

APPENDICES

Appendix 1. Description of the included and excluded studies

Appendix 1a displays excluded studies based on publication year.

Appendix 1b shows the included studies.

Appendix 2. Search Strategy

Search strategies for various databases.

Appendix 3. Cochrane Collaboration's tool for assessment of risk of bias in randomized controlled trials.

Appendix 4. Newcastle-Ottawa Scale (NOS) for assessing the quality of non-randomized studies.

Appendix 1a. Excluded Studies based on publication year

Author/Year	Country	Design	Medication(s) Used	No. of Patients	No. of Sedations	Mean (SD) Age	Male (%)	Procedure(s)
Acworth/2001	Australia	Single blind RCT	INM (50%);IVKM (50%)	52	52	INM: 3.5 (2.0); IVKM:4.6 (2.9)	29 (55.8)	Minor Procedures: Laceration repair; Foreign Body Removal
Bassett/2003	USA	Prospective cohort	Propofol	392	393	8.0 (1-18)	67 (17.1)	Fracture reduction; Joint dislocations; Ocular burn examination
Bates/1994	USA	Single-blind, RCT	IN SM; IM MPC	SM: 19; MPC: 23	SM: 19; MPC: 23	SM, m: 27.9±12.9; MPC: 28.5±11.2	SM: 12(63);MP C: 17 (76)	Sutures lacerations
Bauman/2002	USA	RCT	PF; MR	PF: 88; MR: 87	PF: 88; MR: 87	NA	NA	NA
Billmire/1985	USA	Single Cohort Study	F	2000	2000	NA	NA	Laceration repair, orthopedic procedures
Binder/1991	USA	prospective, observational, non- randomized clinical trial	CH	42	42	3.017	29 (69)	Wound repair, I&D, Foreign body removal, etc
Connors/1994	USA	double-blind, double-P trial	M:Oral vs Nasal drops	Oral: 26; Nasal: 28	Oral: 26; Nasal: 28	Mean(SD); Nasal:3.5(1.9);Ora 14.4(2.5)	Oral:16, Nasal:11	NA
Dachs/1996	USA	Prospective Cohort	K IV	30	30	Median, m: 38; Range: 18 m-8 y	21 (70)	Laceration repair
Davies/1998	UK	Prospective, randomized double blind 2-stage trial	M Oral	50	50	Median, y: 4; Range, y:1-13	NA	Laceration repair, foreign body removal, burn dressing, earring removal, replacing avulsed incisor, orthopedic reduction
Dickinson/2001	USA	Retrospective descriptive chart review	Etomidate	53	53	Mean±SD, y: 9.7±4; Range, y: 2-17	31 (58.5)	Fracture or joint reduction
Ellis/2004	UK	Prospective cohort study	K IM	89	89	Range, y: 1-10	51 (57)	Suturing, foreign body removal, I&D, excision of skin tag, dressing
Frampton/2003	Australia	Retrospective review	Nitrous Oxide	224	224	Range, y: 1-18	138 (61.6)	Wound examination, orthopedic manipulation, dressing, investigative procedures (IV line etc.)
Godambe/2003	USA	prospective, partially blind controlled comparative trial	P/F; KM	P/F: 59;KM: 54	P/F: 59; KM: 54	P/F: 9.3 y (3.9);KM: 9.1 y (3.1);Range, y: 3.1-16.3	P/F: 49 (83.1);KM: 39 (72.2)	Orthopedic procedures
Graff/1996	USA	Retrospective review	FM	339	339	Mean, y: 8.4	220 (65)	Fracture reduction and joint relocation
Green/1998	USA	Retrospective cohort	K IV	156	156	Mean: 6.3 (3.2)	108 (69)	Orthopedic procedures, wound and dermal procedures, intubation, CT scan, foreign body removal, hernia reduction, lumbar puncture etc
Green/1998	USA	Retrospective cohort	K IM	1022	1022	Mean, y: 4.5;Median, y: 3.9	609 (60)	Orthopedic procedures, wound and dermal procedures, intubation, CT scan, foreign body removal, hernia reduction, lumbar puncture etc
Hart/1997	USA	Randomized, controlled study	FIV; FM; MPC	FIV: 20;FM: 13; MPC: 9	FIV: 20;FM: 13;MPC: 9	Mean, y: 4.8 (range: 2-11)	NA	Lacerations, fractures, dental procedures, I&D

