

A procedure-specific systematic review and consensus recommendations for postoperative analgesia following total hip arthroplasty. Fischer and Simanski on behalf of the PROSPECT Working Group.

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Abstract

Total hip replacement is a major surgical procedure usually associated with significant pain in the early postoperative period. Several anaesthetic and analgesic techniques are in common clinical use for this procedure but, to date, clinical studies of pain after total hip replacement have not been systematically assessed. Using the Cochrane protocol, we have conducted a systematic review of analgesic, anaesthetic and surgical interventions affecting postoperative pain after total hip replacement. In addition to the review, transferable evidence from other relevant procedures and clinical practice observations collated by the Delphi method were used to develop evidence-based recommendations for the treatment of postoperative pain. For primary total hip replacement, PROSPECT recommends either general anaesthesia combined with a peripheral nerve block that is continued after surgery or an intrathecal (spinal) injection of local anaesthetic and opioid. The primary analgesic technique should be combined with a step-down approach using paracetamol plus conventional non-steroidal anti-inflammatory drugs, with strong or weak opioids as required.

Qualitative record of analgesic trials in total hip arthroplasty

Systemic analgesia						
Study ID	Quality Grade Score	N treat/control	Drug, dose, route and timing	Postoperative pain scores	Time to first analgesic request	Use of supplemental analgesic
<i>Non-steroidal anti-inflammatory drugs (NSAIDs), placebo-controlled</i>						
Dahl V 1995 ¹	B/4	48/48/25	When spinal anaesthesia about to wear off, oral ibuprofen 800 mg (I) vs. ibuprofen 800 mg and oral codeine 60 mg (IC) vs. placebo	I superior to placebo at 4 h ($p < 0.001$); NS at all other times ($p \geq 0.05$)	Not reported	I superior to control ($p < 0.001$)
Fletcher D 1995 ²	B/4	20/20/20	Before induction, ketorolac 60 mg IV; at skin closure, normal saline 2 mL IV (PRE) vs. before induction, normal saline 2 mL IV; at skin closure, ketorolac 60 mg IV (POST) vs. before induction, normal saline 2 mL IV; at skin closure, normal saline 2 mL IV (placebo)	On arrival in recovery room, PRE superior to placebo at rest ($p = 0.0003$) and movement ($p = 0.0002$); NS over 48 h ($p \geq 0.05$). On arrival in recovery room, POST superior to control ($p = 0.01$); NS over 48 h	Not reported	Cumulative dose: PRE superior to control for titration dose in recovery room ($p < 0.001$) and until 6 h ($p < 0.0125$). POST vs. placebo NS at all times ($p \geq 0.05$)

Fogarty DJ 1995 ³	B/4	30/30	IM ketorolac 30 mg vs. saline placebo, given after induction of spinal anaesthesia, then at three 6 h intervals	Ketorolac superior to placebo at 10 h & morning after surgery ($p<0.05$); NS at all other times	NS	Ketorolac superior to placebo for morphine use per h ($p<0.03$) and cumulative use for 18 h ($p<0.02$)
Iohom G 2002 ⁴	B/3	15/15	Oral dexketoprofen 25 mg three times a day (D) vs. same regimen saline (placebo), for 24 h before and 48 h after surgery	Treatment superior to control at 15 h ($p<0.05$); NS at all other times ($p\geq 0.05$)	Treatment superior to control ($p=0.03$)	Treatment superior to control at 6 & 48 h ($p<0.05$)
Laitinen J 1992 ⁵	B/3	18/20	IV diclofenac 75 mg loading dose over 60 min immediately after surgery, then IV diclofenac 5 mg/h infusion over 15 h vs. same regimen saline placebo	Treatment superior to control at 16 h ($p<0.05$); NS at all other times ($p\geq 0.05$)	Not reported	Treatment superior to control ($p<0.01$)
Segstro R 1991 ⁶	A/4	25/22	At end of surgery and every 8 h thereafter, rectal indomethacin 100 mg vs. placebo	Treatment superior to control at 20, 28 and 42 h ($p<0.05$)	Not reported	Treatment superior to control ($p<0.01$)
Serpell MG 1989 ⁷	B/3	12/12	Oral piroxicam 40 mg on evening of day before surgery & on evening of day of surgery, & oral piroxicam 20 mg on evening of day after surgery vs. placebo capsules at the same times	NS (stats not done)	Not reported	Treatment superior to control ($p<0.002$)

Bugter MLT 2003 ⁸	B/3	17/19	All patients were pretreated during a two-week period before surgery, either with ibuprofen 600 mg or placebo	At rest: NS between groups in 1st 24 h	Not reported	PCA morphine NS between groups
<i>Non-steroidal anti-inflammatory drugs (NSAIDs), other</i>						
Fletcher D 1995 ²	B/4	20/20/20	Before induction, IV ketorolac 60 mg; at skin closure, IV saline 2 mL (PRE) vs. before induction, IV saline 2 mL; at skin closure, IV ketorolac 60 mg (POST) vs. before induction, IV saline 2 mL; at skin closure, IV saline 2 mL	On arrival in recovery room, PRE superior to POST at rest ($p=0.03$) and on movement ($p=0.0002$); NS at all other times over 48 h ($p\geq 0.05$)	Not reported	PRE superior to POST for titration dose in recovery room ($p<0.001$), until 6 h ($p<0.0125$)

