EOR | volume 5 | july 2020
DOI: 10.1302/2058-5241.5.190024
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EFORT open reviews

Three-dimensional printing in orthopaedic surgery: a scoping review

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- Three-dimensional printing (3DP) has become more frequently used in surgical specialties in recent years. These uses include pre-operative planning, patient-specific instrumentation (PSI), and patient-specific implant production.
- The purpose of this review was to understand the current uses of 3DP in orthopaedic surgery, the geographical and temporal trends of its use, and its impact on peri-operative outcomes
- One-hundred and eight studies ($N = 2328$) were included, published between 2012 and 2018, with over half based in China.
- The most commonly used material was titanium.
- Three-dimensional printing was most commonly reported in trauma ($N = 41$) and oncology ($N = 22$). Pre-operative planning was the most common use of 3DP ($N = 63$), followed by final implants ($N = 32$) and PSI ($N = 22$).
- Take-home message: Overall, 3DP is becoming more common in orthopaedic surgery, with wide range of uses, particularly in complex cases. 3DP may also confer some important peri-operative benefits.

Keywords: 3D printing; additive manufacturing; orthopaedic surgery; patient-specific instrumentation

Cite this article: *EFORT Open Rev* 2020;5:430-441.
DOI: 10.1302/2058-5241.5.190024

Introduction

Three-dimensional (3D) printing is a process of design and manufacturing that was invented in the early 1980s.[1] Three-dimensional printing is considered a type of 'additive manufacturing', in that the final product is achieved by building up in layers of a given material.[2] This is in contrast to the more traditional subtractive manufacturing, in which elements are removed from a block of material to achieve the desired product (see Fig. 1). As the technology has matured, 3D printing has become easier to utilize, less expensive, and more readily available.[3] This has helped to expand its uses into many fields including manufacturing, art, industry, and medicine.

Current medical applications of 3D printing include custom medication dosage delivery,[4,5] custom design and manufacturing of medical equipment,[6] and the creation of anatomic models.[7,8] Orthopaedic surgery, with its focus on implants, instruments, and surgical devices, is well suited to applications of 3D printing. Multiple studies have shown that the use of 3D-printed models based on real patient imaging improve the inter-rater reliability of complex acetabular fracture classification compared to the use of radiographs and cross-sectional imaging alone.[9,10] The use of 3D printing also has many clinical applications, including pre-operative planning,[11–13] manufacturing of patient-specific instrumentation (PSI),[14–16] and the manufacture of case-specific implants (e.g. plates and arthroplasty components).[17–19] Overall, there is great potential to be able to provide patients with personalized implants and instrumentation that are created quickly and at low cost.[20]

As would be expected with new applications of a relatively new technology, there has been a sharp increase in the amount of published literature presenting orthopaedic applications of 3D printing. In addition, a number of narrative reviews have provided an overview of the topic.[20,21] As well, there is a recent systematic review on the applications of 3D printing in spine surgery, which found that 3D printing allows for better implant properties, reduced operative time, and better patient outcomes.[22] Finally, a recent systematic review on the use of

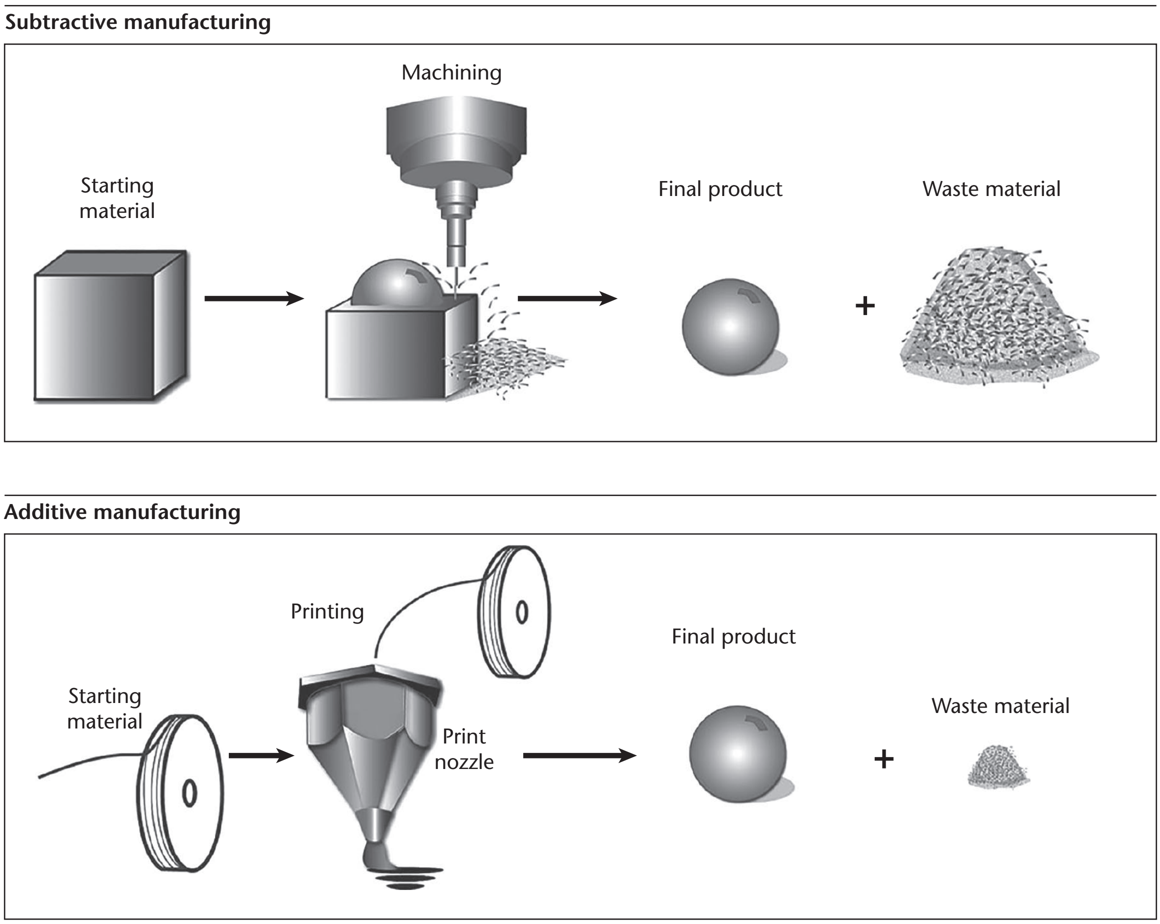

Fig. 1 Conceptual representation of additive vs. subtractive manufacturing.
Source. Modified from the United States Government Accountability Office.

