 0.70α	5		
	Acrylic denture tooth	Portrait IPN A1/55F, Dentsply Sirona	4.50 ± 1.00α	5		
	Milled *PS*	Lucitone 199 Denture Base Disc, Dentsply Sirona	2.10 ± 0.10α	5		
	Milled *TS*		4.80 ± 0.70α	5		

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Table 12 (*continued*)

First author (Year)	Fabrication methods	Brand/ Manufacturer	Color differenceΔE (mean ± SD)	n	Testing methods(Sample dimension)	Conclusion
		Monolithic A1, AvaDent Global Dental Science LLC				
Dayan et al. (2019) [81]	Autopolymerization *PS*	Weropress, Merz Dental GmbH	NS	15	Thermocycling then immersion in coffee, cola c, redwine and distilled water for 7 days and 30 days. (disc-shaped; 15(⌀) × 2 mm)	The color stability of CAD-CAM denture base resins is better than any of the other kinds of denture base resins. The color change values of all groups except Eclipse stored in red wine had clinically detectable values.
	Heat-activated polymerization *PS*	Paladent 20, Kulzer GmbH	NS	15		
	Light-activated polymerization *PS*	Eclipse, Dentsply	NS	15		
	Milled *PS*	M-PM Disc, Merz Dental GmbH	NS	15		

α, this value is a 7-day measurement in coffee solution; ⌀, diameter; *n*, sample size; *NS*, not specified; *PS*, pink shade; *SD*, standard deviation; *TS*, tooth shade; †, study used for meta-analysis.

Table 13
Studies reporting residual monomer from denture bases.

First author (Year)	Fabrication methods	Brand/Manufacturer	Residual monomerin mean ± SD ppm	n	Testing methods(Sample dimension)	Conclusion
†Engler et al. (2020) [82]	Compression-molding	PalaXpress, Kulzer GmbH	14.65 ± 2.14α	40	Stored in distilled water, then the MMA elution was measured by spectrophotometry at 1, 7, 30 and 60 days (14 × 12 × 2 mm)	The differences in elution were material-dependent. CAD-CAM dental polymers, as well as the conventional compression-molded polymers, eluted residual monomer within the aging time.
	Milled	AVADENT Core XCL-1 Base material, AVADENT Digital Dental Solutions	11.96 ± 4.35α	40		
	Milled	AVADENT Teeth material, AVADENT Digital Dental Solutions	15.14 ± 5.77α	40		
	Milled	PMMA Mono Blank A1, AnaxDENT	6.00 ± 1.18α	40		
	Milled	PMMA Multi Blank A3, AnaxDENT	6.33 ± 1.52α	40		
	Milled	Ceramill Temp, Amann Girrbach AG	13.48 ± 4.83α	40		
	Milled	Zirkonzahn Temp Premium, Zirkonzahn	9.56 ± 2.86α	40		
	Milled	SHOFU Block HC, SHOFU Dental Corporation	19.61 ± 7.1α	40		
	Milled	Telio CAD, Ivoclar Vivadent	18.29 ± 2.86α	40		
Ayman et al. (2017) [68]	Compression-molding	Vertex Rapid Simplified, Vertex-Dental B.V.	NS	15	Stored in distilled water, then the MMA elution was measured by gas chromatography after processing, at 2 and 7 days (65 × 10 × 3 mm)	The compression-molded group demonstrated a higher residual monomer content than the milled group.
	Milled	PINK CAD-CAM DISC, Polident d.o.o.	NS	15		
†Steinmassl et al. (2017) [83]	Compression-molding	AESTHETIC RED, CANDULOR AG	1.5 ± 1.6	10	Stored in water (37°C) for 7 days then the MMA elution was measured by high-performance liquid chromatography chromatograms (Maxillary denture fabrication)	All tested dentures released very low amounts of methacrylate monomer but not significantly less than conventional dentures.
	Milled	Baltic Denture System, Merz Dental GmbH	0.6 ± 0.4	10		
	Milled	Whole You Nexteeth, Whole You Inc.	6.0 ± 2.7	10		
	Milled	Vita VIONIC, Vita Zahnfabrik	NS	10		
	Milled	Wieland Digital Dentures, Wieland Dental + TechnikGmbH & Co. KG	NS	10		

α, this value is 7-day measurement; *n*, sample size; *NS*, not specified; *MMA*, methyl-methacrylate; *SD*, standard deviation; †, study used for meta-analysis.

Table 14
Studies reporting denture retention.

First author (Year)	Fabrication methods	Brand/ Manufacturer	Retentive force(mean ± SD in N)	n	Testing methods(Sample dimension)	Conclusion
†Tasaka et al. (2019) [42]	Compression-molding	Acron No.5, GC	1.62 ± 0.46	1	Denture was pulled by a device from a silicon maxillary edentulous jaw model (Maxillary denture fabrication)	3D-printed denture demonstrated a higher retentive force than compression-molded denture
	3D-printing	Vero Clear RGD835, Stratasys	6.36 ± 1.8	1		
AlRumaih et al. (2018) [53]	Compression-molding	Lucitone 199 Denture Base Resin, Dentsply Sirona	52.81 ± 24.23α	20	Four spots of 0.2 ml of denture adhesive (Fixodent; Procter & Gamble Co) were applied to the maxillary denture base's intaglio surface. A portable clinical motorized test stand and advance digital force gauge were modified to measure the amount of denture base retention.	No significant difference in retention was demonstrated between milled and compression-molded heat polymerized complete dentures when using denture adhesive.
	Milled	AvaDent Denture base puck, AvaDent Global Dental Science	58.79 ± 32.43α	20		
†AlHelal et al. (2017) [54]	Compression-molding	Lucitone 199 Denture Base Resin, Dentsply Sirona	54.23 ± 27.36	20	Denture was pulled from patients mouth using a custom-built device. (Maxillary denture fabrication)	The milled group demonstrated a higher retentive force than the compression-molded group.
	Milled§	Avadent, Global Dental Science	74.14 ± 32.56	20		

α, retention of denture while using denture adhesive; *n*, sample size; *SD*, standard deviation; †, study used for meta-analysis.

were included after reference searching and hand searches to leave a final shortlist of 73 articles [8,14–85]. The flow of the entire systematic search and article identification process is illustrated in Fig. 1. The various CD processing techniques identified in this review has been summarized in Fig. 2. The overall κ scores calculated for the various parameters extracted by the two investigators ranged between 0.897 and 1.000, hence indicating an excellent degree of inter-investigator agreement.

From the final list of 73 publications included in the systematic review, 39 studies [8,22,24,33–40,42,43,45–49,54,58,61–70,72–76,79,80,82,83] were identified as suitable for inclusion in a series of meta-analyses. They were undertaken on the following characteristics: trueness of fit, flexural strength, flexural modulus, yield strength, strain at yield point, toughness, fracture toughness, hardness, surface wettability, surface roughness, color stability, residual monomer content, retention and esthetic.

All 73 publications in the final shortlist were analyzed and extracted data included outcome values, sample size, method, conclusions as well as the fabrication technique including brand and manufacturer of materials used in each study. The studies were categorized according to their measured outcomes as follows: trueness of fit, bonding ability to other materials, flexural strength, flexural modulus, elastic modulus, yield strength, strain at yield point, toughness, fracture toughness, hardness, surface wettability, surface roughness, color stability, biocompatibility, microbial adhesion *(Candida albicans)*, residual monomer content, treatment time or cost, retention, esthetics, clinical outcomes and patient-related outcomes.

3.2. Meta-analysis of the searched outcomes

3.2.1. Trueness of fit

A series of meta-analyses were undertaken to compare the trueness of fit for milled CDs; conventional (flask-pack-press) CDs; injection-molded CDs and 3D-printed CDs. When the trueness of fit was compared between CAD-CAM and conventional (flask-pack-press) CDs the meta-analysis illustrated no significant difference of the milled CDs versus conventional (flask-pack-press): $p = 0.053$ (95% CI: -1.329, 0.009; $I^2 = 73.620\%$). For milled CDs compared to injection-molding, no significant difference was noted: $p = 0.854$ (95% CI: -1.248, 1.507; $I^2 = 91.312\%$), with the same result as compared to 3D-printing: $p = 0.360$ (95% CI: -2.547, 0.926; $I^2 = 94.026\%$) (Fig. 3). A further meta-analysis illustrated that the trueness of fit for 3D-printed CDs was superior to conventional flask-pack-press CDs: $p = 0.039$ (95% CI: -1.795, -0.048; $I^2 = 67.531\%$) but no significant difference was noted in comparison to injection-molded CDs: $p = 0.945$ (95% CI: -2.987, 3.207; $I^2 = 95.755$ %), milled CDs: $p = 0.360$ (95% CI: -0.926, 2.547; $I^2 = 94.03\%$) or fused deposition modeling (FDM) CDs: $p = 0.928$ (95% CI: -1.183, 1.297; $I^2 = 0.00\%$) (Fig. 4, Table 2).

3.2.2. Flexural strength and flexural modulus

The flexural strength of milled CDs was higher than composite resin CDs: $p < 0.0001$ (95% CI: -2.006, -1.055; $I^2 = 55.10\%$), conventional (flask-pack-press) CDs: $p = 0.001$ (95% CI: -3.710, -0.959; $I^2 = 94.79\%$), injection-molded CDs: $p = 0.002$ (95% CI: -4.876, -1.061; $I^2 = 93.07\%$) and 3D-printed CDs: $p < 0.0001$ (95% CI: -5.490, -2.906; $I^2 = 62.30\%$; n = 1 study) (Fig. 5, Table 3).

The f flexural modulus of milled CDs was observed to be superior to 3D-printed CDs: $p < 0.0001$ (95% CI: -10.317, -4.875; $I^2 = 81.56\%$). However, no significant difference between milled CDs and conventional (flask-pack-press): $p = 0.192$ (95% CI: -4.647, 0.931; $I^2 = 97.17\%$) and injection molded: $p = 0.603$ (95% CI: -21.278, 12.356; $I^2 = 98.39\%$) (Fig. 6, Table 4).

3.2.3. Yield strength and strain at yield-point

Yield strength for milled CDs was superior to injection-molded: $p = 0.004$ (95% CI: -1.428, -0.271; $I^2 = 0.00\%$); and 3D-printed CDs: $p = 0.001$ (95% CI: -1.760, -0.439; $I^2 = 91.34\%$) (Fig. 7, Table 5). No statistically significant differences were noted in yield strength between milled and conventional (flask-pack-press) CDs: $p = 0.636$ (95% CI: -5.368, 8.781; $I^2 = 98.19\%$). The strain at yield point of conventional (flask-pack-press) CDs was significantly higher than milled CDs: $p < 0.0001$ (95% CI: 2.148, 6.781; $I^2 = 0.00\%$); there were no statistically

Table 15
Studies reporting esthetics, clinical outcomes and patient-related outcomes.

First author (Year)	Study Design	Fabrication methods	Brand/ Manufacturer	Outcomes	n	Method	Conclusion
Arakawa et al. (2021) [14]	Retrospective study	Compression-molding	NS	Number of visits Duration (days) between visits Financial costs Post-delivery adjustments	16	Clinical records from patients who received either CAD-CAM or conventional treatment between 2015 and 2019 were analyzed.	CAD-CAM dentures required fewer visits and costed less than conventional compression-molded dentures.
		Milled	Avadent Digital Dental Solution Wieland Digital Denture		16		
Wei et al. (2021) [15]	Non-randomized, crossover trial	Compression-molding	NS	Oral health impact profile; OHIP-20E (reported by patients) Oral health-related quality of life; OHRQoL (reported by patients)	20	Each patient was delivered with two sets of dentures; conventional and CAD-CAM dentures.	Patients rated higher scores for CAD-CAM on general satisfaction, ease of cleaning, ability to speak, esthetics, stability and oral health status.
		Milled	NS		20		
Cristache et al. (2020) [16]	Prospective cohort study	3D-printing	E-Dent 100, EnvisionTec GmbH (modified with 0.4% TiO2-nanoparticle reinforcement)	Oral health impact profile for edentulous patients; OHIP-EDENT Score (reported by patients) Patient-centered outcomes (reported by patients) such as esthetics, speech, masticatory ability	35	All patients' edentulous arches were restored with 3D-printed complete dentures. Patients completed the questionnaires, the OHIP-EDENT score and VAS in various aspects before treatment and at 1 week, 12 months and 18 months after treatment	OHIP-EDENT scored significantly better after 18 months of denture wearing compared to before treatment. Mean VAS was improved for all parameters assessed.
Drago et al. (2019) [17]	Non-randomized controlled trial	Injection-molding	SR Ivocap Injection System, Ivoclar Vivadent AG	Number of unscheduled post-insertion-adjustment visits	33	The first 33 patients received dentures fabricated using an injection-molding system, and the other 73 were milled using a CAD-CAM milled system. They were treated in a private practice setting and followed up for 1 year after the insertion.	There were no significant differences in the number of unscheduled post-insertion visits for participants whose dentures were fabricated following injection-molding or milled protocols.
		Milled	AvaDent CORE, Global Dental Sciences		73		
Schlenz et al. (2019) [18]	Retrospective cohort study	Milled	Digital Denture, Ivoclar Vivadent	Number of appointments required for treatment Number of interventions during the initial (≤ 4 weeks after insertion) and functional periods (> 4 weeks after insertion) Survival	10	Data from 10 patients who received CAD-CAM milled dentures between 2015 and 2016 were analyzed.	The milled dentures showed acceptable clinical performance in terms of survival and maintenance.
Bidra et al. (2016) [19]	Prospective cohort study	Milled	Avadent, Global Dental Science	Clinical outcomes (reported by prosthodontists) such as retention, stability, extensions, lip support. Patient-centered outcomes (reported by patients) such as tightness, absence of rocking, bulkiness, cosmetics	20	The old dentures were replaced with milled complete dentures. The participants and the 2 prosthodontists judged independently completed a survey using the visual analog scale (VAS) to record baseline and 1-year follow-up evaluations for various patient-centered and clinical outcomes.	CAD-CAM dentures were rated better by the patients than by the clinicians.
Saponaro et al. (2016a) [20]	Retrospective cohort study	Milled	Avadent, Global Dental Science	Patient-centered outcomes (reported by patients) such as i improvement on previous denture, ability to chew, esthetics, speech, ease of cleaning, fit, expectation fulfillment, comfort, recommendation to others, overall satisfaction	19	A questionnaire (agree, neutral, disagree) was mailed to the patients who received CAD-CAM complete dentures between 2012-2014 to assess their satisfaction with their milling denture experience.	Patients were satisfied with their milled complete dentures. However, the patients' ratings of milled complete dentures did not differ significantly in comparison to their previous conventional complete dentures.
	Retrospective cohort study	Milled	Avadent, Global Dental Science	Number of appointments needed for denture insertion	48	Data from patients, who received milled complete	The average number of appointments needed for

