Appendix 1. Search strategy.

Database: Embase <1988 to 2016 Week 39>, Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) <1946 to Present>
Search Strategy:
---

1 (harmonic* adj2 (blade? or dissect* or hook? or incis* or scalpel? or shear? or scalpel?)).tw,kw. (2454)
2 (ultrasonic* adj2 (blade? or dissect* or hook? or incis* or scalpel? or shear? or scalpel?)).tw,kw. (2161)
3 (ultrasound* adj2 (blade? or dissect* or hook? or incis* or scalpel? or shear? or scalpel?)).tw,kw. (838)
4 ultracision?.tw,kw. (376)
5 ultra-cision?.tw,kw. (5)
6 (harmonic* adj (ACE* or Focus* or Synergy* or Wave*)).tw,kw. (812)
7 "ACE+ 7".tw,kw. (21)
8 "Harmonic 7".tw,kw. (3)
9 "CS 14-C".tw,kw. (1)
10 "HD 1000i Shears".tw,kw. (0)
11 HF005.tw,kw. (1)
12 Ultrasonic Surgical Procedures/ (654)
13 ((ultrason* or ultrasound*) adj2 surg* adj3 (device* or instrument* or procedur* or technique*)).tw,kw. (306)
14 or/1-13 (6556)
15 exp Animals/ not (exp Animals/ and Humans/) (13727370)
16 14 not 15 (4336)
17 (comment or editorial or interview or news or newspaper article).pt. (1671785)
18 (letter not (letter and randomized controlled trial)).pt. (1762745)
19 16 not (17 or 18) (4233)
20 limit 19 to systematic reviews [Limit not valid in Embase; records were retained] (1899)
21 meta analysis.pt. (73990)
22 exp meta-analysis as topic/ (49955)
23 (meta-analy* or metanaly* or metaanaly* or met analy* or integrative research or integrative review* or integrative overview* or research integration or research overview* or collaborative review*).tw,kw. (242010)
24 (systematic review* or systematic overview* or evidence-based review* or evidence-based overview* or (evidence adj3 (review* or overview*)) or meta-review* or meta-overview* or meta-synthes* or rapid review* or "review of reviews" or technology assessment* or HTA or HTAs).tw,kw. (282350)
25 exp Technology assessment, biomedical/ (20902)
26 (cochrane or health technology assessment or evidence report).jw. (34521)
27 ((indirect* or mixed or multi-treatment*) adj2 compar*).tw,kw. (8665)
28 ((network* or network-based) adj (MA or MAs)).kw,tw. (11)
29 or/21-28 (519420)
30 19 and 29 (65)
31 20 or 30 [SYSTEMATIC REVIEWS] (1908)

32 (controlled clinical trial or randomized controlled trial).pt. (519165)
33 clinical trials as topic.sh. (179761)
34 exp Randomized Controlled Trials as Topic/ (231226)
35 (randomi#ed or randomly or RCT$1 or placebo*).tw,kw. (1740069)
36 ((singl* or doubl* or trebl* or tripl*) adj (mask* or blind* or dumm*)).tw,kw. (316622)
37 trial.ti. (354659)
38 or/32-37 (2254804)
39 19 and 38 [RCTs] (498)
40 controlled clinical trial.pt. (91760)
41 Controlled Clinical Trial/ or Controlled Clinical Trials as Topic/ (540950)
42 (control* adj2 trial*).tw,kw. (436814)
43 Non-Randomized Controlled Trials as Topic/ (10101)
44 (nonrandom* or non-random* or quasi-random* or quasi-experiment*).tw,kw. (91083)
45 (nRCT or nRCTs or non-RCT$1).tw,kw. (1182)
46 Controlled Before-After Studies/ (167992)
47 (control* adj3 ("before and after" or "before after")).tw,kw. (7222)
48 Interrupted Time Series Analysis/ (152036)
49 (time series adj3 interrupt*).tw,kw. (3539)
50 (pre- adj3 post-).tw,kw. (147710)
51 (pretest adj3 posttest).tw,kw. (7838)
52 Historically Controlled Study/ (187204)
53 (control* adj2 stud$3).tw,kw. (415123)
54 Control Groups/ (255317)
55 (control* adj2 group$1).tw,kw. (895570)
56 trial.ti. (354659)
57 or/40-56 (2531267)
58 19 and 57 [NON-RCTs] (397)
59 exp Cohort Studies/ (1888851)
60 cohort$1.tw,kw. (988452)
61 Retrospective Studies/ (841566)
62 (longitudinal or prospective or retrospective).tw,kw. (2212090)
63 ((followup or follow-up) adj (study or studies)).tw,kw. (91014)
64 Observational study.pt. (26695)
65 (observation$2 adj (study or studies)).tw,kw. (167950)
66 ((population or population-based) adj (study or studies or analys#s)).tw,kw. (38289)
67 ((multidimensional or multi-dimensional) adj (study or studies)).tw,kw. (184)
68 Comparative Study.pt. (1770466)
69 ((comparative or comparison) adj (study or studies)).tw,kw. (178703)
70 exp Case-Control Studies/ (952195)
71 ((case-control* or case-based or case-comparison) adj (study or studies)).tw,kw. (185277)
72 or/59-71 (5817869)
73 19 and 72 [OBSERVATIONAL STUDIES] (1301)
74 31 or 39 or 58 or 73 [ALL STUDY DESIGNS] (2894)
75 74 use ppez (1044) [MEDLINE RECORDS]
76 harmonic.dv. (603)

