

Clinical Benefit of Hydroxyapatite-Coated Versus Uncoated External Fixation: A Systematic Review

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ABSTRACT

AIM: Common complications of external fixators include pin-loosening, infection and loss of reduction/malunion. These are increased with prolonged fixation. The main aim of this systematic review was to investigate HA-coated versus uncoated external fixator and determine benefits in terms of pin loosening, infection and loss of reduction/malunion.

MATERIAL AND METHODS: A systematic literature search using PubMed, EMBASE, OVID SP, Cochrane database, ClinicalTrials.gov website and the references of the studies identified was undertaken on 26th August 2014. Comparative trials investigating HA-coated versus uncoated external fixation pins were identified. These were limited using strict eligibility criteria and critically appraised as per the CASP and CONSORT guidelines. Primary outcome measures included pin loosening and infection. Secondary outcome measures included loss of reduction/malunion.

RESULTS: Seven studies were identified of which five studies demonstrated a statistically significant reduction in loosening with HA-coated pins. There was insufficient evidence to demonstrate any clinical benefits, such as numbers needed to treat to avoid early removal of pins. Review of the studies included also demonstrated insufficient evidence to determine any significant clinical benefit with regards to infection and malunion. Critical appraisal demonstrated average methodological quality of the studies.

CONCLUSION: HA-coating of external fixator pins improves bone fixation and reduces loosening in patients undergoing prolonged fixation procedures, such as leg-lengthening, but the influence on infection and malunion is not clear. Further large, well-designed randomised controlled trials with observer blinding, standardized pin insertion and pin care investigating clinically relevant pin loosening, infection and malunion are recommended. Patient reported, functional outcome measures should also be considered.

Key words: External fixation; Hydroxyapatite-coated external fixator pins; External fixator pins; Leg lengthening

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INTRODUCTION

The external fixator has been used for more than a century^[1]. Despite many advances in the development of external fixation techniques, pin-tract infection and loosening are still significant complications. They are the most commonly occurring complications during limb lengthening using external fixation, with some studies reporting an

incidence of up to 80%^[2-4].

Indications for external fixators include damage control orthopaedics^[5] and definitive treatment frames used in managing acute fractures, bone loss/deformity and limb lengthening. The ability of current external fixator designs to allow gradual reduction and realignment with frequent, small adjustments makes them extremely useful for treating these problems. Ilizarov began to develop the basic concepts of definitive external fixator treatment in 1951 after seeing many WWII veterans with tibial fractures. Since then, external fixation techniques have developed considerably and are now essential components in the treatment of congenital and post-traumatic short limbs. Clinical success or failure of limb lengthening is gauged by the amount of length produced, quality of bone generated and avoidance of complications during and after the lengthening process^[6].

Loosening and infection are common complications of external fixation. The exact frequency of these problems is difficult to ascertain from the literature as different definitions are used for diagnosis^[7]. However, major infections of the pin track, which require intravenous antibiotics and pin removal, have been reported as occurring in 5.8% of cases^[7]. Some studies have reported overall rates of infection, including less severe infections, as high as 100%^[8]. It is not always clear whether loosening or pin infection occurs first, but there is an association. Pin site infection is also associated with osteomyelitis and loss of reduction. Loosening may result in fluid accumulation around the pin and subsequent increased risk of infection^[9].

These complications are especially important to consider for limb lengthening treatments due to the prolonged duration of fixation and high mechanical loads. Diminution of extraction torque with time occurs even in ideal fixation conditions with no infection^[10,11].

Pin loosening may occur as a result of thermal and mechanical cortical damage that occurs on pin insertion. Insertion technique and frame stiffness are the most frequently considered of several important factors in pin loosening^[12]. The use of tapered self-drilling, self-tapping half pins on power drills with diligent soft tissue care seems to be optimal^[11]. Other factors to consider for improving fixation at the pin-bone interface include mechanical pin design and number of pins^[13]. Regular pin site cleaning regimes should also be considered to reduce infection. However, there is still no consensus regarding optimal pin care^[14].

The use of pin coatings to enhance fixation and reduce infection has been increasingly investigated over the last 10 years^[1]. These coatings include hydroxyapatite, titanium and silver. Pins coated with silver have been shown to be associated with less bacterial colonisation than uncoated pins, but their clinical performance has not been found to be definitively superior to that of uncoated pins^[1]. Masse *et al* showed there is a potential for systemic silver absorption with their use and discontinued their study on safety and ethical grounds.

Hydroxyapatite is a crystalline molecule which constitutes 65% of the mineral component of human bone^[15]. It has widely and effectively been used in orthopaedic surgery as a bone substitute and prosthetic coating^[16] due to its osteoconductive^[17] and osteoinductive properties^[18]. Studies investigating the use of hydroxyapatite as a coating for external fixator pins have shown promising results in terms of fixation^[13,19,20].

It is clear that pin loosening and infection are significant problems associated with external fixators, especially in limb lengthening procedures. Hydroxyapatite coated pins have been previously investigated in animal studies with good results^[20].

