



Overview of randomised controlled trials in orthopaedic research: search for significant findings

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Abstract

Background The majority of recent orthopaedics randomised controlled trials (RCTs) have been non-inferiority trials with no significant clinical or statistical differences between treatment groups. The aim of this study was to evaluate randomised trials for significant findings in the orthopaedic literature based on the main elective procedures undertaken across different subspecialties.

Methods We evaluated the following procedures: anterior cervical discectomy and fusion (ACDF), subacromial decompression (SAD), carpal tunnel decompression (CTD), total hip replacement (THR), anterior cruciate ligament reconstruction (ACLR), total knee replacement (TKR) and hallux valgus correction (HVC). Following PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines, we searched the Cochrane Central Register of Controlled Trials (CENTRAL, 2018, Issue 1), Ovid MEDLINE (1946 to 12 January 2018) and Embase (1980 to 12 January 2018). Trials that met our inclusion criteria were assessed using a binary outcome measure of whether they reported statistically significant findings.

Results We included 1078 RCTs across seven most commonly performed elective procedures. Of those, only 16% (172/1078) reported significant findings [ACDF 26/77 (33.8%); SAD 2/22 (9%); CTD 11/72 (15.3%); THR 52/281 (18.5%); ACLR 21/239 (8.8%); TKR 55/357 (15.4%); HVC 5/30 (16.7%)]. The number of RCTs per year of publication has increased dramatically particularly since early 2000s—with over 100 RCTs of those seven procedures published in 2017 alone.

Conclusions This is the first study to undertake a comprehensive review of orthopaedic RCTs in elective practice. The number of RCTs in orthopaedic research is steadily increasing. However, only 16% of trials reports significant differences between interventions.

Clinical relevance For trials comparing different surgical techniques, this evidence provides treating surgeons with the flexibility to utilise available resources and infrastructure to deliver patients care without compromising clinical outcomes. Further, for trials comparing different treatment modalities, this study helps to inform the shared decision-making process when counselling patients on the effectiveness of surgical interventions.

Keywords Orthopaedic interventions · Randomised controlled trials · Non-inferiority trials

Introduction

High-quality randomised controlled trials (RCTs) provide strong evidence for the efficacy of healthcare interventions and inform evidence-based medicine [1, 10]. In particular, RCTs with a statistically significant difference in the results of two treatments or the absence of such a significant difference but a narrow confidence interval indicate a positive effect of a treatment [19, 21]. The number of RCTs in the orthopaedic literature has increased steadily over the last few years [12, 23]. However, most of these trials seem to yield inconclusive results with no significant

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clinical or statistical differences between treatment groups [5, 11]. The majority of these trials are non-inferiority trials demonstrating similar effects of the studied interventions and lack equipoise [5, 15, 18, 25, 27]. Evidence suggests that well-conducted, high-quality orthopaedic RCTs impact surgeon's clinical practice such as the recent UK-DRAFFT and PROFHER trials [7, 8, 14, 22].

In a review of orthopaedic trauma literature, Sung et al. identified 76 RCTs with statistically significant findings although trials had small sample sizes and few outcome events. Therefore, positive findings should be interpreted with caution in these trials [24]. In this study, we aim to provide an overview of RCTs in elective orthopaedic literature and the proportion of RCTs with significant findings. This was based on the main elective procedures undertaken across different subspecialties of elective orthopaedic practice.

Materials and methods

We selected the most commonly performed operations by different orthopaedic subspecialties excluding paediatrics; these were anterior cervical discectomy and fusion (ACDF), subacromial decompression (SAD), carpal tunnel decompression (CTD), total hip replacement (THR), anterior cruciate ligament reconstruction (ACLR), total knee replacement (TKR) and hallux valgus correction (HVC) [9].