(continued on next page)

Table 15 (*continued*)

First author (Year)	Study Design	Fabrication methods	Brand/ Manufacturer	Outcomes	n	Method	Conclusion
Saponaro et al. (2016b) [21]				Number of post-insertion adjustments Number of reported complications		dentures between 2012-2014, were evaluated for objective treatment outcomes.	insertion was 2.39. Common problems included lack of retention, inaccurate vertical dimension and incorrect centric relation.
†Schwindling et al. (2016) [22]	Non-randomized crossover trial	Injection-molding	Ivobase, Ivoclar Vivadent AG	Clinical outcomes (reported by clinicians) such as fit, retention, esthetics, phonetics, retention, occlusion	5	Each patient was delivered with two sets of dentures; injection-molded and milled dentures. Clinicians evaluated the outcomes on a 6-point scales ranging from poor (grade 6) to excellent (grade 1).	Both injection-molded and milled dentures could be produced without significant complications. No pronounced difference was found between the prostheses concerning functional aspects. The definitive esthetic outcome was rated as very good.
		Milled	IvoBase CAD for Zenotec, Wieland Dental		5		
Kattadiyil et al. (2015) [23]	Non-randomized crossover trial	Compression-molding	Lucitone 199, Dentsply Intl	Total clinical chair time Clinical outcomes (reported by prosthodontists) such as denture base contour, tooth arrangement, fit, esthetics. Patient-centered outcomes (reported by patients) such as fit, esthetics, ability to chew, comfort. Questionnaire (reported by predoctoral dental students) such as confidence to perform, preference.	15	Predoctoral dental students delivered two sets of dentures, compression molding and milling dentures, for each patient. Experienced and certified prosthodontists assessed denture quality. The students and patients were asked to complete the questionnaires.	The average clinical chair time was 205 mins longer for the compression-molded group than for the milled group. According to clinical outcomes, significantly higher average scores were observed for milling dentures than for compression-molded dentures. Both students and patients preferred milled dentures more than compression-molded dentures.
		Milled	Avadent, Global Dental Science		15		
†Inokoshi et al. (2012) [24]	Non-randomized crossover trial	Conventional wax trial denture	NS	Clinical outcomes (reported by prosthodontists) such as esthetics, stability, overall satisfaction. Patient-centered outcomes (reported by patients) such as esthetics, predictability of final denture shape, stability, comfort of the dentures, overall satisfaction.	10	Prosthodontists performed a denture try-in for one patient using both trial dentures from conventional and 3D-printing methods. The prosthodontists and patients rated satisfaction for both methods using a visual analog scale; VAS.	Regarding prosthodontist's ratings, esthetics and stability were rated significantly higher with the conventional method than with the 3D-printing method, whereas chair time was rated significantly longer with the 3D-printing method than with the conventional method.
		3D-printing	FullCure720, Objet Geometries		10		

n, sample size; *NS*, not specified; †, study used for meta-analysis.

significant differences in strain at yield point for milled CDs compared to 3D-printed CDs: $p = 0.856$ (95% CI: -0.552, 0.667; $I^2 = 43.9\%$) (Fig. 8, Table 6).

3.2.4. *Toughness, fracture toughness and hardness*

Toughness of milled CDs was superior to conventional (flask-pack-press) CDs: $p < 0.0001$ (95% CI: -11.167, -4.051; $I^2 = 0.00\%$) and 3D-printed CDs: $p < 0.0001$ (95% CI: -2.613, -1.362; $I^2 = 22.46\%$) (Fig. 9, Table 7). Fig. 10 demonstrates that there were no statistically significant differences in fracture toughness for milled CDs compared to conventional (flask-pack-press): $p = 0.690$ (95% CI: -1.399, 2.112; $I^2 = 93.73\%$); injection-molded: $p = 0.074$ (95% CI: -2.322, 0.109; $I^2 = 0.00\%$) and auto-polymerized materials: $p = 0.875$ (95% CI: -1.957, 1.665; $I^2 = 93.83\%$) (Table 8). The hardness of milled CDs was not significantly different to conventional (flask-pack-press): $p = 0.125$ (95% CI: -4.945, 0.605; $I^2 = 97.03\%$); injection-molded CDs: $p = 0.962$ (95% CI: -4.493, 4.716; $I^2 = 97.99\%$) and 3D-printed CDs: $p = 0.240$ (95% CI: -3.454, 0.866; $I^2 = 89.68\%$; n = 1 study) (Fig. 11, Table 9).

3.2.5. *Wettability and surface roughness*

Data available on surface wettability did not demonstrate any statistically significant differences for milled CDs compared to conventional (flask-pack-press): $p = 0.545$ (95% CI: -1.238, 0.654; $I^2 = 92.11\%$) and injection molded: $p = 0.266$ (95% CI: -1.396, 0.385; $I^2 = 0.00\%$) (Fig. 12, Table 10). Fig. 13 demonstrates that the surface roughness for milled CDs was smoother than conventional (flask-pack-press): $p < 0.0001$ (95% CI: -2.152, -0.766; $I^2 = 86.79\%$); injection-molded: $p < 0.0001$ (95% CI: -5.650, -2.560; $I^2 = 0.00\%$) and 3D-printed CDs: $p < 0.0001$ (95% CI: -1.602, -0.642; $I^2 = 0.00\%$) (Table 11). However, polyamide showed superiority to milled: $p < 0.0001$ (95% CI: 28.372, 72.766; $I^2 = 0.00\%$). No significance difference was found between milled and auto-polymerized: $p = 0.129$ (95% CI: -18.080, 142.093; $I^2 = 95.20\%$).

3.2.6. *Color stability*

A series of meta-analyses were undertaken to compare the color stability data for milled CDs; conventional (flask-pack-press) CDs;

Table 16
Studies reporting treatment time or costs involved in delivering dentures.

First author (Year)	Fabrication method	Brand/ Manufacturer	Timein mean ± SD	Costin mean ± SD	n	Method	**Conclusion**
Arakawa et al. (2021) [14]	Compression-molding	NS	NS	NS	16	Clinical records from patients who received either CAD-CAM or conventional treatment between 2015 and 2019 were analyzed.	CAD-CAM dentures required fewer visits and costed less than conventional dentures.
	Milled	Avadent Digital Dental Solution Wieland Digital Denture	NS Number of visits Duration (days) between visits	NS Dental treatment cost Laboratory cost Total cost	16		
Smith et al. (2020) [84]	Compression-molding	NS	NS Number of visits	NS Profitability per chair hour Material costs	NS	Time and cost were analyzed between conventional workflow and digital workflow in university clinics.	A significant cost saving was achieved, both in terms of material cost and chair time cost compared to traditional laboratory fabricated complete dentures.
	Milled	Ivoclar Vivadent process					
Schlenz et al. (2019) [18]	Milled	Digital Denture, Ivoclar Vivadent	4.6 ± 0.7 visits Number of appointments required for treatment	N/A	10	Data from 10 patients who received treatment between 2015 and 2016 were analyzed.	More than four appointments were required for treatment with milled denture (4.6 ± 0.7), mainly for esthetic concerns. An average of 1.7 ± 0.05 appointments during the initial period and 2.07 ± 0.32 during the functional period were noted as a consequence of functional concerns.
†Srinivasan et al. (2019) [8]	Compression-molding	NS	10.7 ± 0.9 h	1999.26 ± 505.39 CHF	12	Undergraduate final-year dental students utilized both the digital denture protocol and the conventional complete denture protocol to construct two sets of complete dentures for patients. Overall time spent and costs (clinical, materials, and laboratory) were calculated.	In a university setting student clinic, the digital denture protocol was found to be less costly when compared with the conventional complete denture protocol. The clinical chair-side time, laboratory and the overall costs were significantly lower for the digital denture protocol, even though the materials costs for this protocol were higher.
	Milled	AVADENT, Global Dental Science	6.9 ± 0.6 h Clinical chair-side time spent for both upper and lower complete dentures in hours	1022.70 ± 74.09 CHF Overall costs for clinical materials and laboratory fees for both upper and lower complete dentures in Swiss francs	12		
Wei et al. (2017) [85]	Conventional wax trial denture	NS	31.1 ± 5.7 mins	N/A	20	Two custom trays were fabricated for each patient. One was a functional, suitable denture system through the CAD-CAM process. The other was manually conventional methods. The production time was recorded.	The average time spent on fabricating custom trays using the digital protocol was less than conventional protocol.
	3D-printing	NS	28.6 ± 2.9 mins Average time spent on fabricating a custom tray in minutes	N/A	20		
Bidra et al. (2016) [19]	Milled	Avadent, Global Dental Science	NS VAS scores, higher scores mean more favorable perception by patients	N/A	20	The old dentures were replaced with milling complete dentures. The participants and the 2 prosthodontist judges independently completed a survey instrument using a visual analog scale (VAS) to record baseline and 1-year follow-up evaluations for various patient-centered and clinical outcomes.	Patients rated the treatment time to make the milled dentures as favorable.
Saponaro et al.	Milled		2.39 ± 0.085 visits Appointments	N/A	48	Data from patients, who received milled complete	The average number of appointments needed for

(continued on next page)

Table 16 (*continued*)

First author (Year)	Fabrication method	Brand/ Manufacturer	Timein mean ± SD	Costin mean ± SD	n	Method	**Conclusion**
(2016) [21]		Avadent, Global Dental Science	needed prior to insertion			dentures between 2012-2014, were evaluated for objective treatment outcomes.	insertion was 2.39. Common problems were lack of retention, inaccurate vertical dimension and incorrect centric relation.
Kattadiyil et al. (2015) [23]	Compression-molding	Lucitone 199, Dentsply Intl	NS	N/A	15	Predoctoral dental students delivered two sets of dentures, compression molding and milled dentures, for each patient.	The average clinical chair time was 205 mins longer for the compression molded group than for the milled group.
	Milled	Avadent, Global Dental Science	NS	N/A			
Inokoshi et al. (2012) [24]	Conventional wax trial denture	NS	41.6 ± 26.1 VAS score	N/A	10	Prosthodontists performed a denture try-in for one patient using both trial dentures from conventional and 3D-printing methods. The prosthodontists and patients rated satisfaction for both methods using a visual analog scale; VAS.	Clinician rated chair time significantly longer with the 3D-printing method than with the conventional method.
	3D-printing	FullCure720, Objet Geometries	74.1 ± 20.6 VAS score VAS scores, higher scores mean a longer time	N/A	10		

n, sample size; *N/A*, not applicable; *NS*, not specified; *SD*, standard deviation; †, study used for meta-analysis.

injection-molded CDs and 3D-printed CDs both, pink-shade material (P) and tooth-shade material (T) (Fig. 14, Table 12). For pink-shade material, when the color stability data was compared between milled and conventional (flask-pack-press) CDs the meta-analysis did not illustrate any statistically significant differences between the two groups: $p = 0.313$ (95% CI: -0.315, 0.982; $I^2 = 46.87\%$). In comparison, injection-molded CDs demonstrated superior color stability compared to milled: $p = 0.013$ (95% CI: 0.405, 3.390; $I^2 = 0.00\%$) but milled CDs were superior to 3D-printed: $p = 0.015$ (95% CI: -2.600, -0.278; $I^2 = 50.99\%$). For tooth-shade material, no significance was found between milled and conventional (flask-pack-press): $p = 0.283$ (95% CI: -4.025, 1.177; $I^2 = 87.97\%$); injection-molded: $p = 0.585$ (95% CI: -0.901, 1.596; $I^2 = 0.00\%$; $n = 1$ study), and 3D-printed: $p = 0.322$ (95% CI: -3.394, 1.115; $I^2 = 81.62\%$).

A further meta-analysis (Fig. 15, Table 12) illustrated that color stability for pink-shade conventional (flask-pack-press) CDs was also superior to 3D-printed CDs: $p = 0.012$ (95% CI: 0.490, 4.042; $I^2 = 0.00\%$). However, tooth-shade conventional (flask-pack-press) CDs had the same color stability as tooth-shade 3D-printed: $p = 0.093$ (95% CI: -2.837, 0.217; $I^2 = 0.00\%$).

3.2.7. Residual monomer content

The forest plot in Fig. 16 illustrates that the data available on residual monomer content did not demonstrate any statistically significant differences for milled CDs compared to conventional CDs: $p = 0.090$ (95% CI: -1.997, 0.144; $I^2 = 92.11\%$) (Table 13).

3.2.8. Clinical and patient reported outcome (retention and esthetics)

Fig. 17 demonstrates that the limited data available on retention shows that 3D-printed and milled CDs were, in a clinical context, measured to be more retentive than conventional (flask-pack-press) CDs: $p = 0.015$ (95% CI: 0.152, 1.400; $I^2 = 68.51\%$) (Table 14).

Fig. 18 demonstrates that the limited data available on esthetics indicated that conventional (flask-pack-press) CDs were superior to 3D-printed CDs: $p < 0.0001$ (95% CI: -3.729, -1.369; $I^2 = 0.00\%$) but that there were no significant differences reported when milled and injection-molded CDs were compared: $p = 1.000$ (95% CI: -1.240, 1.240; $I^2 = 0.00\%$) (Table 15).