Table 1 Summary of eligibility criteria.

Inclusion criteria	Exclusion criteria
Patients undergoing external fixator treatment	Non-comparative studies
Studies comparing hydroxyapatite coated and uncoated external fixation pins	Duplicate studies excluded
Randomized and non-randomized comparative trials	Case reports, editorials, comments, letters, guidelines, protocols, abstracts, demographic studies, unpublished studies
English language articles only	Animal studies
Human studies	Osteoarthritis treatment

Therefore, the purpose of this systematic review is to evaluate their use specifically in the treatment of limb lengthening/distraction osteogenesis in humans as well as other procedures involving external fixation therapy including orthopaedic trauma surgery.

The main objectives of this review are to: (1) Conduct a reproducible literature search identifying studies comparing the use of hydroxyapatite coated versus uncoated external fixation pins; (2) Evaluate whether there is any clinical benefit with primary outcome measures being pin infection and pin loosening (extraction torque) and secondary outcome being malunion/loss of reduction; (3) Critically appraise the evidence and describe the findings in light of existing studies.

METHODS

Literature Search

The Pubmed database was searched on 26th August 2014 using keywords and strict eligibility criteria with no limit regarding the year of publication. The search terms “external fixators” and “hydroxyapatite” were used. The studies identified were further limited by selecting “humans” and “English language articles” only. Each of the remaining studies was carefully analysed. Only comparative (randomized and non-randomized) studies evaluating infection and loosening in hydroxyapatite coated versus uncoated external fixation pins were included. A systematic search of EMBASE using OVID SP, Cochrane database, ClinicalTrials.gov website and the references of the studies identified was also conducted. This did not reveal any additional studies. No statistical analyses were performed due to inhomogeneity between study populations, types of external fixator/pins used and lack of consistency in definition of outcome measures.

Eligibility Criteria

Eligibility criteria for exclusion and inclusion of studies for this systematic review are summarised in Table 1. Below is a breakdown of eligibility criteria for the trials to be included in terms of population (participants), intervention, comparator and outcomes: (1) Participants: Patients undergoing treatment using external fixation; (2) Intervention: Hydroxyapatite-coated external fixation pins; (3) Comparator: Uncoated external fixation pins; (4) Outcomes: Primary - infection (pin-site, osteomyelitis), loosening (extraction torque); Secondary-malunion, loss of reduction/bone apposition, radiological (osteolysis), other complications.

Study Selection and Abstraction

Two authors (AP and AG) independently reviewed the abstract of each publication and included or excluded papers. The authors

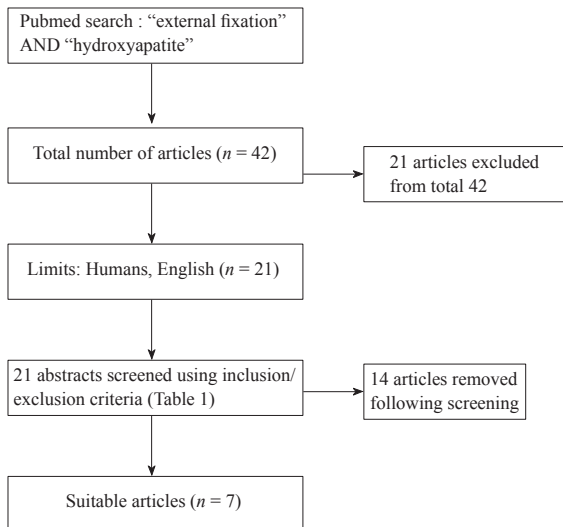


Figure 1 Flow diagram illustrating literature search and selection procedure.

discussed all studies included/excluded. If there were any disagreements or discrepancies in selection, the third author (AA) was consulted. When inclusion or exclusion was not possible based on the abstract, the full text versions were downloaded. In addition, the reference lists of the studies included were reviewed by hand to identify any articles not originally identified during initial electronic search.

After having passed the initial selection process of identifying suitable studies based on inclusion and exclusion criteria, the selected studies were further assessed on methodological quality using the critical appraisal checklist (adapted from Critical Appraisal Skills Programme- CASP, Oxford^[21]) for an article on treatment and the revised CONSORT checklist^[22] for reporting randomized trials were utilized.

Each study was assessed and scored on three different aspects adapted from the CASP checklist: (1) Whether the results of the trial were valid (Section A); (2) What the results were (section B); and (3) Whether the results would help locally (section C).

Each reviewer scored each study based on answering the 11 different questions from the CASP checklist. These scores were used to guide assessment as to whether the study was to be included or excluded into the review. Where there were discrepancies in scores between different studies, consensus was sought using the third reviewer (AA).

All checklists were used to guide assessment of the studies identified from the literature search. All checklists have limitations; therefore the CONSORT and CASP tools were only used as guidelines.