3D printing in orthopaedic trauma demonstrated significant interest in and rapid growth of 3D printing in that subspecialty. To the authors' knowledge, however, there does not exist a broad, up-to-date review of the clinical applications of 3D printing in the entire field of orthopaedic surgery. Thus, the objectives of the current review were to answer the following questions: (1) what are the current clinical uses of 3D printing in orthopaedic surgery?, and (2) what are the geographical and temporal trends in the use of 3D printing in orthopaedic surgery?, and (3) does the use of 3D printing in orthopaedic surgery have an impact on peri-operative outcome?

Materials and methods

This review was performed in large part in adherence to the *Cochrane handbook for systematic reviews of interventions*[23] and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).[24] This review was prospectively registered on PROSPERO (Registration ID: CRD42018099144). However, it was felt that, given the novelty of this technology, it would be useful and important to include all reported uses of 3D printing; thus the search and inclusion strategy are more broad than a traditional systematic review.

Search strategy

A search strategy was developed by two of the authors (SE and JRY) in collaboration with a health sciences research methodology librarian. Given that the use of 3D printing is a relatively new concept within the field of orthopaedic surgery, the search strategy was kept intentionally broad. The keywords used included "3D print*", "three-dimensional print*", and "surg*" (Appendix 1). Four databases (PubMed, Embase, MEDLINE, and Web of Science) were searched from the earliest available date up to and including 13 November 2018. Inclusion criteria were (1) clinical studies reporting on the peri-operative use of 3D printing in orthopaedic surgery. Exclusion criteria were (1) review articles, and (2) articles pertaining to surgical education.

Study screening

Two authors (JNL and AS) independently reviewed all of the titles, abstracts, and full texts, assessing agreement at each stage. Any discrepancies at the title and abstract stages were resolved by automatic inclusion. At the full text stage, disagreements were resolved by consensus. Where consensus could not be reached, a third, more senior author (SE) was consulted.

Quality assessment

The quality of included studies was assessed based on the type of study. Randomized controlled trials (RCTs) were assessed for risk of bias using the Cochrane Risk of Bias Assessment Tool. The Risk of Bias Assessment Tool assesses the likelihood of bias in RCTs across seven primary domains, rating each domain as having a 'low', 'high', or 'unclear' likelihood of demonstrating bias.[25] The Methodological Index for Non-Randomized Studies (MINORS) was used to assess the quality of non-randomized studies. The MINORS tool consists of a total of 12 questions applicable to comparative studies, eight of which are applicable to non-comparative studies. Each item is rated on a three-point scale from 0 to 2, for a maximum score of 16 for non-comparative studies and 24 for comparative studies.[26]

Data abstraction

Data was abstracted by two authors (JNL and AS) into a Microsoft Excel (Version 16.12) spreadsheet designed a priori. The authors verified one another's data abstraction using a random spot-check method. Data extracted included information on study type, location of study, type of 3D printing material used, cost of 3D printing, patient demographics, the specific application of 3D printing, and peri-operative outcomes.

Statistical analysis

Agreement for each stage of the screening process was calculated using a Kappa (κ) statistic, and the results were interpreted as follows: 0 = no agreement, 0–0.2 = slight agreement, 0.2–0.4 = fair agreement, 0.4–0.6 = moderate agreement, 0.6–0.8 = substantial agreement, and 0.8–1.0 = almost perfect agreement.[27] Descriptive statistics (frequencies, mean or median, and 95% confidence intervals, standard deviation, or interquartile ranges) were used to report study characteristics, basic demographic information, uses of 3D printing, and patient outcomes. Due to broad inclusion criteria and expected low quality of evidence overall, a meta-analysis was not planned. A qualitative assessment of peri-operative outcomes (estimated blood loss (EBL), operative time, and fluoroscopy use) was performed using high-quality (i.e. Level I and Level II) studies.

Results

Characteristics of included studies

The initial search of the online databases returned 5124 studies, of which 108 met the inclusion and exclusion criteria (Fig. 2). There was satisfactory agreement among reviewers at the title ($\kappa = 0.777$; 95% CI, 0.754 to 0.801), abstract ($\kappa = 0.605$; 95% CI, 0.543 to 0.667), and full-text ($\kappa = 1.0$; 95% CI, 1.000 to 1.000) stages.

The 108 included studies were published between 2012 and 2018. There was a trend towards an increasing number of publications in more recent years, with 20 studies published from 2012–2015, and 88 studies published from 2016–2018 (Fig. 3). Of these studies, 42 were case reports, 39 case series, 16 cohort studies and 11 randomized controlled trials (Table 1). Over half of all included studies were conducted in China ($N = 55$, 50.9%), with the next highest numbers of studies coming from the United States ($N = 12$, 11.1%), followed by Australia and Spain ($N = 5$ each, 4.6%). Considering geographical regions, Asia produced the most studies ($N = 66$, 61.1%), followed by Europe ($N = 22$, 20.4%), and North America ($N = 13$, 12.0%).

A total of 2328 patients were included in the 108 studies, and 1558 patients were treated with the use of 3D printing technology. The mean age of the combined patient population in 99 of the 108 studies (2126 patients) was 47.0 years old (range, 3 to 90 years), with the remaining studies not reporting age. Table 1 outlines the basic characteristics of all included studies. Appendix 2 contains a full reference list of all included studies.

The mean MINORS score for the 78 non-comparative studies was 8.3 out of 16 (range, 0–14) and for the 19 non-randomized comparative studies it was 17.7 out of 24 (range, 6–23). A risk of bias assessment was performed on the 11 RCTs using the Cochrane Collaboration Risk of Bias Assessment Tool (Fig. 4). High bias was observed in 100% of RCTs for performance and detection bias. Due to the nature of 3D printing technology, it would be extremely difficult to blind surgeons to the intervention used. Additionally, EBL was measured subjectively, which could have been influenced by the lack of blinding. Low bias was observed in all RCTs for attrition bias, reporting bias, and other bias. Nearly half (45%) of RCTs had a low risk of bias for random sequence generation, and 45% of RCTs had an unclear risk of bias in this domain. All RCTs had an unclear risk of bias in allocation concealment.