Following PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines [20], we searched the Cochrane Central Register of Controlled Trials (CENTRAL, 2018, Issue 1), Ovid MEDLINE (including Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE Daily, Ovid MEDLINE and Versions) (1946 to 12 January 2018) and Embase (1980 to 12 January 2018). We limited our searches to the English language literature. In MEDLINE, we combined the subject-specific search strategy with the sensitivity maximising version of the Cochrane Highly Sensitive Search Strategy for identifying randomised trials [17]. We examined the titles and abstracts of articles identified in the search as potentially relevant trials. We obtained the full texts of trials that fulfilled our inclusion criteria and those that were unclear from perusal of the abstracts. We excluded non-randomised trials, systematic reviews and meta-analyses. Trials that met our inclusion criteria were assessed using a binary outcome measure of whether they reported statistically significant findings. Results expressed descriptively in numbers and percentages. SPSS 16.0 software (SPSS Inc., Chicago, Illinois, USA) was used for descriptive statistical analysis and graph demonstrations.

Results

The electronic searches were completed in January 2018 and resulted in the identification of 1078 included randomised controlled trials across seven most commonly performed procedures (Figs. 1, 2; Table 1, “Appendix 1”). Of those, only 16% (172/1078) reported significant findings. ACDF trials were mainly comparing disc replacements versus fusion surgery, different techniques of fusion or physiotherapy. Subacromial decompression for shoulder impingement

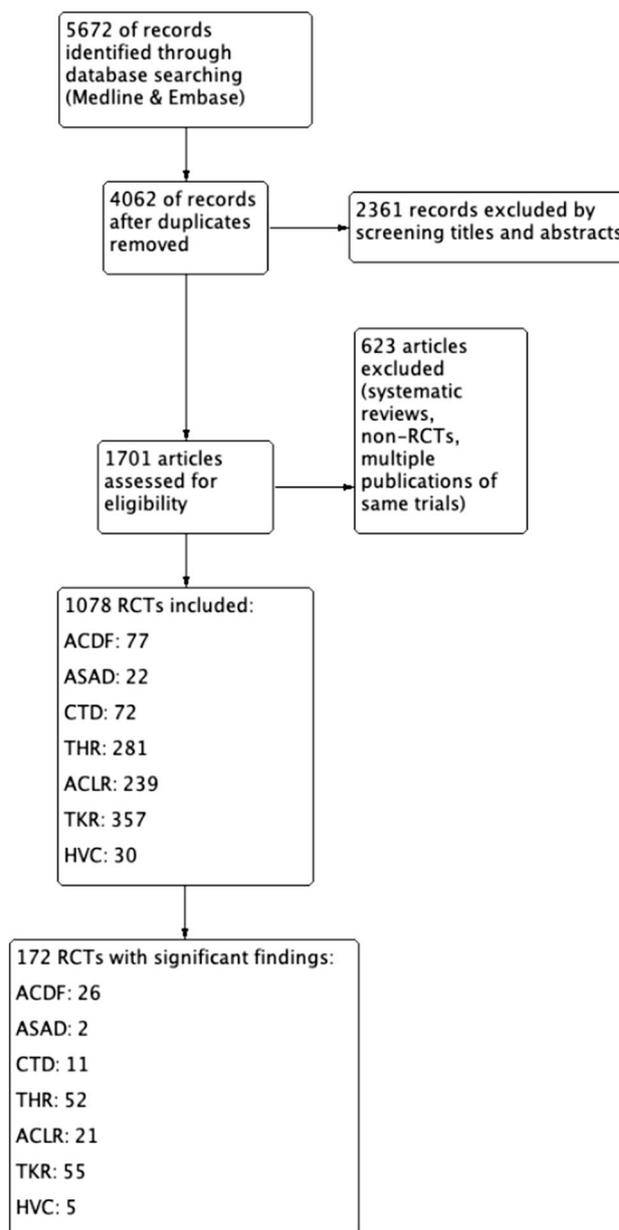


Fig. 1 Flow chart of the literature searches and results of included trials

Fig. 2 Number of RCTs and proportion of trials with significant findings. *ACDF* anterior cervical discectomy and fusion, *SAD* subacromial decompression, *CTD* carpal tunnel decompression, *THR* total hip replacement, *ACLR* anterior cruciate ligament reconstruction, *TKR* total knee replacement, *HVC* hallux valgus correction

