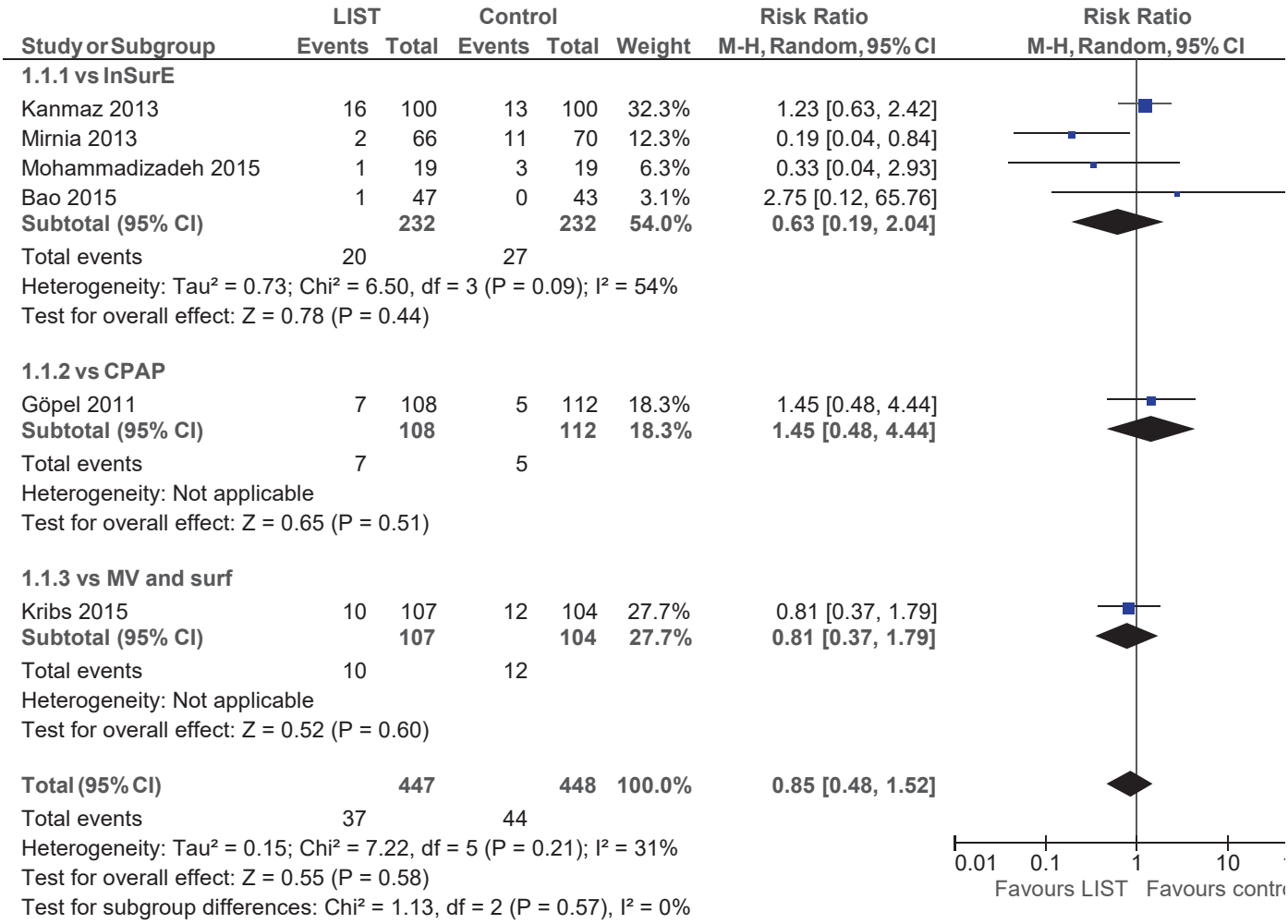
1 Main analysis

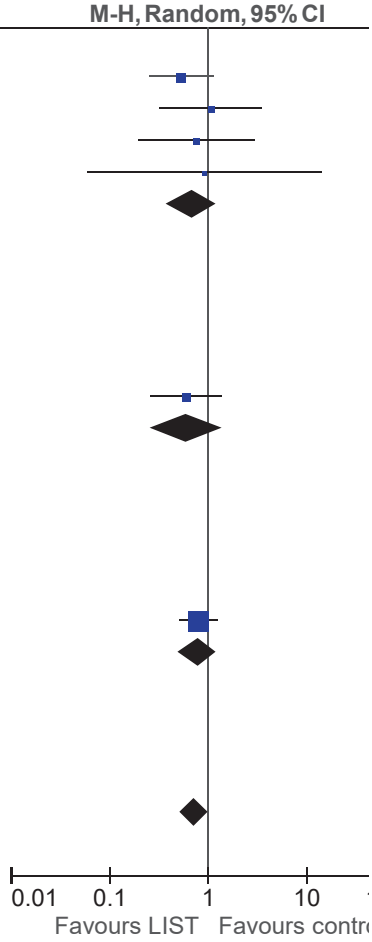
1.1 Death



LIST: Less invasive surfactant therapy
InSurE: Intubation- surfactant- extubation
MV and surf: mechanical ventilation and surfactant

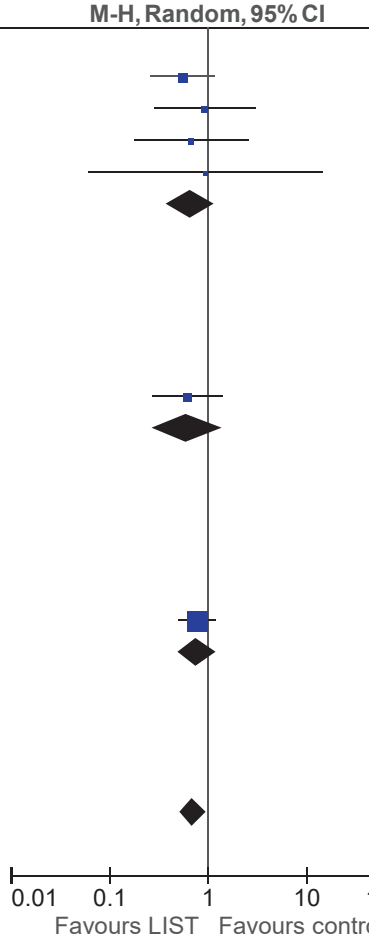
1.2 BPD at 36 weeks, all patients

Study or Subgroup	LIST Events	LIST Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
1.2.1 vs InSurE						
Kanmaz 2013	9	100	17	100	18.4%	0.53 [0.25, 1.13]
Mirnia 2013	5	66	5	70	7.4%	1.06 [0.32, 3.50]
Mohammadizadeh 2015	3	19	4	19	5.8%	0.75 [0.19, 2.91]
Bao 2015	1	47	1	43	1.4%	0.91 [0.06, 14.18]
Subtotal (95% CI)		**232**		**232**	**32.9%**	**0.67 [0.38, 1.19]**
Total events	18		27			
Heterogeneity: Tau² = 0.00; Chi² = 1.02, df = 3 (P = 0.80); I² = 0%						
Test for overall effect: Z = 1.37 (P = 0.17)						
1.2.2 vs CPAP						
Göpel 2011	8	108	14	112	15.4%	0.59 [0.26, 1.36]
Subtotal (95% CI)		**108**		**112**	**15.4%**	**0.59 [0.26, 1.36]**
Total events	8		14			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.24 (P = 0.22)						
1.2.3 vs MV and surf						
Kribs 2015	25	107	31	104	51.6%	0.78 [0.50, 1.23]
Subtotal (95% CI)		**107**		**104**	**51.6%**	**0.78 [0.50, 1.23]**
Total events	25		31			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.05 (P = 0.29)						
Total (95% CI)		**447**		**448**	**100.0%**	**0.71 [0.52, 0.99]**
Total events	51		72			
Heterogeneity: Tau² = 0.00; Chi² = 1.42, df = 5 (P = 0.92); I² = 0%						
Test for overall effect: Z = 2.03 (P = 0.04)						
Test for subgroup differences: Chi² = 0.40, df = 2 (P = 0.82), I² = 0%						



