NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of intramedullary distraction for lower limb lengthening

People can have different length legs from birth, or because of disease or injury. In this procedure, under general anaesthesia, a bone in the shorter leg is cut surgically and a metal lengthening device (distractor) is put inside the bone (intramedullary) across the cut bone. It may be done to a bone in the upper or lower leg. After the operation, the device is gradually lengthened while new bone forms across the cut, so increasing the length of the bone. There are different techniques used to lengthen the distractor depending on the device used. The process of lengthening and healing takes several months, during which partial weight bearing is possible. The main aim is to lengthen the leg and reduce disability.

Contents

Abbreviations

Word or phrase	Abbreviation
Bone healing index	BHI
Bone marrow aspirate concentrate	BMAC
Confidence interval	CI
Energy dispersive x-ray spectroscopy	EDX
Iliotibial band	ITB
Intramedullary skeletal kinetic distractor	ISKD
Intramedullary	IM
Limb reconstruction system	LRS
Lengthening and then nailing technique	LATN
Limb length discrepancy	LLD
Lengthening over the nail	LON
Limb Deformity-Scoliosis Research Society score	LD-SRS score
Mean difference	MD
Non-randomised study	NRS
Not reported	NR
Risk difference	RD
Range of motion	ROM
Randomised controlled trial	RCT
Scanning electron microscopy	SEM
Visual analogue score	VAS

Introduction

The National Institute for Health and Care Excellence (NICE) prepared this interventional procedure overview to help members of the interventional procedures advisory committee (IPAC) make recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and professional opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This overview was prepared in June 2021.

Procedure name

- intramedullary distraction for lower limb lengthening

Professional societies

- British Limb Reconstruction Society
- British Orthopaedic Association
- British Society for Children's Orthopaedic Surgery

Description of the procedure

Indications and current treatment

People may have different or deficient limb lengths because of trauma or infection (acquired) or, because of hypoplasia or dysplasia of the femur or tibia (congenital). Unequal leg length can cause a limp, and limit functional ability and have effect on other joints.

Lengthening of an abnormally short lower limb can be done after an osteotomy using an external fixation device. This exerts force along the long axis of the bone to induce new bone formation (distraction osteogenesis). The main problems with external fixation include: infection of the pin tracts, and external frames that are impractical and aesthetically unacceptable. Once the external fixation is removed, in some people with underlying bone pathology, new bone is augmented by either an internal plate fixation or an IM nail.

What the procedure involves

Once inserted and fixed, IM distraction systems can be lengthened over time using different technique. The aim is to lengthen the bone in a controlled manner.

With this procedure, under general anaesthesia, an osteotomy is done while avoiding damage to the periosteum and its blood supply. The adjustable IM nail-like device is then implanted into the IM space. Its proximal and distal sections are fixed to the relevant section of the bone with sterile locking screws. It then exerts a force along the long axis of the bone, which stimulates new bone formation (distraction osteogenesis) in the gap, causing bone lengthening. Over

days, weeks or months, sequential distractions are used to produce the target limb length.

Different devices achieve distraction in different ways.

Soon after the procedure, with help from the physiotherapy team, people are able to partially weight bear. After clinical assessment, and when there is radiological evidence of adequate bone consolidation across the gap, full weight bearing is possible. The intramedullary device is then usually removed after about 2 years using standard surgical techniques.

Efficacy summary

Mean lengthening achieved

In a systematic review of 10 studies comparing 3 methods of lower limb lengthening, patients who had external fixation alone (in 2 studies) had a greater increase in lengthening (mean 60 mm) than those who had external fixation with an IM nail (5 studies, mean 54 mm) or an IM nail alone (3 studies, mean 44 mm; Brewster 2010).

In a systematic review and meta-analysis of 4 studies comparing LATN with the conventional Ilizarov method for limb lengthening, patients who had LATN gained no more length than those who had the conventional procedure. The pooled results (from 2 studies) showed that there was no statistically significant difference in length gained between the 2 treatment groups (MD = −0.30, 95% CI, −0.72 to 0.12; p=0.16, I^2=80%; Xu 2017).

In a Canadian Agency for Drugs and Technologies in Health (CADTH) report of 3 NRS on lower limb lengthening with a magnetically driven IM nail, 2 studies (Laubscher 2016, Szymczuk 2017) reported that mean lengthening was higher in the LRS external fixation group than in the magnetically driven IM nail group (Laubscher 2016: 59.7 mm compared with 51.4 mm; Szymczuk 2017: 5.55 cm compared with 4.75 cm, p=0.052) but did not achieve statistical significance. One study (Hammouda 2017) reported that there was no statistically significant difference in the mean lengthening between the magnetically driven IM nail group and the mechanically activated ISKD group (5.6 cm compared with 5.2 cm, p=0.35). The lengthening goal was achieved in most patients and in all treatment groups in the 3 studies (Young 2017).

In a systematic review of 15 studies on mechanically activated ISKD for bone lengthening in the femur or tibia, 9 studies reported that the mean lengthening achieved in patients ranged from 31 mm to 49 mm across the studies.

Lengthening goals were not explicitly stated in this systematic review (Nageeb 2014).

In a retrospective comparison of femoral lengthening with 2 different magnetically controlled IM nails (Precice and Stryde nails), statistically significant differences were found between the 2 groups for distraction rate (average of 0.6 mm/day for Stryde and 0.9 mm/day Precice for, p=0.003; Galal 2021).

Mean lengthening time

In the systematic review of 10 studies, the mean time to lengthening was less in patients who had IM nail alone (18 days/cm) than those who had external fixation with IM nail (23 days/cm) or external fixation alone (46 days/cm; Brewster 2010).

Percentage of limbs in which target lengthening was achieved

In the systematic review of 15 studies, 8 studies reported that target lengthening was achieved in 89% to 100% of operated limbs. Two studies reported that target lengthening was achieved in 35% to 100% of limbs (Nageeb 2014).

Mean lengthening rate (mm/day)

In the systematic review of 15 studies, 5 studies reported that the mean lengthening rate ranged from 0.62 mm/day to 1.9 mm/day (Nageeb 2014).

In a retrospective cohort study of 56 patients, the rate of distraction was statistically significantly higher with magnetically driven IM nails (39 limbs,1.0 mm/day) than with LON (20 limbs, 0.8 mm/day) for femoral lengthening ($p<0.001$; Fragomen 2018).

LLD

In the retrospective cohort study of 56 patients, patients in the IM nail group had a lower mean postoperative residual LLD (difference between desired length and final length) than those in the LON group (0.3 mm compared with 3.6 mm, p=0.007; Fragomen 2018).

Bone healing (mean distraction and consolidation or healing index)

In the systematic review and meta-analysis of 4 studies, patients who had the LATN procedure had better consolidation indices than those who had the conventional Ilizarov method. Pooled analysis of 3 studies showed that there was a statistically significant difference in the consolidation indices between the

2 groups (MD = −19.97; 95% CI, −21.59 to −18.35; p<0.00001, I^2=100%; Xu 2017).

In the systematic review of 15 studies, 3 studies reported that the mean consolidation time ranged between 80 to 152 days. The mean consolidation index across 7 studies ranged between 2.2 mm/day to 12.7 mm/day and the mean distraction index across 6 studies ranged between 0.2 mm/day to 1.7 mm/day (Nageeb 2014).

In the CADTH report, 1 study (Szymczuk 2017) reported that distraction index (0.7 mm/day compared with 0.7 mm/day, p=0.99) and consolidation index (34.77 cm/day compared with 29.33 cm/day, p=0.08) were similar in the magnetically driven IM nail group and LRS external fixation groups. Also, 1 study (Laubscher 2016) reported that the mean healing index was statistically significantly shorter in the magnetically driven IM nail group than the LRS external fixation group (31.3 days/cm compared with 47.1 days/cm, p<0.001; Young 2017).

In the retrospective cohort study of 56 patients, time to union was statistically significantly shorter in the IM nail group than that in the LON group (3.3 months compared with 4.5 months, p=0.001. Also, BHI was not statistically significant different between the groups (1.0 month/cm compared with 1.4 month'/cm, p=0.101; Fragomen 2018).

In a retrospective matched pair analysis of 34 patients, the distraction index was statistically significantly different in the mechanically activated ISKD group than in the motorised IM nail (Fitbone) group (0.99 mm/day compared with 0.55 mm/day, p=0.001). Also, the mean weight bearing index differed statistically significantly between the mechanically activated ISKD group and the motorised IM nail (Fitbone) group (32 days/cm compared with 52 days/cm, p=0.001;Thaller 2020).

In the retrospective comparison of femoral lengthening with Precice and Stryde nail), statistically significant differences were found between the 2 groups for BHI (average of 0.84 months/cm for Stryde and 0.67 months/cm for groups, p=0.04; Galal 2021).

Mean time to full weight bearing

In the systematic review of 15 studies, 3 studies reported that mean time to full weight bearing ranged from 1 week to 20.5 weeks (Nageeb 2014).

In the CADTH report, 1 study (Laubscher 2016) reported that mean time to full weight bearing was statistically significantly shorter in the magnetically driven

IM nail group than the LRS external fixation group (3.6 months compared with 4.8 months, p=0.02; Young 2017).

ROM

In the CADTH report, 2 studies (Szymczuk 2017, Laubscher 2016) reported that the ROM was not statistically significantly better in the magnetically driven IM nail group than in the LRS external fixation groups. In 1 study (Szymczuk 2017), ROM was better retained at the end of lengthening and at consolidation (p<0.001) in the magnetically driven IM nail group than in LRS external fixation group. In 1 study (Laubscher 2016), there was a higher rate of preservation of knee range of movement after lengthening in the magnetically driven IM nail group (100%) than in the LRS external fixation group (92% [12/13]; p value not reported; Young 2017).

In the retrospective cohort study of 56 patients, knee flexion at the end of distraction was greater in IM nail group than in the LON group (103 degrees compared with 89 degrees, p=0.006), but this difference was no longer seen after 1 year (123 degrees compared with 119 degrees, p=0.464; Fragomen 2018).

In the retrospective comparison of femoral lengthening with Precice and Stryde nails, there were no statistically significant differences between the 2 groups for loss of ROM for adjacent joints (hip, knee). There was also no statistically significant difference between the tw2o groups for LD-SRS score at 6 months compared with preoperative scores (preoperative score 3.9 for Stryde and 4 for Precice, p=0.09; 6-month postoperative score 4.1 4.4 for Stryde and 4.4 for Precice, p=0.07; Galal 2021).

External fixation index

In the systematic review and meta-analysis of 4 studies, patients who had LATN had better external fixation indices than those who had the conventional Ilizarov method. The pooled results (from 3 studies) showed a statistically significant difference in the external fixation index between the 2 treatment groups (MD −50.21, 95% CI, −51.83 to −48.59; p<0.00001; I^2 = 99%; Xu 2017).

Patient reported outcomes (measured by patient interviews)

In the CADTH report, 1 study (Laubscher 2016) reported that, after treatment, patients interviewed in the magnetically driven IM nail group were more satisfied with the cosmetic appearance of their scar after femoral lengthening, experienced less pain (as measured with the mean VAS score) and were more able to do activities of daily living throughout lengthening than patients in the LRS external fixation group (Young C 2017).

Safety summary

Overall complications

The overall complication rate was 34% (332/983) in a systematic review of 41 studies of externally controlled (motorised or magnetically driven) IM bone lengthening nails. Of these, 3% (28/983) were type 3B complications (with new pathology or permanent sequelae), 5% (45/983) were type 3A complications (not achieving the lengthening goal), 15% (146/983) were type 2 complications (with substantial change in treatment) and 11% (113/983) were type 1 complications (with minimal intervention). The overall complication rate per bone segment was 46% for studies reporting the use of an externally controlled motorised IM nail and 31% for studies reporting the use of an externally controlled magnetically driven IM nail (Frost 2021).

The complication rate in the mechanically activated ISKD group was not statistically significantly higher than in the magnetically driven IM nail cohort (39% [3/13] compared with 23% [7/18], p=0.45) in an NRS (Hammouda 2017) included in the CADTH report. In the same report, in another NRS (Szymczuk 2017), adverse events classified as 'problems' were statistically significantly lower in the magnetically driven IM nail group than in the LRS external fixation group (8 compared with 32, p<0.001; Young 2017).

Complications in the magnetically driven IM nail cohort were lower than in the LON cohort (18% [7/39] compared with 45% [9/20], p=0.027) in the retrospective cohort study of 56 patients (Fragomen 2018).

Device-related complications

Device-related complications were seen in 12% (122/983) of segments in the systematic review of 41 studies. These were mainly related to the distraction mechanism (in 5%, 45/983), mechanical strength (in 5%, 44/983, 2 of these were type 3B complications) and attachment failure in 3% (33/983) of bone segments. One per cent (13/983) of segments failed to achieve the planned lengthening goal because of device-related type 3A complications (Frost 2021).

Hardware malfunction complications ranging from 6% to 33% were reported in 7 studies in the systematic review of 15 studies. Runaway nails (uncontrolled rapid lengthening of more than 1.5 mm/day) ranging from 8% to 100% were reported in 10 studies. Non-distracting or difficult-to-distract nails (defined as 'nails that fail to distract in-situ despite increasing the activity level and manually rotating the lower extremities by the patients themselves or with assistance from family members') ranging from 2% to 50% were reported in 9 studies. Jammed nails were reported in 1% to 33% of operated limbs (in which the lengthening

mechanism jammed because of implantation procedure) in 3 studies (Nageeb 2014).

Broken magnetically controlled IM nails were reported in a case report of 2 patients. In 1 patient, 2 femoral Stryde implants broke through the proximal locking screw hole, 1 on the right at 413 days and 1 on the left at 504 days during nail removal. In another patient, 1 femoral nail broke through the area containing the magnet at 325 days during walking. All these nails were removed using 2 different surgical techniques and reimplanted with different nails (Rolfing 2021).

Mechanical nail failure needing exchange with other nails was reported in 3 femoral lengthening procedures in the Precice nail group compared with none in the Stryde nail group in a retrospective comparison of treatment with 2 different magnetically controlled IM nails. Delayed consolidation that needed a BMAC injection was reported in 1 patient in Precice group and 4 patients in the Stryde group (Galal 2021).

Bone-related complications

In the systematic review and meta-analysis of 4 studies, pooled analysis (3 studies) showed that there was no statistically significant difference in refracture between the LATN group and the conventional method group (RD = -0.02, 95% CI –0.06, 0.01; p=0.21, I^2=69%). Pooled analysis (3 studies) showed that there was no statistically significant difference in axial deviation between the LATN group and the conventional method group (RD = -0.10, 95% CI –0.15, –0.05; p=0.22, I^2=57%; Xu 2017).

Complications related to bone regeneration were seen in 8% (78/983) of bone segments in the systematic review of 41 studies. These were mainly due to premature consolidation in 2% (19/983) of segments, or delayed healing in 5% (46/78) of segments. Other causes include secondary malalignment in 3 fractures in 8 segments and other reasons in 2 segments. Four of these complications were type 3B (with new pathology or permanent sequelae) and 7 were type 3A complications (not achieving the lengthening goal; Frost 2021).

Insufficient bone regeneration causing delayed healing or non-union (needing additional surgical procedures to achieve union) are other common complications reported in the systematic review of 15 studies. This ranged from 8% to 38% across 6 studies. Premature consolidation (ranging from 7 to 36%) was reported in 5 studies. Non-union (ranging from 1% to 33%) was reported in 4 studies. Angular deformity was reported in 2 patients in 1 study (Nageeb 2014).

In a retrospective analysis of 366 removed magnetically controlled IM lengthening devices, there were radiological bone abnormalities at the junction of the telescopic nails at the time of nail removal (mean 434 days). The difference in

bone abnormalities were statistically significantly different between the 3 types of IM lengthening devices used (Stryde nails 77% [20/26] versus Fitbone nails 2% [4/242] and Precice nails 1% [1/98]; p<0.001). Focal osteolysis with periosteal reaction at the telescoping interface was seen in 12% (3/26) for Stryde nails, but not in either Fitbone or Precice nails. The authors stated that this was likely to be related to corrosion. Bony overgrowth covering the interlocking screws were noticed in many of these patients (Iobst CA 2021).