Kostamovaara PA 1998 ⁹	B/3	28/28/29	IV ketorolac 30 mg loading dose then IV ketorolac 90 mg infusion vs. IV diclofenac 75 mg loading dose then IV diclofenac 75 mg infusion vs. IV ketoprofen 100 mg loading dose then IV ketoprofen 100 mg infusion; all started in recovery room for 11 h	All outcomes at rest: NS (p≥0.05)	Not reported	NS (p≥0.05)
<i>COX-2 inhibitors</i>						
Camu F 2002 ¹⁰	B/3	73/73/71	Valdecoxib 20 mg (V20) vs. valdecoxib 40 mg (V40) vs. placebo. All given orally 1–3 h before surgery and 12, 24 and 36 h after first dose	V20 and V40 superior to placebo at 4 h (p<0.01), 6, 12 & 18 h (p<0.05). NS at all other times and NS for dose comparison (p≥0.05)	Not reported	V20 and V40 superior to control (p<0.001). NS for dose comparison (p>0.3)
<i>Strong opioid, placebo-controlled</i>						
O'Sullivan G 1983 ¹¹	B/3	19/19/18/18	Sublingual buprenorphine 0.4 mg 2 h before surgery vs. IM buprenorphine 0.3 mg 1 h before surgery vs. IM morphine sulphate 10 mg 1 h before surgery vs. matching placebo regimen (sublingual or IM placebo given to each group to maintain blinding)	NS (p≥0.05)	Not reported	Not reported

<i>Strong opioid, other</i>						
Bourke M 2000 ¹²	B/2	19/20	Oral morphine sulphate sustained-release tablet 20 mg with premedication and every 12 h thereafter for 48 h (MSRT) vs. IM morphine 10 mg after regression of spinal motor block and at 6 h intervals thereafter (MIM) (corresponding IM and oral placebo doses given to maintain blinding)	NS at rest & on movement: (p≥0.05)	Not reported	MIM superior to MSRT at 36 h (p=0.03); NS at all other times (p≥0.05)
Fee JPH 1989 ¹³	B/3	40/40	IM nalbuphine 0.3 mg/kg vs. IM morphine 0.15 mg/kg, each given 1 h before surgery, as soon as requested after surgery and 3 h later if required	Morphine superior to nalbuphine at 2 & 4 h (p<0.02)	Not reported	Morphine superior to nalbuphine (p<0.05)
Frater RAS 1989 ¹⁴	B/3	26/23	After surgery, meptazinol 20 mg boluses on demand via PCA device (10-min lockout; max. dose 120 mg/h) vs. morphine 2 mg boluses on demand via PCA device (10-min lockout; max. dose 12 mg/h)	Morphine superior to meptazinol at 8 h (p<0.05); NS at all other times	Not reported	Not reported
Keita H 2003 ¹⁵	A/2	20/20	Postoperative IV PCA morphine 1 mg with a lockout period of 8 min (PCA group) vs. SC morphine 0.1 mg/kg every 4 h or earlier if VAS≥30 (SC group)	VAS scores on rest and on movement sig. lower in PCA group at all times (24 and 48 h)	Not reported	Postop morphine consumption NS between groups

McCormack JP 1993 ¹⁶	B/4	23/24	Postoperatively, oral morphine 20 mg (5 mg/mL) with 5 mg increments every 4 h and rescue of 10 mg oral morphine; (oral regular) vs. IM morphine 5–10 mg on demand (IM on demand); both groups received corresponding oral or IM placebo doses	Oral regular superior to IM on demand for average scores on day 1 and 2 (p<0.05)	Not reported	Not reported
Robinson SL 1991 ¹⁷	B/3	16/20	After surgery, morphine 2 mg on demand via PCA device vs. diamorphine 1 mg on demand via PCA device	NS (p=0.74)	Not reported	Number of PCA demands: diamorphine superior to morphine (p=0.004)
<i>Weak opioids</i>						
Stubhaug A 1995 ¹⁸	B/4	33/35/36/33	Oral tramadol 50 mg (T50) vs. oral tramadol 100 mg (T100) vs. oral paracetamol 1000 mg plus codeine 60 mg (PC) vs. matching regimen of placebo tablets , all given on day after surgery, (same number of tablets/capsules administered to each group – made up with placebos)	PC superior to T50, T100 and placebo at 2, 3, 4, 5 and 6 h (p<0.05); NS for T50 and T100 vs. placebo	PC superior to T50 (p=0.03), T100 (p=0.005) and placebo (p=0.004)	PC superior to T50 (p=0.002), T100 (p=0.009) and placebo (p=0.0002), for reducing the proportion of patients requiring rescue analgesia
Dahl V 1995 ¹	B/4	48/48/25	When spinal anaesthesia about to wear off, oral ibuprofen 800 mg (I) vs. oral ibuprofen 800 mg plus oral codeine 60 mg (IC) vs. placebo	NS for I vs. IC (p≥0.05). IC superior to placebo	Not reported	NS for I vs. IC (p≥0.05). IC superior to placebo for 0–5 h