The next step involved extracting the information from each study. This included the data such as the intervention, comparator, baseline characteristics of each study (*e.g.*, study design, sample size, research size, study period, participant demographics) as well as the primary and secondary outcomes of each study. The data extracted is summarised in Table 2.

Methods used for assessing risk of bias in individual studies

To assess the reliability of results from the studies, investigations into potential sources of bias was carried out, looking at potential sources at both the study and outcome level. Once studies were selected into the review, a key part of the analysis stage was considering the risk of bias in the methodology of each study. The

Delphi list^[23] was used to help assess the risk of bias for the RCT selected in this review. Points were only awarded when a criterion was clearly satisfied.

Two authors (AP and AG) reviewed each study for its internal validity using the Delphi list and scored each study with a quality score. Any discrepancies amongst scores were reviewed by a third reviewer (AA) and a final decision was made based on the agreement of all reviewers. Other risks of bias also investigated for, included; selection bias, performance bias, attrition bias, detection bias and reporting bias.

The stages adopted in assessing the risk of bias was guided by recommended approaches from the Agency for healthcare research and quality methods guide (AHRQ)^[24].

RESULTS

Search Results

The PubMed search identified a total of 42 articles. Following limitation to “English language articles” and “human species”, 21 studies remained. The abstracts were thoroughly screened and 7 studies comparing hydroxyapatite coated with uncoated external fixation pins were identified. These are summarised in Table 2 and Table 3. The flow diagram in Figure 1 illustrates the search strategy.

DISCUSSION

The main purpose of this systematic review was to determine whether HA-coating of external fixation pins has a beneficial effect on rates of loosening and pin-track infections compared to uncoated pins. The secondary objective was to determine whether HA-coating influenced malunion and loss of reduction.

Five of the studies in this review found that HA-coating of pins improves bone fixation and therefore reduces loosening in patients undergoing external fixation. However, the results of the studies of Pieske *et al*^[25,26] found that although there was a trend towards a superior clinical outcome, the results showed no significant superiority of HA-coated pins against uncoated pins and that the majority of clinical pin-site parameters were comparable in both groups. At the end of the fixator therapy, Pieske *et al*^[26], found there were a total of 9 loose pins out of 76 in the steel group (11.8%) compared to 6 loose pins out of 76 in the HA-coated group (7.9%), whilst Pieske *et al*^[25], showed there were 10 loose pins in the titanium group (12.5%) compared to 6 loose pins in the HA-coated group (7.9%). Pieske *et al*^[26] found that although there was a lower rate of loose pins in the HA group, this was not significant ($P = 0.864$) and that the benefit of advanced pin-bone bonding in the HA group was clinically irrelevant. Furthermore the fixation therapy in both of these studies was only for a period of 6 weeks. In other studies which have demonstrated a significant improvement in bone fixation, such as for lower leg lengthening, external fixation treatment time is much longer, extending on average up to 500 days^[25]. During long-term fixator treatment, the beneficial effects of HA-coated pins becomes more evident, with improved bone fixation and low rates of pin-loosening seen, compared with the shorter duration of fixation therapy used for this wrist study.

The definitions of pin loosening were extremely variable. Both Moroni *et al*^[13] and Placzek *et al*^[16] did not use a standardized definition of loosening. Placzek *et al*^[16] used the fixation index which they developed to determine screw fixation strength. Pommer *et al*^[28] used both clinical and radiological criteria to define loosening. Piza *et al*^[27] and Caja *et al*^[12] used the same definition of

Table 2 Summary of included studies comparing hydroxyapatite coated and uncoated external fixation pins.