3D printing characteristics

Uses of 3D printing

The uses of 3D printing were divided into three main categories: surgical models for pre-operative planning, PSI (e.g. cutting guides, etc. that are then used intra-operatively), and

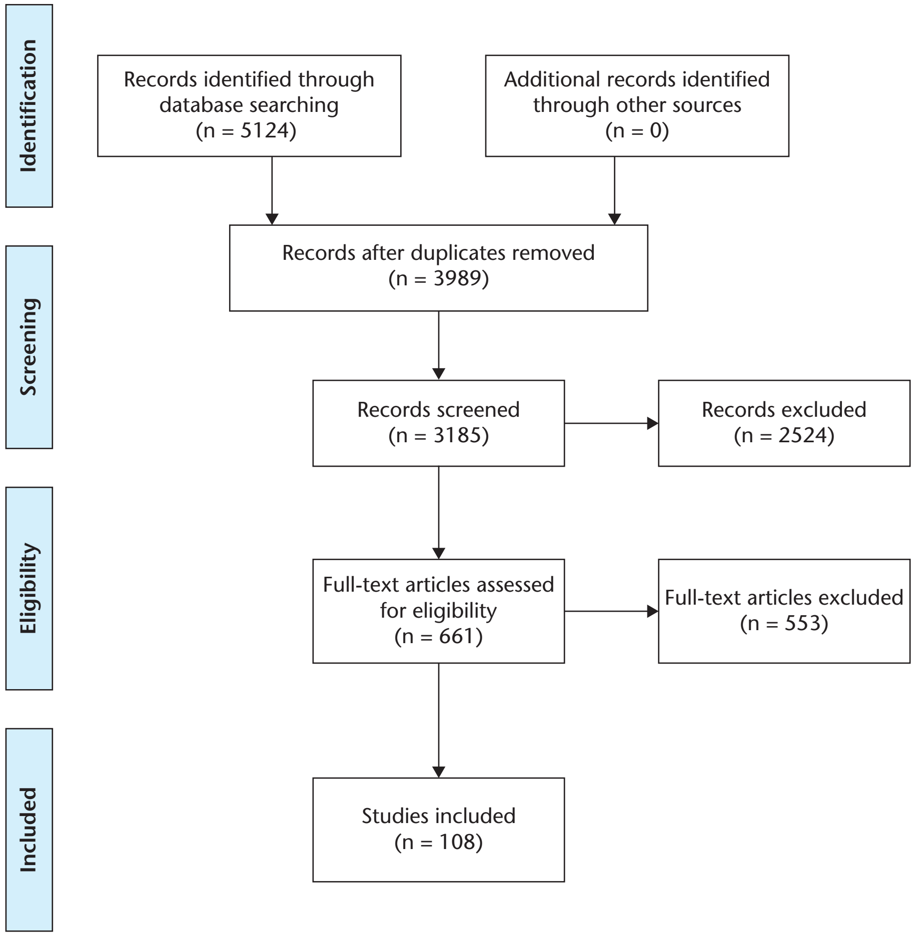

Fig. 2 PRISMA flow diagram.

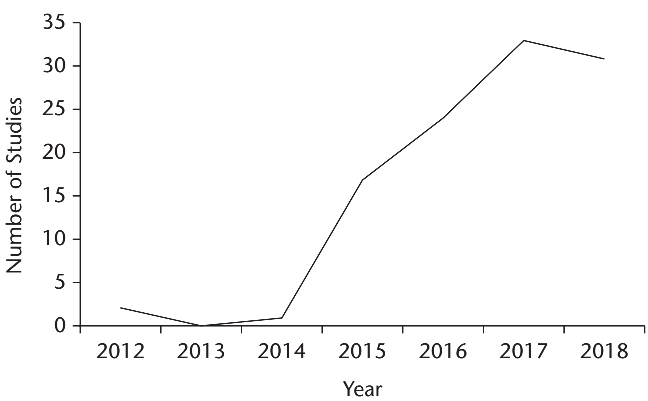

Fig. 3 Number of included studies by year.
Note. Data from 2018 does not include the full year as the search was performed in November 2018.

final implants (e.g. custom plates, etc.). The most common use of 3D printing was for pre-operative planning (*N* = 63), followed by final implants (*N* = 32) and PSI (*N* = 22). Some studies reported more than one category of use.

Three-dimensional printing was most commonly used in trauma (*N* = 41), oncology (*N* = 22), and arthroplasty/reconstruction (*N* = 18) (Table 2). There were some differences in the categories of 3D printing use between subspecialties. Though pre-operative planning was the most common use of 3D printing in most subspecialties, printing of final implants was the most common purpose of 3D printing in oncology and foot and ankle. Finally, PSI was relatively more common in paediatrics, where it accounted for 60.0% of the reported applications of 3D printing.

Materials used in 3D printing

The most commonly used 3D printing materials were titanium (16 studies, 27.1%), acrylonitrile butadiene styrene (13 studies, 22.0%), and polylactic acid (13 studies, 22.0%). Table 3 outlines the details of all reported material. The majority of surgical models were made of acrylonitrile butadiene styrene, and most final implants used titanium. Only four studies reporting use of titanium specified details about the composition of the alloy utilized: all four used Ti_6Al_4V with a patented truss structure.