77 (harmonic* adj2 (blade? or dissect* or hook? or incis* or scalpel? or shear? or scalpel?)).tw,kw. (2454)
78 (ultrason* adj2 (blade? or dissect* or hook? or incis* or scalpel? or shear? or scalpel?)).tw,kw. (2300)
79 (ultrasound* adj2 (blade? or dissect* or hook? or incis* or scalpel? or shear? or scalpel?)).tw,kw. (838)
80 ultracision?.tw,kw. (376)
81 ultra-cision?.tw,kw. (5)
82 (harmonic* adj (ACE* or Focus* or Synergy* or Wave*)).tw,kw. (812)
83 "ACE+ 7".tw,kw. (21)
84 "Harmonic 7".tw,kw. (3)
85 "CS 14-C".tw,kw. (1)
86 "HD 1000i Shears".tw,kw. (0)
87 HF005.tw,kw. (1)
88 ultrasound surgery/ (387)
89 ((ultrason* or ultrasound*) adj2 surg* adj3 (device* or instrument* or procedur* or technique*)).tw,kw. (306)
90 or/76-89 (6828)
91 exp animal experimentation/ or exp models animal/ or exp animal experiment/ or nonhuman/ or exp vertebrate/ (39067187)
92 exp human/ or exp human experimentation/ or exp human experiment/ (31426764)
93 91 not 92 (7641574)
94 90 not 93 (6291)
95 editorial.pt. (906336)
96 letter.pt. not (letter.pt. and randomized controlled trial/) (1757763)
97 94 not (95 or 96) (6158)
98 meta-analysis/ (221672)
99 "systematic review"/ (139042)
100 "meta analysis (topic)"/ (34527)
101 (meta-analy* or metanaly* or metaanaly* or met analy* or integrative research or integrative review* or integrative overview* or research integration or research overview* or collaborative review*).tw,kw. (242010)
102 (systematic review* or systematic overview* or evidence-based review* or evidence-based overview* or (evidence adj3 (review* or overview*)) or meta-review* or meta-overview* or meta-synthes* or rapid review* or "review of reviews" or technology assessment* or HTA or HTAs).tw,kw. (282350)
103 biomedical technology assessment/ (19793)
104 (cochrane or health technology assessment or evidence report).jw. (34521)
105 ((indirect* or mixed or multi-treatment*) adj2 compar*).tw,kw. (8665)
106 ((network* or network-based) adj (MA or MAs)).kw,tw. (11)
107 or/98-106 (561546)
108 97 and 107 [SYSTEMATIC REVIEWS] (132)
109 randomized controlled trial/ or controlled clinical trial/ (1109541)
110 exp "clinical trial (topic)"/ (256945)
111 (randomi#ed or randomly or RCT$1 or placebo*).tw,kw. (1740069)
112 ((singl* or doubl* or trebl* or tripl*) adj (mask* or blind* or dumm*)).tw,kw. (316622)

