Online Supplementary Figure

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Figure S1. Risk of bias item presented as percentages across all included studies.

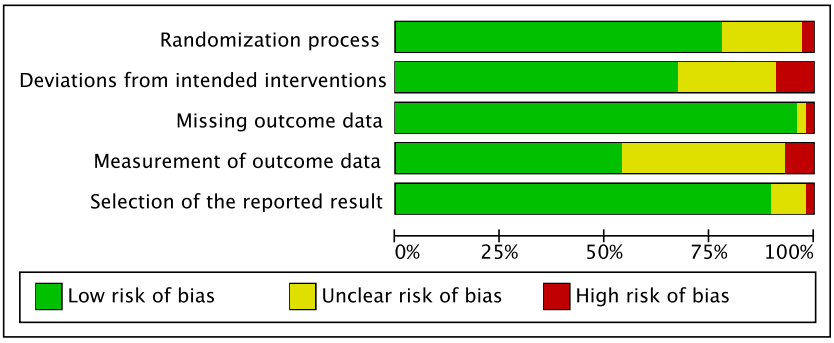
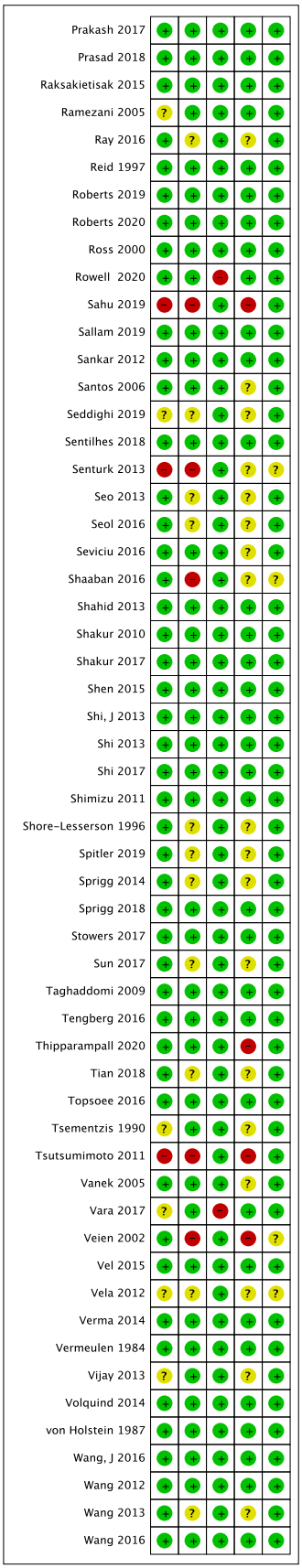


Figure S2. Risk of bias summary and graph.


Prakash 2017
Prasad 2018
Raksakietisak 2015
Ramezani 2005
Ray 2016
Reid 1997
Roberts 2019
Roberts 2020
Ross 2000
Rowell 2020
Sahu 2019
Sallam 2019
Sankar 2012
Santos 2006
Seddighi 2019
Sentilhes 2018
Senturk 2013
Seo 2013
Seol 2016
Seviciu 2016
Shaaban 2016
Shahid 2013
Shakur 2010
Shakur 2017
Shen 2015
Shi, J 2013
Shi 2013
Shi 2017
Shimizu 2011
Shore-Lesserson 1996
Spitler 2019
Sprigg 2014
Sprigg 2018
Stowers 2017
Sun 2017
Taghaddomi 2009
Tengberg 2016
Thipparampall 2020
Tian 2018
Topsoee 2016
Tsementzis 1990
Tsutsumimoto 2011
Vanek 2005
Vara 2017
Veien 2002
Vel 2015
Vela 2012
Verma 2014
Vermeulen 1984
Vijay 2013
Volquind 2014
von Holstein 1987
Wang, J 2016
Wang 2012
Wang 2013
Wang 2016

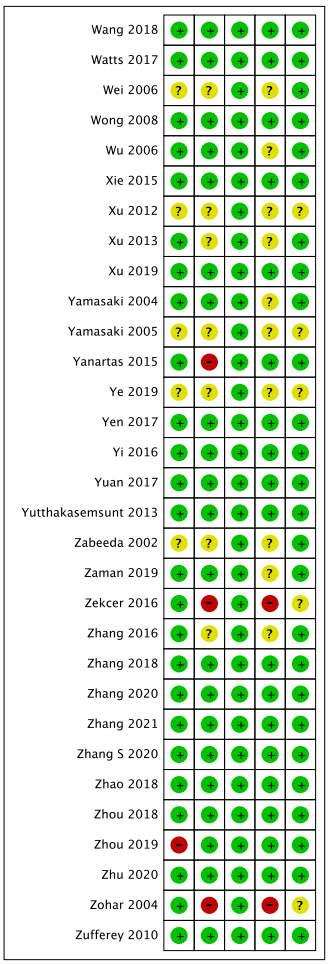

Wang 2018
Watts 2017
Wei 2006
Wong 2008
Wu 2006
Xie 2015
Xu 2012
Xu 2013
Xu 2019
Yamasaki 2004
Yamasaki 2005
Yanartas 2015
Ye 2019
Yen 2017
Yi 2016
Yuan 2017
Yutthakasemsunt 2013
Zabeeda 2002
Zaman 2019
Zekcer 2016
Zhang 2016
Zhang 2018
Zhang 2020
Zhang 2021
Zhang S 2020
Zhao 2018
Zhou 2018
Zhou 2019
Zhu 2020
Zohar 2004
Zufferey 2010

Figure S3. Funnel plot of the thrombotic events.

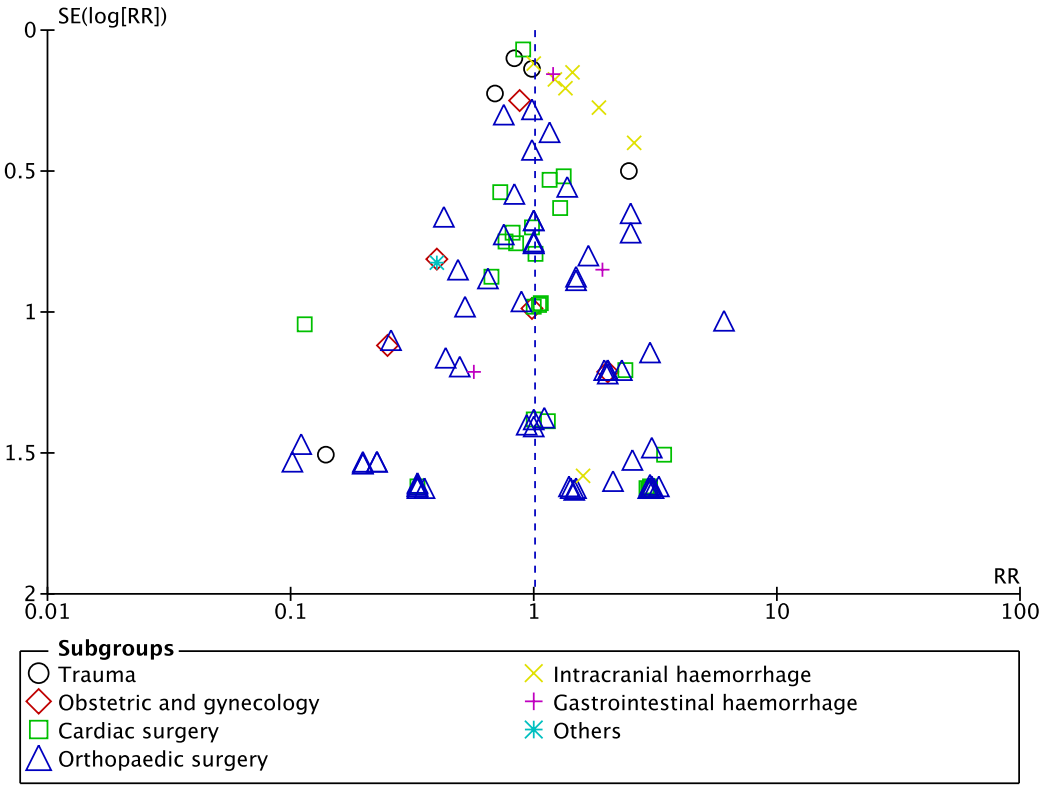


Figure S4. Funnel plot of the seizures.

