

## Appendix B: Non-inferiority trials

Author	Year	Country	Specialty	Pediatric patients included	Mortality as single or composite outcome	Industry funding	Conclusion	Estimated risk of event in control (%)	Observed event in control (%)	Absolute non-inferiority margin (% difference)	Relative non-inferiority margin
African Neonatal Sepsis Trial (AFRINEST) group	2015	international	infectious diseases	yes	composite	no	non-inferior	10	8	5	1.5
Ahn et al.	2013	Korea	oncology	no	single	not explicit/unclear	non-inferior	41.2	23	13	1.32
Aliberti et al.	2017	Italy	infectious diseases	no	composite	no	stopped early	10	7.4	5	1.5
Baqui et al.	2015	Bangladesh	infectious diseases	yes	composite	no	non-inferior	10	10	5	1.5
Bertrand et al.	2006	Canada	thrombosis	no	composite	yes	non-inferior	23	18.2	8	1.35
Beyer-Westendorf et al.	2017	Germany	thrombosis	no	composite	yes	non-inferior	3	1.7	4.5	2.5
Borchmann et al.	2017	international	oncology	no	composite	yes	non-inferior	12	8.8	6	1.5
Brack et al.	2012	international	infectious diseases	yes	composite	yes	not non-inferior	1	2.9	3.5	4.5
Budde et al.	2014	international	transplant	no	composite	yes	non-inferior	15	19.6	10	1.67
The Matisse Investigators	2003	international	thrombosis	no	composite	yes	non-inferior	5	5	3.5	1.7
Bunnapradist et al.	2013	international	transplant	no	composite	yes	non-inferior	6	2.5	9	2.5
Cai et al.	2014	China	transplant	no	composite	yes	non-inferior	20	16.7	20	2
Chastre et al.	2003	France	infectious diseases	no	single	no	non-inferior	40	17.2	10	1.25
Cordonnier et al.	2009	France	infectious diseases	no	single	no	non-inferior	9.2	2.7	8	1.87
de Kraker et al.	2004	international	oncology	yes	composite	no	non-inferior	15	8.6	10	1.67
De Simone et al.	2012	international	transplant	no	composite	yes	non-inferior	24	9.5	12	1.5
Diener et al.	2006	international	thrombosis	no	composite	yes	non-inferior	9.3	8.8	5	1.54
Eckardt et al.	2006	international	oncology	no	single	yes	non-inferior	62	69	10	1.16
Eriksson et al.	2011	international	thrombosis	no	composite	yes	non-inferior	20	8.8	7.7	1.39
Eriksson et al.	2007	international	thrombosis	no	composite	yes	non-inferior	48	37.7	9.2	1.19

Eriksson et al.	2007	international	thrombosis	no	composite	yes	non-inferior	20	6.7	7.7	1.39
Feres et al.	2013	Brazil	thrombosis	no	composite	yes	non-inferior	9	5.8	2.7	1.3
Ferre et al.	2017	international	oncology	yes	composite	no	non-inferior	10	10.1	10	2
Gaston et al.	2009	US	transplant	yes	composite	yes	non-inferior	20	27.9	10	1.5
Giamarellou et al.	2000	Greece	infectious diseases	no	composite	not explicit/unclear	non-inferior	25	49.2	10	1.4
Gilard et al.	2015	international	thrombosis	no	composite	yes	non-inferior	3	1.5	2	1.67
Gulizia et al.	2008	Italy	cardiology	no	composite	not explicit/unclear	non-inferior	38	40	10	1.26
Gwon et al.	2012	Korea	thrombosis	no	composite	yes	non-inferior	10	4.3	4	1.4
Sibbing et al.	2017	international	thrombosis	no	composite	yes	non-inferior	10.5	9	30	3.86
Han et al.	2016	China	thrombosis	no	composite	yes	non-inferior	8.3	5.9	3.7	1.45
Harris et al.	2018	international	infectious diseases	no	single	no	not non-inferior	14	3.7	5	1.36
Hofheinz et al.	2012	Germany	oncology	no	single	yes	non-inferior	42.5	33	12.5	1.29
Huh et al.	2017	Korea	transplant	no	composite	yes	non-inferior	10	13.3	15	2.5
Iversen et al.	2019	Denmark	infectious diseases	no	composite	no	non-inferior	10	12.1	10	2
Jeng et al.	2018	international	transplant	no	composite	yes	non-inferior	20	5.8	12	1.6
Johnson et al.	2016	international	oncology	no	composite	no	not non-inferior	5	14.3	5	2
Jones et al.	2016	Canada	anesthesia	no	composite	no	non-inferior	25	30	10	1.4
Kim et al.	2012	Korea	thrombosis	no	composite	yes	non-inferior	11	4.7	4	1.36
Park et al.	2013	Korea	thrombosis	no	composite	no	non-inferior	3	1.4	0.75	1.25
Hahn et al.	2018	Korea	thrombosis	no	composite	yes	non-inferior	4.5	4.2	2	1.44
Kirchhof et al.	2012	Germany	cardiology	no	composite	yes	not non-inferior	29.8	na	12	1.4
Kirchhof et al.	2018	international	thrombosis	no	composite	no	non-inferior	17	7.3	7.5	1.44
Kutner et al.	2015	US	cardiology	no	single	no	not non-inferior	21	20.3	5	1.24
Le et al.	2017	Vietnam	infectious diseases	no	single	no	non-inferior	15	6.5	10	1.67
Lee et al.	2018	Korea	thrombosis	no	composite	yes	non-inferior	7	0.6	4	1.57
Lee et al.	2009	UK	oncology	not explicit	single	no	non-inferior	80	69	10	1.13