Ref.	Study design	Sample Size	Study period	Participants	Indication	Intervention	Comparator	Observer blinding	Primary outcome	Secondary Outcome	Conclusion
Pieske <i>et al</i> ^[25] , 2011	Prospective, randomised controlled cohort study	Total no. of pts: 39 HA pts: 19 HA pins: 76 Non-HA patients: 20 Non-HA pins: 80	2005-2007	Average age (years): - HA: 65.0 (+/- 17.8) - Non HA 66.4 (+/- 16.0) Sex: - HA 3 M/16 F - Non HA 3 M/17 F	Patients presenting after wrist trauma requiring distal radial fracture fixation.	HA coated steel pins -ASTM (F1185). Orthofix tapered half pins (3.3/3.0 mm) with shank diameter of 4.0 mm)	Non-HA coated pins- consisting of titanium alloy (Ti6Al4V-group) (ASTM F136) Orthofix tapered half pins (3.3/3.0 mm) with shank diameter of 4.0 mm)	Not described	Grade of extraction torque: Grade 1 and 2 (> 0.4 Nm = 'strong' to 'good' pin-extraction force) HA = 69.3% Non HA = 56.6% Grade 3 (< 0.4 Nm = low pin extraction force) HA = 22.1% Non HA = 30.3% Grade 4 (Manually Extractable) HA = 7.9% Non HA = 12.5% Pin loosening: HA = 7.9% Non- HA = 12.5% No Sig diff (<i>P</i> > 0.05). Pin tract Infection: HA = 2.7% Non HA = 0% Not stat. significant (<i>P</i> > 0.05).		In external fixation of the wrist, the use of HA-coated pins yields no clinical advantages: there is a trend toward a superior pin-bone anchorage, but a tendency of increased susceptibility for minor pin-track infections.
Pieske <i>et al</i> ^[26] , 2010	Prospective, randomised controlled cohort study	Total no. of pts: 38 HA pts: 19 HA pins: 76 Non-HA patients: 19 Non-HA pins: 76	Not Stated	Average age (years): - HA: 65.0 (+/- 17.8) - Non HA 69.8 (+/- 12.2) Sex: - HA 3 M/16 F - Non HA 4 M/15 F	Patients presenting after wrist trauma requiring distal radial fracture fixation.	HA coated steel pins -ASTM (F1185), orthofix tapered half pins (3.3/3.0 mm) with shank diameter of 4.0 mm)	Non-HA coated pins- consisting of stainless steel (steel group) (ASTM F136), orthofix tapered half pins (3.3/3.0 mm) with shank diameter of 4.0 mm)	Not described	Grade of extraction torque Grade 1 and 2 (> 0.4 Nm = 'strong' to 'good' pin-extraction force)) HA = 69.1% Non HA = 56.6% Grade 3 (< 0.4 Nm- low pin extraction force) HA = 22.1% Non HA = 31.6% Grade 4 (Manually Extractable) HA = 7.9% Non HA = 11.8% Pin loosening HA = 7.9% Non- HA = 11.8% No Sig diff (<i>P</i> = 0.846). Pin tract Infection: HA = 2.6% Non HA = 5.3% Not stat. significant (<i>P</i> = 0.601).		The use of HA-coated pins compared with standard stainless-steel pins in external fixation for unstable wrist fractures yields only a trend towards a superior clinical outcome
Placzek <i>et al</i> ^[16]	Prospective non-randomised comparative study .	Total no. of pts: 21 HA pts: 12 HA pins: 47 Non-HA pts: 9 Non-HA pins: 45	Not stated	Average age (years): - HA 20 (9 – 44) - Non HA 30 (9 - 47) Sex: - HA 6 M / 6 F - Non HA 5 M / 4 F Average implantation time (days): - HA 213 (91 – 335) - Non HA 165 (91 – 305)	Patients treated for congenital and post-traumatic leg length discrepancies for short stature	HA coated steel 6mm Schanz pin with taper shank and non-tapered thread	Non-HA coated steel 6mm Schanz pin with taper shank and non-tapered thread	Not described	Fixation index (F.I.) = max. extraction torque / max insertion torque Pins with no infection:- HA F.I. = 1.92 Non HA F.I. = 0.76 Sig diff <i>P</i> < 0.001 Pins with infection:- HA F.I. = 0.39 Non HA F.I. = 0.13 No sig diff <i>P</i> > 0.05 Pin track infectiona: HA = 11% Non HA = 9% No sig diff		HA coating improved fixation of Schanz screws in bone and may be useful in prolonged lower leg external fixation. No significant difference with regards to infection.