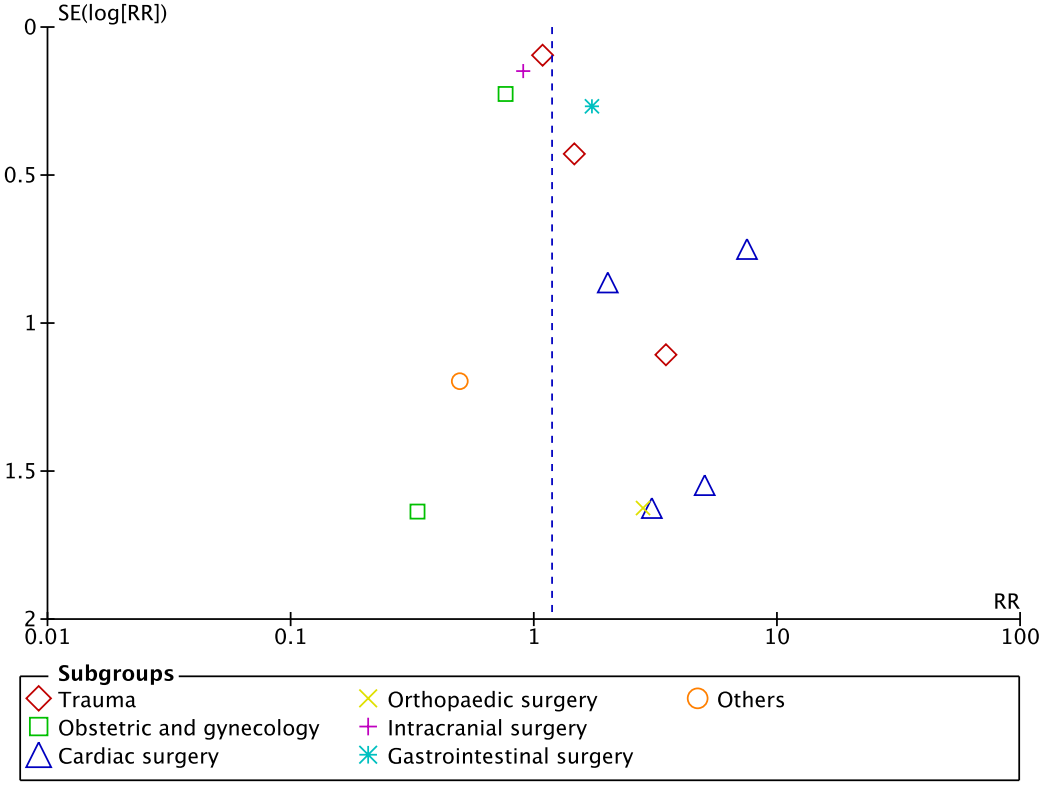
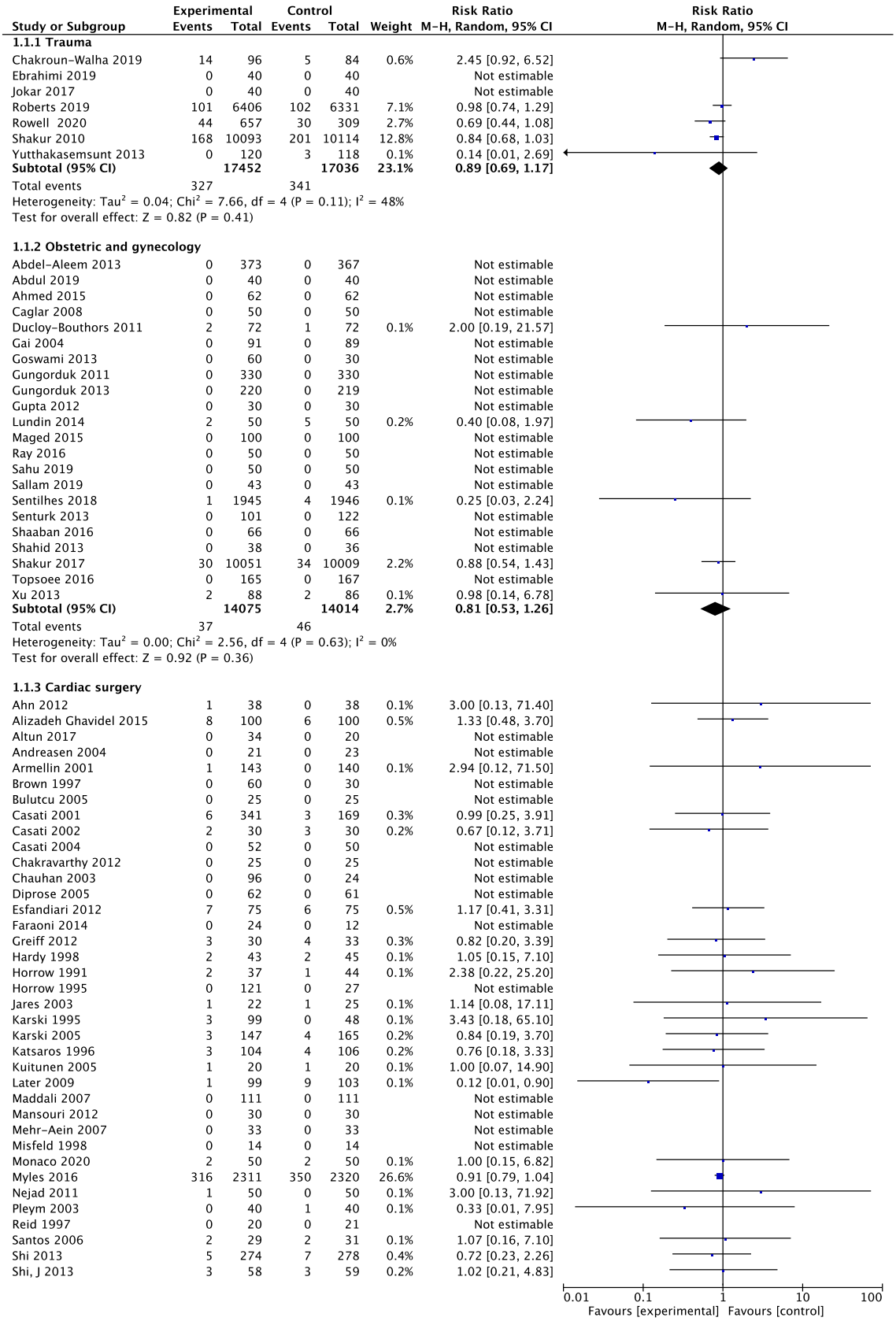
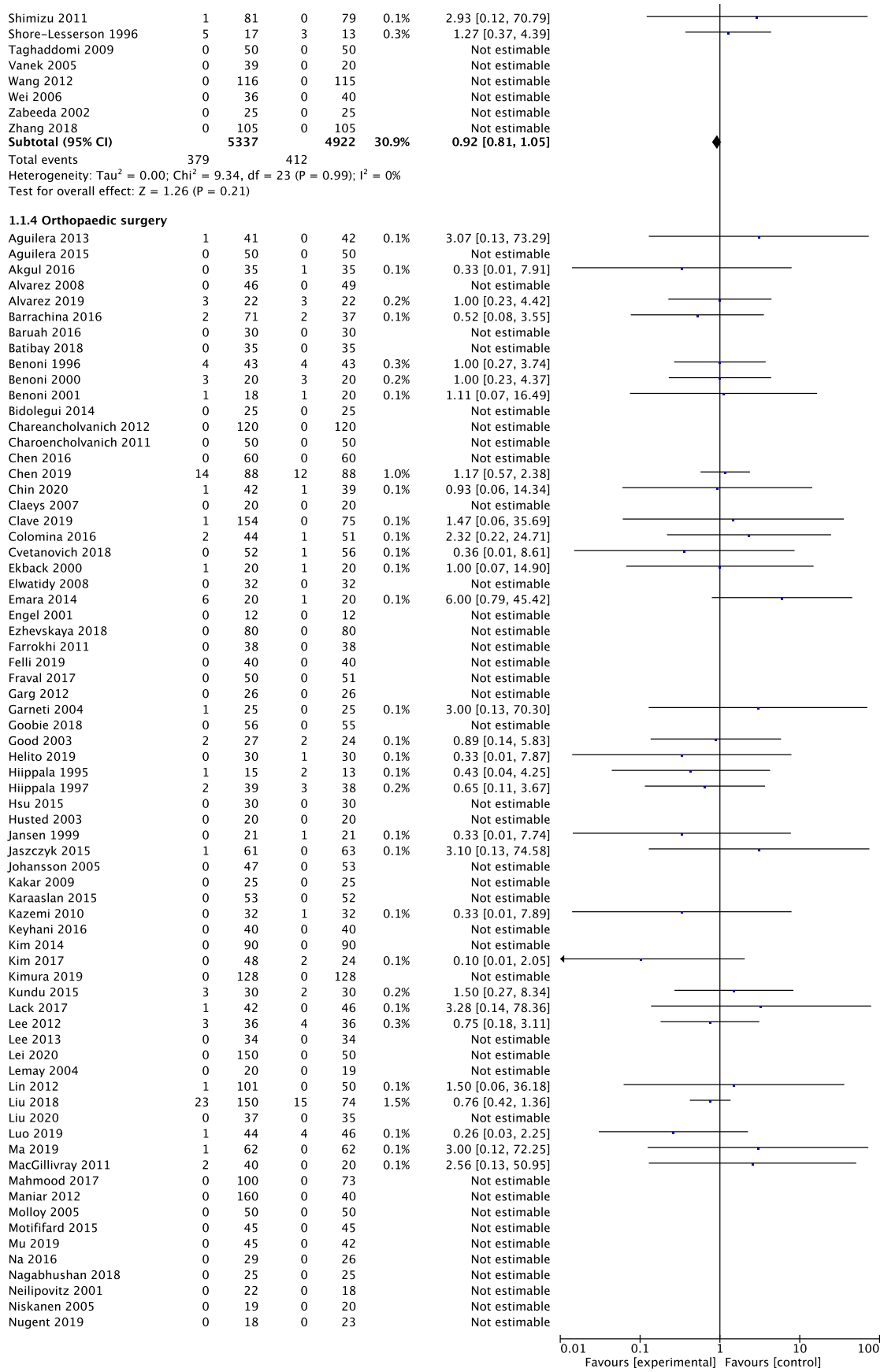
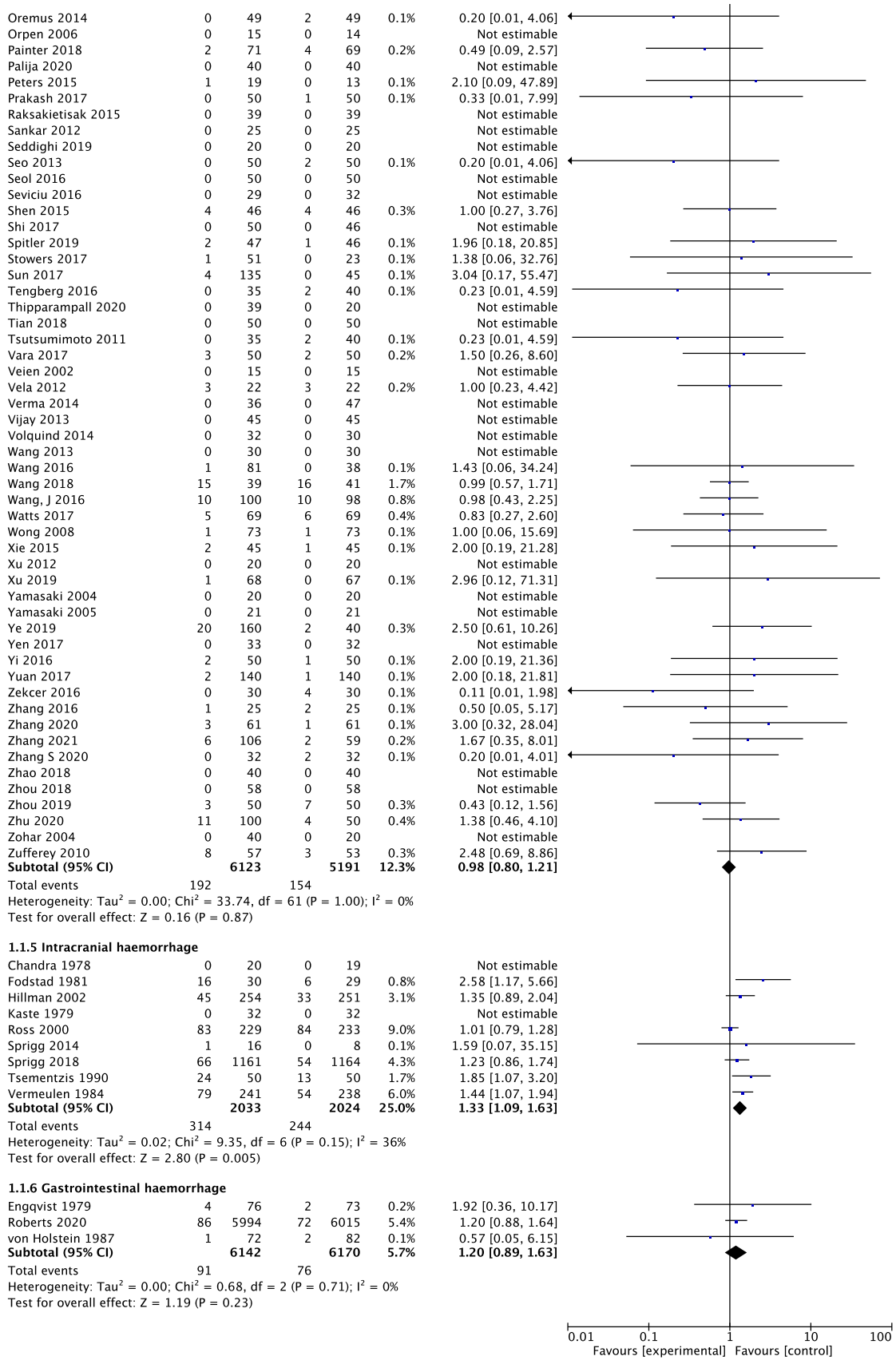
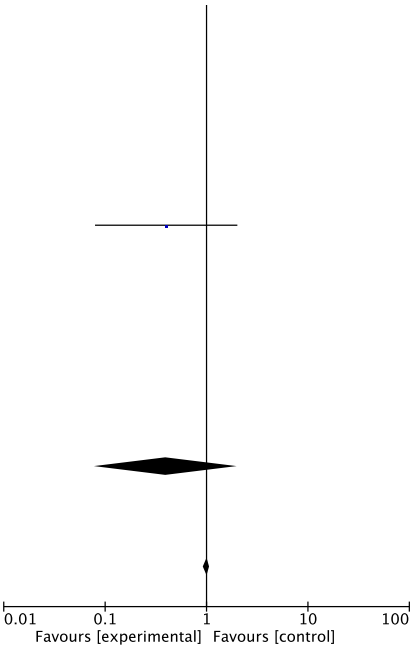


Figure S5. Forest plot of the thrombotic events: subgroup analysis by underlying disease.