Table 1. Study demographics

Author (reference numbers in Appendix 2)	Year	Country	Subspecialty	Study type	LOE	*N*	3DP Patients	% Female	Mean age (years)	MINORS score
Bagaria and Chaudhary[1]	2017	India	Multiple	Case series	IV	50	50	NR	NR	11/16
Beliën et al[2]	2017	Belgium	Upper extremity	Case series	IV	5	5	20.0	49.0	9/16
Bizzotto et al[3]	2016	Italy	Trauma	Case series	IV	40	40	NR	NR	9/16
Bizzotto et al[4]	2016	Italy	Trauma	Case series	IV	102	102	55.9	(20.0–78.0)	8/16
Cai et al[5]	2018	China	Trauma	Retrospective cohort study	III	137	65	40.1	32.8	23/24
Chae et al[6]	2015	Australia	Foot and ankle	Case report	IV	1	1	NR	82.0	4/16
Chana-Rodriguez et al[7]	2016	Spain	Trauma	Case report	IV	1	1	NR	45.0	5/16
Chen et al[8]	2018	China	Trauma	Case series	IV	48	16	33.3	52.4	15/24
Chen et al[9]	2016	China	Oncology	Case report	IV	1	1	NR	62.0	10/16
Cherkasskiy et al[10]	2017	USA	Pediatrics	Retrospective cohort study	III	15	5	53.3	13.5	20/24
Citak et al[11]	2016	Germany	Arthroplasty/ reconstructive	Case report	IV	1	1	100.0	61.0	6/16
Corona et al[12]	2018	Spain	Foot and ankle	Retrospective cohort study	III	9	9	33.3	51.4	8/24
Dekker et al[13]	2018	USA	Foot and ankle	Case series	IV	15	15	60.0	3.3	14/16
Dong et al[14]	2017	China	Oncology	Case report	IV	1	1	0.0	65.0	9/16
Duan et al[15]	2018	China	Foot and ankle	Prospective cohort study	II	29	15	48.0	55.0	15/24
Duncan et al[16]	2015	UK	Trauma	Case report	IV	1	1	0.0	48.0	2/16
Fan et al[17]	2015	China	Oncology	Case series	IV	3	3	100.0	37.3	14/16
Fang et al[18]	2015	China	Trauma	Case report	IV	1	1	100.0	88.0	7/16
Fang et al[19]	2018	China	Oncology	Case report	IV	1	1	100.0	43.0	9/16
Gemalmaz et al[20]	2017	Turkey	Upper extremity	Case report	IV	1	1	0.0	18.0	11/16
Giannetti et al[21]	2016	Italy	Trauma	Prospective cohort study	II	40	16	45.0	43.2	22/24
Giovinco et al[22]	2012	USA	Foot and ankle	Case report	IV	1	1	NR	NR	2/16
Hamada et al[23]	2017	Japan	Upper extremity	Case report	IV	1	1	0.0	21.0	11/16
Hamid et al[24]	2016	USA	Trauma	Case report	IV	1	1	100.0	46.0	9/16
Han et al[24]	2018	China	Oncology	Case report	IV	1	1	100.0	32.0	9/16
Holt et al[26]	2017	USA	Pediatrics	Case report	IV	1	1	100.0	10.0	10/16
Hsu and Ellington[27]	2015	USA	Foot and ankle	Case report	IV	1	1	0.0	63.0	9/16
Hsu et al[28]	2018	China	Trauma	Retrospective cohort study	III	29	12	13.8	37.6	17/24
Hughes et al[29]	2017	Ireland	Arthroplasty/ reconstructive	Case series	IV	2	2	NR	NR	4/16
Hung et al[30]	2018	China	Trauma	Retrospective cohort study	III	30	16	40.0	35.5	23/24
Imanishi and Choong[31]	2015	Australia	Oncology	Case report	IV	1	1	0.0	71.0	8/16
Inge et al[32]	2018	Netherlands	Upper extremity	Case report	IV	1	1	100.0	16.0	9/16
Jastifer and Gustafson[33]	2016	USA	Foot and ankle	Case report	IV	1	1	0.0	46.0	8/16
Jentzsch et al[34]	2016	Switzerland	Oncology	Case series	IV	4	4	25.0	40.0	11/6
Jeuken et al[35]	2017	Netherlands	Pediatrics	Case report	IV	1	1	100.0	15.0	7/16
Kieser et al[36]	2018	New Zealand	Arthroplasty/ reconstructive	Case series	IV	36	36	44.4	68.0	12/16
Kim et al[37]	2015	South Korea	Trauma	Case series	IV	7	7	NR	NR	7/16
Kim et al[38]	2018	South Korea	Arthroplasty/ reconstructive	Retrospective cohort study	III	40	20	82.5	55.4	14/24
Lau et al[39]	2018	China	Trauma	Case report	IV	1	1	NR	57.0	8/16
Li et al[40]	2018	China	Arthroplasty/ reconstructive	Prospective cohort study	II	40	20	37.5	41.0	17/24
Li et al[41]	2016	China	Arthroplasty/ reconstructive	Case series	IV	24	24	66.7	65.0	14/16
Li et al[42]	2017	China	Trauma	Retrospective cohort study	III	64	28	28.1	33.6	21/24
Lin et al[43]	2018	Taiwan	Trauma	Case report	IV	1	1	0.0	64.0	5/16
Liu et al[44]	2018	China	Oncology	Case report	IV	1	1	0.0	16.0	5/16
Lou et al[45]	2017	China	Trauma	RCT	II	72	34	47.2	53.4	N/A, see Fig. 4

(continued)

Table 1 (continued)