3.2.9. Manufacturing costs and chair-side-time

A meta-analysis of the costs involved for the various manufactured CDs, revealed that the conventional (flask-pack-press) CDs, were more cost-effective than the CAD-CAM milled CDs when it came to clinical costs: $p < 0.0001$ (95% CI:7.182, 13.321; $I^2 = 47.07\%$). However, the CAD-CAM milled CDs were most cost effective than the conventional (flask-pack-press) CDs when analyzing the laboratory: $p < 0.0001$ (95% CI: -5.328, -2.532; $I^2 = 47.61\%$) and overall: $p < 0.0001$ (95% CI: -4.166, -1.827; $I^2 = 0.00\%$) costs (Fig. 19, Table 16). Fig. 20 illustrates the time analysis demonstrating that the CAD-CAM milled CDs required much lesser clinical chairside time than the conventional (flask-pack-press) CDs: $p = 0.037$ (95% CI: -6.448, -0.206; $I^2 = 81.58$) (Table 16).

3.3. Publication bias

Funnel plots analyses were performed to rule out publication bias for the investigated parameters. Egger's regression identified publication biases for the following meta-analyses, flexural strength ($p = 0.005$), flexural modulus ($p = 0.001$), strain at yield point ($p = 0.0184$), toughness ($p < 0.001$), hardness ($p = 0.008$), color stability ($p = 0.022$), cost analysis ($p = 0.038$) (Appendices 1-7). The remaining meta-analysis were free from publication bias.

Table 17
Studies reporting elastic modulus of denture bases.

First author (Year)	Fabrication methods	Brand/ Manufacturer	Elastic modulus (mean ± SD in MPa)	n	Testing methods(Sample dimension)	**Conclusion**
Perea-Lowery et al. (2020) [60]	Compression-molding	Paladon 65, Kulzer GmbH	NS	8	Nanoindentation test on dry-stored and water-stored specimens (10 × 10 × 2 mm)	CAD-CAM milled dentures resins were not generally found to be suoperior superior than conventional denture resins in terms of elastic modulus.
	Autopolymerization	Palapress, Kulzer GmbH	NS	8		
	Milled	Degos Dental L-Temp, Degos Dental GmbH	NS	8		
	Milled	IvoBase CAD, Ivoclar Vivadent AG	NS	8		
	Milled	Zirkonzahn Temp Basic Tissue, Zirkonzahn SRL	NS	8		
Srinivasan et al. (2018) [67]	Compression-molding	AESTHETIC RED, CANDULOR AG	3900 ± 200α [3.9 ± 0.2 GPa]	2	Nanoindentation test (11 × 11 × 2 mm)	Similar elastic modulus between compression molded and milled group.
	Milled	AvaDent Digital Dentures, Global Dental Science Europe BV	4100 ± 200α [4.1 ± 0.2 GPa]	2		
Steinmassl et al. (2018) [69]	Compression-molding	AESTHETIC RED, CANDULOR AG	3570.24 ± 450.75	10	Three-point bending test (39 × 8 × 4 mm)	CAD-CAM denture resins were not generally found to be superior than conventional denture resins in terms of elastic modulus. Four of six CAD-CAM groups had a higher elastic modulus than the compression molding group. Five of six CAD-CAM groups had a higher elastic modulus than the auto polymerization group.
	Autopolymerization	AESTHETIC BLUE, CANDULOR AG	3405.01 ± 178.52	10		
	Milled *i*	Whole You Nexteeth, Whole You Inc.	4921.05 ± 87.85	10		
	Milled *ii*	Whole You Nexteeth, Whole You Inc.	4777.01 ± 110.72	10		
	Milled	AvaDent Digital Dentures, Global Dental Science Europe BV	4649.15 ± 1110.93	10		
	Milled	Baltic Denture System, Merz Dental GmbH	4606.38 ± 325.93	10		
	Milled	Vita VIONIC, Vita Zahnfabrik	4569.16 ± 267.40	10		
	Milled	Wieland Digital Dentures, Wieland Dental + TechnikGmbH & Co. KG	4009.95 ± 200.00	10		

α, this value is converted from the original value GPa to MPa; *i*, without light-curing topcoat; *ii*, with light-curing topcoat; *n*, sample size; *NS*, not specified; *SD*, standard deviation.

Table 18
Studies reporting biocompatibility of denture material.

First author (Year)	Fabrication methods	Brand/ Manufacturer	Outcomein mean ± SD	n	Testing methods(Sample dimension)	Conclusion
Müller et al. (2019) [63]	Milled *PS*	AvaDent Denture base puck, AvaDent Global Dental Science Europe	387.540 ± 113.912α	18	Human epithelial cells (n = 9) and Human gingival cells (n = 9) were cultured for Resazurin assays on days 3, 7, 14 and 21. (10 × 10 × 2 mm)	Milled groups showed no difference from 3D-printed groups in terms of biocompatibility with human epithelial cell growth and human gingival cell growth.
	Milled *TS*	Avadent Extreme CAD CAM shaded puck YW10, AvaDent Global Dental Science Europe	372.767 ± 98.014α	18		
	3D-printing *PS*	NextDent Base, Vertex-Dental B.V.	364.672 ± 71.464α	18		
	3D-printing *TS*	NextDent C&B, Vertex-Dental B.V.	346.354 ± 77.538α	18		
Srinivasan et al. (2018) [67]	Compression-molding	AESTHETIC RED, CANDULOR AG	10.936±5.71β	18	Human primary osteoblasts (n = 9) and mouse embryonic fibroblasts (n = 9) were cultured for Resazurin assays on days 3, 7, 14 and 21. (11 × 11 × 2 mm)	This study concluded that the tested CAD/CAM resin was equally biocompatible to the traditional heat-polymerized PMMA resin
	Milled	AvaDent Digital Dentures, Global Dental Science Europe BV	15.836±7.51β	18		

α, day-21 cell growth value from human epithelial cells; β, day-21 cell growth value from human primary osteoblasts; *n*, sample size; *PS*, pink shade; *SD*, standard deviation; *TS*, tooth shade.

Table 19
Studies reporting microbial adhesion *(Candida albicans)* to denture bases.

First author (Year)	Fabrication methods	Brand/ Manufacturer	Outcomein mean ± SD	n	Testing methods(Sample dimension)	Conclusion
Murat et al. (2019) [73]	Compression-molding	Promolux, Merz Dental GmbH	279.06 ± 3.34α	10	An adhesion test was performed by incubating the disk specimens in *Candida albicans* suspensions at 37 °C for 2 hours, and the adherent cells were counted under an optical microscope. (disk-shaped; 10(⌀) × 2 mm)	The milled groups may help reduce Candida-associated denture stomatitis in the long-term.
	Milled	PINK CAD-CAM DISC, Polident d.o.o.	22.44 ± 4.64α	10		
	Milled	AvaDent Puck Disc, Avadent Global Dental Science LLC	60.28 ± 5.59α	10		
	Milled	M-PM Disc, Merz Dental GmbH	18.30 ± 2.39α	10		
Al-Fouzan et al. (2017) [77]	Compression-molding	MAJOR.BASE 20, MAJOR PRODOTTI DENTARI S.P.A	2.3 × 103 ± 8.4 × 102 β	10	Candida colonization was performed on all the specimens using four *Candida albicans* isolates. The number of adherent yeast cells was calculated by the colony-forming units (CFU) and by Fluorescence microscopy. (disk-shaped; 10(⌀) × 3 mm)	The milled group displayed promising potential for reducing the adherence of candida.
	Milled	Wieland Digital Denture, Ivoclar Vivadent	1.1 × 103 ± 6.0 × 102 β	10		

α cell count per field; β, CFU/ml; *n*, sample size; *SD*, standard deviation.

3.4. Descriptive analysis and quality assessment of the included clinical studies

Parameters where a meta-analysis was not possible were reported descriptively. Elastic-modulus, biocompatibility, anti-microbial adhesion, and the bonding ability of the CAD-CAM resins are reported descriptively in Tables 17–20. The characteristics of all the included studies, including all the extracted data, the outcome variables, sample sizes, methods, conclusions as well as the fabrication techniques enlisting the brand and manufacturer of materials are presented in the tables. A quality assessment of the included clinical studies was performed using the Newcastle-Ottawa scale for assessing the quality of non-randomized studies and is reported in Table 21.

4. Discussion

This systematic review identified a large number of studies with data relevant to CAD-CAM CDs. The data extracted from these studies facilitated a large number of meta-analyses focused on trueness of fit [25–51], biocompatibility [62,66], mechanical properties [57–71], surface characteristics [62,65–67,69,71–77], color stability [58,75, 78–80], residual monomer content [67,81,82], anti-microbial properties [72,76], bonding ability [52,54–56], clinical/patient reported outcomes [14–24,42,52,53], and time-cost efficiency [8,14,18,19,21,23, 24,83,84]. The quality of the included studies varied , but funnel plot analyses largely ruled out publication bias.

Good adaptation of the denture base to the denture bearing tissues is essential for the adequate retention and stability of any CD [38]. Trueness of fit refers to the closeness of agreement between the expectation of a measurement result and a true value [85]. This review demonstrated that the trueness of fit for milled CDs was not significantly different from conventional, 3D-printed and injection-molded CDs, all techniques led to an clinically acceptable trueness of the intaglio surface. The clinical retention of a CD depends, apart from the morphology and resilience of the denture bearing tissues, on adaptation of the intaglio surface to the tissues, border seal, and salivary flow-related effects associated with viscosity and film thickness of the oral fluid [86,87]. Deformation of conventional denture body during processing is affected by the shape (palatal vault and residual ridge), thickness, denture base materials, and denture processing steps [88,89]. Mucosal adaptation, which is associated with retention, stability, and support, is influenced by distortion [49], hence all attempts to minimize distortion must be made. In conventional fabrication techniques, the deformation of heat-polymerized resin may diminish the degree of base adaptation This clinical misfit is being compensated by deliberately compressing the posterior palatal seal area and hence creating a suction effect, as well as a primary remount of the denture to correct the occlusal discrepancies which result from the denture deformation through polymerization.

Given the data on trueness of fit, this review also examined the issue of clinical denture retention. It is widely reported that successful CD therapy requires satisfactory stability, support and retention [90]. For conventional CDs posterior palatal seal design, palatal surface design, denture base surface enhancement and adhesives contribute to denture retention [91,92]. In the long term, denture wearing in neurologically healthy patients these parameters might be complemented or compensated by muscular skills. However, polymerization shrinkage of conventional CD bases can negatively impact on adaptation and retention [93]. This review demonstrated that the retention of CAD-CAM CDs was superior to conventional (flask-pack-press) ($p = 0.015$) CDs.

Data on a large number of mechanical properties were examined in this review. From the data analyzed CAD-CAM CDs exhibited superior performance in flexural strength; flexural modulus; yield strength; toughness; and surface roughness.

Hardness is a measure of the resistance to localized plastic deformation induced by either mechanical indentation or abrasion. CDs made of a material with low surface hardness can be damaged by mechanical brushing, causing plaque retention and pigmentations, which can decrease the life of the prostheses. Conventional CD bases are prone to

Table 20
Studies reporting bonding ability to other materials of denture bases.

First author (Year)	Fabrication methods	Brand/ Manufacturer	Outcomein mean ± SD	n	Testing methods	Conclusion
Choi et al. (2021) [55]	Compression-molding	Vertex Rapid Simplified, Vertex	0.88 ± 0.14	10	Two denture reline materials (low and high viscosity) were bonded to testing materials forming 50 × 4 × 3 mm samples. Flexural bond strength and fracture toughness were measured.	The compression-molded group produced the highest flexural bond strength and fracture toughness when bonded to denture characterizing composite. The high viscosity denture characterizing material showed significantly higher flexural bond strength and fracture toughness than the lower viscosity material.
	Milled	IvoCAD, Ivoclar Vivodent	0.69 ± 0.18	10		
	3D-printing	Kulzer 3D Dima, Kulzer	0.73 ± 0.23 Flexural bond strength between high-viscosity denture characterizing composite and testing materials in MPa	10		
Li et al. (2021) [56]	3D-printing	FREEPRINT denture, Detax	NS Shear bond strength between repair resin and testing material	20	3D-printed denture base material was treated with different surface treatments (no surface treatment, monomer applying, carbide paper grinding and sandblasting). Then repair resin was used to bond to the 3D printed materials. Shear bond strength was measured.	The 3D-printed denture base material exhibited favorable repairability. Different surface treatments showed the same shear bond strength.
AlRumaih et al. (2018) [53]	Compression-molding	Lucitone 199 Denture Base Resin, Dentsply Sirona	52.81 ± 24.23	20	Four spots of 0.2 ml of denture adhesive (Fixodent; Procter & Gamble Co) were applied to the maxillary denture base's intaglio surface. A portable clinical motorized test stand and advance digital force gauge were modified to measure the amount of denture base retention.	No significant difference was found in retention between milled and heat-activated complete dentures when using denture adhesive.
	Milled	AvaDent Denture base puck, AvaDent Global Dental Science	58.79 ± 32.43 Retention of denture while using denture adhesive in N	20		
Choi et al. (2018) [57]	Auto-polymerization	Vertex Self-Curing, Vertex-Dental B.V.	NS	16	Three subgroups for resilient materials (Ufi Gel SC, Silagum-Comfort, and Vertex Soft) were used to bond between a pair of samples in each denture material group. A universal testing machine to measure the tensile bond strength between resilient denture liners and denture materials.	Resilient denture liners bonded to CAD-CAM denture bases produced the weakest tensile bond strengths. Silicone-based resilient denture liners produced the highest tensile bond strength to all denture bases tested.
	Heat-activated polymerization	Vertex Rapid Simplified, Vertex-Dental B.V.	NS	20		
	Milled	IvoBase CAD, Ivoclar Vivadent AG	NS Tensile bond strength between resilient material and testing materials in MPa	10		

n, sample size; *NS*, not specified; *SD*, standard deviation.