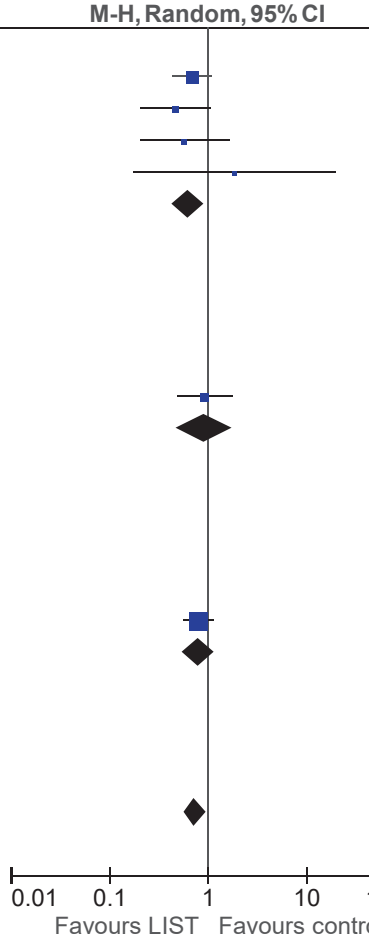
1.3 BPD at 36 weeks, survivors

Study or Subgroup	LIST Events	LIST Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
1.3.1 vs InSurE						
Kanmaz 2013	9	84	17	87	18.2%	0.55 [0.26, 1.16]
Mirnia 2013	5	64	5	59	7.3%	0.92 [0.28, 3.02]
Mohammadizadeh 2015	3	18	4	16	5.7%	0.67 [0.18, 2.54]
Bao 2015	1	46	1	43	1.4%	0.93 [0.06, 14.48]
Subtotal (95% CI)		**212**		**205**	**32.6%**	**0.65 [0.37, 1.14]**
Total events	18		27			
Heterogeneity: Tau² = 0.00; Chi² = 0.60, df = 3 (P = 0.90); I² = 0%						
Test for overall effect: Z = 1.50 (P = 0.13)						
1.3.2 vs CPAP						
Göpel 2011	8	101	14	107	15.1%	0.61 [0.27, 1.38]
Subtotal (95% CI)		**101**		**107**	**15.1%**	**0.61 [0.27, 1.38]**
Total events	8		14			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.19 (P = 0.23)						
1.3.3 vs MV and SURF						
Kribs 2015	25	97	31	92	52.3%	0.76 [0.49, 1.19]
Subtotal (95% CI)		**97**		**92**	**52.3%**	**0.76 [0.49, 1.19]**
Total events	25		31			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.19 (P = 0.24)						
Total (95% CI)		**410**		**404**	**100.0%**	**0.70 [0.51, 0.97]**
Total events	51		72			
Heterogeneity: Tau² = 0.00; Chi² = 0.94, df = 5 (P = 0.97); I² = 0%						
Test for overall effect: Z = 2.18 (P = 0.03)						
Test for subgroup differences: Chi² = 0.34, df = 2 (P = 0.85), I² = 0%						

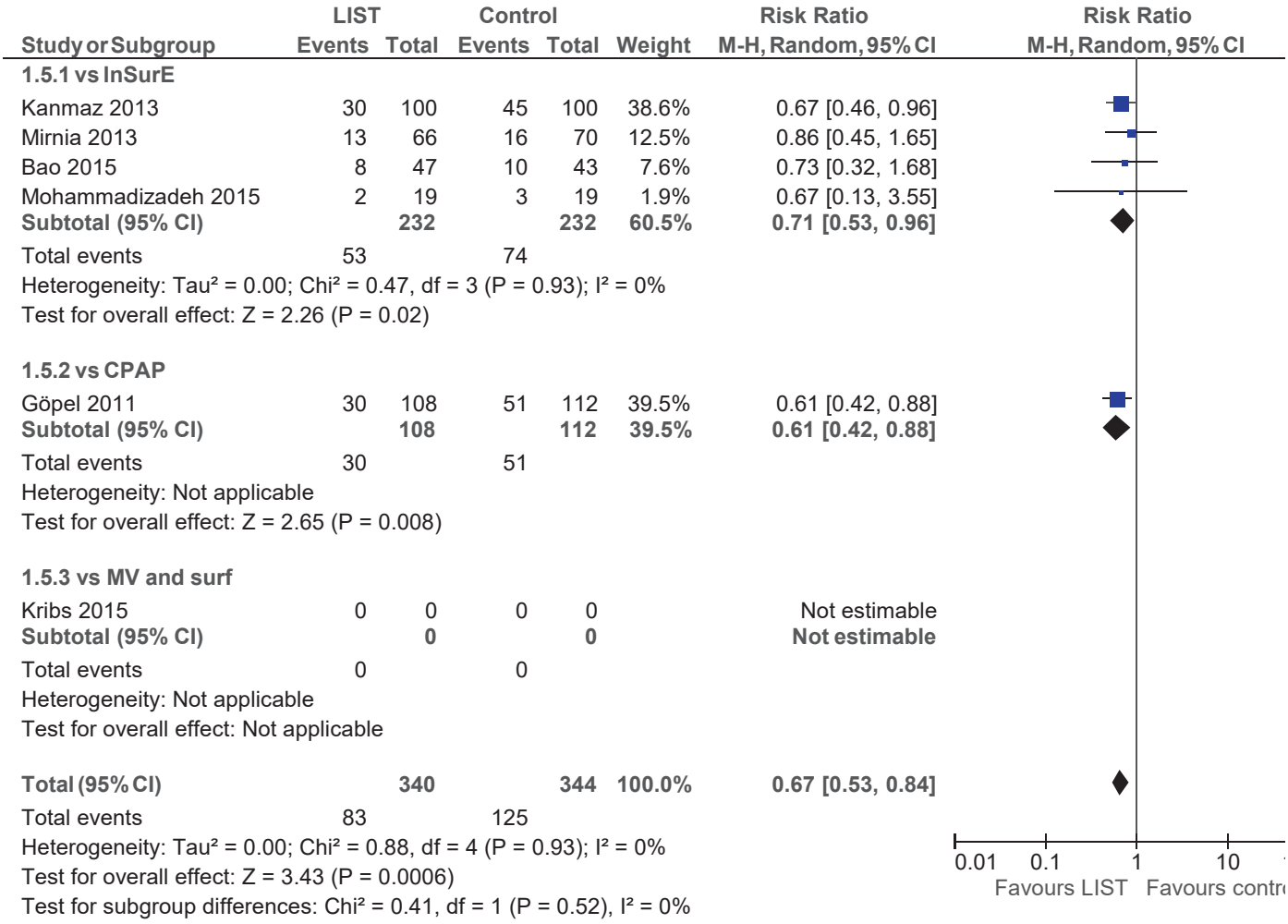


1.4 Death or BPD

Study or Subgroup	LIST Events	LIST Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
1.4.1 vs InSurE						
Kanmaz 2013	22	100	32	100	26.2%	0.69 [0.43, 1.10]
Mirnia 2013	7	66	16	70	8.5%	0.46 [0.20, 1.06]
Mohammadizadeh 2015	4	19	7	19	5.2%	0.57 [0.20, 1.63]
Bao 2015	2	47	1	43	1.0%	1.83 [0.17, 19.47]
Subtotal (95% CI)		**232**		**232**	**40.9%**	**0.63 [0.44, 0.92]**
Total events	35		56			
Heterogeneity: Tau² = 0.00; Chi² = 1.48, df = 3 (P = 0.69); I² = 0%						
Test for overall effect: Z = 2.38 (P = 0.02)						
1.4.2 vs CPAP						
Göpel 2011	15	108	17	112	13.9%	0.92 [0.48, 1.74]
Subtotal (95% CI)		**108**		**112**	**13.9%**	**0.92 [0.48, 1.74]**
Total events	15		17			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.27 (P = 0.79)						
1.4.3 vs MV and surf						
Kribs 2015	35	107	43	104	45.3%	0.79 [0.55, 1.13]
Subtotal (95% CI)		**107**		**104**	**45.3%**	**0.79 [0.55, 1.13]**
Total events	35		43			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.29 (P = 0.20)						
Total (95% CI)		**447**		**448**	**100.0%**	**0.74 [0.58, 0.94]**
Total events	85		116			
Heterogeneity: Tau² = 0.00; Chi² = 2.69, df = 5 (P = 0.75); I² = 0%						
Test for overall effect: Z = 2.50 (P = 0.01)						
Test for subgroup differences: Chi² = 1.21, df = 2 (P = 0.55), I² = 0%						