				at 4 h		
<i>Paracetamol</i>						
Peduto VA 1998 ¹⁹	B/3	42/47	After extubation, four doses of propacetamol 2 g at 6 h intervals via IV drip infusion (dextrose 5%, 100 mL in 15 min) vs. matching placebo regimen	NS ($p \geq 0.05$)	Not reported	Treatment superior to control ($p < 0.001$)
Stubhaug A 1995 ¹⁸	B/4	33/35/36/33	Oral tramadol 50 mg (T50) vs. oral tramadol 100 mg (T100) vs. oral paracetamol 1000 mg plus codeine 60 mg (PC) vs. matching regimen of placebo tablets , all given on day after surgery, (same number of tablets/capsules administered to each group – made up with placebos)	PC superior to T50, T100 and placebo at 2, 3, 4, 5 and 6 h ($p < 0.05$); NS for T50 and T100 vs. placebo	PC superior to T50 ($p = 0.03$), T100 ($p = 0.005$) and placebo ($p = 0.004$)	PC superior to T50 ($p = 0.002$), T100 ($p = 0.009$) and placebo ($p = 0.0002$), for reducing the proportion of patients requiring rescue analgesia
<i>Other systemic medication</i>						
Kandler D 1993 ²⁰	B/3	17/23	IV metoclopramide 1 mg/kg in saline 100 mL bolus over 15 min, then IV metoclopramide 1.5 mg/kg in saline 150 mL infusion over the following 9 h vs. same placebo regimen, given after spinal block but before surgery	NS ($p \geq 0.05$)	Treatment superior to control ($p < 0.05$)	Treatment superior to control ($p < 0.05$)

IV = intravenous; IM = intramuscular; SC = subcutaneous; PCA = patient controlled; $p < 0.05$ = significant difference in favour of treatment *versus* control; NS = no significant difference between groups ($p \geq 0.05$)

Peripheral neural block						
Study ID	Quality Grade Score	N treat/control	Drug, dose, route and timing	VAS scores/Type of pain, where specified	Time to first analgesic request	Use of supplemental analgesic
Biboulet P 2004 ²¹		16/15/14	Femoral nerve block following Winnie's landmarks (FNB) vs. posterior lumbar plexus (PCB), each at the end of surgery before patient wakes using 2 mg/kg 0.375% bupivacaine and 2 µg/kg clonidine vs. no block . All patients received: general anaesthesia, 2 mg/5 min morphine in PACU if VAS >30 mm, morphine PCA 1 mg with 10-min lockout, paracetamol 2 g/6 h IV and indomethacin 50 mg rectally at end of surgery and then 25 mg orally every 12 h	At rest: PCB superior to FNB and to no block at 0 and 4 h (p=0.001). FNB vs. placebo: NS On mobilisation: NS	Not reported	PCB superior to FNB and to no block for morphine use for 0–4 h (p<0.002). FNB vs. placebo NS
Fournier R 1998 ²²	B/4	20/20	'3-in-1' femoral nerve block following Winnie's landmarks with nerve stimulation (40 mL bupivacaine 0.5% with epinephrine 1:200,000) vs. sham femoral nerve block	NS (p≥0.05)	Block superior to control (p<0.05)	NS (p≥0.05)
Stevens RD 2000 ²³	B/4	30/30	Posterior lumbar plexus block using nerve stimulation (0.5% bupivacaine 0.4 mL/kg with epinephrine 1/200,000) vs. needle perforation of	At rest: block superior to control in PACU for 0-60	Not reported	Block superior to control for morphine 0–6 h (p<0.0001) and 0–12 h (p<0.05)

			lumbar skin	min ($p < 0.001$) and at ($p = 0.007$)		
Singelyn FJ 2001 ²⁴	B/3	15/15/15	Extended femoral nerve sheath block with continuous infusion of 0.125% bupivacaine with clonidine 1 $\mu\text{g}/\text{mL}$ and sufentanil 0.1 $\mu\text{g}/\text{mL}$ at 10 mL/h vs. 10 mL boluses of 0.125% bupivacaine with clonidine 1 $\mu\text{g}/\text{mL}$ and sufentanil 0.1 $\mu\text{g}/\text{mL}$ via PCA device with 60-min lockout vs. 5 mL boluses of 0.125% bupivacaine with clonidine 1 $\mu\text{g}/\text{mL}$ and sufentanil 0.1 $\mu\text{g}/\text{mL}$ via PCA device	At rest: NS ($p \geq 0.05$) On movement: NS ($p \geq 0.05$)	Not reported	NS ($p \geq 0.05$)

PCA = patient controlled; PACU = postanesthesia care unit; $p < 0.05$ = significant difference in favour of treatment *versus* control; NS = no significant difference between treatment and control ($p \geq 0.05$)