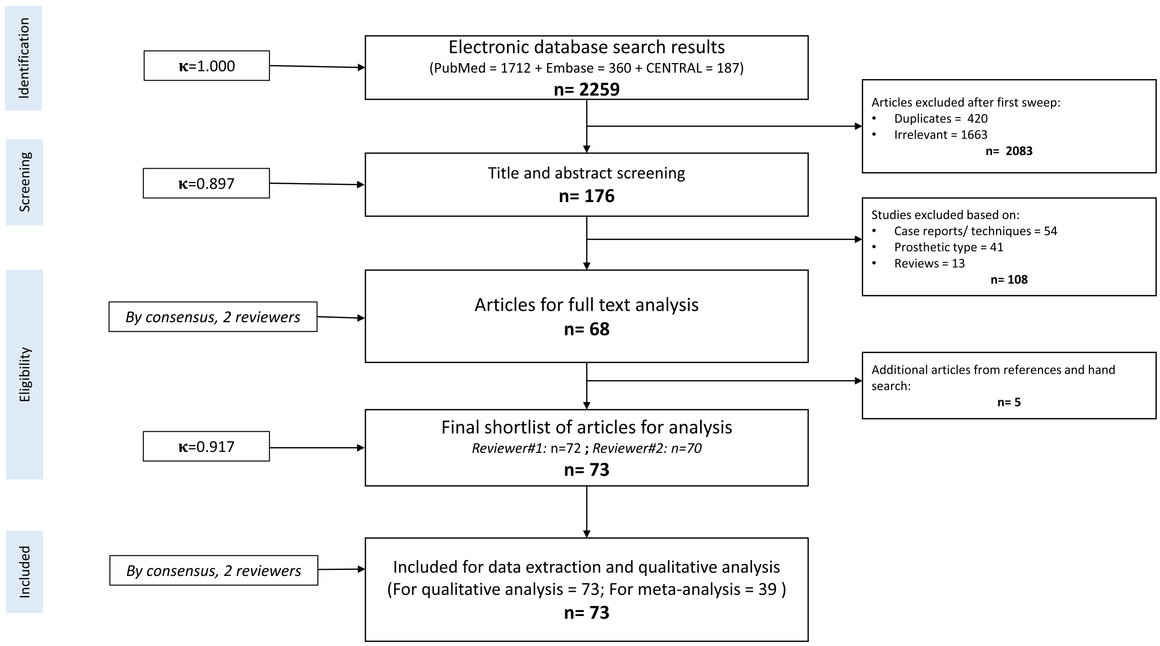


Fig. 1. PRISMA flow diagram showing the identification, screening, eligibility and inclusion process of the studies. n: number, κ: Cohen's unweighted kappa (inter-investigator reliability).

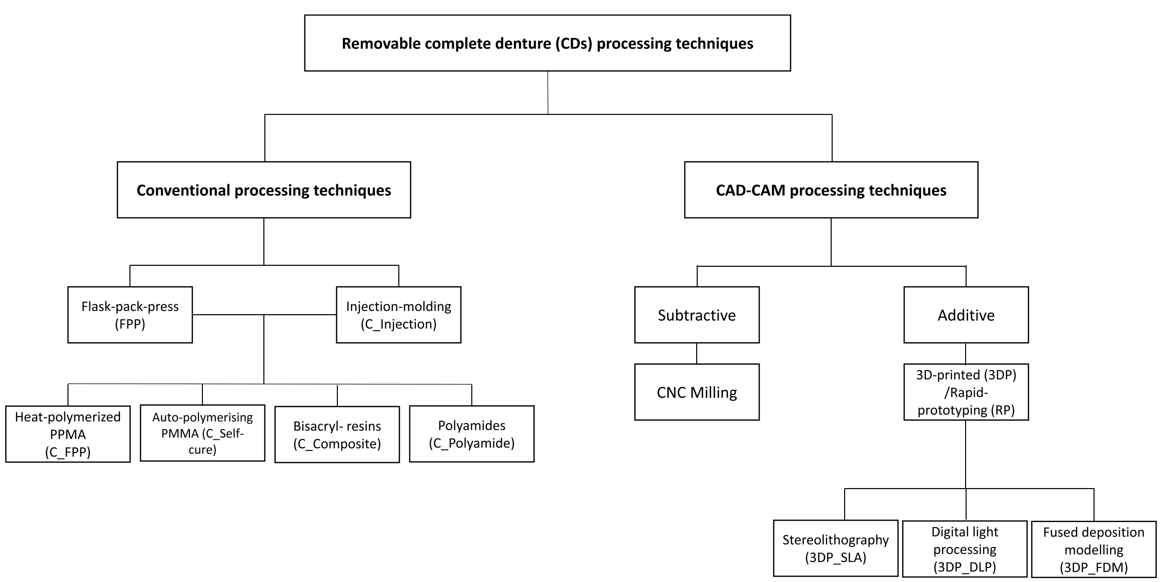
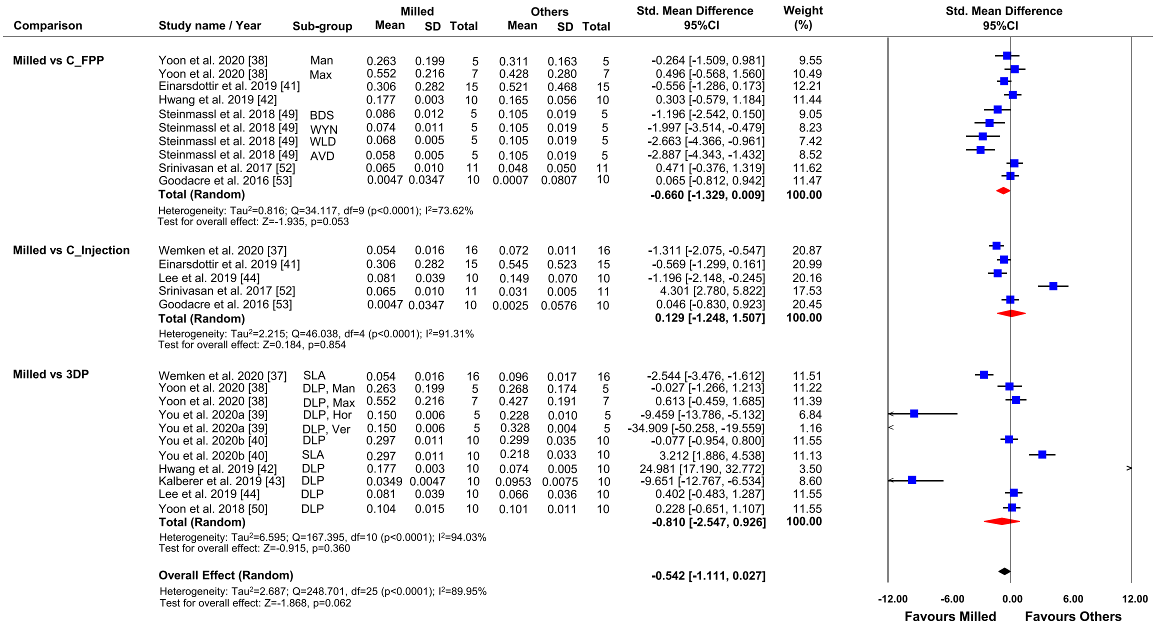


Fig. 2. Removable complete denture (CDs) processing techniques as identified and the various subgroups as classified in this review. CNC, computerized numeric control.

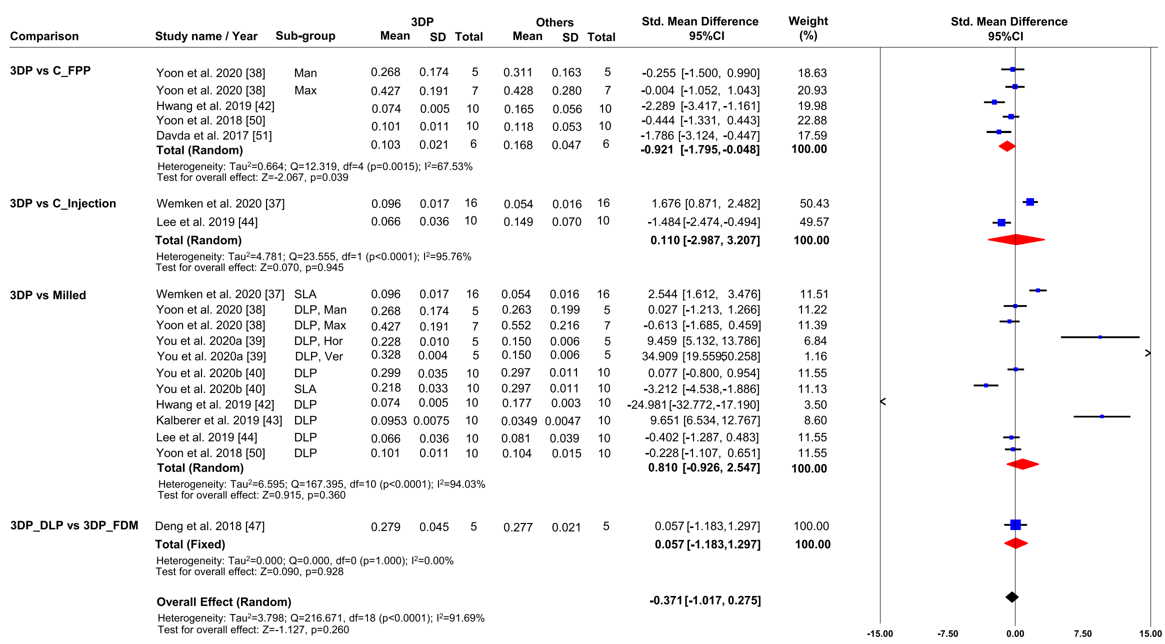
fracture, particularly with impacts sustained when the denture is out of the mouth or while in service in the mouth due to flexural fatigue as the base undergoes cyclical loading during mastication [94,95]. High flexural strength is imperative for sustained successful CD wear as alveolar resorption is a continual and irregular process which can lead to uneven prosthesis support [96]. To ensure that the stresses applied during mastication do not cause permanent deformation, wear and ultimately fracture, the CD base material must exhibit a high elastic modulus.

A number of properties are responsible for microbial colonization of denture bases including surface roughness. Microbial contamination of denture surfaces can elicit localized intra-oral mucosal infections but have also been implicated in the aetiology of aspiration pneumonia in dependent older adults [97]. The surface roughness of conventional CD bases is primarily determined by processing which gives rise to gaseous porosities and surface irregularities. Although these irregularities can be countered by applying packing pressure, the amount of applicable pressure is limited in conventional CD manufacturing, as too high pressure may cause fractures of the mold or the flask [98,99]. By contrast, in CAD/CAM CD manufacturing, the bases are milled from industrially polymerized resin pucks, and the resin in these pucks is highly condensed because of the high pressure the manufacturers apply during polymerization. As illustrated in this review, the fully automated



Comparison	Study name / Year	Sub-group	Milled Mean	Milled SD	Milled Total	Others Mean	Others SD	Others Total	Std. Mean Difference 95%CI	Weight (%)
Milled vs C_FPP	Yoon et al. 2020 [38]	Man	0.263	0.199	5	0.311	0.163	5	-0.264 [-1.509, 0.981]	9.55
	Yoon et al. 2020 [38]	Max	0.552	0.216	7	0.428	0.280	7	0.496 [-0.568, 1.560]	10.49
	Einarsdottir et al. 2019 [41]		0.306	0.282	15	0.521	0.468	15	-0.556 [-1.286, 0.173]	12.21
	Hwang et al. 2019 [42]		0.177	0.003	10	0.165	0.056	10	0.303 [-0.579, 1.184]	11.44
	Steinmassl et al. 2018 [49]	BDS	0.086	0.012	5	0.105	0.019	5	-1.196 [-2.542, 0.150]	9.05
	Steinmassl et al. 2018 [49]	WYN	0.074	0.011	5	0.105	0.019	5	-1.997 [-3.514, -0.479]	8.23
	Steinmassl et al. 2018 [49]	WLD	0.068	0.005	5	0.105	0.019	5	-2.663 [-4.366, -0.961]	7.42
	Steinmassl et al. 2018 [49]	AVD	0.058	0.005	5	0.105	0.019	5	-2.887 [-4.343, -1.432]	8.52
	Srinivasan et al. 2017 [52]		0.065	0.010	11	0.048	0.050	11	0.471 [-0.376, 1.319]	11.62
	Goodacre et al. 2016 [53]		0.0047	0.0347	10	0.0007	0.0807	10	0.065 [-0.812, 0.942]	11.47
	Total (Random)								**-0.660 [-1.329, 0.009]**	**100.00**
	Heterogeneity: Tau^2=0.816; Q=34.117, df=9 (p<0.0001); I^2=73.62%									
	Test for overall effect: Z=-1.935, p=0.053									
Milled vs C_Injection	Wemken et al. 2020 [37]		0.054	0.016	16	0.072	0.011	16	-1.311 [-2.075, -0.547]	20.87
	Einarsdottir et al. 2019 [41]		0.306	0.282	15	0.545	0.523	15	-0.569 [-1.299, 0.161]	20.99
	Lee et al. 2019 [44]		0.081	0.039	10	0.149	0.070	10	-1.196 [-2.148, -0.245]	20.16
	Srinivasan et al. 2017 [52]		0.065	0.010	11	0.031	0.005	11	4.301 [2.780, 5.822]	17.53
	Goodacre et al. 2016 [53]		0.0047	0.0347	10	0.0025	0.0576	10	0.046 [-0.830, 0.923]	20.45
	Total (Random)								**0.129 [-1.248, 1.507]**	**100.00**
	Heterogeneity: Tau^2=2.215; Q=46.038, df=4 (p<0.0001); I^2=91.31%									
	Test for overall effect: Z=0.184, p=0.854									
Milled vs 3DP	Wemken et al. 2020 [37]	SLA	0.054	0.016	16	0.096	0.017	16	-2.544 [-3.476, -1.612]	11.51
	Yoon et al. 2020 [38]	DLP, Man	0.263	0.199	5	0.268	0.174	5	-0.027 [-1.266, 1.213]	11.22
	Yoon et al. 2020 [38]	DLP, Max	0.552	0.216	7	0.427	0.191	7	0.613 [-0.459, 1.685]	11.39
	You et al. 2020a [39]	DLP, Hor	0.150	0.006	5	0.228	0.010	5	-9.459 [-13.786, -5.132]	6.84
	You et al. 2020a [39]	DLP, Ver	0.150	0.006	5	0.328	0.004	5	-34.909 [-50.258, -19.559]	1.16
	You et al. 2020b [40]	DLP	0.297	0.011	10	0.299	0.035	10	-0.077 [-0.954, 0.800]	11.55
	You et al. 2020b [40]	SLA	0.297	0.011	10	0.218	0.033	10	3.212 [1.886, 4.538]	11.13
	Hwang et al. 2019 [42]	DLP	0.177	0.003	10	0.074	0.005	10	24.981 [17.190, 32.772]	3.50
	Kalberer et al. 2019 [43]	DLP	0.0349	0.0047	10	0.0953	0.0075	10	-9.651 [-12.767, -6.534]	8.60
	Lee et al. 2019 [44]	DLP	0.081	0.039	10	0.066	0.036	10	0.402 [-0.483, 1.287]	11.55
	Yoon et al. 2018 [50]	DLP	0.104	0.015	10	0.101	0.011	10	0.228 [-0.651, 1.107]	11.55
	Total (Random)								**-0.810 [-2.547, 0.926]**	**100.00**
	Heterogeneity: Tau^2=6.595; Q=167.395, df=10 (p<0.0001); I^2=94.03%									
	Test for overall effect: Z=-0.915, p=0.360									
	Overall Effect (Random)								**-0.542 [-1.111, 0.027]**	
	Heterogeneity: Tau^2=2.687; Q=248.701, df=25 (p<0.0001); I^2=89.95%									
	Test for overall effect: Z=-1.868, p=0.062									

