Appendices

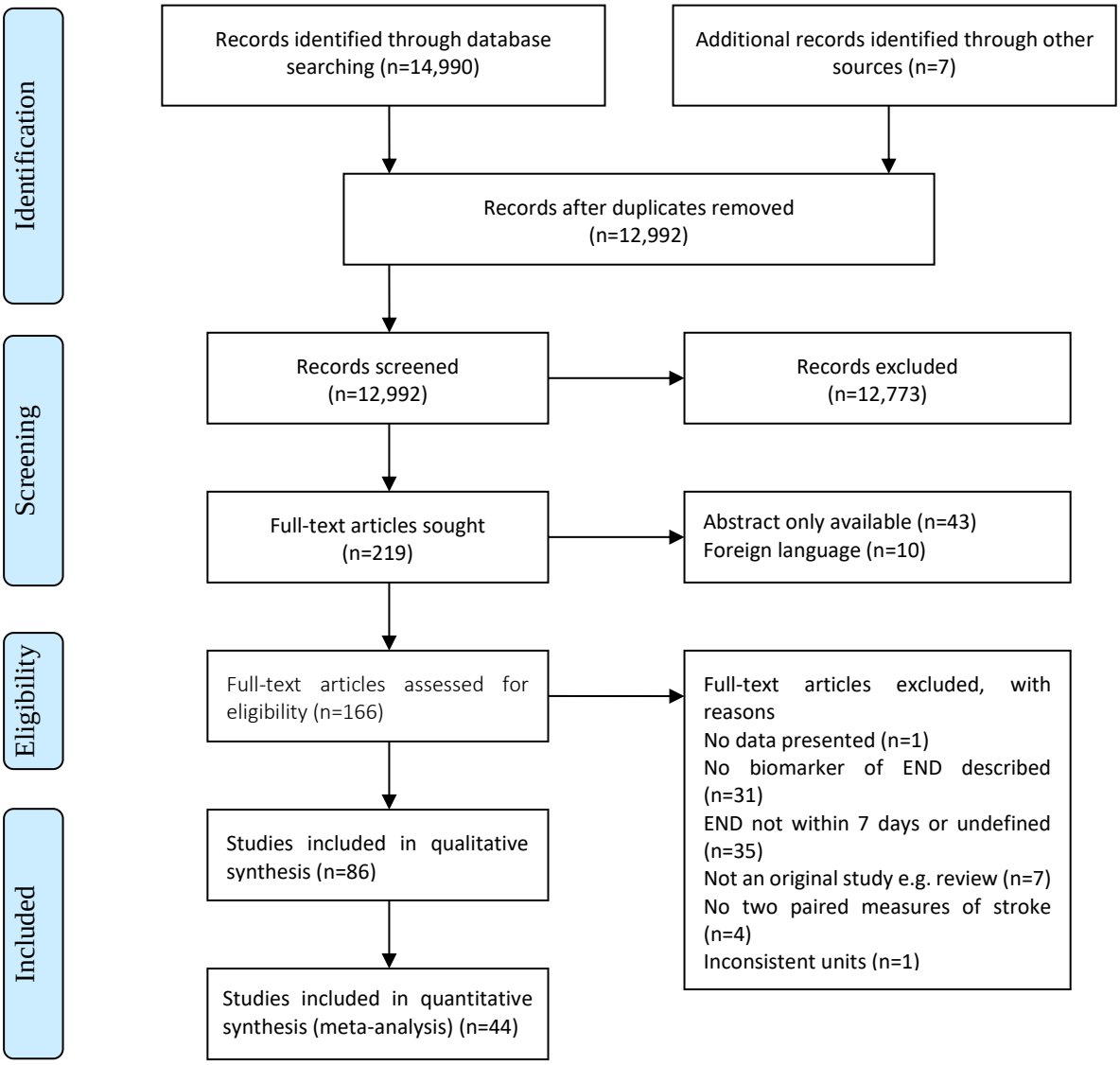
Appendix 1 - Search strategy and data items

Medline		Embase	
1	progress$.mp.	1	progress$.mp.
2	evol$.mp.	2	evol$.mp.
3	deteriorat$.mp.	3	deteriorat$.mp.
4	worse$.mp.	4	worse$.mp.
5	acute phase.mp.	5	acute phase.mp.
6	early neurologic$.mp.	6	early neurologic$.mp.
7	early outcome.mp.	7	early outcome.mp.
8	short-term outcome.mp.	8	short-term outcome.mp.
9	Stroke/	9	*cerebrovascular accident/
10	Humans/	10	human/
11	(1 or 2 or 3 or 4 or 5 or 6 or 7 or 8) and 9	11	(1 or 2 or 3 or 4 or 5 or 6 or 7 or 8) and 9
12	10 and 11	12	10 and 11
13	limit 12 to yr="1990-2017"	13	limit 12 to yr="1990-2017"