Author (reference numbers in Appendix 2)	Year	Country	Subspecialty	Study type	LOE	*N*	3DP Patients	% Female	Mean age (years)	MINORS score
Lu et al[46]	2018	China	Oncology	Case series	IV	11	11	45.5	38.0	13/16
Lu et al[47]	2018	China	Oncology	Case report	IV	1	1	0.0	15.0	10/16
Luo et al[48]	2017	China	Oncology	Case series	IV	4	4	75.0	49.0	14/16
Ma et al[49]	2017	China	Oncology	Case series	IV	12	12	16.7	22.8	13/16
Ma et al[50]	2016	China	Oncology	Case series	IV	8	8	37.5	17.5	14/16
Maini et al[51]	2016	India	Trauma	RCT	I	21	11	14.3	38.7	N/A, see Fig. 4
Mao et al[52]	2015	China	Arthroplasty/ reconstructive	Case series	IV	22	22	NR	60.9	12/16
Merema et al[53]	2017	Netherlands	Trauma	Case report	IV	1	1	0.0	48.0	10/16
Nie et al[54]	2018	China	Trauma	Case series	IV	30	30	40.0	30.4	5/16
Niikura et al[55]	2014	Japan	Trauma	Case series	IV	5	5	NR	NR	7/16
Nizam and Batra[56]	2018	Australia	Arthroplasty/ reconstructive	Case series	IV	188	188	62.8	67.7	7/16
Ogura et al[57]	2018	USA	Arthroplasty/ reconstructive	Case series	IV	55	55	64.0	51.0	8/16
Okoroha et al[58]	2018	USA	Sports	Case report	IV	1	1	100.0	26.0	4/16
Osagie et al[59]	2017	UK	Upper extremity	Case series	IV	3	3	0.0	34.3	6/16
Pérez-Mananes et al[60]	2016	Spain	Arthroplasty/ reconstructive	Retrospective cohort study	III	28	8	NR	44.7	19/24
Ranalletta et al[61]	2017	Argentina	Upper extremity	Case report	IV	1	1	100.0	28.0	7/16
Ren et al[62]	2017	China	Oncology	Case report	IV	1	1	100.0	17.0	7/16
Roner et al[63]	2018	Switzerland	Upper extremity	Case series	IV	15	8	NR	NR	6/24
Sánchez-Perez et al[64]	2018	Spain	Arthroplasty/ reconstructive	Case report	IV	1	1	0.0	43.0	9/16
Sanghavi and Jankharia[65]	2016	India	Trauma	Case report	IV	1	1	0.0	45.0	0/16
Schneider et al[66]	2018	Australia	Arthroplasty/ reconstructive	Case series	IV	30	30	50.0	63.9	7/16
Sheth et al[67]	2015	Canada	Sports	Case report	IV	1	1	0.0	29.0	6/16
Shi et al[68]	2018	China	Arthroplasty/ reconstructive	Prospective cohort study	II	33	12	63.6	47.3	16/24
Shon et al[69]	2018	South Korea	Trauma	Case series	IV	5	5	40.0	41.4	8/16
Shuang et al[70]	2016	China	Trauma	RCT	II	13	6	23.1	43.0	N/A, see Fig. 4
Simal et al[71]	2016	Spain	Oncology	Case report	IV	1	1	0.0	14.0	6/16
Smith et al[72]	2016	USA	Foot and ankle	Case series	IV	2	2	100.0	40.0	10/16
So et al[73]	2018	USA	Foot and ankle	Case series	IV	3	3	100.0	44.0	11/16
Stoffelen et al[74]	2015	Belgium	Upper extremity	Case report	IV	1	1	100.0	56.0	8/16
Tam et al[75]	2012	UK	Oncology	Case report	IV	1	1	100.0	65.0	2/16
Tran et al[76]	2018	Australia	Oncology	Case report	IV	1	1	100.0	39.0	6/16
Upex et al[77]	2016	France	Trauma	Case report	IV	1	1	0.0	39.0	2/16
Wada et al[78]	2018	Japan	Arthroplasty/ reconstructive	Case report	IV	1	1	100.0	79.0	8/16
Wang et al[79]	2017	China	Oncology	Case series	IV	11	11	54.5	47.0	12/16
Wang et al[80]	2017	China	Trauma	Case report	IV	1	1	100.0	53.0	6/16
Wang et al[81]	2017	China	Oncology	RCT	II	66	33	42.4	43.6	N/A, see Fig. 4
Wang et al[82]	2018	China	Trauma	Retrospective cohort study	III	46	21	69.6	71.5	15/24
Wang et al[83]	2017	China	Trauma	Case series	IV	6	6	50.0	43.7	8/16
Wang et al[84]	2017	China	Arthroplasty/ reconstructive	Retrospective cohort study	III	74	17	50.0	62.7	22/24
Wong et al[85]	2015	China	Oncology	Case report	IV	1	1	0.0	65.0	8/16
Wu et al[86]	2015	China	Trauma	Case series	IV	9	9	22.2	47.0	10/16
Xie et al[87]	2017	China	Upper extremity	Case report	IV	1	1	NR	41.0	10/16
Xu et al[88]	2015	China	Arthroplasty/ reconstructive	Case series	IV	10	10	90.0	57.8	13/16
Yang et al[89]	2016	China	Oncology	Case report	IV	1	1	100.0	78.0	6/16
Yang et al[90]	2017	China	Trauma	RCT	I	40	20	30.0	38.6	N/A, see Fig. 4

Table 1 (continued)

Author (reference numbers in Appendix 2)	Year	Country	Subspecialty	Study type	LOE	*N*	3DP Patients	% Female	Mean age (years)	MINORS score
Yang et al[91]	2016	China	Trauma	RCT	II	30	15	46.7	36.5	N/A, see Fig. 4
Yang et al[92]	2016	China	Trauma	Case series	IV	7	7	57.1	44.0	12/16
You et al[93]	2016	China	Trauma	RCT	I	66	34	59.1	66.2	N/A, see Fig. 4
Yu et al[94]	2015	UK	Trauma	Case series	IV	2	2	NR	52.0	1/16
Zang et al[95]	2017	China	Upper extremity	Case series	IV	5	5	20.0	28.0	10/16
Zeng et al[96]	2015	China	Trauma	Case series	IV	38	38	34.2	32.0	13/16
Zeng et al[97]	2016	China	Trauma	Case series	IV	10	10	50.0	19.0–52.0	8/16
Zerr et al[98]	2016	USA	Arthroplasty/ reconstructive	Case report	IV	1	1	100.0	70.0	7/16
Zhang et al[99]	2017	China	Trauma	Case series	IV	78	78	47.4	56.0	10/16
Zhang et al[100]	2017	China	Oncology	Case report	IV	1	1	0.0	36.0	6/16
Zhang et al[101]	2018	China	Arthroplasty/ reconstructive	Case series	IV	30	30	36.7	41.7	9/16
Zheng et al[102]	2017	China	Paediatrics	Prospective cohort study	II	25	12	84.0	10.9	23/24
Zheng et al[103]	2017	China	Paediatrics	Retrospective cohort study	III	11	11	36.4	6.6	18 /24
Zheng et al[104]	2017	China	Trauma	Prospective cohort study	II	39	19	43.6	66.0	23/24
Zheng et al[105]	2017	China	Trauma	RCT	II	91	43	46.2	44.6	N/A, see Fig. 4
Zheng et al[106]	2018	China	Trauma	RCT	I	100	50	NR	41.9	N/A, see Fig. 4
Zheng et al[107]	2017	China	Trauma	RCT	I	75	35	41.3	45.7	N/A, see Fig. 4
Zhuang et al[108]	2016	China	Trauma	Case series	IV	12	12	33.3	49.0	10/16

Note. LOE, level of evidence; 3DP, three-dimensional printing; MINORS, Methodological Index for Non-Randomized Studies; NR, not reported; RCT, randomized controlled trial.

Cost

Twenty-five studies (23.1%) reported on 3D printing cost, with a range from 'less than $10' to $20,000 dollars. Not surprisingly, the highest costs were associated with studies that were 3D printing a final implant (range $4,750–$20,000). Interestingly, the two studies which reported on the cost of printing PSI reported costs of 'less than 5 euros' and $150. The cost of pre-operative planning models ranged from 'less than $10' to $2,200. Time required to edit and print 3D models was also quite variably reported in 32 studies (29.6%), ranging from three hours to six weeks. Most studies did not distinguish between the time required for each stage of the 3D printing process (image editing, physical printing, sterilization, etc.).