Piza <i>et al</i> ^[27]	Prospective, randomized comparative study	Total no. of pts: 23 HA pts: 23 HA pins: 161 Non-HA pts: 23 Non-HA pins: 161 Each patient had bilateral limb lengthening, HA pins used on one side and non-HA other side	1995-1997	Average age (years): - HA 12.7 - Non HA 12.7 Sex: - HA 12 M / 11 F - Non HA 12 M / 11 F Average implantation time (days): - HA 549 (+/- 180) - Non HA 512 (+/- 151)	Patients treated for short stature by bilateral leg lengthening	HA coated Orthofix tapered 6 to 5 mm steel pins	Non-HA coated Orthofix tapered 6 to 5 mm steel pins	Not described	Mean extraction torque (Nmm per degree): HA = 7612 +/- 3101 Non HA = 85 +/- 1942 Sig diff $P < 0.001$ Pin loosening: HA = 4% Non HA = 80% Sig diff $P < 0.001$ Pin track infection: HA = 64% Non HA = 69% No sig diff	Bone apposition: HA 73% Non HA 22% Sig diff $P < 0.001$ Bicortical osteolysis: HA 4% Non HA 32% Sig diff $P < 0.001$	HA coating effective in reducing pin loosening in external fixation with long implantation time. No significant diff btw groups with regards to pin-track infections.
Caja <i>et al</i> ^[12]	Prospective, randomized comparative study	Total no. of pts: 17 HA pts: 17 HA pins: 102 Non-HA pts: 17 Non-HA pins: 102 Each patient had bilateral limb lengthening, HA pins used on one side and non-HA other side	1995-1997	Average age (years): - HA 12 - Non HA 12 Sex: - HA 8 M / 9 F - Non HA 8 M / 9 F Average implantation time (days): - HA 583 (+/- 147) - Non HA 583 (+/- 147)	Patients treated with symmetrical tibial elongation for short stature	HA coated standard steel Orthofix 6mm cortical pins with tapered threads (6 mm and 5 mm)	Non-HA coated standard steel Orthofix 6mm cortical pins with tapered threads (6 mm and 5 mm)	Not described	Mean extraction torque (Nmm per degree): HA = 7801 +/- 2106 Non HA = 41 +/- 104 Sig diff $P < 0.001$ Pin loosening: HA = 7% Non HA = 95% Sig diff $P < 0.001$	Average coronal axial deviation: HA 6.5° Non HA 12.5° Sig diff ($P = 0.023$) Closed MUA for axial deviation: HA 0 patients Non HA 3 patients	Tibial lengthening with HA coated pins results in less axial deviation compared with use of uncoated pins. Significantly increased loosening in uncoated pins.
Pomer <i>et al</i> ^[28]	Prospective, randomized comparative study	Total no. of pts: 46 HA pts: 23 HA pins: 165 Non-HA pts: 23 Non-HA pins: 169	1996-1998	Average age (years): - HA 38.2 (+/- 15.3) - Non HA 40.1 (+/- 12.8) Sex: - HA 17 M / 6 F - Non HA 18 M / 5 F Average implantation time (days): - HA 270 (97 - 503) - Non HA 241 (132 - 326)	Patients treated with external fixation for distraction osteogenesis to fill tibial defect or lengthen short tibia	HA coated stainless-steel Schanz pins (50 µm thick coating, core diameter 3.8 mm, thread depth 50 mm)	Non-HA coated titanium Schanz pins (core diameter 3.8 mm, thread length 50 mm)	Not described	Mean extraction torque (Nmm per degree): HA = 430 +/- 180 Non HA = 100 +/- 90 Sig diff $P < 0.001$ Pin loosening: HA = 0% Non HA = 13% Sig diff $P < 0.001$ Pin track infection: HA = 0% Non HA = 12% Sig diff $P < 0.001$	Pin breakage: HA = 1 pin Non HA = 0 Mean local bone density around pin decrease: HA = 4% Non HA = 9%	HA coating of pins increases their fixation and reduces infection and loosening. HA coated pins should be considered in situations requiring prolonged ex fixation.
Moroni <i>et al</i> ^[29]	Prospective, randomized comparative study	Total no. Of pts: 20 HA pts: 10 HA pins: 40 Non-HA pts: 10 Non-HA pins: 40	Not stated	20 consecutive female patients > 60 years of age with osteoporosis and an AO classification A2 or A3 distal radius fracture.	Osteoporotic wrist fractures	3.3-3 mm tapered HA coated pins.	3.3-3 mm tapered non-HA coated pins	Not described	Mean extraction torque (Nmm per degree): HA = 600 +/- 214 Non HA = 191 +/- 155 Sig diff $P < 0.001$ Pin track infection: HA = 0% Non HA = 20% No sig diff		HA coated tapered external-fixation pins provided improved fixation in the treatment of wrist fractures in patients with osteoporosis.

a: As per Schmidts classification of infection (see appendices); b: As per Checketts classification of pin-track infection (see appendices); c: Microbiological criteria of Mahan *et al*^[30].

loosening (extraction torque < 150 Nmm per degree). However, as discussed in the critical appraisal, this did not correlate well with clinical results such as the requirement of removing or changing pins. Pieske *et al*^[25,26] defined loose pins as those that were manually extractable with an extraction torque value of grade 4. Despite the

difference in definitions used, it is reasonable to say that all of the papers excluding Pieske *et al*^[25,26] show that HA-coating reduces the risks of pin loosening. All of the studies stated that the extraction torque of uncoated pins was lower than HA-coated pins; this was highly statistically significant in all the studies except for Pieske

Table 3 Critical Analysis of Data.