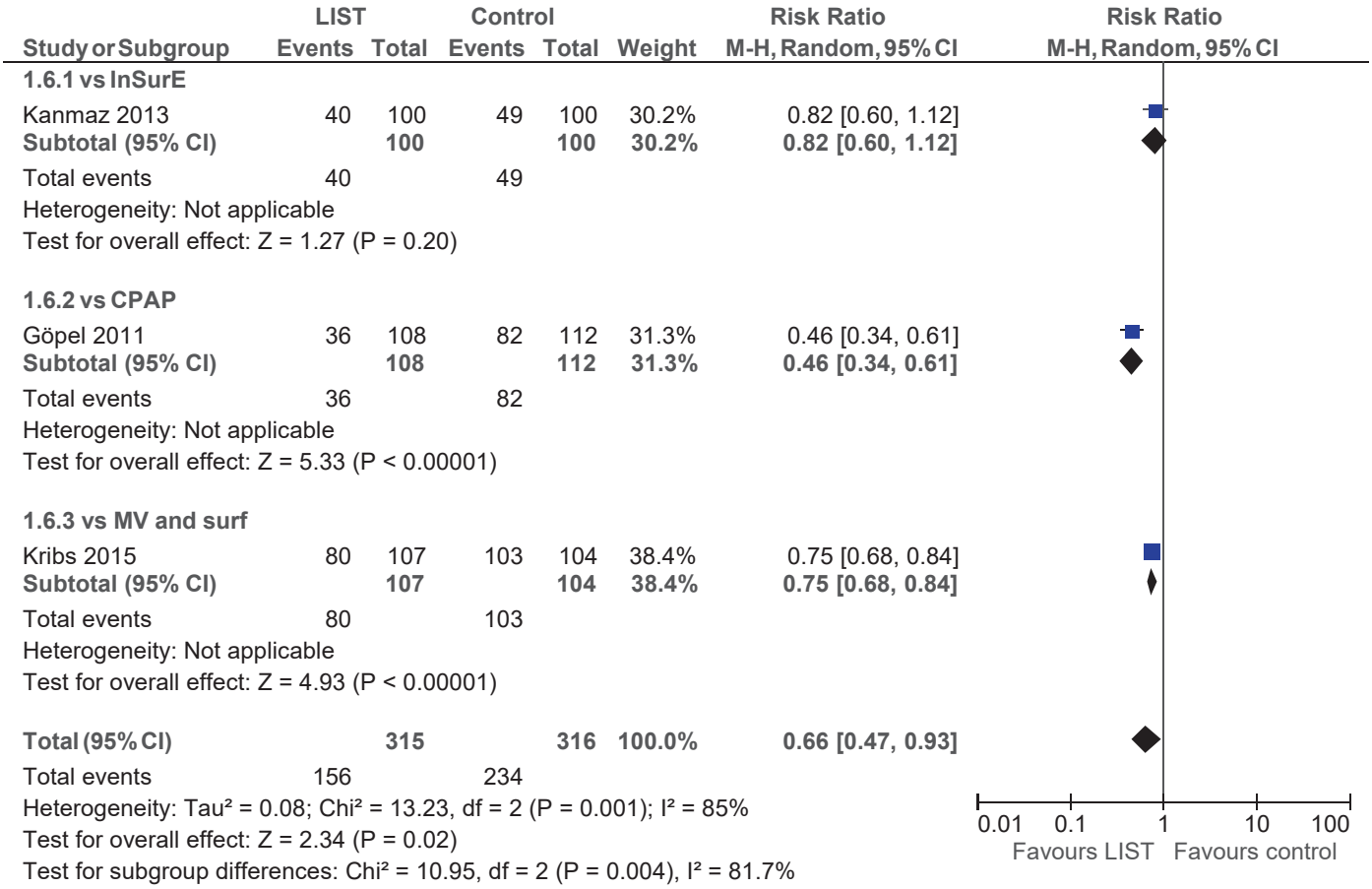


1.5 Early MV (by 72H)



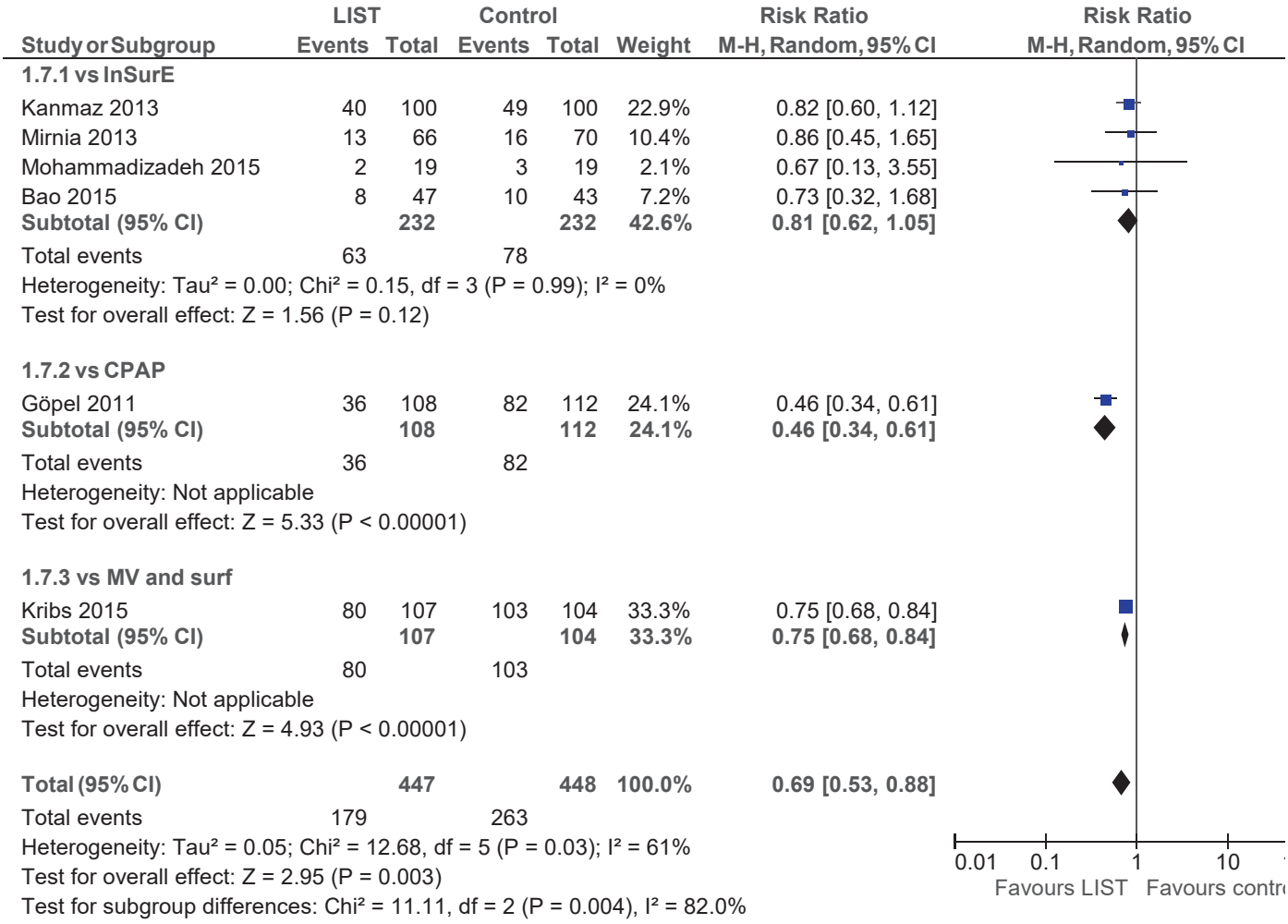
Kribs 2015 not included: early mechanical ventilation mandatory for control group.