Epidural analgesia						
Study ID	Quality Grade Score	N treat/control	Drug, dose, route and timing	VAS scores/Type of pain, where specified	Time to first analgesic request	Use of supplemental analgesic
<i>Epidural anaesthesia and analgesia vs. general anaesthesia and systemic analgesia</i>						
Wulf H 1999 ²⁵	B/2	46/44	Epd anaesthesia then, when regression of motor block obvious, continuous epd infusion of ropivacaine 2 mg/mL at 4–6 mL/h (8–12 mg/h) plus ropivacaine 6 mL top-up doses on demand with ≥30 mins between top-ups, for 24 h, then ropivacaine 20 mg top-up doses at investigator's discretion for 24 h (epd) vs. general anaesthesia (thiopental/fentanyl then isoflurane/enflurane, fentanyl, nitrous oxide/oxygen) then in PACU, morphine 10 mg max. IV loading dose followed by morphine 1.0–1.5 mg IV boluses on demand via PCA device with 5-min lockout, for 48 h (GA)	At rest: epd superior to GA during 24 h (area under the curve, p=0.007) and a greater proportion of patients in the GA had VAS score >30 mm (p<0.05). On mobilisation: scores with GA higher than with epd but NS. After epd stopped: NS	Not reported	Greater proportion of patients required rescue morphine in the GA group (9%) compared with the epidural (67%), no p values

Moiniche S 1994 ²⁶	B/2	10/10	General anaesthesia (midazolam, fentanyl then nitrous oxide, fentanyl and midazolam), then conventional analgesia with IV morphine 5 mg, IM morphine 0.125 mg/kg and oral acetaminophen on demand (GA) vs. epd anaesthesia, then continuous epd infusion of bupivacaine 0.625 mg/mL plus morphine 0.05 mg/mL at 4 mL/h for 48 h postoperatively, plus oral piroxicam 40 mg on evening before surgery and 1 h before surgery, then oral piroxicam 20 mg/day for 7 days (epd)	During 48 h: epd superior to GA (at rest p=0.001, during flexion p=0.0002, during walk p=0.01). When epd stopped: epd superior to GA during flexion (p=0.02) but NS at rest (p=0.44) & during walk (p =0.7)	Not reported	NS (assessed when epd stopped p=0.31)
<i>Epidural analgesia vs. systemic analgesia</i>						
Gustafsson LL 1986 ²⁷	B/2	07/07/07	After surgery when severe pain experienced, one dose administered: IM pethidine hydrochloride 1 mg/kg in saline 0.02 mL/kg (IM) vs. epidural pethidine hydrochloride 20 mg in 0.9% saline 10 mL (Epd20) vs. epidural pethidine hydrochloride 60 mg in 0.9% saline 10 mL (Epd60) (each group had corresponding IM or epd saline regimen)	Epd60 superior to IM at 0.5 and 1 h after dose (p<0.05), but NS for 2, 3 and 4 h. Epd20 vs. IM: NS (p≥0.05). Epd20 vs. Epd60: NS	NS (p≥0.05)	NS (p≥0.05)

<i>Epidural local anaesthetic vs. epidural without local anaesthetic</i>						
Carabine UA 1992 ²⁸	B/4	30/30/30	~30 min before end of surgery, epidural clonidine 150 µg (1 mL) diluted to 10 mL in 0.9% saline (C) vs. epidural 10 mL plain bupivacaine 0.25% (B) vs. epidural clonidine 150 µg (1 mL) in 9 mL plain bupivacaine 0.25% (CB)	CB superior to B at 30 and 60 min (p<0.05); CB superior to C at 60 min (p<0.05). C superior to B at 60 min (p<0.05)	CB superior to C (p<0.05); CB and C superior to B (p<0.05)	CB superior to B (p<0.05); C superior to B (p<0.05); CB vs. C NS
Kostamovaara PA 2001 ²⁹	B/4	20/19	In PACU, fentanyl 10 µg/mL plus ropivacaine 1 mg/mL as 3 mL/h continuous infusion plus 3 mL boluses on demand via PCEA device (FR) vs. fentanyl 10 µg/mL as 3 mL/h continuous infusion plus 3 mL boluses on demand via PCEA device (F)	At rest & on movement: NS (p≥0.05)	Not reported	Not reported
Milligan KR 2000 ³⁰	B/4	27/30/29	Levobupivacaine 0.125% epd infusion at 6 mL/h for 24 h (L) vs. levobupivacaine 0.125% plus clonidine 8.3 µg/mL epd infusion at 6 mL/h for 24 h (LC) vs. clonidine 8.3 µg/mL epd infusion at 6 mL/h for 24 h (C)	On movement: NS for all comparisons (p≥0.05)	LC superior to L (p<0.01), but not C. C superior to L (p<0.05)	LC superior to L and C (p<0.01); and C superior to L (p<0.05), for total morphine use