113 trial.ti. (354659)
114 or/109-113 (2404037)
115 97 and 114 [RCTs] (821)
116 exp controlled clinical trial/ (1109665)
117 exp "controlled clinical trial (topic)"/ (125448)
118 (control* adj2 trial*).tw,kw. (436814)
119 (nonrandom* or non-random* or quasi-random* or quasi-experiment*).tw,kw. (91083)
120 (nRCT or nRCTs or non-RCT$1).tw,kw. (1182)
121 (control* adj3 ("before and after" or "before after")).tw,kw. (7222)
122 time series analysis/ (23164)
123 (time series adj3 interrupt*).tw,kw. (3539)
124 (pre- adj3 post-).tw,kw. (147710)
125 (pretest adj3 posttest).tw,kw. (7838)
126 controlled study/ (5135971)
127 (control* adj2 stud$3).tw,kw. (415123)
128 control group/ (255317)
129 (control* adj2 group$1).tw,kw. (895570)
130 trial.ti. (354659)
131 or/116-130 (6991487)
132 97 and 131 [NON-RCTs] (1248)
133 cohort analysis/ (495917)
134 cohort$1.tw,kw. (988452)
135 retrospective study/ (1095490)
136 longitudinal study/ (205538)
137 prospective study/ (803888)
138 (longitudinal or prospective or retrospective).tw,kw. (2212090)
139 follow up/ (1160020)
140 ((followup or follow-up) adj (study or studies)).tw,kw. (91014)
141 observational study/ (145370)
142 (observation$2 adj (study or studies)).tw,kw. (167950)
143 population research/ (87063)
144 ((population or population-based) adj (study or studies or analys#s)).tw,kw. (38289)
145 ((multidimensional or multi-dimensional) adj (study or studies)).tw,kw. (184)
146 exp comparative study/ (2681728)
147 ((comparative or comparison) adj (study or studies)).tw,kw. (178703)
148 exp case control study/ (952195)
149 ((case-control* or case-based or case-comparison) adj (study or studies)).tw,kw. (185277)
150 or/133-149 (7156712)
151 97 and 150 [OBSERVATIONAL STUDIES] (2311)
152 108 or 115 or 132 or 151 [ALL STUDY DESIGNS] (2829)
153 152 use emed (1897) [EMBASE RECORDS]
154 75 or 153 [BOTH DATABASES] (2941)
155 remove duplicates from 154 (2081) [TOTAL UNIQUE RECORDS]
156 155 use ppez [MEDLINE UNIQUE RECORDS] (1016)
157 155 use emed [EMBASE UNIQUE RECORDS] (1065)

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Cochrane Library

ID	Search Hits
#1	(harmonic* near/2 (blade* or dissect* or hook* or incis* or scalpel* or shear* or scalpel*)):ti,ab,kw 213
#2	(ultrason* near/2 (blade* or dissect* or hook* or incis* or scalpel* or shear* or scalpel*)):ti,ab,kw 157
#3	(ultrasound* near/2 (blade* or dissect* or hook* or incis* or scalpel* or shear* or scalpel*)):ti,ab,kw 54
#4	ultracision*:ti,ab,kw 38
#5	ultra-cision*:ti,ab,kw 1
#6	(harmonic* next (ACE* or Focus* or Synergy* or Wave*)):ti,ab,kw 44
#7	"ACE+ 7":ti,ab,kw 1
#8	"Harmonic 7":ti,ab,kw 0
#9	"CS 14-C":ti,ab,kw 0
#10	"HD 1000i Shears":ti,ab,kw 0
#11	HF005:ti,ab,kw 0
#12	[mh ^"Ultrasonic Surgical Procedures"] 36
#13	(((ultrason* or ultrasound*) near/2 surg*) near/3 (device* or instrument* or procedur* or technique*)):ti,ab,kw 107
#14	{or #1-#13} 458

Appendix 2. Calculation of ratio of means (RoM) and ratio of geometric means (RoGM) effect measures.

Ratio of Geometric Means (RoGM) basic calculation based on methods proposed by Friedrich et al. [1]

$RoGM_{Taylor}$ should be considered for pooling continuous outcomes in meta-analysis when data are skewed. Calculate the natural logarithm of the RoGM for each trial, and its standard error (SE) using Equation 1 and Equation 2, respectively.

Equation 1

$$\ln(\boldsymbol{RoGM}) = \boldsymbol{ln}\left(\frac{\boldsymbol{mean^2_{X,exp}}}{\sqrt{\boldsymbol{mean^2_{X,exp}} + \boldsymbol{SD^2_{X,exp}}}}\right) - \boldsymbol{ln}\left(\frac{\boldsymbol{mean^2_{X,contr}}}{\sqrt{\boldsymbol{mean^2_{X,contr}} + \boldsymbol{SD^2_{X,contr}}}}\right)$$

Equation 2

$$\boldsymbol{Var_{Taylor}}(\ln[\mathbf{RoGM}]) = \boldsymbol{Var_{Taylor}}(\boldsymbol{mean_{ln(X),exp}}) + \boldsymbol{Var_{Taylor}}(\boldsymbol{mean_{ln(X),exp}})$$