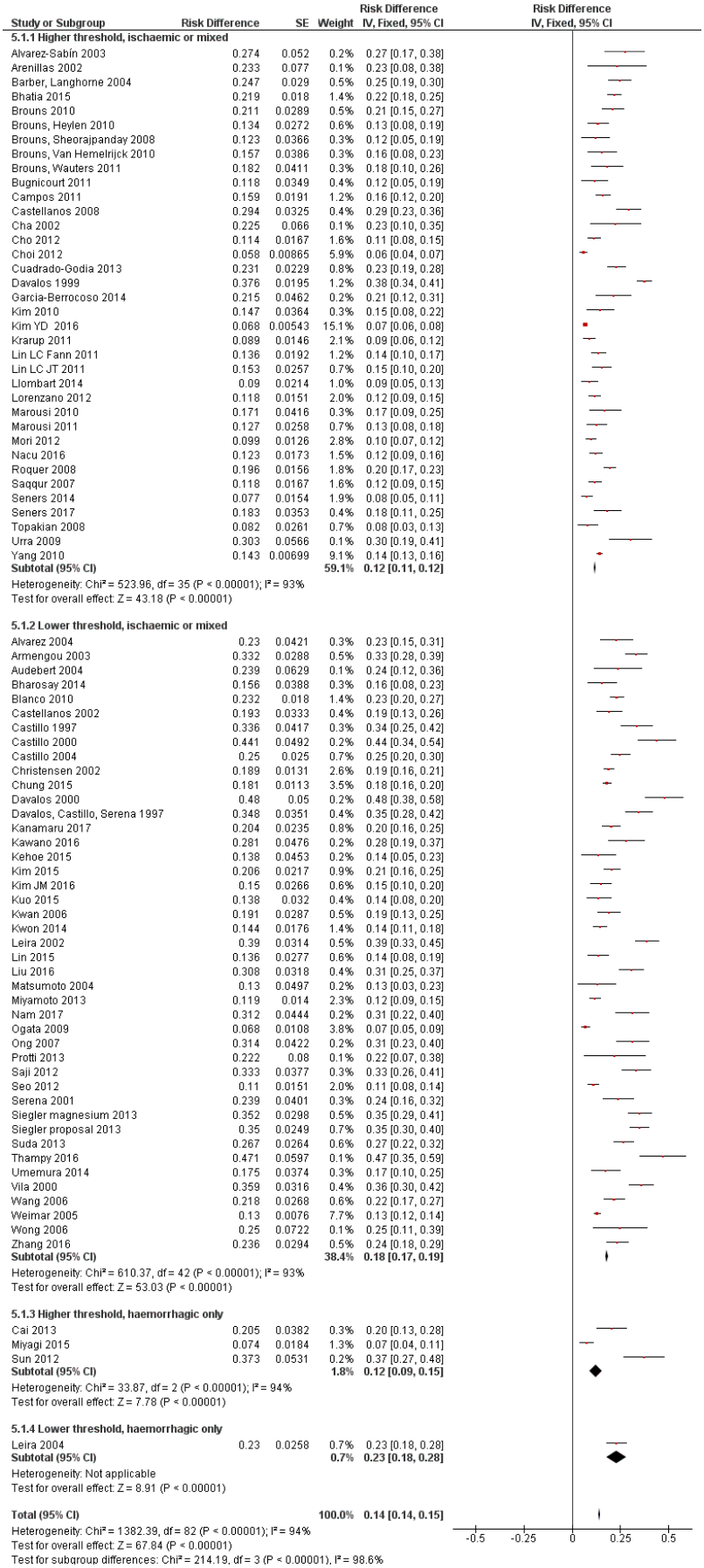
Appendix 2 - Data items

- Author, year, study type
- Number of patients in END and non-END groups
- Biomarker – any eligible biomarker that was reported in both the END and non-END groups
- Time from onset of biomarker measurement
- Patient details in each group
    - % Female
    - Mean/median admission delay
    - Mean/median initial stroke severity
    - Mean/median systolic and diastolic blood pressure
    - Distribution of stroke subtypes
- Stroke types included in the study
- Definition of END
    - Heterogenous definitions of END were categorised into higher neurological threshold and lower neurological threshold
- Time window of END
    - Categorised into second stroke severity measurement within <24 hours, <48 hours, 72 hours and <7 days of the first

Appendix 3 Systematic Review & Meta-analysis PRISMA (1) flowchart



Appendix 4 Incidence forest plot (2-79)



Appendix 5 - Metabolic non-meta-analysis biomarkers

Citations in **bold** agree with the conclusions of meta-analysis studies.

UACR = Urinary albumin:creatinine ratio

#	Biomarker	Author [ref]	END definition, time	n	END: Median (IQR) or Mean ± SD	non-END: Median (IQR) or Mean ± SD	Cut-off	n END with outcome	n nEND with outcome	OR (95% CI)	p
A	Adiponectin [mg/dl]	**Marousi 2010 (26)**	EPSS 72 hours	82	11.82 ± 9.05	11.02 ± 8.47	-	-	-	Binary regression OR 1.1 (0.97-1.19)	0.184
B	Adrenomedullin [pg/ml]	**Wang 2014 (34)**	NIHSS 4+ 24 hours	114	126.5 ± 28.8	89 ± 36.6	-	-	-	-	<0.001
C	Albumin ratio	Brouns, Wauters (9)	EPSS 72 hours	88	8.8 ± 3.5	5.6 ± 2	-	-	-	Logistic regression OR 14.9	<0.001
D	Alkaline phosphatase ALP[IU/l]	Bhatia 2015 (5)	NIHSS 3+ 72 hours	114	384.4 ± 159	346.6 ± 111.1	-	-	-	-	0.144
E	Aspartate [µM]	Brouns 2010(7)	EPSS 72 hours	89	0.53 (0.34-0.73)	0.59 (0.47-0.70)	-	-	-	-	0.723
		Wong 2006	EPSS 72 hours	36	13 ± 3	12 ± 2	-	-	-	-	NS
F	Bilirubin	Bhatia 2015 (5)	NIHSS 3+ 72 hours	114	0.64 ± 0.11	0.55 ± 0.1	-	-	-	-	0.001
G	Blood glucose [mmol/l]	**Alvarez 2004 (36)**	CSS ≤-1 72 hours	100	8.94 (5.55-15.65)	8.66 (3.89-29.36)	-	-	-	-	0.148
		Alvarez-Sabin 2003 (2)	NIHSS 4+ 24 hours	73	In normoglycaemic (n=42), END 17%; in hyperglycaemic (n=31) END 42%						0.02
		Barber, Wright 2004 (80)	EPSS, 72 hours	359	-	-	>10	36 (21%)	32 (17%)	-	0.442
		Castillo 2004 (79)	CSS 1- 48 hours	300	7.94 (6.83-9.55)	7.55 (6.22-9.32)	-	-	-	-	-
		Christensen 2002 (44)	SSS drop 2+, 72 hours	727	7.30 (6.90-7.80)	7.00 (6.80-7.30)	-	-	-	-	-
		Kim 2016 (20)	NIHSS 4+ 72 hours	2150	-	-	>7.5	56 (38.4%)	644 (32.1%)	-	0.121
		Liu 2016 (58)	NIHSS 2+ 72 hours	211	5.00 (4.60-5.70)	5.20 (4.70.6.30)	-	-	-	-	0.246
		Seners 2017 (31)	NIHSS 4+ 24 hours	120	7.5 (6.2-8.3)	6.8 (5.9-8.5)	-	-	-	-	0.44
		Siegler, Boehme 2013 (69)	NIHSS 2+ 24 hours	366	6.99 (4.22-36.80)	6.33 (4.00-31.58)	-	-	-	-	0.0036
		Topakian 2008 (32)	NIHSS 4+ 24 hours	110	6.44 (4.66-14.71)	6.55 (4.22-18.32)	-	-	-	-	0.46
		Umemura 2014 (72)	NIHSS 2+ 5 days	85	-	-	Per +1 SD	-	-	OR 1.22 (0.72-1.94)	0.490
		Weimar 2005 (76)	NIHSS 1+ 72 hours	1964	-	-	>11mmol/l	15.6%	6.0%	-	<0.01

