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

Akash Patel, Anik Ghai, Amarjit Anand

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

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
showed there is a potential for systemic silver 
Osteoarthritis treatment

Exclusion criteria
Patel et al. previously investigated in animal studies with good results
lengthening procedures. Hydroxyapatite coated pins have been 
and osteoinductive properties
substitute and prosthetic coating
and effectively been used in orthopaedic surgery as a bone
coatings include hydroxyapatite, titanium and silver. Pins coated
improving fixation at the pin-bone interface include mechanical pin
tissue care seems to be optimal
important factors in pin loosening
and frame stiffness are the most frequently considered of several
time occurs even in ideal fixation conditions with no infection
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
Other factors to consider for improving fixation at the pin-bone interface include mechanical pin
design and number of pins.
Regular pin site cleaning regimes should also be considered to reduce infection. However, there is
still no consensus regarding optimal pin care.
The use of pin coatings to enhance fixation and reduce infection
has been increasingly investigated over the last 10 years. 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. 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. It has widely
and effectively been used in orthopaedic surgery as a bone
substitute and prosthetic coating due to its osteoconductive and
osteoinductive properties. Studies investigating the use of
hydroxyapatite as a coating for external fixator pins have shown
promising results in terms of fixation.

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.

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
Both definitions of pin loosening were extremely variable. However, the results of the studies considering the risk of bias in the methodology of each study. The selected into the review, a key part of the analysis stage was the identification of potential sources of bias was carried out, looking at potential risks of 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)\(^{[24]}\).

### METHODS

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\(^{[23]}\)) 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.

### 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\(^{[25]}\) 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\(^{[12]}\) did not use a standardized definition of loosening. Placzek et al\(^{[12]}\) used the fixation index which they developed to determine screw fixation strength. Pomer et al\(^{[20]}\) used both clinical and radiological criteria to define loosening. Piza et al\(^{[27]}\) and Caja et al\(^{[15]}\) used the same definition of

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**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.

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**LIMITATIONS**

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)\(^{[24]}\). 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\(^{[25]}\) 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\(^{[12]}\) did not use a standardized definition of loosening. Placzek et al\(^{[12]}\) used the fixation index which they developed to determine screw fixation strength. Pomer et al\(^{[20]}\) used both clinical and radiological criteria to define loosening. Piza et al\(^{[27]}\) and Caja et al\(^{[15]}\) used the same definition of
### Table 2 Summary of included studies comparing hydroxyapatite coated and uncoated external fixation pins.

<table>
<thead>
<tr>
<th>Ref.</th>
<th>Study design</th>
<th>Sample Size</th>
<th>Study period</th>
<th>Participants</th>
<th>Indication</th>
<th>Intervention</th>
<th>Comparator</th>
<th>Observer blinding</th>
<th>Primary outcome</th>
<th>Secondary Outcome</th>
<th>Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pieske et al (2011)</td>
<td>Prospective, randomised controlled cohort study</td>
<td>Total no. of pts: 39</td>
<td>2005-2007</td>
<td>HA pts: 19</td>
<td>Non-HA pts: 76</td>
<td>Average age (years): - HA: 65.0 (+/- 17.8) - Non HA: 66.4 (+/- 16.0) Sex: HA: 3M/16 F - Non HA: 3M/17 F</td>
<td>Patients presenting after wrist trauma requiring distal radial fracture fixation.</td>
<td>HA coated steel pins -ASTM (F1185). Orthofix tapered half pins (3.3/3.0 mm with shank diameter of 4.0 mm)</td>
<td>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</td>
<td>Grade of extraction torque: - Grade 1 and 2 (&gt; 0.4 Nm = ‘strong’ to ‘good’ pin-extraction force)</td>
<td>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.</td>
</tr>
<tr>
<td>Pieske et al (2010)</td>
<td>Prospective, randomised controlled cohort study</td>
<td>Total no. of pts: 38</td>
<td>2010</td>
<td>HA pts: 19</td>
<td>Non-HA pts: 76</td>
<td>Average age (years): - HA: 65.0 (+/- 17.8) - Non HA: 69.8 (+/- 12.2) Sex: HA: 3M/16 F - Non HA: 4M/15 F</td>
<td>Patients presenting after wrist trauma requiring distal radial fracture fixation.</td>
<td>HA coated steel pins -ASTM (F1185). Orthofix tapered half pins (3.3/3.0 mm with shank diameter of 4.0 mm)</td>
<td>Non-HA coated pins - consisting of stainless steel (group) (ASTM F136), Orthofix tapered half pins (3.3/3.0 mm) with shank diameter of 4.0 mm</td>
<td>Grade of extraction torque: - Grade 1 and 2 (&gt; 0.4 Nm = ‘strong’ to ‘good’ pin-extraction force)</td>
<td>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</td>
</tr>
<tr>
<td>Placzek et al (2011)</td>
<td>Prospective non-randomised comparative study</td>
<td>Total no. of pts: 23</td>
<td>Not stated</td>
<td>HA pts: 12</td>
<td>Non-HA pts: 47</td>
<td>Average age (years): - HA: 20 (9 - 44) - Non HA: 30 (9 - 47) Sex: HA: 6M/6 F - Non HA 5 M/4 F Average implantation time (days): HA: 213 (91 - 335) Non HA: 165 (91 - 305)</td>
<td>Patients treated for congenital and post-traumatic leg length discrepancies for short stature</td>
<td>HA coated steel 6mm Schanz pin with taper shank and non-tapered thread</td>
<td>Non-HA coated steel 6mm Schanz pin with taper shank and non-tapered thread</td>
<td>Fixation index (F.I.) = max. extraction torque / max insertion torque Pins with no infection: HA F.I. &gt; 1.92 Non HA F.I. = 0.76 Sig diff P &lt; 0.001 Pins with infection: HA F.I. &gt; 0.39 Non HA F.I. &gt; 0.13 No sig diff P &gt; 0.05</td>
<td>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.</td>
</tr>
</tbody>
</table>
All in all the studies except for Pieske; t pins.