Where,

$$\begin{aligned} Var_{Taylor}(\text{mean}_{\text{ln(X),exp}}) &= \frac{1}{n_{exp}}(CV^2{}_{exp})\left(1+\frac{CV^2{}_{exp}}{1+CV^2{}_{exp}}\right)^2 \\ &- \frac{1}{n_{exp}}\left(1+\frac{CV^2{}_{exp}}{1+CV^2{}_{exp}}\right)\left[(1+CV^2{}_{exp})^2 - 3 + \frac{2}{(1+CV^2{}_{exp})}\right] \\ &+ \frac{1}{4n_{exp}}\left[(1+CV^2{}_{exp})^4 - 4(1+CV^2{}_{exp}) - 1 + \frac{8}{(1+CV^2{}_{exp})}\right. \\ &\left. - \frac{4}{(1+CV^2{}_{exp})^2}\right] \end{aligned}$$

Ratio of Means (RoM) basic calculation based on methods proposed by Friedrich et al. [1, 2]

Calculate the natural logarithm of the RoM for each trial, and its standard error (SE) using Equation 3 and Equation 4, respectively.

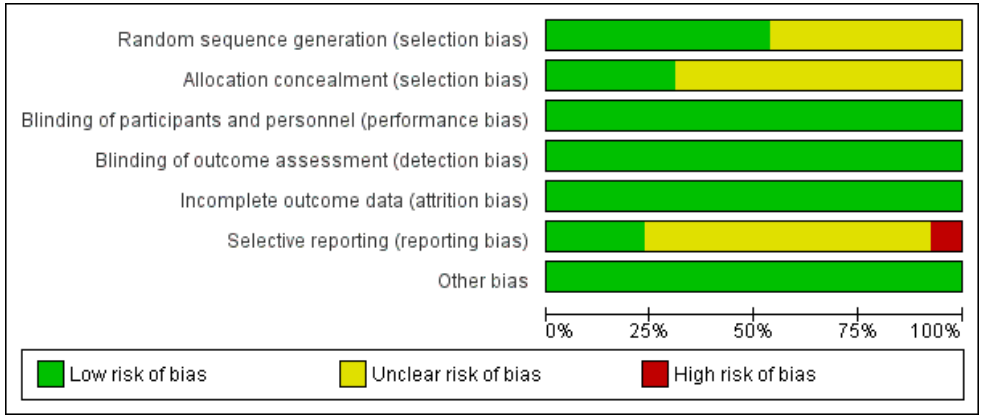
Equation 3 $$\ln(\boldsymbol{RoM}) = \boldsymbol{ln}\left(\frac{\boldsymbol{mean_{exp}}}{\boldsymbol{mean_{contr}}}\right)$$

Equation 4 $$\boldsymbol{SE}[\ln(\boldsymbol{RoM})] = \sqrt{\frac{\boldsymbol{1}}{\boldsymbol{n_{exp}}}\left(\frac{\boldsymbol{SD_{exp}}}{\boldsymbol{mean_{exp}}}\right)^{\boldsymbol{2}} + \frac{\boldsymbol{1}}{\boldsymbol{n_{contr}}}\left(\frac{\boldsymbol{SD_{contr}}}{\boldsymbol{mean_{contr}}}\right)^{\boldsymbol{2}}}$$