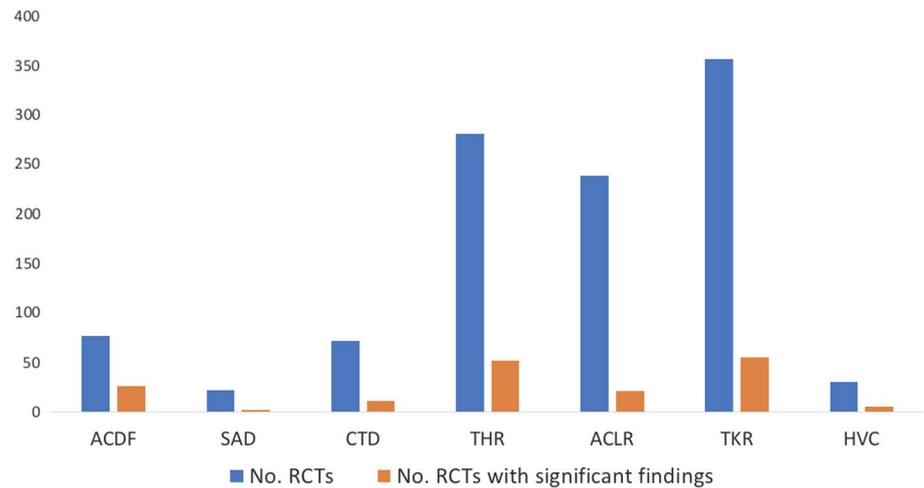


Table 1 Summary of randomised controlled trials per procedure and significant findings

Surgical procedure	No. RCTs	No. RCTs with significant findings	Percentage (%)
ACDF	77	26	33.8
SAD	22	2	9.0
CTD	72	11	15.3
THR	281	52	18.5
ACLR	239	21	8.8
TKR	357	55	15.4
HVC	30	5	16.7
Total	1078	172	16

ACDF anterior cervical discectomy and fusion, *SAD* subacromial decompression, *CTD* carpal tunnel decompression, *THR* total hip replacement, *ACLR* anterior cruciate ligament reconstruction, *TKR* total knee replacement, *HVC* hallux valgus correction

was studied in 22 trials comparing surgery versus conservative management or arthroscopic versus open techniques; only two trials reported significant findings. In patients with carpal tunnel syndrome, 72 trials were included mainly focused on standard decompression versus minimally invasive endoscopic surgery, physiotherapy, additional procedures such as epineurotomy or timing or surgery. Eleven trials (15.3%) reported significant differences.

In total hip replacements, we identified 281 trials comparing different surgical approaches, bearing surfaces, different head sizes, cemented versus uncemented implants or the use of navigation techniques. Of these, 52 (18.5%) trials reported significant findings. Similarly, in total knee replacement, trials compared different implant designs, standard versus patient-specific instrumentations, robotic versus conventional techniques and patella management techniques. Fifty-five trials (15.4%) reported significant findings.

Anterior cruciate ligament reconstruction trials compared single- versus double-bundle reconstructions, different graft choices, methods of graft fixation and structured physiotherapy with only 8.8% (21/239) of trials reporting significant differences. Finally, 30 trials compared different types of osteotomies and different methods of fixation to correct hallux valgus deformity with only five trials (16.7%) reporting significant findings.

The number of RCTs per year of publication has increased dramatically particularly since early 2000s—with over 100 RCTs of those seven procedures published in 2017 alone (Fig. 3). Similarly, the number of RCTs reporting significant findings has proportionately increased (Fig. 4).