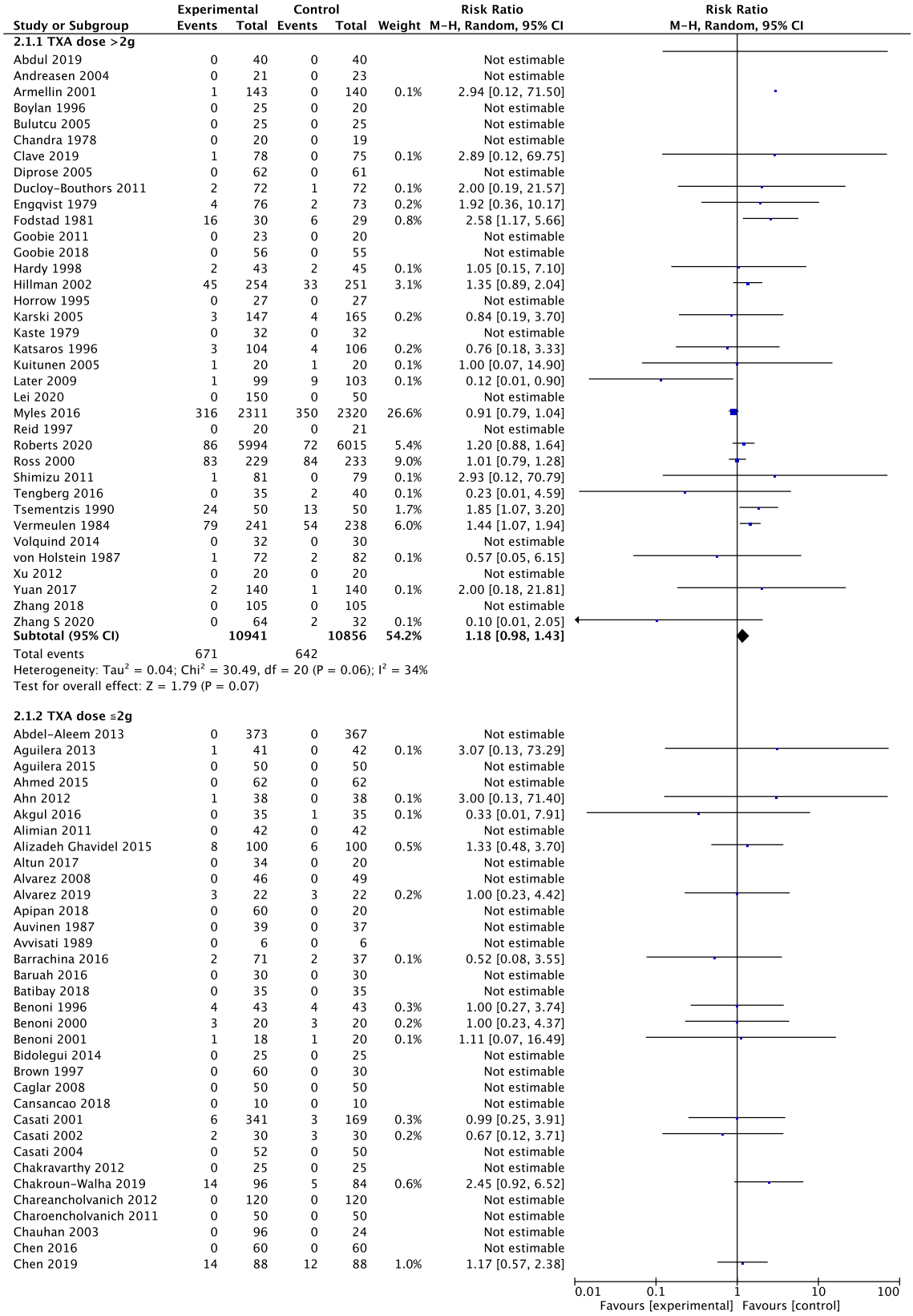

Shimizu 2011 1 81 0 79 0.1% 2.93 [0.12, 70.79]
Shore-Lesserson 1996 5 17 3 13 0.3% 1.27 [0.37, 4.39]
Taghaddomi 2009 0 50 0 50 Not estimable
Vanek 2005 0 39 0 20 Not estimable
Wang 2012 0 116 0 115 Not estimable
Wei 2006 0 36 0 40 Not estimable
Zabeeda 2002 0 25 0 25 Not estimable
Zhang 2018 0 105 0 105 Not estimable
Subtotal (95% CI) 5337 4922 30.9% 0.92 [0.81, 1.05]
Total events 379 412
Heterogeneity: Tau² = 0.00; Chi² = 9.34, df = 23 (P = 0.99); I² = 0%
Test for overall effect: Z = 1.26 (P = 0.21)
1.1.4 Orthopaedic surgery
Aguilera 2013 1 41 0 42 0.1% 3.07 [0.13, 73.29]
Aguilera 2015 0 50 0 50 Not estimable
Akgul 2016 0 35 1 35 0.1% 0.33 [0.01, 7.91]
Alvarez 2008 0 46 0 49 Not estimable
Alvarez 2019 3 22 3 22 0.2% 1.00 [0.23, 4.42]
Barrachina 2016 2 71 2 37 0.1% 0.52 [0.08, 3.55]
Baruah 2016 0 30 0 30 Not estimable
Batibay 2018 0 35 0 35 Not estimable
Benoni 1996 4 43 4 43 0.3% 1.00 [0.27, 3.74]
Benoni 2000 3 20 3 20 0.2% 1.00 [0.23, 4.37]
Benoni 2001 1 18 1 20 0.1% 1.11 [0.07, 16.49]
Bidolegui 2014 0 25 0 25 Not estimable
Chareancholvanich 2012 0 120 0 120 Not estimable
Charoencholvanich 2011 0 50 0 50 Not estimable
Chen 2016 0 60 0 60 Not estimable
Chen 2019 14 88 12 88 1.0% 1.17 [0.57, 2.38]
Chin 2020 1 42 1 39 0.1% 0.93 [0.06, 14.34]
Claeys 2007 0 20 0 20 Not estimable
Clave 2019 1 154 0 75 0.1% 1.47 [0.06, 35.69]
Colomina 2016 2 44 1 51 0.1% 2.32 [0.22, 24.71]
Cvetanovich 2018 0 52 1 56 0.1% 0.36 [0.01, 8.61]
Ekback 2000 1 20 1 20 0.1% 1.00 [0.07, 14.90]
Elwatidy 2008 0 32 0 32 Not estimable
Emara 2014 6 20 1 20 0.1% 6.00 [0.79, 45.42]
Engel 2001 0 12 0 12 Not estimable
Ezhevskaya 2018 0 80 0 80 Not estimable
Farrokhi 2011 0 38 0 38 Not estimable
Felli 2019 0 40 0 40 Not estimable
Fraval 2017 0 50 0 51 Not estimable
Garg 2012 0 26 0 26 Not estimable
Garneti 2004 1 25 0 25 0.1% 3.00 [0.13, 70.30]
Goobie 2018 0 56 0 55 Not estimable
Good 2003 2 27 2 24 0.1% 0.89 [0.14, 5.83]
Helito 2019 0 30 1 30 0.1% 0.33 [0.01, 7.87]
Hiippala 1995 1 15 2 13 0.1% 0.43 [0.04, 4.25]
Hiippala 1997 2 39 3 38 0.2% 0.65 [0.11, 3.67]
Hsu 2015 0 30 0 30 Not estimable
Husted 2003 0 20 0 20 Not estimable
Jansen 1999 0 21 1 21 0.1% 0.33 [0.01, 7.74]
Jaszczyk 2015 1 61 0 63 0.1% 3.10 [0.13, 74.58]
Johansson 2005 0 47 0 53 Not estimable
Kakar 2009 0 25 0 25 Not estimable
Karaaslan 2015 0 53 0 52 Not estimable
Kazemi 2010 0 32 1 32 0.1% 0.33 [0.01, 7.89]
Keyhani 2016 0 40 0 40 Not estimable
Kim 2014 0 90 0 90 Not estimable
Kim 2017 0 48 2 24 0.1% 0.10 [0.01, 2.05]
Kimura 2019 0 128 0 128 Not estimable
Kundu 2015 3 30 2 30 0.2% 1.50 [0.27, 8.34]
Lack 2017 1 42 0 46 0.1% 3.28 [0.14, 78.36]
Lee 2012 3 36 4 36 0.3% 0.75 [0.18, 3.11]
Lee 2013 0 34 0 34 Not estimable
Lei 2020 0 150 0 50 Not estimable
Lemay 2004 0 20 0 19 Not estimable
Lin 2012 1 101 0 50 0.1% 1.50 [0.06, 36.18]
Liu 2018 23 150 15 74 1.5% 0.76 [0.42, 1.36]
Liu 2020 0 37 0 35 Not estimable
Luo 2019 1 44 4 46 0.1% 0.26 [0.03, 2.25]
Ma 2019 1 62 0 62 0.1% 3.00 [0.12, 72.25]
MacGillivray 2011 2 40 0 20 0.1% 2.56 [0.13, 50.95]
Mahmood 2017 0 100 0 73 Not estimable
Maniar 2012 0 160 0 40 Not estimable
Molloy 2005 0 50 0 50 Not estimable
Motififard 2015 0 45 0 45 Not estimable
Mu 2019 0 45 0 42 Not estimable
Na 2016 0 29 0 26 Not estimable
Nagabhushan 2018 0 25 0 25 Not estimable
Neilipovitz 2001 0 22 0 18 Not estimable
Niskanen 2005 0 19 0 20 Not estimable
Nugent 2019 0 18 0 23 Not estimable
0.01 0.1 1 10 100
Favours [experimental] Favours [control]

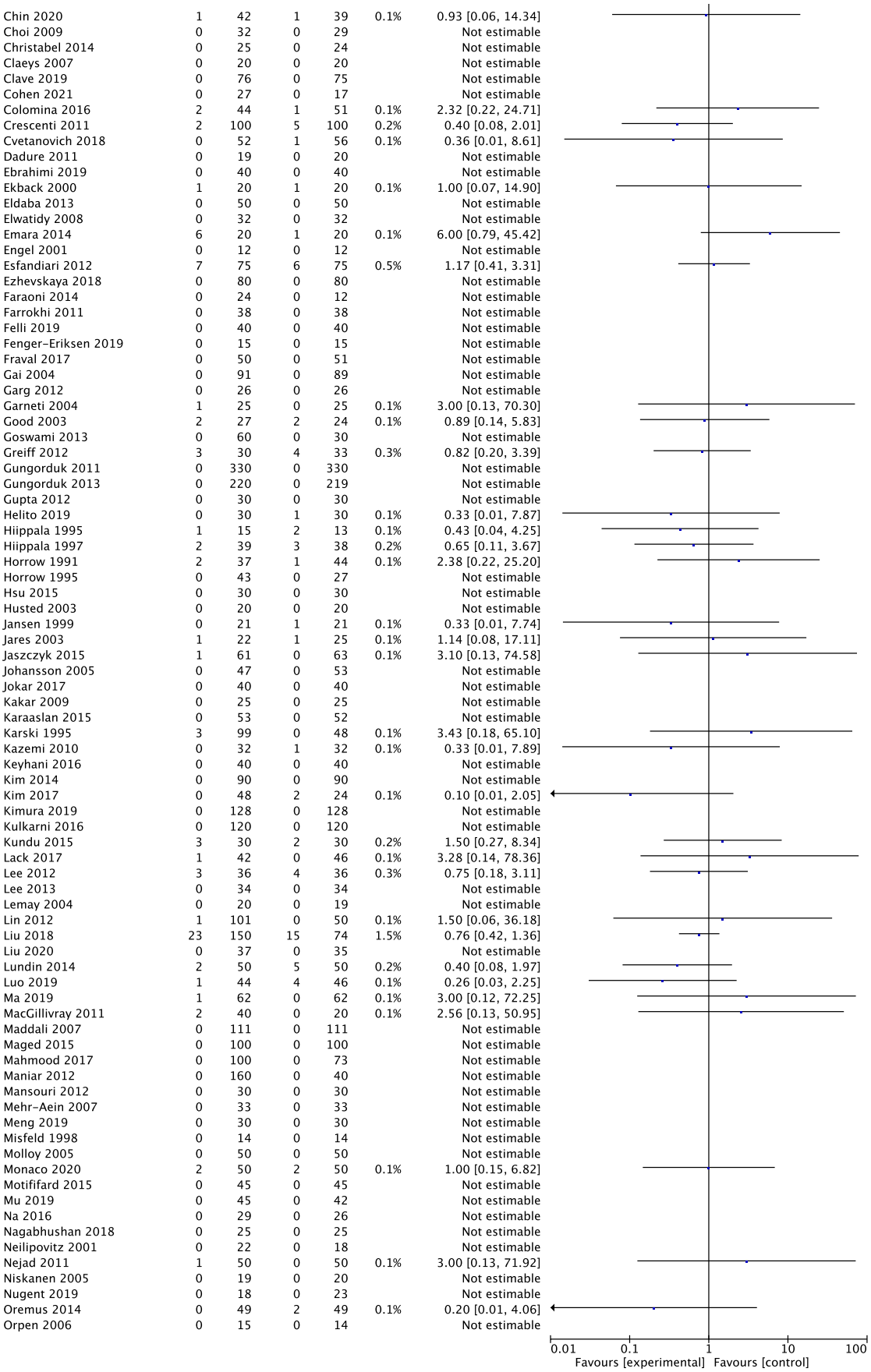

Oremus 2014 0 49 2 49 0.1% 0.20 [0.01, 4.06]
Orpen 2006 0 15 0 14 Not estimable
Painter 2018 2 71 4 69 0.2% 0.49 [0.09, 2.57]
Palija 2020 0 40 0 40 Not estimable
Peters 2015 1 19 0 13 0.1% 2.10 [0.09, 47.89]
Prakash 2017 0 50 1 50 0.1% 0.33 [0.01, 7.99]
Raksakietisak 2015 0 39 0 39 Not estimable
Sankar 2012 0 25 0 25 Not estimable
Seddighi 2019 0 20 0 20 Not estimable
Seo 2013 0 50 2 50 0.1% 0.20 [0.01, 4.06]
Seol 2016 0 50 0 50 Not estimable
Seviciu 2016 0 29 0 32 Not estimable
Shen 2015 4 46 4 46 0.3% 1.00 [0.27, 3.76]
Shi 2017 0 50 0 46 Not estimable
Spitler 2019 2 47 1 46 0.1% 1.96 [0.18, 20.85]
Stowers 2017 1 51 0 23 0.1% 1.38 [0.06, 32.76]
Sun 2017 4 135 0 45 0.1% 3.04 [0.17, 55.47]
Tengberg 2016 0 35 2 40 0.1% 0.23 [0.01, 4.59]
Thipparampall 2020 0 39 0 20 Not estimable
Tian 2018 0 50 0 50 Not estimable
Tsutsumimoto 2011 0 35 2 40 0.1% 0.23 [0.01, 4.59]
Vara 2017 3 50 2 50 0.2% 1.50 [0.26, 8.60]
Veien 2002 0 15 0 15 Not estimable
Vela 2012 3 22 3 22 0.2% 1.00 [0.23, 4.42]
Verma 2014 0 36 0 47 Not estimable
Vijay 2013 0 45 0 45 Not estimable
Volquind 2014 0 32 0 30 Not estimable
Wang 2013 0 30 0 30 Not estimable
Wang 2016 1 81 0 38 0.1% 1.43 [0.06, 34.24]
Wang 2018 15 39 16 41 1.7% 0.99 [0.57, 1.71]
Wang, J 2016 10 100 10 98 0.8% 0.98 [0.43, 2.25]
Watts 2017 5 69 6 69 0.4% 0.83 [0.27, 2.60]
Wong 2008 1 73 1 73 0.1% 1.00 [0.06, 15.69]
Xie 2015 2 45 1 45 0.1% 2.00 [0.19, 21.28]
Xu 2012 0 20 0 20 Not estimable
Xu 2019 1 68 0 67 0.1% 2.96 [0.12, 71.31]
Yamasaki 2004 0 20 0 20 Not estimable
Yamasaki 2005 0 21 0 21 Not estimable
Ye 2019 20 160 2 40 0.3% 2.50 [0.61, 10.26]
Yen 2017 0 33 0 32 Not estimable
Yi 2016 2 50 1 50 0.1% 2.00 [0.19, 21.36]
Yuan 2017 2 140 1 140 0.1% 2.00 [0.18, 21.81]
Zekcer 2016 0 30 4 30 0.1% 0.11 [0.01, 1.98]
Zhang 2016 1 25 2 25 0.1% 0.50 [0.05, 5.17]
Zhang 2020 3 61 1 61 0.1% 3.00 [0.32, 28.04]
Zhang 2021 6 106 2 59 0.2% 1.67 [0.35, 8.01]
Zhang S 2020 0 32 2 32 0.1% 0.20 [0.01, 4.01]
Zhao 2018 0 40 0 40 Not estimable
Zhou 2018 0 58 0 58 Not estimable
Zhou 2019 3 50 7 50 0.3% 0.43 [0.12, 1.56]
Zhu 2020 11 100 4 50 0.4% 1.38 [0.46, 4.10]
Zohar 2004 0 40 0 20 Not estimable
Zufferey 2010 8 57 3 53 0.3% 2.48 [0.69, 8.86]
Subtotal (95% CI) 6123 5191 12.3% 0.98 [0.80, 1.21]
Total events 192 154
Heterogeneity: Tau² = 0.00; Chi² = 33.74, df = 61 (P = 1.00); I² = 0%
Test for overall effect: Z = 0.16 (P = 0.87)
1.1.5 Intracranial haemorrhage
Chandra 1978 0 20 0 19 Not estimable
Fodstad 1981 16 30 6 29 0.8% 2.58 [1.17, 5.66]
Hillman 2002 45 254 33 251 3.1% 1.35 [0.89, 2.04]
Kaste 1979 0 32 0 32 Not estimable
Ross 2000 83 229 84 233 9.0% 1.01 [0.79, 1.28]
Sprigg 2014 1 16 0 8 0.1% 1.59 [0.07, 35.15]
Sprigg 2018 66 1161 54 1164 4.3% 1.23 [0.86, 1.74]
Tsementzis 1990 24 50 13 50 1.7% 1.85 [1.07, 3.20]
Vermeulen 1984 79 241 54 238 6.0% 1.44 [1.07, 1.94]
Subtotal (95% CI) 2033 2024 25.0% 1.33 [1.09, 1.63]
Total events 314 244
Heterogeneity: Tau² = 0.02; Chi² = 9.35, df = 6 (P = 0.15); I² = 36%
Test for overall effect: Z = 2.80 (P = 0.005)
1.1.6 Gastrointestinal haemorrhage
Engqvist 1979 4 76 2 73 0.2% 1.92 [0.36, 10.17]
Roberts 2020 86 5994 72 6015 5.4% 1.20 [0.88, 1.64]
von Holstein 1987 1 72 2 82 0.1% 0.57 [0.05, 6.15]
Subtotal (95% CI) 6142 6170 5.7% 1.20 [0.89, 1.63]
Total events 91 76
Heterogeneity: Tau² = 0.00; Chi² = 0.68, df = 2 (P = 0.71); I² = 0%
Test for overall effect: Z = 1.19 (P = 0.23)
0.01 0.1 1 10 100
Favours [experimental] Favours [control]



1.1.7 Others						
Alimian 2011	0	42	0	42		Not estimable
Apipan 2018	0	60	0	20		Not estimable
Auvinen 1987	0	39	0	37		Not estimable
Avvisati 1989	0	6	0	6		Not estimable
Boylan 1996	0	25	0	20		Not estimable
Cansancao 2018	0	10	0	10		Not estimable
Choi 2009	0	32	0	29		Not estimable
Christabel 2014	0	25	0	24		Not estimable
Cohen 2021	0	27	0	17		Not estimable
Crescenti 2011	2	100	5	100	0.2%	0.40 [0.08, 2.01]
Dadure 2011	0	19	0	20		Not estimable
Eldaba 2013	0	50	0	50		Not estimable
Fenger-Eriksen 2019	0	15	0	15		Not estimable
Goobie 2011	0	23	0	20		Not estimable
Kulkarni 2016	0	120	0	120		Not estimable
Meng 2019	0	30	0	30		Not estimable
Prasad 2018	0	40	0	20		Not estimable
Ramezani 2005	0	32	0	30		Not estimable
Vel 2015	0	50	0	50		Not estimable
Wu 2006	0	108	0	106		Not estimable
Zaman 2019	0	88	0	88		Not estimable
Subtotal (95% CI)		**941**		**854**	**0.2%**	**0.40 [0.08, 2.01]**
Total events	2		5			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.11 (P = 0.27)						
Total (95% CI)		**52103**		**50211**	**100.0%**	**1.00 [0.93, 1.08]**
Total events	1342		1278			
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 81.71$, df = 106 (P = 0.96); $I^2 = 0\%$						
Test for overall effect: Z = 0.11 (P = 0.91)						
Test for subgroup differences: $Chi^2 = 13.60$, df = 6 (P = 0.03), $I^2 = 55.9\%$						

Figure S6. Forest plot of the thrombotic events: subgroup analysis by TXA (tranexamic acid) dose.