Fig. 3. Forest plot comparing the trueness of fit (mean and SD in mm) between milled, conventional flask-pack-press (C_FPP), injection-molded (C_injection), and 3D-printed (3DP) complete dentures. AVD, 'AvaDent Digital Dentures' (milled); BDS, 'Baltic Denture System' (milled); CI, confidence interval; DLP, digital light processing (3DP); Hor, 3D-printed in horizontal orientation (3DP); Man, mandibular denture fabrication; Max, maxillary denture fabrication; SD, standard deviation; SLA, stereolithography (3DP); Std., standardized; Ver, 3D-printed in vertical orientation; WLD, 'Wieland Digital Dentures'(milled); WYN, 'Whole You Nexteeth' (milled)



Comparison	Study name / Year	Sub-group	3DP Mean	3DP SD	3DP Total	Others Mean	Others SD	Others Total	Std. Mean Difference 95%CI	Weight (%)
3DP vs C_FPP	Yoon et al. 2020 [38]	Man	0.268	0.174	5	0.311	0.163	5	-0.255 [-1.500, 0.990]	18.63
	Yoon et al. 2020 [38]	Max	0.427	0.191	7	0.428	0.280	7	-0.004 [-1.052, 1.043]	20.93
	Hwang et al. 2019 [42]		0.074	0.005	10	0.165	0.056	10	-2.289 [-3.417, -1.161]	19.98
	Yoon et al. 2018 [50]		0.101	0.011	10	0.118	0.053	10	-0.444 [-1.331, 0.443]	22.88
	Davda et al. 2017 [51]		0.103	0.021	6	0.168	0.047	6	-1.786 [-3.124, -0.447]	17.59
	Total (Random)								**-0.921 [-1.795, -0.048]**	**100.00**
	Heterogeneity: Tau^2=0.664; Q=12.319, df=4 (p=0.0015); I^2=67.53%									
	Test for overall effect: Z=-2.067, p=0.039									
3DP vs C_Injection	Wemken et al. 2020 [37]		0.096	0.017	16	0.054	0.016	16	1.676 [0.871, 2.482]	50.43
	Lee et al. 2019 [44]		0.066	0.036	10	0.149	0.070	10	-1.484 [-2.474, -0.494]	49.57
	Total (Random)								**0.110 [-2.987, 3.207]**	**100.00**
	Heterogeneity: Tau^2=4.781; Q=23.555, df=1 (p<0.0001); I^2=95.76%									
	Test for overall effect: Z=0.070, p=0.945									
3DP vs Milled	Wemken et al. 2020 [37]	SLA	0.096	0.017	16	0.054	0.016	16	2.544 [1.612, 3.476]	11.51
	Yoon et al. 2020 [38]	DLP, Man	0.268	0.174	5	0.263	0.199	5	0.027 [-1.213, 1.266]	11.22
	Yoon et al. 2020 [38]	DLP, Max	0.427	0.191	7	0.552	0.216	7	-0.613 [-1.685, 0.459]	11.39
	You et al. 2020a [39]	DLP, Hor	0.228	0.010	5	0.150	0.006	5	9.459 [5.132, 13.786]	6.84
	You et al. 2020a [39]	DLP, Ver	0.328	0.004	5	0.150	0.006	5	34.909 [19.55950.258]	1.16
	You et al. 2020b [40]	DLP	0.299	0.035	10	0.297	0.011	10	0.077 [-0.800, 0.954]	11.55
	You et al. 2020b [40]	SLA	0.218	0.033	10	0.297	0.011	10	-3.212 [-4.538, -1.886]	11.13
	Hwang et al. 2019 [42]	DLP	0.074	0.005	10	0.177	0.003	10	-24.981 [-32.772, -17.190]	3.50
	Kalberer et al. 2019 [43]	DLP	0.0953	0.0075	10	0.0349	0.0047	10	9.651 [6.534, 12.767]	8.60
	Lee et al. 2019 [44]	DLP	0.066	0.036	10	0.081	0.039	10	-0.402 [-1.287, 0.483]	11.55
	Yoon et al. 2018 [50]	DLP	0.101	0.011	10	0.104	0.015	10	-0.228 [-1.107, 0.651]	11.55
	Total (Random)								**0.810 [-0.926, 2.547]**	**100.00**
	Heterogeneity: Tau^2=6.595; Q=167.395, df=10 (p<0.0001); I^2=94.03%									
	Test for overall effect: Z=0.915, p=0.360									
3DP_DLP vs 3DP_FDM	Deng et al. 2018 [47]		0.279	0.045	5	0.277	0.021	5	0.057 [-1.183, 1.297]	100.00
	Total (Fixed)								**0.057 [-1.183, 1.297]**	**100.00**
	Heterogeneity: Tau^2=0.000; Q=0.000, df=0 (p=1.000); I^2=0.00%									
	Test for overall effect: Z=0.090, p=0.928									
	Overall Effect (Random)								**-0.371 [-1.017, 0.275]**	
	Heterogeneity: Tau^2=3.798; Q=216.671, df=18 (p<0.0001); I^2=91.69%									
	Test for overall effect: Z=-1.127, p=0.260									

Fig. 4. Forest plot comparing the trueness of fit (mean and SD in mm) between 3D-printed (3DP), conventional flask-pack-press (C_FPP), injection-molded (C_injection), and milled, complete dentures. CI, confidence interval; 3DP_DLP, 3D-printed using digital light processing (3DP); 3DP_FDM, 3D-printed using fused deposition modeling (3DP); Hor, 3D-printed in horizontal orientation; Man, mandibular denture fabrication; Max, maxillary denture fabrication; 3DP, 3D-printed; SD, standard deviation; SLA, stereolithography (3DP); Std., standardized; Ver, 3D-printed in vertical orientation

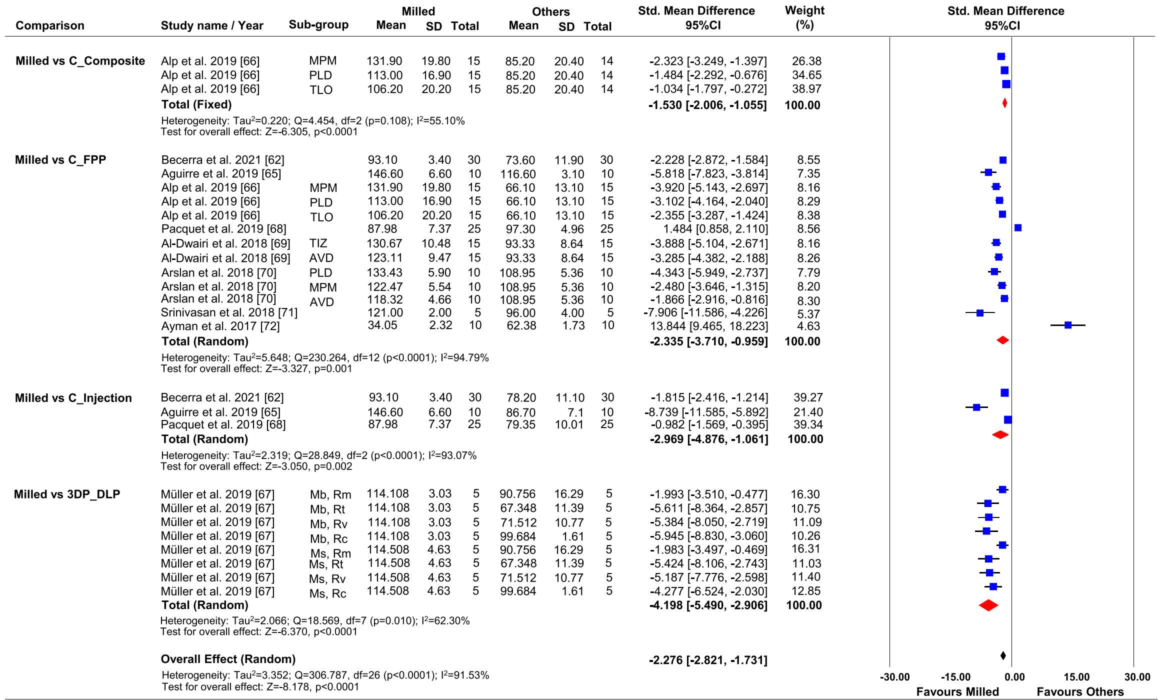


Fig. 5. Forest plot comparing the flexural strength (mean and SD in MPa) between milled, conventional flask-pack-press (C_FPP), 3D-printed (3DP), and injection-molded (C_Injection) complete dentures. AVD, 'Avadent' (milled); CI, confidence interval; Mb, 'AvaDent Denture base disc' (milled); MPM, 'M-PM Disc' (milled); Ms, 'Avadent Extreme CAD-CAM shaded disc YW10' (milled); PLD, 'Polident' (milled); Rc, 'NextDent C&B' (3DP); Rm, 'NextDent Base' 3D-printed using a manufacturer-recommended 3D-printer (3DP); Rt, 'NextDent Base' 3D-printed using a third-party 3D-printer (3DP); Rv, 'NextDent Base' 3D-printed in vertical orientation (3DP); SD, standard deviation; Std. standardized; TIZ, 'Tizian' (milled); TLO, 'Telio CAD' (milled)

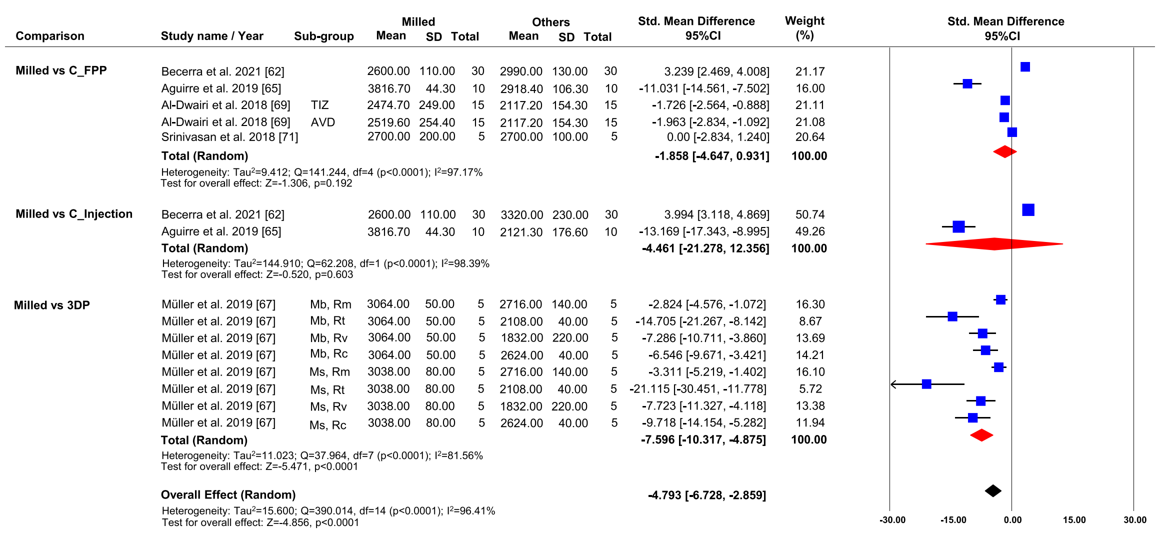


Fig. 6. Forest plot comparing the flexural modulus (mean and SD in MPa) of milled, conventional flask-pack-press (C_FPP), injection-molded (C_injection) and 3D-printed (3DP) complete dentures. AVD, 'Avadent' (milled); CI, confidence interval; Mb, 'AvaDent Denture base disc' (milled); Ms, 'Avadent Extreme CAD-CAM shaded disc YW10' (milled); Rc, 'NextDent C&B' (3DP); Rm, 'NextDent Base' 3D-printed using a manufacturer-recommended 3D-printer (3DP); Rt, 'NextDent Base' 3D-printed using a third-party 3D-printer (3DP); Rv, 'NextDent Base' 3D-printed using a vertical orientation (3DP); SD, standard deviation; Std., standardized; TIZ, 'Tizian' (milled).