Havel/1999	USA	Prospective, blind, randomized, clinical trial	Propofol, M	Propofol: 43; M: 46	Propofol: 43; M: 46	Mean, y: Propofol: 9.0±3.8; M: 8.6±4.2	Propofol: 25 (58.1); M: 35 (76.1)	Orthopedic reduction
Holloway/2000	UK	Retrospective review	K	100	105	Range, y: 0-12	56 (56)	Laceration repairs, foreign body removal, I&D, fracture manipulation, lump excision, dressing change, knee aspiration
Hostetler/2002	USA	Retrospective review	KM; FM	KM: 57; FM: 28	KM: 57; FM: 28	Mean(SD), m; KM: 44.9 (37.2); FM: 31.6 (25.5); Range, y: 0-18	KM: 28 (50); FM: 17 (65.4)	Esophageal Foreign body removal
Ip/2000	Canada	Retrospective review of prospectively gathered sedation data	K; FM; M	K: 138; FM: 28; M: 1	K: 138; FM: 28; M: 1	Range: 6 m-16 y	103 (62)	Orthopedic procedures, wound repair, foreign body removal, ophthalmologic examination, dorsal slit of the penis, TMJ reduction, fecal impaction, rectal prolapse reduction
Kenegaye/2003	USA	Randomized, double-blind, controlled study	SDM; HDM	SDM: 32; HDM: 33	SDM: 32; HDM: 33	Mean±SD, m: HDM 30.0 ± 11.3; SDM: 25.5 ± 10.6; Range, m: 8-47	SDM: 22 (69); HDM: 20 (61)	Wound repair
Kennedy/1998	USA	Single-blind, randomized, controlled trial	FM; KM	FM: 130; KM: 130	FM: 130; KM: 130	Mean±SD, y: FM: 9.7±3.01; KM: 9.7±3.27; Range, y: 5-15	FM: 94 (72); KM: 88 (68)	Orthopedic procedures
Kim/2003	USA	Prospective, observational case series	K IV	20	20	Median, y: 6.5; Range, y: 1.7-13.0	8 (40)	Fracture reduction, Laceration, I&D, central venous access, wound exploration
Klein/2002	USA	Randomized, double-blind, P-controlled, clinical trial	MF; M	MF: 28; M: 23	MF: 28; M: 23	MF: 3.8 y; M: 3.7 y; Range: 2-8 y	MF: 15 (54); M: 12 (52)	Laceration Repair
Luhmann/2001	USA	Randomized, 4-armed, controlled trial	M; N2O; MN	M: 51; N2O: 51; MN: 52	M: 51; N2O: 51; MN: 52	Mean, y (SD); M: 4.2 (1.4); N2O: 4.2 (1.4); MN: 4.0 (1.4)	M: 33 (65); N2O: 35 (69); MN: 34 (65)	Laceration repair
Luhmann/2002	USA	Retrospective Cohort	KM; MoM; MeM; MN	KM: 36; MoM: 3; MeM: 2; MN: 1	KM: 36; MoM: 3; MeM: 2; MN: 1	Mean, y (SD); 11.3 (4.3)	16 (36)	Peritonsillar Abscess
McCarty/2000	USA	Prospective cohort	K	114	114	Mean, y (range); 5.3 (1-10.9)	64 (56.1)	Fracture and dislocation reduction
McGlone/1998	UK	Prospective cohort	K; M	K: 50; M: 50	K: 50; M: 50	Median; K: 3.6 (1-7); M: 3.6 (1-7)	NA	Suturing
McGlone/2001	UK	Prospective cohort	M; MF	M: 20; MF: 20	M: 20; MF: 20	y (SD) M: 3.4 (1.7); MF: 2.9 (1.4)	NA	Suturing
McGlone/2004	UK	Prospective cohort	K	501	501	Mean, y: 3.6 y (median 3, mode	NA	Wound toilet, suturing and foreign body removal

						2, range 0–12)		
McQuillen/2000	USA	Prospective cohort	M; KM; MO; K; KMO	M: 13;KM: 44;MO: 46;K: 1;KMO: 2	M: 13;KM: 44;MO: 46;K: 1;KMO: 2	Mean, y (range):6.8 (1.2-16.6)	64 (60)	Fracture reduction, laceration repair, I&D, LP
Pena/1999	USA	Prospective cohort	MFIV; MIV;MPO;INM; FIV; IMKM;IVKM; KPO; PIV; CPO; DPO; LIV; LPO; MS; MM; CH	MFIV: 391; MIV: 67; MPO: 62; INM: 3; FIV: 21; IMKM: 180; IVKM: 40; KPO: 2; PIV: 93; CPO: 122; DPO: 1; LIV: 9; LPO: 1; MS: 25; MM: 1; N2O: 168; CH: 4	MFIV: 391; MIV: 67; MPO: 62; INM: 3; FIV: 21; IMKM: 180; IVKM: 40; KPO: 2; PIV: 93; CPO: 122; DPO: 1; LIV: 9; LPO: 1; MS: 25; MM: 1; N2O: 168; CH: 4	Median, m: 48;Range: 1 m-21 y	733^ (62)	Imaging, laceration repair, arthrocentesis, bone marrow aspiration, foreign body removal, hernia reduction
Pershad/2004	USA	Retrospective cohort	Propofol	52	54	Mean (SD); 4.25 (1.86) mg/kg	31 (59)	I&D, imaging, laceration repair, burn debridement, fracture manipulation
Petrack/1996	USA	RCT	K;MPC	K: 15;MPC: 12	K: 15;MPC: 12	Mean, m (SD); K: 31 (20) MPC: 39 (22)	K: 10 (67);MPC: 10 (83)	Suturing, wound/burn debridement and LP
Pitetti/2003	USA	Prospective Cohort	MFIV; IVKM; IMKM; IV MoM; MIV; N2O; IV F and Lorazepam	1215	1244	Mean, Median (range):5.9, 6.9 (2 m-19.4 y)	791 (65.1%)	Laceration repair, fracture reduction
Pohlgeers/1995	USA	Retrospective cohort (retrospective chart review)	IV Diazepam and IV F	133	138	Mean, y (SD): 8.6 (3.7); Range, y: 2-18	84 (63)	Orthopedic procedures
Priestley/2001	Australia	Prospective cohort	K (IV or IM)	28	28	Median, y (range); IV: 4.9 (2-12); IM: 4.0 (1.5-10.0).	NA	Fracture reduction, I&D, splinter removal, steroid injection.
Pruitt/1995	USA	Prospective cohort	K + M + Glycopyrrolate	37	37	Mean, y (range); 2.7 (1.0-7.0)	23 (62)	Laceration repair, tooth extraction/correction
Qureshi/1995	USA	RCT	K;P	K: 15;P: 15	K: 15;P: 15	Mean, y (SD);K: 3.3 (2.0);P: 3.5 (2.0)	14 (93)	Laceration repair
Schutzman/1996	USA	RCT	OTFC; MPC	OTFC: 20; MPC: 19	OTFC: 20; MPC: 19	Mean, y (SD); OTFC: 4.8 (1.4); MPC: 4.6 (0.9)	OTFC: 13 (65); MPC: 12 (63)	Laceration repair
Shane/1994	USA	RCT	M, Rectal; P	M: 16; P: 18	M: 16; P: 18	Mean, m (SD); M: 25.5 (9.3); P: 27.2 (10.8)	M: 10 (63); P: 12 (67)	Laceration repair
Sherwin/2000	USA	RCT	K; KM	K: 51; KM: 53	K: 51; KM: 53	Median, y (IQR); KM: 7.3 (4.1-10.9); K: 6.1 (2.2-10.7)	K: 30 (59); KM: 40 (75)	NA
Skokan/2001	USA	Prospective cohort	Propofol + Opioid	40	40	Mean, y: 7.4	26(65)	Hernia reduction, laceration repair, etc