Chin 2020 1 42 1 39 0.1% 0.93 [0.06, 14.34]
Choi 2009 0 32 0 29 Not estimable
Christabel 2014 0 25 0 24 Not estimable
Claeys 2007 0 20 0 20 Not estimable
Clave 2019 0 76 0 75 Not estimable
Cohen 2021 0 27 0 17 Not estimable
Colomina 2016 2 44 1 51 0.1% 2.32 [0.22, 24.71]
Crescenti 2011 2 100 5 100 0.2% 0.40 [0.08, 2.01]
Cvetanovich 2018 0 52 1 56 0.1% 0.36 [0.01, 8.61]
Dadure 2011 0 19 0 20 Not estimable
Ebrahimi 2019 0 40 0 40 Not estimable
Ekback 2000 1 20 1 20 0.1% 1.00 [0.07, 14.90]
Eldaba 2013 0 50 0 50 Not estimable
Elwatidy 2008 0 32 0 32 Not estimable
Emara 2014 6 20 1 20 0.1% 6.00 [0.79, 45.42]
Engel 2001 0 12 0 12 Not estimable
Esfandiari 2012 7 75 6 75 0.5% 1.17 [0.41, 3.31]
Ezhevskaya 2018 0 80 0 80 Not estimable
Faraoni 2014 0 24 0 12 Not estimable
Farrokhi 2011 0 38 0 38 Not estimable
Felli 2019 0 40 0 40 Not estimable
Fenger-Eriksen 2019 0 15 0 15 Not estimable
Fraval 2017 0 50 0 51 Not estimable
Gai 2004 0 91 0 89 Not estimable
Garg 2012 0 26 0 26 Not estimable
Garneti 2004 1 25 0 25 0.1% 3.00 [0.13, 70.30]
Good 2003 2 27 2 24 0.1% 0.89 [0.14, 5.83]
Goswami 2013 0 60 0 30 Not estimable
Greiff 2012 3 30 4 33 0.3% 0.82 [0.20, 3.39]
Gungorduk 2011 0 330 0 330 Not estimable
Gungorduk 2013 0 220 0 219 Not estimable
Gupta 2012 0 30 0 30 Not estimable
Helito 2019 0 30 1 30 0.1% 0.33 [0.01, 7.87]
Hiippala 1995 1 15 2 13 0.1% 0.43 [0.04, 4.25]
Hiippala 1997 2 39 3 38 0.2% 0.65 [0.11, 3.67]
Horrow 1991 2 37 1 44 0.1% 2.38 [0.22, 25.20]
Horrow 1995 0 43 0 27 Not estimable
Hsu 2015 0 30 0 30 Not estimable
Husted 2003 0 20 0 20 Not estimable
Jansen 1999 0 21 1 21 0.1% 0.33 [0.01, 7.74]
Jares 2003 1 22 1 25 0.1% 1.14 [0.08, 17.11]
Jaszczyk 2015 1 61 0 63 0.1% 3.10 [0.13, 74.58]
Johansson 2005 0 47 0 53 Not estimable
Jokar 2017 0 40 0 40 Not estimable
Kakar 2009 0 25 0 25 Not estimable
Karaaslan 2015 0 53 0 52 Not estimable
Karski 1995 3 99 0 48 0.1% 3.43 [0.18, 65.10]
Kazemi 2010 0 32 1 32 0.1% 0.33 [0.01, 7.89]
Keyhani 2016 0 40 0 40 Not estimable
Kim 2014 0 90 0 90 Not estimable
Kim 2017 0 48 2 24 0.1% 0.10 [0.01, 2.05]
Kimura 2019 0 128 0 128 Not estimable
Kulkarni 2016 0 120 0 120 Not estimable
Kundu 2015 3 30 2 30 0.2% 1.50 [0.27, 8.34]
Lack 2017 1 42 0 46 0.1% 3.28 [0.14, 78.36]
Lee 2012 3 36 4 36 0.3% 0.75 [0.18, 3.11]
Lee 2013 0 34 0 34 Not estimable
Lemay 2004 0 20 0 19 Not estimable
Lin 2012 1 101 0 50 0.1% 1.50 [0.06, 36.18]
Liu 2018 23 150 15 74 1.5% 0.76 [0.42, 1.36]
Liu 2020 0 37 0 35 Not estimable
Lundin 2014 2 50 5 50 0.2% 0.40 [0.08, 1.97]
Luo 2019 1 44 4 46 0.1% 0.26 [0.03, 2.25]
Ma 2019 1 62 0 62 0.1% 3.00 [0.12, 72.25]
MacGillivray 2011 2 40 0 20 0.1% 2.56 [0.13, 50.95]
Maddali 2007 0 111 0 111 Not estimable
Maged 2015 0 100 0 100 Not estimable
Mahmood 2017 0 100 0 73 Not estimable
Maniar 2012 0 160 0 40 Not estimable
Mansouri 2012 0 30 0 30 Not estimable
Mehr-Aein 2007 0 33 0 33 Not estimable
Meng 2019 0 30 0 30 Not estimable
Misfeld 1998 0 14 0 14 Not estimable
Molloy 2005 0 50 0 50 Not estimable
Monaco 2020 2 50 2 50 0.1% 1.00 [0.15, 6.82]
Motififard 2015 0 45 0 45 Not estimable
Mu 2019 0 45 0 42 Not estimable
Na 2016 0 29 0 26 Not estimable
Nagabhushan 2018 0 25 0 25 Not estimable
Neilipovitz 2001 0 22 0 18 Not estimable
Nejad 2011 1 50 0 50 0.1% 3.00 [0.13, 71.92]
Niskanen 2005 0 19 0 20 Not estimable
Nugent 2019 0 18 0 23 Not estimable
Oremus 2014 0 49 2 49 0.1% 0.20 [0.01, 4.06]
Orpen 2006 0 15 0 14 Not estimable
0.01
0.1
1
10
100
Favours [experimental]
Favours [control]

Painter 2018	2	71	4	69	0.2%	0.49 [0.09, 2.57]
Palija 2020	0	40	0	40		Not estimable
Peters 2015	1	19	0	13	0.1%	2.10 [0.09, 47.89]
Pleym 2003	0	40	1	40	0.1%	0.33 [0.01, 7.95]
Prakash 2017	0	50	1	50	0.1%	0.33 [0.01, 7.99]
Prasad 2018	0	40	0	20		Not estimable
Raksakietisak 2015	0	39	0	39		Not estimable
Ramezani 2005	0	32	0	30		Not estimable
Ray 2016	0	50	0	50		Not estimable
Roberts 2019	101	6406	102	6331	7.1%	0.98 [0.74, 1.29]
Rowell 2020	44	657	30	309	2.7%	0.69 [0.44, 1.08]
Sahu 2019	0	50	0	50		Not estimable
Sallam 2019	0	43	0	43		Not estimable
Sankar 2012	0	25	0	25		Not estimable
Santos 2006	2	29	2	31	0.1%	1.07 [0.16, 7.10]
Seddighi 2019	0	20	0	20		Not estimable
Sentilhes 2018	1	1945	4	1946	0.1%	0.25 [0.03, 2.24]
Senturk 2013	0	101	0	122		Not estimable
Seo 2013	0	50	2	50	0.1%	0.20 [0.01, 4.06]
Seol 2016	0	50	0	50		Not estimable
Seviciu 2016	0	29	0	32		Not estimable
Shaaban 2016	0	66	0	66		Not estimable
Shahid 2013	0	38	0	36		Not estimable
Shakur 2010	168	10093	201	10114	12.8%	0.84 [0.68, 1.03]
Shakur 2017	30	10051	34	10009	2.2%	0.88 [0.54, 1.43]
Shen 2015	4	46	4	46	0.3%	1.00 [0.27, 3.76]
Shi 2013	5	274	7	278	0.4%	0.72 [0.23, 2.26]
Shi 2017	0	50	0	46		Not estimable
Shi, J 2013	3	58	3	59	0.2%	1.02 [0.21, 4.83]
Shore-Lesserson 1996	5	17	3	13	0.3%	1.27 [0.37, 4.39]
Spitler 2019	2	47	1	46	0.1%	1.96 [0.18, 20.85]
Sprigg 2014	1	16	0	8	0.1%	1.59 [0.07, 35.15]
Sprigg 2018	66	1161	54	1164	4.3%	1.23 [0.86, 1.74]
Stowers 2017	1	51	0	23	0.1%	1.38 [0.06, 32.76]
Sun 2017	4	135	0	45	0.1%	3.04 [0.17, 55.47]
Taghaddomi 2009	0	50	0	50		Not estimable
Thipparampall 2020	0	39	0	20		Not estimable
Tian 2018	0	50	0	50		Not estimable
Topsoee 2016	0	165	0	167		Not estimable
Tsutsumimoto 2011	0	35	2	40	0.1%	0.23 [0.01, 4.59]
Vanek 2005	0	39	0	20		Not estimable
Vara 2017	3	50	2	50	0.2%	1.50 [0.26, 8.60]
Veien 2002	0	15	0	15		Not estimable
Vel 2015	0	50	0	50		Not estimable
Vela 2012	3	22	3	22	0.2%	1.00 [0.23, 4.42]
Verma 2014	0	36	0	47		Not estimable
Vijay 2013	0	45	0	45		Not estimable
Wang 2012	0	116	0	115		Not estimable
Wang 2013	0	30	0	30		Not estimable
Wang 2016	1	81	0	38	0.1%	1.43 [0.06, 34.24]
Wang 2018	15	39	16	41	1.7%	0.99 [0.57, 1.71]
Wang, J 2016	10	100	10	98	0.8%	0.98 [0.43, 2.25]
Watts 2017	5	69	6	69	0.4%	0.83 [0.27, 2.60]
Wei 2006	0	36	0	40		Not estimable
Wong 2008	1	73	1	73	0.1%	1.00 [0.06, 15.69]
Wu 2006	0	108	0	106		Not estimable
Xie 2015	2	45	1	45	0.1%	2.00 [0.19, 21.28]
Xu 2013	2	88	2	86	0.1%	0.98 [0.14, 6.78]
Xu 2019	1	68	0	67	0.1%	2.96 [0.12, 71.31]
Yamasaki 2004	0	20	0	20		Not estimable
Yamasaki 2005	0	21	0	21		Not estimable
Ye 2019	20	160	2	40	0.3%	2.50 [0.61, 10.26]
Yen 2017	0	33	0	32		Not estimable
Yi 2016	2	50	1	50	0.1%	2.00 [0.19, 21.36]
Yutthakasemsunt 2013	0	120	3	118	0.1%	0.14 [0.01, 2.69]
Zabeeda 2002	0	25	0	25		Not estimable
Zaman 2019	0	88	0	88		Not estimable
Zekcer 2016	0	30	4	30	0.1%	0.11 [0.01, 1.98]
Zhang 2016	1	25	2	25	0.1%	0.50 [0.05, 5.17]
Zhang 2020	3	61	1	61	0.1%	3.00 [0.32, 28.04]
Zhang 2021	6	106	2	59	0.2%	1.67 [0.35, 8.01]
Zhang S 2020	0	32	2	32	0.1%	0.20 [0.01, 4.01]
Zhao 2018	0	40	0	40		Not estimable
Zhou 2018	0	58	0	58		Not estimable
Zhou 2019	3	50	7	50	0.3%	0.43 [0.12, 1.56]
Zhu 2020	11	100	4	50	0.4%	1.38 [0.46, 4.10]
Zohar 2004	0	40	0	20		Not estimable
Zufferey 2010	8	57	3	53	0.3%	2.48 [0.69, 8.86]
Subtotal (95% CI)		**41175**		**39489**	**45.8%**	**0.94 [0.84, 1.05]**
Total events	671		638			
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 51.10$, df = 86 (P = 1.00); $I^2 = 0\%$						
Test for overall effect: Z = 1.15 (P = 0.25)						
Total (95% CI)		**52116**		**50345**	**100.0%**	**1.00 [0.93, 1.08]**
Total events	1342		1280			
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 84.32$, df = 107 (P = 0.95); $I^2 = 0\%$						
Test for overall effect: Z = 0.09 (P = 0.93)						
Test for subgroup differences: $Chi^2 = 4.50$, df = 1 (P = 0.03), $I^2 = 77.8\%$						

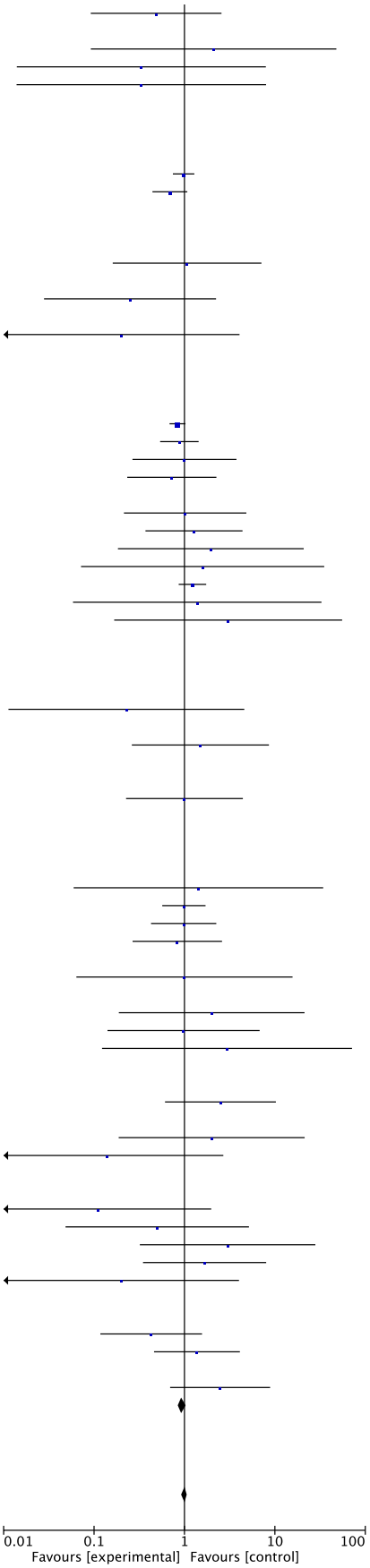


Figure S7. Forest plot of the thrombotic events: subgroup analysis in children.