1.6 Any MV



Kribs 2015: MV mandatory for control patients. RR 0.61 [0.34, 1.08] if not included

1.7 Any MV reported

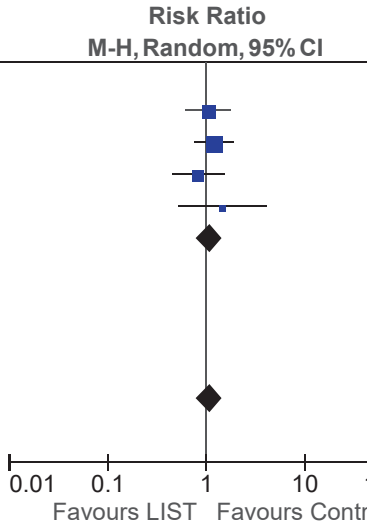


Kribs 2015 : MV mandatory in control patients. RR 0.66 [0.47, 0.94] if not included. Mirnia 2013, Mohammadizadeh 2015 and Bao 2015 reported mechanical ventilation by day 3 of life only.

1 Main analysis

1.8 Need for extra surfactant dose

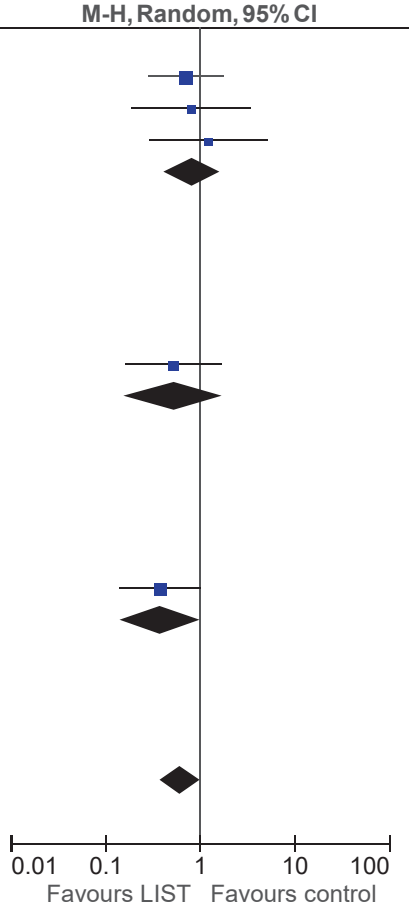
Study or Subgroup	LIST Events	LIST Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
1.8.1 vs InSurE						
Kanmaz 2013	22	100	21	100	30.1%	1.05 [0.62, 1.78]
Mirnia 2013	25	66	22	70	39.3%	1.21 [0.76, 1.92]
Mohammadizadeh 2015	9	19	11	19	22.7%	0.82 [0.44, 1.51]
Bao 2015	8	47	5	43	7.8%	1.46 [0.52, 4.13]
Subtotal (95% CI)		**232**		**232**	**100.0%**	**1.07 [0.80, 1.44]**
Total events	64		59			
Heterogeneity: Tau² = 0.00; Chi² = 1.38, df = 3 (P = 0.71); I² = 0%						
Test for overall effect: Z = 0.48 (P = 0.63)						
Total (95% CI)		**232**		**232**	**100.0%**	**1.07 [0.80, 1.44]**
Total events	64		59			
Heterogeneity: Tau² = 0.00; Chi² = 1.38, df = 3 (P = 0.71); I² = 0%						
Test for overall effect: Z = 0.48 (P = 0.63)						
Test for subgroup differences: Not applicable						



Göpel 2011 and Kribs 2015 reported the median number of surfactant doses per infant, with no difference.

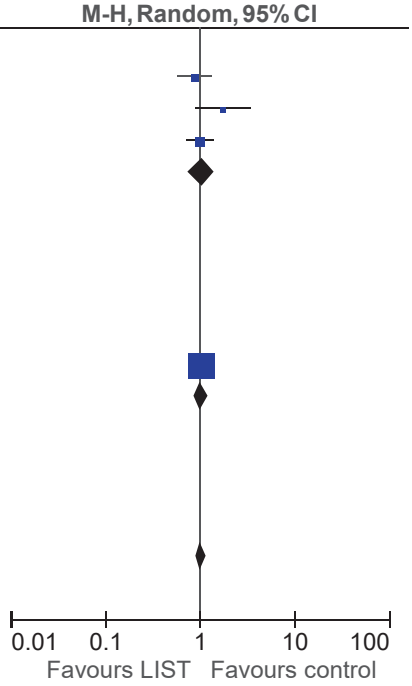
1.9 Pneumothorax

Study or Subgroup	LIST Events	LIST Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
1.9.1 vs InSurE						
Kanmaz 2013	7	100	10	100	30.3%	0.70 [0.28, 1.77]
Mirnia 2013	3	66	4	70	12.2%	0.80 [0.18, 3.42]
Bao 2015	4	47	3	43	12.5%	1.22 [0.29, 5.14]
Subtotal (95% CI)		**213**		**213**	**54.9%**	**0.82 [0.41, 1.62]**
Total events	14		17			
Heterogeneity: Tau² = 0.00; Chi² = 0.41, df = 2 (P = 0.82); I² = 0%						
Test for overall effect: Z = 0.58 (P = 0.56)						
1.9.2 vs CPAP						
Göpel 2011	4	108	8	112	18.9%	0.52 [0.16, 1.67]
Subtotal (95% CI)		**108**		**112**	**18.9%**	**0.52 [0.16, 1.67]**
Total events	4		8			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.10 (P = 0.27)						
1.9.3 vs MV and surf						
Kribs 2015	5	105	13	103	26.2%	0.38 [0.14, 1.02]
Subtotal (95% CI)		**105**		**103**	**26.2%**	**0.38 [0.14, 1.02]**
Total events	5		13			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.92 (P = 0.05)						
Total (95% CI)		**426**		**428**	**100.0%**	**0.61 [0.37, 1.02]**
Total events	23		38			
Heterogeneity: Tau² = 0.00; Chi² = 2.08, df = 4 (P = 0.72); I² = 0%						
Test for overall effect: Z = 1.89 (P = 0.06)						
Test for subgroup differences: Chi² = 1.67, df = 2 (P = 0.43), I² = 0%						