Similar results were reported in 30 bone segments with magnetically controlled IM nails in a cross-sectional study of 27 patients (periosteal reaction in 12 segments, cortical hypertrophy in 12 segments and discolouration in many removed nails; Rolfing 2021).

In another retrospective study of 57 lengthening procedures done with the magnetically controlled IM Stryde nails, there were implant-specific osteolytic changes in 35% (20/57) of segments 10 months after surgery. Forty per cent (8/20) of these patients reported pain at rest and ambulation during consolidation, 42% (24/57) of nails were removed and 83% (20/24) of patients reported macroscopic corrosion at the nail's telescoping junction. Before implant removal, there was osteolysis in 55% (11/20) of lengthened segments. Implant retrieval analysis using SEM showed pitting and crevice corrosion at the nail junction. EDX analysis detected chromium as the main metallic element of corrosion (Frommer 2021).

Joint-related complications

In the meta-analysis of 4 studies, pooled analysis (3 studies) showed that there was a statistically significant difference in joint contracture between the LATN group and the conventional method group (RD = –0.04, 95% CI–0.10, 0.02; p=0.0003, I^2=69%; Xu 2017).

Joint-related complications were reported in 6% (61/983) of segments in the systematic review of 41 studies. These included contractures in 5% of segments (53/983), joint subluxation in 6 segments, and dislocation or pain in 1 segment each (Frost 2021).

Joint contractures were reported in 2 patients in 1 study included in the systematic review of 15 studies (Nageeb 2014).

Infections

In the systematic review and meta-analysis of 4 studies, the pooled analysis of 4 studies showed that there was a statistically significant difference in pin tract infection between the LATN procedure and the conventional method group (RD = −0.13; 95% CI, −0.19 to 0.06; p=0.0002, I^2=79%) (Xu 2017). The pooled

analysis of 3 studies showed that there was no statistically significant difference in IM infection between the LATN and the conventional method group (RD = 0.05, 95% CI –0.01, 0.11; p=0.11, I^2=56%; Xu 2017).

Infection rates were lower for the IM nail alone group (0%) than the external fixation alone group (39%) and external fixation with IM nail group (6.9%) in the systematic review of 10 studies. There were more superficial pin tract infections (36%) and fewer deep infections (3%) in the external fixation alone group. In the external fixation with IM nail group, there were more deep infections (6%) and fewer superficial pin tract infections (1%) (Brewster 2010).

Complications such as pin site or superficial infections were reported less frequently with externally controlled magnetically driven IM nail lengthening than with LRS external fixation in 2 non-randomised studies included in the CADHT report (Young C 2017).

Infections were reported in fewer than 1% of bone segments (8/983) in the systematic review of 41 studies with externally controlled motorised or magnetically driven IM bone lengthening nails. These included superficial soft tissue infection in 3 operated segments, deep soft tissue infection in 1 limb and osteomyelitis in 4 segments (3 type 3A and 1 type 3B complications; Frost 2021).

Infections (superficial in 2 operated limbs and deep in 1 limb) were reported in 3 included studies in the systematic review of 15 studies (Nageeb 2014).

Soft tissue complications

Soft tissue related complications were reported in 1% (13/983) of segments in the systematic review of 41 studies. These included pain in 5 segments (type 1), skin problems in 3 segments (type 1 and 2), and other complications in 5 segments, of which 2 were compartment syndrome problems (with new pathology or permanent sequelae; Frost 2021).

Compartment syndrome was reported in 1 patient in a study included in the systematic review of 15 studies (Nageeb 2014).

Late onset of pain was reported in 8 patients with magnetically controlled IM nail lengthening in a cross-sectional study of 27 patients (Rolfing 2021).

Vascular complications

Vascular complications were reported in 1% (10/983) of segments in the systematic review of 41 studies with externally controlled motorised or magnetically driven IM bone lengthening nails. These included 6 type 3B complications (vascular damage in 1, deep vein thrombosis in 4 and

arteriovenous fistula of the posterior tibial artery decompensated during tibial lengthening in 1) and 4 type 1 complications (haemorrhage in 2 and other complications in 2 segments; Frost 2021).

Neurological complications

Neurological complications were reported in less than 1% of segments (8/983) in the systematic review of 41 studies with externally controlled motorised or magnetically driven IM bone lengthening nails. These included paraesthesia in 5 segments (of which 1 was a type 3A complication) (Frost 2021).

Other complications

Other complications (6 patient related, 11 surgical related and 1 other) were reported in 2% (18/983) of segments in the systematic review of 41 (Frost 2021).

Anecdotal and theoretical adverse events

In addition to safety outcomes reported in the literature, professional experts are asked about anecdotal adverse events (events which they have heard about) and about theoretical adverse events (events which they think might possibly occur, even if they have never happened). For this procedure, we received no questionnaires.

The evidence assessed

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to IM distraction for lower limb lengthening. The following databases were searched, covering the period from their start to 14.04.2021: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the Internet were also searched. No language restriction was applied to the searches (see the literature search strategy). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The inclusion criteria were applied to the abstracts identified by the literature search. Where selection criteria could not be determined from the abstracts the full paper was retrieved.

Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, or a laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising study methodology, unless they reported specific adverse events that were not available in the published literature.
Patient	Patients with limb length deficiency of any aetiology.
Intervention/test	IM distraction (or distraction osteogenesis) for lower limb lengthening (implants can either be mechanically activated nails, motorised nails, or magnetically driven nails).
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

List of studies included in the IP overview

This IP overview is based on 2,714 patients from 5 systematic reviews, 2 retrospective cohort studies, 2 case series, 1 retrospective matched case series, 1 cross-sectional study and 1 case report.

Other studies that were considered to be relevant to the procedure but were not included in the main summary of the key evidence are listed in the appendix.

Summary of key evidence on intramedullary distraction for lower limb lengthening

Study 1 Brewster MB (2010)

Study details

Study type	Systematic review
Country	UK
Study period	Search period NR. Databases searched: PubMed; additional studies were identified from reference lists of included studies.
Study population and number	n=619 patients who had limb lengthening (10 studies: 3 prospective case series, 2 retrospective case series, 3 retrospective reviews, 1 retrospective matched case series, 1 prospective non-randomised cohort study). 3 methods of lengthening were compared: 1. external fixation alone (n=335, 2 studies) 2. IM nail alone (n=54, 3 studies) 3. IM nail with external fixation (n=230, 5 studies)
Age and gender	NR
Study selection criteria	Inclusion criteria: studies in English, limited to humans, on limb lengthening involving the tibia or femur, with a minimum of 10 bones, reporting lengthening of bone achieved and timing of lengthening and infection data. Exclusion criteria: lengthening using Taylor special frames were excluded due to prolonged, complex correction process involved. Studies with inadequate raw data available to recalculate lower limb results were excluded.
Technique	1. external fixation alone (n=335, 2 studies) 2. IM nails alone (n=54, 3 studies) 3. IM nail with external fixation (n=230, 5 studies)
Follow up	Varied across studies and between comparator groups.
Conflict of interest/source of funding	No conflicts of interest were declared. Authors declared that no funding was received for this study.

Analysis

Follow-up issues: length of follow up was varied and not consistent in the included studies and between treatment groups.

Study design issues: search was done in only 1 database; study selection criteria were described but lacked details on screening and critically appraisal of included studies. Most of the included studies were retrospective comparisons and susceptible to bias. Confounding factors were not considered when comparisons were made and outcomes were analysed. There is variation in reporting data across studies and data on infection rates were limited. Mean scores were calculated.

Study population issues: patient population and demographic characteristics were clearly stated but they were diverse. 4 papers included some patients who had concurrent angulation corrections.

Key efficacy findings

- Number of patients analysed: 619

Study details	Median follow up, months (range)	Lengthening method	Median lengthening index, days/cm (range)	Mean length increase, mm (range)	Infection rates %
External fixation with IM nail					
Lee 1997 retrospective review	37 (24-59)	14 external fixations	50 (36-76)	40 (37-78)	29% pin tract infections
	30 (24-42)	7 external fixations + IM nail	14 (13-18)	48 (36-60)	0
Huang 1997 prospective cohort	27 (24-80)	59 external fixations	57 (31–134)	37 (30–80)	0 deep infections
		12 external fixations +IM nail	20 (12–29)	40 (32–50)	8% deep infections
Wang 1999 retrospective review	73 (30-100)	23 external fixations	41 (6-80)	67 (30-145)	30% pin tract infections
	48	1 external fixation + IM nail	28	63	0
Paley 1997 retrospective matched case series	44 (24-72)	32 external fixations	51	58 (20-130)	3% nail removal for infection
	34 (24-60)	32 external fixations + IM nail	21	52 (20-130)	3% pin removal
Kocaoglu 2004 retrospective case series	44 (26-62)	42 external fixations + IM nail	31.2	63 (25-115)	Pin tract infections unspecified; 2.5 pins removed for infection
External fixation alone					
Maffuli 1996 Retrospective review	>12	281 external fixations	35.3 (26-43)	93 (30-80)	62-78% pin tract infections 5% pin removal 1 case of osteomyelitis

Catagni 2005 prospective case series	75 (12-192)	54 external fixations	41	70 (50-110)	48.2% pin tract infections, some nails removed
IM nail alone					
Baumgart 1997 prospective case series	>24	12 motorised IM nail	12.4 42 healing index	NR	0
Singh 2006 retrospective case series	36 (12-48)	22 motorised IM nail	28.5 (18.8–70.9)	40 (27–60)	0
Cole 2001 prospective case series	28 (12-48)	20 ratcheted IM nail	12 (6-25)	49 (29-110)	0

Mean lengthening index, days/cm

	Mean lengthening index, days/cm	**Mean length increase, mm (range)**
External fixation alone (2 studies)	45.9	60
IM nail alone (3 studies)	17.6	44
External fixation with IM nail (5 studies)	22.8	54

Key safety outcomes

Complications

	External fixation alone	**IM nail alone**	**External fixation with IM nail**
Superficial infections, %	36.2	0	1.4
Deep infections, %	2.5	0	5.5

Study 2 Xu WG (2017)

Study details

Study type	Systematic review and meta-analysis
Country	China
Study period	Search period: inception to 22 May 2015 Databases searched: Cochrane Central Register of Controlled Trials (CENTRAL), PubMed, EMBASE, and the ISI Web of Knowledge. References of included studies were searched for additional studies, grey literature was also identified. Further internet searches were done from articles from Congress, such as those of the European Federation of National Associations of Orthopaedic Sports Traumatology and British Orthopaedic Association Annual Congress.
Study population and number	n=212 patients (354 limbs) who had lower limb lengthening (4 studies: 1 RCT), 2 clinical controlled trials and 1 retrospective cohort study) lengthening and then nailing (LATN [94 patients, 183 limb]) versus conventional Ilizarov method (118 patients,171 limbs) number of tibiae: LATN (n=142), conventional method (n=187)
Age and gender	Age range between 22 to 30 years.
Study selection criteria	Inclusion criteria: clinical controlled trials (RCT or non-RCT); patients having leg lengthening operations with 1 group having the LATN method and 1 group having the conventional Ilizarov method; and reported surgical outcomes (external fixation index, percentage length increase, consolidation index, and incidence of complications).
Technique	Intervention: longitudinal osteotomy combined with the LATN or LON technique. After the desired length was achieved, the fixator was removed and 2 distal interlocking screws were inserted; partial weight bearing was continued until full consolidation. Comparator: in the conventional Ilizarov technique the fixator was removed when there was a radiographic confirmation of 3 cortices in the regenerate column of both anterio–posterior and lateral X-ray images, and then the individual could try to bear weight fully.
Follow up	Varied across studies and between comparator groups.
Conflict of interest/source of funding	No conflicts of interest were declared. Authors declared that no funding was received for this study.

Analysis

Follow-up issues: length of follow up was varied and not consistent in the included studies and between treatment groups.

Study design issues: comprehensive searches were done; study selection was done independently by authors and any disagreements were resolved by consensus. Quality assessment of RCT was assessed using the

Cochrane collaboration's tool for assessing risk of bias and the non-RCTs were assessed using a methodological index for NRS (MINORS) form. The RCT had a low risk of bias and the non-RCTs had a high risk of bias (inadequate information on the randomisation methods and blinding methods). Authors of the studies were contacted for missing data or further information. A meta-analysis was done.

Very few studies were included in the review. Studies were heterogenous in terms of indications, devices used, and the surgical techniques used for limb lengthening).

Key efficacy findings

- Number of patients analysed: 212 patients (354 limbs)

External Fixation Index between LATN and conventional method (3 studies)

The pooled results (from 3 studies) demonstrated a significant difference in the external fixation index between the 2 treatment groups (MD −50.21, 95% CI, −51.83 to −48.59; $p < 0.00001$; $I^2 = 99\%$). So, patients who had LATN procedure had better external fixation indices than those who had the conventional procedure.

Length gained between LATN and conventional methods (2 studies)

The pooled results (from 2 studies) demonstrated that there was no significant difference in length gained between the 2 treatment groups (MD = −0.30, 95% CI, −0.72 to 0.12; p=0.16, I^2=80%). Therefore, patients who had LATN procedure gained no more length than those who had the conventional procedure.

Consolidation Index between LATN and conventional methods (3 studies)

Pooled analysis (from 3 studies) showed a statistically significant difference in the consolidation indices between the 2 groups (MD = −19.97; 95% CI, −21.59 to −18.35; p<0.00001, I^2=100%). Therefore, patients who had the LATN procedure had better consolidation indices than those who had the conventional procedure.

Key safety outcomes

Adverse events between LATN and conventional methods (4 studies)

Adverse event	LATN Method (n)				Conventional method (n)			
	Rozburch 2008	Guo 2012	Lan 2013	El Husseini 2013	Rozburch 2008	Guo 2012	Lan 2013	El Husseini 2013
Pin tract infections	1	8	2	5	1	11	11	9
IM infection	1	0	0	3	0	0	0	0
Refracture	0	-	0	0	0	-	0	3
Axial deviation	-	0	0	0	-	1	8	5
Joint contracture	0	-	6	1	0	-	8	6
Delayed consolidation	-	1	-	3	-	2	-	0
Total	**2**	**9**	**8**	**12**	**1**	**14**	**27**	**23**

Pin tract infections
Pooled analysis (of 4 studies) showed that there was a significant difference in pin tract infections between the LATN group and the conventional method group (RD = −0.13; 95% CI, −0.19 to 0.06; p=0.0002, I^2=79%). Therefore, patients who had the LATN procedure had fewer pin tract infections than those who had the conventional procedure.

IM infection
Pooled analysis (of 3 studies) showed that there was no statistically significant difference in IM infection between the LATN group and the conventional method group (RD = 0.05, 95% CI –0.01, 0.11; p=0.11, I^2=56%).

Refracture
Pooled analysis (of 3 studies) showed that there was no significant difference in refracture between the LATN group and the conventional method group (RD = -0.02, 95% CI –0.06, 0.01; p=0.21, I^2=69%).

Axial deviation
Pooled analysis (of 3 studies) showed that there was no significant difference in axial deviation between the LATN group and the conventional method group (RD = -0.10, 95% CI –0.15, –0.05; p=0.22, I^2=57%).

Joint contracture
Pooled analysis (of 3 studies) showed that there was a significant difference in joint contracture between the LATN group and the conventional method group (RD = –0.04, 95% CI–0.10, 0.02; p=0.0003, I^2=69%).

Study 3 Nageeb MA (2014)

Study details

Study type	Systematic review
Country	Egypt
Study period	Search was done between August to November 2012. Databases searched: PubMed, Ovid Medline, Ovid Full Text, Springer link, EBSCO Medline, Science Direct, ISI Web of Knowledge, and Google Scholar. References of included articles and previous reviews and meta-analyses were reviewed to identify additional relevant articles.
Study population and number	n=440 patients (484 operated limbs: femora 222; tibiae 43) 15 studies (case series) Causes of LLD needing ISKD implantation: trauma (n=185), congenital (n=162), cosmetic (n=29), infection (n=14), tumour (n=9), burn, polio, knee arthrodesis (1 each), and other causes (n=31).
Age and sex	mean age ranging from 24 years to 40 years 173 male and 101 female patients.
Study selection criteria	Inclusion criteria: peer reviewed studies (prospective, retrospective, cross-sectional, or interventional) published in the English language, reporting ISKD implantation in the femur or tibia of skeletally mature patients, with extractable data about the study population and outcomes. Exclusion criteria: studies in languages other than English; animal studies; studies describing lengthening techniques using devices other than ISKDs; and unpublished data and abstracts.
Technique	ISKD bone lengthening in femora and tibiae. Tibial lengthening reported in 5 studies Femoral tibial lengthening in 12 studies
Follow up	Mean follow up ranged from 14 to 76 months
Conflict of interest/source of funding	The authors declare that they have no financial or non-financial conflicts of interest.