<i>Local anaesthetic comparison</i>						
Bertini L 2001 ³¹	B/3	26/25	After surgery, ropivacaine 2 mg/mL continuous epd infusion at 6 mL/h and ropivacaine 4 mg boluses on demand via PCEA (R) vs. bupivacaine 2 mg/mL continuous epd infusion at 6 mL/h and bupivacaine 4 mg boluses on demand via PCEA (B)	At rest and during physio: NS (p≥0.05)	Not reported	NS (p≥0.05)
Casati A 2003 ³²	A/4	15/15/15	Levobupivacaine (L) vs. bupivacaine (B) (both given intra-op in 10 mL at 0.5% and postop 0.125% set at 5 mL/h, with 2 mL incremental boluses and a lockout time of 20 min) vs. ropivacaine (R) (given intra-op at 0.5% and postop analgesia with PCEA epidural infusion of ropivacaine 0.2% set at 5 mL/h, with 2 mL incremental boluses and a lockout time of 20 min)	NS at 0, 6 and 12 h postop	Not reported	NS between groups
<i>Strong opioid vs. different type or dose of strong opioid</i>						
Berti M 1998 ³³	B/3	15/15	Immediately after surgery, 5 mL epd bolus of morphine 0.05 mg/mL in bupivacaine 0.125%, then continuous epd infusion of same solution at 4 mL/h for 24 h (M) vs. 5 mL epd bolus of fentanyl 0.005 mg/mL in bupivacaine 0.125%, then continuous epd infusion of same solution at 4 mL/h for 24 h (F)	NS (p≥0.05)	Not reported	NS (p≥0.05)

Kampe S 2003 ³⁴	A/3	11/10/11	Continuous epidural infusion (started postop) with ropivacaine 0.1% combined with: sufentanil 0.5 µg/mL (S0.5) vs. sufentanil 0.75 µg/mL (S0.75) vs. sufentanil 1 µg/mL (S1)	At rest and on movement: NS between groups	Not reported	IV PCA use NS between groups
<i>Clonidine vs. LA, strong opioid or combination</i>						
Carabine UA 1992 ²⁸	B/4	30/30/30	~30 min before end of surgery, epidural clonidine 150 µg (1 mL) diluted to 10 mL in 0.9% saline (C) vs. epidural 10 mL plain bupivacaine 0.25% (B) vs. epidural clonidine 150 µg (1 mL) in 9 mL plain bupivacaine 0.25% (CB)	CB superior to B at 30 and 60 min (p<0.05); CB superior to C at 60 min (p<0.05). C superior to B at 60 min (p<0.05)	CB superior to C (p<0.05); CB and C superior to B (p<0.05)	CB superior to B (p<0.05); C superior to B (p<0.05); CB vs. C NS
Carabine UA 1992 ³⁵	B/3	20/20/20/20	~30 min before end of surgery, epidural clonidine 150 µg (1 mL) diluted to 10 mL in 0.9% saline, then epidural clonidine 25 µg/mL infusion at 1 mL/h for 24 h (C25) vs. epidural clonidine 150 µg (1 mL) diluted to 10 mL in 0.9% saline, then epidural clonidine 50 µg/mL infusion at 1 mL/h for 24 h (C50) vs. epidural morphine 1 mg diluted to 10 mL in 0.9% saline, then epidural morphine 0.1 mg/mL infusion at 1 mL/h for 24 h (M) vs. epidural clonidine 150 µg (1 mL) plus morphine 1 mg diluted to 10 mL in 0.9% saline, then epidural morphine 0.1 mg/mL	CM, C25 and C50 superior to M at 30 & 60 min (p<0.05) CM vs. C25 vs. C50: NS	CM and C50 both superior to M and C25 groups (p<0.05)	CM superior to C25 and M (p<0.05); C50 superior to C25 (p<0.05); C25 vs. M: NS; CM vs. C50: NS

			infusion at 1 mL/h for 24 h (CM)			
Milligan KR 2000 ³⁰	B/4	27/30/29	Levobupivacaine 0.125% epd infusion at 6 mL/h for 24 h (L) vs. levobupivacaine 0.125% plus clonidine 8.3 µg/mL epd infusion at 6 mL/h for 24 h (LC) vs. clonidine 8.3 µg/mL epd infusion at 6 mL/h for 24 h (C)	On movement: NS for all comparisons (p≥0.05)	LC superior to L (p<0.01), but not C. C superior to L (p<0.05)	LC superior to L and C (p<0.01); and C superior to L (p<0.05), for total morphine use

IV = intravenous; IM = intramuscular; epd = epidural; exd = extradural; PCA = patient controlled; PCEA = patient controlled epidural analgesia; PACU = postanaesthesia care unit; p<0.05 = significant difference in favour of treatment vs. control; NS = no significant difference between treatment and control (p≥0.05)

Spinal anaesthesia and analgesia						
Study ID	Quality Grade Score	N treat/control	Drug, dose, route and timing	VAS scores/Type of pain, where specified	Time to first analgesic request	Use of supplemental analgesic
<i>Spinal technique vs. different technique</i>						
Maurer K 2003 ³⁶	A/3	31/34	Continuous IT anaesthesia with 15 mg isobaric bupivacaine 5 mg/mL (1 mL) and postoperative analgesia with IT isobaric bupivacaine 2.5–5 mg/h (CS) vs. single-shot IT anaesthesia consisting of 15 mg isobaric bupivacaine 5 mg/mL (3 mL) and postoperative IV PCA morphine 3 mg bolus and 5-min lockout (IV)	Pain scores sig lower 3–24 h in the (CS) group (p<0.05)	Not reported	Not reported
Möllmann M 1999 ³⁷	B/3	51/51	Continuous IT anaesthesia, then bupivacaine 0.25% 1 mL bolus followed by bupivacaine 0.25% 10 mL continuous infusion over 24 h (IT) vs. continuous epd anaesthesia, then bupivacaine 0.25% 10 mL bolus followed by bupivacaine 0.25% 2 mL/h continuous infusion (epd)	At rest: IT superior to epd (p<0.05) for 6–57 h After movement: IT superior to epd (p<0.05)	Not reported	IT superior to epd (p<0.05)