		Yang 2010 (35)	EPSS, 72 hours	2511	-	-	Fasting >7.8, random >11.1	136 (37.82%)	483 (22.45%)	-	-
		Zhang 2016 (78)	NIHSS 2+ motor 1+ 7 days	208	8 (5.9-9.9)	5.4 (5.0-6.1)	-	-	-	-	0.001
H	Blood urea nitrogen: creatinine ratio	Lin, Yang 2011 (23)	NIHSS 3+ 72 hours	196	-	-	>15	16 (59.3%)	37 (31.1%)	3.22 (1.36-7.62)	0.008
		Bhatia 2015 (5)	NIHSS 3+ 72 hours	114	20.2 ± 5.7	15.6 ± 2.7	-	-	-	-	<0.001
I	Creatinine phosphokinase [U/l]	Leira, 2004 (81)	CSS 1+ 48 hours	226	220 ± 231	151 ± 150	-	-	-	-	0.043
J	Estimated glomerular filtration rate [ml/min/m^2]	**Miyagi 2015 (82)**	GCS 2+/NIHSS 4+ 72 hours	203	-	-	<60	-	-	2.44 (0.72-7.36)	0.169
		Saji 2012 (65)	NIHSS 2+, 7 days	156	43.4 (30.1-51.7)	50.3 (40.4-62.2)	-	-	-	-	0.005
		Umemura 2014 (72)	NIHSS 2+ 5 days	85	-	-	<60	-	-	3.47 (1.20-10.09)	0.021
K	Glycosylated haemoglobin [%]	Ogata 2009 (62)	NIHSS 2+ 7 days	543	5.4	5.8	-	-	-	-	0.035
		Siegler 2013 (69)	NIHSS 2+ 24 hours	366	6.1 (4.6-12.7)	5.8 (4.5-13.7)	-	-	-	-	0.0104
L	High density lipoprotein mmol/l	**Siegler 2013 (69)**	NIHSS 2+ 24 hours	366	1.17 (0.28-2.59)	1.09 (0.49-2.59)	-	-	-	-	0.1876
		Zhang 2016 (78)	NIHSS 2+ 7 days	208	1.4 (1.1-1.6)	1.3 (1.1-1.5)	-	-	-	-	0.192
M	Low density lipoprotein mmol/l	Siegler 2013 (69)	NIHSS 2+ 24 hours	366	103 (29-540)	105 (17-540)	-	-	-	-	0.3318
		Zhang 2016 (78)	NIHSS 2+ 7 days	208	2.3 (1.7-2.9)	2.3 (1.9-2.9)	-	-	-	-	0.75
N	Magnesium reduction	Siegler 2013 (68)	NIHSS 2+ 24 hours	256	-	-	-	46 (51.1%)	93 (56.0%)	-	-
O	Methionine	Wong 2006 (77) (77)	Undefined, 48 hours	36	22 ± 6	22 ± 8	-	-	-	-	NS
P	Microalbuminuria mg albumin/g creatinine	**Cho 2012 (15)**	NIHSS 4+ 5 days	361	-	-	30-300	25 (61.0%)	114 (35.6%)	-	0.002
		Thampy 2016 (71)	NIHSS change, 24 hours	70	-	-	30-300	28 (84.8%)	14 (37.8%)	Multivariate regression OR 15.69 (1.08-227.88)	
Q	Osmolarity mmol/l	Barber, Wright 2004 (80)	EPSS, 72 hours	349	-	-	>300	59 (34%)	51 (29%)	-	0.24
R	Plasma osmolality [mOsml/l]	Bhatia 2015 (5)	NIHSS 3+ 72 hours	114	294.02 ± 3.42	292.24 ± 4.3	-	-	-	-	0.047
S	Total cholesterol (mmol/l)	Liu 2016 (58)	NIHSS 2+ 72 hours	211	4.4 (3.8-5.3)	4.5 (3.9-4.9)	-	-	-	-	0.903

T	Triglycerides (mmol/l)	Zhang 2016 (78)	NIHSS 2+ 7 days	208	1.3 (1.0-2.2)	1.3 (1.0-1.7)	-	-	-	-	0.307
U	Triglyceride/HDL-c ratio	Choi 2012 (16)	NIHSS 4+ 7 days	553	4 ± 3.2	3 ± 2.6	-	-	-	-	N
V	Urinary albumin [mg]: creatinine [g] ratio	Umemura 2014(72)	NIHSS 2+ 5 days	85	-	-	>30	-	-	5.88 (1.81-18.85)	0.002
W	UACR [excl. macroalbuminuria]	Cho 2012 (15)	NIHSS 4+ 5 days	361	77 ± 75.44	39.08 ± 57.36	-	-	-	-	0.003
X	UACR [incl. macroalbuminuria]	Kanamaru 2017 (49)	NIHSS 2+ 7 days	294	652.8 ± 1089.8	227.2 ± 513.4	-	-	-	-	<0.001
Y	Uric acid change	Brouns, Wauters 2011 (9)	EPSS 72 hours	88	8.8 ± 3.5	5.6 ± 2	-	-	-	-	0.012
Z	Urine specific gravity	Bhatia 2015 (5)	NIHSS 3+ 72 hours	114	1.0 18 ± 0.005	1.015 ± 0.005	-	-	-	-	0.03
		Lin, Fann 2011 (22)	NIHSS 3+ 72 hours	317	34 (85.0%)	143 (68.1%)	>1.010	-	-	-	0.031

Appendix 6 – Inflammatory & excitotoxic non-meta-analysis biomarkers

Citations in **bold** agree with the conclusions of meta-analysis studies
15-dPGJ2 = 15-deoxy delta prostaglandin J2; 5-HIAA = 5-hydroxyindoleacetic acid; BD-2 = beta defensin-2; CRP = C-reactive protein; MMP-9 = matrix metalloproteinase-9; F2isop = F2-isoprostane (index of endogenous oxidant stress); FMPPs = fluorescent molecular peroxidation products; hsCRP = high-sensitivity c-reactive protein; IL = interleukin; NO-m = nitric oxide metabolites; sICAM-1 = soluble intercellular adhesion molecule-1; sTNF-R = soluble tumour necrosis factor receptor; svCAM-1 = soluble vascular cell adhesion molecule-1;

#	Biomarker	Author [ref]	END definition, time	n	END: Median (IQR) or Mean ± SD	Non-END: Median (IQR) or Mean ± SD	Cut-off	n END with outcome	n nEND with outcome	OR (95% CI)	p
A	15-dPGJ2 [pg/ml] all	Blanco 2005 (40)	CSS -1 48 hours	552	69.5 (12.8-69.5)	50.9 (11.2-111.1)	-	-	-	-	0.880
B	15-dPGJ2 [pg/ml] atherothrombotic	Blanco 2005 (40)	CSS -1 48 hours	221	77.5 (56.9-121.3)	120.5 (99.3-151.2)	-	-	-	-	<0.0001
C	5-HIAA	Brouns, Van Hemelrijck. 2010 (7)	EPSS 72 hours	89	102.9 (66.6-144.8)	51.9 (36.3-82.2)	-	-	-	-	0.001
D	BD-2 [ng/ml]	Garcia-Berrocoso 2014 (18)	NIHSS 4+ 24 hours	79	-	-	>1.15	14 (82.4%)	32 (51.6%)	4.87 (1.13-20.91)	0.033
E	Monocyte CD14high, CD16-	Urra 2009 (33)	NIHSS 4+ 7 days	46	-	-	1% increment in subtype	-	-	Logistic regression only: 1.29 (1.03-1.63)	<0.05
F	CD34+ cells [/ul]	Kawano 2016 (50)	NIHSS 1+, IQR for END 1-3 days	89	0.5 (0.31-0.88)	0.79 (0.46-1.1)	-	-	-	-	0.03
G	CRP	**Barber, Langhorne 2004 (4)**	EPSS 72 hours	219	8.66 (3.69-30.45)	5.26 (1.54-18.4)	-	-	-	-	0.049
		Krarup 2011 (21)	SSS 3+ 48 hours	382	6 (5-11)	7 (5-12)	-	-	-	-	0.74
		Nam 2017 (61)	NIHSS 2+ 72 hours	109	2.48 (1.75-8.23)	1.39 (0.35-7.20)	-	-	-	-	0.05
		Ong 2007 (63)	NIHSS 2+ 7 days	121	-	-	>0.8	19 (50%)	15 (18.1%)	-	0.0003
		Saji 2012 (65)	NIHSS 2+ or 1+ limb 7 days	156	1 (0-3)	1 (0-3)	-	-	-	-	0.355
		Topakian 2008 (32)	NIHSS 4+ 24 hours	110	2.0 (1.0-7.0)	4.0 (0-5.9)	-	-	-	-	0.09
H	Cysteine [µmol/l]	Wong (77)	Undefined 48 hours	36	77 ± 15	65 ± 11	-	-	-	-	<0.02