Discussion

This study provides an overview of orthopaedic randomised controlled trials of the most commonly performed orthopaedic operations by subspecialty. RCTs are considered the best means of providing evidence in support of or against specific treatment modalities. However, careful planning throughout the different stages of conducting an RCT is needed to provide the high-quality evidence needed.

Historically, surgical RCTs have faced significant ethical and practical challenges from methodological design to implementation [3, 6, 26]. For example, hip replacement surgery for severe hip arthritis is considered one of the most cost-effective orthopaedic interventions [16]. However, questions related to surgical technique, approach, head sizes or bearing surfaces have been covered by a large number of RCTs with no significant differences found. While the lack of significant findings in those trials did not influence the decision to offer patients hip replacements, it rather reflected the lack of marginal effects of those variations in surgical interventions.

Fig. 3 Number of trials per year of publication

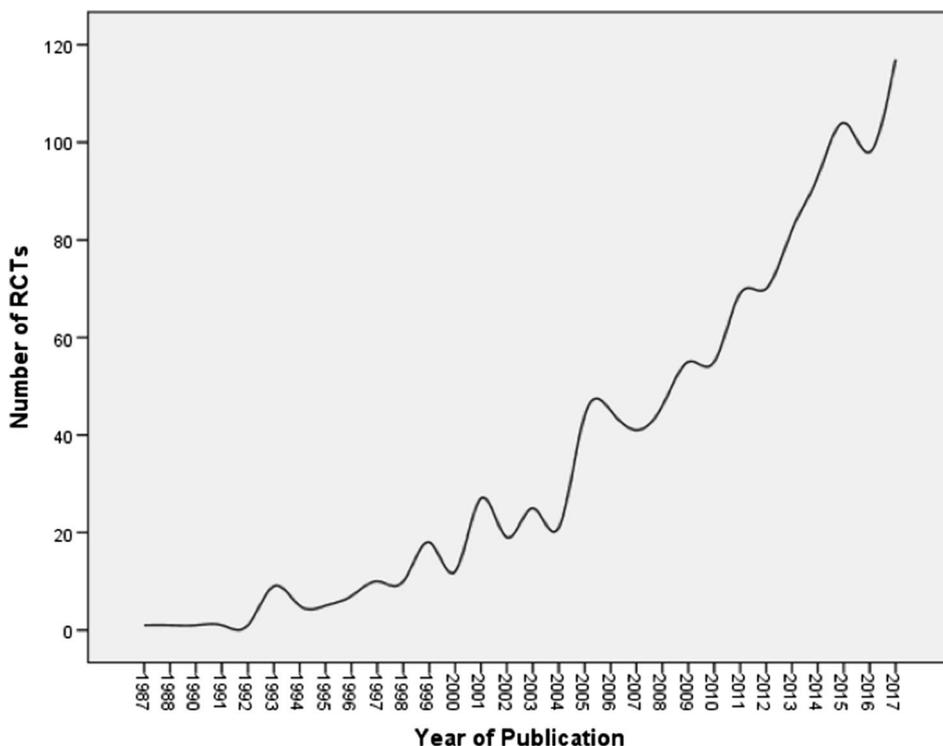
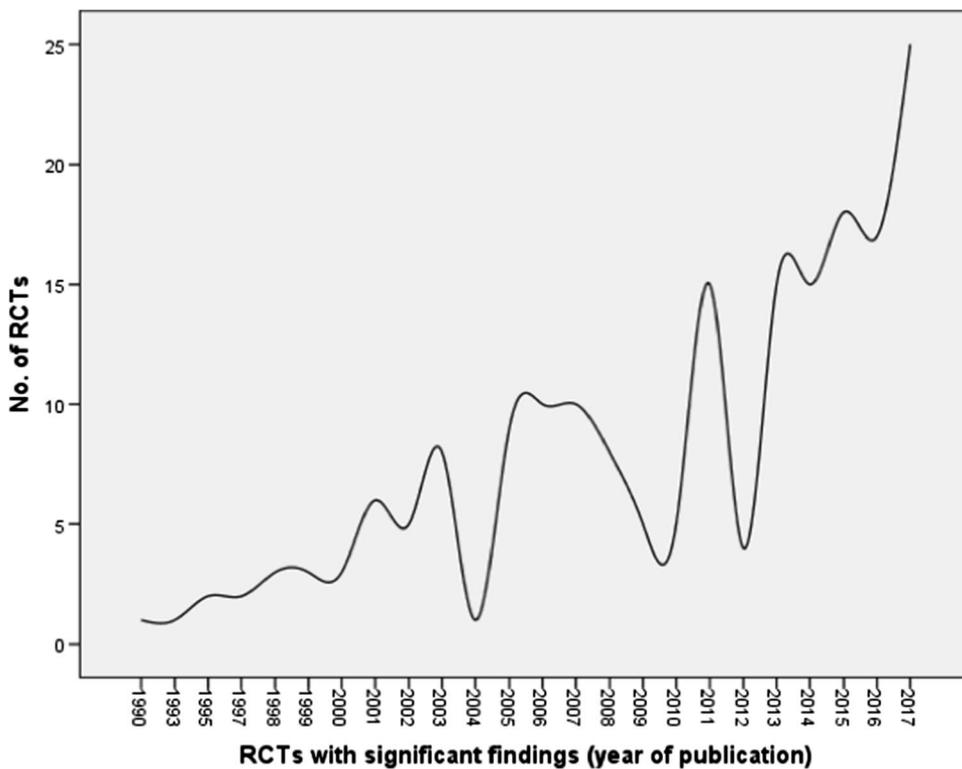