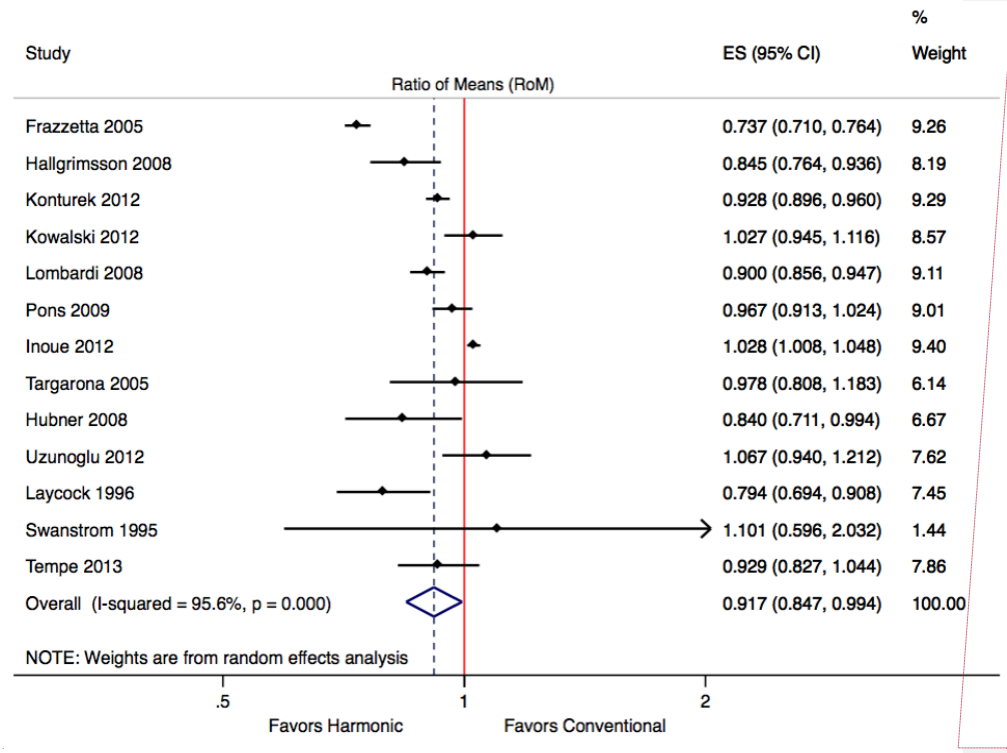
Let the mean, standard deviation, and number of patients in the experimental group be denoted by mean_{exp}, SD_{exp}, and n_{exp}, respectively, and by $\text{mean}_{\text{contr}}$, SD_{contr}, and n_{contr}, respectively, in the control group.

Appendix 3. Risk of bias assessment.

Study	Random Sequence Generation	Allocation Concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other bias
Frazzetta et al., 2005[3]	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Unclear risk	Low risk
Hallgrimsson et al., 2008[4]	Low risk	Low risk	Low risk	Low risk	Low risk	Unclear risk	Low risk
Hubner et al., 2008[5]	Low risk	Low risk	Low risk	Low risk	Low risk	Unclear risk	Low risk
Inoue et al., 2012[6]	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk
Konturek et al., 2012[7]	Low risk	Low risk	Low risk	Low risk	Low risk	Unclear risk	Low risk
Kowalski et al., 2012[8]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Laycock et al., 1996[9]	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Unclear risk	Low risk
Lombardi et al., 2008[10]	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Unclear risk	Low risk
Pons et al., 2009[11]	Low risk	Unclear risk	Low risk	Low risk	Low risk	High risk	Low risk
Targarona et al., 2005[12]	Low risk	Unclear risk	Low risk	Low risk	Low risk	Unclear risk	Low risk
Uzunoglu et al., 2012[13]	Low risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk
Tempe et al., 2013[14]	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Unclear risk	Low risk
Swanstrom & Pennings, 1995[15]	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Unclear risk	Low risk



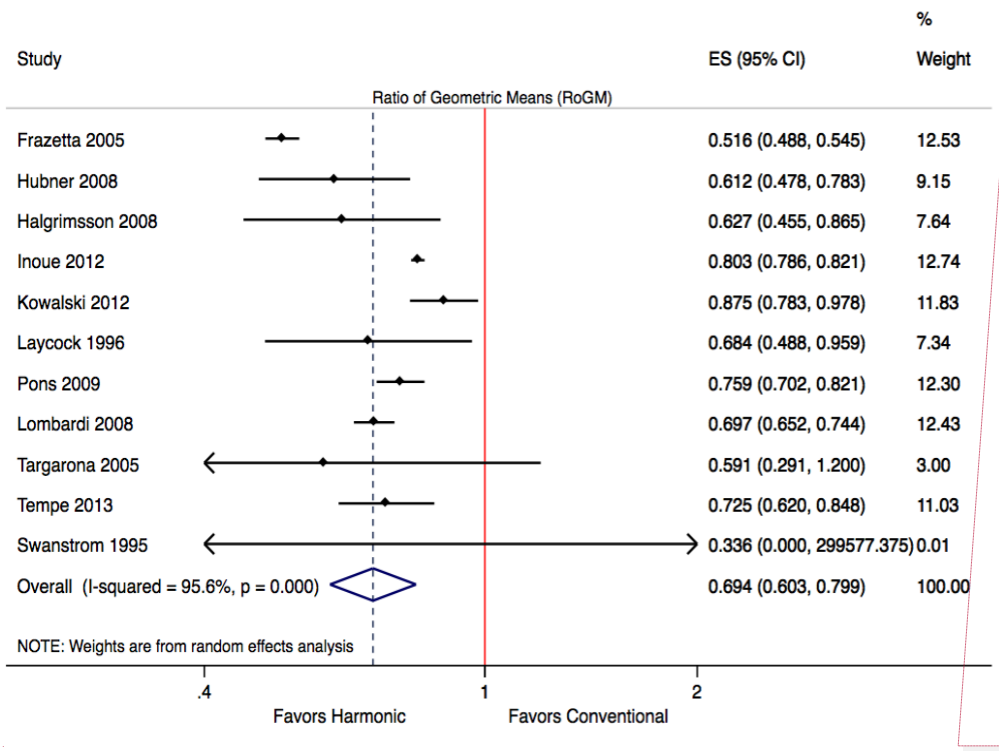
Appendix 4. Forest plot of primary meta-analysis results for procedure costs (2016 USD) expressed as ratio of means (RoM); p-value [test of effect size (ES)=1] = 0.034.