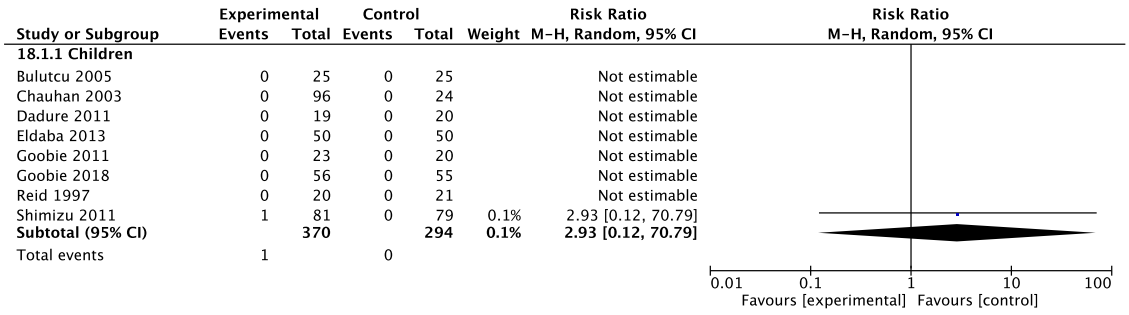
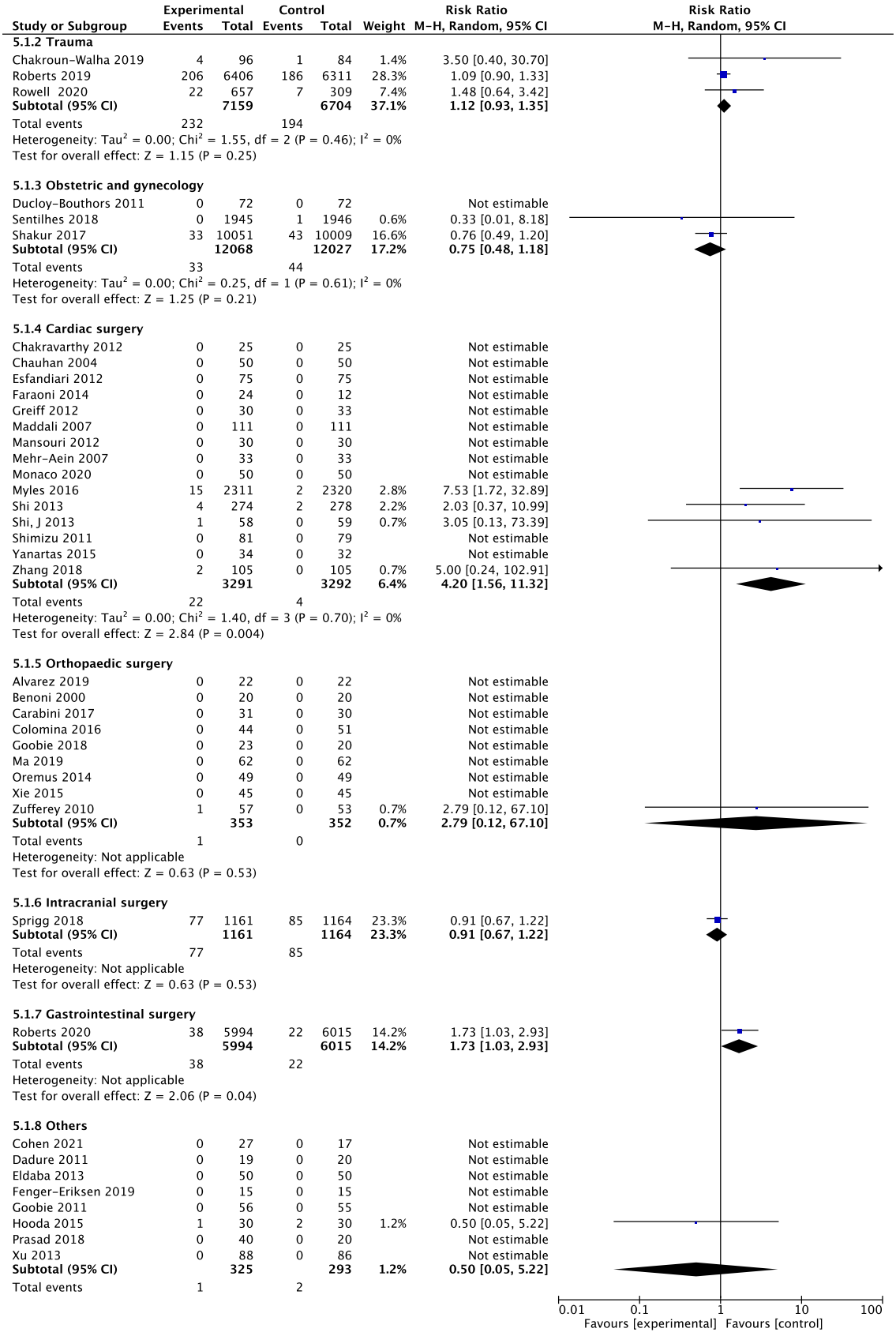


Figure S8. Forest plot of the seizures: subgroup analysis by underlying disease



Heterogeneity: Not applicable
Test for overall effect: Z = 0.58 (P = 0.56)

Total (95% CI)		**30351**	**29847**	**100.0%**	**1.18 [0.91, 1.53]**
Total events	404		351		

Heterogeneity: $Tau^2 = 0.05$; $Chi^2 = 18.31$, df = 12 (P = 0.11); $I^2 = 34\%$
Test for overall effect: Z = 1.24 (P = 0.21)
Test for subgroup differences: $Chi^2 = 15.05$, df = 6 (P = 0.02), $I^2 = 60.1\%$

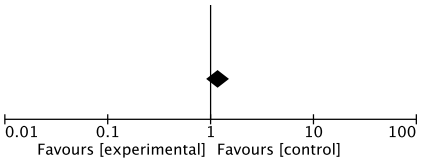


Figure S9. Forest plot of the seizures: subgroup analysis by TXA (tranexamic acid) dose.

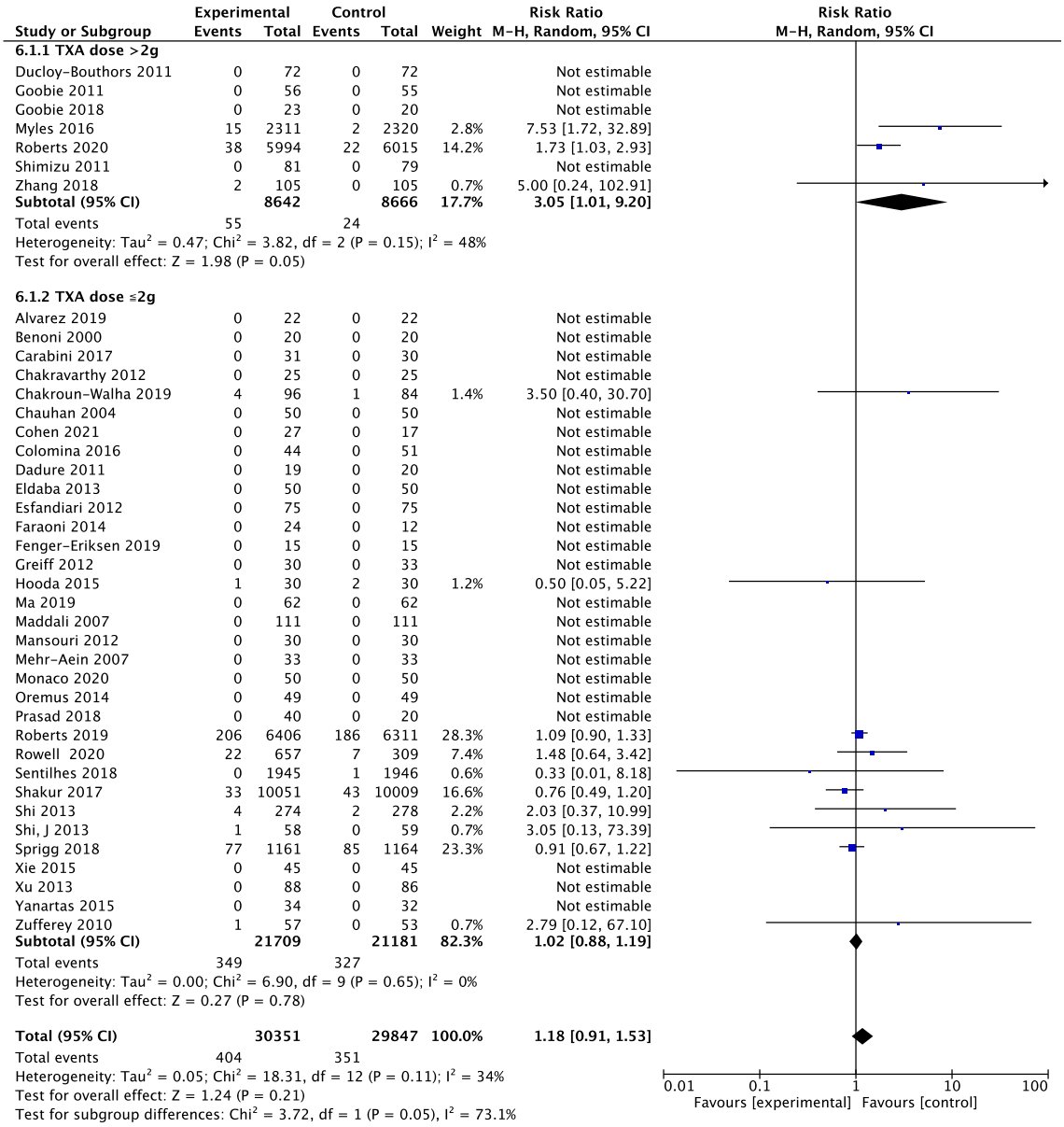


Figure S10. Forest plot of the seizures: subgroup analysis in children.