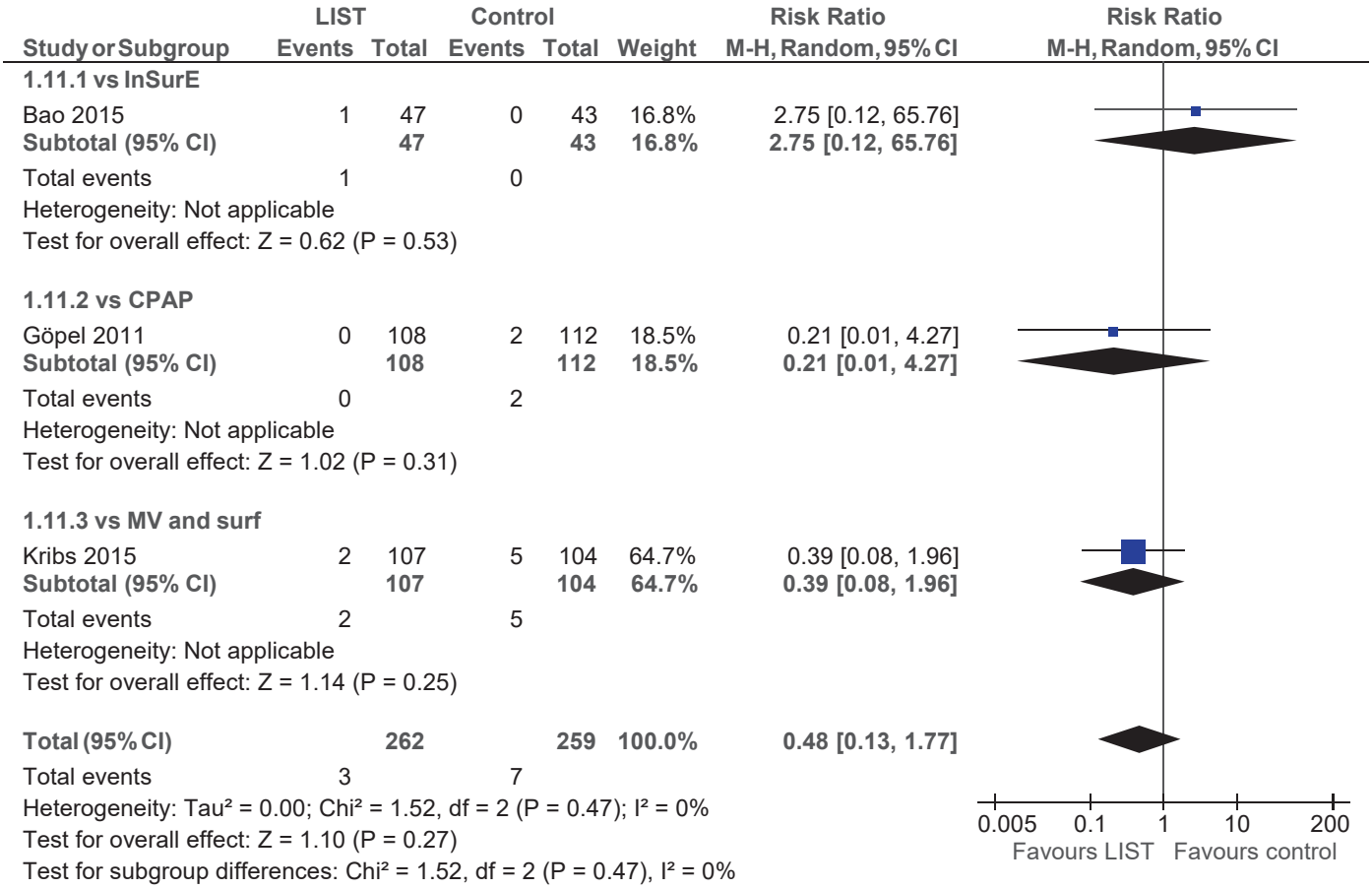
1.10 PDA

Study or Subgroup	LIST Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
1.10.1 vs InSurE						
Kanmaz 2013	28	100	32	100	10.3%	0.88 [0.57, 1.34]
Mirnia 2013	18	66	11	70	4.2%	1.74 [0.89, 3.39]
Bao 2015	28	47	26	43	16.4%	0.99 [0.70, 1.38]
Subtotal (95% CI)		**213**		**213**	**30.9%**	**1.05 [0.76, 1.44]**
Total events	74		69			
Heterogeneity: Tau² = 0.03; Chi² = 3.00, df = 2 (P = 0.22); I² = 33%						
Test for overall effect: Z = 0.28 (P = 0.78)						
1.10.2 vs MV and surf						
Kribs 2015	79	107	75	104	69.1%	1.02 [0.87, 1.21]
Subtotal (95% CI)		**107**		**104**	**69.1%**	**1.02 [0.87, 1.21]**
Total events	79		75			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.28 (P = 0.78)						
Total (95% CI)		**320**		**317**	**100.0%**	**1.02 [0.89, 1.17]**
Total events	153		144			
Heterogeneity: Tau² = 0.00; Chi² = 2.99, df = 3 (P = 0.39); I² = 0%						
Test for overall effect: Z = 0.33 (P = 0.74)						
Test for subgroup differences: Chi² = 0.02, df = 1 (P = 0.90), I² = 0%						



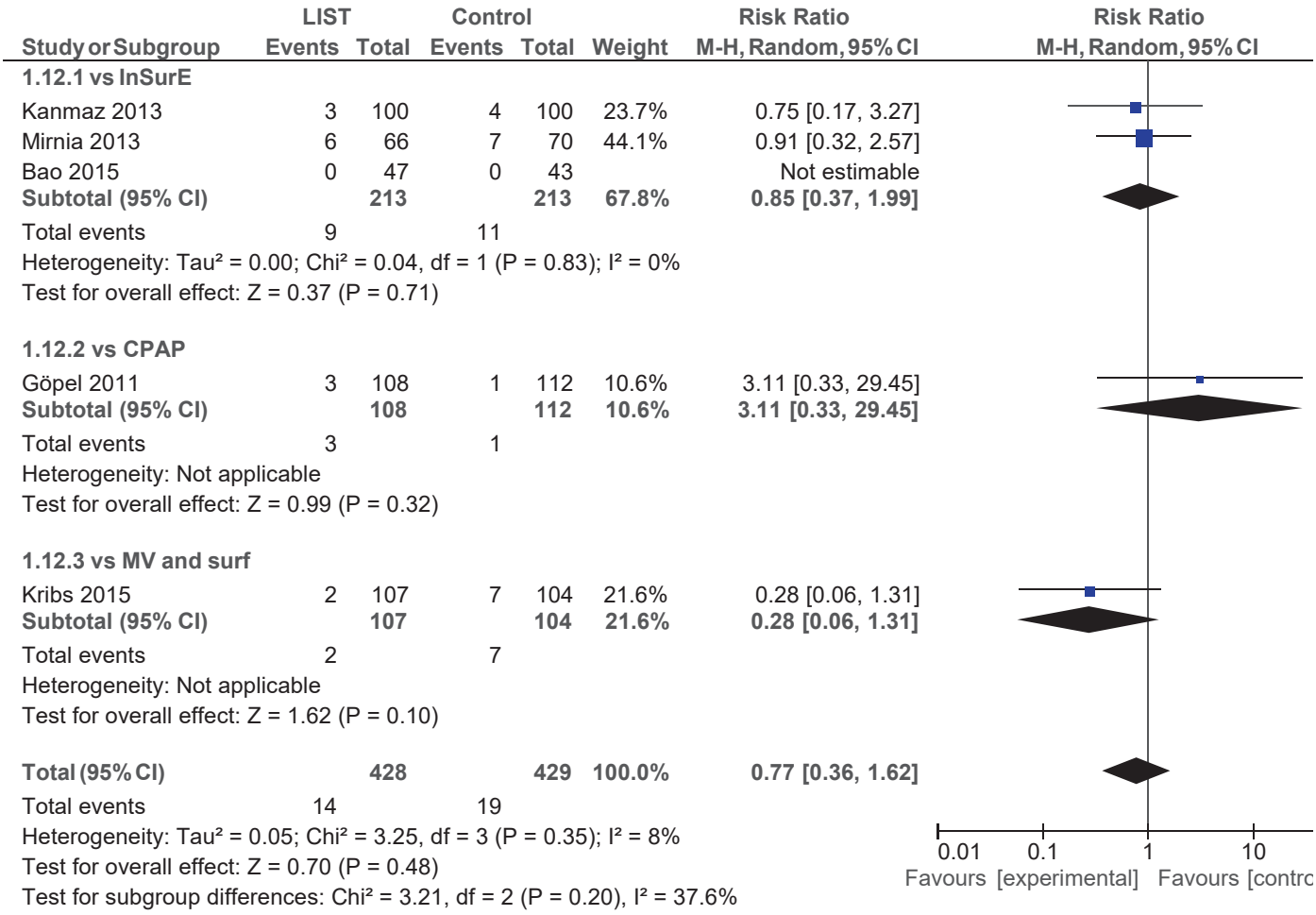
Mirnia 2013: we used data for PDA requiring therapy.