Analysis

Follow-up issues: follow up was reported in only 8 studies and varied across studies.

Study design issues: comprehensive search was done; 2 reviewers independently reviewed abstracts to identify relevant studies and any disagreements were resolved by consensus. Quality assessment of included studies was done using a checklist of potential sources of bias. Only 6 studies stated inclusion and exclusion criteria and 8 reported the consolidation and distraction indices. Blinding was not possible and there was no

allocation concealment in all studies. Studies were too heterogenous and there is no standardised reporting so a narrative synthesis was done.

Study population issues: studies included different groups of patients; 2 studies did not report which limbs were operated.
Other issues: authors state that the patient's level of activity may not be homogeneous and may be responsible for the variability in daily lengthening.

Key efficacy findings

Number of patients analysed: 440

Clinical outcomes

Clinical outcome	Data are presented as n (%), n (range), or mean ± SD.	Study
Mean time to full weight bearing (week)	1	Cole 2001
	10 (7-14)	Hankemeier 2004
	20.5	Kucukayya 2011
Mean lengthening achieved (mm)	49 (29-110)	Cole 2001
	31 (26-40)	Hankemeier 2004
	46 (15-80)	Simpson 2009
	42.8 ± 12.9 (25-70)	Kenawey 2011
	31 (0-60)	Pappanna 2011
	35 (21-75)	Wang and Edwards 2012
	38 (20-52)	Kucukayya 2011
	40.8 (10-80)	Schiedel 2011
	43 ± 16 (2-10)	Kenawey 2011
Mean lengthening rate (mm/day)	0.82 (0.4-1.7)	Cole 2001
	1.2 ± 0.4 (0.7-2.8)	Kenawey 2011
	0.62	Pappanna 2011
	in 10 patients:1.9 (1.43-2.56) In 2 patients:0.84 (0.75-0.93)	Mahboubian 2012
	1	Kenawey 2011
% of limbs in which satisfactory lengthening was achieved	4 (100%)	Hankemeier 2004
	32 (97%)	Simpson 2009
	37 (100%)	Kenawey 2011
	2 (66%)	Pappanna 2011
	16 (100%)	Wang and Edwards 2012
	8 (89%)	Kucukayya 2011

	88 (53-100%)	Mahboubian 2012
	63 (91%)	Schiedel 2011
	168 (93%)	Burghardt 2011
	57 (100%)	Kenawey 2011
Mean consolidation time (days)	80 (51-111)	Hankemeier 2004
	152 (77-365)	Wang and Edwards 2012
	133 (56-477)	Schiedel 2011
Mean consolidation index (mm/day)	2.9 (1.8-4.1)	Hankemeier 2004
	3.6 ± 0.9 (1.8-6.3) (n=29)	Kenawey 2011
	12.66	Pappanna 2011
	4.87 (2.78-11.2)	Wang and Edwards 2012
	2.2 (1.2-3.5)	Kucukayya 2011
	9.09 (1.26-51.6)	Mahboubian 2012
	3.39 (2.37-9.54)	Schiedel 2011
Mean distraction index (mm/day)	1.2 (0.9-1.8)	Hankemeier 2004
	1.1 ± 0.3 (n=29)	Kenawey 2011
	0.63 (0-1.25)	Pappanna 2011
	0.2-2.5	Wang and Edwards 2012
	1.0 (0.1-2.5)	Schiedel 2011
% of patients in whom additional surgical procedures were done	3 (75%)	Hankemeier 2004
	7 (78%)	Kubiak 2007
	3 (100%)	Pappanna 2011
	6 (38%)	Wang and Edwards 2012
	2 (22%)	Kucukayya 2011
	30 (43%)	Schiedel 2011

Mean time to patient discharge: ranged from 7-10 days (in 3 studies).

Key safety findings

Complications with ISKD procedures

	% (n, ISKDs)	Study	Number of patients	Number of inserted ISKDs
Infection				
Deep	(1/12)	Mahboubian 2012	11	12
Superficial	(1/3)	Pappanna 2011	3	3
	1.75 (1/57)	Kenawey 2011	53	57
Compartment syndrome	(1/57)	Kenawey 2011	53	57

IP overview: intramedullary distraction for lower limb lengthening

Insufficient bone regenerate (causing delayed union)	21 (12/57)	Kenawey 2011	53	57
	8.3 (1/12)	Mahboubian 2012	11	12
	9 (3/33)	Simpson 2009	30	33
	21.6 (8/37)	Kenawey 2011	35	37
	33.3 (1/3)	Pappanna 2011	3	3
	37.5 (6/16)	Wang and Edwards 2012	16	16
Runaway nail (uncontrolled rapid lengthening of > 1.5 mm per day)	21.2 (7/33)	Simpson 2009	30	33
	18.9 (7/37)	Kenawey 2011	35	37
	9.09 (1/11))	Kubiak 2007	9	11
	33.3 (1/3)	Pappanna 2011	3	3
	31.2 (5/16)	Wang and Edwards 2012	16	16
	1	Reynders 2009	1	1
	44.4 (4/9)	Kucukkaya 2011	9	9
	8.33 (1/12)	Mahboubian 2012	11	12
	15.78 (9/57)	Kenawey 2011	53	57
	10 (4/41)	Thonse 2005	41	41
Jammed nail (lengthening mechanism jammed)	0.7 (1/210)	Burghardt 2011	180	242
	33.3 (1/3)	Pappanna 2011	3	3
	27.2 (3/11)	Kubiak 2007	9	11
Difficult to distract nails^	24.2 (8/33)	Simpson 2009	30	33
	2.7 (1/37)	Kenawey 2011	35	37
	33.3 (1/3)	Pappanna 2011	3	3
	18.7 (3/16)	Wang and Edwards 2012	16	16
	10.1 (7/69)	Schiedel 2011	69	69
	1.65 (4/210)	Burghardt 2011	180	242
	1.75 (1/57)	Kenawey 2011	53	57
	50(1/2)	Vitale 2006	2	2
	20 (8/41)	Thonse 2005	41	41
Premature consolidation	36.3 (4/11)	Kubiak 2007	9	11
	33.3 (1/3)	Pappanna 2011	3	3
	11.1 (1/9)	Kucukkaya 2011	9	9
	8.3 (1/12)	Mahboubian 2012	11	12
	7.01 (4/57)	Kenawey 2011	53	57
Non-union	33.3 (1/3)	Pappanna 2011	3	3
	11.1 (1/9)	Kucukkaya 2011	9	9

	8.3 (1/12)	Mahboubian 2012	11	12
	1.2 (3/210)	Burghardt 2011	180	242
Angular deformity	12.5 (2/16)	Wang and Edwards 2012	16	16
Joint contracture	3.5 (2/57)	Kenawey 2011	53	57
Hardware malfunction	10 (2/20)	Cole 2001	18	20
	6.06 (2/33)	Simpson 2009	30	33
	33.3 (1/3)	Pappanna 2011	3	3
	6.2 (1/16)	Wang and Edwards 2012	16	16
	8.3 (1/12)	Mahboubian 2012	11	12
	8.9 (6/69)	Schiedel 2011	69	69
	6.2 (15/210)	Burghardt 2011	180	242
Technique abandoned	33.3 (1/3)	Pappanna 2011	3	3
	33.3 (4/12)	Mahboubian 2012	11	12
	10.1 (7/69)	Schiedel 2011	69	69

^Non-distracting nails were defined as nails that fail to distract in situ despite increasing the activity level and manually rotating the lower extremities by the patients themselves or with assistance from family members.

Study 4 Young C (2017)

Study details

Study type	Systematic review
Country	Canada
Study period	Search period: January 2012 to November 2017 Databases searched: MEDLINE, The Cochrane Library, University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies; a focused internet search was also done.
Study population and number	n=112 patients who had limb lengthening with the Precice IM limb lengthening system or alternative limb lengthening system (LRS external fixation system or ISKD) (3 NRS/retrospective reviews) 1. Szymczuk [2017, US]: n=62 patients with congenital femoral deficiency, with or without fibular hemimelia, who had femoral lengthening (30 Precice IM nail and 32 LRS monoliteral external fixation) 2. Hammouda [2017, US]: n=28 skeletally immature patients who had a reamed IM lengthening nail inserted through the greater trochanter (31 femurs, 13 in Precice group and 18 in ISKD group). 3. Laubscher [2016, UK]: 22 skeletally mature patients that had femoral lengthening procedures (33 femurs, 20 in Precice group and 13 in LRS external fixation group)
Age and gender	1. Szymczuk 2017: mean age 15.4 years in Precice group and 9.4 years in LRS external fixation group; 24 male and 38 female 2. Hammouda 2017: age 7 to 17 years; 17 male and 11 female 3. Laubscher 2016: age 15 to 57 years; 11 male and 11 female
Study selection criteria	Inclusion criteria: published studies (health technology assessments, systematic reviews, meta-analyses, RCTs, NRS, and guidelines), in humans, limited to English language; patients who have growth disturbances secondary to trauma or congenital abnormalities, post-traumatic growth arrests, congenital deformity, infection, bone loss, tumours, non-unions, or achondroplasia; correction of lower or upper limb deformities in adults and children with Precice IM limb lengthening system; reporting clinical benefit (e.g., rate of lengthening, overall lengthening, ROM, gait, pain, functional ability) and Harms (e.g., femoral fissure, spontaneous bony section, transient palsy, pain, fracture, mechanical failure, poor bone formation, lengthening at an inappropriate rate, fat embolisation, deep vein thrombosis, respiratory distress syndrome, equinus ankle deformity). Exclusion criteria: duplicate publications, studies published before 2012, uncontrolled, single-arm trials were excluded.
Technique	Intervention: Precice magnetically motorised IM nail was used for femoral lengthening. Comparators: external fixation using the LRS (2 studies, Szymczuk [2017] and Laubscher [2016]). ISKD (Hammouda 2017).

IP overview: intramedullary distraction for lower limb lengthening

Follow up	Varied across studies and between compactor groups. Szymczuk 2017: mean 86 years and 4.47 years for the Precice and the LRS external fixation groups Hamaoudda 2017: 1.9 years and 4.6 years for the Precice and ISKD groups Laubascher 2016: 14.7 months and 28.8 months for the Precice and LRS fixation groups
Conflict of interest/source of funding	No conflicts of interest were declared. Authors of 1 study (Hammouda 2017) declared financial support from device companies (Precice technologies, Ellipse technologies).

Analysis

Follow-up issues: length of follow up was varied and not consistent in the included studies and between treatment groups.

Study design issues: systematic review followed preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines. comprehensive search was done; studies were screened and selected by 1 reviewer. Included studies had small sample sizes (ranging from 22 to 62 patients), lacked randomisation, patients were unblinded to treatments, and were critically appraised using the Downs and Black checklist. All 3 studies were retrospective comparisons and susceptible to bias. Confounding factors were not considered when comparisons were made and outcomes were analysed. Patient selection criteria, interventions, outcomes were explicitly described in included studies.

Study population issues: patient population and demographic characteristics were clearly stated but they were diverse (in terms of aetiology and age) between comparisons and studies. All studies considered patients having femoral lengthening only.

Key efficacy findings

- Number of patients analysed: 112

Hammouda 2017	**Outcomes**	**Precice (n=13 segments)**	**ISKD (n=18 segments)**	**P value**
	Mean lengthening achieved, cm (range)	5.6 (3-6.7)	5.2 (3.8-6.5)	0.35
Szymczuk 2017	**Outcomes**	**Precice (n=30)**	**LRS external fixation (n=32)**	**P value**
	Lengthening goal, cm (range)	4.97 ± 1.43	5.58 ± 1.82	0.15
	Lengthening goal achieved % (n)	87 (26/30)	88 (28/32)	NR
	Mean lengthening achieved, cm (range)	4.75 ± 1.40	5.55 ± 1.74	0.052
	Distraction index, mm/day (±SD)	0.7 ± 0.18	0.7 ± 0.17	0.99

	Consolidation index, cm/day (±SD)	34.77 ± 11.23		29.33 ± 12.68		0.08
	ROM degrees, (± SD)	**Extension**	**Flexion**	**Extension**	**Flexion**	**P value**
	Preoperative	0.8±3.1	127.7±22.9	0.47±2.18	123.3±12.2	0.35
	Post distraction	0.93 (± 3.3)	96.3 (± 28.2)	-0.6 (± 4.3)	69.9 (± 30.2)	0.0007
	Post consolidation	-0.4 (± 2.1)	121.5 (± 23.1)	0.74 (± 4.9)	81.3 (± 30.1)	< 0.0001
	Final follow up	-0.4 (± 2.0)	119.6 (± 16.5)	-0.7 (± 4.8)	120.2 (± 19.9)	0.90
Laubscher 2016	**Outcomes**	**Precice (n=20)**		**LRS external fixation (n=12)**		**P value**
	Planned lengthening achieved % (n)	100 (20/20)		92 (12/13)		NR
	Mean lengthening, mm (range)	51.4 (25-68)		59.7 (50-70)		NR
	Mean lengthening rate, mm (range)	0.93 (0.67-1.09)		0.83 (0.55-1.13)		NR
	Preservation of knee ROM % (n)	100 (20/20)		92 (12/13)		NR
	Mean healing index, cm/day (range)	31.3 (21.1-43.0)		47.1 (34.4-67)		<0.001
	Mean time to full weight bearing, months (range)	3.6 (2-7)		4.8 (3-7)		0.02

Patient reported outcomes (measured by patient interviews), Laubscher 2016

Outcome	Precice (n=20)	LRS external fixation (n=13)	P value
Cosmetic appearance of scars, mean score* (range)	3.0 (1-5)	7.5 (6-10)	<0.001
Pain, mean VAS score (range)	during lengthening: 4.4 (1-7.5) during consolidation: 2.2 (1-6)	during lengthening: 8.1(5-10) during consolidation: 5.3 (3-7)	<0.001 <0.001
Ability to do daily activities of living, n (%)	90 (18/20)	38 (5/13)	NR
Choose to have treatment again, n (%)	100 (20/20)	68 (9/13)	NR

*0 being best and 10 being worst

Key safety outcomes

Complications

Hammouda 2017	**Precice (n=13 segments)**		**ISKD (n=18 segments)**		**P value**
Complication rate % (n)	23 (3/13)		39 (7/18)		0.45
Szymczuk 2017	**Precice (n=30)**		**LRS external fixation (n=32)**		**P value**
Adverse events*	**Total events**	**Affected segments**	**Total events**	**Affected segments**	**P value**
Problems % (n)	25.8 (8)	23.3 (7)	55.2 (32)	62.5 (20)	<0.001
Obstacles % (n)	61.3 (19)	36.7 (11)	34.5 (20)	31.3 (10)	0.66
Complications % (n)	12.9 (4)	13.3 (4)	10.3 (6)	15.6 (5)	0.99
Total	31	60 (18)	58	81.3 (26)	0.07

*Authors classified adverse events as problems, obstacles, or complications.