Commented [RQ1]: References for this figure:

Frazzetta 2005[3]
Hallgrimsson 2008[4]
Konturek 2012[7]
Kowalski 2012[8]
Lombardi 2008[10]
Pons 2009[11]
Inoue 2012[6]
Targarona 2005[12]
Hubner 2008[5]
Uzunoglu 2012[13]
Laycock 1996[9]
Swanstrom 1995[15]
Tempe 2013[14]

Appendix 5. Forest plot of meta-analysis results for operating time costs (2016 USD) expressed as ratio of geometric means (RoGM); p-value for difference [test of effect size (ES)=1]<0.001.



Commented [RQ2]: References for this figure:

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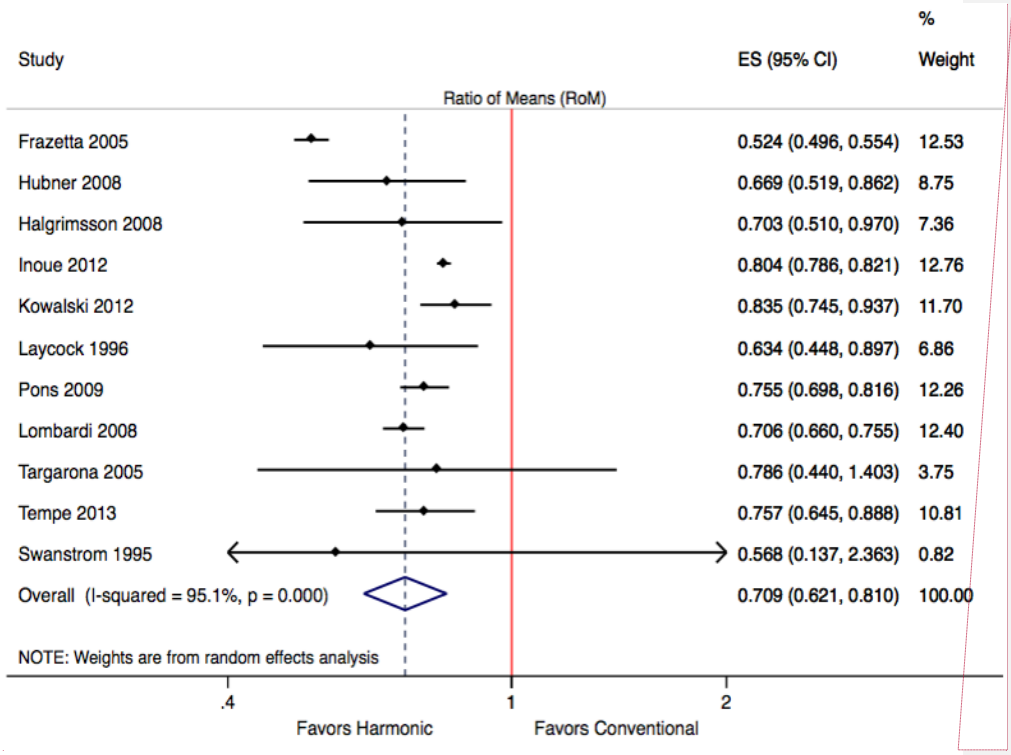
Hubner 2008[5]
Hallgrimsson 2008[4]
Inoue 2012[6]
Kowalski 2012[8]
Laycock 1996[9]
Pons 2009[11]
Lombardi 2008[10]
Targarona 2005[12]
Tempe 2013[14]
Swanstrom 1995[15]