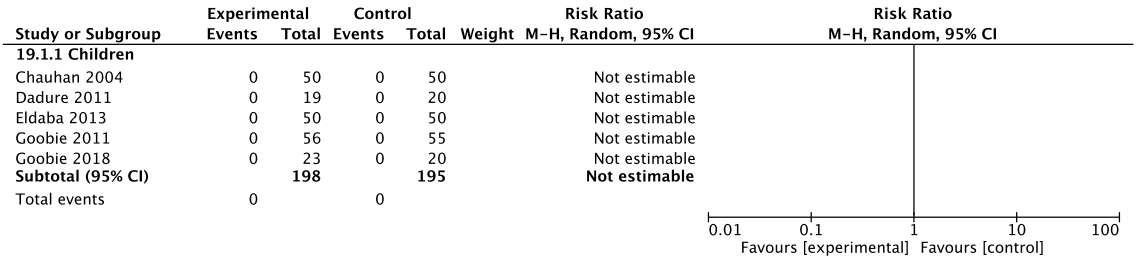
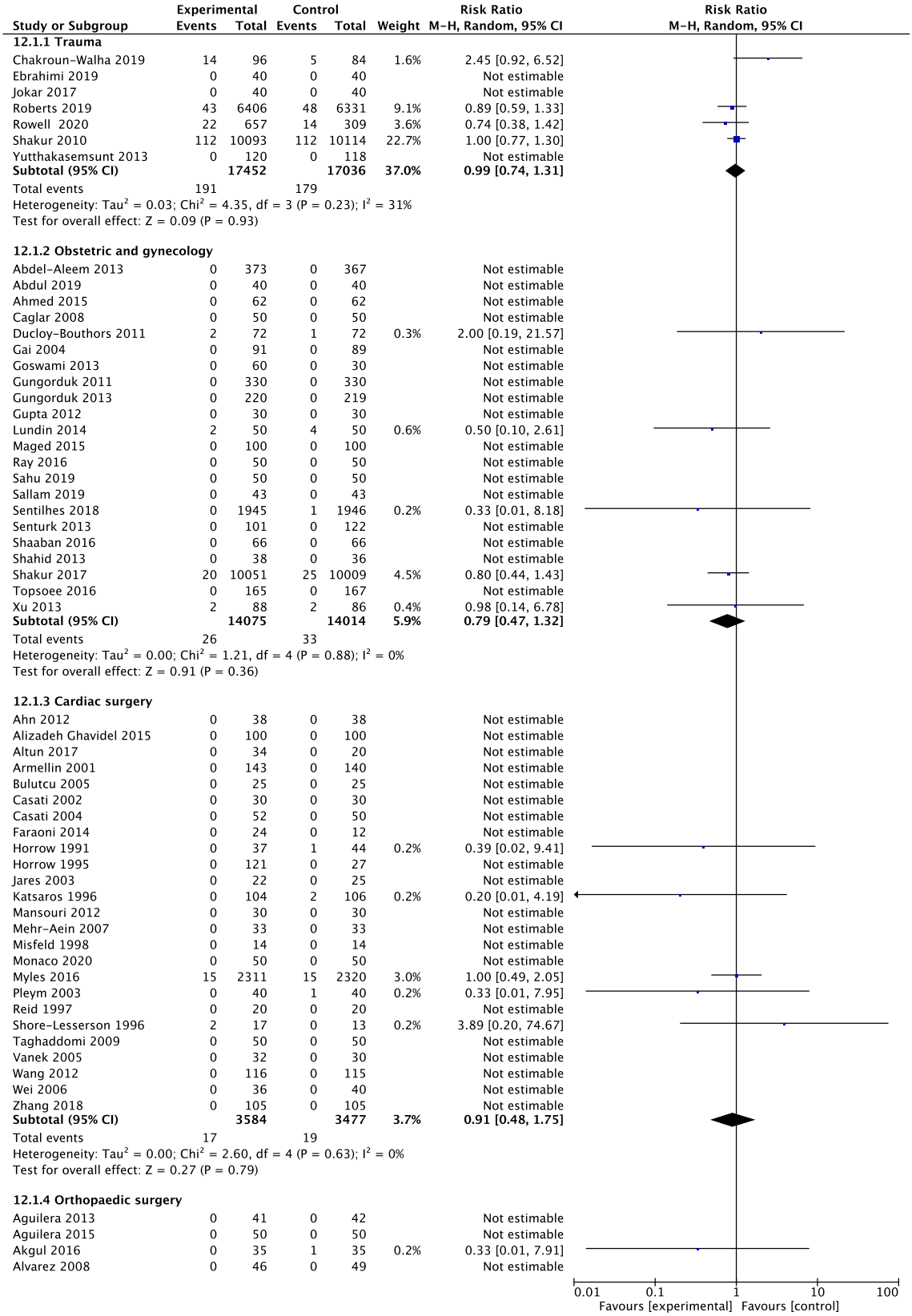
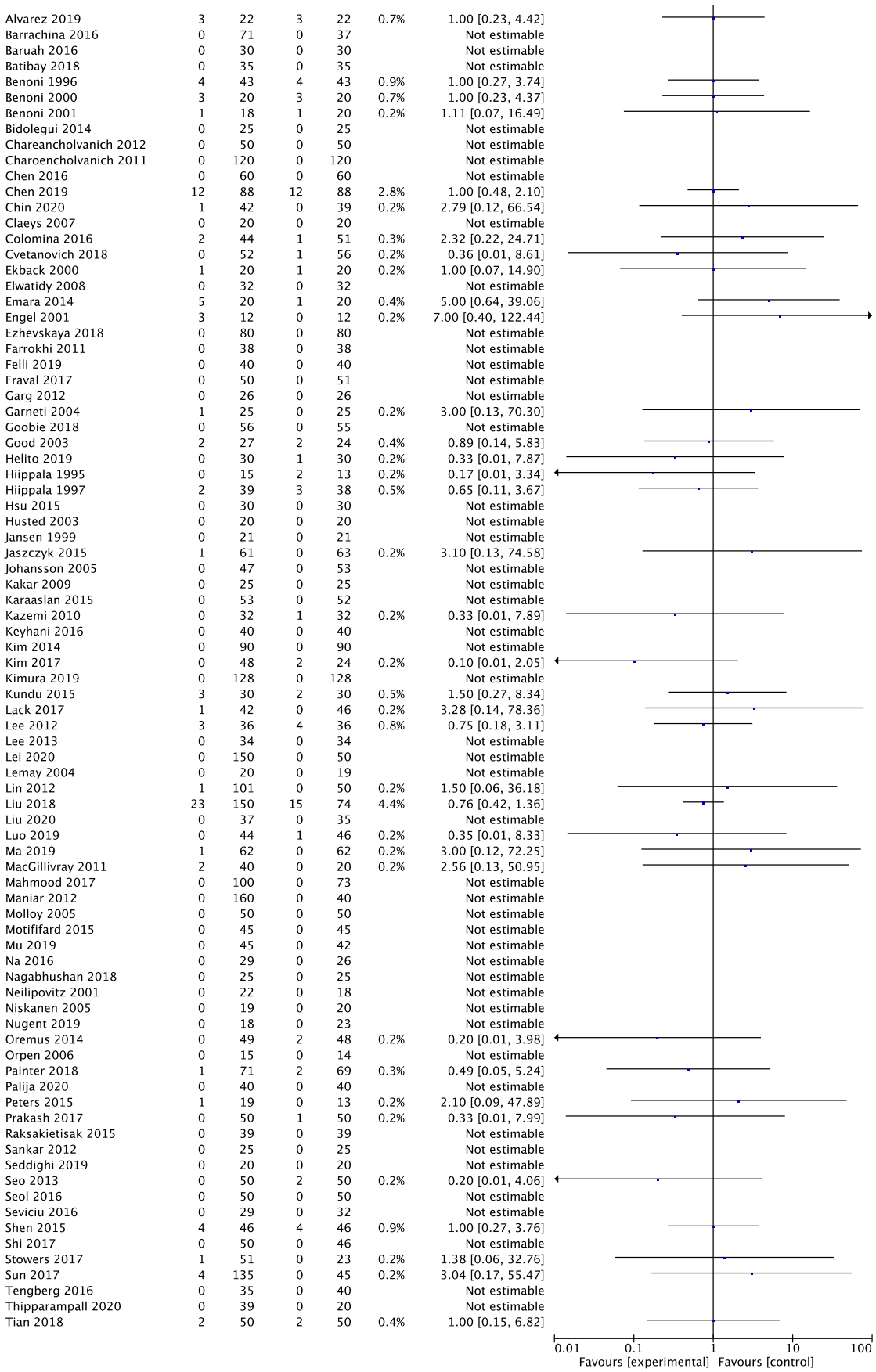
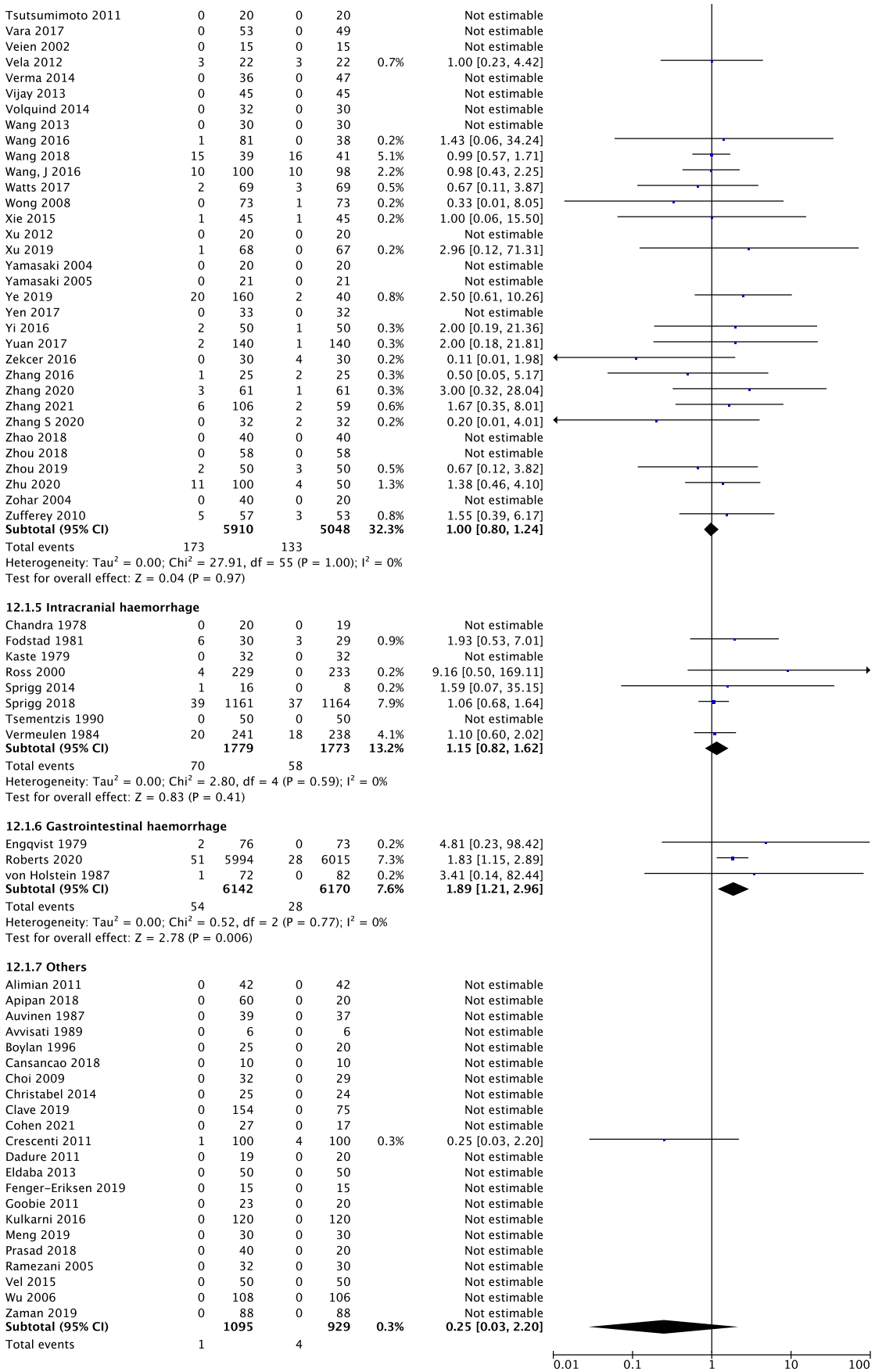


Figure S11. Forest plot of the venous thromboembolism: subgroup analysis by underlying disease.




Alvarez 2019 3 22 3 22 0.7% 1.00 [0.23, 4.42]
Barrachina 2016 0 71 0 37 Not estimable
Baruah 2016 0 30 0 30 Not estimable
Batibay 2018 0 35 0 35 Not estimable
Benoni 1996 4 43 4 43 0.9% 1.00 [0.27, 3.74]
Benoni 2000 3 20 3 20 0.7% 1.00 [0.23, 4.37]
Benoni 2001 1 18 1 20 0.2% 1.11 [0.07, 16.49]
Bidolegui 2014 0 25 0 25 Not estimable
Chareancholvanich 2012 0 50 0 50 Not estimable
Charoencholvanich 2011 0 120 0 120 Not estimable
Chen 2016 0 60 0 60 Not estimable
Chen 2019 12 88 12 88 2.8% 1.00 [0.48, 2.10]
Chin 2020 1 42 0 39 0.2% 2.79 [0.12, 66.54]
Claeys 2007 0 20 0 20 Not estimable
Colomina 2016 2 44 1 51 0.3% 2.32 [0.22, 24.71]
Cvetanovich 2018 0 52 1 56 0.2% 0.36 [0.01, 8.61]
Ekback 2000 1 20 1 20 0.2% 1.00 [0.07, 14.90]
Elwatidy 2008 0 32 0 32 Not estimable
Emara 2014 5 20 1 20 0.4% 5.00 [0.64, 39.06]
Engel 2001 3 12 0 12 0.2% 7.00 [0.40, 122.44]
Ezhevskaya 2018 0 80 0 80 Not estimable
Farrokhi 2011 0 38 0 38 Not estimable
Felli 2019 0 40 0 40 Not estimable
Fraval 2017 0 50 0 51 Not estimable
Garg 2012 0 26 0 26 Not estimable
Garneti 2004 1 25 0 25 0.2% 3.00 [0.13, 70.30]
Goobie 2018 0 56 0 55 Not estimable
Good 2003 2 27 2 24 0.4% 0.89 [0.14, 5.83]
Helito 2019 0 30 1 30 0.2% 0.33 [0.01, 7.87]
Hiippala 1995 0 15 2 13 0.2% 0.17 [0.01, 3.34]
Hiippala 1997 2 39 3 38 0.5% 0.65 [0.11, 3.67]
Hsu 2015 0 30 0 30 Not estimable
Husted 2003 0 20 0 20 Not estimable
Jansen 1999 0 21 0 21 Not estimable
Jaszczyk 2015 1 61 0 63 0.2% 3.10 [0.13, 74.58]
Johansson 2005 0 47 0 53 Not estimable
Kakar 2009 0 25 0 25 Not estimable
Karaaslan 2015 0 53 0 52 Not estimable
Kazemi 2010 0 32 1 32 0.2% 0.33 [0.01, 7.89]
Keyhani 2016 0 40 0 40 Not estimable
Kim 2014 0 90 0 90 Not estimable
Kim 2017 0 48 2 24 0.2% 0.10 [0.01, 2.05]
Kimura 2019 0 128 0 128 Not estimable
Kundu 2015 3 30 2 30 0.5% 1.50 [0.27, 8.34]
Lack 2017 1 42 0 46 0.2% 3.28 [0.14, 78.36]
Lee 2012 3 36 4 36 0.8% 0.75 [0.18, 3.11]
Lee 2013 0 34 0 34 Not estimable
Lei 2020 0 150 0 50 Not estimable
Lemay 2004 0 20 0 19 Not estimable
Lin 2012 1 101 0 50 0.2% 1.50 [0.06, 36.18]
Liu 2018 23 150 15 74 4.4% 0.76 [0.42, 1.36]
Liu 2020 0 37 0 35 Not estimable
Luo 2019 0 44 1 46 0.2% 0.35 [0.01, 8.33]
Ma 2019 1 62 0 62 0.2% 3.00 [0.12, 72.25]
MacGillivray 2011 2 40 0 20 0.2% 2.56 [0.13, 50.95]
Mahmood 2017 0 100 0 73 Not estimable
Maniar 2012 0 160 0 40 Not estimable
Molloy 2005 0 50 0 50 Not estimable
Motififard 2015 0 45 0 45 Not estimable
Mu 2019 0 45 0 42 Not estimable
Na 2016 0 29 0 26 Not estimable
Nagabhushan 2018 0 25 0 25 Not estimable
Neilipovitz 2001 0 22 0 18 Not estimable
Niskanen 2005 0 19 0 20 Not estimable
Nugent 2019 0 18 0 23 Not estimable
Oremus 2014 0 49 2 48 0.2% 0.20 [0.01, 3.98]
Orpen 2006 0 15 0 14 Not estimable
Painter 2018 1 71 2 69 0.3% 0.49 [0.05, 5.24]
Palija 2020 0 40 0 40 Not estimable
Peters 2015 1 19 0 13 0.2% 2.10 [0.09, 47.89]
Prakash 2017 0 50 1 50 0.2% 0.33 [0.01, 7.99]
Raksakietisak 2015 0 39 0 39 Not estimable
Sankar 2012 0 25 0 25 Not estimable
Seddighi 2019 0 20 0 20 Not estimable
Seo 2013 0 50 2 50 0.2% 0.20 [0.01, 4.06]
Seol 2016 0 50 0 50 Not estimable
Seviciu 2016 0 29 0 32 Not estimable
Shen 2015 4 46 4 46 0.9% 1.00 [0.27, 3.76]
Shi 2017 0 50 0 46 Not estimable
Stowers 2017 1 51 0 23 0.2% 1.38 [0.06, 32.76]
Sun 2017 4 135 0 45 0.2% 3.04 [0.17, 55.47]
Tengberg 2016 0 35 0 40 Not estimable
Thipparampall 2020 0 39 0 20 Not estimable
Tian 2018 2 50 2 50 0.4% 1.00 [0.15, 6.82]
0.01
0.1
1
10
100
Favours [experimental]
Favours [control]