Study	Clear statement of aims	Is qualitative methodology appropriate?	Design appropriate to address aims?	Appropriate recruitment strategy?	Appropriate Data collection?	Appropriate consideration of researcher/participant role?	Ethical issues/Funding?	Sufficiently rigorous data analysis?	Clear statement of findings?	How valuable is research?
Pieske <i>et al</i> ^[25] , 2011	Yes	Yes	Yes	* Indications for recruitment into study were clear; pt's presenting with unstable wrist fractures. * Inclusion/exclusion criteria clearly defined. * Patients were randomised using a computer generated list. * Patients were blinded into one of three treatment arms.	* Prospective, randomized comparative study. * Surgical technique well described. * Follow up period and investigations clearly described. * Short follow up period of only 6 weeks. * Small sample size; total of 40 patients.	* Number/ experience of surgeons undertaking the procedure was not discussed. * Post-operative radiological findings clearly defined and independently verified by radiologists who were blinded to treatment arms. * Other clinical findings were investigated by the co-author who was not blinded to treatment groups.	* Study approved by the institutional Ethics Committee	* The study had a small sample size. * No power calculations were carried out. * Statistical analyses were adequate.	* Clear statement of findings. * Outcomes pre-specified and well defined.	* This study showed that in external fixation of the wrist, the use of HA-coated pins yields no clinical advantages: there is a trend toward a superior pin-bone anchorage, but a tendency of increased susceptibility for minor pin-track infections.
Placzek <i>et al</i> ^[16]	Yes	Yes	Yes	* Indications for recruitment into study are clear- short stature. * Eligibility criteria not clearly stated. * Assessor blinding was not undertaken.	* Prospective, non-randomised comparative study. * Data was collected at two separate centres in Germany, one centre evaluated HA-coated screws and the other centre evaluated non-HA coated screws. * Surgical technique was not described.	* Baseline characteristics of patients included in this study were not clearly stated. * Number/ experience of surgeons undertaking the procedure was not discussed. * Post-operative clinical and radiographic findings were clearly defined, although the author did not state if these were independently verified. * No assessor blinding undertaken.	* The author did not state whether external funding or ethical approval was obtained.	* The study had a small sample. * No power calculations were carried out. * For comparison of both groups, the Mann-Whitney U Test was applied, and for statistical analysis within the group, the Wilcoxon test was performed. * Confidence intervals used.	* Clear statement of findings, although the primary and secondary outcomes were not well defined. * The authors stated there was no significant difference in rates of infection between the two groups; but this was only specified for grades 3/4 infection. They do not mention of any grade 1 or 2 infections in the results.	* Results of the study were consistent with findings from other similar studies although with major reservations regarding methodology. * The results showed there was no difference in rates of infection, but HA-coating improved bone fixation in Schanz screws.
Pommer <i>et al</i> ^[28]	Yes	Yes	Yes	* Indications for recruitment into study are clear. * Eligibility criteria clearly defined. * Patients were randomised into treatment arms, however randomisation technique was poor. There was no discussion regarding sequence generation, implementation or observer blinding.	* Prospective, randomized comparative study. * Surgical technique and follow up was well described and standardized. * Patients were reviewed 2 weekly, with radiographs taken on alternate visits.	* Number/ experience of surgeons undertaking the procedure was not discussed. * Definition of pin loosening was based on clinical and radiological findings, rather than extraction torque measurements; however the author does not mention whether these were independently verified.	* The author did not discuss ethical approval.	* Power calculations were not performed in this study. * Confidence intervals were not discussed. * The overall statistical analyses were adequate.	* Clear statement of findings, although the primary and secondary outcomes were not well defined.	* Whilst this study demonstrates a significant difference between rates of loosening and infection between the two groups (p < 0.001), the study was comparing stainless steel HA-coated pins against titanium pins and therefore the assessment was not simply of the HA coating.
Piza <i>et al</i> ^[27]	Yes	Yes	Yes	* Indications for recruitment into study are clear- pts with short stature undergoing bilateral limb lengthening.	* Prospective, randomized comparative study. * Surgical technique well described. * The	* Baseline characteristics of patients undergoing the lengthening procedures were clearly illustrated. * Number/ experience of	* Ethical approval was obtained from the	* The study had a small sample. * No power calculations were carried out. * Statistical	* Clear statement of findings. * Outcomes pre-specified and well defined however	* Results of the study were consistent with findings from other similar studies; therefore studies are linked to current

