

Supplementary table 1a: Trial characteristics of the Non-inferiority trials registered either in clinicaltrials.gov / ISRCTN (2000 to 2007) contributing to our analyses (N-62):

S.No.	Study id (reference)	Trial register id	Health/Disease condition studied in the trial	Type of drug/procedure/intervention	Comparison between	Primary outcome of non- inferiority in the trial
1	NI001(1)	NCT01163812	Gastric cancer	Gastrectomy, surgical procedure	Less invasive Laproscopic New vs Invasive Open Standard	Proportion of cases with no more than one missing lymph node station
2	NI004(2)	NCT00142350	Gastric cancer	Anti tumour chemotherapy agent	Oral New vs Intravenous Standard	One year overall survival
3	NI006(3)	NCT00527137	Anemia in chronic kidney disease	Erythropoiesis stimulating agent	New vs Standard	Change in serum Haemoglobin
4	NI008(4)	NCT00249223	Schizophrenia	Antipsychotic drug, route of administration	Injection New vs Oral Standard	Change in Positive and Negative syndrome scale (PANSS) score
5	NI011(5)	NCT00783744	Diabetes	Anti diabetic drug combination	New vs Standard	Change in HbA1c
6	NI023(6)	NCT00114608	Venous thromboembolism	Prophylactic procedure	New vs Standard	Change in blood flow velocity
7	NI024(7)	NCT00398684	HIV	Prophylactic drug	New vs Standard	Rate of transmission from mother to child
8	NI031(8)	NCT00051753	Otitis Media	Antibiotic drug	New vs Standard	Clinical cure rate
9	NI034(9)	NCT00950794	Asthma	Anti asthmatic drug	New vs Standard	Change in Peak Expiratory Flow

10	NI038(10)	NCT00751829	hypertension	Anti hypertensive drug	New vs Standard	Change in systolic blood pressure
11	NI039(11)	NCT00253955	Pneumonia	Antibiotic drug	New vs Standard	Clinical cure rate
12	NI0310(12)	NCT00383136	Acute myocardial infarction	Adjunctive therapy to angioplasty	New vs Standard	Rate of complete ST resolution
13	NI0311(13)	NCT00139815	Acute coronary syndrome	Anti coagulant drug	Safer New vs Standard	Rate of composite of hazard events
14	NI0313(14)	NCT00274612	hypertension	anti hypertensive drug	New vs Standard	Change in systolic and diastolic blood pressure
15	NI0315(15)	NCT00208299	Myocardial perfusion	Diagnostic procedure	Safer , Well tolerated New vs Standard	Agreement rate
16	NI0318(16)‡	NCT00058682	Candidemia	Antifungal drug	New vs Standard	Clinical success rate
17	NI0320(17)	NCT00106288	Candidemia	Antifungal drug	Safer New vs Standard	Treatment success rate
18	NI0323(18)	NCT00062803	Venous thromboembolism	Anti coagulant drug	Fixed dose new vs Monitored dose adjusted Standard	Incidence rate
19	NI0324(19)	NCT00070655	Stroke and Systemic thromboembolism	Anti coagulant drug	Fixed dose new vs Monitored dose adjusted Standard	Cumulative Incidence
20	NI0325(20)	NCT00334386	hypertension	Anti hypertensive drug	Prolonged release vs Immediate release	Change in diastolic blood pressure
21	NI115(21)	NCT00150735	Epilepsy	Treatment drug	Better tolerable New vs Standard	Seizure free rate
22	NI116(22)	NCT00093067	Bacteremia and endocarditis	Antibiotic drug	New vs Standard	Success rate