Study 5 Frost MW 2021

Study details

Study type	Systematic review
Country	Denmark
Study period	Search done in 2019 and updated in March 2020. Databases searched: PubMed, EMBASE, and the Cochrane Library. Additional studies were identified from reference lists of included studies.
Study population and number	n=782 patients; 983 bone segments (813 femurs ([n 40 studies] and 170 tibiae [in 28 studies]) 41 studies (26 case series, 6 cohort studies, 1 case-control study and 8 case reports) Indications for lengthening (in accordance with the modified Stricker and Hunt classification): 208 with congenital shortening (in 22 studies), 305 with acquired limb shortening (in 29 studies), 111 with short stature (in 14 studies), 158 with unidentified aetiology.
Age and gender	Age range 8-74 years (in 39 studies) 384 were male (in 29 studies), 34 were female (in 33 studies) and 164 were unidentified.
Study selection criteria	Inclusion criteria: published studies (RCTs, prospective and retrospective cohort studies, case-control studies, case series, and case reports with less than 5 segments), conducted in humans in both English and German with no limit on publishing date; studies on bone lengthening (with FITBONE and/or PRECICE nails) on lower extremities, with descriptions of complications (origin, severity, and management) or a statement of no complications. Exclusion criteria: cross-sectional studies or different study designs, duplicate studies, other operation types (studies reporting bone transport treatment, nails used for compression), other indications (no involvement of lower extremities, stump lengthening), other nail types, insufficient description of complications.
Technique	Magnetically driven (PRECICE) and externally controlled motorised (FITBONE) IM nails were used for lower limb lengthening. 214 FITBONE nails (in 15 studies), 747 PRECICE nails (in 27 studies), 22 either FITBONE or PRECICE nails.
Follow up	Varied across studies.
Conflict of interest/source of funding	No conflicts of interest were declared. Study was funded by the authors' institution.

Analysis

Study design issues: systematic review was done according to meta-analysis of observational Studies in epidemiology (MOOSE) guidelines; comprehensive search was done and 2 reviewers independently reviewed, selected studies, evaluated and graded complications. Any disagreements were resolved by consensus. There were no standardised reporting methods in studies. Complications were assessed in relation to segments

lengthened and according to origin (8 main groups and 33 sub-groups) and severity (graded according to modified Black classification 2015 into 4 types) to achieve consistent reporting. Some complications that were not well described might have been downgraded. The Oxford Centre for Evidence-Based Medicine-Levels of Evidence 2009 grading of Harm was used to assess the level of evidence in the included studies. Studies were quality assessed using validated scores (MINORS and Murad et al) and the level of evidence was low. The primary outcome was the risk of type 3B complications resulting in a new pathology or permanent sequelae.

Study population issues: patient population and demographics were diverse.

Key safety findings

- Number of patients analysed: 782 (983 segments)

Complications (categorised **according to origin** (8 groups (soft tissue, joint, vascular, bone, neurological, infection, device-related, others) **and severity:** type 1 (minimal intervention); type 2 (substantial change in treatment); Type 3A (failure to achieve planned lengthening due to a complication); and Type 3B (resulted in new pathology or permanent sequelae).

14 complications could not be categorised due to missing descriptions.

	Severity				
	Grade 1	**Grade 2**	**Grade 3A**	**Grade 3B**	**Total**
Total number of complications, n	113	146	45	28	332
Complications per segment, %	11	15	5	3	34
Complications per segment using Precice nail %					31
Complications per segment using Fitbone nail %					46
Complications per patient, %	14	19	6	4	42
Groups					
Soft tissue, n					**13**
Skin	2	1			3
Pain	5				5
Others	2	1		2*	5
Soft tissue complications per segment %					1
Joint, n					**61**
Pain	1				1
Contracture	19	24	5	5	53
Subluxation				6	6
Dislocation				1	1
Joint complications % of segments					6
Vascular, n					**10**
Vascular damage				1	1

Deep vein thrombosis				4	4
Haemorrhage/haematoma	2				2
Others	2			1 AV^	3
Vascular complications per segment %					1
Bone, n					**78**
Premature consolidation		15	4		19
Delayed healing	16	27	2	1	46
Secondary alignment		1		2	3
Fracture		6	1	1	8
Others	1	1			2
Bone complications per segment %					8
Neurology					8
Paraesthesia	2	2	1		5
Others	3				3
Neurology complications per segment %					0.8
Infection, n					**8**
Superficial soft tissue	2	1			3
Deep soft tissue		1			1
Osteomyelitis			3	1	4
Infection complications per segment %					0.8
Device related, n					**122**
Distraction mechanism	16	20	9		45
Mechanical strength	25	14	3	2	44
Attachment failure	8	24	1		33
Device related complications per segment %					12
Others, n					**18**
Patient (request to stop lengthening procedure)			6		6
Surgical (intra-articular nail placement causing irritation and residual deformity)		3	7	1	11
Others			1		1
Others, complications per segment %					1.8

*compartment syndrome

^ arteriovenous fistula of the posterior tibial artery decompensated during tibial lengthening and an embolisation procedure had to be done.

6% (11/177) of complications occurred intraoperatively (n=5) or perioperatively (n=6) before the start of distraction, and 94% of complications (166/177) occurred during distraction (in 85 segments), or after the end of distraction (in 81 segments).

Subgroup analysis of complications was not possible between nail types due to low numbers. Authors state that studies with fewer than 20 patients had more complications per segment compared with studies with more than 40 patients.

Study 6 Fragomen AT (2018)

Study details

Study type	Retrospective cohort study
Country	USA
Recruitment period	LON (2005-9) Magnetic remote controlled IM nail (2012- 14)
Study population and number	n= 56 patients who had femoral or lower limb lengthening . (35 patients with IM nail lengthening (40 femurs) and 21 with LON technique (22 femurs) Indications for lengthening: • posttraumatic incident (malunion): 12 in IM nail group, 11 in LON group • congenital: 11 in IM nail group, 1 in LON group • metabolic: 4 in IM nail group, 2 in LON group • short stature: 7 in IM nail group, 3 in LON group.
Age and gender	IM nail group: mean 29.7 years; LON group: 32.4 years IM nail group: 78% (31/40) male; LON group: 90% (18/20) male
Study selection criteria	Inclusion criteria: Exclusion criteria: patients with active infection or irregular bone diameter or deformity that would prevent insertion of an IM device.
Technique	LON technique used an antegrade nailing method. First IM nail is inserted and external fixator (frame) is applied with pin insertion. Then at the end of lengthening phase, the nail is locked and the fixator is removed. Magnetically driven IM lengthening nail is done with a Precice nail. Both antegrade and retrograde nailing approaches are used. The ITB is released in these patients and also extended posteriorly to include the lateral intramuscular septum. All patients were given anticoagulants for 4 weeks. Physical therapy focused on ambulation with weight bearing restrictions. Weight bearing as tolerated was allowed for LON patients and for IM nail patients, it was dependent on the nail diameter. In both groups IM nails were removed after 1 year.
Follow up	LON group: minimum follow up was 13 months (average, 27 months; range, 13–38 months) IM nail group: 21 months (average, 31 months; range, 21–43 months).
Conflict of interest/source of funding	Authors declare that they have no conflicts of interest. Some authors received fees from the company outside the submitted work.

Analysis

Follow-up issues: 2 patients in the LON group (n=22) were lost to follow up 3 to 4 months after removal of the external frame and 1 patient in the IM nail group (n=35) was lost to follow up after postoperative visit.

Study design issues: study was conducted according to the strengthening the reporting of observational studies in epidemiology (STROBE) guidelines. Patients in the 2 cohorts were retrospectively identified from registry. All procedures were done by 2 trained surgeons. Lengthening technique (osteotomy, IM canal reaming, and IM nail) were similar in both methods except the ITB release in the IM nail technique and external fixator in the LON group. Data were collected retrospectively from medical records and radiographs. Regenerate assessment was done by only 1 observer.

Study population issues: patient population, demographics and pre-evaluation were similar between the groups but there were more patients with congenital femoral shortening in the IM nail group.

Key efficacy findings

- Number of patients analysed: 56
  59 limbs (39 IM nail group versus 20 LON group)

	IM nail group (39 limbs)	LON (20 limbs)	P value (between groups)
Pre-operative LLD (mm)	26.8±23.5	43.3±20.4	0.007
Femur length distracted (mm)	38.0±16.8	40.5±22.9	0.666
mean postoperative LLD^ (accuracy, mm)	0.3±1.6	3.6±7.0	0.007
Rate of distraction (mm/day)	1.0±00	0.8±0.2	<0.001
BHI* (months/cm)	1.0±0.5	1.4±0.8	0.101
Time to union^^ (months)	3.3±1.0	4.5±1.7	0.001
Regenerate quality (measured with modified Li score)			
Homogenous, %	35±88	14±70	0.082
Heterogenous, %	5±12	4±20	0.565
Sparse	0	2±10	0.188

^ difference between desired length and final length.
^^ defined as the time at which there was bridging bone on 3 of 4 cortices on the AP and lateral femur radiographs.

* rate at which bone heals after lengthening.

Knee ROM

	IM nail group (39 limbs)	LON (20 limbs)	P value (between groups)
Knee extension			
Pre-operative	0.4±2.8	-0.5±3.6	0.385
Distraction	1.8±5.4	2.7±4.4	0.481
Postoperative	0.5±1.6	0.9±5.7	0.739
P value (within group)	0.239	0.070	
Knee flexion			
Pre-operative	125.9±9.52	122.2±8.9	0.426
Distraction	103.3±25.2	88.8±20.0	0.006
Postoperative	122.6±14.9	119.2±11.5	0.464
P value (within group)	0.000	0.000	
Knee arc of motion			

Pre-operative	125.5±9.5	116.3±29.9	0.145
Distraction	101.5±26.9	80.0±30.7	0.002
Postoperative	122.0±16.0	111.9±30.8	0.112
P value (within group)	0.000	0.000	

Key safety findings

Complications

Complications	**IM nail group (39 limbs)**	**LON (20 limbs)**
Total	**18% (7/39)**	**45% (9/20) (p=0.027)**
Number of events	**n**	**n**
Delayed union	1	0
LLD (over-lengthening, treated by reversing the motor for 4 days)	1	1
Varus deformity of regenerate	2	1
IM nail fracture/breakage (changed nail)	1	0
Premature consolidation (1 with varus deformity)	2	0
Unplanned surgeries	5	4
Skin dehiscence (around pin site)	0	1
Excessive pain	0	3
Knee flexion contracture	0	1

Study 7 Thaller 2020

Study details

Study type	Retrospective matched comparative case series
Country	Germany
Recruitment period	1999-2011
Study population and number	n=34 patients who had femoral or lower limb lengthening with IM limb lengthening devices (ISKD®; Fitbone®). (17 patients with ISKD versus 17 with Fitbone) site: 4 proximal femoral, 7 distal femoral, and 6 proximal tibial
Age and gender	Age range 14-63 years; 11 male, 23 female
Study selection criteria	Inclusion criteria: patients in both groups meeting 5 criteria were matched. Criteria include similar surgical technique and pre and postoperative treatment protocol, site of osteotomy (proximal femur, distal femur or proximal tibia), simultaneous realignment of the mechanical axis, amount of lengthening (maximum variation 10%), age (maximum variation 20%). Exclusion criteria: subsequent lengthening of another bone, implant failure due to malpractice by the patient or accidental trauma, or nicotine abuse during lengthening.
Technique	Lower limb lengthening with IM limb lengthening devices (ISKD®; Fitbone®).
Follow up	Mean 2.5 years (range 1.3–7.0) years
Conflict of interest/source of funding	None, no financial support received.

Analysis

Study design issues: small, matched pair analysis; surgeries were all done by 1 surgeon with the same technique and managed with equivalent pre and postoperative treatment protocols. Complications were rated according to Paley's classification for external lengthening.

Study population issues: aetiology was not included in the matching criteria.

Key efficacy findings

- Number of patients analysed: 34

	ISKD nail group (n=17)	Fitbone nail group (n=17)	P value (between groups)
Distraction index, mm/day (range)	0.99 (0.55-1.67)	0.55 (0.14-0.92)	0.001

Mean weight bearing index, day/cm	32 (16.4-64)	51.6 (25.8-95)	0.001

Differences between the 3 osteotomy sites independent from group 1 or 2 were not significant (p= 0.875).

There was only 1 ISKD patient who had a distraction index of more than 1.5 mm/day and none in the fitbone group.

Key safety findings

Complications

Complications	**ISKD group (n=17)**	**Fitbone (n=17)**
Implant related, n	**4^**	**11^^**
pain (treated with peridural catheter or analgesic)	3	
accelerated nail (treated with peridural catheter and had 3 additional blocking screws to increase the friction)	1	
early consolidation treated by re-osteotomy	2	
thrombosis of the popliteal vein	1	
Superficial wound infection	1	
Defect in external controller		1
Back tracking of the nail (distraction index<0.5mm/day)		7
Temporary peroneal nerve irritation	2	3
Periostitis		1
Equinus foot (treated with physiotherapy)	2	1
Loosening of interlocking bolts (retightening or exchanged)		3
Broken interlocking bolt	1	
insufficient regenerate by following cancellous bone grafting		2
osteophyte needing removal		1

^1 accelerated nail, 2 early consolidations, 1 broken bolt.

^^ 1 defect controller, 7 back tracking, 3 loosening of interlocking bolts.

Study 8 lobst CA 2020

Study details

Study type	Retrospective case series
Country	USA 3 centres
Recruitment period	Procedures done between 2006 and 2021
Study population and number	306 patients who had 366 limb-lengthening nails removed. LLD causes: congenital (n=121), post-traumatic (n=94), developmental (n=47) and short stature (n=26). Mean LLD: 3 cm (range 0-14 cm).
Age and gender	Mean age 27 years; 55% (168/306) male
Study selection criteria	Patients were included if they had either of the 3 limb-lengthening nails (STYDE, PRECICE, or FITBONE) removed at 1 of the 3 centres. Bone transport nails and stump-lengthening nails were excluded.
Technique	Limb lengthening procedures were done using 3 different nails. FITBONE n=202 (242 nails), PRECICE n=82 (98 nails), STRYDE n=22 (26 nails). Bone segments: femur 292, tibia 68, humerus 6 Nail approach used: antegrade 138; retrograde 228 267 patients had 1 nail removal, 39 patients had 99 nail removals (2-6 removals per patient).
Follow up	Mean 434 days (range 36 to 3,015 days) from nail insertion to radiological evaluation. Mean 507days (range 55 to 2,372) to nail removal.
Conflict of interest/source of funding	Authors have received some financial benefits from companies.

Analysis

Study design issues: large study, retrospective analysis of radiographs before removal of nails was done to examine bone abnormalities at the junction of the nail ends in the area of interlocking screws. Patients' charts were also reviewed. Comparison between different nail designs were made.

Study population issues: Most nails were Fitbone and the femur was the most predominant lengthened segment.

Other issues: 19 Stryde nail evaluations in this study were also reported in study 12.

Key safety findings

- Number of patients analysed: 306 (366 IM nails)

	Total % (n=366)	Stryde nails % (n=26)	Fitbone nails % (n=242)	Precice nails % (n=98)
Radiological bone abnormalities at the telescopic nail junctional	**7 (20/366)**	**77 (20/26)**	**2 (4/242)**	**1 (1/98) P<0.001**
Focal osteolysis	1 (2/366)	0	0	1 (1/98)
Periosteal reaction	1 (2/366)	8 (2/26)	0	0
Cortical hypertrophy	2 (7/366)	15 (4/26)	3 (1/242)	0
Focal osteolysis, periosteal reaction	1 (3/366)	12 (3/26)	0	0
Cortical hypertrophy, periosteal reaction	1 (5/366)	19 (5/26)	0	0
Focal osteolysis, periosteal reaction and cortical hypertrophy	2 (6/366)	23 (6/26)	0	0
Bone abnormalities at the locking screw in the thin part of nail				
Cortical hypertrophy at the interlocking screws	39 (143/366)	35 (9/26)	44 (106/242)	30 (29/98)
Focal osteolysis and periosteal reaction	0 (1/366)	4 (1/26)	0	0

Study 9 Frommer 2021

Study details

Study type	Retrospective case series
Country	Germany (single centre)
Recruitment period	2019-2020
Study population and number	N=50 patients (with 57 IM lengthening procedures of the lower limb) Bone segments: 38 femoral, 19 tibial Indications: LLD n=43, short stature n=7
Age and gender	Median 16.5 years; 54% (31/57) female
Study selection criteria	All patients who had the Stryde IM lengthening system were included
Technique	Stryde intramedullary lengthening nail used for IM lower limb lengthening Bilateral treatments in 4 femoral, 3 tibial segments
Follow up	Median 12.2 months (range 3 to 22 months)
Conflict of interest/source of funding	Conflicts of interest not reported. Study was supported by open access publication fund of the University of Muenster.