I	DOPAC (nM)	Brouns, Van Hemelrijck. 2010 (7)	EPSS 72 hours	89	0.44 (0.27-0.97)	0.78 (0.50-1.03)	-	-	-	-	0.295
J	Erythrocyte sedimentation rate (mm)	Leira 2004 (81)	CSS 1- 48 hours	216	39 ± 14	22 ± 19	-	-	-	-	<0.001
K	Excitotoxic index	Serena 2001 (67)	CSS 1- 48 hours	113	279 ± 121	43 ± 31	-	-	-	-	n
L	FMPPs	Llombart 2014 [uf/ml] (24)	NIHSS 4+ 48 hours	186	-	-	>48.2	13 (81.3%)	70 (43.2%)	Adjusted 5.203 (1.338-20.240)	0.017
M	GABA [nmol/l]	Serena 2001 (67)	CSS 1- 48 hours	113	140 ± 63	411 ± 97	-	-	-	-	n
N	Glutamate (plasma) [µmol/l]	Castellanos 2008 (13)	NIHSS 4+ 72 hours	197	267.8 (176.6-356.6)	54.4 (38.2-78.6)	-	-	-	-	<0.0001
		Davalos 2000 (46)	CSS 1- 48 hours	100	304 (119-408)	98 (49-254)	-	-	-	-	<0.001
O	Glutamate (CSF) [µmol/l]	Brouns, Van Hemelrijck. 2010 (7)	EPSS 72 hours	89	1.32 (1.06-1.50)	1.24 (1.10-1.43)	-	-	-	-	0.879
		Davalos 2000 (46)	CSS 1- 48 hours	100	13 (5-22)	4.5 (2-17)	-	-	-	-	<0.001
		Davalos 1997 (48)	CSS 1- 48 hours	184	12.5 (5-22)	4.0 (2-17)	-	-	-	-	<0.0001
P	Glutamine [µmol/l]	Brouns, Van Hemelrijck 2010 (7)	EPSS, 72 hours	89	367.7 (272.3-397.9)	340.3 (310.2-373.3)	-	-	-	-	0.543
Q	Glycine CSF [µmol/l]	Castillo 1997 (42)	CSS 1- 48 hours	128	13.9 ± 4.1	9.9 ± 7.7	-	-	-	-	0.0028
R	Glycine [µmol/l]	Brouns, Van Hemelrijck 2010 (7)	EPSS, 72 hours	89	2.71 (2.16-3.55)	2.47 (1.85-3.23)	-	-	-	-	0.3
S	Homocysteine (µmol/l)	Zhang 2016 (78)	NIHSS 2+ 7 days	208	14.4 (12.0-21.7)	11.1 (13.0-18.0)	-	-	-	-	0.049
T	HVA (nM)	Brouns, Van Hemelrijck. 2010 (7)	EPSS 72 hours	89	386.8 (277.5-696.9)	386.7 (289.8-476.6)	-	-	-	-	0.589
U	ICAM-1 [pg/ml]	Castellanos 2002 (41)	CSS -1 48 hours	140	285 (219-315)	158 (137-187)	>208			Adjusted 315 (17-5748)	<0.001
		Zhang 2016 (78)	NIHSS 2+ 7 days	208	6.0 (2.0-11.5)	2.0 (0.9-5.0)	-	-	-	-	0.001
V	IL-10 [pg/ml]	Christensen 2002 (44)	SSS -2 72 hours	162	2.7 (1.53-4.70)	1.6 (1.32-1.98)	-	-	-	-	0.039
		Protti 2013 (64)	NIHSS 1+ 72 hours	27	-	-	>925.5			Sens 76.2%, spec 80%	
W	IL-1B [pg/ml]	Christensen 2002 (44)	SSS -2 72 hours	162	0.3 (0.06-1.10)	0.1 (0.06-0.28)	-	-	-	-	0.419
X	IL-1RA [pg/ml]	Christensen 2002 (44)	SSS -2 72 hours	162	284 (168-479)	171 (111-262)	-	-	-	-	0.232
Y	IL-4R [pg/ml]	Garcia-Berrocosco 2014 (18)	NIHSS 4+ 24 hours				503.4	9 (52.9%)	17 (27.9%)	Adj 3.5 (1.0-12.1)	0.045
Z	IL-6 [pg/ml]	Castellanos 2002 (41)	CSS 1- 48 hours	113	28.8 (22.5-35.7)	11.5 (8.5-16.2)	-	-	-	-	<0.001