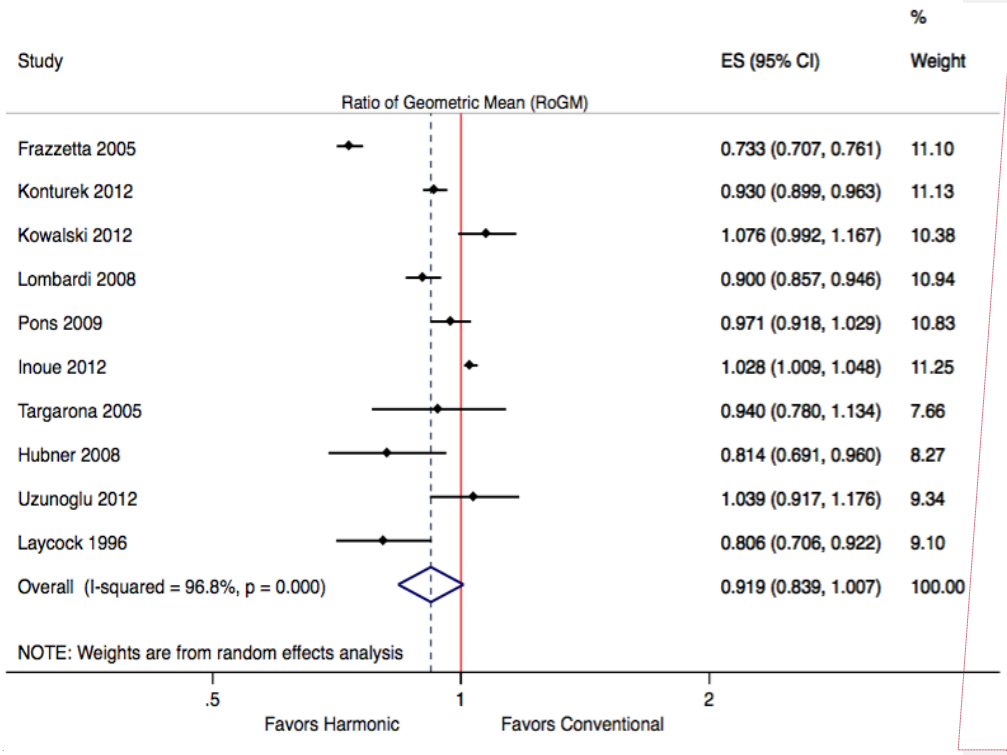
Appendix 6. Forest plot of meta-analysis results for operating time costs (2016 USD) expressed as ratio of means (RoM); p-value for difference [test of effect size (ES)=1]<0.001.



Commented [RQ3]: References for this figure:

Frazzetta 2005[3]
Hubner 2008[5]
Hallgrimsson 2008[4]
Inoue 2012[6]
Kowalski 2012[8]
Laycock 1996[9]
Pons 2009[11]
Lombardi 2008[10]
Targarona 2005[12]
Tempe 2013[14]
Swanstrom 1995[15]

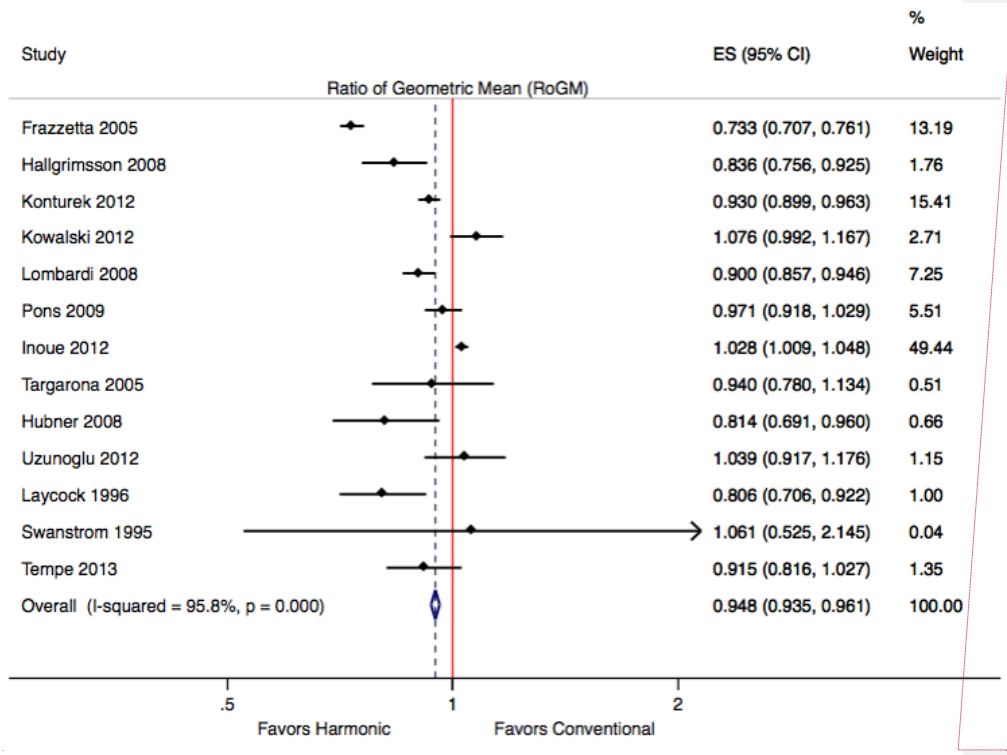
Appendix 7. Forest plot of meta-analysis results for procedure costs (2016 USD) after removing studies that required imputation of standard deviations (SD) expressed as ratio of geometric means (RoGM); p-value for difference [test of effect size (ES)=1] = 0.071.