Analysis

Follow-up issues: no patient was lost to follow up.

Study design issues: small retrospective study where only some nails have been explanted. Clinical and radiological changes from medical records and radiographs were assessed. Pain was assessed on the numeric rating scale (NRS) (0 = no pain, 10 = worst pain). Macro- and microscopic metallographic analysis of only 4 retrieved nails was conducted. SEM and EDX were done to assess corrosion at telescoping junction, bolts and locking holes. Explanted implants were analysed intraoperatively by the authors.

Study population issues: heterogenous study population in terms of indications.

Key efficacy findings

- Number of patients analysed: 50 (57 procedures)

Limb lengthening outcomes

Median planned distraction distance, mm	47.5 (20 to 65)
Median achieved distraction distance, mm	46 (26 to 67)
No of segments finished distraction %	95 (54/57)
Median distraction period, days (range)	55.5 (27 to 134)
Mean distraction index, mm/day (95% CI)	0.74 (0.69 to 78)
No of segments with complete consolidation %	86 (49/57)
Median consolidation period, days (range)	118 (68 to 262)
Median consolidation index, days/cm (range)	30.4 (16.2 to 59)
Median LLD before surgery, mm (range)	37 (20 to 94)
Median LLD at final follow up, mm (range)	0 (-26 to 46)
Median gained leg length in DSS, mm (range)	55 (47 to 65)

Clinical and radiological outcomes

	% (n)
Pain during distraction (not relieved by NSAIDs)	28 (16/57)
Pain during consolidation	25 (14/57)
Full weight bearing during distraction	46 (26/57)
Full weight bearing during consolidation	68 (37/57)
Additional medication (analgesics or antibiotics)	18 (31/57)
Additional imaging	13 (23/57)

Key safety findings

Complications

Complications	**% (n)**
Nails explanted (6 removed prematurely [due to osteomyelitis in 2, nail dislocation during distraction in 1, non-union during consolidation in 1] and 18 after consolidation as per treatment plan).	42 (24/57)
Macroscopic signs of corrosion at nail junction, locking holes, bolts^	83 (20/24)
Implanted related osteolysis (at the nail telescoping junction)*	40 (20/50)
Persistent or new onset of rest and ambulation pain during consolidation	40 (8/20)
Revision surgery (for dislocation of proximal tibiofibular screw in 4, dislocation of the nail in 2, delayed consolidation/non-union in 5, premature consolidation 4, osteomyelitis in 4)	10 (19/57)

* *average 9.5 months after surgery and 7 months after distraction. Before implant removal 11 of these nails revealed osteolysis.

^Implant retrieval analysis of 4 nails by means of SEM showed pitting and crevice corrosion at the telescopic junction. EDX analysis detected chromium as the main metallic element of corrosion deposits.

Study 10 Galal 2021

Study details

Study type	Retrospective cohort study
Country	Single centre
Recruitment period	2017-2020
Study population and number	N=46 patients (with 66 femoral lengthening procedures) N=16 STRYDE® group (30 femoral procedures)_ N=30 PRECICE® group (36 femoral procedures)
Age and gender	Mean age was 31 years and 33 years for the Stryde and Precice groups; 83-87% male patients in both groups.
Study selection criteria	Patients who had femoral lengthening using a Stryde IM nail with a lengthening goal of 8 cm, no associated deformity and no medical co-morbidities were included. Patients who had Precice IM nail lengthening procedures were matched for age (± 2 years), lengthening goal (± 1 cm) and aetiology to maximise homogeneity between groups.
Technique	2 different IM nails (Stryde and PRECICE nails) for both unilateral and bilateral femoral lengthening procedures were used. Patients in both cohorts had identical surgical procedures. Stryde group-14 patients with short stature had bilateral procedures and 2 patients with post-traumatic physeal arrest had unilateral procedures. Precice group-17 patients with short stature and 1 patient had Prader–Willi syndrome had bilateral procedures. Post-operative distraction started on day 7 at 0.8 mm/day, patients were followed up every 2 weeks during the distraction phase, then every month during the consolidation phase. Measurement of distraction gap was done on femur radiographs while measurements of lateral distal femoral angle (LDFA) were 1 on long leg films. In the STRYDE® group if the patient's weight was below the implant weight limit, they were allowed to be weight bearing as tolerated, while in the Precice group post-operative weight bearing was limited to the manufacturer-recommended implant weight limit until regenerate if fully consolidated.
Follow up	14 months (range 12-30 months)
Conflict of interest/source of funding	No conflicts of interest nor any financial support was received.

Analysis

IP overview: intramedullary distraction for lower limb lengthening

Follow-up issues: no patients were lost to follow up.

Study design issues: small retrospective study on only femoral IM lengthening procedures. Patients' medical records were reviewed to collect data on these procedures. All radiographic measurements were done by 2 authors. The LD-SRS questionnaire is composed of 30 questions and covers 5 domains: pain, function, self-image, mental health and satisfaction. Responses are scored from 1 (worst) to 5 (best), and the sum of all scores is then divided by the number of questions for a final score from 1(worst) to 5 (best).

Study population issues: patient groups were similar in terms of age, gender, nail size i(10.7 to 11.5mm), and lengthening done.

Key efficacy findings

- Number of patients analysed: 66 lengthening procedures (36 Precice versus 30 Stryde nail)

	PRECICE group (n=30)	**STRYDE group (n=36)**	**P value**
Preop LD-SRS score	4 (2.9-4.6)	3.9 (3.2-4.8)	0.09
Post-op LD-SRS score	4.4 (3.8-4.8)	4.1 (3.5-4.9)	0.07
Change in LD-SRS score	0.4 (0.8 improvement to 0.5 worsening)	0.2 (1 improvement to 1 worsening)	0.50
Pre-op LDFA	87.4° (84–93)	87.4° (85–93)	0.33
Post-op LDFA	87.8° (84–92)	88.8° (84–94)	0.09
Change in LDFA	1.6° varus (3 valgus–5 varus)	0.25° varus (5 valgus–4 varus)	0.08
Hip adjacent ROM	-	(15º and 30º)	NS
Knee adjacent ROM	5º and 10º	5º and 10º	NS
BHI, months/cm	0.67 (0.44 to 1.2)	0.84 (0.53 to 1.5)	0.04
Average distraction rate mm/day (range)	0.9 (0.6 to 1)	0.6 (0.4 to 0.9)	0.003
Average lengthening achieved, cm	6.8 (4-8)	7.1 (4.1 -8)	0.5

Key safety findings

Complications

Complications	**PRECICE group**	**STRYDE group**
Type 2 complications (substantial change in treatment plan but treatment goal still achieved, for example, return to operating room for BMAC injection, exchange nailing)	**4**	
Mechanical nail complications (nail failure)	3	0
femurs needed BMAC injection for delayed healing/consolidation	1	4

Type 3A complications in the form of "crown breakage" when achieved more than 7 cm of length but less than the lengthening goal of 8 cm	3	

No non-union, VTE, or infection reported in this study.

Study 11 Rolfing 2021

Study details

Study type	Cross-sectional study
Country	Denmark (nationwide study)
Recruitment period	2018- 2021
Study population and number	N=27 patients (30 bone segments)
Age and gender	Mean age 20 years
Study selection criteria	All bone lengthening surgeries of the lower limb using the fully weight-bearing Stryde implant included.
Technique	Stryde bone lengthening nail in femur (n=19) and tibia (n=11) implanted. Planned lengthening was mean 35mm
Follow up	Radiographs were evaluated at mean 11 months (range 2-23 months)
Conflict of interest/source of funding	Authors declared no conflicts of interest.

Analysis

Study design issues: Patients were identified by searching electronic records. Radiographs of all bone segments were evaluated for radiographic changes (osteolysis, periosteal reaction, cortical hypertrophy in the nail junction) before removal. The radiographic changes were classified based on a consensus decision of 3 authors. Late onset of symptoms such as pain or swelling were also assessed.

Study population issues: 37% (10/27) patients were younger than 18 years.

Other issues: 19 Stryde nail evaluations in this study were also reported in study 8. The company has recalled all Stryde implants.

Key safety findings

- Number of patients analysed: 27 (30 bone segments)

Complications

	N=27 patients	n=30 segments
Radiographic changes*	**20**	**21**
Radiographically confirmed osteolysis		19
Periosteal reaction (most often multi-layered onion skin type)		12
Cortical hypertrophy in the area of the junction between the telescoping nail parts		12
Late onset of pain after consolidation of the regenerate (likely to be due to bony changes)	8	
Broken IM nails (in femoral segment within 1 year, reoperated)		2

*9 bone segments had no radiographic junctional changes, while 1 radiographic abnormality was present in 4 and 17 had 2 or all 3 radiographic signs. The time from onset of symptoms to radiographic changes ranged from 15 to 48 days.

Discoloration (potential corrosion) at the nail interface was seen in multiple removed nails. 15/30 nails that were not yet removed were still at risk of developing complications.

Study 12 Rolfing 2021

Study details

Study type	Case report
Country	Denmark
Recruitment period	Not reported
Study population and number	N= 2 patients (with 3 broken magnetically controlled nails)
Age and gender	17 and 65 years old.
Study selection criteria	-
Technique	2 different techniques for removal of broken Precice Stryde intramedullary bone lengthening nails were used. Solid core technique- bilateral broken Stryde nails were removed with a retrograde trauma nail and Fitbone tube system. A retrograde guide wire is placed and a rod inserted through the Fitbone tube system protecting the knee joint. Then a blocking guide wire narrowing the medullary cavity directing the tip of the rod is inserted to prevent iatrogenic fractures. Hollow core technique- broken nail components are removed with long pilers and implant extraction set. A distal locking screw is reinserted in its hole to establish a firm grip and prevent subsidence of the nail. A jamming technique was applied with a coned extraction device correcting malalignment and guiding the nail through the trochanteric area.
Follow up	Nails were removed between 325 to 504 days.
Conflict of interest/source of funding	The authors declare no conflicts of interest.

Analysis

Study population issues: 1 of the patients were also reported in study 11.

Key safety findings

Number of patients analysed: 2**Complications**

Complication	**n**
Broken implants within IM canal (because of hardware failure) In 1 patient 2 femoral Stryde implants broke through the proximal locking screw hole on the right side and left side (at 413 and 504 days during nail removal). They were asymptomatic.	3

In another patient 1 nail broke through the area containing the magnet (at 325 days after index surgery) during walking. All these nails were removed using techniques described above and implanted with different types of nails.	

Validity and generalisability of the studies

- Several IM limb lengthening devices with variation in techniques (mechanically activated nails, motorised nails, and magnetically driven nails) are used for distraction and stimulating lower limb lengthening and all these are considered in this review.

- There are no RCTs comparing the use of IM limb lengthening nails alone for lower-limb lengthening with current standard of care/conventional lengthening procedures (external fixation devices).

- 5 systematic reviews are included in this overview and evidence is mainly based on NRS, case series and case reports that are prone to a number of biases. NRS compared IM nail lengthening with LON or with external fixation. There were differences in the time of follow up and no standardised reporting methods were used in studies.

Existing assessments of this procedure

There were no published assessments from other organisations identified at the time of the literature search.

Related NICE guidance

There is currently no NICE guidance related to this procedure.

Additional information considered by IPAC

Professional experts' opinions

Expert advice was sought from consultants who have been nominated or ratified by their professional Society or Royal College. The advice received is their individual opinion and is not intended to represent the view of the society. The advice provided by professional experts, in the form of the completed questionnaires, is normally published in full on the NICE website during public consultation, except in circumstances but not limited to, where comments are

considered voluminous, or publication would be unlawful or inappropriate. No professional expert questionnaires for IM distraction for unilateral lower limb lengthening were submitted.

Patient commentators' opinions

NICE's Public Involvement Programme sought patient commentary for this procedure but none was received.

Company engagement

A structured information request was sent to 2 companies who manufacture a potentially relevant device for use in this procedure. NICE received 2 completed submissions. These was considered by the IP team and any relevant points have been taken into consideration when preparing this overview.

Issues for consideration by IPAC

- Lengthening of bones other than the tibia and femur is not considered in the overview.
- It is unclear from the evidence whether (and when) removal of device after lengthening and consolidation is recommended.
- One company representative informed that 'the ISKD system is older technology that they have decided to stop actively marketing and is very much superseded by FITBONE®'.
- Some of the other IM nails are also no longer available (Phenix nail, Albizzia nail, Bliskunov nail, Stryde system).

References

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12. Rolfing JD, Mathias B; Petruskevicius J et al. (2021) Removal of broken PRECICE Stryde intramedullary lengthening nails. Orthopaedics and Traumatology: Surgery and Research; 102958.

Literature search strategy

Databases	Date searched	Version/files
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	05/10/2021	Issue 10 of 12, October 2021
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	05/10/2021	Issue 10 of 12, October 2021
International HTA database (INAHTA)	05/10/2021	-
MEDLINE (Ovid)	05/10/2021	1946 to October 04, 2021
MEDLINE In-Process (Ovid)	05/10/2021	1946 to October 04, 2021
MEDLINE Epubs ahead of print (Ovid)	05/10/2021	October 04, 2021
EMBASE (Ovid)	05/10/2021	1974 to 2021 October 04
EMBASE Conference (Ovid)	05/10/2021	1974 to 2021 October 04

Literature search strategy

The following search strategy was used to identify papers in MEDLINE. A similar strategy was used to identify papers in other databases.

1 orthopedic fixation devices/ or external fixators/
2 ((Intramedullar* or internal* or implant*) adj4 (lenghten* or distract*)).tw.
3 ISKD.tw.
4 intramedullary skeletal kinetic distractor.tw.
5 ((orthoped* or external*) adj4 fixat*).tw.
6 ilizarov technique/ or osteogenesis, distraction/
7 (albizia* or albizzia).tw.
8 or/1-7
9 Bone Malalignment/
10 Bone Lengthening/
11 or/9-10
12 exp Femur/
13 Tibia/
14 Femur*.tw.
15 Tibia*.tw.
16 femora.tw.
17 or/12-16
18 11 and 17
19 ((leg or lower limb or femora* or femur* or tibia*) adj4 (lengthen* or elongat*)).tw.
20 Leg Length Inequality/
21 leg lengt* inequal*.tw.
22 or/19-21
23 18 or 20

24 8 and 23
25 fitbone.tw.
26 illzarov.tw.
27 precice.tw.
28 or/25-27 (47)
29 24 or 28 (995)
30 Animals/ not Humans/
31 29 not 30
32 limit 31 to ed=20190801-20211005

Appendix

The following table outlines the studies that are considered potentially relevant to the IP overview but were not included in the summary of the key evidence. It is by no means an exhaustive list of potentially relevant studies.