		Castellanos 2008 (13)	NIHSS 4+ 72 hours	197	44.6 (33.1-54.6)	21.4 (16.3-30.0)	-	-	-	-	<0.0001
		Christensen 2002 (44)	SSS 2- 72 hours	162	-	-	21.5	16.7%	17.5%	-	0.912
		Kawano 2016 (50)	NIHSS 1+ END IQR 1-3 days	89	4.8 (2.3-7.95)	2.45 (1.3-4.15)	-	-	-	-	0.009
		Vila 2000 (73)	CSS 1- 48 hours	231	35 ± 13	10.2 ± 8	-	-	-	-	<0.0001
AA	L-arginine plasma [µmol/l]	Armengou 2003 (37)	CSS 1- 48 hours	268	65 (59-69)	68 (61-82)	-	-	-	-	0.002
		Castellanos 2008 (13)	NIHSS 4+ 72 hours	197	60.2 (49.6-70.6)	97.9 (78.8-129.4)	-	-	-	-	<0.0001
AB	L-arginine CSF [µmol/l]	Armengou 2003 (37)	CSS 1- 48 hours	268	6.4 (4.5-11.4)	15 (9.2-17.6)	-	-	-	-	<0.001
AC	Lactate CSF [mmol/l]	Brouns, Sheorajpanday 2008 (10)	NIHSS 2+ 72 hours	85	1.9 ± 0.9	1.5 ± 0.3	>2	-	-	7.6	0.022
AD	Leucocytes [$x10^9$/l]	**Barber, Langhorne 2004 (4)**	EPSS 72 hours	219	10.25 (8.05-12.78)	9.30 (7.40-11.50)	-	-	-	-	0.017
		Saji 2012 (65)	NIHSS 2+ or 1+ in limb 7 days	156	6 (4-7.4)	6.30 (5.4-7.1)	-	-	-	-	0.519
		Sun 2012 (83)	GCS ≥3 72 hours	89	-	-	>10,000 ml^3	27 (87.1%)	32 (61.5%)	-	0.014
AE	MMP-9 change	Brouns, Wauters 2011 (9)	EPSS 72 hours	67	-	-	-	-	-	13.5	<0.001
AF	Neutrophils [$x1000/mm^3$]	Leira 2004 (81)	CSS 1+ 48 hours	266	10.8 ± 2.9	6.3 ± 4.3	-	-	-	-	<0.001
AG	NO-m	Castillo 2000 (43)	CSS 1- 48 hours	102	4 (1.7-7.8)	1.6 (1.0-2.5)	-	-	-	-	<0001
AH	Norepinephrine [nM]	Brouns, Van Hemelrijck 2010 (7)	EPSS, 72 hours	89	0.56 (0.44-1.08)	0.70 (0.49-1.18)	-	-	-	-	0.407
AI	Phosphorylated axonal filament subunit H [pg/ml]	Cai 2013 (84)	NIHSS 4+ 24 hours	112	910.9 ± 381.6	611.8 ± 426.9	>748.6	-	-	1.25 (1.1-1.5)	<0.001
AJ	Proline [µM]	Brouns, Van Hemelrijck 2010 (7)	EPSS 72 hours	89	0.28 (0.18-0.58)	0.23 (0.14-0.36)	-	-	-	-	0.24
AK	p-selectin [MFI]	Cha 2002 (14)	NIHSS 4+ 7 days	40	110.7 ± 39.5	103.7 ± 33.9	-	-	-	-	NS
AL	Segmented & band leucocytes [$x10^9$/l]	Lin, Yang 2011 (23)	NIHSS 3+ 72 hours	196	5.3 ± 2.4	5.3 ± 2.5	-	-	-	-	n
AM	Segmented neutrophils [$x10^9$/l]	Lin, Yang (23)	NIHSS 3+ 72 hours	196	0.7 ± 0.1	0.6 ± 0.1	-	-	-	-	0.795
AN	SE-selectin [ng/ml]	Wang 2006 (75)	NIHSS 1+ 7 days	238	43.9 ± 6.5	42.5 ± 6.1	-	-	-	-	0.367
AO	sICAM-1 [ng/ml]	Wang 2006 (75)	NIHSS 1+ 7 days	238	261 ± 43.3	223 ± 41.4	-	-	-	-	<0.001

AP	sTNF-R1 [pg/ml]	Christensen 2002 (44)	SSS 2- 72 hours	162	1422 (1140-1794)	1340 (1233-1456)	-	-	-	-	0.549
AQ	sTNF-R2 [pg/ml]	Christensen 2002 (44)	SSS 2- 72 hours	162	2218 (1845-2667)	2432 (2270-2606)	-	-	-	-	0.259
AR	svCAM-1	Wang 2006 (75)	NIHSS 1+ 7 days	238	731 ± 84.3	715 ± 79.6	-	-	-	-	0.232
AS	Taurine [nM]	Brouns, Van Hemelrijck 2010 (7)	EPSS, 72 hours		4.02 (2.33-4.91)	4.28 (3.54-5.28)	-	-	-	-	0.295
AT	TNF-a plasma [pg/ml]	Christensen 2002 (44)	SSS 2- 72 hours	162	1.9 (1.06-3.20)	3.0 (2.02-4.40)					0.218
		Castellanos 2002 (41)	CSS 1- 48 hours	113	16.5 (13.7-21.2)	7.5 (6.2-9.0)	-	-	-	Adj 511 (17-4937)	<0.001
		Castellanos 2008 (13)	NIHSS 4+ 72 hours	197	20.3 (13.5-29.8)	18.6 (12.2-26.0)	-	-	-	-	0.182
		Vila 2000 (73)	CSS 1- 48 hours	231	21.1 ± 8.1	15.1 ± 6.1	-	-	-	-	<0.0001
AU	TNF-a CSF [pg/ml]	Vila 2000 (73)	CSS 1- 48 hours	231	22.8 ± 15.4	11.1 ± 11.1	-	-	-	-	0.001

Appendix 7 - Coagulation and haematological non-meta-analysis biomarkers

Citations in **bold** agree with the conclusions of meta-analysis studies

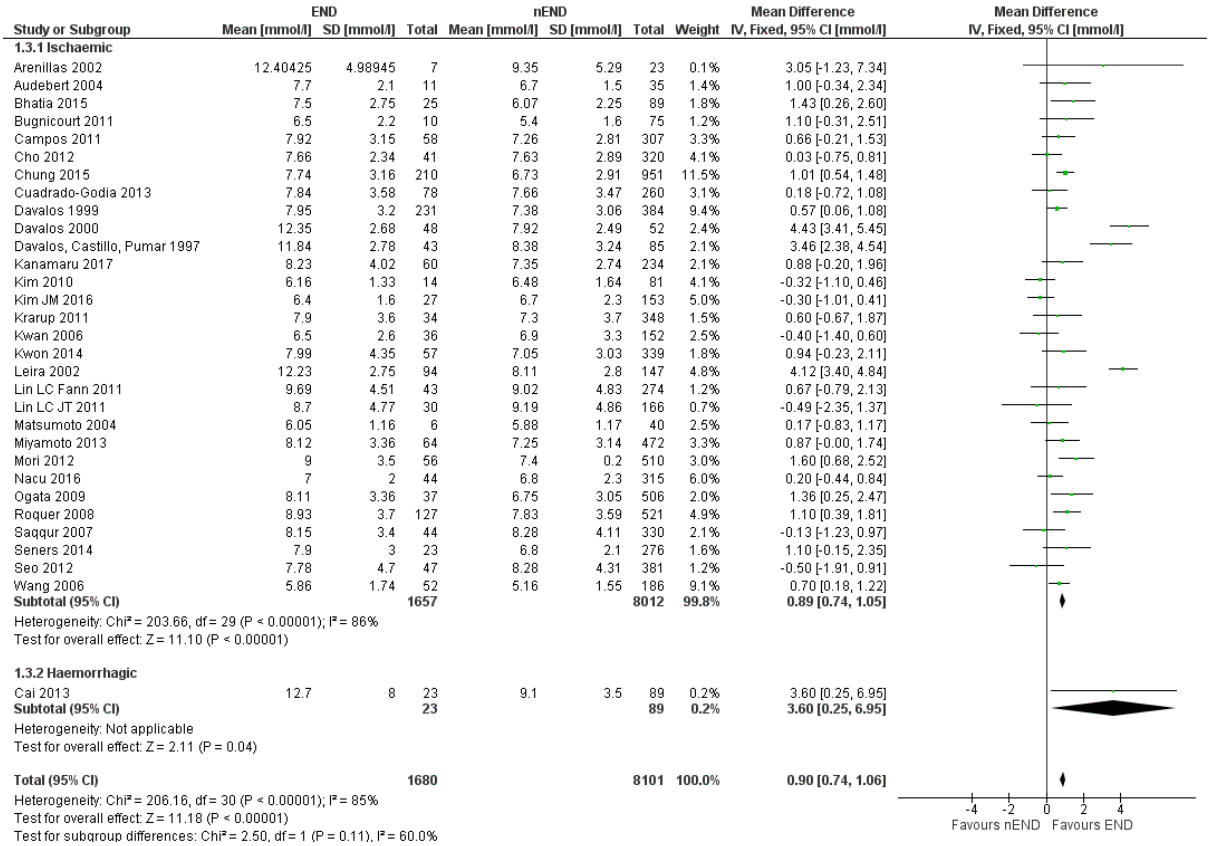
APC ratio = Activated protein C ratio; APTT = Activated partial thromboplastin time; ARU = Aspirin reaction unit; mPa = millipascal-second; PRCP = Prolyl carboxypeptidase; TAT = Thrombin-antithrombin III complex; tPa = tissue plasminogen activator; vWF = Von Willebrand factor