Commented [RQ4]: References for this figure:

Frazzetta 2005[3]
Konturek 2012[7]
Kowalski 2012[8]
Lombardi 2008[10]
Pons 2009[11]
Inoue 2012[6]
Targarona 2005[12]
Hubner 2008[5]
Uzunoglu 2012[13]
Laycock 1996[9]

Appendix 8. Forest plot of meta-analysis results for procedure costs (2016 USD) expressed as ratio of geometric means (RoGM) using a fixed effects model; p-value for difference [test of effect size (ES)=1]<0.001.



Commented [RQ5]: References for this figure:

Frazzetta 2005[3]
Hallgrimsson 2008[4]
Konturek 2012[7]
Kowalski 2012[8]
Lombardi 2008[10]
Pons 2009[11]
Inoue 2012[6]
Targarona 2005[12]
Hubner 2008[5]
Uzunoglu 2012[13]
Laycock 1996[9]
Swanstrom 1995[15]
Tempe 2013[14]

Reference List

1. Friedrich JO, Adhikari NK, Beyene J. Ratio of geometric means to analyze continuous outcomes in meta-analysis: comparison to mean differences and ratio of arithmetic means using empiric data and simulation. Stat Med. 2012 Jul 30;31(17):1857-86. PubMed PMID: 22438170.
2. Friedrich JO, Adhikari NK, Beyene J. Ratio of means for analyzing continuous outcomes in meta-analysis performed as well as mean difference methods. J Clin Epidemiol. 2011 May;64(5):556-64. PubMed PMID: 21447428.
3. Frazzetta M, Furgiuele G, Raimondo D, et al. [Ultrasonic dissector for total thyroidectomy: results of prospective randomized study]. G Chir. 2005 Aug-Sep;26(8-9):295-301. PubMed PMID: 16329770. Tiroidectomia totale con impiego del dissettore ad ultrasuoni: risultati di uno studio prospettico randomizzato.
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6. Inoue K, Nakane Y, Michiura T, et al. Ultrasonic scalpel for gastric cancer surgery: a prospective randomized study. Journal of Gastrointestinal Surgery. 2012;16(10):1840-6.
7. Konturek A, Barczynski M, Stopa M, Nowak W. Total thyroidectomy for non-toxic multinodular goiter with versus without the use of harmonic FOCUS dissecting shears - a prospective randomized study. Wideochir Inne Tech Maloinwazyjne. 2012 Dec;7(4):268-74. PubMed PMID: 23362426. Pubmed Central PMCID: 3557734.
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9. Laycock W, Trus T, Hunter J. New technology for the division of short gastric vessels during laparoscopic Nissen fundoplication. Surgical endoscopy. 1996;10(1):71-3.
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11. Pons Y, Gauthier J, Ukkola-Pons E, et al. Comparison of LigaSure vessel sealing system, harmonic scalpel, and conventional hemostasis in total thyroidectomy. Otolaryngol Head Neck Surg. 2009 Oct;141(4):496-501. PubMed PMID: 19786219.
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13. Uzunoglu FG, Stehr A, Fink JA, et al. Ultrasonic dissection versus conventional dissection techniques in pancreatic surgery: a randomized multicentre study. Annals of surgery. 2012;256(5):675-80.

14. Tempé F, Jänes A, Cengiz Y. Cost analysis comparing ultrasonic fundus-first and conventional laparoscopic cholecystectomy using electrocautery. Surgical endoscopy. 2013;27(8):2856-9.
15. Swanstrom LL, Pennings JL. Laparoscopic control of short gastric vessels. Journal of the American College of Surgeons. 1995;181(4):347-51.