Souron V 2003 ³⁸	A/2	27/26	IT morphine 0.1 mg admin over 15 s (IT) vs. psoas compartment block with 25 mL ropivacaine 0.475% (PCB); each administered 30 min before general anaesthesia	Sig lower in IT at 30 min, 90 min, 6 h, 12 h and 18 h (p<0.05). NS at 60 min, 120 min, 24 and 48 h	Not reported	Morphine consumption lower in IT in PACU, during 24 h to 48 h (p<0.05)
<i>Spinal local anaesthetic plus strong opioid vs. spinal local anaesthetic alone</i>						
Fernandez-Galinski D 1996 ³⁹	B/2	11/11	Hyperbaric bupivacaine 12.5 mg plus fentanyl 25 µg in a final volume of 3.5 mL (BF) vs. hyperbaric bupivacaine 12.5 mg plus saline in a final volume of 3.5 mL (B)	BF superior to B (p<0.05)	Not reported for hip	Not reported for hip
Fogarty DJ 1993 ⁴⁰	B/3	30/30/30	IT anaesthesia with 2.75 mL plain bupivacaine 0.5% over 10 s then morphine 1 mg diluted to 1 mL with saline 0.9% (BM) vs. 2.75 mL plain bupivacaine 0.5% over 10 s then clonidine 75–100 µg (depending on weight) diluted to 1 mL with saline 0.9% (BC) vs. 2.75 mL plain bupivacaine 0.5% over 10 s then 1 mL saline 0.9% (B)	BM superior to BC 4, 6, 8 & 10 h (4, 8 & 10 h postop, p<0.01; 6 h postop, p<0.001); BM superior to B at 4, 6, 8 and 10 h (p<0.05); B superior to BC and BM at 24 h (p<0.05).	BM superior to B (p<0.05). BC superior to B (p<0.05)	BM superior to B (p<0.05). BC vs. B: NS

Grace D 1994 ⁴¹	B/3	30/30/30	Pethidine 0.75 mg/kg and clonidine 75 µg (0.5 mL) made up to 3.75 mL with 0.9% sodium chloride (PC) vs. 0.5% isobaric bupivacaine 13.75 mg (2.75 mL), then morphine sulphate 0.5 mg (0.25 mL) and 0.9% sodium chloride (0.75 mL) (BM) vs. 0.5% isobaric bupivacaine (B)	At rest: BM superior to B 2 h (p=0.04), 4 h (p<0.018) & 6 h (p<0.02) postop; NS 10 h postop (p≥0.05)	BM superior to B (p<0.001).	BM superior to B (p<0.001)
Grace D 1995 ⁴²	B/3	30/30/30	Morphine sulphate 0.5 mg (0.25 mL) plus clonidine hydrochloride 75 µg (0.5 mL) (BMC) vs. morphine sulphate 0.5 mg (0.25 mL) (BM) vs. 0.9% sodium chloride (1 ml) (B) ; all groups received 0.5% isobaric bupivacaine 13.75 mg (2.75 mL)	At rest: BM superior to B at 2 h (p<0.04) & 4 h (p<0.001) postop; NS at all other times (p≥0.05). BMC superior to B at 2 h (p<0.04), 4 h (p<0.001), 6 h (p<0.002) & 24 h (p<0.009) postop	BM superior to B (p<0.001). BMC superior to B (p<0.001)	BM superior to B (p<0.001). BMC superior to B (p<0.001)
Milligan KR 1993 ⁴³	B/4	30/30	1 mL diamorphine (0.75–1 mg, depending on weight) (BD) vs. 1 mL saline (B) ; both groups received 2.75 mL plain bupivacaine 0.5% over 10 s	BD superior to B 6 h (p<0.001), 8 h (p<0.01), 10 h (p<0.05) & 12 h (p<0.01) postop; NS at all other	BD superior to B (p<0.001)	BD superior to B (p<0.001)

				times		
Murphy PM 2003 ⁴⁴	B/2	20/20/20/20	IT anaesthesia with hyperbaric bupivacaine 15 mg + IT morphine 50 µg vs. IT anaesthesia with bupivacaine 15 mg + IT morphine 100 µg vs. IT anaesthesia with bupivacaine 15 mg + IT morphine 200 µg vs. IT anaesthesia with bupivacaine 15 mg (control)	Pain scores sig lower in 100 and 200 µg morphine groups vs. 50 µg and control group (p<0.05). 100 vs. 200 µg group: NS at all time points	Sig longer in 100 and 200 µg morphine groups vs. 50 µg and control group (p<0.05). 100 vs. IT 200 µg group: NS	Mean suppl morphine consumption over 1st 24 h sig lower in 100 and 200 µg morphine groups vs. 50 µg and control group (p<0.05). 100 vs. IT 200 µg group: NS
<i>Spinal local anaesthetic comparison</i>						
Glaser C 2002 ⁴⁵	A/4	40/40	isobaric levobupivacaine 0.5% 3.5 mL vs. isobaric bupivacaine 0.5% 3.5 mL; both single shot for anaesthesia	NS (p≥0.05)	Not reported	Similar (stats not done)
<i>Spinal strong opioid comparison</i>						