				<p>* Eligibility criteria poorly defined -no clear exclusion and inclusion criteria.</p> <p>* Randomisation technique was poor- consisted of tossing a coin.</p> <p>* Observer blinding was not discussed.</p>	<p>accuracy of measurements was not checked following modification of the DIGITORK (electronic torque wrench), required for attaching to the external fixator pins.</p> <p>* No follow up period mentioned.</p>	<p>surgeons undertaking the procedure was not discussed.</p> <p>* Post-operative clinical findings clearly defined; pin loosening defined as an extraction torque of < 150 N mm per degree.</p>	<p>hospital ethics committee and the no external sources of funding were obtained.</p>	<p>analyses were adequate.</p> <p>* There was no significant difference between the groups with respect to number of pins removed due to loosening.</p>	<p>not always correlating with clinical findings.</p>	<p>knowledge/ trends.</p>
Caja <i>et al</i> ^[12]	Yes	Yes	Yes	<p>* Indications for recruitment into study are clear.</p> <p>* Eligibility criteria were not well defined.</p> <p>*Randomisation was used however the author did not discuss the process used.</p>	<p>* Prospective, non-randomised comparative study.</p> <p>* Surgical technique was reported to be the same as that by Piza <i>et al</i></p> <p>* Post-operative rehabilitation, indication for pin removed and pin assessment were clearly discussed.</p> <p>* The study did not record infection as an outcome measure and therefore did not report it.</p>	<p>* Number/ experience of surgeons undertaking the procedure was not discussed.</p> <p>* Post-operative clinical findings clearly defined; pin loosening defined as an extraction torque of < 150 N mm per degree.</p> <p>* The author does not discuss if assessor blinding was undertaken or if results were independently verified.</p>	<p>* The study was approved by the hospital ethics committee and the authors did not receive any external sources of funding.</p>	<p>* Power calculations were not performed in this study.</p> <p>* Confidence intervals were not discussed.</p> <p>* The overall statistical analyses were adequate.</p>	<p>* Clear statement of findings, although the primary and secondary outcomes were not well defined.</p>	<p>* This study by Caja <i>et al</i> reported on the association of axial deformity with the use of HA-coated pins,</p>
Moroni <i>et al</i> ^[29]	Yes	Yes	Yes	<p>* Indications for recruitment into study are clear.</p> <p>* Eligibility criteria clearly defined.</p> <p>Randomisation was used; however there was no description on the process other than stating it was done "with use of a computer generated list".</p>	<p>* Prospective, randomized comparative study.</p> <p>* Surgical technique well described.</p> <p>* There was no evidence of the torque wrench device being calibrated before use to measure the pin extraction torque.</p>	<p>Baseline characteristics of patients undergoing the lengthening procedures were clearly illustrated.</p> <p>* Number/ experience of surgeons undertaking the procedure was not discussed.</p> <p>* Post-operative clinical findings clearly defined.</p>	<p>* The study had a small sample.</p> <p>* Power calculations were carried out; although only brief details were given.</p> <p>* Statistical analyses were adequate.</p> <p>* Confidence intervals were used.</p>	<p>* Clear statement of findings.</p> <p>* Outcomes pre-specified and well defined.</p> <p>Clinical analysis of pin tracts was performed using the classification system of 'Checketts and Otterburn'.</p>	<p>* The authors recommend the use of HA-coated pins for external fixation of distal radial fractures in osteoporotic bone. However, the results do not justify the conclusion; although the mean extraction torque is greater for HA coated pins, there is no evidence to suggest this is relevant clinically; in terms of pin loosening and malunion.</p>	
Pieske <i>et al</i> ^[26]	Yes	Yes	Yes	<p>* Indications for recruitment into study were clear; pt's presenting with unstable wrist fractures.</p> <p>*Inclusion/exclusion criteria clearly defined.</p> <p>* Patients were randomised using a computer generated list.</p>	<p>* Prospective, randomized comparative study.</p> <p>* Surgical technique well described.</p> <p>* Follow up period and investigations clearly described.</p> <p>* Short follow up period of</p>	<p>* Number/ experience of surgeons undertaking the procedure was not discussed.</p> <p>Post-operative radiological findings clearly defined and independently verified by radiologists who were blinded to treatment arms.</p>	<p>* Study approved by the institutional Ethics Committee</p>	<p>* The study had a small sample size.</p> <p>* No power calculations were carried out.</p> <p>* Statistical analyses were adequate.</p>	<p>* Clear statement of findings.</p> <p>* Outcomes pre-specified and well defined.</p>	<p>* The study is consistent with other studies looking at HA-coated pins in demonstrating reduced rates of pin loosening, however this was a non-significant result and so compared with standard stainless steel pins; HA-</p>

* Patients were blinded into one of three treatment arms.	only 6 weeks. * Small sample size; total of 40 patients.	* Other clinical findings were investigated by the co-author who was not blinded to treatment groups.	coated pins demonstrate only a trend towards a superior clinical outcome.
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et al^[25,26]. However, there is insufficient evidence to comment of clinical benefit such as numbers needed to treat to avoid removal of external fixator pins.

Six of the seven studies included evaluated pin-track infection as a specific outcome measure. The study by Caja *et al*^[12] did not evaluate pin-track infection. Each of these studies used a different definition for infection. Placzek *et al*^[16] used the classification by Schmidt *et al* (1990) and reported no significant difference in rates of pin-track infection between HA-coated and uncoated pins. Piza *et al*^[27] used Checketts classification (see Appendices) to define pin-track infection and again reported no significant differences in rates of infection between the two groups. Pommer *et al*^[28] used the microbiological criteria of Mahan *et al*^[30] and reported a significantly lower rate of infection in the HA-coated group. Pieske *et al*^[25,26] evaluated infection at each pin-site specifically assessing for signs of erythema surrounding the pin, grading the drainage as well as scoring pain intensity using a numeric rating scale (NRS) (0-10) for each pin-site. In Pieske *et al*^[26], two pin-track infections requiring daily pin-site care and oral antibiotics occurred in the HA group (2.6%) compared with four in the steel group (5.3%) ($P = 0.601$). These were non-significant results. Therefore, with regards to pin-track infection, there is insufficient evidence to determine whether the use of HA-coated external fixator pins has any significant beneficial effect. The only study to evaluate the effect of HA-coated pins on malunion was undertaken by Caja *et al*^[12]. They concluded HA-coated pins reduced axial deformity, however there was no significant difference between groups in the final bone angle achieved and in the number of patients requiring manipulation. Despite the significant difference in axial deformity, it is not clear whether this has any effect on functional outcome, which is extremely important to consider.