23	NI117(23)	NCT00439855	Coronary artery disease	Anticoagulant drug	Safer, Convenient New vs Standard	Incidence of composite ischaemic endpoint
24	NI1110(24)	NCT00118638	Chemotherapy induced anemia	Treatment drug	Less frequent New vs Frequent standard treatment regimen	Incidence of blood transfusion
25	NI1111(25)	NCT00206128	Schizophrenia	Treatment drug	Extended release vs Immediate release	Failure rate
26	NI1112(26)	NCT00254878	Attention Deficit Disorder	Treatment drug	Extended release vs Immediate release	Attention and deportment rating scale
27	NI1113(27)	NCT00311961	COPD exacerbation	Treatment drug	Oral vs Intravenous	Failure rate
28	NI1115(28)	NCT00093158	Acute coronary syndrome	Antithrombotic regimen	Safer New vs Standard	Incidence of composite ischaemic endpoint
29	NI1118(29)	NCT00240474	hypertension	antihypertensive drug	New vs Standard	Change in systolic blood pressure
30	NI1122(30)	NCT00682760	Blepharospasm	Treatment drug	New vs Standard	Proportion of improvement in spasm severity
31	NI1126(31)	NCT00484900	malaria	Anti malarial drug combination	Easy to use New vs Standard	Parasitological cure rate
32	NI127(32)	NCT00299403	Depression	Treatment procedure	Safer New vs Standard	Rate of partial remission
33	NI129(33)	NCT00358176	Postmenopausal osteoporosis	treatment drug	Less frequent New vs Frequent standard	Change in bone mineral density
34	NI1211(34)	NCT00279344	Cancer	Anti analgesic drug	Well controlled New vs Standard	Change in pain intensity rating scale
35	NI1219(35)	NCT00486694	malaria	Anti malarial drug	New vs Standard	Parasitological cure rate

36	NI1222(36)	NCT00117169	Pulmonary embolism	Diagnostic procedure	Single drug versus Combination	3 month thromboembolic risk
37	NI1223(37)	NCT00325637	Ischemic stroke	antihypertensive drug	New vs Standard	Change in cerebral blood flow
38	NI1230(38)	NCT00150046	cardiac transplantation	Immunosuppressant	New vs Standard	Creatinine clearance rate
39	NI1235(39)	NCT00208312	Myocardial perfusion	Diagnostic procedure	Safer Well tolerated New vs Standard	Agreement rate
40	NI1239(40)	NCT00158405	HIV	Treatment strategies	Non continuous New vs Continuous standard treatment strategy	Proportion of patients with CD4 count < 350 per mm3
41	NI1240(41)	NCT00088491	Schizophrenia	Treatment regimens	Long acting injection vs Oral	Exacerbation rate
42	NI1246(42)	NCT00094523	HIV	treatment regimens	New vs Standard	Proportion of HIV RNA < 400 copies/ml
43	NI1254(43)	NCT00298350	HIV	Treatment drug	New vs Standard	Change in HIV RNA level
44	NI1255(44)	NCT00375713	Dermatitis & Eczema	Anti allergic drug	New vs Standard	Pruritis severity score
45	NI1256(45)	NCT00650598	Knee arthroscopy procedure	Analgesic drug	New vs Standard	VAS pain scale
46	NI1259(46)	NCT01082471	Abdominal surgery	Anasthetic drug	Well tolerated New vs Standard	VRS-11 pain intensity score
47	NI1260(47)	NCT00299884	Dyslipidemia	Treatment drug	Well tolerated New vs Standard	Change in LDL cholesterol
48	NI1263(48)	NCT00399464	Benign prostatic hyperplasia	Treatment drug	New vs Standard	Change in I-PSS score
49	NI1265(49)	NCT00417872	Clostridium difficile Colitis	Antibiotic drug	Less expensive New vs Standard	Response rate