Liu et al.	2013	China	oncology	yes	single	no	stopped early	15	na	15	2
Maertens et al.	2016	international	infectious diseases	no	single	yes	non-inferior	20	20	10	1.5
Mai et al.	2016	international	oncology	no	composite	yes	non-inferior	50	na	15	1.3
Matsumura-Nakano et al.	2019	Japan	thrombosis	no	composite	yes	not non-inferior	8	13.6	4	1.5
Mavroudis et al.	2016	Greece	oncology	no	composite	no	not non-inferior	15	10.5	7	1.47
Mavroudis et al.	2015	Greece	oncology	no	composite	no	not non-inferior	15	4.3	8	1.53
Merle et al.	2014	international	infectious diseases	no	composite	no	not non-inferior	20	17.2	6	1.3
Mesu et al.	2018	international	infectious diseases	yes	composite	no	non-inferior	6	2.4	13	3.17
Meynard et al.	2018	France	infectious diseases	no	composite	yes	not non-inferior	15	29	10	1.67
Mir et al.	2017	Pakistan	infectious diseases	yes	composite	no	non-inferior	10	11.8	5	1.5
Molloy et al.	2018	international	infectious diseases	no	single	no	non-inferior	15	21.4	10	1.67
Nakamura et al.	2017	Japan	thrombosis	no	composite	no	non-inferior	4.5	1.5	2	1.44
Nathan et al.	2005	Niger	infectious diseases	yes	composite	no	non-inferior	15	9	10	1.67
Park et al.	2014	Korea	gastroenterology	no	single	no	not non-inferior	10	na	15	2.5
Paul et al.	2015	Israel	infectious diseases	no	composite	no	not non-inferior	30	27	15	1.5
Ponticelli et al.	2014	Italy	transplant	no	composite	not explicit/unclear	inconclusive	3	2.8	10	4.33
Postma et al.	2015	Netherlands	infectious diseases	no	single	no	non-inferior	5	na	3	1.6
Pritchard-Jones et al.	2015	international	oncology	yes	composite	no	non-inferior	14	7.4	10	1.71
Pujade-Lauraine et al.	2010	international	oncology	no	composite	yes	non-inferior	77	80	7.9	1.1
Qazi et al.	2017	international	transplant	no	composite	yes	not non-inferior	25	20.4	10	1.4
Reynolds et al.	2010	Uganda	infectious diseases	no	composite	no	non-inferior	5	29.8	15	4
Riess et al.	2010	Germany	thrombosis	no	composite	yes	non-inferior	4.7	4.52	3.45	1.73
Russ et al.	2013	international	transplant	no	composite	yes	unclear	10	14	15	2.5
Schrappe et al.	2018	international	oncology	yes	composite	no	not non-inferior	4	4.4	4	2
Schroder et al.	2004	international	oncology	no	single	no	inconclusive	50	24.04	15	1.3