Terndrup/1991	USA	Prospective cohort	IM Meperidine + IM Promethazine + IM Chlorpromazine	63	63	Mean, y, (SD) range: 3.6 (2.0), 1-9	40 (63)	Laceration repair, fracture reduction, foreign body removal, joint aspiration, I&D
Terndrup/1993	USA	RCT	MPC; MP	MPC: 44;MP: 43	MPC: 44;MP: 43	Mean, y (SD):MPC: 4.0 (2.2);MP: 4.4 (2.5)	MPC: (64);MP: (72)	Laceration repair, fracture reduction
Theroux/1993	USA	RCT	M	27	27	Median, m; M: 34.2	NA	Laceration repair
Treston/2004	Australia	Prospective cohort	K	272	272	Range, y: 1-12	173 (64)	Laceration repair, fracture reduction, plaster change, foreign body removal, dressing change, I&D
Wathen/2000	USA	RCT	KM;K	KM: 137;K: 129	KM: 137;K: 129	Median, y (IQR):KM: 5.6 (3.4-9.6);K: 6.8 (4.4-10.3).	KM: 76 (55.5);K: 73 (56.6)	Fractures, Lacerations, other
Yealy/1992	USA	Retrospective cohort	M	38	38	Mean, m (SD): 32 (9)	NA	Laceration repair
Younge/2001	UK	RCT	M; K	M: 28; K: 29	M: 28; K: 29	Mean, y; M: 4.1; K: 4.1	M: 15 (54); K: 15 (52)	Wound repair

Abbreviations: CH, Chloral Hydrate; CPO, Chloral Hydrate Oral; CT, Computed Tomography; DPO, Diazepam Oral; F, Fentanyl; FIV, Fentanyl Intravenous; FM, Fentanyl + Midazolam; HDM, High Dose Rectal Midazolam; I&D, incision and drainage; IM, Intramuscular; IMKM, Ketamine + Midazolam; INM, Intranasal Midazolam; IV, Intravenous; IVKM, Intravenous Ketamine + Midazolam; K, Ketamine; kg, kilogram; KM, Ketamine + Midazolam; KMO, Ketamine + Midazolam + Opiate; KPO, Ketamine Oral; LIV, Lorazepam Intravenous; LP, lumbar puncture; LPO, Lorazepam Oral; M, Midazolam; m, months; MeM, Meperidine and Midazolam, MF, Midazolam/Flumazenil; MFIV, Intravenous Midazolam + Fentanyl; MIV, Midazolam Intravenous; mg, milligram; MM, Morphine + Midazolam; MN, Midazolam + N2O; MO, Midazolam + Opiate; MoM, Morphine and Midazolam; MP, Meperidine + Promethazine; MPC, Meperidine + Promethazine + Chlorpromazine; MPO, Midazolam Oral; MR, Methohexital + Remifentanyl; MS, Midazolam + Sufentanyl; P/F, Propofol/Fentanyl; PIV, Phentobarbital Intravenous; OTFC, Oral Transmucosal Fentanyl Citrate; P, Placebo; RCT, Randomized Controlled Trial; SDM, Standard Dose Rectal Midazolam; SM, Sufentanyl + Midazolam; TMJ, Temporomandibular Joint; y, years