50	NI1270(50)	NCT00209300	Ulcerative colitis	treatment drug	Less frequent New vs Frequent standard	Remission rate
51	NI1278(51)	NCT00140049	Glaucoma	Anti glaucoma drug	Less frequent New vs Frequent standard	Change in intra ocular pressure
52	NI1301(52)	ISRCTN65487167	Osteoarthritis	Treatment procedure	More accessible treatment vs less accessible	Pain assessment visual score
53	NI1302(53)	ISRCTN51678883	Esophagogastric cancer	Treatment drug	Convenient, less toxic drug vs Standard drug	Overall survival
54	NI1303(54)	ISRCTN11611768	Chronic Obstructive Pulmonary Disease	Treatment procedure	More tolerable New procedure vs less tolerable Standard	Chronic respiratory questionnaire score
55	NI1305(55)	ISRCTN81306618	Malaria	Treatment drug	Cheaper New vs Standard drug	Cure rate
56	NI1312(56)	ISRCTN62825862	Acute MI	Treatment procedure	Safer New stent vs Standard stent	In-lesion late loss at 9 months
57	NI1315(57)	ISRCTN89458845	Aortailiac occlusive disease	Treatment procedure	New vs Standard	Restenosis rate
58	NI1317(58)	ISRCTN27914471	Malaria	Treatment drug	Cheap tolerable New vs Standard	Failure rate
59	NI1318(59)	ISRCTN87811512	Abortion	Treatment drug	Safer New vs Standard	Abortion rate
60	NI1319(60)	ISRCTN89831716	Fertilisation	Treatment procedure	Safer New vs Standard	Fertilisation rate
61	NI1320(61)	ISRCTN07576538	Malaria	Treatment drug	Easier to administer , fixed New vs Standard dosing procedure	Cure rate
62	NI1321(62)†	ISRCTN36773557	Parturition	Treatment drug	Cheaper, easy-to-store New vs Standard	Vaginal delivery in 24 hrs

‡ Trial registered by principal investigator as a non-inferiority trial but registered by sponsor with no reference to non-inferiority

† the two identical trials had a pooled analysis

Supplementary table 1b: Trial characteristics of the Non-inferiority trials published in the four major journals (2005 to 2011) contributing to our analyses (N-112):

S.No.	Study id (reference)	Health/Disease condition studied in the trial	Type of drug/procedure/intervention	Comparison between	Primary outcome of non- inferiority in the trial
1	MJ001(63)	Malaria	Anti malarial drug, form of tablet	Easy to use New vs Standard	PCR corrected 28-day cure rate
2	MJ002(64)	Diabetes	Anti diabetic drug combination	Less frequent New vs Standard	Change in HbAc
3	MJ003(65)	Diabetes	Anti diabetic drug	Less frequent New vs Standard	Change in HbAc
4	MJ004(66)	Stroke	Anti coagulant drug	Fixed dose new vs Monitored dose adjusted Standard	Incidence of stroke or embolism
5	MJ005(67)	Colorectal surgery	Surgical procedure	Better tolerable New vs Standard	Rate of leakage
6	MJ007(68)	Diabetes	Anti diabetic drug	Less frequent New vs Standard	Change in HbAc
7	MJ008(69)	Thromboprophylaxis - hip replacement	Anti coagulant drug	Oral New vs Standard	Rate of composite of thromboembolism and death
8	MJ009(70)	HIV	Treatment drug	New vs Standard	Proportion of RNA count <400/ml
9	MJ010(71)	Head Injury	Treatment procedure	Less time consuming New vs Standard	Rate of no recovery
10	MJ011(72)	Infertility	Treatment procedure	Less expensive, More tolerable New vs Standard	Proportion with Pregnancy at 1 yr
11	MJ012(73)	Atrial fibrillation	Treatment procedure	Better tolerable New vs Standard	Incidence of composite failure endpoint