Qualitative analysis of peri-operative outcomes

Seventeen high-quality studies (ten RCTs, seven prospective cohorts) including 864 patients, examined the difference in operative time between cases where 3D printing was used and controls. Fifteen of 17 studies (88.2%) found significantly shorter operative times in 3D printing cases as opposed to standard cases. Two studies found statistically non-significant differences between the two groups: one study found shorter operative time in the 3D printing group, while the other found the opposite. Among studies with statistical significance, the difference in mean operative time between the two groups ranged from 9 to 27 minutes (see Fig. 5a).

Thirteen high-quality studies (eight RCTs, five prospective cohorts) including 780 patients, assessed the difference in estimated blood loss (EBL) between 3D printing patients and control patients. Of these, 11 studies (84.6%) found significantly lower EBL in the 3D printing groups. The other two studies also found lower EBL in the 3D printing groups though this difference was not statistically significant. Among studies with significant findings, the difference in mean EBL ranged from 14 mL to 100 mL (see Fig. 5b).

Thirteen high-quality studies (four RCTs, six prospective cohorts) including 631 patients, compared the number of fluoroscopy shots used intra-operatively. All 13 studies (100%) found significantly fewer fluoroscopy shots during cases that used 3D printing compared to controls. The difference in mean number of fluoroscopy shots taken ranged from 1 to 29 shots (see Fig. 5c).

Discussion

The key findings of this review were that 3D printing is being used with increasing frequency in peri-operative

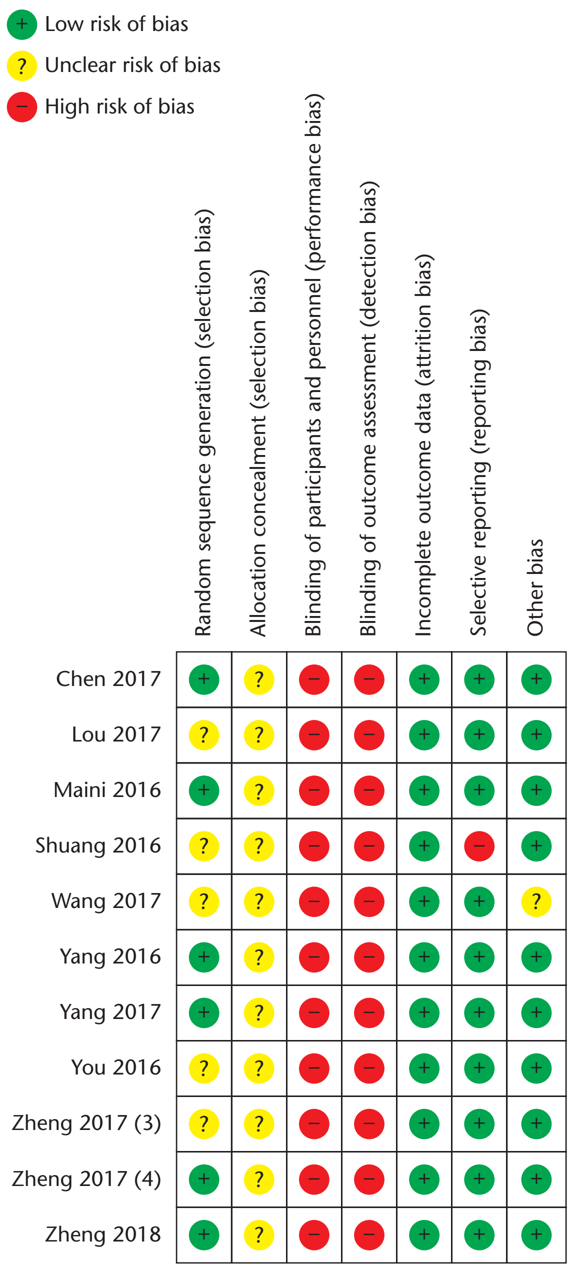

Fig. 4 Risk of bias assessment diagram.

Table 2. Subspecialties most commonly reporting the use of three-dimensional printing

Subspecialty	Number of studies reporting (%)
Trauma	41 (38.0%)
Oncology	22 (20.4%)
Arthroplasty/reconstruction	18 (16.7%)
Upper extremity	10 (9.3%)
Foot and ankle	9 (8.3%)
Paediatrics	5 (4.6%)
Sports	2 (1.9%)
Multiple subspecialties	1 (0.9%)

Note. Based on all 108 studies; some studies reported on more than one subspecialty.

Table 3. Materials used for three-dimensional printing

Material	Number of studies reporting (%)
Titanium	16 (27.1%)
Acrylonitrile butadiene styrene	13 (22.0%)
Polylactic acid	13 (22.0%)
Plaster	5 (8.5%)
Polyamide	4 (6.8%)
Polyethylene	4 (6.8%)
Other polymer	3 (5.1%)
Ultraviolet curable resin	1 (1.7%)

Note. Based on 57 studies reporting; two studies each reported two different materials used.

orthopaedics and is most commonly reported in trauma and oncology. The most common application of 3D printing is for pre-operative planning. The majority of 3D printing research in orthopaedics is based in Asia, particularly in China. In addition, the Level I and Level II evidence consistently finds shorter operative times,[28–43] less blood loss,[28–30,32–38,41–43] and less fluoroscopy use[28,30,31,33–37,44,45] when 3D printing is used.

Across an overwhelming majority of the high-quality literature, the use of 3D printing significantly reduced operative time,[28–43] EBL,[28–30,32–38,41–43] and the number of fluoroscopy shots.[28,30,31,33–37,44,45] It is difficult to evaluate the clinical significance of these findings given the significant heterogeneity in terms of clinical context between the different studies. Nonetheless, a reduction in operative time is certainly beneficial from a cost perspective, and, given that the risk of complications increases with longer operative times,[46] it is reasonable to hypothesize that this is beneficial to the patient as well. Similarly, a reduction in EBL has a theoretical safety benefit to the patient, though it is unclear what the threshold for clinical benefit would be. Certainly, if blood transfusion rates were to be decreased, this would represent an important patient benefit.[47] Finally, fewer fluoroscopy shots may not necessarily have a direct impact on the patient, but are important for the safety of operating room staff, particularly in the long term.[48] Given the wide range of different operations included in this review, it is difficult to know whether or not these benefits of 3D printing are globally present or clinically important. That being said, the consistently significant findings across the majority of prospective comparative studies suggest the possibility of a true signal, and this warrants further study with larger RCTs to clarify the magnitude of this effect.