#	Biomarker	Author [ref]	END definition, time	n	END: Median (IQR) or Mean ± SD	Non-END: Median (IQR) or Mean ± SD	Cut-off	n END with outcome	n nEND with outcome	OR (95% CI)	p
A	ARU [IU]	Kim 2015 (85)	NIHSS 1+ 5 days	349	475.5 ± 62.14	476.4 ± 70.6	≥550	6 (10.2%)	52 (17.9%)	-	0.67
B	APC ratio	Barber, Langhorne 2004 (4)	EPSS, 72 hours	219	2.73 (2.44-3.07)	2.81 (2.53-3.12)	-	-	-	-	0.43
C	APTT [s]	**Lin 2015 (57)**	NIHSS 1+ 72 hours	154	-	-	<1	17 (80.9%)	74 (55.6%)	-	0.028
D	Aspirin non-responder status [PFA-100s]	Bugnicourt 2011 (11)	NIHSS 4+ 72 hours	85	176 ± 68	239.1 ± 72.5	-	-	-	-	0.011
E	ATIII [%]	Matsumoto 2004 (59)	NIHSS 2+ 7 days	46	91 ± 14.3	88.1 ± 13.6	-	-	-	-	0.55
F	D-dimer	**Barber, Langhorne 2004 (4)**	EPSS 72 hours	219	443 ng/ml (164-1091)	194 (92-481)	-	-	-	-	<0.001
		Krarup 2011 (21)	SSS 3+ 48 hours	382	1025 ng/ml (610-2261)	970 (621-1779)	-	-	-	-	0.73
		Lin, Yang 2011 (23)	NIHSS 3+ 72 hours	196	-	-	>1000ug/l	16 (53.3%)	57 (35.2%)		0.06
		Lin, Fann 2011 (22)	NIHSS 3+ 72 hours	317	-	-	>1000ug/l	15 (34.9%)	85 (31.8%)	-	0.691

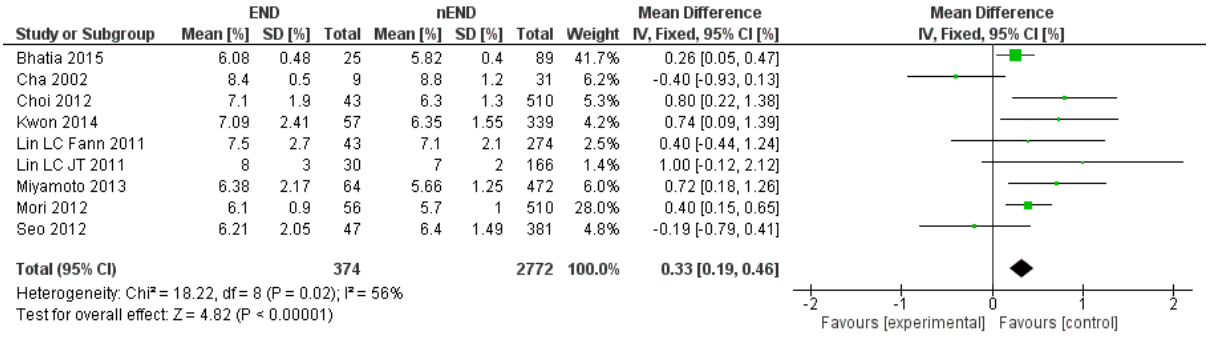
		Nam 2017 (61)	NIHSS 2+ 72 hours	109	12.68 (4.96-20.00)	1.39 (0.35-7.20)	-	-	-	-	<0.01
		Ong 2007 (63)	NIHSS 2+ 7 days	121	-	-	>324ng/ml	9 (23.7%)	13 (15.7%)	-	0.286
G	Factor IXc [IU/dl]	Barber, Langhorne 2004 (4)	EPSS, 72 hours	219	170 (148-188)	156 (142-184)	-	-	-	-	0.085
H	Factor VIIc [IU/dl]	Barber, Langhorne 2004 (4)	EPSS, 72 hours	219	139 (111-171)	148 (127-165)	-	-	-	-	0.126
I	Factor VIII [IU/dl]	Kuo 2015 (53)	NIHSS 1+ 72 hours	116	152.9 ± 49.9	123.5 ± 52	-	-	-	-	n
J	Factor VIIIc [IU/dl]	Barber, Langhorne 2004 (4)	EPSS, 72 hours	219	204 (166-240)	195 (162-235)	-	-	-	-	0.15
K	Ferritin plasma	Christensen 2002 (44) [pmol/l]	SSS drop 2+ 72 hours	162	284 (212-380)	255 (222-292)	>618	11.1%	12.0%		0.884
		Davalos 2000 (46) [ng/ml]	CSS 1- 48 hours	100	391 (119-500)	148 (21-399)	>275ng/ml	-	-	33.5 (4.7-235) PPV 79% (65-89)	<0.001
L	Ferritin CSF [ng/ml]	Davalos 2000 (46)	CSS 1- 48 hours	100	17.4 (6.8-82)	4.8 (0.6-14)	>11ng/ml	-	-	11.4 (3.1-41) PPV 79% (62-90)	<0.001
M	Fibrinogen [g/l]	**Barber, Langhorne 2004 (4)**	EPSS, 72 hours	219	3.97 (3.50-5.02)	3.9 (3.16-4.54)	-	-	-	-	0.079
		Castillo 2004 (79)	CSS 1- 48 hours	300	3.56 (3.22-4.15)	3.48 (3.16-4.12)	-	-	-	-	-
		Yang 2010 (35)	EPSS, 72 hours	2511	-	-	>4.0	72 (19.83%)	640 (29.75%)	-	-
N	Haematocrit [%]	Alvarez 2004 (36)	CSS 1- 72 hours	100	42 (40-44)	42 (39-45)	-	-	-	-	0.565
		Barber, Langhorne 2004 (4)	EPSS, 72 hours	219	40 (37-43)	40 (36-43)	-	-	-	-	0.467
O	Plasma iron [ug/ml]	Davalos 2000 (46)	CSS 1- 48 hours	100	1.2 (0.3-9.1)	1.3 (0.2-3.6)					0.389
P	CSF iron [ng/ml]	Davalos 2000 (46)	CSS 1- 48 hours	100	0.06 (0.01-02)	0.05 (0.01-0.2)	-	-	-	-	0.087
Q	Plasma viscosity [mPa.s]	Barber, Langhorne 2004 (4)	EPSS, 72 hours	219	1.32 (1.21-1.38)	1.26 (1.20-1.34)	-	-	-	-	0.066
R	Platelets [x10^9/l]	Zhang 2016 (78)	NIHSS 2+ or motor 1+ 7 days	208	186 (156-228)	190 (145-210)	-	-	-	-	0.817
S	PRCP [U/l]	Kehoe 2015 (51)	CSS 1- 72 hours	50	0.99 ± 0.24	0.97 ± 0.21	-	-	-	-	0.82
T	proCPU change [U/l]	Brouns 2010 (8)	EPSS 72 hours	157	147 ± 179	36 ± 114	-	-	-	-	<0.001
U	Prothrombin fragment 1&2 [nmol/l]	Krarup 2011 (21)	SSS 3+ 48 hours	382	1.9 ± 1.6	1.9 ± 1.7	-	-	-	-	0.72
V	Prothrombin time [seconds]	Cai 2013 (84)	NIHSS 4+ 24 hours	112	16.4 ± 2.2	16.4 ± 2.7	-	-	-	-	NS
W	Soluble fibrin monomer	Krarup 2011 (21)	SSS 3+ 48 hours	382	12.6 ± 2.7	12.1 ± 3.5	-	-	-	-	0.86