Fournier R 2000 ⁴⁶	B/4	12/12	When postop VAS pain score >3 cm, IT nalbuphine 400 µg in 4 mL normal saline over 1 min (N) vs. IT morphine 160 µg in 4 mL normal saline over 1 min (M)	N superior to M 5–15 min after IT injection (p<0.05); NS at all other times (p> 0.05)	M superior to N (p<0.05)	M superior to N (p<0.001)
Fournier R 2000 ⁴⁷	B/4	21/21	When postop VAS pain score >3/10, IT fentanyl 40 µg in 2 mL normal saline over 30 s (F) vs. IT sufentanil 7.5 µg in 2 mL normal saline over 30 s (S)	NS (p> 0.05)	NS (p> 0.05)	NS (p> 0.05)
Fogarty DJ 1995 ⁴⁸	B/4	30/30	2.75 mL plain bupivacaine 0.5% over 10 s, then morphine 1 mg (made up to 1 mL in normal saline) (BM) vs. 2.75 mL plain bupivacaine 0.5% over 10 s, then diamorphine 0.75 mg (made up to 1 mL in normal saline) (BD)	2, 6, 8, 10, 12 h postop: NS 4 h postop: BM superior to BD (p<0.01). 24 h postop: BD superior to BM (p<0.05)	NS (p≥0.05)	BM superior to BD (p<0.05)
Grace D 1996 ⁴⁹	B/4	25/25/25	0.5% plain bupivacaine 13.75 mg, then morphine sulphate 500 µg (0.25 mL) and 0.9% sodium chloride 0.75 mL (M) vs. 0.5% plain bupivacaine 13.75 mg, then morphine-6-glucuronide 100 µg (0.8 mL) (M6G100) and 0.9% sodium chloride (0.2 mL) vs. 0.5% plain bupivacaine 13.75 mg, then morphine-6-glucuronide 125 µg (1 mL) (M6G125)	At rest & on movement: NS (p≥0.05)	NS (p≥0.05)	NS (p≥0.05)

Murphy PM 2003 ⁴⁴	B/2	20/20/20/20	IT anaesthesia with bupivacaine 15 mg + IT morphine 50 µg vs. IT anaesthesia with bupivacaine 15 mg + IT morphine 100 µg vs. IT anaesthesia with bupivacaine 15 mg + IT morphine 200 µg vs. IT anaesthesia with bupivacaine 15 mg (control)	Pain scores sig lower in 100 and 200 µg morphine groups vs. 50 µg and control group (p<0.05). 100 vs. 200 µg group NS at all time points	Sig longer in 100 and 200 µg morphine groups vs. 50 µg and control group (p<0.05). 100 vs. IT 200 µg group: NS	Mean suppl morphine consumption over 1st 24 h sig lower in 100 and 200 µg morphine groups vs. 50 µg and control group (p<0.05). 100 vs. IT 200 µg group: NS
Slappendel R 1999 ⁵⁰	B/2	35/37/37/34	Bupivacaine 20 mg plus morphine 0.025 mg (BM0.025) vs. bupivacaine 20 mg plus morphine 0.05 mg (BM0.05) vs. bupivacaine 20 mg plus morphine 0.1 mg (BM0.1) vs. bupivacaine 20 mg plus morphine 0.2 mg (BM0.2)	NS (p≥0.05)	Not reported	BM0.1 superior to BM0.025 (p<0.01); BM0.2 superior to BM0.025 (p<0.01). Other combinations NS (p≥0.05)

Spinal clonidine, placebo-controlled

Fogarty DJ 1993 ⁴⁰	B/3	30/30/30	IT anaesthesia with 2.75 mL plain bupivacaine 0.5% over 10 s then morphine 1 mg diluted to 1 mL with saline 0.9% (BM) vs. 2.75 mL plain bupivacaine 0.5% over 10 s then clonidine 75–100 µg (depending on weight) diluted to 1 mL with saline 0.9% (BC) vs. 2.75 mL plain bupivacaine 0.5% over 10 s then 1 mL saline 0.9% (B)	BM superior to BC 4, 6, 8 & 10 h (4, 8 & 10 h, $p < 0.01$; 6 h, $p < 0.001$); BM superior to B at 4, 6, 8 and 10 h ($p < 0.05$); BC superior to B at 2 (p<0.05) & 4 h (p<0.001). B superior to BC and BM at 24 h (p<0.05).	BM superior to B and BC (p<0.05). BC superior to B (p<0.05)	BM superior to B and BC (p<0.05). BC vs. B: NS
Fournier R 2002 ⁵¹	B/4	15/15/15	When postop VAS pain score >3/10, IT sufentanil 7.5 µg plus epinephrine 200 µg in 2 mL normal saline, over 30 s (SE) vs. IT sufentanil 7.5 µg plus clonidine 30 µg in 2 mL normal saline, over 30 s (SC) vs. IT sufentanil 7.5 µg in 2 mL normal saline, over 30 s (S)	All comparisons: NS ($p \geq 0.05$)	All comparisons: NS ($p \geq 0.05$)	All comparisons: NS ($p \geq 0.05$)