Pre-operative planning is an essential part of any successful operation. With the increasing availability of 3D printing technology, surgeons and learners can use a physical, high-fidelity model to review and plan for complex cases with accurate depth perception and haptic feedback. In a retrospective study, Mainard et al found that the use of 3D models was more accurate than traditional two-dimensional templating in total hip arthroplasty.[49]

	3DP			Control				Mean Difference
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Random, 95% CI**
Chen 2017	56.58	4.74	52	65.73	6.02	55	11.2%	−9.15 [−11.20, −7.10]
Giannetti 2016	148.2	15.9	16	174.5	22.2	24	2.5%	−26.30 [−38.11, −14.49]
Li 2018	29.93	2.13	20	40.51	2.24	20	12.0%	−10.58 [−11.93, −9.23]
Lou 2017	85.2	0.9	34	99.2	1	38	12.5%	−14.00 [−14.44, −13.56]
Maini 2016	120	35.8	10	132	41.1	11	0.4%	−12.00 [−44.90, 20.90]
Shi 2018	77.76	6.5	12	96.5	8.5	21	7.1%	−18.74 [−23.91, −13.57]
Shuang 2016	70.6	12.1	6	92.3	1.4	7	3.4%	−21.70 [−31.44, −11.96]
Wang 2017	144.8	45.2	33	135.6	32.7	33	1.1%	9.20 [−9.83, 28.23]
Yang 2016	71	23	15	98	20	15	1.6%	−27.00 [−42.42, −11.58]
Yang 2017	61	13	20	82	22	20	2.7%	−21.00 [−32.20, −9.80]
You 2016	77.65	8.09	34	92.03	10.31	32	7.9%	−14.38 [−18.87, −9.89]
Zheng 2017	21.08	4.64	12	46.92	11.51	13	5.4%	−25.84 [−32.63, −19.05]
Zheng 2017 (2)	46.27	6.51	19	60.58	11.92	20	6.2%	−14.31 [−20.30, −8.32]
Zheng 2017 (3)	76.6	7.9	43	92	10.5	48	8.9%	−15.40 [−19.19, −11.61]
Zheng 2017 (4)	71.4	6.8	35	91.3	11.2	40	8.4%	−19.90 [−24.04, −15.76]
Zheng 2018	74.1	8.2	45	90.2	10.9	48	8.7%	−16.10 [−20.00, −12.20]
Total (95% CI)			**406**			**445**	**100.0%**	**−15.58 [−17.66, −13.49]**

Heterogeneity: $Tau^2 = 9.00$; $Chi^2 = 85.08$, df = 15 ($P < 0.00001$); $I^2 = 82\%$
Test for overall effect: Z = 14.64 ($P < 0.00001$)

Mean Difference IV, Random, 95% CI

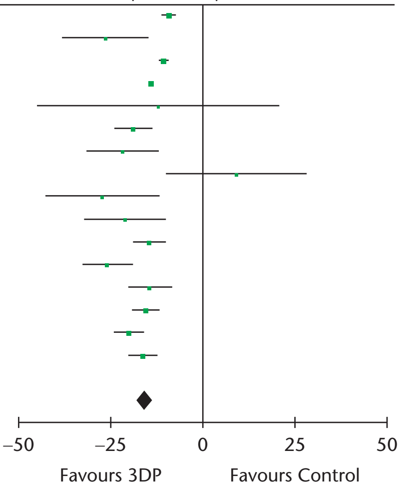

Fig. 5a Forest plot of estimated blood loss based on high-quality studies.

	3DP			Control				Mean Difference
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Random, 95% CI**
Chen 2017	39.25	8.72	52	52.95	9.78	55	12.5%	−13.70 [−17.21, −10.19]
Giannetti 2016	520	11	16	546	0	24		Not estimable
Li 2018	18.04	11.14	20	39.91	13.03	20	11.7%	−21.87 [−29.38, −14.36]
Lou 2017	186.3	5.5	34	216.2	6.9	38	12.5%	−29.90 [−32.77, −27.03]
Maini 2016	620	246.9	10	720	286.3	11	0.2%	−100.00 [−328.13, 128.13]
Wang 2017	647.8	137.8	33	689.3	123.4	33	1.9%	−41.50 [−104.61, 21.61]
Yang 2016	65	26	15	90	38	15	7.1%	−25.00 [−48.30, −1.70]
Yang 2017	47	16	20	69	28	20	9.8%	−22.00 [−36.13, −7.87]
You 2016	235.29	63.4	34	281.25	57.85	32	5.6%	−45.96 [−75.22, −16.70]
Zheng 2017 (2)	98.35	4.76	19	162.57	63.28	20	6.0%	−64.22 [−92.04, −36.40]
Zheng 2017 (3)	231.1	18.1	43	278.6	23	48	11.5%	−47.50 [−55.96, −39.04]
Zheng 2017 (4)	226.1	22.6	35	288.7	34.8	40	10.1%	−62.60 [−75.73, −49.47]
Zheng 2018	117.1	20.7	45	159.8	26.5	48	11.2%	−42.70 [−52.33, −33.07]
Total (95% CI)			**376**			**404**	**100.0%**	**−35.86 [−45.18, −26.55]**

Heterog eneity: $Tau^2 = 178.05$; $Chi^2 = 131.38$, df= 11 ($P < 0.00001$); $I^2 = 92\%$
Test for overall effect: Z = 7.55 ($P < 0.00001$)

Mean Difference IV, Random, 95% CI

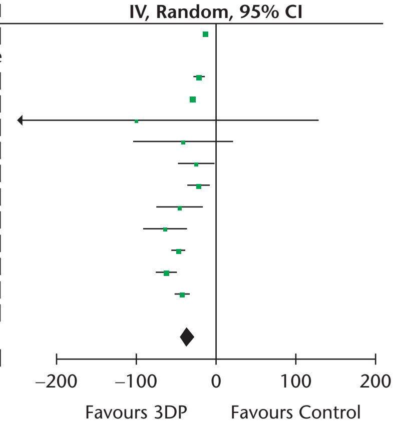

Fig. 5b Forest plot of operative time based on high-quality studies.