X	Thrombin time	Cai 2013 (84)	NIHSS 4+ 24 hours	112	16.4 ± 2.2	16.4 ± 2.7	-	-	-	-	NS
Y	Thrombin-antithrombin III complex [mg/ml]	Barber, Langhorne 2004 (4)	EPSS, 72 hours	219	5.28 (3.90-8.46)	4.07 (3.28-6.25)	-	-	-	-	0.009
		Matsumoto 2004 (59)	NIHSS 2+ 7 days	46	2.9 ± 2.3	5.9 ± 11	-	-	-	-	0.55
Z	tPa antigen [ng/ml]	Barber, Langhorne 2004 (4)	EPSS, 72 hours	219	12.7 (8.9-18.0)	11 (8.2-15.2)	-	-	-	-	0.102
AA	vWF [IU/dl]	Barber, Langhorne 2004 (4)	EPSS, 72 hours	219	216 (178-273)	198 (157-244)	-	-	-	-	0.045

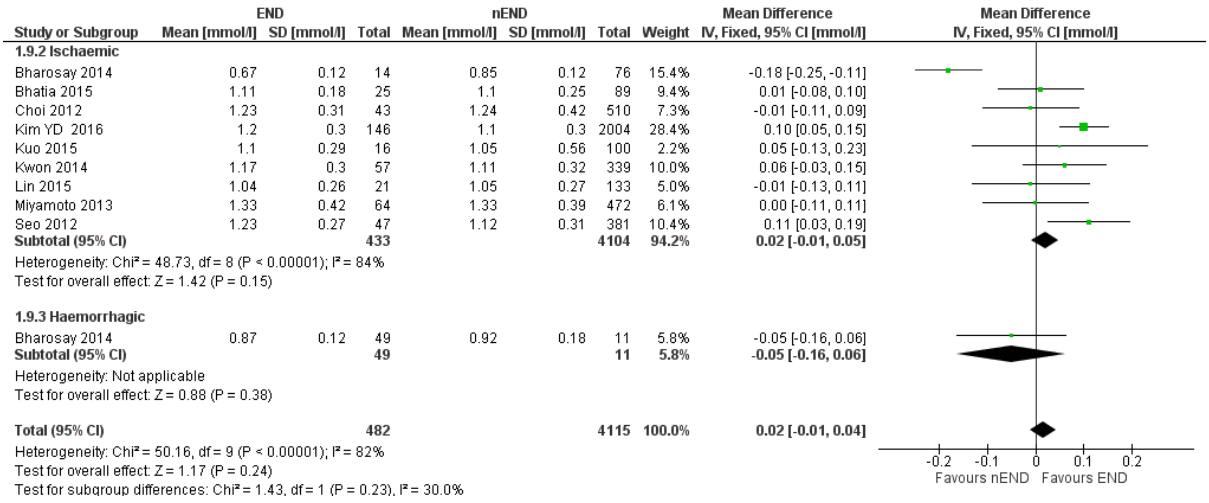
Appendix 8 Glucose [mmol/l] (3, 5, 11, 12, 15, 17, 19, 21-23, 27-30, 38, 45-47, 49, 52, 54-56, 59, 60, 62, 66, 75, 84, 86, 87)



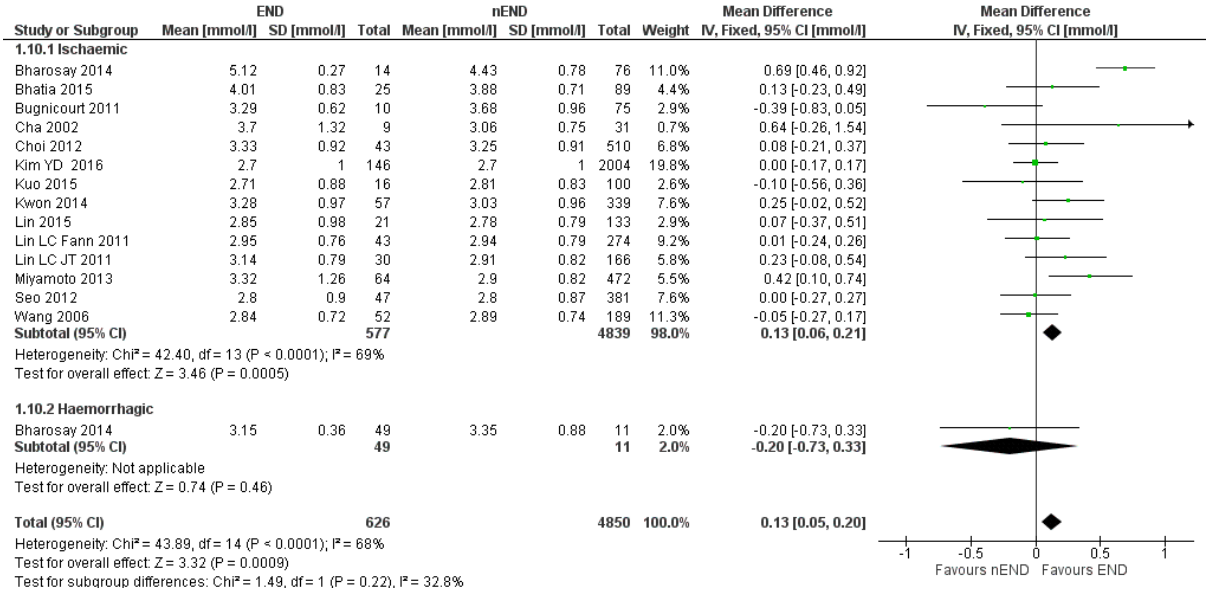
Appendix 9 HbA1c [%] (5, 14, 22, 23, 27, 55, 60, 66)