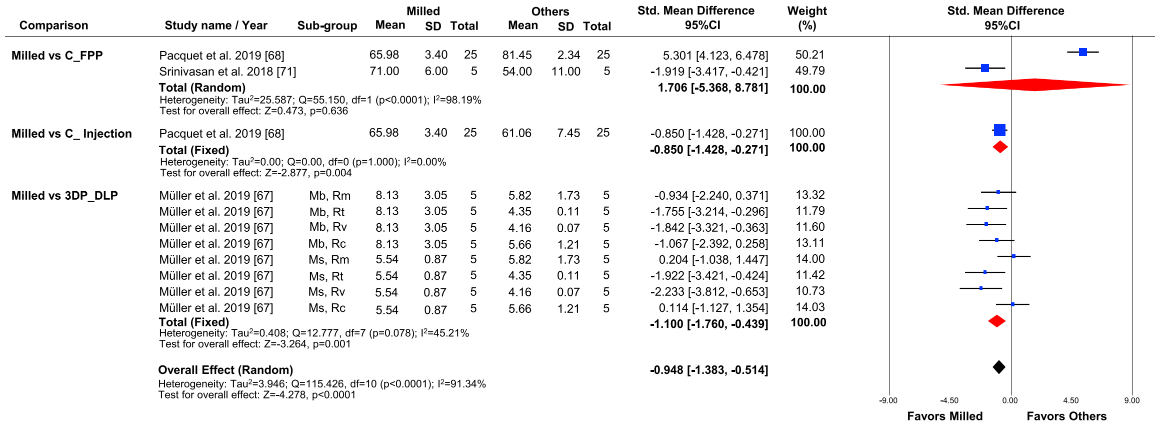


Fig. 7. Forest plot comparing the yield strength (mean and SD in MPa) between milled, 3D-printed (3DP), conventional flask-pack-press (C_FPP), and injection-molded (C_injection) complete dentures. CI, confidence interval; Mb, 'AvaDent Denture base disc' (milled); Ms, 'Avadent Extreme CAD-CAM shaded disc YW10' (milled); Rc, 'NextDent C&B' (3DP); Rm, 'NextDent Base' 3D-printed using a manufacturer-recommended 3D-printer (3DP); Rt, 'NextDent Base' 3D-printed using a third-party 3D-printer (3DP); Rv, 'NextDent Base' 3D-printed using vertical orientation (3DP); SD, standard deviation; Std., standardized.

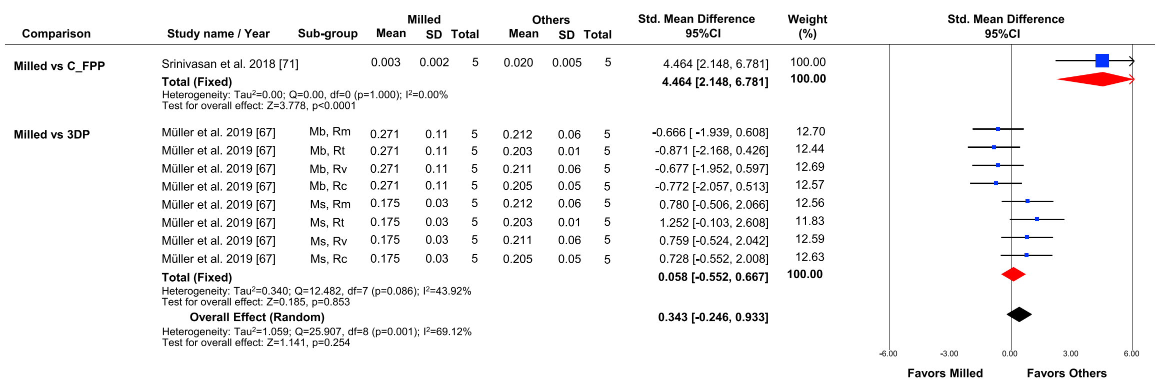


Fig. 8. Forest plot comparing the strain at yield point (mean and SD in unitless) between milled, conventional flask-pack-press (C_FPP), and 3D-printed (3DP) complete dentures. CI, confidence interval; Mb, 'AvaDent Denture base disc' (milled); Ms, 'Avadent Extreme CAD-CAM shaded disc YW10' (milled); Rc, 'NextDent C&B' (3DP); Rm, 'NextDent Base' 3D-printed using a manufacturer-recommended 3D-printer (3DP); 3DP, 3D-printed; Rt, 'NextDent Base' 3D-printed using a third-party 3D-printer (3DP); Rv, 'NextDent Base' 3Dprintred using vertical orientation (3DP); SD, standard deviation; Std., standardized.

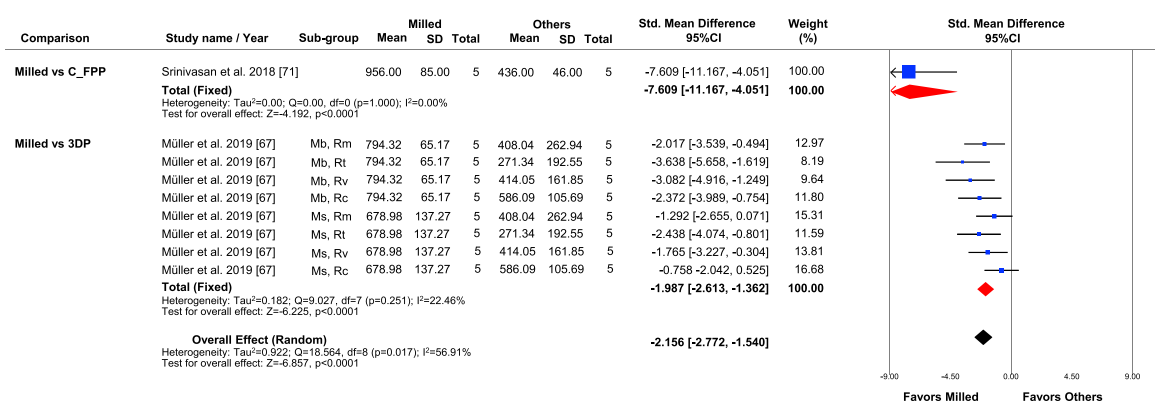


Fig. 9. Forest plot comparing the toughness (mean and SD in N•mm) between milled, 3D-printed (3DP) and conventional flask-pack-press (C_FPP) complete dentures. CI, confidence interval; Mb, 'AvaDent Denture base disc' (milled); Ms, 'Avadent Extreme CAD-CAM shaded disc YW10' (milled); Rc, 'NextDent C&B' (3DP); Rm, 'NextDent Base' 3D-printed using a manufacturer-recommended 3D-printer (3DP); 3DP, 3D-printed; Rt, 'NextDent Base' 3D-printed using a third-party 3D-printer (3DP); Rv, 'NextDent Base' 3D-printed using vertical orientation (3DP); SD, standard deviation; Std., standardized

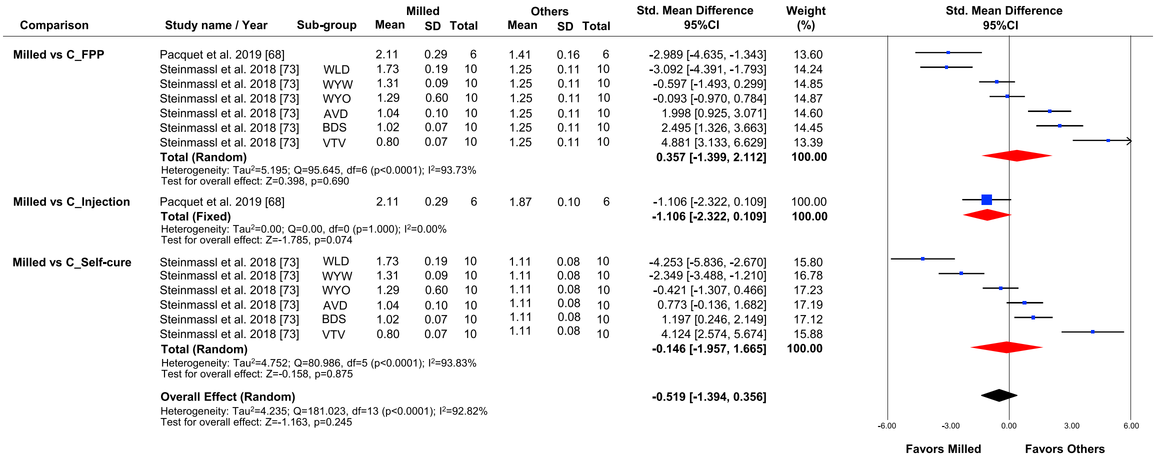


Fig. 10. Forest plot comparing the fracture toughness (mean and SD in MPa•m$^{1/2}$) between milled, conventional flask-pack-press (C_FPP), injection-molded (C_injection) and auto-polymerized (C_Self-cure) complete dentures. AVD, 'AvaDent Digital Dentures' (milled); BDS, 'Baltic Denture System' (milled); CI, confidence interval; SD, standard deviation; Std., standardized; VTV, 'Vita VIONIC' (milled); WLD, 'Wieland Digital Dentures' (milled); WYO, 'Whole You Nexteeth' without light-curing topcoat (milled); WYW, 'Whole You Nexteeth' with light-curing topcoat (milled).

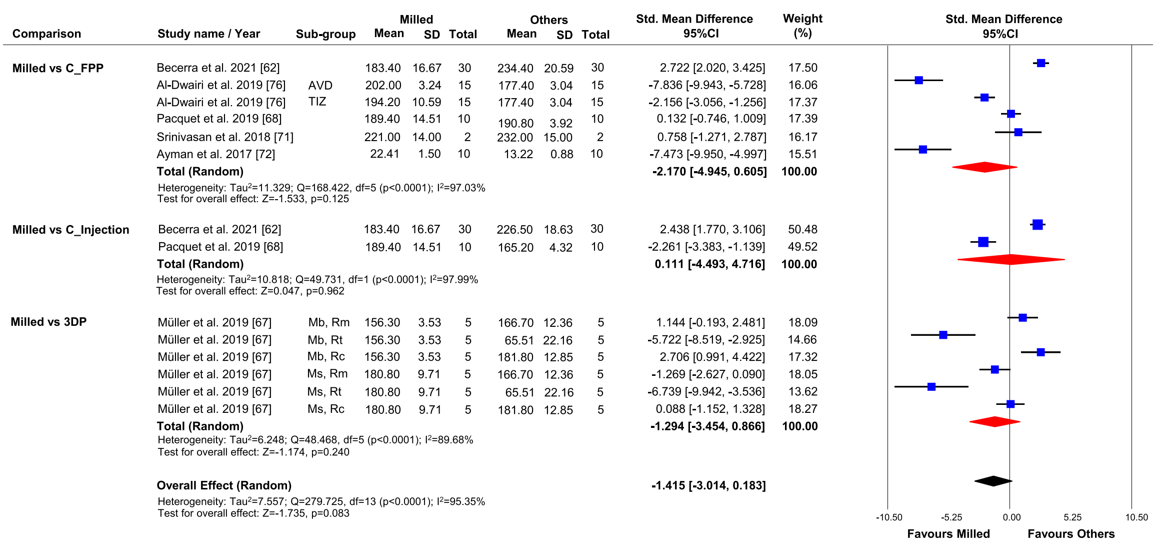


Fig. 11. Forest plot comparing the hardness (mean and SD in MPa) between milled, 3D-printed (3DP), conventional flask-pack-press (C_FPP), and injection-molded (C_Injection) complete dentures. AVD, 'Avadent' (milled); CI, confidence interval; Mb, 'AvaDent Denture base disc' (milled); Ms, 'Avadent Extreme CAD-CAM shaded disc YW10' (milled); Rc, 'NextDent C&B' (3DP); Rm, 'NextDent Base' 3D-printed using a manufacturer-recommended 3D-printer (3DP); Rt, 'NextDent Base' 3D-printed using a third-party 3D-printer (3DP); Rv, 'NextDent Base' 3D-printed using vertical orientation (3DP); SD, standard deviation; Std., standardized; TIZ, 'Tizian' (milled).

milling process produces smoother CD surfaces than the conventional manual fabrication process [74,83]. This was further supported by the studies identified in this review which demonstrated lower levels of microbial adhesion (*Candida Albicans*) to CAD-CAM CDs compared to conventional bases.