Appendix 1b. Included studies

Author/Year	Country	Design	Medication/s Used	No. of Patients	No. of Sedations	Median/Mean Age	Male (%)	Procedure/s
Anderson/2007	USA	Prospective cohort	Propofol	125	NA	Median: 8 (2-17)	81 (65)	Orthopedic Reduction
Andolfatto/2010	Canada	Prospective cohort	K + Propofol	219	219	Median: 13; Range: 1-20; IQR: 8-16	159 (73)	Orthopedic Reduction, Laceration, Chest tube, I&D, Foreign Body Removal, Hernia Repair, Lumbar Puncture, Cardioversion, Laryngoscopy, Pelvic examination
Asadi/2013	Iran	Prospective Double-Blind RCT	K + Atropine; K + P	200	200	Intervention arm, y: Mean(SD): 7.0 (3.6); Control arm, y: Mean(SD): 7.1 (3.7); Range, y: 3-16	137 (68.5)	Fracture, Reduction, Wound Management
Babl/2010	Australia	Retrospective chart review	Nitrous Oxide; K; M	2002	2002	Median: 5.7	1192 (59.5)	Laceration repair, Orthopedic procedures, foreign body removal, vascular access, etc
Babl/2008	Australia	Prospective Observational Study	Nitrous Oxide	124	131	Mean: 8.1, (1.3–17.9); Median: 8.3 (4.9–11.0)	80 (64.5)	Laceration repair, Orthopedic procedures, IV line access, abscess
Barkan/2013	Israel	RCT	KM; M	60	60	Mean; KM: 4.76±2.29; M: 5.26±2.26	KM: 17(54); M: 15(51)	Laceration repair
Bar-Meir/2006	Israel	Prospective cohort	Nitrous Oxide	45	45	Mean: 4.3 (3); Range: 1-16	30 (67)	Facial laceration repair
Bleilberg/2007	USA	Retrospective review	K	72	72	Median, y: 6.1; Range: 10m-14y	NA	Fracture reduction, Laceration repair, I&D, foreign body removal, fingertip amputation repair, inguinal hernia reduction, paraphymosis reduction and arthrocentesis
Chong/2013	Singapore	Retrospective study	K + Atropine; K w/o Atropine	K + Atropine: 164; K w/o Atropine: 119	K + Atropine: 164; K w/o Atropine: 119	Mean; K + Atropine: 5.3 (4.74 to 5.81); K w/o Atropine: 5.5 (4.77 to 6.16)	K + Atropine: 101; K w/o Atropine: 83	Laceration repair, Manipularion and reduction, foreign body removal, I&D
Chun/2009	USA	Retrospective cohort study	MTX; PTB	MTX: 21, PTB: 42	MTX: 21, PTB: 42	Mean (SD), y; MTX: 20.0 (4.9); PTB: 28.8 (4.9)	MTX: 13; PTB: 26	Head CT
Cudny/2013	USA	Prospective observational	K IV vs IM	IV: 91; IM: 49	IV: 91; IM: 49	NA	NA	Fracture reduction, Laceration/suture, I&D, Lumber puncture, sedation for radiology, foreign body removal.
Di Liddo/2006	Canada	Randomized, double-blind trial	E; M	E: 50; M: 50	E: 50; M: 50	Mean; E: 108±45.6 m; M: 100±42.7	E: 25(50); M: 25(50)	Fracture Reduction
Dilli/2008	Turkey	Randomized controlled study	IVKM; K IV	IVKM: 48; K IV: 51	IVKM: 48; K IV: 51	Mean±SD: IVKM: 7.1±3.9; K IV: 6.0±3.5	IVKM: 27 (56.3); K IV: 32 (62.7)	Lumbar Puncture
Ghane/2012	Iran	Interventional non randomized trial	M	30	30	5.50±2.70 y	14 (46.7)	Imaging CT scan