Clinical results such as the requirement of removing or changing criteria of Mahan a: As per Schmidts classification of infection (see appendices); b: As per Checketts classification of pin-track infection (see appendices); c: Microbiological:

Moriani et al (28) Prospective, randomized comparative study

<table>
<thead>
<tr>
<th>Total no. of pts: 20</th>
<th>HA pins: 10</th>
<th>Non-HA pins: 10</th>
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<tbody>
<tr>
<td>20 consecutive female patients ≥ 60 years of age with osteoporosis and an AO classification A2 or A3 distal radius fracture.</td>
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</table>

Osteoporotic wrist fractures

3.3-3 mm tapered HA coated pins. | 3.3-3 mm tapered non-HA coated pins |

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

Bone apposition: HA = 73%  
Non-HA = 22%  
Sig diff P < 0.001

Bicortical osteolysis: HA = 4%  
Non-HA = 32%  
Sig diff P < 0.001

No significant diff btw groups with regards to pin-track infections.

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 (2,26) 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 (2,26) 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>
<thead>
<tr>
<th>Study</th>
<th>Clear statement of aims</th>
<th>Is qualitative methodology appropriate?</th>
<th>Design appropriate to address aims?</th>
<th>Appropriate recruitment strategy?</th>
<th>Appropriate data collection?</th>
<th>Appropriate consideration of researcher/participant role?</th>
<th>Ethical issues/Funding?</th>
<th>Sufficiently rigorous data analysis?</th>
<th>Clear statement of findings?</th>
<th>How valuable is research?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peske et al., 2011</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>* 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.</td>
<td>* Prospective, randomized comparative study. * Surgical technique well described. * The</td>
<td>* 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.</td>
<td>* Study approved by the institutional Ethics Committee. * The study had a small sample size. * No power calculations were carried out. * Statistical analyses were adequate.</td>
<td>* Clear statement of findings. * Outcomes pre-specified and well defined.</td>
<td>* 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.</td>
<td></td>
</tr>
<tr>
<td>Placzek et al. 2014</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>* Indications for recruitment into study were clear; patients treated for short stature. * Eligibility criteria not clearly stated. * Assessor blinding was not undertaken.</td>
<td>* 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.</td>
<td>* 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.</td>
<td>* 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.</td>
<td>* Clear statement of findings, although the primary and secondary outcomes measures were not well defined. * The authors stated there was no significant difference in rates of infection between the two groups; this was only specified for grades 3/4 infection. They do not mention any grade 1 or 2 infections in the results.</td>
<td>* 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.</td>
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<tr>
<td>Pummer et al., 2014</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>* 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.</td>
<td>* Prospective, randomized comparative study. * Surgical technique and follow up was well described and standardised. * Patients were reviewed 2 weekly, with radiographs taken on alternate visits.</td>
<td>* 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.</td>
<td>* The author did not state whether external funding or ethical approval was obtained. * Power calculations were not performed in this study. * Confidence intervals were not discussed. * The overall statistical analyses were adequate.</td>
<td>* Clear statement of findings, although the primary and secondary outcomes were not well defined.</td>
<td>* Whilst this study demonstrates a significant difference between rates of loosening and infection between the two groups (p &lt; 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.</td>
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<tr>
<td>Piza et al. 2011</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>* Indications for recruitment into study are clear: pts with short stature undergoing bilateral limb lengthening.</td>
<td>* Prospective, randomized comparative study. * Surgical technique well described. * The</td>
<td>* Baseline characteristics of patients undergoing the lengthening procedures were clearly illustrated. * Number/experience of</td>
<td>* Ethical approval was obtained from the</td>
<td>* The study had a small sample. * No power calculations were carried out. * Statistical analyses were adequate.</td>
<td>* Clear statement of findings. * Outcomes pre-specified and well defined.</td>
<td>* Results of the study were consistent with findings from other similar studies; therefore studies are linked to current clinical practice.</td>
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</tbody>
</table>