The articles identified in this systematic review did not include an extensive number of studies which utilized patient reported outcome measures (PROMs). Unfortunately, this is a common finding across removable prosthodontics and should be addressed in future research. Data was summarized on esthetics which was gathered from a series of Visual Analogue Scales (VAS) completed by clinicians. These results indicated that clinicians preferred conventional CDs in terms of esthetics ($p = 0.002$). When the CAD-CAM milled base was used in conjunction with conventional artificial teeth, no significance was noted between milled and injection-molded dentures [22]. However, when comparing conventional (flask-pack-press) and 3D-printed CD groups, a clear preference was found for the conventional (flask-pack-press) group [24]. It would appear that limited esthetics continue to be an issue with CAD-CAM CDs with patients expressing concern about the pink and white esthetics of the prostheses [24,100]. This issue should also be

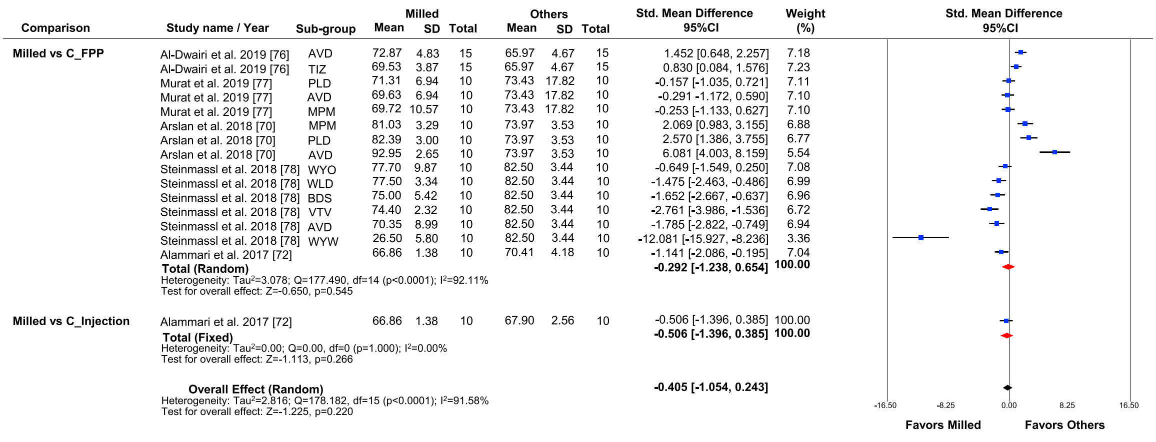


Fig. 12. Forest plot comparing the surface wettability (mean and SD in degree) of milled, conventional flask-pack-press (C_FPP), and injection-molded (C_Injection) complete dentures. AVD, 'Avadent' (milled); BDS, 'Baltic Denture System' (milled); CI, confidence interval; MPM, 'M-PM Disc' (milled); PLD, 'Polident' (milled); SD, standard deviation; Std., standardized; TIZ, 'Tizian' (milled); VTV, 'Vita VIONIC' (milled); WLD, 'Wieland Digital Dentures' (milled); WYO, 'Whole You Nexteeth' without light-curing topcoat (milled); WYW, 'Whole You Nexteeth' with light-curing topcoat (milled).

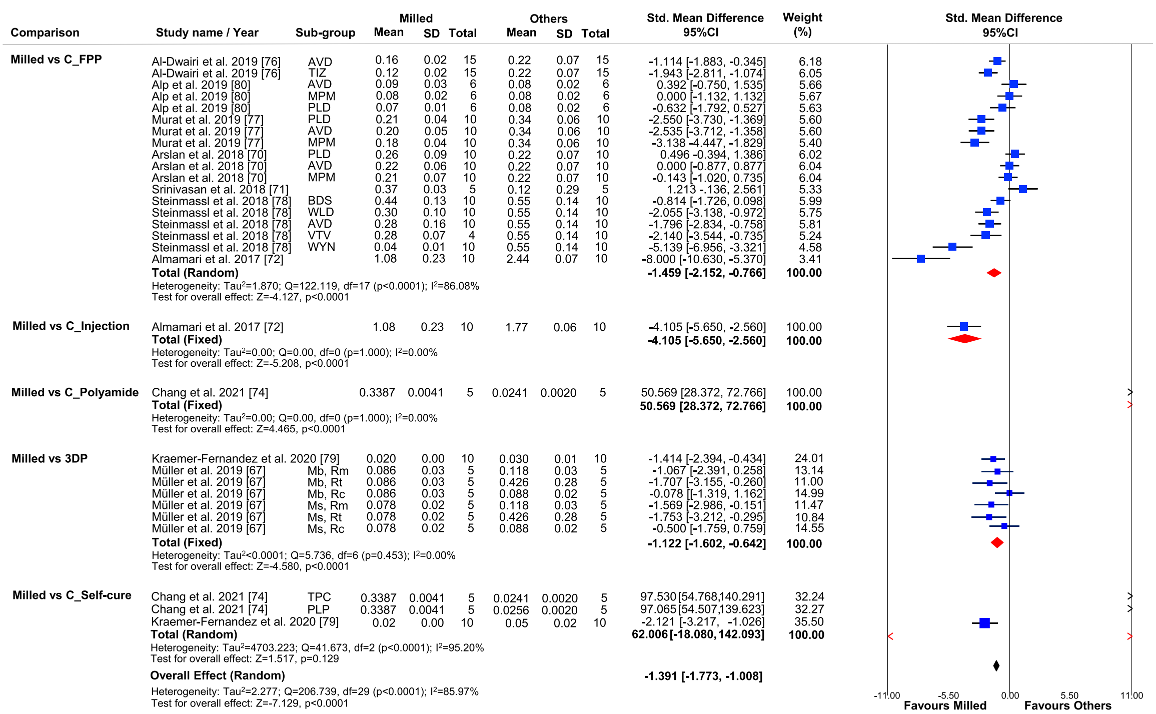


Fig. 13. Forest plot comparing the surface roughness (R_a value, mean and SD in µm) of milled, conventional flask-pack-press (C_FPP), injection-molded (C_Injection), 3D-printed (3DP) and auto-polymerized (C_Self-cure) complete dentures. AVD, 'Avadent' (milled); BDS, 'Baltic Denture System' (milled); CI, confidence interval; Mb, 'AvaDent Denture base disc' (milled); MPM, 'M-PM Disc' (milled); Ms, 'Avadent Extreme CAD-CAM shaded disc YW10' (milled); PLD, 'Polident' (milled); PLP, 'Palapress' (C-Self-cure); Rc, 'NextDent C&B' (3DP); Rm, 'NextDent Base' 3D-printed using a manufacturer-recommended 3D-printer (3DP); Rt, 'NextDent Base' 3D-printed using a third-party 3D-printer (3DP); Rv, 'NextDent Base' 3D-printed using vertical orientation (3DP); SD, standard deviation; Std., standardized; TIZ, 'Tizian' (milled); TPC; 'Triplex Cold' (C-Self-cure); VTV, 'Vita VIONIC' (milled); WLD, 'Wieland Digital Dentures' (milled); WYN, 'Whole You Nexteeth' (milled).

considered in relation to the highly aesthetic conventional CDs which can be produced by high quality dental technicians particularly when working closely with both the clinician and the patient [101–103]. However, it is highly likely that the esthetics of CAD-CAM CDs will evolve rapidly in future with constantly improving technology.

This review is a comprehensive oversight of material properties, clinical and patient centered outcomes for CAD-CAM CDs. This review is particularly timely given the emergence of this clinical technique and research evidence over the last two decades. Certainly, one of the strengths of this review is that the evidence on this topic is contemporaneous with the majority of included studies published within the last 10 years. Unfortunately, this does mean that long term prospective clinical studies on CAD-CAM CDs are scarce and those which have been conducted include small numbers of patients. Given the outcome measures under investigation, long term follow-up is required to adequately assess factors including clinical success, survival of restorations and

Comparison	Study name / Year	Sub-group	Milled Mean	Milled SD	Milled Total	Others Mean	Others SD	Others Total	Std. Mean Difference 95%CI	Weight (%)
Milled vs C_FPP (Pink-Shade)	Gruber et al. 2020 [83]	WLD	0.91	0.13	4	0.39	0.22	4	2.878 [0.901, 4.855]	7.71
	Gruber et al. 2020 [83]	MPM	0.57	0.16	4	0.39	0.22	4	0.936 [-0.524, 2.396]	11.43
	Gruber et al. 2020 [83]	PLD	0.51	0.02	4	0.39	0.22	4	0.768 [-0.668, 2.204]	11.65
	Gruber et al. 2020 [83]	AVD	0.46	0.18	4	0.39	0.22	4	0.348 [-1.048, 1.745]	12.02
	Alp et al. 2019 [80]	AVD	1.52	0.71	6	1.19	0.53	6	0.527 [-0.624, 1.678]	14.64
	Alp et al. 2019 [80]	PLD	1.10	0.38	6	1.19	0.53	6	-0.195 [-1.329, 0.939]	14.83
	Alp et al. 2019 [80]	MPM	0.95	0.67	6	1.19	0.53	6	-0.397 [-1.540, 0.745]	14.73
	Al-Qarni et al.2019 [84]		2.10	0.10	5	2.30	0.30	5	-0.894 [-2.195, 0.406]	12.99
	Total (Fixed)								**0.334 [-0.315, 0.982]**	**100.00**
	Heterogeneity: Tau²=0.403; Q=13.176, df=7 (p=0.068); I²=46.87% Test for overall effect: Z=1.008, p=0.313									
Milled vs C_Injection (Pink-Shade)	Al-Qarni et al. 2019 [84]		2.10	0.10	5	1.80	0.20	5	1.897 [0.405, 3.390]	100.00
	Total (Fixed)								**1.897 [0.405, 3.390]**	**100.00**
	Heterogeneity: Tau²=0.000 Q=0.000, df=0 (p=1.000); I²=0.00% Test for overall effect: Z=2.491, p=0.013									
Milled vs 3DP (Pink-Shade)	Gruber et al. 2020 [83]	WLD	0.91	0.13	4	0.90	0.23	4	0.054 [-1.333, 1.440]	28.91
	Gruber et al. 2020 [83]	MPM	0.57	0.16	4	0.90	0.23	4	-1.666 [-3.274, -0.057]	25.30
	Gruber et al. 2020 [83]	PLD	0.51	0.02	4	0.90	0.23	4	-2.389 [-4.203, -0.575]	22.35
	Gruber et al. 2020 [83]	AVD	0.46	0.18	4	0.90	0.23	4	-2.131 [-3.866, -0.395]	23.44
	Total (Fixed)								**-1.439 [-2.600, -0.278]**	**100.00**
	Heterogeneity: Tau²=0.713; Q=6.121, df=3 (p=0.106); I²=50.99% Test for overall effect: Z=-2.430, p=0.015									
Milled vs C_FPP (Tooth-Shade)	Gruber et al. 2020 [83]	AVD	1.63	0.90	4	1.42	0.30	4	0.313 [-1.081, 1.707]	26.96
	Gruber et al. 2020 [83]	MPM	0.53	0.26	4	1.42	0.30	4	-3.170 [-5.252, -1.089]	24.61
	Gruber et al. 2020 [83]	PLD	0.22	0.13	4	1.42	0.30	4	-5.190 [-8.087, -2.294]	21.45
	Al-Qarni et al. 2019 [84]		4.80	0.70	5	3.80	0.70	5	1.429 [0.040, 2.817]	26.98
	Total (Random)								**-1.424 [-4.025, 1.177]**	**100.00**
	Heterogeneity: Tau²=6.025; Q=24.946, df=3 (p<0.0001); I²=87.97% Test for overall effect: Z=-1.073, p=0.283									
Milled vs C_Injection (Tooth-Shade)	Al-Qarni et al. 2019 [84]		4.80	0.70	5	4.50	1.00	5	0.348 [-0.901, 1.596]	100.00
	Total (Fixed)								**0.348 [-0.901, 1.596]**	**100.00**
	Heterogeneity: Tau²=0.000; Q=0.000, df=0 (p=1.0009); I²=0.00% Test for overall effect: Z=0.545, p=0.585									
Milled vs 3DP (Tooth-Shade)	Gruber et al. 2020 [83]	AVD	1.63	0.90	4	1.00	0.34	4	0.926 [-0.532, 2.384]	35.04
	Gruber et al. 2020 [83]	MPM	0.53	0.26	4	1.00	0.34	4	-1.553 [-3.134, 0.028]	34.16
	Gruber et al. 2020 [83]	PLD	0.22	0.13	4	1.00	0.34	4	-3.030 [-5.062, -0.999]	30.80
	Total (Random)								**-1.139 [-3.394, 1.115]**	**100.00**
	Heterogeneity: Tau²=1.585; Q=10.882, df=2 (p=0.004); I²=81.62% Test for overall effect: Z=-0.990, p=0.322									
	Overall Effect (Random)								**0.080 [-0.389, 0.549]**	
	Heterogeneity: Tau²=1.585; Q=76.078, df=20 (p<0.001); I²=73.71% Test for overall effect: Z=-0.335, p=0.738									

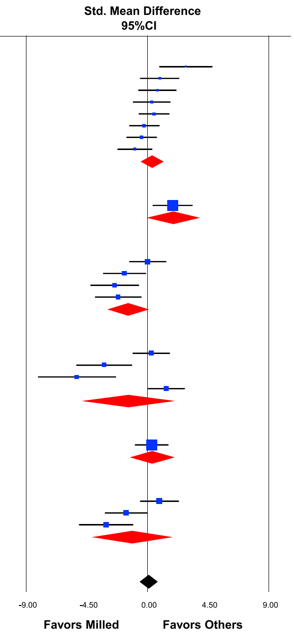


Fig. 14. Forest plot comparing the color stability (color difference ΔE, mean and SD in unitless) between milled, conventional flask-pack-press (C_FPP), injection-molded (C_Injection), and 3D-printed (3DP) complete dentures. AVD, 'Avadent' (milled); CI, confidence interval; MPM, 'M-PM Disc' (milled); PLD, 'Polident' (milled); 3DP, 3D-printed; SD, standard deviation; Std., standardized; WLD, 'Wieland Digital Dentures' (milled).