Heinrich/2014	Germany	Record review	Nitrous Oxide (50:50)	207	207	Mean, y: 9.0; Range, y: 2.7-16.5	NA	Orthopedic reduction, laceration closure, Iv cannulation, Abscess drainage, needle puncture, foreign body removal.
Jasiak/2012	USA	Retrospective cohort study	Prpofol IV	88	88	Mean±SD, y: 10.8±4.5; Range, y:1-18	66 (75)	Fracture/Dislocation manipulation, imaging, LP, eye examination, laceration repair
Jiminez/2012	Spain	Retrospective observational study	F + N2O (FN2O); N2O	F + N2O: 64; N2O: 17	F + N2O: 64; N2O: 17	Range, y: 4-15	F + N2O: 46 (71.9); N2O: 12 (70.6)	Fracture reduction (radial, ulnar)
Khutia/2012	India	Prospective, randomized trial	Propofol + K; Propofol + F	Propofol + K: 48; Propofol + F: 44	Propofol + K: 48; Propofol + F: 44	Range, y: 3-14	NA	Fracture dislocation, I&D, dressing-debridement of wounds
Klein/2011	USA	Randomized clinical trial	M: Oral ; IN, Buccal	Oral: 59; IN: 59; Buccal: 59	Oral: 59; IN: 59; Buccal: 59	Median (range), y; Oral: 2.7 (1.2–6.7); IN: 2.9 (1.2–7.0); Buccal: 3.8 (1.1–6.1)	Oral: 33 (56); IN: 40 (68); Buccal: 40 (68)	Laceration Repair
Koo/2013	Korea	Retrospective review of medical records	CH: 48±2 mg/kg (1); 55±2 mg/kg (2); 66±3 mg/kg (3); 76±3 mg/kg (4); 85±3 mg/kg (5); 97±4 mg/kg (6)	1: 115; 2: 116; 3: 122; 4: 202; 5: 179; 6: 100	1: 115; 2: 116; 3: 122; 4: 202; 5: 179; 6: 100	m; 1: 28±13.9; 2: 28±15.8; 3: 29±14.4; 4: 30±12.1; 5: 32±15.0; 6: 31±13.6	1: 75 (65.2); 2: 80 (69); 3: 80 (65.6); 4: 136 (67.3); 5: 116 (64.8); 6: 66 (66)	Facial laceration repair
Kye/2012	Korea	Prospective, randomized, double-blind, P-controlled trial	K + Atropine; K	K + Atropine: 68; K: 72	K + Atropine: 68; K: 72	y, K + Atropine: 2.9±1.5; K: 2.6±1.3	K + Atropine: 48; K: 49	Laceration repair
Lane/2008	USA	Retrospective chart review	M	205	205	Mean±SD, m: 31.3±13.2; Range, m: 1.5-60	121 (59)	Laceration repair, I&D, nail bed repair or removal, dental procedure, hernia reduction, imaging, g-tube replacement, LP, eye irrigation, arthrocentesis
Langhan/2011	USA	RCT	K	58	58	Median, y: 5; Range, y: 1-19	43 (74)	Fracture reduction, laceration repair, I&D, arthrocentesis
Lee/2012	Korea	Prospective randomized study	N2O (50%-70%); K	N2O: 18; K: 14	N2O: 18; K: 14	Mean±SD, y; N2O: 5.9±1.8; K: 4.7±1.6; Range, y: 3-10	N2O: 14 (77.8); K: 12 (85.7)	Laceration repair
Lee-Jayaram/2010	USA	Prospective, RCT	KM; E + F	KM: 11; E + F: 12	KM: 11; E + F: 12	Mean(SD), Median: KM: 9.64 (2.9), 10.0; E + F: 8.5 (2.6), 8.0	KM: 7 (64); E + F: 11 (92)	Fracture reduction
Lin/2010	Taiwan	Retrospective observational study	Thiamylal: 5 mg/kg (1); 5 mg/kg+2.5 mg/kg (2); 5 mg/kg+ 5 mg/kg (3)	1: 146; 2: 54; 3: 27	1: 146; 2O: 54; 3: 27	y, 1: 3.87±1.34; 2: 4.37±1.77; 3: 4.41±1.55; Range, y: 2-7	1: 64 (43.8); 2: 31 (57.4); 3: 10 (37.0)	Laceration repair
Losek/2006	USA	Retrospective cohort	KM; MoM + K; MeM + K	KM: 33; MoM + K: 32; MeM + K: 15	KM: 33; MoM + K: 32; MeM + K: 15	Mean, m (SD); Total: 91.8 (47.2); KM: 79 (46); MoM + K: 108 (47); MeM + K: 85 (44)	KM: 16 (48); MoM + K: 24 (75); MeM + K: 7 (47)	Fracture/joint dislocation reduction, foreign body removal, I&D, vaginal examination, CT scan, hernia reduction