Tsutsumimoto 2011 0 20 0 20 Not estimable
Vara 2017 0 53 0 49 Not estimable
Veien 2002 0 15 0 15 Not estimable
Vela 2012 3 22 3 22 0.7% 1.00 [0.23, 4.42]
Verma 2014 0 36 0 47 Not estimable
Vijay 2013 0 45 0 45 Not estimable
Volquind 2014 0 32 0 30 Not estimable
Wang 2013 0 30 0 30 Not estimable
Wang 2016 1 81 0 38 0.2% 1.43 [0.06, 34.24]
Wang 2018 15 39 16 41 5.1% 0.99 [0.57, 1.71]
Wang, J 2016 10 100 10 98 2.2% 0.98 [0.43, 2.25]
Watts 2017 2 69 3 69 0.5% 0.67 [0.11, 3.87]
Wong 2008 0 73 1 73 0.2% 0.33 [0.01, 8.05]
Xie 2015 1 45 1 45 0.2% 1.00 [0.06, 15.50]
Xu 2012 0 20 0 20 Not estimable
Xu 2019 1 68 0 67 0.2% 2.96 [0.12, 71.31]
Yamasaki 2004 0 20 0 20 Not estimable
Yamasaki 2005 0 21 0 21 Not estimable
Ye 2019 20 160 2 40 0.8% 2.50 [0.61, 10.26]
Yen 2017 0 33 0 32 Not estimable
Yi 2016 2 50 1 50 0.3% 2.00 [0.19, 21.36]
Yuan 2017 2 140 1 140 0.3% 2.00 [0.18, 21.81]
Zekcer 2016 0 30 4 30 0.2% 0.11 [0.01, 1.98]
Zhang 2016 1 25 2 25 0.3% 0.50 [0.05, 5.17]
Zhang 2020 3 61 1 61 0.3% 3.00 [0.32, 28.04]
Zhang 2021 6 106 2 59 0.6% 1.67 [0.35, 8.01]
Zhang S 2020 0 32 2 32 0.2% 0.20 [0.01, 4.01]
Zhao 2018 0 40 0 40 Not estimable
Zhou 2018 0 58 0 58 Not estimable
Zhou 2019 2 50 3 50 0.5% 0.67 [0.12, 3.82]
Zhu 2020 11 100 4 50 1.3% 1.38 [0.46, 4.10]
Zohar 2004 0 40 0 20 Not estimable
Zufferey 2010 5 57 3 53 0.8% 1.55 [0.39, 6.17]
Subtotal (95% CI) 5910 5048 32.3% 1.00 [0.80, 1.24]
Total events 173 133
Heterogeneity: Tau² = 0.00; Chi² = 27.91, df = 55 (P = 1.00); I² = 0%
Test for overall effect: Z = 0.04 (P = 0.97)
12.1.5 Intracranial haemorrhage
Chandra 1978 0 20 0 19 Not estimable
Fodstad 1981 6 30 3 29 0.9% 1.93 [0.53, 7.01]
Kaste 1979 0 32 0 32 Not estimable
Ross 2000 4 229 0 233 0.2% 9.16 [0.50, 169.11]
Sprigg 2014 1 16 0 8 0.2% 1.59 [0.07, 35.15]
Sprigg 2018 39 1161 37 1164 7.9% 1.06 [0.68, 1.64]
Tsementzis 1990 0 50 0 50 Not estimable
Vermeulen 1984 20 241 18 238 4.1% 1.10 [0.60, 2.02]
Subtotal (95% CI) 1779 1773 13.2% 1.15 [0.82, 1.62]
Total events 70 58
Heterogeneity: Tau² = 0.00; Chi² = 2.80, df = 4 (P = 0.59); I² = 0%
Test for overall effect: Z = 0.83 (P = 0.41)
12.1.6 Gastrointestinal haemorrhage
Engqvist 1979 2 76 0 73 0.2% 4.81 [0.23, 98.42]
Roberts 2020 51 5994 28 6015 7.3% 1.83 [1.15, 2.89]
von Holstein 1987 1 72 0 82 0.2% 3.41 [0.14, 82.44]
Subtotal (95% CI) 6142 6170 7.6% 1.89 [1.21, 2.96]
Total events 54 28
Heterogeneity: Tau² = 0.00; Chi² = 0.52, df = 2 (P = 0.77); I² = 0%
Test for overall effect: Z = 2.78 (P = 0.006)
12.1.7 Others
Alimian 2011 0 42 0 42 Not estimable
Apipan 2018 0 60 0 20 Not estimable
Auvinen 1987 0 39 0 37 Not estimable
Avvisati 1989 0 6 0 6 Not estimable
Boylan 1996 0 25 0 20 Not estimable
Cansancao 2018 0 10 0 10 Not estimable
Choi 2009 0 32 0 29 Not estimable
Christabel 2014 0 25 0 24 Not estimable
Clave 2019 0 154 0 75 Not estimable
Cohen 2021 0 27 0 17 Not estimable
Crescenti 2011 1 100 4 100 0.3% 0.25 [0.03, 2.20]
Dadure 2011 0 19 0 20 Not estimable
Eldaba 2013 0 50 0 50 Not estimable
Fenger-Eriksen 2019 0 15 0 15 Not estimable
Goobie 2011 0 23 0 20 Not estimable
Kulkarni 2016 0 120 0 120 Not estimable
Meng 2019 0 30 0 30 Not estimable
Prasad 2018 0 40 0 20 Not estimable
Ramezani 2005 0 32 0 30 Not estimable
Vel 2015 0 50 0 50 Not estimable
Wu 2006 0 108 0 106 Not estimable
Zaman 2019 0 88 0 88 Not estimable
Subtotal (95% CI) 1095 929 0.3% 0.25 [0.03, 2.20]
Total events 1 4
0.01 0.1 1 10 100

Heterogeneity: Not applicable
Test for overall effect: Z = 1.25 (P = 0.21)

Total (95% CI)	**50037**	**48447**	**100.0%**	**1.04 [0.92, 1.17]**
Total events	532	454		

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 49.90$, df = 78 (P = 0.99); $I^2 = 0\%$
Test for overall effect: Z = 0.59 (P = 0.56)
Test for subgroup differences: $Chi^2 = 10.33$, df = 6 (P = 0.11), $I^2 = 41.9\%$

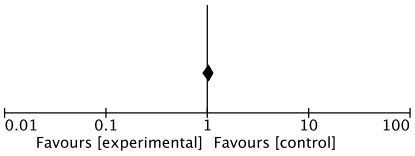
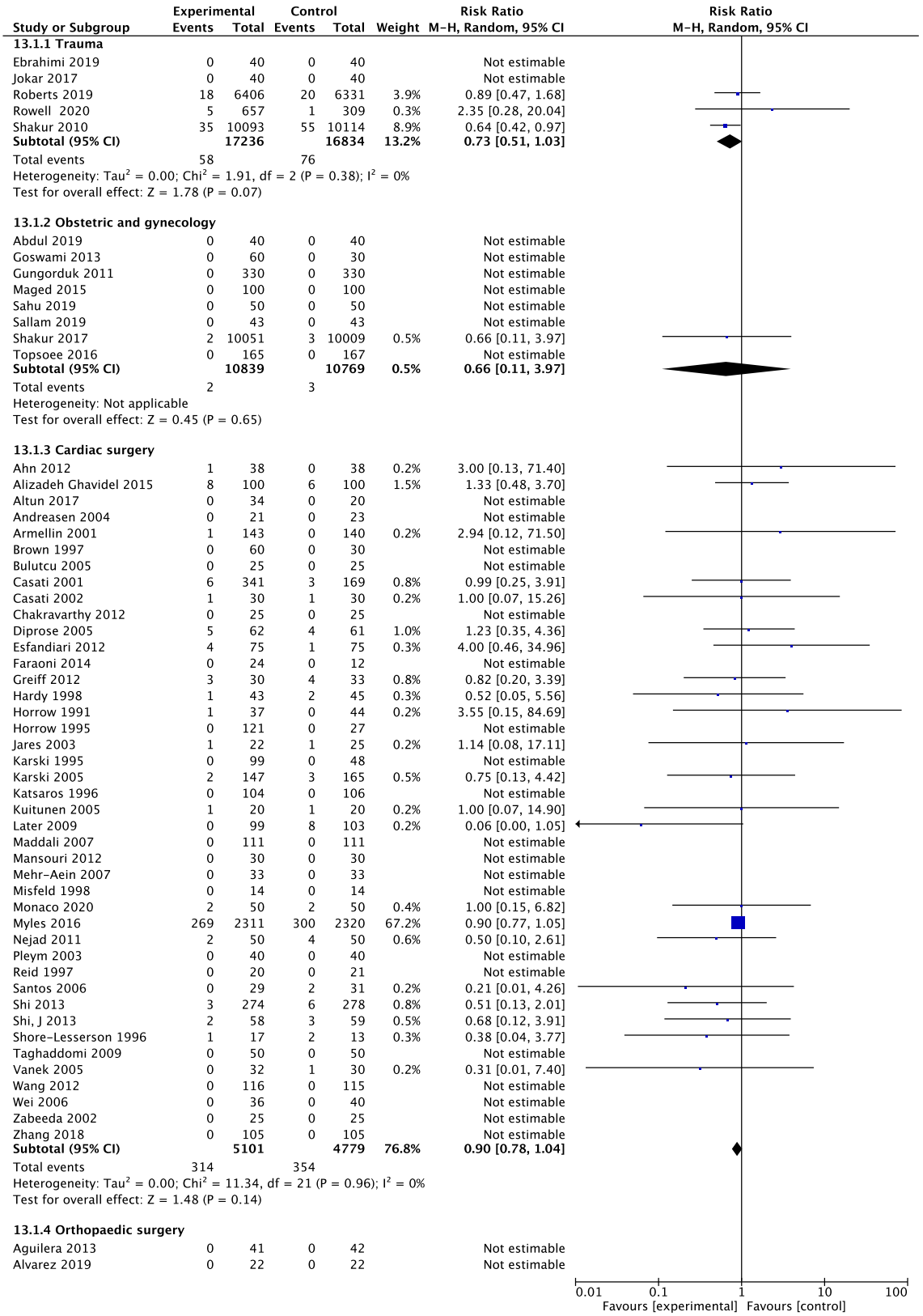


Figure S12. Forest plot of the acute coronary syndrome: subgroup analysis by underlying disease.



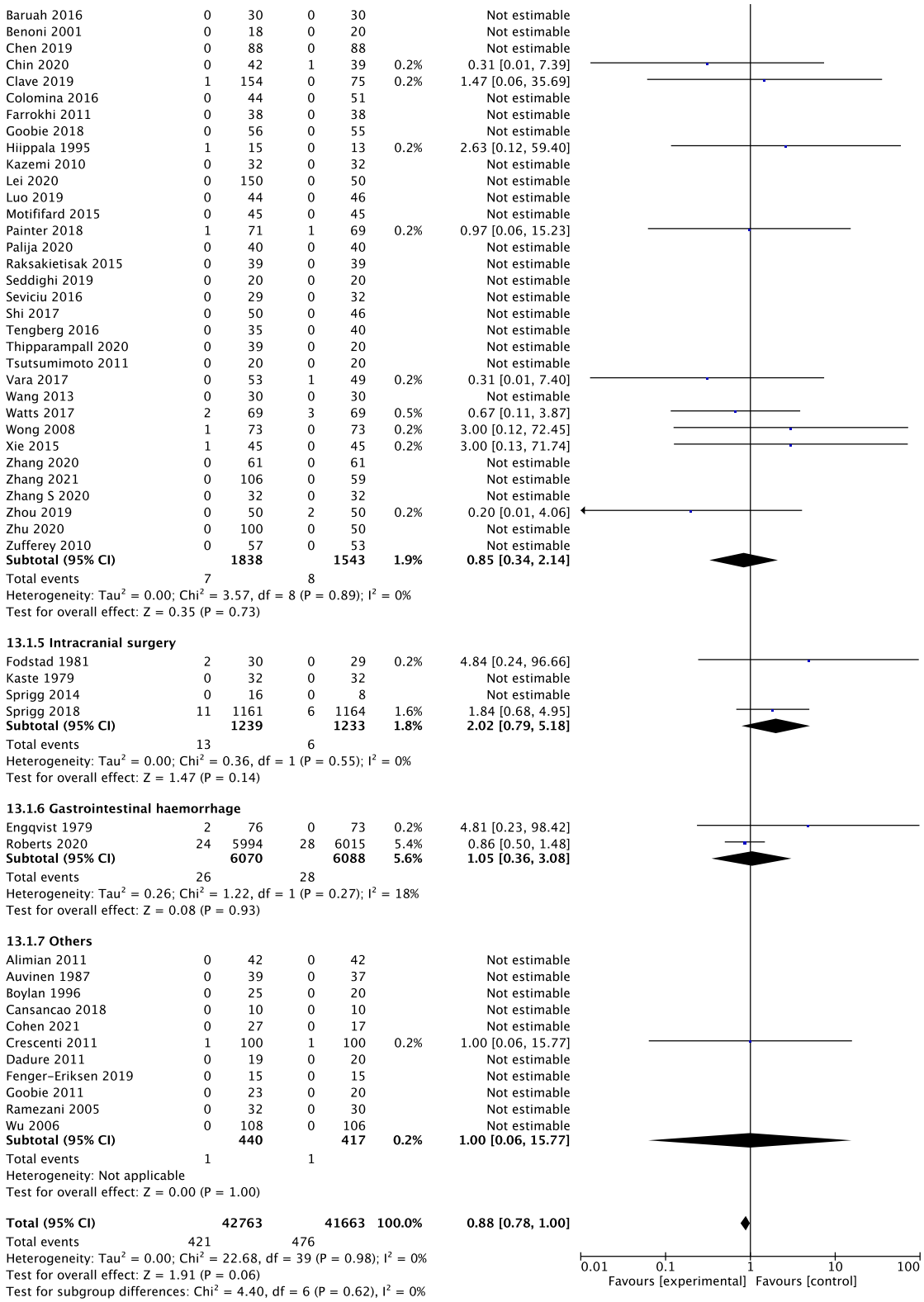
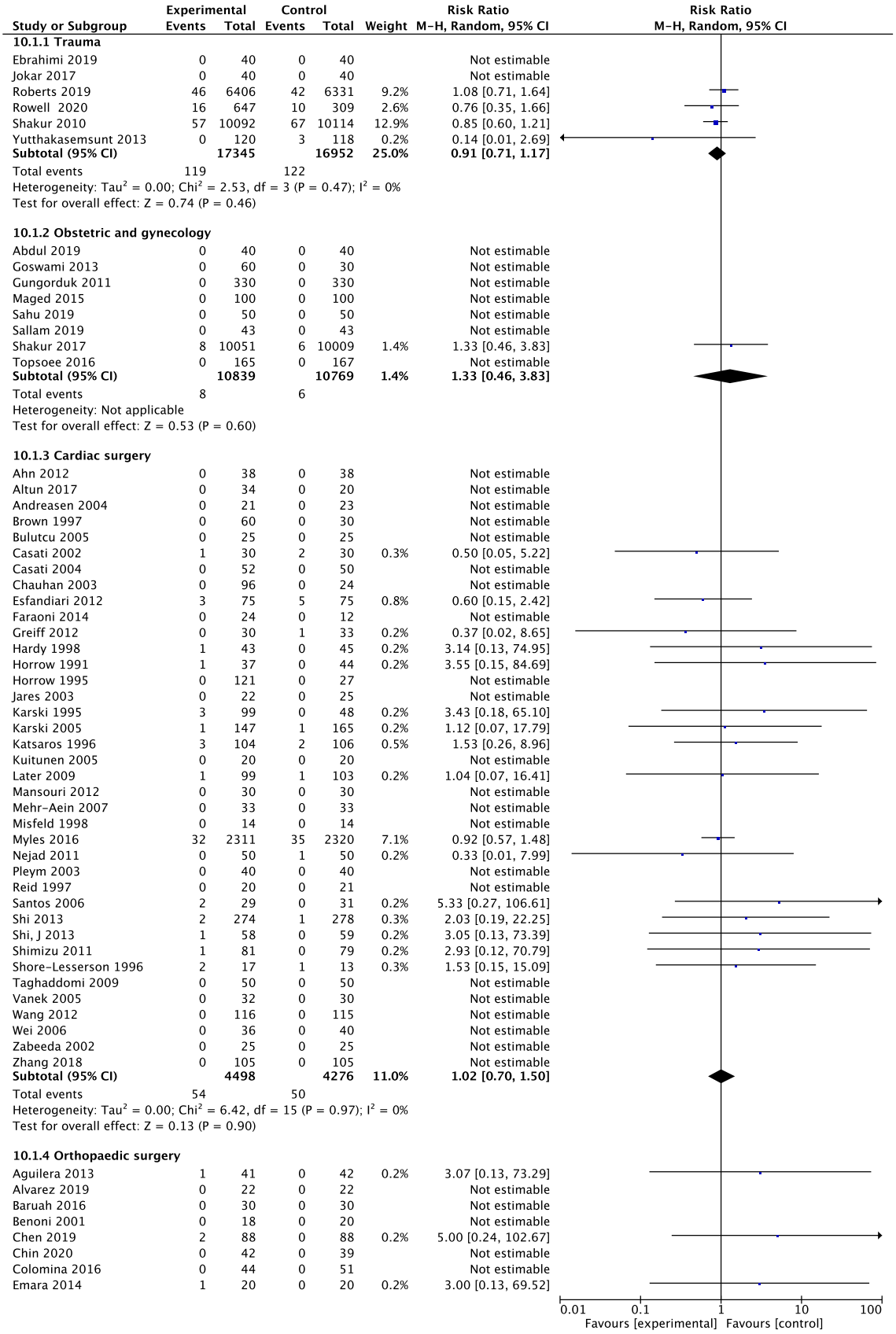
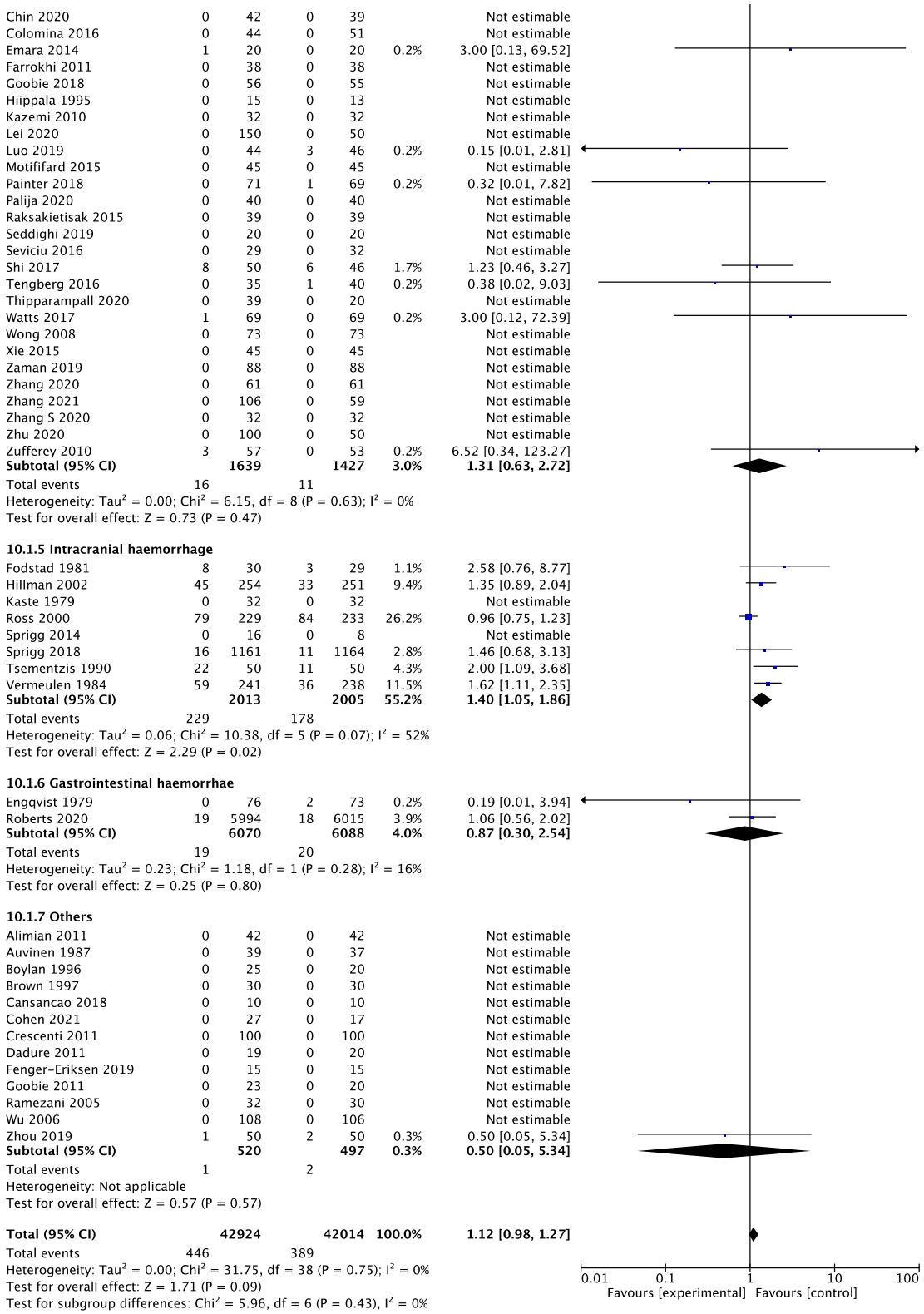