Similar studies investigating the influence of HA-coating of external fixator pins on loosening and pin-track infection have been undertaken in different groups of patients. Moroni *et al*^[31] investigated patients with tibial fractures. The study reported a significantly lower extraction torque than insertion torque for the uncoated groups, whereas the HA-coated group extraction torque was unchanged. Half of the uncoated pins developed infection compared to none of the HA-coated pins. Magyar *et al*^[19] conducted a randomised study investigating patients treated with the hemicallotaxis for osteoarthritis of the medial side of the knee. They reported a significantly higher extraction torque ($P < 0.05$) for the HA-coated pins. Also, 18 of the uncoated screws were loose compared to 1 HA-coated screw. They found no statistically significant difference in pin-site infection.

Overall, with regards to the CASP^[21] and CONSORT^[22] guidelines, the methodological quality of the studies included in this systematic review was average. The specific deficiencies of each study have been discussed previously in the critical appraisal. In summary, however, these deficiencies include: (1) Poorly defined eligibility criteria; (2) Small sample sizes; (3) No discussion regarding use of prophylactic antibiotics; (4) Poor randomisation techniques (inadequate details of sequence generation, allocation concealment and implementation method); (5) No standardization for pin insertion (depth of threads,

number of pins per bone fragment); (6) No power calculations; (7) No confidence intervals; (8) No observer blinding; and (9) No discussion with regards to losses to follow-up.

Other limitations of the studies included in this review include differing surgical techniques and external fixation equipment. This makes comparison of the results of the studies difficult, however it improves the external validity and generalisability of the conclusions of this review as current practices are reflected. Another limitation of this review is the fact that no functional, patient reported outcome measures were considered. Also, none of the studies discussed cost and patient acceptability specifically. These points are important due to the current economic climate and increased, possibly painful, force required to remove HA-coated pins, respectively.

There are other factors which may have affected the findings of this systematic review. Firstly, the selection criteria excluded case reports, non-comparative case-series, editorials, abstracts, and unpublished studies. Although this was undertaken to ensure the studies included were of appropriate high quality and had been through a peer-reviewed process, it may also have introduced publication bias. Secondly, non-English language articles were excluded. This was due to the difficulties with translation. Nonetheless, it may have limited the breadth of literature review. Finally, the search strategy was based on a computer search process. Studies by Colville-Stewart have demonstrated that computer searches may omit some articles, and consequently, limit the scope of this review^[32].

In conclusion, despite variability in definitions and methodological deficiencies, all studies except Pieske *et al*^[25,26] demonstrated a significantly reduced risk of loosening in the HA-coated pins. This is especially important to consider in patients undergoing leg lengthening, who require prolonged fixation. However, clinical benefits in terms of pin removal or exchange are not clear. Only Pommer *et al*^[28] discussed pin removal and demonstrated a higher rate in the uncoated group, conferring a possible clinical benefit. With regards to infection, there is insufficient evidence to confidently state any risk reduction with use of HA-coated pins. There is reduced axial deformity with use of HA-coated pins, however Caja *et al*^[12] reported no significant difference in final bone angle or number patients requiring manipulation. Considering the results of this systematic review and previous studies, there is considerable scope for further trials. A well-designed, large randomised controlled trial with observer blinding and standardisation of pin-insertion, pin-care and post-operative rehabilitation is required. A power calculation should be undertaken. The numbers needed to treat with HA-coated pins to decrease the risk of clinically important loosening, infection and deformity should be calculated. Longer follow-up of patients undergoing leg lengthening procedures would also be useful. Patient reported, functional and disease specific outcome measures as well as cost and patient acceptability should also be considered.

COMPETING INTERESTS

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

Appendices 1 Classification of pin track infection; Schmidt *et al* (1990).

Grade 1	Irritation of pin surrounding area by adhesions and restriction of movement
Grade 2	Infection of the pin surrounding area without secretion
Grade 3	As grade 2, but with definite pin-track secretion, without significant pin loosening
Grade 4	As grade 3, but with significant pin loosening

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A.P is the lead author and carried out the majority of the research for this review as well as the interpretation and analysis of the study results. A.G was responsible for reformatting the original paper as well as contributing to the critical appraisal and selection of papers into this review. A.A assisted in developing the eligibility criteria and selecting papers. He also assisted in critical appraisal.

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Appendices 2 Checketts-Otterburn Classification of pin track infection^[33].

Grade	Characteristics	Treatment
Minor infection		
1	Slight redness, little discharge	Improved pin site care
2	Redness of the skin, discharge, pain and tenderness in the soft tissue	Improved pin site care, oral antibiotics
3	Grade 2 but no improvement with oral antibiotics	Affected pin or pins resited and external fixation can be continued
Major infection		
4	Severe soft tissue infection involving several pins, sometimes with associated loosening of the pin	External fixation must be abandoned
5	Grade 2 but radiographic changes	External fixation must be abandoned
6	Infection after fixator removal. Pin track heals initially, but will subsequently break down and discharge in intervals. Radiographs show new bone formation and sometimes sequestra	Curettage of the pin tract

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