Grace D 1995 ⁴²	B/3	30/30/30	Morphine sulphate 0.5 mg (0.25 mL) plus clonidine hydrochloride 75 µg (0.5 mL) (BMC) vs. morphine sulphate 0.5 mg (0.25 mL) (BM) vs. 0.9% sodium chloride (1 ml) (B); all groups received 0.5% isobaric bupivacaine 13.75 mg (2.75 mL)	At rest: BM superior to B at 2 h (p<0.04) & 4 h (p<0.001); NS at all other times (p≥0.05). BMC superior to B at 2 h (p<0.04), 4 h (p<0.001), 6 h (p<0.002) & 24 h (p<0.009). BMC vs. BM: NS	BM superior to B (p<0.001). BMC superior to B (p<0.001). BMC vs. BM: NS	BM superior to B (p<0.001). BMC superior to B (p<0.001). BMC vs. BM: NS
<i>Other combinations of spinal agents</i>						
Grace D 1994 ⁴¹	B/3	30/30/30	Pethidine 0.75 mg/kg and clonidine 75 µg (0.5 mL) made up to 3.75 mL with 0.9% sodium chloride (PC) vs. 0.5% isobaric bupivacaine 13.75 mg (2.75 mL), then morphine sulphate 0.5 mg (0.25 mL) and 0.9% sodium chloride (0.75 mL) (BM) vs. 0.5% isobaric bupivacaine	At rest: BM superior to B 2 h (p=0.04), 4 h (p<0.018) & 6 h (p<0.02); NS 10 h (p≥0.05). BM superior to PC at 4 h (p < 0.001), 6 h (p < 0.04) & 10 h (p < 0.02), but NS at 2 h (p ≥ 0.05). B superior to PC at	BM superior to B (p<0.001). BM superior to PC (p = 0.001). B vs. PC: NS	BM superior to B (p<0.001). BM superior to PC (p = 0.001) B vs. PC: NS.

				10 h ($p < 0.05$) but NS at 2, 4 & 6 h postop ($p \geq 0.05$)		
Fournier R 2002 ⁵¹	B/4	15/15/15	When postop VAS pain score $>3/10$, IT sufentanil 7.5 μg plus epinephrine 200 μg in 2 mL normal saline, over 30 s (SE) vs. IT sufentanil 7.5 μg plus clonidine 30 μg in 2 mL normal saline, over 30 s (SC) vs. IT sufentanil 7.5 μg in 2 mL normal saline, over 30 s (S)	All comparisons: NS ($p \geq 0.05$)	All comparisons: NS ($p \geq 0.05$)	All comparisons: NS ($p \geq 0.05$)
<i>Different spinal dosing regimens</i>						
Rundshagen I 1997 ⁵²	B/2	20/21	In PACU, infusion of plain bupivacaine 0.125% at 0.6 mg/h plus bupivacaine 0.6 mg boluses on demand via PCA device with 30-min lockout (PCA) vs. first bolus when VAS pain score >50 mm and thereafter on demand bupivacaine 0.25% 3.75 mg subarachnoid boluses on demand (bolus)	At rest: PCA superior to bolus for mean score over 18 h and for every 1-time point between 2 and 18 h (except 3 and 14 h) ($p < 0.01$)	Not reported	PCA superior for reducing total dose of bupivacaine ($p < 0.01$). Supplementary piritramide: NS ($p \geq 0.05$)

IT = spinal administration; epd = epidural; PACU = postanesthesia care unit; $p < 0.05$ = significant difference in favour of treatment *versus* control;

NS = no significant difference between treatment and control ($p \geq 0.05$)

Operative techniques and perioperative procedures						
Study ID	Quality Grade Score	N treat/control	Drug, dose, route and timing	VAS scores/ Type of pain, where specified	Time to first analgesic request	Use of supplemental analgesic
Horwitz BR 1993 ⁵³	C/1	49/51	Modified Hardinge approach vs. transtrochanteric lateral approach	NS ($p \geq 0.05$)	Not reported	Not reported
Borghi B 2004 ⁵⁴	A/4	24/24	Epidural catheter insertion with the tip of the Tuohy needle rotated 45° toward the operative side vs. tip of the Tuohy needle in the conventional position (90° cephalad)	VRS: NS	Not reported	NS
Ravikumar KJ 2001 ⁵⁵	A/4	12/13	Drains, one placed next to joint and one in subcutaneous fat layer, exiting anterior to incision, for 24 h vs. no drains.	Drains had higher pain scores than no drains on days 2 and 4 (no p values reported)	Not reported	Not reported

$p < 0.05$ = significant difference in favour of treatment *versus* control; NS = no significant difference between treatment and control ($p \geq 0.05$)

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