1.11 PDA ligation



1 Main analysis

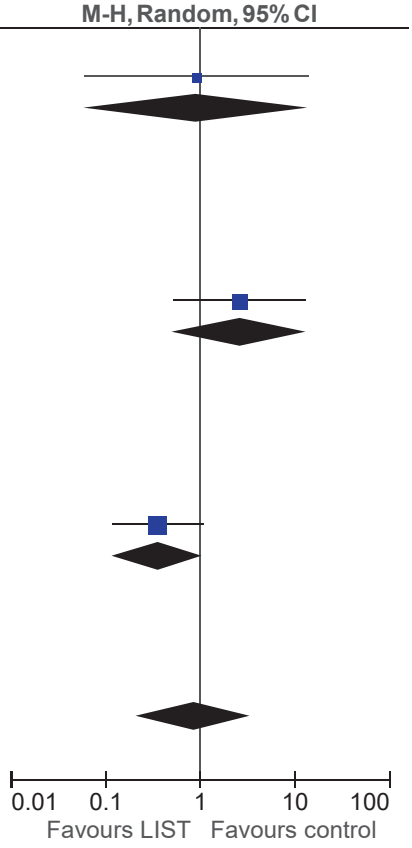
1.12 ROP



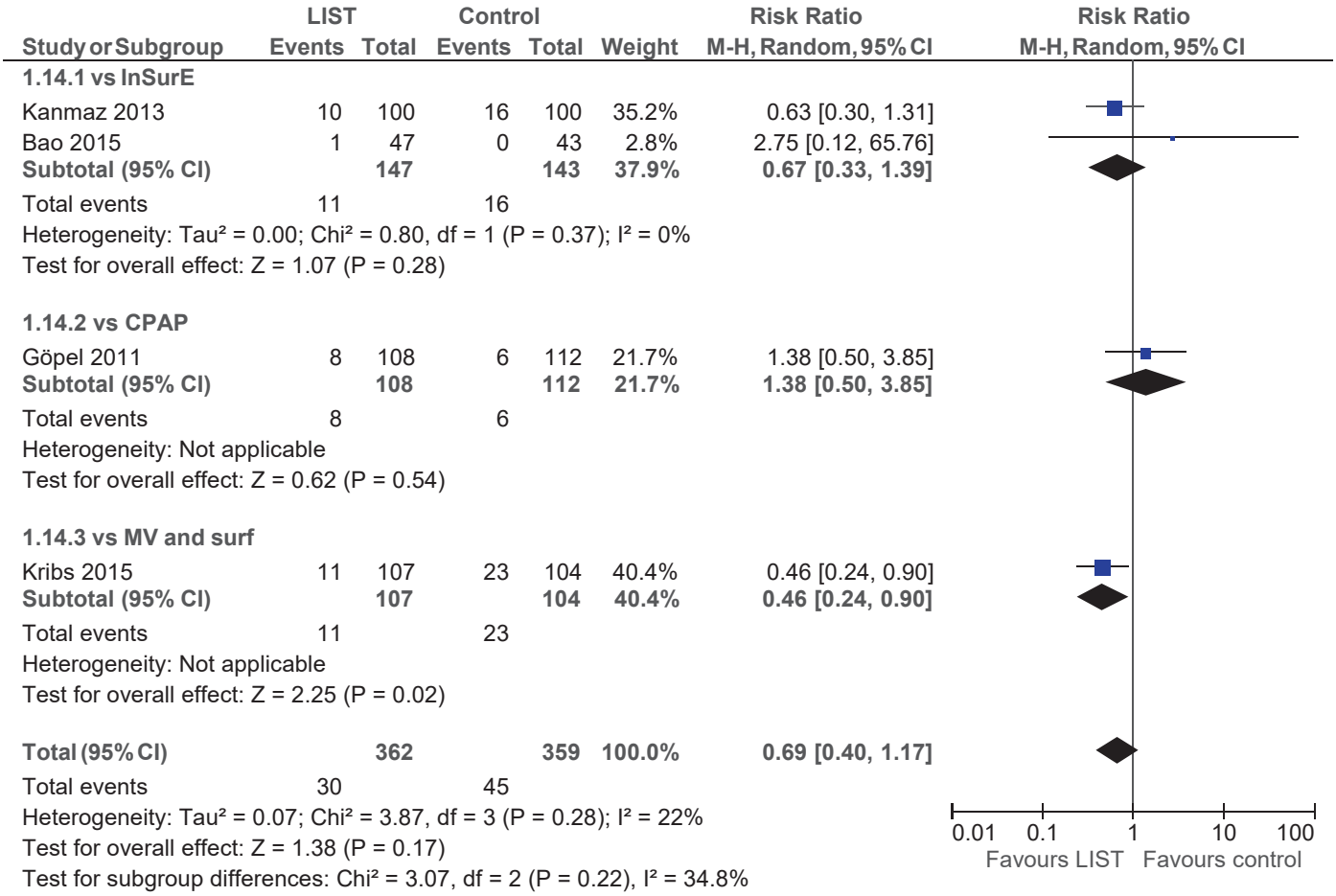
Kanmaz 2013, Mirnia 2013 and Boa 2015 reported on ROP> grade 2.
Göpel 2011 and Kribs 2015 reported on ROP treated by laser or cryotherapy.
Mirnia 2013 also reported data for treated ROP (5/66 and 1/70), associated with a total RR of 1.13 [0.31, 4.10]

1.13 cPVL

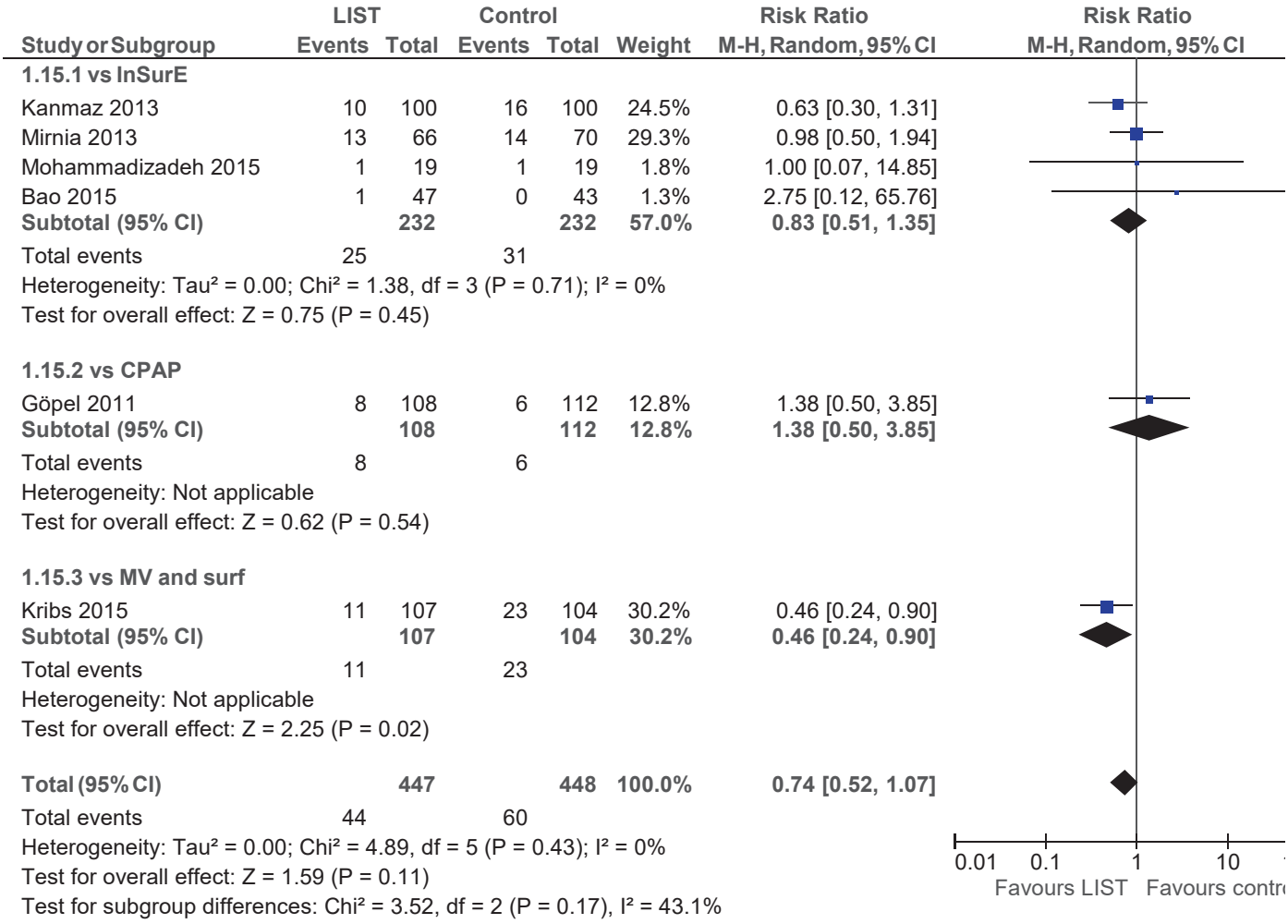
Study or Subgroup	LIST Events	LIST Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
1.13.1 vs InSurE						
Bao 2015	1	47	1	43	18.4%	0.91 [0.06, 14.18]
Subtotal (95% CI)		**47**		**43**	**18.4%**	**0.91 [0.06, 14.18]**
Total events	1		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.06 (P = 0.95)						
1.13.2 vs CPAP						
Göpel 2011	5	108	2	112	34.9%	2.59 [0.51, 13.08]
Subtotal (95% CI)		**108**		**112**	**34.9%**	**2.59 [0.51, 13.08]**
Total events	5		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.15 (P = 0.25)						
1.13.3 vs MV and surf						
Kribs 2015	4	107	11	104	46.7%	0.35 [0.12, 1.07]
Subtotal (95% CI)		**107**		**104**	**46.7%**	**0.35 [0.12, 1.07]**
Total events	4		11			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.83 (P = 0.07)						
Total (95% CI)		**262**		**259**	**100.0%**	**0.84 [0.21, 3.35]**
Total events	10		14			
Heterogeneity: Tau² = 0.74; Chi² = 4.00, df = 2 (P = 0.14); I² = 50%						
Test for overall effect: Z = 0.24 (P = 0.81)						
Test for subgroup differences: Chi² = 4.00, df = 2 (P = 0.14), I² = 50.0%						