Fig. 4 Number of trials with significant findings per year of publication



We evaluated 1078 trials, many of which compared similar interventions with varying quality and small sample sizes. This perhaps reflects the recent shift and evolution of

orthopaedic research from relative scarcity of RCTs in the 1980s to numerous small-scale RCTs in 2000s. However, with increasing awareness of the important role of research

networks in supporting trials, multidisciplinary collaboration and adequate investment in trial infrastructure have proved crucial for successful delivery of more recent multi-centre, high-quality RCTs such as UKFF trial [4], UK FASHIoN trial [13] and CSAW trial [2].

This is the first study to undertake a comprehensive review of orthopaedic RCTs in elective practice. We do, however, acknowledge limitations to its findings. We did not calculate the treatment effect of individual trials with significant statistical findings and whether this correlated with clinically measurable effects nor did we undertake extensive review to confirm equipoise in any of the interventions reviewed. Further, the quality of reporting trials was not addressed as this aspect falls outside the scope of this study.

To conclude, it is evident that the number of RCTs in orthopaedic research is steadily increasing. This is indeed a welcomed development. However, only 16% of trials reports significant differences between interventions. For trials comparing different surgical techniques, this evidence provides the treating surgeon with the flexibility to utilise available resources and infrastructure to deliver patients care without compromising clinical outcomes. Further, for trials comparing different treatment modalities, i.e. surgery versus no surgery, this study helps to inform the shared decision-making process when counselling patients on the effectiveness of surgical interventions. Finally, large multi-centre/international high-quality RCTs adopting unified outcome measures supported by national/international societies with greater focus on the minimal clinically important differences (MCID) in outcome measures can better inform clinicians and patients alike.

Compliance with ethical standards

Conflict of Interest The author(s) declare that they have no competing interests.