12	MJ013(74)	Diabetes	Anti diabetic drug combination	Less adverse effect New vs Standard	Incidence of composite failure endpoint
13	MJ014(75)	Cancer	Treatment drug	Less toxic New vs Standard	Disease rate
14	MJ015(76)	HIV	Treatment drug	New vs Standard	Proportion with RNA count <400/ml
15	MJ016(77)	Psoriasis	Treatment procedure	Home based New vs Outpatient based Standard	Success rate of high Psoriasis severity score
16	MJ017(78)	Candidaemia	Treatment drug	New vs Standard	Proportion with Negative blood culture for candidaemia
17	MJ019(79)	HIV	Treatment drug combination	Better tolerable New vs Standard	Proportion with RNA count <50/ml
18	MJ020(80)	Obsessive compulsive disorder	Treatment procedure	More accessible New vs Standard	Change in score
19	MJ021(81)	Anemia	Treatment drug	Less frequent, less monitored New vs Standard	Change in Hb in g/L
20	MJ022(82)	HIV	Treatment drug combination	New vs Standard	Proportion with RNA count <400/ml
21	MJ023(83)	Epilepsy	Treatment drug	New vs Standard	Retention rate
22	MJ024(84)	Physiotherapy for Neck pain	Treatment procedure	Less time consuming New vs Standard	Change in score
23	MJ025(85)	antibiotic	Treatment procedure	Easy, better tolerable New vs Standard	Rate of renal scarring
24	MJ026(86)	HIV	Treatment drug combination	Less toxic New vs Standard	Proportion with RNA count <50/ml
25	MJ027(87)	Pneumonia	Treatment procedure	Easy, better tolerable New vs Standard	Clinical success rate
26	MJ028(88)	Meningitis	Treatment drug	More accessible New vs Standard	Failure rate
27	MJ029(89)	Cancer	Treatment procedure	Less adverse effect New vs Standard	Relapse free rate
28	MJ030(90)	Trypanosomiasis	Treatment drug combination	Less toxic, easy New vs Standard	Cure rate
29	MJ031(91)	Invasive Candidiasis	Treatment drug	Safer New vs Standard	Proportion with negative blood

					culture for candidaemia
30	MJ032(92)	Osteoporosis	Treatment drug	Less frequent New vs Standard	Percentage change in bone density
31	MJ034(93)	Stroke	Treatment drug	Less adverse effect New vs Standard	Recurrence rate
32	MJ035(94)	Cancer	Treatment drug combination	Lower cost, less toxic New vs Standard	Survival
33	MJ036(95)	Carotid artery stenosis	Treatment procedure	New vs Standard	Incidence of Stroke or death
34	MJ037(96)	Malaria	Anti malarial drug	More accessible, less costly New vs Standard	Failure rate
35	MJ038(97)	Coronary artery disease	Treatment procedure	Safer New vs Standard	Incidence of composite failure endpoint
36	MJ039(98)	Thromboprophylaxis - knee arthroplasty	Anti coagulant drug	Oral New vs Standard	Incidence of thrombosis or embolism or death
37	MJ042(99)	Depression	Treatment drug	Better tolerable New vs Standard	Change in depression score
38	MJ043(100)	Contraception	Contraceptive drug	Better tolerable New vs Standard	12 month severe flareup rate
39	MJ044(101)	Renal transplant	Treatment drug	Less adverse effect New vs Standard	6 month rejection rate
40	MJ045(102)	Coronary heart disease	Treatment procedure	New vs Standard	Insegment late luminal loss
41	MJ046(103)	Colon cancer	Treatment drug	Less adverse effect New vs Standard	Disease free survival rate
42	MJ047(104)	Thromboprophylaxis – total knee replacement	Anti coagulant drug	Easy to use New vs Standard	Incidence of composite endpoint of thrombolism, embolism, death
43	MJ048(105)	Influenza	Prophylactic procedure	More accessible New vs Standard	Incidence rate
44	MJ049(106)	Pulmonary adeno carcinoma	Treatment drug	New vs Standard	12 month progression free survival rate
45	MJ050(107)	Chronic hepatitis	Treatment drug	New vs Standard	Therapeutic response rate
46	MJ053(108)	Coronary artery	Treatment drug	New vs Standard	Incidence of composite of major adverse cardiac/cerebrovascular