Luhmann/2006	USA	RCT	KM; N2OHB	KM: 47; N2OHB: 55	KM: 47; N2OHB: 55	Mean, y (95%CI); KM: 9.4 (8.5 to 10.2); N2OHB: 8.7 (7.9 to 9.4)	KM: 32 (58); N2OHB: 29 (62)	Middle to distal forearm fracture reduction.
Mandt/2012	USA	Prospective cohort	F + E: 0.1 mg/kg (1); 0.2 mg/kg (2); 0.3 mg/kg (3)	1: 4; 2: 40; 3: 16	1: 4; 2: 40; 3: 16	NA	38 (63.3)	Fracture/Joint reduction, I&D, Arthrocentesis
McKee/2008	USA	Retrospective cohort	K; Oral Analgesia + K	K: 270; OAK: 201	K: 270; OAK: 201	Mean, y (SD); K: 8.5 (3.9); OAK: 8.2 (3.6)	K: 192 (71); OAK: 124 (62)	Fracture reduction
McQueen/2009	USA	Prospective cohort	FM; KM; K	FM: 108; KM: 123; K: 422	FM: 108; KM: 123; K: 422	Mean, y (SD) all patients: 7.5 (4.5)	341 (62%)	Fracture reduction, laceration repair.
Melendez/2009	USA	Case-control study	K	4252	4252	NA	NA	Fracture reduction, laceration repair, I&D, Arthrocentesis, LP, bone marrow biopsy
Misra/2008	USA	Retrospective cohort	K; M	173	173	1-2 y; 73% (126/173)	94 (54.3)	I&D, laceration repair
Oktay/2005	Turkey	Prospective cohort	K; KM	K: 91; KM: 50	K: 91; KM: 50	Mean-median (SD), y; 4.52 - 4 (2.60)	78^ (55.3)	Fracture/dislocation reduction, imaging and gynecological examination
Roback/2006	USA	RCT	K: IV vs IM	IV: 109; IM: 99	IV: 109; IM: 99	Median (range), y; IV: 8.1 (1.2-15.8); IM: 7.0 (1.9-15.5)	IV: 71 (65.1); IM: 63 (63)	Orthopedic procedures
Seith/2012	Australia	Prospective cohort	N2O + IN F	41	41	Mean (SD), y: 6.7 (2.9); Median (IQR), y: 6.3 (5.2-8.8)	29 (70.7)	Orthopedic procedures, laceration repair, I&D, foreign body removal, burn dressing
Shah/2011	Canada	RCT	K; K + Propofol	K: 69; K + Propofol: 67	K: 69; K + Propofol: 67	Median, y (IQR); K: 11 (7-13); K + Propofol: 11 (7-14)	K: 46 (69); K + Propofol: 50 (72)	Orthopedic procedures
Sharieff/2007	USA	Prospective cohort	K + Propofol	20	20	Mean, y (SD); 9.6 (3.4)	16 (80)	Fracture Reduction
Street/2014	USA	Prospective cohort	K	43	43	Mean, y (SD); 13.9 (1.5)	35 (81)	Fracture reduction, abscess drainage, chest tube placement
Treston/2009	Australia	Prospective cohort	K: IM vs IV	IM: 54; IV: 691	IM: 54; IV: 691	Mean, y (range); 5.5 (1-14)	NA	Laceration repair, fracture reduction, foreign body removal, I&D, imaging.
Waterman/2006	USA	Retrospective cohort	K; K + Morphine	K: 454; K + Morphine: 857	K: 454; K + Morphine: 857	Mean, y: K: 7; K + Morphine: 8.6	NA	Dislocation reductions, I&D, laceration repair
Wells/2012	USA	Retrospective cohort	Propofol	331	331	NA	218 (66)	Fracture and laceration repair

Abbreviations: CH, Chloral Hydrate; CI, Confidence Interval; CT, Computed Tomography; E, Etomidate; F, Fentanyl; FIV, Fentanyl Intravenous; FM, Fentanyl + Midazolam; HDM, High Dose Rectal Midazolam; I&D, Incision and Drainage; IM, Intramuscular; IMKM, Ketamine + Midazolam; IN, Intranasal; INM, Intranasal Midazolam; IV, Intravenous; IVKM, Intravenous Ketamine + Midazolam; K, Ketamine; kg, kilogram; KM, Ketamine + Midazolam; LIV, Lorazepam Intravenous; LP, Lumbar Puncture; M, Midazolam; m, months; MeM, Meperidine and Midazolam, MF, Midazolam/Flumazenil; MFIV, Intravenous Midazolam + Fentanyl; MIV, Midazolam Intravenous; mg, milligram; MM, Morphine + Midazolam; MN, Midazolam + N2O; MoM, Morphine and Midazolam; MP, Meperidine + Promethazine; MPC, Meperidine + Promethazine + Chlorpromazine; MR, Methohexital + Remifentanyl; MS, Midazolam + Sufentanil; MTX, Methotrexate; N2OHB, Inhaled N2O and Hematoma Block; OAK, Oral Analgesia + Ketamine; P/F, Propofol/Fentanyl; PIV, Phentobarbital Intravenous; PTB, Pentobarbital; OTFC, Oral Transmucosal Fentanyl Citrate; P, Placebo; RCT, Randomized Controlled Trial; SDM, Standard Dose Rectal Midazolam; SM, Sufentanil + Midazolam; TMJ, Temporomandibular Joint; y, years

Appendix 2. Search Strategy

	Search Number	Topic	Limiters/Expanders	Results	Search Type
Ovid MEDLINE® in process and other non-indexed citations					
	1	((conscious or dissociative) adj3 sedat*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]			
	2	Conscious Sedation/ or exp "Hypnotics and Sedatives"/			
	3	1 or 2			
	4	emergen*.mp. or exp emergency medical services/ or emergency medicine/ [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]			
	5	3 and 4			
	6	(procedur* adj3 sedat*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]			
	7	4 and 6			
EMBASE					
	1	((conscious or procedural or dissociative) adj3 sedat*).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]			
	2	conscious sedation/			
	3	emergency patient/ or emergency care/ or emergency nurse practitioner/ or emergency surgery/ or emergency treatment/ or emergency medicine/ or emergency/ or emergency nursing/ or emergency ward/ or emergency health service/			
	4	(1 or 2) and (3 or trauma*.mp.) [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]			
WEB of SCIENCE					
	1	TOPIC: ((conscious OR procedural OR dissociative OR moderate) SAME sedat*) AND TOPIC: (emergen* OR trauma*) Indexes: SCI-EXPANDED			
SCOPUS					
		TITLE-ABS-KEY(((conscious OR procedural OR dissociative OR moderate) W/3 sedat*) AND (emergen* OR trauma*)) 109			
CINAHL					
	S5	S1 AND S4	Limiters - Published Date: 20130101-20141231; Peer Reviewed; Search modes - Boolean/Phrase	48	