Baruah 2016 0 30 0 30 Not estimable
Benoni 2001 0 18 0 20 Not estimable
Chen 2019 0 88 0 88 Not estimable
Chin 2020 0 42 1 39 0.2% 0.31 [0.01, 7.39]
Clave 2019 1 154 0 75 0.2% 1.47 [0.06, 35.69]
Colomina 2016 0 44 0 51 Not estimable
Farrokhi 2011 0 38 0 38 Not estimable
Goobie 2018 0 56 0 55 Not estimable
Hiippala 1995 1 15 0 13 0.2% 2.63 [0.12, 59.40]
Kazemi 2010 0 32 0 32 Not estimable
Lei 2020 0 150 0 50 Not estimable
Luo 2019 0 44 0 46 Not estimable
Motififard 2015 0 45 0 45 Not estimable
Painter 2018 1 71 1 69 0.2% 0.97 [0.06, 15.23]
Palija 2020 0 40 0 40 Not estimable
Raksakietisak 2015 0 39 0 39 Not estimable
Seddighi 2019 0 20 0 20 Not estimable
Seviciu 2016 0 29 0 32 Not estimable
Shi 2017 0 50 0 46 Not estimable
Tengberg 2016 0 35 0 40 Not estimable
Thipparampall 2020 0 39 0 20 Not estimable
Tsutsumimoto 2011 0 20 0 20 Not estimable
Vara 2017 0 53 1 49 0.2% 0.31 [0.01, 7.40]
Wang 2013 0 30 0 30 Not estimable
Watts 2017 2 69 3 69 0.5% 0.67 [0.11, 3.87]
Wong 2008 1 73 0 73 0.2% 3.00 [0.12, 72.45]
Xie 2015 1 45 0 45 0.2% 3.00 [0.13, 71.74]
Zhang 2020 0 61 0 61 Not estimable
Zhang 2021 0 106 0 59 Not estimable
Zhang S 2020 0 32 0 32 Not estimable
Zhou 2019 0 50 2 50 0.2% 0.20 [0.01, 4.06]
Zhu 2020 0 100 0 50 Not estimable
Zufferey 2010 0 57 0 53 Not estimable
Subtotal (95% CI) 1838 1543 1.9% 0.85 [0.34, 2.14]
Total events 7 8
Heterogeneity: Tau² = 0.00; Chi² = 3.57, df = 8 (P = 0.89); I² = 0%
Test for overall effect: Z = 0.35 (P = 0.73)
13.1.5 Intracranial surgery
Fodstad 1981 2 30 0 29 0.2% 4.84 [0.24, 96.66]
Kaste 1979 0 32 0 32 Not estimable
Sprigg 2014 0 16 0 8 Not estimable
Sprigg 2018 11 1161 6 1164 1.6% 1.84 [0.68, 4.95]
Subtotal (95% CI) 1239 1233 1.8% 2.02 [0.79, 5.18]
Total events 13 6
Heterogeneity: Tau² = 0.00; Chi² = 0.36, df = 1 (P = 0.55); I² = 0%
Test for overall effect: Z = 1.47 (P = 0.14)
13.1.6 Gastrointestinal haemorrhage
Engqvist 1979 2 76 0 73 0.2% 4.81 [0.23, 98.42]
Roberts 2020 24 5994 28 6015 5.4% 0.86 [0.50, 1.48]
Subtotal (95% CI) 6070 6088 5.6% 1.05 [0.36, 3.08]
Total events 26 28
Heterogeneity: Tau² = 0.26; Chi² = 1.22, df = 1 (P = 0.27); I² = 18%
Test for overall effect: Z = 0.08 (P = 0.93)
13.1.7 Others
Alimian 2011 0 42 0 42 Not estimable
Auvinen 1987 0 39 0 37 Not estimable
Boylan 1996 0 25 0 20 Not estimable
Cansancao 2018 0 10 0 10 Not estimable
Cohen 2021 0 27 0 17 Not estimable
Crescenti 2011 1 100 1 100 0.2% 1.00 [0.06, 15.77]
Dadure 2011 0 19 0 20 Not estimable
Fenger-Eriksen 2019 0 15 0 15 Not estimable
Goobie 2011 0 23 0 20 Not estimable
Ramezani 2005 0 32 0 30 Not estimable
Wu 2006 0 108 0 106 Not estimable
Subtotal (95% CI) 440 417 0.2% 1.00 [0.06, 15.77]
Total events 1 1
Heterogeneity: Not applicable
Test for overall effect: Z = 0.00 (P = 1.00)
Total (95% CI) 42763 41663 100.0% 0.88 [0.78, 1.00]
Total events 421 476
Heterogeneity: Tau² = 0.00; Chi² = 22.68, df = 39 (P = 0.98); I² = 0%
Test for overall effect: Z = 1.91 (P = 0.06)
Test for subgroup differences: Chi² = 4.40, df = 6 (P = 0.62), I² = 0%
0.01
0.1
1
10
100
Favours [experimental]
Favours [control]

Figure S13. Forest plot of the stroke: subgroup analysis by underlying disease.




Chin 2020 0 42 0 39 Not estimable
Colomina 2016 0 44 0 51 Not estimable
Emara 2014 1 20 0 20 0.2% 3.00 [0.13, 69.52]
Farrokhi 2011 0 38 0 38 Not estimable
Goobie 2018 0 56 0 55 Not estimable
Hiippala 1995 0 15 0 13 Not estimable
Kazemi 2010 0 32 0 32 Not estimable
Lei 2020 0 150 0 50 Not estimable
Luo 2019 0 44 3 46 0.2% 0.15 [0.01, 2.81]
Motififard 2015 0 45 0 45 Not estimable
Painter 2018 0 71 1 69 0.2% 0.32 [0.01, 7.82]
Palija 2020 0 40 0 40 Not estimable
Raksakietisak 2015 0 39 0 39 Not estimable
Seddighi 2019 0 20 0 20 Not estimable
Seviciu 2016 0 29 0 32 Not estimable
Shi 2017 8 50 6 46 1.7% 1.23 [0.46, 3.27]
Tengberg 2016 0 35 1 40 0.2% 0.38 [0.02, 9.03]
Thipparampall 2020 0 39 0 20 Not estimable
Watts 2017 1 69 0 69 0.2% 3.00 [0.12, 72.39]
Wong 2008 0 73 0 73 Not estimable
Xie 2015 0 45 0 45 Not estimable
Zaman 2019 0 88 0 88 Not estimable
Zhang 2020 0 61 0 61 Not estimable
Zhang 2021 0 106 0 59 Not estimable
Zhang S 2020 0 32 0 32 Not estimable
Zhu 2020 0 100 0 50 Not estimable
Zufferey 2010 3 57 0 53 0.2% 6.52 [0.34, 123.27]
Subtotal (95% CI) 1639 1427 3.0% 1.31 [0.63, 2.72]
Total events 16 11
Heterogeneity: Tau² = 0.00; Chi² = 6.15, df = 8 (P = 0.63); I² = 0%
Test for overall effect: Z = 0.73 (P = 0.47)
10.1.5 Intracranial haemorrhage
Fodstad 1981 8 30 3 29 1.1% 2.58 [0.76, 8.77]
Hillman 2002 45 254 33 251 9.4% 1.35 [0.89, 2.04]
Kaste 1979 0 32 0 32 Not estimable
Ross 2000 79 229 84 233 26.2% 0.96 [0.75, 1.23]
Sprigg 2014 0 16 0 8 Not estimable
Sprigg 2018 16 1161 11 1164 2.8% 1.46 [0.68, 3.13]
Tsementzis 1990 22 50 11 50 4.3% 2.00 [1.09, 3.68]
Vermeulen 1984 59 241 36 238 11.5% 1.62 [1.11, 2.35]
Subtotal (95% CI) 2013 2005 55.2% 1.40 [1.05, 1.86]
Total events 229 178
Heterogeneity: Tau² = 0.06; Chi² = 10.38, df = 5 (P = 0.07); I² = 52%
Test for overall effect: Z = 2.29 (P = 0.02)
10.1.6 Gastrointestinal haemorrhae
Engqvist 1979 0 76 2 73 0.2% 0.19 [0.01, 3.94]
Roberts 2020 19 5994 18 6015 3.9% 1.06 [0.56, 2.02]
Subtotal (95% CI) 6070 6088 4.0% 0.87 [0.30, 2.54]
Total events 19 20
Heterogeneity: Tau² = 0.23; Chi² = 1.18, df = 1 (P = 0.28); I² = 16%
Test for overall effect: Z = 0.25 (P = 0.80)
10.1.7 Others
Alimian 2011 0 42 0 42 Not estimable
Auvinen 1987 0 39 0 37 Not estimable
Boylan 1996 0 25 0 20 Not estimable
Brown 1997 0 30 0 30 Not estimable
Cansancao 2018 0 10 0 10 Not estimable
Cohen 2021 0 27 0 17 Not estimable
Crescenti 2011 0 100 0 100 Not estimable
Dadure 2011 0 19 0 20 Not estimable
Fenger-Eriksen 2019 0 15 0 15 Not estimable
Goobie 2011 0 23 0 20 Not estimable
Ramezani 2005 0 32 0 30 Not estimable
Wu 2006 0 108 0 106 Not estimable
Zhou 2019 1 50 2 50 0.3% 0.50 [0.05, 5.34]
Subtotal (95% CI) 520 497 0.3% 0.50 [0.05, 5.34]
Total events 1 2
Heterogeneity: Not applicable
Test for overall effect: Z = 0.57 (P = 0.57)
Total (95% CI) 42924 42014 100.0% 1.12 [0.98, 1.27]
Total events 446 389
Heterogeneity: Tau² = 0.00; Chi² = 31.75, df = 38 (P = 0.75); I² = 0%
Test for overall effect: Z = 1.71 (P = 0.09)
Test for subgroup differences: Chi² = 5.96, df = 6 (P = 0.43), I² = 0%
0.01
0.1
1
10
100
Favours [experimental]
Favours [control]