Appendix 1: References for RCTs with significant findings

Anterior cervical discectomy and fusion (26 trials/45 publications)

Farrokhi 2017, Rožanković 2017, Xia 2017, Lee 2016, Loumeau 2016, Hou 2016, Engquist 2015, Mariappan 2015, Luo 2015, Vaccaro 2013, Chen 2013, Abbott 2013, Auerbach 2011, Cheng 2011, Coric 2011, Garrido 2010, Riina 2008, Wang 2008, Nabhan 2007, Zoega 2000. RCTs with multiple related publications: (Lanman 2017, Gornet 2017), (Sasso 2017, Sasso 2007, Sasso 2011, Heller 2009, Anderson 2008), (Park 2011, Phillips 2015, Phillips 2013),

(Hisey 2016, Radcliff 2016, Ament 2016, Jackson 2016, Hisey 2015, Davis 2015, Hisey 2014, Ament 2014, Davis 2013, Radcliff 2016), (Delamarter 2013, Zigler 2013, Murray 2009), (Mummaneni 2007, Burkus 2014).

Subacromial decompression

Jacquot 2014, Rahme 1998.

Carpal tunnel decompression

De Kleermaeker 2017, Gutiérrez-Monclus 2017, Orak 2016, Tarallo 2014, Chandra 2013, Sørensen 2013, Drosos 2013, Cresswell 2008, Gentili 2003, Padua 2003, Jugovac 2002.

Total hip replacement

Bargar 2017, Atrey 2017, Schouten 2017, Dahlstrand 2017, Scemama 2017, Broomfield 2017, Verdier 2016, Langlois 2015, Gofton 2015, Mjaaland 2015, Briggs 2015, Glyn-Jones 2015, Gerhardt 2015, Meermans 2014, Gustafson 2014, Dienstknecht 2014, Small 2014, Lass 2014, Engh 2014, Tiusanen 2013, Lorenzen 2013, Vendittoli 2013, Penny 2013, Engh 2012, Howie 2012, Stocks 2011, Corten 2011, Thomas 2011, Corten 2011, Mutimer 2010, Smolders, 2010, Stilling 2009, Calvert 2009, Glyn-Jones 2008, Geerdink 2006, Grübl 2006, Luites 2006, Schauss 2006, Faris 2006, Wembridge 2006, von Schewelov 2005, Kalteis 2005, Kim 2005, Flivik 2005, Brodner 2003, Martell 2003, Freund 2003, Visser 2002, Tanzer 2001, Koessler 2001, Bose 2000, Berger 1997.

Anterior cruciate ligament reconstruction

Khare 2017, Mutsuzaki 2017, Venosa 2017, Reda 2016, Bottoni 2014, Kim 2013, Takeda 2013, Mirzatolooei 2012, Sørensen 2011, Zaffagnini 2011, Vogrin 2010, Ferretti 2008, Siebold 2008, Jepsen 2007, Zhao 2007, Zaffagnini 2006, Drogset 2006, Krywulak 2005, Yasuda 1997, Cameron 1995, Dahlstedt 1990.

Total knee replacement

De Vloo 2017, Zhang 2017, Wang 2017, Vide 2017, Li 2017, Todesca 2017, Calliess 2017, Kim 2017, Jawhar 2016, Ahn 2016, Morrison 2016, Bell 2016, Camp 2015, Chen 2015, Alomran 2015, Fransen 2015, Hutt 2015, Dosssett 2014, Nam 2014, Pornrattanama-neewong 2013, Altay 2012, Meijerink 2011, Blakeney 2011, van Jonbergen 2011, Zhang 2011, Varela-Egocheaga 2010, Higuchi 2009, Dutton 2008, Confalonieri 2007, Mullaji 2007, Chin 2007, Weeden 2007, Matziolis 2007, Kalairajah 2006, Cobb 2006, Ishii 2005, Bâthis 2005, Carlsson 2005, Decking 2005, Chauhan

2004, Sparmann 2003, Waters 2003, Price 2003, Reed 2002, Chiu 2002, Wood 2002, Stukenborg-Colsman 2001, Chiu 2001, Roysam 2001, Waikakul 2000, Levy 1999, Jorn 1999, Nilsson 1998, Newman 1998, Abdel-Salam 1995.

Hallux valgus correction

Irha 2016, Buciuo 2014, Torkki 2001, Calder 1999, Klosok 1993.

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