	S4	S2 OR S3	Search modes - Boolean/Phrase	42,433	
	S3	(MH "Trauma+") OR (MH "Emergency Patients") OR (MH "Trauma Centers") OR (MH "Trauma Nursing")	Search modes - Boolean/Phrase	15,870	
	S2	(MH "Emergency Service+") OR (MH "Emergency Medicine") OR (MH "Emergency Nurse Practitioners") OR (MH "Emergency Medical Technician Attitudes") OR (MH "Physicians, Emergency")	Search modes - Boolean/Phrase	31,563	
	S1	(MH "Conscious Sedation"# OR #MH "Hypnotics and Sedatives+"#	Search modes - Boolean/Phrase	8,029	
Ovid MEDLINE®†					
	1	emergen*.mp. or exp emergency medical services/ or emergency medicine/ [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]		313,001	Advanced
	2	conscious sedation/ or ((conscious or moderate or dissociative) adj3 sedat*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]		8,068	Advanced
	3	(procedur* adj3 sedation).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]		1,373	Advanced
	4	(propofol or etomidate or versed or fentanyl or ketamine or midazolam or methohexital or dexmedetomidine or remifentanyl or pentobarbital or "nitrous oxide").mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]		70,089	Advanced
	5	1 and (2 or 3 or 4)		3,550	Advanced
	6	limit 5 to ("newborn infant (birth to 1 month)" or "infant (1 to 23 months)" or "preschool child (2 to 5 years)" or "child (6 to 12 years)" or "adolescent (13 to 18 years)")		1,335	Advanced
	7	conscious sedation/ae or (propofol/ae or etomidate/ae or versed/ae or fentanyl/ae or ketamine/ae or midazolam/ae or methohexital/ae or dexmedetomidine/ae or remifentanyl/ae or pentobarbital/ae or "nitrous oxide"/ae)		7,736	Advanced
	8	6 and 7		319	Advanced
	9	6 and ci.fs.		163	Advanced
	10	8 or 9		377	Advanced
	11	5 and (child* or pediater* or paediatric* or boy* or girl* or preschool* or school*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]		1,196	Advanced
	12	11 and (7 or ci.fs.)		314	Advanced
	13	10 or 12		393	Advanced
	14	remove duplicates from 13		387	
Cochrane*					
	1	emergen*.mp. or exp emergency medical services/ or emergency medicine/ [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]		359,289	Advanced
	2	conscious sedation/ or ((conscious or moderate or dissociative) adj3 sedat*).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]		5,990	Advanced

	3	(procedur* adj3 sedation).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]		2,978	Advanced
	4	(propofol or etomidate or versed or fentanyl or ketamine or midazolam or methohexital or dexmedetomidine or remifentanyl or pentobarbital or "nitrous oxide").mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]		118,093	Advanced
	5	emergency ward/		60,820	Advanced
	6	1 or 5		359,289	Advanced
	7	conscious sedation/		4,105	Advanced
	8	2 or 3 or (7 and 4)		8,348	Advanced
	9	6 and 8		1,020	Advanced
	10	exp adverse drug reaction/		232,623	Advanced
	11	conscious sedation/ae or (propofol/ae or etomidate/ae or versed/ae or fentanyl/ae or ketamine/ae or midazolam/ae or methohexital/ae or dexmedetomidine/ae or remifentanyl/ae or pentobarbital/ae or "nitrous oxide"/ae)		14,223	Advanced
	12	9 and (10 or 11)		293	Advanced
	13	limit 9 to (infant <to one year> or child <unspecified age> or preschool child <1 to 6 years> or school child <7 to 12 years> or adolescent <13 to 17 years>)		346	Advanced
	14	12 and (child* or infant* or preschool* or pediatr* or paediatr* or teen* or adolescen*).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]		166	Advanced
	15	13 or 14		386	Advanced
	16	15 not case report/		362	
WEB of SCIENCE					
		TOPIC: (((procedur* OR moderate OR conscious OR dissociative OR propofol OR etomidate OR versed OR fentanyl OR ketamine OR midazolam OR methohexital OR dexmedetomidine OR remifentanyl OR pentobarbital OR "nitrous oxide") SAME sedat*) AND emergency) AND TOPIC: (pediatr* OR paediatr* OR child* OR infant* OR adolescen* OR preteen* OR teen*) AND TOPIC: (adverse OR Death* OR mortal* OR fatal* OR "life threatening" OR intub* OR ventilat* OR nausea* OR emesis OR aspirat* OR vomit* OR hypoxi* OR bradycard* OR hypotens* OR myoclon* OR laryngospas* OR intraocular OR letharg* OR headache OR sleep OR apne* OR apnoe* OR hallucinat*) 421			
SCOPUS					
		(TITLE-ABS-KEY(((procedur* OR moderate OR conscious OR dissociative OR propofol OR etomidate OR versed OR fentanyl OR ketamine OR midazolam OR methohexital OR dexmedetomidine OR remifentanyl OR pentobarbital OR "nitrous oxide") W/5 sedat*) AND TITLE-ABS-KEY(emergency AND (pediatr* OR paediatr* OR infant* OR preschool* OR adolescen* OR child* OR teen*))) AND TITLE-ABS-KEY((adverse OR death* OR mortal* OR fatal* OR "life threatening" OR intub* OR ventilat* OR nausea* OR emesis OR aspirat* OR vomit* OR hypoxi* OR bradycard* OR hypotens* OR myoclon* OR laryngospas* OR intraocular OR letharg* OR apne* OR apnoe* OR hallucinat*))) 473			

*Same Strategy for Cochrane.