Additional papers identified

Article	Number of patients/follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
Acharya A, Guichet JM (2006) Effect on knee motion of gradual intramedullary femoral lengthening. Acta Orthop Belg 72, 569-577.	Case series N=27 patients had bilateral simultaneous femoral lengthening using Albizzia nails. Mean follow up was 28.6 months.	The mean gain was 6.2 cm. No significant difference was noted between the mean preoperative and final knee flexions (148.3° vs. 148.4°) and the mean preoperative and final knee extensions (2.3° vs. 3.4°). All patients were flexing to at least 120° and only 1 patient had a flexion deformity over 5°.	Larger studies included in the summary of key evidence.
Accadbled F, Pailhé R, Cavaignac E et al. (2016) Bone lengthening using the Fitbone motorized intramedullary nail: the first experience in France. Orthop Traumatol Surg Res; 102(2): 217-22.	Prospective case series N=23 patients had 26 limb lengthening (15 in femur and 11 in tibia) using IM limb lengthening systems (Fitbone and Precice) Mean follow up was 3.4 years (range: 2–5.3 years)	Limb lengthening obtained in 23 cases (88%) and the mean lengthening was 45.3 ± 18 mm (range: 20–80 mm). The mean time to healing was 277 ± 167 days (range: 86–638 days). The mean healing index was 73 ± 57 days/cm for the femurs and 83.5 ± 65 days/cm for the tibias. The	Study included in systematic review added to the summary of key evidence.

		mean complication rate was 15.4%.	
Al-Sayyad MJ. (2012) Lower limb lengthening and deformity correction using the Fitbone motorized nail system in the adolescent patient. J Pediatr Orthop Part B; 21(2): 131-6.	Prospective case series N=10 patients had leg lengthening with a motorised IM lengthening device (the Fitbone System) 9 femoral nails and 5 tibial nails	leg lengthening combined with correction of the mechanical axis alignment seen in 3 patients. The consolidation index was 24 days/cm. No bone or soft tissue infections noted. 1 patient had irritation and pain from the antenna system after lengthening and recovered after antenna removal.	Study included in systematic review added to the summary of key evidence.
Aleksey D, Zhang DT, Fragomen, AT et al. (2021) Cost comparison of tibial distraction osteogenesis using external lengthening and then nailing vs internal magnetic lengthening nails. Strategies in Trauma and Limb Reconstruction; 16 (1); 14-19.	Retrospective review comparing consecutive tibial lengthening using either LATN (n = 17) or MLN (n = 15).	Patients who had MLN had fewer surgeries (3.6 vs 2.8; $p < 0.001$) but had a longer time to union as compared with patients who had with LATN (19.79 vs 27.84 weeks; $p = 0.006$). Total costs were similar ($50,345 vs $46,162; $p = 0.249$) although surgeon fees were lower for MLN as compared with LATN ($6,426 vs $4,428; $p < 0.001$). LATN and MLN had similar overall costs in patients having tibial lengthening. MLN was associated with fewer procedures but a longer time to union as compared with LATN. Despite an increased upfront cost in MLN, there	Costs out of remit of IP guidance.

		was no difference in total cost between LATN and MLN when used for tibial lengthening.	
Alfie V; Bardach A; Klappenbach R et al. (2021) Sistema de clavo endomedular motorizado Precice® en discrepancia de longitud de miembros. INAHTA HTA (Other)	HTA	High-quality evidence comparing lower limb-lengthening using the Precice® system with other lengthening and fixation methods was not identified. Low-quality evidence from observational studies suggests that using the Precise® motorised intramedullary nail system would be as efficacious as using the monoplanar external fixator and fixator-assisted nailing in achieving the desired bone length for the treatment of limb-length discrepancy. The advantages of the Precice® system, when compared to the fixator-assisted nailing, would be a faster lengthening speed, shorter consolidation time and better motion during treatment. Those patients who used the endomedullary system would experience less pain, fewer complications and greater	Non-English To add summary under existing assessments in the overview.

		satisfaction for cosmesis and system use when compared with external fixation treatments. No clinical practice guidelines about limb-length discrepancy treatment were found, so absolute recommendations about this technology cannot be made. One United States private health sponsor covers the use of the Precice® system for bone lengthening. The remaining public and private sponsors consulted from Argentina and other selected countries, do not mention this technology. No economic studies carried out in Argentina were found on the cost-effectiveness of this technology.	
Axelrod D, Rubinger L, Shah A et al. (2021) How should we lengthen post-traumatic limb defects? a systematic review and comparison of motorized lengthening systems, combined internal and external fixation and external` fixation alone. European journal of orthopaedic	Systematic review comparative studies of lengthening techniques for treating post-traumatic long bone deformity. N=13 studies (1 RCT and 12 cohort studies with 725 patients,	The mean limb lengthening achieved, lengthening index, and rate of reoperation were similar among the MLN, EF, and CIF groups. The purported decreased the duration of lengthening and the risk of reoperation	Similar studies included.

surgery & traumatology: orthopedie traumatologie; 31 (6); 1015-1022.	mean age: 29.6 years) Treatment groups were pooled into external fixation (EF) alone, combined internal and external fixation (CIF), and mechanical lengthening nail (MLN).	associated with MLNs was not demonstrated in this review. Patients with post-traumatic leg length deformities remain a challenging patient population to treat, with intervention being associated with high rates of infectious complications and need for revision operations.	
Burghardt RD, Herzenberg JE, Specht SC, et al. (2021) Mechanical failure of the Intramedullary Skeletal Kinetic Distractor in limb lengthening. J Bone Joint Surg Br; 93:639e43.	Case series (retrospective) n=180 patients (had 242 lower-limb segments using the ISKD.	15 ISKDs in 12 patients (13 limbs) failed mechanically (overall failure rate of 6.2%), with device fracture in 10/15 failures. 2 nails in 1 patient failed to lengthen and had to be replaced. The manufacturer detected an error in the assembly of the nail, which prompted a wide recall. 1 nail jammed after being forcefully inserted, and 2 nails failed to lengthen fully. Lengthening was achieved in all 12 patients, although 3 needed a second operation to exchange a defective nail for a new, functioning device.	Study included in systematic review added to the summary of key evidence.
Bafor A, Duncan ME, Iobst CA. (2020) Evaluating the utility of the Pixel value ratio in	Retrospective case series N= 42 patients had unilateral	The pixel value ratio is a reliable method to objectively assess the state of healing	More relevant studies included in the

the determination of time to full weight-bearing in patients undergoing intramedullary limb lengthening. Strategies Trauma Limb Reconstr;15(2):74–78.	lengthening of the femur for LLD using the PRECICE nail. Follow up ranged from 4 to 35 months.	of the regenerate bone during distraction osteogenesis. There were no adverse effects when subjects commenced full weight-bearing when 3/4 cortices had a PVR of at least 0.93.	summary of key evidence.
Burghardt RD, Paley D, Specht SC et al. (2012) The effect on mechanical axis deviation of femoral lengthening with an intramedullary telescopic nail. J Bone Joint Surg Br; 94 (9): 1241–5.	Case series (retrospective) N=24 patients (27 femoral lengthening using the ISKD)	The mean lengthening achieved was 4.4 cm (1.5 to 8.0). In 26 of 27 limbs, the mechanical axis shifted laterally by a mean of 1.0 mm/cm of lengthening (0 to 3.5). In 1 femur that was initially in varus, a 3 mm medial shift occurred during a lengthening of 2.2 cm	Larger studies included in the summary of key evidence.
Calder PR, McKay JE, Timms AJ et al. (2019) Femoral lengthening using the Precice intramedullary limb-lengthening system: outcome comparison following antegrade and retrograde nails. Bone Joint J; 101-B (9): 1168-76.	Case series (retrospective) N=92 (107 femoral lengthening operations (73 antegrade nails and 34 retrograde nails inserted.	This study confirms excellent results in femoral lengthening with antegrade and retrograde Precice nails. There is a trend for better healing and less restriction in hip and knee movement following antegrade nails. Minor implant complications included locking bolt migration, deformity of the nail u(in 1),delayed union (in 3), surgical intervention for joint contracture (in 5).	Study included in systematic review added to the summary of key evidence.

Cosic F, Edwards E. (2020) PRECICE intramedullary nail in the treatment of adult leg length discrepancy. Injury 51,1091–1096.	Case series N=21 patients had lengthening with PRECICE IM nail (17 femoral and 4 tibial) . Mean follow up 15.1 months.	All patients achieved correct lengthening (mean gain 36.5 mm). All patients consolidated their regenerate bone (mean 268 days). Mean femoral consolidation index was 6.5, mean tibial consolidation index was 16.1 (p=0.002). 6 patients had delayed consolidation of regenerate bone. 19%(4/21) patients suffered a complication, with 1 implant failure.	Study included in systematic review added to the summary of key evidence.
Dinçyürek H, Kocaoğlu M, Eralp IL et al. (2012) Functional results of lower extremity lengthening by motorized intramedullary nails. Acta Orthop Traumatol Turc; 46(1): 42-9.	Case series N=14 patients (11 femoral and 4 tibiae) had limb lengthening using motorised IM femoral nails (Fitbone). Mean follow up was 33.5 (range: 7 to 88) months.	Functional scores were excellent for 12 patients. Complications such as dysfunction of the distraction mechanism in 2, restricted transient knee motion in 4, and delayed consolidation in 4 were noted. Other complications included valgus deformities and superficial infections surrounding the antenna of the IM nail, as well as femur fractures at the proximal end of the nail.	Study included in systematic review added to the summary of key evidence.
Fragomen AT, Rozbruch R. (2017) Retrograde magnetic internal lengthening nail for acute femoral	Review	The phenomenal bone healing ability for the retrograde Precice nail after femoral osteotomy	Review

deformity correction and limb lengthening. Expert review of medical devices, 4 (10): 811–820.		for lengthening, even after acute deformity correction, is recognised. The few failures that have occurred appear to be attributable to excessive loading of the femur and implant during a vulnerable time of bone healing. Further studies with more uniform outcome criteria need to be conducted to better standardise user's experiences. The higher 1-time cost of the implant is offset by the reduced number of surgeries needed when compared with the gold standard of lengthening-over-nail-technique, and patients return to work sooner due to the ability to wear normal clothing and the reduction in pain throughout the entire lengthening process.	
Fragomen AT, Rozbruch R. (2016) Lengthening of the femur with a remote-controlled magnetic intramedullary nail-retrograde technique. JBJS Essential Surgical Techniques, 6(2): e20(1-15).	Surgical technique is described.	retrograde approach is used for special occasions.	Surgical technique.
Gigi, R., Hemo, Y., Danino, B. et al. (2021)	Case series (retrospective) n=	The osteotomy level co-efficient (OLC)	More relevant studies added

Changes in the femoral osteotomy level coefcient and neck shaft angle during limb lengthening with an intramedullary magnetic nail. Archives of orthopaedic and trauma Surgery, doi: 10.1007/s00402-020-03740-9. Online ahead of print.	30 patients with 31 femoral lengthening procedures with the PRECICE antegrade IM lengthening nail. Trochanteric entry points were used in 24 femurs, and piriformis entry points in 7 femurs. Average follow up was 10.15 months.	ranged from 0.16 to 0.34. The average postoperative neck shaft angle (NSA) significantly reduced from 133.5º to 128.5º p=0.000]. There was no correlation between the OLC and the change in the NSAs. The trochanteric entry points have a greater tendency to reduce the NSA compared to the piriformis entry points.	to the summary of key evidence.
Hammouda AI, Jauregui JJ, Gesheff MG et al. (2017) Treatment of post-traumatic femoral discrepancy with PRECICE magnetic-powered intramedullary lengthening nails. J Orthop Trauma; 31(7): 369-74.	Case series (retrospective) N=17 patients with post-traumatic femoral shortening had femurs lengthened with Precice nail. Mean follow up was 2.2 years	16patients achieved the planned lengthening, a mean of 3.8 cm. Regenerate consolidation occurred at a mean of 119 days The mean consolidation index was 32 d/cm. 3 patients (18%) experienced complications.	Study included in systematic review added to the summary of key evidence.
Hidden KA, Dahl MT, Ly TV. (2020) Management of a Broken PRECICE Femoral Nail at an Ununited Distraction Osteogenesis Site. A Case Report. JBJS The Journal of Bone and Joint Surgery, Case Connect;10:e0267	Case report A 20-year-old man with a right lower extremity fibular hemimelia treated with PRECICE femoral nail lengthening presented with a broken magnetic nail and a displaced fracture through an ununited distraction osteogenesis site.	Using a combination of techniques, the broken implant was removed while maintaining the achieved limb length and preserving the native biology without bone grafting.	Implant removal reported in studies included in the summary of key evidence.

Havitcioglu H, Gursan O, Isin Y. (2020) Cosmetic bilateral leg lengthening using intramedullary nail experience of 9 cases. J Orthop; 20: 232-5.	Retrospective case series N=9 patients with short stature had IM nail lengthening for cosmetic purposes (16 femoral and 2 tibial segments) Mean follow up was 22 ± 11 months	The mean lengthening gained in all was 8.7 cm; healing index with normal bone healing was 46.8 ± 16 months/ cm. Complications included insufficient bone regeneration (n = 2), quadriceps contracture (n = 1), proximal locking screw runaway (n = 1).	Study included in systematic review added to the summary of key evidence.
Hawi N, Kenawey M, Panzica M et al. (2015) Nail–medullary canal ratio affects mechanical axis deviation during femoral lengthening with an intramedullary distractor. Injury, 46: 2258–2262.	Retrospective case series N=20 patients had unilateral femoral-lengthening procedures using IM distractors. Analysed pretreatment and posttreatment radiographs.	Compared to the preoperative axis, the mechanical axis shifted medially in 7 patients (varisation group) and laterally in 13 patients (valgisation group). The nail–medullary canal ratio significantly differed between groups ($p < 0.001$), being <85% in the varisation group and >85% in the valgisation group. The nail–medullary canal ratio should be considered during preoperative planning.	More comprehensive studies included in the summary of key evidence.
Horn J, Grimsrud Ø, Dagsgard AH et al. (2015) Femoral lengthening with a motorized intramedullary nail: a matched-pair comparison with external ring fixator lengthening in 30 cases.	Case control study N=30 femoral lengthening (15 with a motorised IM nail (Fitbone) compared with 15 lengthening with	Mean lengthening was 35 mm in the nail group and 38 mm in the fixator group. The mean radiographic consolidation index in the Fitbone group, at 1.5 months/cm, was better than the	Study included in systematic review added to the summary of key evidence.

Acta Orthop; 86(2): 248-56.	an external ring fixation.	mean value for the fixator group 1.9 months/cm (p=0.01). Knee ROM was better in the nail group during the lengthening, after 6 weeks, and 6 months (p<0.001). A larger number of complications were seeb in the fixator group than in the nail group.	
Horn J, Hvid I, Huhnstock S et al. (2019) Limb lengthening and deformity correction with externally controlled motorized intramedullary nails: evaluation of 50 consecutive lengthenings. Acta Orthop; 90(1): 81-7.	Retrospective case series N=47 patients (50 lengthenings -34 Precice and 16 Fitbone devices) ≥ 12 months follow up.	Lengthening was achieved in all but 2 patients. 5 patients who had simultaneous axial correction showed minor residual deformity. The consolidation index was 1.2 months/cm in the femur and 2.5 months/ cm in the tibia. 2 femoral fractures occurred in retrograde femoral lengthenings after consolidation due to substantial trauma. There were 8 complications, all correctable by surgery.	Study included in systematic review added to the summary of key evidence.
Hothi H, Bergiers S, Henckel J et al. (2021) Analysis of retrieved STRYDE nails. Bone & Joint Open 2(8): 599-610.	Retrieval analysis findings of 10 PRECICE STRYDE intermedullary nails removed from 6 patients who achieved lengthening and after consolidation.	All nails were removed at the end of treatment, having achieved their intended lengthening (20 mm to 65 mm) and after regenerate consolidation. All nails had evidence of corrosion localised to the screw holes and	Larger studies included concerning clinical and radiological findings.

	Macro- and microscopic analysis of all surfaces and graded the presence of corrosion using validated semiquantitative scoring methods. Metrology analysis.	the extendable junctions; corrosion was graded as moderate at the junction of 1 nail and severe at the junctions of 5 nails. Energy dispersive x-ray spectroscopy analysis showed surface deposits to be chromium rich. Plain radiographs showed cortical thickening and osteolysis around the junction of 6 nails, corresponding to the same nails with moderate – severe junction corrosion. In fully united bones, evidence of cortical thickening and osteolysis appeared to be associated with corrosion at the extendable junction; when corrosion was present, cortical thickening was adjacent to this junction. Further work, with greater numbers of retrievals, is needed to fully understand this association between corrosion and bony changes, and the influencing surgeon, implant, and patient factors involved.	
Iliadis AD, Palloni V, Wright J et al. (2021) Pediatric lower limb	Retrospective case series	Mean achieved lengthening was 46.5 mm. Mean	More comprehensive studies

lengthening using the PRECICE nail: our experience with 50 cases. J Pediatr Orthop; 41: e44–e49.	n= 42 paediatric and adolescent patients who had IM lengthening for lower LLD using the PRECICE and STRYDE IML nails (50 procedures, 43 femoral and 7 tibial nails).	percentage lengthening was 12.6%. Nail accuracy was 96% and reliability 90%. Average distraction rate was 0.92 mm/d for femur and 0.64 mm/d for tibias. Consolidation index was 28 d/cm and 39 d/cm, respectively. Time from completion of lengthening to independent full weight-bearing was 45 days and 34.2 days, respectively. Bone and functional scores were favourable and PROMS demonstrated high patient satisfaction. No significant complications were seen.	included in the summary of key evidence.
Iliadis AD, Wright J, Stoddart MT et al. (2021) Early results from a single centre's experience with the STRYDE nail : a cause for concern?. The bone & joint journal; 103b (6); 1168-1172.	Retrospective review of prospective data N=9 patients with 14 STRYDE nails (an evolution of the PRECICE Intramedullary Limb Lengthening System). Mean age 33 years	At the time of reporting, 8 patients (13 implants) had completed lengthening. Osteolysis and periosteal reaction at the junction of the telescopic nail was evident in 9 implants. 5 patients experienced localised pain and swelling. Macroscopic appearances following retrieval were consistent with corrosion at the telescopic junction.	Larger studies included concerning clinical and radiological findings.