		disease			events
47	MJ054(109)	Venous thrombo embolism (VTE)	Treatment drug	Less cost, easy to use New vs Standard	Recurrence rate of venous thromboembolism
48	MJ055(110)	Pulmonary embolism	Diagnostic procedure	More informative New vs Standard	Incidence of thromboembolism
49	MJ057(111)	Catheter related infection	Treatment procedure	Less cost, easy to use New vs Standard	Catheter colonisation rate
50	MJ058(112)	Lower respiratory tract infection	Treatment procedure	Easy, less adverse effect New vs Standard	Incidence of composite adverse outcomes
51	MJ060(113)	Coronary artery disease - stent	Treatment procedure	New vs Standard	In segment late loss
52	MJ061(114)	Heart failure	Treatment drug combination	Less adverse effect New vs Standard	Survival
53	MJ062(115)	Acute myocardial infarction	Treatment procedure	Less adverse effect, less costly New vs Standard	Recovery rate at 90 mts
54	MJ063(116)	Atrial fibrillation	Anti coagulant drug	Less adverse effect New vs Standard	Incidence of stroke or embolism
55	MJ064(117)	Deep vein thrombosis (DVT)	Treatment drug	Less monitored New vs Standard	Recurrence rate
56	MJ065(118)	Parkinsons	Treatment drug	New vs Standard	Rate of change of score
57	MJ066(119)	Hepatoblastoma	Treatment drug	Less toxic New vs Standard	Rate of resection
58	MJ067(120)	Acute VTE	Treatment drug	Less monitored New vs Standard	6 month recurrence rate
59	MJ068(121)	Intensive care unit (ICU)	Treatment procedure	Ease of use New vs Standard	Multiple organ dysfunction rate
60	MJ069(122)	Lupus nephritis	Treatment drug	Better tolerable, Oral New vs Standard	Rate of remission
61	MJ072(123)	Carotid stenosis	Treatment procedure	Less invasive New vs Std	Incidence of composite failure endpoint
62	MJ074(124)	Leishmaniasis	Treatment drug	Less expensive, less time consuming New vs Standard	Cure rate

63	MJ075(125)	Viral hepatitis	Treatment drug combination	Shorter duration New vs Standard	Virological response rate
64	MJ076(126)	DVT	Treatment drug	Less adverse effect New vs Standard	Recurrence rate
65	MJ078(127)	Prostate Cancer	Treatment procedure	Less adverse effect New vs Standard	Survival
66	MJ079(128)	breast cancer	Treatment drug combination	Easy to use New vs Standard	Recurrence rate
67	MJ081(129)	Percutaneous endoscopic gastrostomy	Treatment procedure	Simpler New vs Standard	Rate of wound infection
68	MJ082(130)	Diabetes	Treatment drug combination	Less adverse effect New vs Standard	Change in HbA1c
69	MJ083(131)	Breast cancer	Treatment procedure	Less adverse effect New vs Standard	Survival
70	MJ084(132)	Septic shock	Treatment procedure	Less cost, less time consuming New vs Standard	In-Hospital mortality rate
71	MJ085(133)	Hearing loss	Treatment procedure	Less adverse effect New vs Standard	Change in hearing threshold
72	MJ086(134)	Atrial fibrillation	Anti coagulant drug	Less monitored, less adverse effect New vs Standard	Incidence of cardiovascular major event
73	MJ087(135)	Aortic valve replacement	Treatment procedure	Less invasive New vs Std	Survival
74	MJ088(136)	Hepatitis	Treatment drug	Shorter duration New vs Standard	Sustained virologic response rate
75	MJ089(137)	Atrial fibrillation	Anti coagulant drug	Less adverse effect New vs Standard	Incidence of stroke or systemic embolism
76	MJ090(138)	Coronary artery disease	Treatment procedure	New vs Standard	Cumulative event rate
77	MJ091(139)	Macular degeneration	Treatment drug	New vs Standard	Change in visual acuity
78	MJ092(140)	Atrial fibrillation	Anti coagulant drug	Less monitored, less adverse effect New vs Standard	Ischemic/hemorrhagic event rate
79	MJ094(141)	Ovarian cancer	Treatment procedure	New vs Standard	Survival
80	MJ095(142)	Breast cancer	Treatment procedure	Shorter duration New vs Standard	Risk of local breast cancer