1.14 Severe IVH

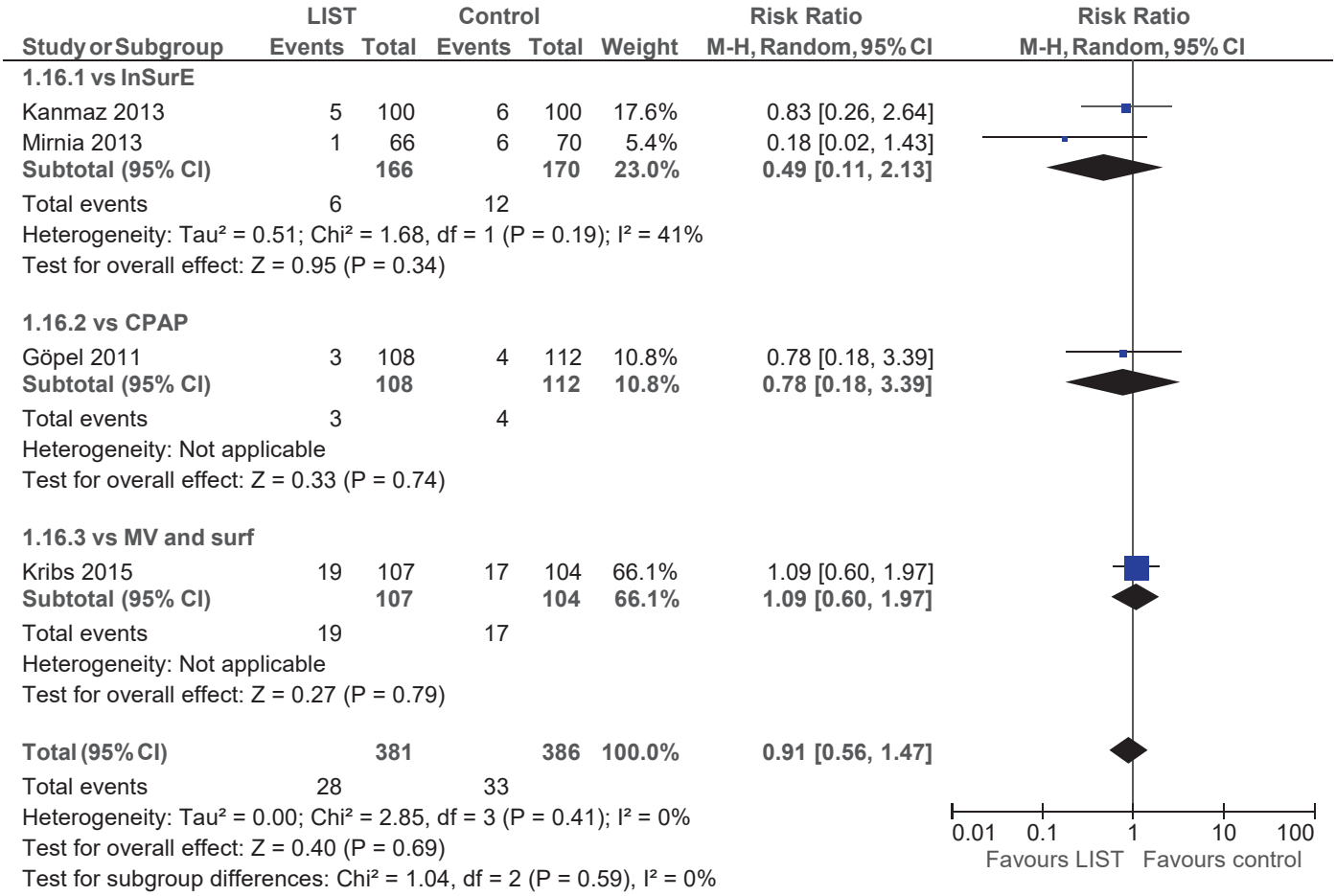


1.15 Any IVH reported



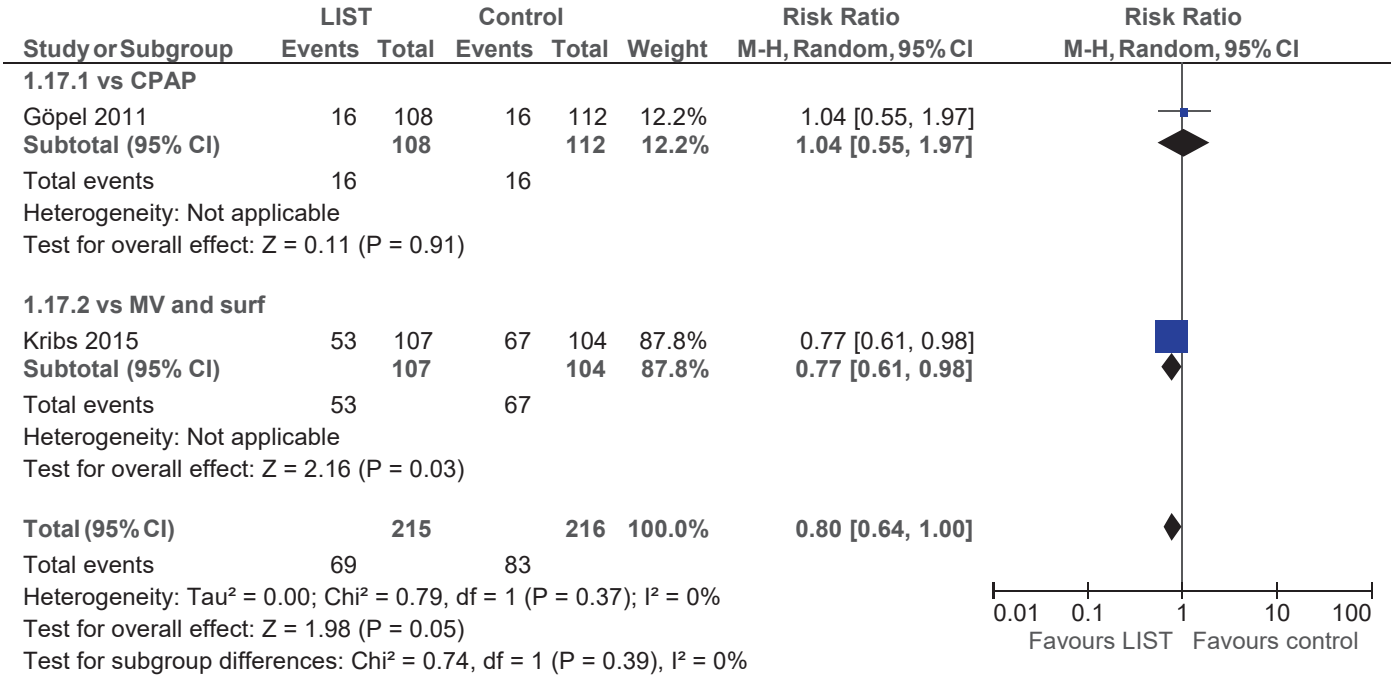
Kanmaz 2013, Bao 2015, Göpel 2015 and Kribs 2015 reported grade 3-4 IVH.
Mirnia 2013 reported grade 2-4 IVH.
Mohammadizadeh 2015 reported grade 1-4 IVH

1.16 NEC (as reported)



Göpel 2015 and Kribs 2015 reported a combined outcome of NEC or focal intestinal perforation requiring surgery.
Kanmaz 2013 and Mirnia 2013 reported NEC Bell stages 2 and 3.