		Tissue histology was consistent with effects of focal metallic wear debris.	
Karakoyun O, Sokucu S, Erol MF et al. (2016) Use of a magnetic bone nail for lengthening of the femur and tibia. J Orthop Surg; 24(3): 374-8.	Case series (retrospective) N=23 patients with trauma and other reasons had limb lengthening with 27 precice nails (femur 21, tibia 6) Mean follow up was 20.72 months.	The mean lengthening was 48.20 mm, and the mean acute angular correction was 15.5º. The mean time to full weight-bearing was 5.15 months, and the mean consolidation index was 1.12 months/cm. The mean maturation index was 0.78 months/cm. 1 patient had nail breakage during the consolidation phase. The nail was replaced, 8 patients had over-lengthening and the nails were driven back to the desired length.	Study included in systematic review added to the summary of key evidence.
Karakoyun Ö, Küçükkaya M, Erol MF. (2015) Does lengthening after acute correction negatively affect bone healing during distraction osteogenesis? Acta Orthop Traumatol Turc; 49(4): 405-9.	Case series (retrospective) Group 1 (9 patients, 9 femora) had lengthening IM distraction devices after acute correction. Group 2 (13 patients, 16 femora) had lengthening using IM distraction devices. Group 3 (12 patients,13 femora) had lengthening ≥4 cm with lengthening and the retrograde	Acute correction had no negative effect on bone healing after distraction osteogenesis using new-generation IM distraction devices. We suggest that the negative impact on healing and the prolonged consolidation index in patients having LORN may be due to impaired periosteal blood supply due to fixator pins.	Study included in systematic review added to the summary of key evidence.

	nailing method (LORN) following acute correction.		
Kenawey M, Krettek C, Liodakis E et al. (2011) Insufficient bone regenerate after intramedullary femoral lengthening: risk factors and classification system. Clin Orthop Relat Res; 469:264e73.	Case series N= 35 patients (with 37 ISKD femoral lengthening procedures) Follow up 12 months	The average length gain was 42.8 ± 12.9 mm. Distraction problems with the ISKD were related mostly to internal malfunction of the lengthening mechanism (in 8). A distraction rate greater than 1.5 mm/day should be avoided in femoral IM lengthening. Smoking should be a contraindication for femoral lengthening.	Larger studies included in the summary of key evidence.
Kenawey M, Krettek C, Liodakis E et al. (2011) Leg lengthening using intramedullary skeletal kinetic distractor: results of 57 consecutive applications. Injury; 42:150e5	Case series N=53 patients (femoral = 45 and tibial = 12) had lengthening procedures using ISKD nail. Mean follow up was 23±12 months.	Emphasises the rule of distraction rates above 1.5 mm/day in the development of insufficient bone regenerate. Distraction problems with these nails are due to dysfunction within the ratcheting mechanism, which may be related to the diameter of the nail. New designs for mechanically activated nails with a better control mechanism for the distraction rate are needed.	Study included in systematic review added to the summary of key evidence.
Kirane YM, Fragomen AT, Rozbruch SR. (2014) Precision of the PRECICE internal bone lengthening nail. Clin Orthop Relat Res; 472 (12): 3869-78.	Case series (retrospective) N=24 patients had femoral and/or tibial lengthening procedures using the PRECIC nail	Mean total lengthening was 35 mm with an accuracy of 96% and precision of 86%. All patients achieved target lengthening with	Study included in systematic review added to the summary of key evidence.

	for varied aetiology. Mean14 follow up was weeks	minimal unintentional effects on bone alignment. The knee and ankle ROM were minimally affected. Implant failure by a non-functional distraction mechanism in 1, premature consolidation in 1 patient, delayed bone healing in 2, delayed equinus contracture in 2 and toe clawing in 1 were reported.	
Krieg AH, Speth BM, Foster BK. (2008) Leg lengthening with a motorized nail in adolescents: an alternative to external fixators? Clin Orthop Relat Res; 466(1): 189-97.	Case series (prospective) N=8 had leg lengthening with a motorised IM lengthening device (Fitbone).	In 6 patients, leg lengthening was combined with successful correction of the mechanical axis alignment. The consolidation index averaged 26 days/cm. No bone or soft tissue infections were seen.	Study included in systematic review added to the summary of key evidence.
Krieg AH, Lenze U, Speth BM (2011). Intramedullary leg lengthening with a motorized nail: indications, challenges, and outcome in 32 patients. Acta Orthop; 82(3): 344-50.	Case series (retrospective) N=32 had limb lengthening with IM motorised nail (fitbone) -femur 21, tibia 11	Leg lengthening was successful in 30/32 cases. No intraoperative complications were seen. The consolidation index was significantly different (p=0.04) between femoral lengthening (mean 35 days/cm) and tibial lengthening (mean 48 days/cm). 10 complications noted and 4 were implant-associated.	Study included in systematic review added to the summary of key evidence.
Küçükkaya M, Karakoyun Ö, Sökücü S	Case series (retrospective)	The mean lengthening was 5.8	Study included in systematic

et al. (2015) Femoral lengthening and deformity correction using the Fitbone motorized lengthening nail. J Orthop Sci; 20(1): 149-54.	N=22 patients with femoral shortening and deformity (had 25 Fitbone lengthening nail). Follow up was 30.8 months.	(range 2–14) cm. The degree of acute angular correction was 9° (5–22°) in 9 cases. The time to full weight-bearing was 5.9 months. The consolidation index was 1.07 (0.75–1.62) months/cm. Complete consolidation was obtained in all cases except 2.	review added to the summary of key evidence.
Karakoyun O, Kucukkaya M, Sokucu S (2014). Intramedullary skeletal kinetic distractor in lower extremity lengthening. Acta Orthop Traumatol Turc; 48 (3): 307-312.	Case series N=12 patients (10 femoral and 2 tibial lengthening with ISKD)	IM extensible nails decrease the risk of joint contractures and infection. This procedure can be well tolerated by the patients and they can return to their daily activities earlier.	Larger studies included in the summary of key evidence.
Kariksiz M, Karakoyun O. (2019) Limb lengthening with one Precice nail over its capacity. Saudi Med J; 40(10): 1058-62.	Case report N=37-year-old patient with a 14 cm LLD was treated with a Precice nail.	This surgical technique can be used safely and satisfactorily in cases with more shortness as we can correct the extremity length discrepancy using only 1 nail.	Study included in systematic review added to the summary of key evidence.
Laubscher M, Mitchell C, Timms A et al. (2016) Outcomes following femoral lengthening: an initial comparison of the Precice intramedullary lengthening nail and the LRS external fixator monorail system. Bone Joint J; 98-B(10): 1382-8.	Case series (retrospective) N=22 patients had femoral lengthening (15 precice lengthening nail versus 7 patients, 13 LRS external fixator system)	Femoral lengthening with the Precice femoral nail achieved excellent functional results with fewer complications and greater patient satisfaction when compared to LRS external fixation.	Study included in systematic review and CADTH report added to the summary of key evidence.
Lee HD, Ryu KJ, Song HR et al. (2014)	Case series	Rate control was not achieved with the	Larger studies included in the

Complications of the Intramedullary Skeletal Kinetic Distractor (ISKD) in Distraction Osteogenesis. Clin Orthop Relat Res, 472: 3852–3859.	N=19 patients (35 lengthening segments-(26 femurs, 9 tibias) ISKD Follow up was 15 months (mean, 26 months; range, 15–38 months) after first-stage surgery.	ISKD nail for femoral and tibial lengthenings, complications were relatively common, and among these patients, pain levels were high. Complications occurred in 10 patients (53%) with decreased ankle ROM during distraction, 4 with delayed bone healing, and 1 with mechanical device failure during distraction. Based on our findings, we believe that surgeons should avoid use of this nail.	summary of key evidence.
Lee DH, Kim S, Lee JW et al. (2017) A comparison of the device-related complications of intramedullary lengthening nails using a new classification system. Biomed Res Int. 2017:8032510	115 segments of lower limb lengthening using IM lengthening nails (35 ISKD, 34 PRECICE1, and 46 PRECICE2)	Most common complications were distraction mechanism issues (type 1) in ISKD and mechanical strength related ones (type 2) in PRECICE1 and PRECICE2. Sixty percent (21/35) of ISKD had device-related problems. In PRECICE1 group, 8.8% (3/34) had device-related problems, and 8.8% (3/34) showed device-related obstacle. In PRECICE2, 44% (20/46) had device-related problems.	Study included in systematic review added to the summary of key evidence.
Lecoanet P, Legallois Y, Ribes C et al. (2020)	Case series (retrospective)	Lengthening was achieved in 79% of	Larger studies included in the

Medium-term evaluation of leg lengthening by ISKD® intramedullary nail in 28 patients: Should we still use this lengthening system? Orthopaedics & Traumatology: Surgery & Research 106, 1433–1440	N=28 patients with limb-lengthening by ISKD nails (24 femoral and 4 tibial). Mean follow up was 75 months.	cases, for a mean lengthening of 34.5 mm. Mean lengthening and consolidation indices were respectively 0.94 mm/day and 105 days/cm. Length discrepancy showed significant correction, with improvement in functional scores ($p < 0.01$). The overall complications rate was 68%, 76% of which were specific to the ISKD® nail.	summary of key evidence.
Mahboubian S, Seah M, Fragomen AT, et al. (2012) Femoral lengthening with lengthening over a nail has fewer complications than intramedullary skeletal kinetic distraction. Clin Orthop Relat Res; 470: 1221e31.	Case series (retrospective) N=11 patients had 12 ISKD procedures 21 patients had LON procedures (22 femoral lengthenings) ISKD average follow up was 76 months (range, 62–93 months) Lengthening over nail (average 27 months; range, 13–38 months).	No difference in achieving the lengthening goals between the 2 procedures. LON technique for femoral lengthening is associated with fewer complications than the ISKD.	Study included in systematic review added to the summary of key evidence.
Mazeau P, Assi C, Louahem D et al. (2012) Complications of Albizzia femoral lengthening nail: an analysis of 36 cases. Journal of Pediatric Orthopaedics B, 21:394–399.	Case series N=36 patients with femoral lengthening using the Albizzia nail for various indications. Follow up average was 5.8 years.	Bone consolidation was achieved faster than with external fixation. The patient's comfort during lengthening as well as the speed of functional restoration also improved. In 3 cases, the program	More comprehensive studies included in the summary of key evidence.

		failed, in 6 the lengthening was achieved with a second procedure, and 8 patients needed 1 ratcheting or more under general anaesthesia.	
Morrison T, Sontich J.(2016) Premature consolidation with resultant implant failure using PRECICE femoral nail lengthening. JBJS Case Connect; 6(2): E2.	Case report describes a failure to lengthen with the PRECICE femoral nail and the subsequent steps taken to determine the root cause.	This failure represents the first reported case of malfunction of the PRECICE femoral nail distraction mechanism since its 2013 redesign.	Study included in systematic review added to the summary of key evidence.
Nasto LA, Coppa V, Riganti S et al. (2020) Clinical results and complication rates of lower limb lengthening in paediatric patients using the PRECICE 2 intramedullary magnetic nail: a multicentre study. J Pediatr Orthop B; 29, 6: 611-617.	Retrospective case series N=26 patients had limb lengthening using the Precice 2 system Follow up was more than 6 months.	average achieved lengthening was 44.4 ± 11.6mm. Average distraction and consolidation indexes were 11.9 ± 2.1 days/cm and 25.1 ± 8.1 days/cm, respectively. Nail accuracy and reliability were 91.1% , 88.5%, respectively. 5 joint contractures, 1 femur fracture and 1hip joint subluxation, 1 deep infection and 1 nail running back) were reported.	Study included in systematic review added to the summary of key evidence.
Paley D, Harris M, Debiparshad K et al. (2014) Limb lengthening by implantable limb lengthening devices. Tech Orthop; 29 (2): 72-85.	Retrospective case series N=48 patients had treatment of LLD (unilateral) and short stature (bilateral) with Precice nails (n=65) at different locations .	Successful lengthening was achieved in all patients. There were numerous distraction and hardware complications. Despite these, implantable limb lengthening appears	Study included in systematic review added to the summary of key evidence.

		to be the direction for the future.	
Paley D, Debiparshad K, Balci H et al. (2015) Stature lengthening using the precice intramedullary lengthening nail. Tech Orthop; 30 (3): 167-82.	Retrospective case series N=51 patients 116 bone segments lengthened using Precice nails (P1 and P2).	All patients consolidated the distraction gap of the femurs and/or tibias without additional surgery. All returned to previous activities including sports. There were 7/58 (12.1%) implant failures for P1 and 1/58 (1.7%) for P2. The P2 had the lowest complication rate with the best overall reported results.	Study included in systematic review added to the summary of key evidence.
Pappana M, Monga P, Wilkes R. (2011) Promises and difficulties with the use of femoral intra-medullary lengthening nails to treat limb length discrepancies. Acta Orthop Belg, 77, 788-794.	Case series N=8 femoral lengthening procedures done in adults using intra-medullary lengthening nails (Albizzia nails 5, ISKD 3). Average follow up was 26.5 months	Target lengthening was achieved in 6/8 femurs with an average of 38.77 mm length gained. The distraction index (length gained per day) was 0.58 on average and the consolidation index average was 5039 days/cm. Premature consolidation was noted in 4 cases, runaway acute lengthening in 1 patient; prominent metalwork in 4 patients and a bent nail were frequent obstacles.	Larger studies included in the summary of key evidence.
Paley D (2015) PRECICE intramedullary limb lengthening system. Expert Rev. Med. Devices 12(3), 231–249.	Review	PRECICE IM limb lengthening system reported and published results in over 250 cases has been excellent with less pain and lower	Review

		complication rates than with external fixation methods or previous implantable nail systems.	
Panagiotopoulou VC, Davda K, Hothi HS et al. (2018) A retrieval analysis of the Precice intramedullary limb lengthening system. Bone & Joint Research.7(7):476-84.	Retrieval analysis of 15 Precice nails from 13 patients following lower-limb lengthening. Macro- and microscopic analysis of all surfaces, evaluated differences following design modification.	All patients obtained the desired length with no implant failure. Surface degradation was noted on the telescopic part of every nail design, less on the latest implants. Microscopical analysis confirmed fretting and pitting corrosion. Following sectioning, black debris was noted in all implants. The early designs were found to have fractured actuator pins and the pin and bearings showed evidence of corrosive debris. The latest designs showed evidence of biological deposits suggestive of fluid ingress within the nail but no corrosion. This study confirms less internal corrosion following modification, but evidence of titanium debris remains. Authors recommend no change to current clinical practice. However, potential reuse of the Precice nail, for secondary	Larger studies included concerning clinical and radiological findings.