Table 3 Critical Analysis of Data.
<table>
<thead>
<tr>
<th>作者和参考文献</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
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<tbody>
<tr>
<td>Patel A et al.</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Caja et al [26]</td>
<td>* Indications for recruitment into study are clear. * Eligibility criteria were not well defined. * Randomisation was used; however the author did not discuss the process used. * Prospective, non-randomised comparative study. * Surgical technique was well described. * There was no evidence of the torque wrench device being calibrated before use to measure the pin extraction torque. * The study did not record infection as an outcome measure and therefore did not report it.</td>
<td></td>
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</tr>
<tr>
<td>Moroni et al [29]</td>
<td>* Indications for recruitment into study are clear. * Eligibility criteria clearly defined. * Randomisation was used; however there was no description on the process other than stating it was done &quot;with use of a computer generated list&quot;. * Prospective, randomized comparative study. * Surgical technique well described. * There was no evidence of the torque wrench device being calibrated before use to measure the pin extraction torque. * The study had a small sample.</td>
<td></td>
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<tr>
<td>Pieske et al [27]</td>
<td>* Indications for recruitment into study were clear; p's presenting with unstable wrist fractures. * Inclusion/exclusion criteria clearly defined. * Patients were randomised using a computer generated list. * Prospective, randomized comparative study. * Surgical technique well described. * Follow up period and investigations clearly described. * Short follow up period of 587</td>
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</table>

**Studied outcome:**

Clinical benefit of hydroxyapatite-coated versus uncoated external fixation

**Rationale:**

The clinical benefit of hydroxyapatite-coated pins compared with conventional stainless steel pins was not always correlated with clinical findings. There was no significant difference between the groups with respect to number of pins removed due to loosening. The study by Caja et al reported on the association of axial deformity with the use of HA-coated pins, but there is no evidence to suggest this is relevant clinically; in terms of pin loosening and malunion.

**Methods:**

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-
et al.[12]. However, there is insufficient evidence to comment on 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.[14] used the classification by Schmidt et al.[19] and reported no significant difference in rates of pin-track infection between HA-coated and uncoated pins. Piza et al.[21] 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.[23] 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.[15] 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.[31] conducted a randomised study investigating patients treated with the hemicallostasis 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[22] 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 size; (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 et al. have demonstrated that computer searches may omit some articles, and consequently, limit the scope of this review[12].

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.[23] 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.
Characteristics
Infection after fixator removal.
Improved pin site care
1996;
Severe soft tissue infection
1997;
2011;
As grade 2, but with definite pin-track secretion, without
External fixation must be
Irritation of pin surrounding area by adhesions and restriction
Treatment
Slight redness, little discharge
J Orthop Trauma
14. Sabharwal S, Green S, McCarthy J, Hamdy R. What's New in
11. Pettine K, Chao E, Kelly P. Analysis of external fixation pin-bone
9. Clasper J, Cannon L, Stapley S. Fluid accumulation and the rapid
8. Leyes M, Noonan K, Forriol F, Canadell J. Statistical analysis of
5. Dahl M, Guli B, Berg T. Complications of limb lengthening. A
4. Maffulli N Fixsen J. Distraction osteogenesis in congenital limb
2. Dahl M, Guli B, Berg T. Complications of limb lengthening. A
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AUTHORS' CONTRIBUTIONS
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.

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

<table>
<thead>
<tr>
<th>Grade</th>
<th>Characteristics</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Minor infection</td>
<td>Improved pin site care</td>
</tr>
<tr>
<td>2</td>
<td>Redness of the skin, discharge, pain, and tenderness in the soft tissue</td>
<td>Improved pin site care, oral antibiotics</td>
</tr>
<tr>
<td>3</td>
<td>Grade 2 but no improvement with oral antibiotics</td>
<td>Affected pin or pins restated and external fixation can be continued</td>
</tr>
<tr>
<td>4</td>
<td>Severe soft tissue infection involving several pins, sometimes with associated loosening of the pin</td>
<td>External fixation must be abandoned</td>
</tr>
<tr>
<td>5</td>
<td>Grade 2 but radiographic changes</td>
<td>External fixation must be abandoned</td>
</tr>
<tr>
<td>6</td>
<td>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</td>
<td>Curettage of the pin track</td>
</tr>
</tbody>
</table>


Appendices 2 Checketts-Otterburn Classification of pin track infection

<table>
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</table>
Patel A et al. Clinical benefit of hydroxyapatite-coated versus uncoated external fixation

infection in leg lengthening for short stature. *JBJS (Br)* 2004; 86-B: 892-897.


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