					recurrence
81	MJ096(143)	Atrial fibrillation	Treatment procedure	Less adverse effect New vs Standard	Incidence of composite CV endpoint
82	MJ098(144)	VTE	Treatment drug	Less monitored New vs Standard	Recurrent rate of VTE
83	MJ099(145)	Latent TB infection	Treatment drug combination	Shorter duration New vs Standard	Cumulative rate of TB confirmed
84	MJ100(146)	Visceral Leishmaniasis	Treatment drug	Less frequent New vs Standard	Cure rate
85	MJ101(147)	Coronary artery disease	Treatment procedure	New vs Standard	Incidence of composite CV endpoint
86	MJ102(148)	ANCA vasculitis	Treatment drug	Safer New vs Standard	Rate of remission of vasculitis
87	MJ103(149)	thromboprophylaxis - hip replacement	Anti coagulant drug	Ease of use New vs Standard	Incidence of composite CV endpoint
88	MJ104(150)	Coronary artery stenosis	Treatment procedure	Safer New vs Standard	Incidence of composite CV endpoint
89	MJ105(151)	Cardiac transplantation	Treatment procedure	Tolerable, Safer New vs Standard	Cumulative rate of composite rejection endpoint
90	MJ106(152)	HIV	Treatment drug	Tolerable, Safer New vs Standard	Confirmed response rate
91	MJ107(153)	Prostate cancer	Treatment drug	Less toxic, easy New vs Standard	Time to skeletal related event
92	MJ108(154)	Appendicitis	Treatment procedure	Less invasive New vs Std	Incidence of post intervention peritonitis
93	MJ109(155)	Leishmaniasis	Treatment drug combination	Safer, shorter duration New vs Standard	Cure rate
94	MJ112(156)	HIV	Treatment drug	Tolerable, Safer New vs Standard	Confirmed response rate
95	MJ113(157)	H pylori eradication	Treatment drug combination	New vs Standard	Rate of H pylori eradication
96	MJ114(158)	Post partum Haemorrhage	Treatment drug	More accessible New vs Standard	Cessation of active bleeding at 20 min

97	MJ115(159)	Cerebral ischemia	Treatment drug	Safer New vs Standard	Incidence of composite CV endpoint
98	MJ116(160)	Acute pulmonary embolism	Treatment procedure	Less cost, less time consuming New vs Standard	Incidence of symptomatic recurrent VTE
99	MJ117(161)	Breast cancer	Treatment procedure	Safer, more tolerable New vs Std	5 yr local recurrence rate
100	MJ118(162)	Malaria	Treatment drug combination	Ease of use New vs Standard	ACPR response rate
101	MJ120(163)	HIV	Treatment procedure	Easily accessible New vs Standard	Cumulative treatment failure rate
102	MJ121(164)	Diabetes	Treatment procedure	Safer, convenient New vs Standard	Change in HbAc
103	MJ122(165)	Diabetes	Treatment drug	Better tolerable New vs Standard	Change in HbAc
104	MJ123(166)	Endometrial cancer	Treatment procedure	Less adversr effects New vs Standard	5 yr vaginal recurrence rate
105	MJ124(167)	HIV	Treatment procedure	Easy, more accessible New vs Standard	Incidence of composite HIV endpoint
106	MJ125(168)	Thromboprophylaxis - knee replacement	Anti coagulant drug	Easy, less adverse effect New vs Standard	Incidence of composite CV endpoint
107	MJ126(169)	Emergency contraception	Treatment drug	New vs Standard	Pregnancy rate
108	MJ127(170)	HIV	Treatment drug combination	Less adverse effect New vs Standard	Response rate
109	MJ128(171)	ICU	Treatment procedure	Shorter duration, less adverse effect New vs Standard	Mortality at day28
110	MJ129(172)	TB	Treatment procedure	Convenient, more compliant, less adverse effect New vs Standard	Cure rate
111	MJ131(173)	Post partum Haemorrhage	Treatment drug	More accessible New vs Standard	Rate of bleeding cessation
112	MJ132(174)	Syphilis	Treatment drug	Convenient New vs Standard	Cure rate

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