	3DP			Control				Mean Difference
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Random, 95% CI**
Chen 2017	4.85	1.39	52	5.85	1.64	55	11.1%	−1.00 [−1.57, −0.43]
Duan 2018	2.3	0.1	15	3.5	0.3	14	11.8%	−1.20 [−1.37, −1.03]
Li 2018	0.92	0.41	20	4.14	0.73	20	11.5%	−3.22 [−3.59, −2.85]
Lou 2017	5.3	0.2	34	7.1	0.2	38	11.8%	−1.80 [−1.89, −1.71]
Shi 2018	6.1	1.25	12	34.7	7.75	21	3.5%	−28.60 [−31.99, −25.21]
You 2016	7.12	1.57	34	10.59	1.36	32	10.8%	−3.47 [−4.18, −2.76]
Zheng 2017	3.92	0.9	12	6.69	1.49	13	10.0%	−2.77 [−3.73, −1.81]
Zheng 2017 (3)	5.3	1.9	43	8.7	2.7	48	10.0%	−3.40 [−4.35, −2.45]
Zheng 2017 (4)	5.6	1.9	35	8.6	2.7	40	9.7%	−3.00 [−4.05, −1.95]
Zheng 2018	7.6	2.2	45	11	2.9	48	9.7%	−3.40 [−4.44, −2.36]
Total (95% CI)			**302**			**329**	**100.0%**	**−3.46 [−4.22, −2.70]**

Heterogeneity: $Tau^2 = 1.27$; $Chi^2 = 406.02$, df = 9 ($P < 0.00001$); $I^2 = 98\%$
Test for overall effect: Z = 8.92 ($P < 0.00001$)

Mean Difference IV, Random, 95% CI

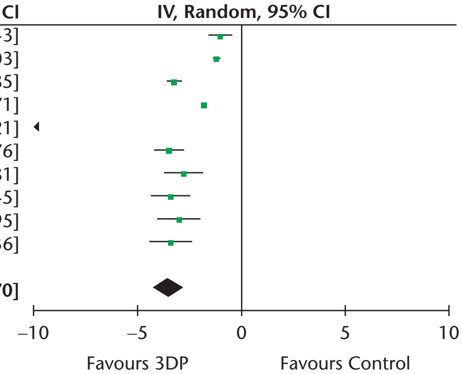

Fig. 5c Forest plot of fluoroscopy shots based on high-quality studies.

They hypothesized that the ability to plan using an actual size model (as opposed to magnified images), and the ability to simultaneously assess length, alignment, and rotation in multiple planes were some reasons for improved accuracy.[49] With the advent of the use of virtual reality (VR) in surgical planning and education,[50] future studies comparing VR and 3D printing can elucidate the importance of the haptic feedback.

As it is a new technology, the cost of 3D printing is a concern, particularly when being considered for use in a publicly funded healthcare system. It can be difficult to gauge the true cost of any new piece of technology: beyond the cost of the hardware itself, there are costs associated with energy usage, personnel training, ancillary software costs, and maintenance and repair expenditures. In the case of 3D printing in orthopaedics, other specific costs such as storage, encryption, and sterilization are also important to consider. The studies included in this review reported cost in a number of different ways, if at all, making it difficult to draw direct comparisons. Overall, however, there is no doubt that the cost of 3D printing technology, including both hardware and software, has decreased dramatically in recent years.[51] Interestingly, many of the included studies were able to achieve their 3D printing requirements for less than US$100. Given the potential for reduced operative time and fluoroscopy use, a careful economic analysis is needed to assess the cost-effectiveness of 3D printing technology in orthopaedic surgery.

With the increasing focus on competency-based education, combined with reduced work hours for surgical residents,[52] there is a growing need for high-fidelity educational models that can be deployed outside the operating room. Though this review focused on the clinical applications of 3D printing, its educational uses are also abundant and increasing. Three dimensional printing of complex fracture patterns such as acetabular and calcaneal fractures has been shown to improve consistency in fracture classification and patient understanding of the fracture and surgical plan.[9,34] With the growing focus on minimizing patient harm and competency-based education, 3D printing has the potential to play a key role in the future of orthopaedic education.

Strengths

The strengths of this review stem from its thorough methodology, broad inclusion criteria, and current relevance. Inclusion criteria were kept intentionally broad given that this is a relatively new field and thus keywords and Medical Subject Heading terms may be heterogeneously used. Additionally, strict adherence to PRISMA guidelines make this a methodologically sound review. Finally, the qualitative analysis of high-quality evidence provides important insights into the potential peri-operative benefits of 3D printing.

Limitations

This review was primarily limited by the overall low level of evidence available, with the majority of studies being Level IV evidence. In addition, data on the cost and time required to complete 3D prints was inconsistently reported, making it difficult to draw conclusions on these important facets of the technology. As discussed above, the heterogeneity of the included studies precluded a meta-analysis. Finally, the heterogeneity in population, applications, and reporting of outcomes meant that an analysis of functional outcomes could not be performed.

Future directions

As the orthopaedic applications of 3D printing continue to grow, it is important that they are critically evaluated to ensure that these applications are in the best interest of patients. There is a need for larger RCTs to further assess the potential benefits of 3D printing. More consistent reporting of detailed cost breakdown is important to aid future economic analyses of 3D printing in order to ascertain its cost-effectiveness and optimal indications. Finally, an evaluation of the educational uses of 3D printing in orthopaedics is required.

Conclusions

The uses of 3D printing in orthopaedic surgery are growing rapidly, with its use being most common in trauma and oncology. Pre-operative planning is the most common use of 3D printing in orthopaedics. The use of 3D printing significantly reduces EBL, operative time, and fluoroscopy use compared to controls. Future research is needed to confirm and clarify the magnitude of these effects.

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ICMJE CONFLICT OF INTEREST STATEMENT

SE reports grants from the Research Institute of St. Joseph's Healthcare Hamilton, PSI Foundation and Michael G. DeGroote Fellowship, not related to the submitted work. DSW is a consultant for Stryker and Intellijoint.

The other authors declare no conflict of interest relevant to this work.

FUNDING STATEMENT

The author or one or more of the authors have received or will receive benefits for personal or professional use from a commercial party related directly or indirectly to the subject of this article.

SUPPLEMENTAL MATERIAL

Supplemental material is available for this paper at https://online.boneandjoint.org.uk/doi/suppl/10.1302/2058-5241.5.190024

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