1.17 Death or severe morbidity

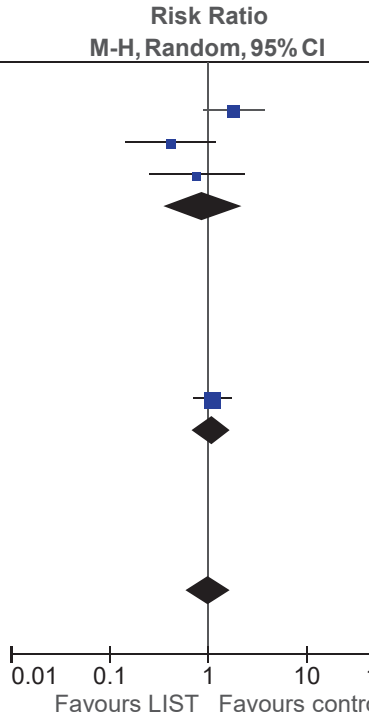


Both studies reported a combined ouctome of death, BDP, severe IVH, PVL, or surgery for NEC, FIP or ROP.
Kribs 2015 also include BPD

1 Main analysis

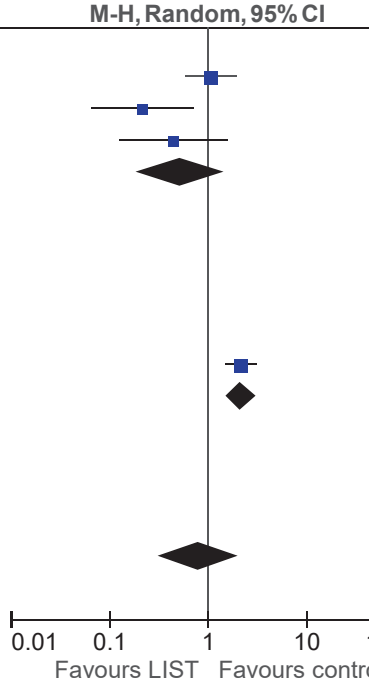
1.18 Failed first attempt

Study or Subgroup	LIST Events	LIST Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
1.18.1 vs InSurE						
Kanmaz 2013	18	100	10	100	27.2%	1.80 [0.87, 3.70]
Mohammadizadeh 2015	4	35	10	36	16.9%	0.41 [0.14, 1.19]
Bao 2015	5	47	6	43	15.9%	0.76 [0.25, 2.32]
Subtotal (95% CI)		**182**		**179**	**60.0%**	**0.89 [0.36, 2.21]**
Total events	27		26			
Heterogeneity: Tau² = 0.41; Chi² = 5.45, df = 2 (P = 0.07); I² = 63%						
Test for overall effect: Z = 0.26 (P = 0.80)						
1.18.2 vs MV and surf						
Kribs 2015	29	107	28	112	40.0%	1.08 [0.69, 1.69]
Subtotal (95% CI)		**107**		**112**	**40.0%**	**1.08 [0.69, 1.69]**
Total events	29		28			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.35 (P = 0.72)						
Total (95% CI)		**289**		**291**	**100.0%**	**1.00 [0.59, 1.68]**
Total events	56		54			
Heterogeneity: Tau² = 0.13; Chi² = 5.47, df = 3 (P = 0.14); I² = 45%						
Test for overall effect: Z = 0.00 (P = 1.00)						
Test for subgroup differences: Chi² = 0.15, df = 1 (P = 0.70), I² = 0%						



1.19 Desaturation during procedure

Study or Subgroup	LIST Events	LIST Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
1.19.1 vs InSurE						
Kanmaz 2013	18	100	17	100	28.2%	1.06 [0.58, 1.93]
Mirnia 2013	3	66	15	70	21.1%	0.21 [0.06, 0.70]
Mohammadizadeh 2015	3	35	7	36	20.2%	0.44 [0.12, 1.57]
Subtotal (95% CI)		**201**		**206**	**69.6%**	**0.51 [0.18, 1.44]**
Total events	24		39			
Heterogeneity: Tau² = 0.57; Chi² = 6.37, df = 2 (P = 0.04); I² = 69%						
Test for overall effect: Z = 1.26 (P = 0.21)						
1.19.2 vs MV and surf						
Kribs 2015	60	107	27	104	30.4%	2.16 [1.50, 3.11]
Subtotal (95% CI)		**107**		**104**	**30.4%**	**2.16 [1.50, 3.11]**
Total events	60		27			
Heterogeneity: Not applicable						
Test for overall effect: Z = 4.13 (P < 0.0001)						
Total (95% CI)		**308**		**310**	**100.0%**	**0.78 [0.30, 2.02]**
Total events	84		66			
Heterogeneity: Tau² = 0.73; Chi² = 19.83, df = 3 (P = 0.0002); I² = 85%						
Test for overall effect: Z = 0.50 (P = 0.61)						
Test for subgroup differences: Chi² = 6.59, df = 1 (P = 0.01), I² = 84.8%						



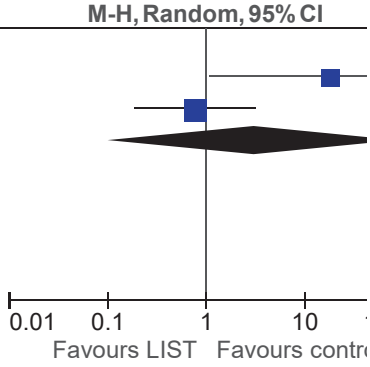
1 Main analysis

1.20 Cough during procedure

Study or Subgroup	LIST Events	LIST Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
1.20.1 vs InSure						
Mirnia 2013	8	66	0	70	43.6%	18.01 [1.06, 306.05]
Mohammadizadeh 2015	3	35	4	36	56.4%	0.77 [0.19, 3.20]
Subtotal (95% CI)		**101**		**106**	**100.0%**	**3.05 [0.10, 90.71]**
Total events	11		4			

Heterogeneity: Tau² = 4.79; Chi² = 4.66, df = 1 (P = 0.03); I² = 79%

Test for overall effect: Z = 0.64 (P = 0.52)

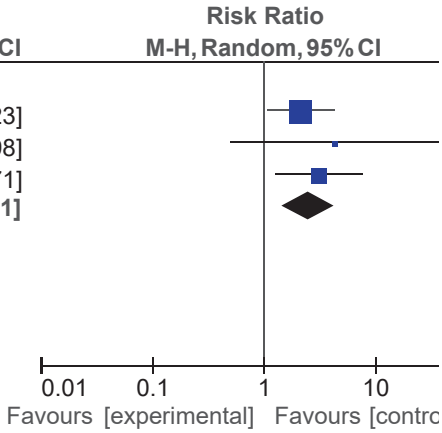


1.21 Surfactant reflux during procedure

Study or Subgroup	LIST Events	LIST Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
1.21.1 vs InSurE						
Kanmaz 2013	21	100	10	100	58.8%	2.10 [1.04, 4.23]
Mirnia 2013	4	66	1	70	6.2%	4.24 [0.49, 36.98]
Bao 2015	17	47	5	43	35.0%	3.11 [1.26, 7.71]
Subtotal (95% CI)		**213**		**213**	**100.0%**	**2.52 [1.47, 4.31]**
Total events	42		16			

Heterogeneity: Tau² = 0.00; Chi² = 0.69, df = 2 (P = 0.71); I² = 0%

Test for overall effect: Z = 3.37 (P = 0.0008)



Test for subgroup differences: Not applicable