Comparison	Study name / Year	Sub-group	Rapidly-Prototyped Mean	Rapidly-Prototyped SD	Rapidly-Prototyped Total	Others Mean	Others SD	Others Total	Std. Mean Difference 95%CI	Weight (%)
3DP vs C_FPP (Pink-Shade)	Gruber et al. 2020 [83]		0.90	0.23	4	0.39	0.22	4	2.266 [0.490, 4.042]	100.00
	Total (Fixed)								**2.266 [0.490, 4.042]**	**100.00**
	Heterogeneity: Tau²=0.000; Q=0.000, df=1 (p=1.000); I²=0.00% Test for overall effect: Z=2.501, p=0.012									
3DP vs Milled (Pink-Shade)	Gruber et al. 2020 [83]	WLD	0.90	0.23	4	0.91	0.13	4	-0.054 [-1.440, 1.333]	28.91
	Gruber et al. 2020 [83]	MPM	0.90	0.23	4	0.57	0.16	4	1.666 [0.057, 3.274]	25.30
	Gruber et al. 2020 [83]	PLD	0.90	0.23	4	0.51	0.02	4	2.389 [0.575, 4.203]	22.35
	Gruber et al. 2020 [83]	AVD	0.90	0.23	4	0.46	0.18	4	2.131 [0.395, 3.866]	23.44
	Total (Fixed)								**1.439 [0.278, 2.600]**	**100.00**
	Heterogeneity: Tau²=0.713; Q=6.121, df=3 (p=0.106); I²=50.99% Test for overall effect: Z=2.430, p=0.015									
3DP vs C_FPP (Tooth-Shade)	Gruber et al. 2020 [83]		1.00	0.34	4	1.42	0.30	4	-1.310 [-2.837, 0.217]	100.00
	Total (Fixed)								**-1.310 [-2.837, 0.217]**	**100.00**
	Heterogeneity: Tau²=0.000; Q=0.000, df=0 (p=1.000); I²=0.00% Test for overall effect: Z=-1.681, p=0.093									
3DP vs Milled (Tooth-Shade)	Gruber et al. 2020 [83]	AVD	1.00	0.34	4	1.63	0.90	4	-0.926 [-2.384, 0.532]	35.04
	Gruber et al. 2020 [83]	MPM	1.00	0.34	4	0.53	0.26	4	1.553 [-0.028, 3.134]	34.16
	Gruber et al. 2020 [83]	PLD	1.00	0.34	4	0.22	0.13	4	3.030 [0.999, 5.062]	30.80
	Total (Random)								**1.139 -1.115, 3.394]**	**100.00**
	Heterogeneity: Tau²=3.223; Q=10.882, df=2 (p=0.004); I²=81.62% Test for overall effect: Z=0.990, p=0.322									
	Overall Effect (Random)								**0.860 [0.090, 1.631]**	
	Heterogeneity: Tau²=1.769; Q=28.424, df=8 (p<0.0001); I²=71.86% Test for overall effect: Z=2.188, p=0.029									

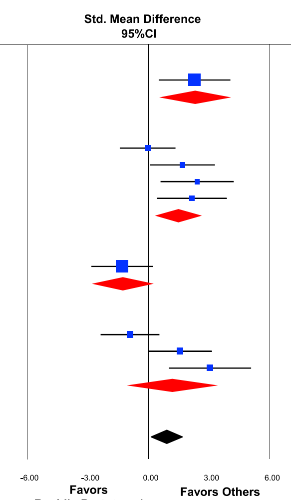


Fig. 15. Forest plot comparing the color stability (color difference ΔE, mean and SD in unitless) between 3D-printed, conventional flask-pack-press (C_FPP), and milled complete dentures. AVD, 'Avadent' (milled); CI, confidence interval; MPM, 'M-PM Disc' (milled); PLD, 'Polident' (milled); 3DP, 3D-printed; SD, standard deviation; Std., standardized; WLD, 'Wieland Digital Dentures' (milled).

Comparison	Study name / Year	Sub-group	Milled Mean	Milled SD	Milled Total	Conventional Mean	Conventional SD	Conventional Total	Std. Mean Difference 95%CI	Weight (%)
Milled vs C_FPP	Engler et al. 2020 [86]	AVC	11.96	4.35	40	14.65	2.14	40	-0.785 [-1.240, -0.330]	10.23
	Engler et al. 2020 [86]	AVT	15.14	5.77	40	14.65	2.14	40	0.113 [-0.326, 0.551]	10.25
	Engler et al. 2020 [86]	AD1	6.00	1.18	40	14.65	2.14	40	-5.006 [-5.897, -4.115]	9.72
	Engler et al. 2020 [86]	AD3	6.33	1.52	40	14.65	2.14	40	-4.483 -5.304, -3.661]	9.82
	Engler et al. 2020 [86]	TLO	18.29	5.24	40	14.65	2.14	40	0.909 [0.449, 1.370]	10.23
	Engler et al. 2020 [86]	CRM	13.48	4.83	40	14.65	2.14	40	-0.313 [-0.754, 0.128]	10.24
	Engler et al. 2020 [86]	ZKZ	9.56	2.86	40	14.65	2.14	40	-2.015 [-2.553, -1.477]	10.16
	Engler et al. 2020 [86]	SFB	19.61	7.10	40	14.65	2.14	40	0.946 [0.484, 1.408]	10.23
	Steinmassl et al. 2017 [87]	BDS	0.60	0.40	40	1.50	1.60	40	-0.772 [-1.680, 0.137]	9.70
	Steinmassl et al. 2017 [87]	WYN	6.00	2.70	40	1.50	1.60	40	2.028 [0.949, 3.106]	9.43
	Overall Effect (Random)								**-0.926 [-1.997, 0.144]**	**100.00**
	Heterogeneity: Tau²=3.078; Q=177.490, df=14 (p<0.0001); I²=92.11% Test for overall effect: Z=-1.696, p=0.090									

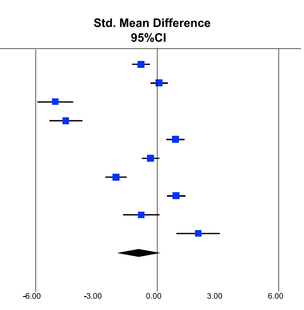


Fig. 16. Forest plot comparing the residual monomer content (mean and SD in ppm) of milled and conventional flask-pack-press (C_FPP) complete dentures. AD1, 'AnaxDent A1' (milled); AD3, 'AnaxDent A3' (milled); AVC, 'AVADENT Core ' (milled); AVT, 'AVADENT Teeth' (milled); BDS, 'Baltic Denture System' (milled); CI, confidence interval; CRM, 'Ceramill' (milled); SD, standard deviation; SFB, 'SHOFU Block' (milled); Std., standardized; TLO, 'Telio' (milled); WYN, 'Whole You Nexteeth' (milled); ZKZ, 'Zirkonzahn' (milled).

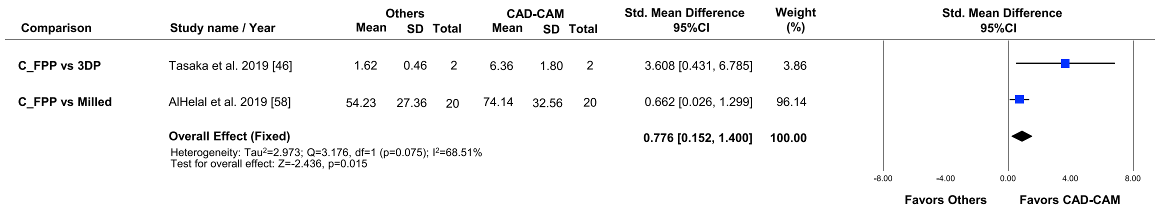


Fig. 17. Forest plot comparing the retention (mean and SD in N) of conventional flask-pack-press (C_FPP), 3D-printed (3DP) and milled complete dentures. CI, confidence interval; SD, standard deviation; Std., standardized.

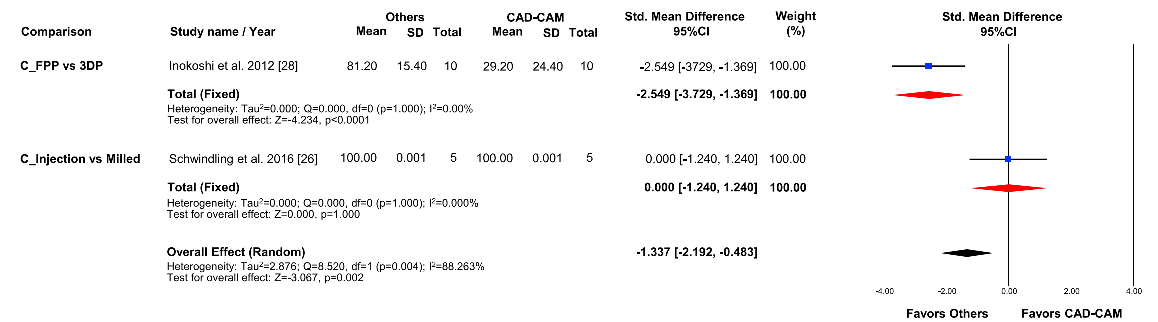


Fig. 18. Forest plot comparing the aesthetics (VAS scores reported by clinician, mean and SD in unitless) of conventional flask-pack-press (C_FPP), 3D-printed (3DP), milled, and injection-molding (C_Injection) complete dentures. CI, confidence interval; SD, standard deviation; Std., standardized.

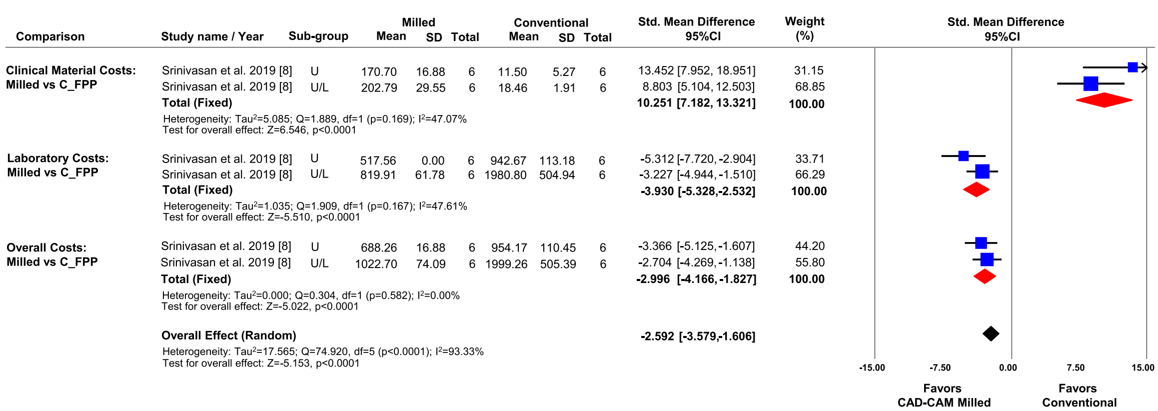


Fig. 19. Forest plot comparing the costs (mean and SD in Swiss francs) involved for the fabrication of conventional flask-pack-press (C_FPP), and milled complete dentures. CI, confidence interval; SD, standard deviation; Std., standardized; U, upper complete denture fabrication; U/L, upper and lower complete denture fabrication.

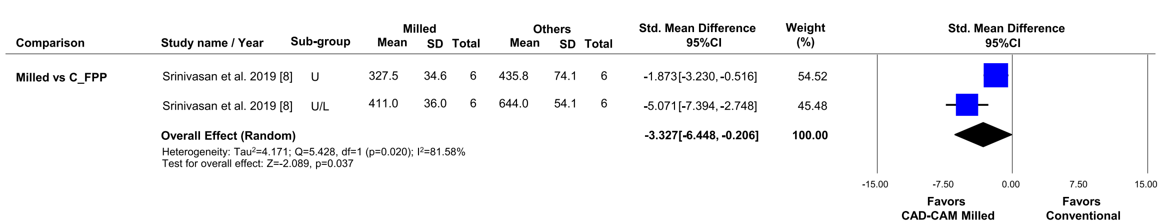


Fig. 20. Forest plot comparing the chair-side time (mean and SD in minutes) involved in fabricating conventional flask-pack-press (C_FPP), and milled complete dentures. CI, confidence interval; SD, standard deviation; Std., standardized; U, upper complete denture fabrication; U/L, upper and lower complete denture fabrication.

Table 21
The Newcastle-Ottawa Scale for assessing the quality of non-randomized studies.

First author (Year)	Selection				Comparability	Outcome			Total
	Representativeness of the exposed cohort	Selection of the non exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Comparability of cohorts on the basis of the design or analysis	Assessment of outcome	Was follow-up long enough for outcomes to occur	Adequacy of follow-up of cohorts	
Arakawa et al. (2021) [14]		*	*	*	*	*	*	*	7
Wei et al. (2021) [15]		*	*	*	**	*	*	*	8
Cristache et al. (2020) [16]			*	*	*	*	*	*	6
Drago et al. (2019) [17]		*	*	*	**	*	*	*	8
Schlenz et al. (2019) [18]			*	*	*	*	*	*	6
†Srinivasan et al. (2019) [8]		*	*	*	**	*	*	*	8
Wei et al. (2017) [85]		*	*	*	**	*	*	*	8
Bidra et al. (2016) [19]			*	*	**	*	*	*	7
Saponaro et al. (2016a) [20]			*	*	*	*	*	*	6
Saponaro et al. (2016b) [21]			*	*	*	*	*	*	6
†Schwindling et al. (2016) [22]		*	*	*	**	*	*	*	8
Kattadiyil et al. (2015) [23]		*	*	*	**	*	*	*	8
†Inokoshi et al. (2012) [24]		*	*	*	*	*	*	*	7

†, used in the meta-analysis

serviceability. Unfortunately, there is an extremely small number of clinical studies which have utilized validated PROMs. Given that successful CD therapy is often built on a positive relationship between patient and clinician, incorporating the patient's opinions into the final prostheses, is very important [104]. This review did not identify any clinical studies which utilized Quality of Life measures, despite a number of instruments specifically developed for edentate older adults [105]. This should be addressed in future clinical studies with appropriate long-term follow-up. The majority of the studies included in this review were in vitro studies; currently, a universal methodological assessment tool for in vitro studies that assesses all critical aspects of in vitro metanalysis does not exist [106], hence quality assessment of these in vitro studies could not be performed. It is also important to mention the heterogeneity of the included studies, which may be considered a further limitation of this review. Although these limitations might have impacted the findings of this review, the methodology of this review adhered to all the recommended protocols for performing systematic reviews and therefore may be considered robust.

5. Conclusions

The introduction of CAD-CAM CDs has brought many advantages including fewer patient appointments, reduced clinical time and digital archiving of completed prostheses. Some CAD-CAM techniques also result in reduced manufacturing costs. This systematic review concludes that CAD-CAM CDs offer a number of improved mechanical/surface properties and are not inferior when compared to conventional CDs. However, further long-term follow-up studies are required to fully evaluate these CAD-CAM CDs with particular regard to estheticsand PROMs .

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Conflicts of interest Statement

The authors declare that they have no conflict of interests.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jdent.2021.103777.

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