		limb lengthening in the same patient, should be done with caution.	
Richardson SS, Schairer WW, Fragomen AD et al. (2019) Cost comparison of femoral distraction osteogenesis with external lengthening over a nail versus internal magnetic lengthening nail. Journal of the American Academy of Orthopaedic Surgeons. 27, 9: e430-436.	retrospective review comparing femoral lengthenings using either LON (n = 19) or MLN (n = 39).	No difference was seen in the length of femoral distraction. Patients who had MLN had fewer surgeries (3.1 versus 2.1; P , 0.001) and had a shorter time to union (136.7 versus 100.2 days; p=0.001). Total costs were similar ($50,255 versus $44,449; p=0.482), although surgeon fees were lower for MLN ($4,324 versus $2,769; p=0.001).	Costs out of remit
Robbins C, Paley D. (2020) Stryde Weight-bearing Internal Lengthening Nail. *Tech Orthop*. 35(3):201–208.	Case series N=106 patients implanted with STRYDE nails. 57 skeletally mature patients had cosmetic stature lengthening 49 other patients with a variety of limb length discrepancy aetiologies including metabolic, congenital, genetic, and posttraumatic, had unilateral lengthening.	Immediate full weight-bearing was allowed in all. Patients with secondary ipsilateral acute deformity corrections had restricted weight-bearing until sufficient healing was present at the metaphyseal site. 52 stature patients and 43 unilateral patients lengthened to within 10 and 5mm. 1 tibial nail stopped functioning prematurely and was exchanged to complete the lengthening. 7 patients needed secondary	Larger studies included.

		unplanned operations. There were no issues related to biological incompatibility of the Biodur 108 alloy stainless steel from which the implant was fabricated.	
Rozbruch R, Fragomen AT (2016) Lengthening of the femur with a remote-controlled magnetic intramedullary nail- antegrade technique. JBJS Essential Surgical Techniques, 6(1): e2(1-11).	Surgical technique described.	antegrade technique is the first choice for lengthening.	Surgical technique.
Schiedel FM, Pip S, Wacker S, et al. (2011) Intramedullary limb lengthening with the Intramedullary Skeletal Kinetic Distractor in the lower limb. J Bone Joint Surg Br; 93:788e92.	69 unilateral ISKD lengthenings (58 femora and 11 tibiae). Mean follow up was 16 months (6-49)	Successful femoral lengthening was achieved in 52 of the 58 patients (90%). However, successful tibial lengthening was only achieved in 5 of 11 patients (45%).	Study included in systematic review added to the summary of key evidence.
Schiedel F M, Vogt B, Tretow HL et al. (2014) How precise is the PRECICE compared to the ISKD in intramedullary limb lengthening? Reliability and safety in 26 procedures. Acta Orthop; 85 (3): 293-8.	Prospective case series N=24 patients with PRECICE IM limb lengthening system (26 procedures)	24/26 nails obtained 37 mm lengthening. There were 2 nail breakages, 1 in the welding seam and 1 because of a fall that occurred during consolidation. 15 cases had implant-associated problems, 5 had obstacles and 4 had complications.	Study included in systematic review added to the summary of key evidence.
Simpson AH, Shalaby H, Keenan G (2009). Femoral lengthening with the Intramedullary Skeletal Kinetic	Case series N=30 (33 femoral lengthening with ISKDs)	Lengthening was achieved in 32/33 limbs. Problems encountered included difficulty in achieving length in 8	Study included in systematic review added to the

Distractor. J Bone Joint Surg Br; 91:955e61.		femora (24%) and uncontrolled lengthening in 7(21%).	summary of key evidence.
Shabtai L, Specht SC, Standard SC et al. (2014) Internal lengthening device for congenital femoral deficiency and fibular hemimelia. Clin Orthop Relat Res; 472 (12): 3860-8.	Case series (prospective) N=18 patients with congenital limb shortening (21 bone segments lengthened using Precice nails) Mean follow up was 14 months	satisfactory joint motion during treatment in most patients. Lengthening was achieved in an accurate, controlled manner, and all patients reached their goal length. Complications remain a concern, as is the case with all approaches to this complex patient population. Both future comparative studies and longer-term follow up are needed.	Study included in systematic review added to the summary of key evidence.
Singh S, Lahiri A, Iqbal M (2006) The results of limb lengthening by callus distraction using an extending intramedullary nail (Fitbone) in non-traumatic disorders. J Bone Jt Surg, Br 88 (7): 938–942	Retrospective case series N=22 motorised IMN (Fitbone) Femoral and tibial lengthenings were done with no angulation corrections. Follow up was 36 months (range 12–48).	Mean length increase 40 mm (range 27-60). Median LI 28 days/cm (range 18.8 -70.9). infection rates 0%	Study included in systematic review added to the summary of key evidence.
Stendahl JM, Lomholt TN, Hansen, RQ et al. (2021) The STRYDE limb lengthening nail is susceptible to mechanically assisted crevice corrosion: an analysis of 23 retrieved implants. Acta	Retrospective metallurgical analysis N= 23 first version of the STRYDE limb-lengthening nails retrieved.	20/23 retrieved nails had visible signs of corrosion, i.e., discoloration at the telescopic junction. Micro-CT verified corrosion attacks in 12/12 scanned bushings. Corrosion, predominantly	Larger studies included concerning clinical and radiological findings.

Orthopaedica; 92(5):621-627.		mechanically assisted crevice corrosion, was seen at the locking screws and screw holes in 20/23 nails. Biological material inside the nail was seen in addition to oozing from the junction of 2 nails during hardware removal, which was experimentally reproducible. Notably, the mechanical construction of the bushing changed from PRECICE P2 to STRYDE nails. Interpretation - STRYDE nails are not hermetically sealed, and liquid can pass the bushing. Biodur 108 itself is corrosion resistant; however, mechanically assisted crevice corrosion of the bushing, locking screws, and screw holes may be aggravated due to manufacturing aiming for increased strength and hardness of the alloy. Observing several adverse events, we recently published a nationwide cross-sectional analysis of all 30 STRYDE limb-lengthening nails	

		(NuVasive, Specialized Orthopedics, San Diego, CA) that were implanted in Denmark (Rolfing et al. 2021a). 27/30 STRYDE nails have now been removed and we present data from metallurgical analysis of 23 of the retrieved implants.	
Szymczuk VL, Hammouda AI, Gesheff MG et al. (2019) Lengthening with monoliteral external fixation versus magnetically motorized intramedullary nail in congenital femoral deficiency. J Pediatr Orthop; 39: 458–465.	Retrospective non-randomised comparative study N=62 (30 in PRECICE group and 32 in LRS external fixation group) Mean follow up was 4.47± 2.7 and 1.86± 0.7 years.	Mean lengthening achieved was 5.6± 1.7 and 4.8 ± 1.4 cm for group A and group B, respectively (p=0.052). Mean distraction index was 0.7± 0.2 mm/d for group A and 0.7 ± 0.2 mm/d for the group B (p=0.99). Mean consolidation index for group A was 29.3± 12.7 and 34.8± 11.2 d/cm for group B (p=0.08). Mean arc of motion before surgery and at final follow up were similar between groups (p=0.35). Group A had significantly less ROM at the end of distraction (p=0.0007) and at consolidation (P < 0.0001). Both groups had similar rates of obstacles and complications. A significant difference between groups was found in the total	Study included in CADTH review added to the summary of key evidence.

		problems (P < 0.001) specifically with pin site/superficial infection (P < 0.0001).	
Tiefenboeck TM, Zak L, Bukaty A et al. (2016) Pitfalls in automatic limb lengthening: first results with an intramedullary lengthening device. Orthop Traumatol Surg Res; 102 (7): 851-5.	Retrospective case series N=10 patients with LLD of lower extremity, treated with an Ellipse PRECICE® nail (6 tibia, 4 femur). Mean follow up was 18 months	In all patients, limb lengthening goals were reached within a range of ± 0.5 cm after a mean time of 53 days. In 2 patients, mechanical failures with unintended shortening were seen. In a further patient, nail breakage occurred. Overall, 7 patients presented with complications.	Study included in systematic review added to the summary of key evidence.
Thaller PH, Furmetz J, Wolf F et al. (2014) Limb lengthening with fully implantable magnetically actuated mechanical nails (PHENIX1)—Preliminary results. Injury, 45S, S60–S65.	N=10 patients had 6 femoral and 4 tibial procedures with Phenix M21 bone lengthening nail.	The intended distraction goal was achieved in 8/10 patients. In simultaneously malalignment was corrected. Average lengthening was 4.6 cm, average distraction index was 0.85 mm/day Average weight bearing index was 27 days/cm. 3 patients had revisions due to early distraction arrest.	Larger studies included in the summary of key evidence.
Tiefenboeck TM, Wozasek GE. (2015) Unusual complication with an intramedullary lengthening device 15 months after implantation. Injury, 46, 2069–2072	Case report N=1 An IM lengthening device (PRECICE1 P1 nail) was implanted in a 74	After bone lengthening of 6 cm and obvious radiological callus formation a nail breakage with severe deformity	Adverse event reported in papers included in the summary of key evidence.

	year old male patient with a congenital leg length discrepancy.	occurred 15 months after implantation.	
Tomaszewski R, Wikor L, Kler J et al. (2020) Results of femoral elongation treatment using electromagnetic intramedullary nail. Preliminary report. Ortopedia Traumatologia Rehabilitacja, 3 (6), 22, 173-179.	Case series N=5 adolescent patients who had treatment for lower limb discrepancy by femoral lengthening using Precice IM nail.	Femoral lengthening was successful in all patients. Femur was lengthened by a mean 49mm , a knee flexion contracture of 10 degrees occurred in 1 patient.	Larger studies included in the summary of key evidence.
Teulieres M, Langlais T, Sales De Gauzy J et al. (2021) Bone lengthening with a motorized intramedullary nail in 34 patients with posttraumatic limb length discrepancies. Journal of Clinical Medicine; 10 (11); 2393.	Prospective case series N=34 patients with symptomatic LLD of 20 mm treated with motorised lengthening nails (Fitbone). mean age of 28.8 ± 9.7 years mean follow up of 27.8 months.	The mean LLD was 44 mm in 29 femoral and 32 mm in 4 tibial cases, which was reduced to less than 10 mm in 25/34 (74%) patients. The mean healing index was 84.6 days/cm for femurs and 92 days/cm for tibias. The mean time to resume full weight-bearing without walking aids was 226 days. There was no significant difference between preoperative and final follow-up alignment angles and ROM. The mechanical lateral distal femoral angle (mLDFA) was corrected in the subgroup of 10 LLD patients with varus deformity of the femur (preoperative 95.7 degree vs.	Larger studies included.

		postoperative 91.5 degree, p = 0.008). According to Paley's classification, there were 14 problems, 10 obstacles and 2 complications. 6 instances of locking screw pull out, often needed reoperation.	
Vogt B, Roedl R, Gosheger G et al. (2020) Tibial lengthening using a retrograde magnetically driven intramedullary lengthening device in 10 patients with preexisting ankle and hindfoot fusion. Acta Orthopaedica; 91 (6): 761–769	Retrospective case series N=10 patients with LLD and pre-existing ankle and hindfoot fusion had tibial lengthening with a retrograde ILN (PRECICE). LLD indications were congenital in 9 and post trauma resection in 1. Mean follow up was 18 months	All patients achieved the goal of lengthening. Toe contractures in 2 patients were resolved with physiotherapy or tenotomy. At last follow up (mean 18 months [12–30]) no true complications were encountered, knee motion remained unaffected, and full osseous consolidation occurred in all patients.	Larger and more comprehensive studies were included in the summary of key evidence.
Wang K, Edwards E. (2012) Intramedullary skeletal kinetic distractor in the treatment of leg length discrepancy-a review of 16 cases and analysis of complications. J Orthop Trauma; 26: e138e44.	Case series (retrospective) N=16 patients who had ISKD (11 femora and 5 tibiae).	Mean lengthening 35mm. The ISKD is an effective method for correcting leg length discrepancies. Complications are frequent but are manageable with standard techniques.	Study included in systematic review added to the summary of key evidence.
Wiebking U, Liodakis E, Kenawey M et al. (2016) Limb lengthening using the PRECICETM nail system: complications and results. Arch Trauma Res; 5(4): e36273.	Retrospective case series N=9 patients with a PRECICE nail for a leg length discrepancy (posttraumatic 5 and congenital 4).	The mean distraction rate was 0.5 ± 0.1 mm/day. Average lengthening was 34.7 ± 10.7 mm. All patients reached normal alignment and normal joint orientation. An	Study included in systematic review added to the summary of key evidence.

	5 femoral, 4 tibial implants Follow up was 2 months.	unintentional loss of the achieved length during the consolidation phase was noticed in 2 patients. 1 nail broke and was replaced.	
Wagner P, Burghardt RD, Green SA et al. (2017) PRECICE magnetically-driven, telescopic, intramedullary lengthening nail: pre-clinical testing and first 30 patients. SICOT J, 3, 19	Retrospective case series N=30 patients with LLD had a Precice IM nail (24 femoral, 8 tibial implants) Follow up was 19 months	Mean postoperative length achieved was 4.3 cm. Average consolidation index was 36.4 days/cm. Mean nail accuracy was 97.3% with a precision of 92.4%.The preoperative and 12-month postoperative SF-12 physical and mental component scores were not statistically different. 9 complications (2 partial femoral unions, 3 DVT, 1 delayed tibial union, 1 fibular non-union, 1 peroneal nerve irritation, 1 knee joint subluxation) resolved. 91% (/29/32) limb segments achieved successful bone healing without revision surgery.	Larger and more comprehensive studies included in the summary of key evidence.
Wright SE, Goodier WD, Calder P. (2020) Regenerate deformity with the Precice tibial nail. Strategies in Trauma and Limb Reconstruction; 10.5005/jp-journals-10080-1457	Case series N= 17 Precice tibial lengthenings (slightly modified surgical technique) Median follow up was 17 months	All the nails lengthened at the desired rate. There were no complications of infection or poor regenerate formation. Progressive valgus and procurvatum was prevented in	Larger studies included in the summary of key evidence.

		later cases by the positioning of Poller blocking screws at the time of nail insertion. The recommended technique was insufficient to control the deforming forces from the lower limb muscle compartments during lengthening. We therefore recommend the addition of multiple blocking screws in an amended technique.	
Young C, Farrah K, Frey N (2017). Intramedullary distraction devices for lower-limb lengthening: clinical effectiveness and guidelines. Ottawa: CADTH; 2017 Apr. (CADTH rapid response report: reference list).	Systematic review and critical appraisal.	One RCT and 22 NRS were identified about the clinical benefit and safety of IM distraction devices for lower-limb lengthening in adults.	Similar reviews added to the summary of key evidence.
Youssef AR, Mohammed G, Hosny, GA. (2021) Are internal lengthening devices effective and associated with less complications compared to other lengthening devices? A systematic review and meta-analysis. Journal of pediatric orthopedics. Part B.	Systematic review and meta-analysis of femoral internal lengthening devices' n=5 randomised and non-randomised studies.	For healing index, there is limited evidence that internal lengthening devices lower healing index by 0.45 months/cm (95% CI, -0.62 to -0.28; P < 0.01) compared to LON/external fixators. The incidence of major complications, that were directly related to the procedures, did not differ between internal	Similar studies included.

		lengthening devices and other fixators (risk ratio=0.97; 95% CI, 0.39-2.44; P < 0.95). This review provides evidence that supports lower healing index and similar complications associated with internal lengthening devices compared to other procedures of femoral lengthening. However, the evidence is very limited to draw a solid conclusion.	
Zak L, Arnhold R, Tiefenboeck, TM et al. (2021) The influence of advanced age in bone healing after intramedullary limb lengthening. Orthopaedics and Traumatology: Surgery and Research; 103055	Case series Retrospective analysis n=19 patients after intramedullary telescopic nailing (PRECICE) on the lower limb. Mean age of 43 years with a mean distraction distance of 38.9 mm.	Younger patients showed a shorter distraction distance, a lower distraction-consolidation time (DCT), a lower distraction index (DI), a higher healing index (HI), and a higher consolidation index (CI) than older patients. The complication rate needing nail exchange was higher among the younger patients. Advanced age did not influence bone healing or complication rate in intramedullary lengthening. However, the conclusion is limited by the small patient numbers.	Large studies included.
Zhang J, Zhang Y, Wang C et al. (2021)	Review	Intramedullary lengthening nails	Review

[Research progress of intramedullary lengthening nail technology]. Chinese journal of reparative and reconstructive surgery; 35 (5); 642-647.		provide a new option for limb lengthening, and the initial effectiveness is good. It is 1 development direction of limb lengthening technology.	