†In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) 1946 to Present

‡Cochrane =74; Embase 1988 to 2014 week 24.

Appendix 3. Cochrane Collaboration's tool for assessment of risk of bias in randomized controlled trials.

Author/Year	Adequate Sequence Generation	Allocation concealment	Blinding					Incomplete Outcome Data addressed	Free of selective outcome reporting	Free of other bias
			Patients	ED Physicians	Follow-up Physician	Data Collectors	Outcome Assessors			
Asadi /2013	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes
Barkan /2013	Yes	Yes	Yes	Yes	Unclear	Yes	Unclear	No	Unclear	No
Di Liddo/2006	Yes	Yes	Unclear	Unclear	Unclear	Unclear	Unclear	Yes	Yes	No
Dilli 2008	Yes	Yes	No	No	No	Yes	No	Yes	Yes	No
Ghane/2012	No	Yes	No	No	No	No	No	Yes	Yes	No
Khutia/2012	Unclear	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No
Klein/2011	Unclear	Unclear	No	Yes	No	No	Yes	Yes	Yes	No
Kye /2012	Yes	Yes	Yes	Yes	No	Yes	Unclear	Yes	Yes	No
Langhan /2011	Unclear	Unclear	Yes	No	No	Yes	Unclear	Yes	Yes	No
Lee/2012	Yes	Yes	No	Yes	No	No	No	Yes	Yes	No
Lee-Jayaram /2010	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No
Luhmann/2006	Yes	Yes	No	No	NA	No	No	Yes	Yes	No
Roback/2006	Yes	No	No	No	No	No	No	Yes	Yes	No
Shah/2011	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	Yes	No

Abbreviations: ED, Emergency Department

Appendix 4: Newcastle-Ottawa Scale (NOS) for assessing the quality of non-randomized studies

		Selection			Comparability			Outcome	
Author/Year	Was the cohort representative?	Was the selection of non-exposed cohort adequate?	Was the ascertainment of exposure credible?	Was the outcome of interest demonstrated to not exist in the study enrollment?	Were the cohorts comparable on the basis of the design?	Were the cohorts comparable on the basis of the analysis?	Was the outcome assessed by credible means?	Was follow-up long enough for outcomes to occur?	Was the amount of patients followed adequate?
Anderson/2007	Yes	NA	Yes	Yes	NA	NA	Yes	Yes	Yes
Andolfatto/2010	Yes	NA	Yes	Yes	NA	NA	Yes	Yes	Yes
Babl/2010	Yes	NA	Yes	Yes	NA	NA	Yes	Yes	Yes
Babl/2008	Yes	NA	Yes	Yes	NA	NA	Yes	Yes	Yes
Bar-Meir/2006	Somewhat	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Bleilberg/2007	Yes	NA	Yes	Yes	NA	NA	Yes	Yes	Yes
Chong/2013	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Chun/2009	Somewhat	NA	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Cudny/2013	Yes	NA	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Heinrich/2014	Yes	NA	Yes	Yes	NA	NA	Yes	Yes	Yes
Jasiak/2012	Yes	NA	Yes	Yes	NA	NA	Yes	Yes	Yes
Jiminez/2012	Somewhat	NA	Yes	Yes	NA	NA	Yes	Yes	Yes
Koo/2013	Somewhat	NA	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Lane/2008	Yes	NA	Yes	Yes	NA	NA	Yes	Yes	Yes
Lin/2010	Yes	NA	Yes	Yes	Yes	NA	Yes	Yes	Yes
Losek/2006	Yes	NA	Yes	Yes	Yes	NA	Yes	Yes	Yes
Mandt/2012	Yes	NA	Yes	Yes	NA	NA	Yes	Yes	Yes

McKee/2008	Yes	NA	Yes	Yes	No	No	Yes	Yes	Yes
McQueen/2009	Unclear	NA	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Melendez/2009	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Misra/2008	No	NA	Yes	Yes	NA	NA	Yes	Yes	Yes
Oktay/2005	Yes	NA	Yes	Yes	NA	NA	Yes	Yes	Yes
Seith/2012	Yes	NA	Yes	Yes	NA	NA	Yes	Yes	Yes
Sharieff/2007	Yes	NA	Yes	Yes	NA	NA	Yes	Yes	Yes
Street/2014	No	NA	Yes	Yes	NA	NA	Yes	Yes	Yes
Treston/2009	Yes	NA	Yes	Yes	NA	NA	Yes	Yes	Yes
Waterman/2006	Yes	NA	Yes	Yes	Yes	NA	Yes	Yes	Yes
Wells/2012	Yes	NA	Yes	No	NA	NA	Yes	Yes	Yes