Schulz-Schupke et al.	2015	international	thrombosis	no	composite	yes	stopped early	10	1.6	2	1.2
Tedesco Silva et al.	2010	international	transplant	no	composite	yes	non-inferior	20	24.2	10	1.5
Sinha et al.	2005	international	respirology	yes	single	yes	non-inferior	45	na	14.5	1.32
Stabile et al.	2008	Italy	thrombosis	not explicit	composite	not explicit/unclear	non-inferior	2.5	3.7	5.5	3.2
Stellbrink et al.	2004	Germany	thrombosis	no	composite	yes	non-inferior	4	4.8	2	1.5
Stets et al.	2019	international	infectious diseases	no	composite	yes	non-inferior	21	17.3	10	1.48
Stone et al.	2007	international	thrombosis	no	composite	yes	not non-inferior	5.9	7.1	1.48	1.25
Swaminathan et al.	2011	India	infectious diseases	no	composite	no	not non-inferior	10	15	15	2.5
The GUSTO V Investigators	2001	international	thrombosis	no	single	yes	non-inferior	7.4	5.9	0.74	1.1
Turpie et al.	2009	international	thrombosis	no	composite	yes	non-inferior	27	10.1	4	1.15
Walsh et al.	2004	international	infectious diseases	yes	composite	yes	non-inferior	50	66.3	10	1.2
Willenheimer et al.	2005	international	cardiology	no	composite	yes	not non-inferior	40	36.8	5	1.13
Yahav et al.	2019	international	infectious diseases	no	composite	not explicit/unclear	non-inferior	35	48.3	10	1.29
Yakoub-Agha et al.	2012	international	oncology	no	single	not explicit/unclear	inconclusive	50	27.2	14.64	1.29
Yang et al.	2018	China	oncology	yes	composite	no	non-inferior	5	na	10	3
Daniels et al.	2019	South Africa	infectious diseases	yes	composite	no	non-inferior	7	11.4	5	1.71
Cisneros et al.	2019	international	infectious diseases	no	single	no	not non-inferior	20	25.3	10	1.5
Hahn et al.	2019	Korea	thrombosis	no	composite	yes	non-inferior	4	2.5	1.8	1.45
Jain et al.	2019	India	respirology	yes	composite	no	not non-inferior	40	39.1	10	1.25
Kollef et al.	2019	international	infectious diseases	no	single	yes	non-inferior	20	25.3	10	1.5
Nunn et al.	2019	international	infectious diseases	no	composite	no	non-inferior	30	20.2	10	1.33
Watanabe et al.	2019	Japan	thrombosis	not explicit	composite	yes	non-inferior	4.4	3.7	2.2	1.5
Charbonnier et al.	1998	international	thrombosis	no	composite	yes	non-inferior	7	7.2	5	1.71
Colombo et al.	2014	international	thrombosis	no	composite	yes	non-inferior	4.5	3.7	2	1.44
Lassen et al.	2010	international	thrombosis	not explicit	composite	yes	non-inferior	16	24.37	5.6	1.35

Lassen et al.	2009	international	thrombosis	no	composite	yes	not non-inferior	16	8.8	5.6	1.35
Le Deley et al.	2014	international	oncology	yes	composite	no	inconclusive	30	21.8	10	1.33
Noguchi et al.	2016	international	oncology	no	composite	yes	non-inferior	30	39.8	17.5	1.58
Patte et al.	1991	international	oncology	yes	composite	not explicit/unclear	non-inferior	10	10.7	15	2.5
Platzbecker et al.	2017	international	oncology	no	composite	no	non-inferior	15	13.2	5	1.33
Raffi et al.	2014	international	infectious diseases	no	composite	yes	non-inferior	20	13.8	9	1.45
Rubinstein et al.	2011	international	infectious diseases	no	composite	yes	non-inferior	40	40.5	20	1.5
Schulman et al.	2009	international	thrombosis	no	composite	yes	non-inferior	2	2.1	3.6	2.8
Schulman et al.	2013	international	thrombosis	no	composite	yes	non-inferior	2	1.3	2.8	2.4
Seo et al.	2014	Korea	gastroenterology	yes	composite	no	non-inferior	30	na	10	1.33
Continuous Infusion versus Double-Bolus Administration of Alteplase (COBALT) Investigators	1997	international	thrombosis	not explicit	single	yes	not non-inferior	6.3	7.53	0.4	1.06
Assessment of the Safety and Efficacy of a New Thrombolytic (ASSENT-2) Investigators	1999	international	thrombosis	no	single	yes	non-inferior	7.2	6.151	1	1.14
Vilas-Boas et al.	2014	Brazil	infectious diseases	yes	composite	no	non-inferior	20	23	9	1.45
International Joint Efficacy Comparison of Thrombolytics (INJECT)	1995	international	thrombosis	no	single	yes	non-inferior	2.7	9.53	2.1	1.78
Nitz et al.	2019	Germany	oncology	no	composite	yes	non-inferior	28.9	10.2	4.4	1.15