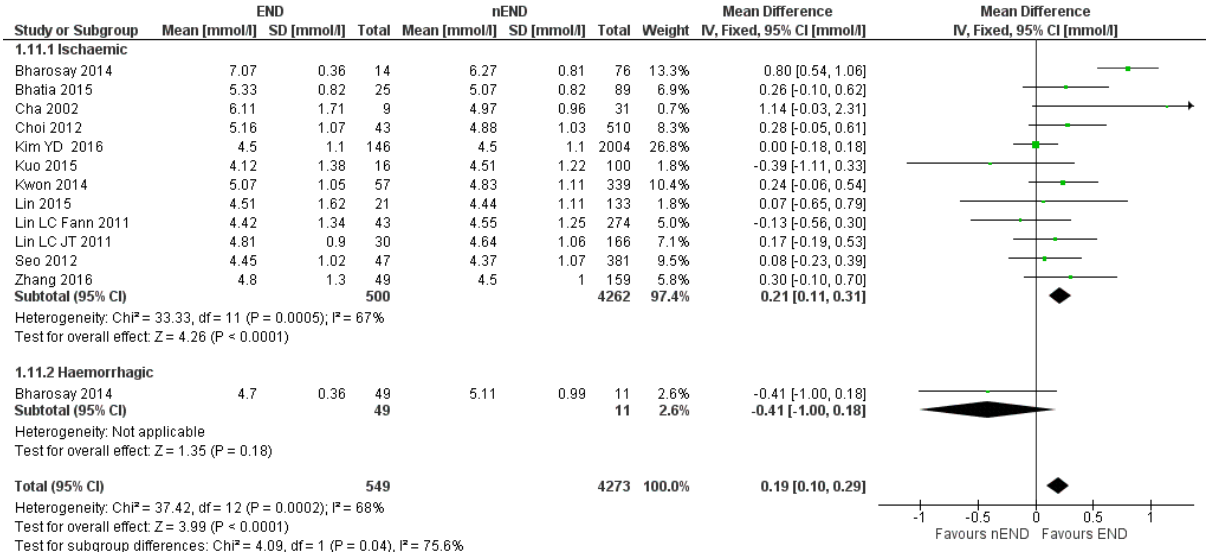
Appendix 10 HDL [mmol/l] (5, 16, 20, 39, 53, 55, 57, 60, 66)



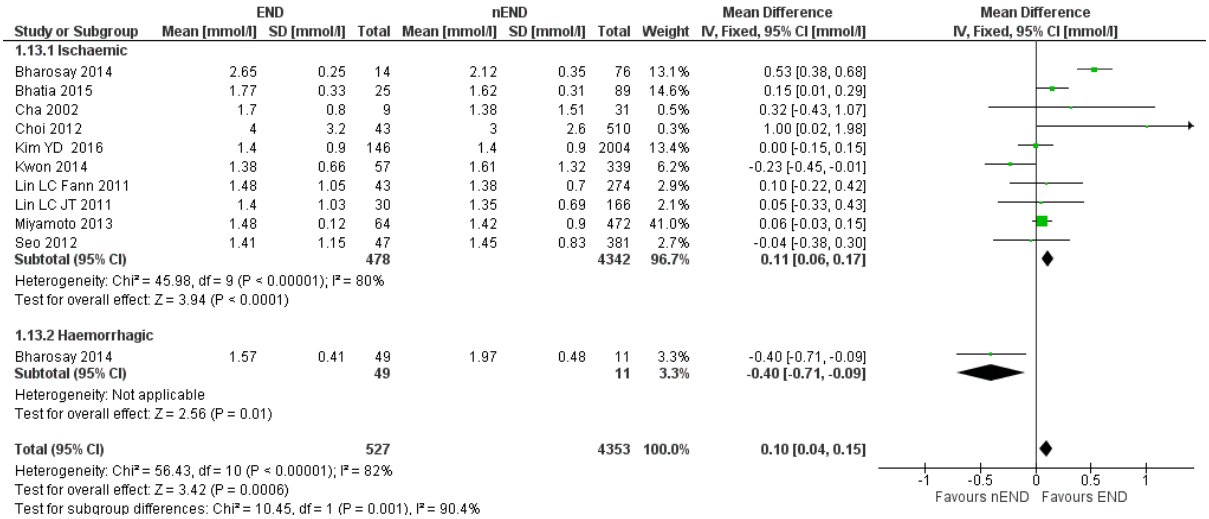
Appendix 11 LDL (5, 11, 14, 16, 20, 22, 23, 39, 53, 55, 57, 60, 66, 78)



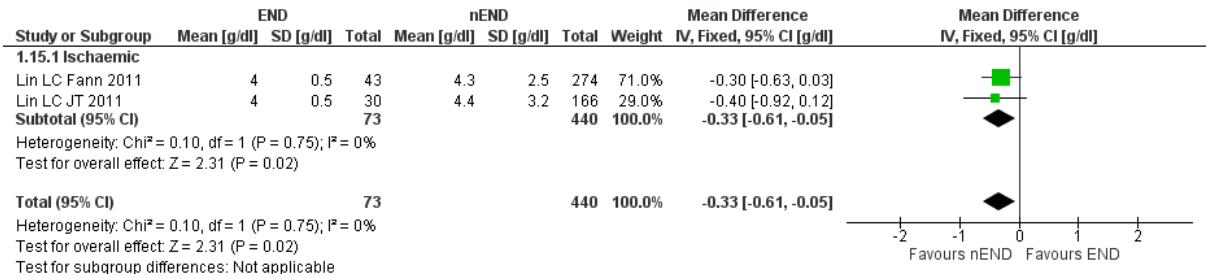
Appendix 12 Total cholesterol [mmol/l] (5, 14, 16, 20, 22, 23, 39, 53, 55, 57, 66, 78)



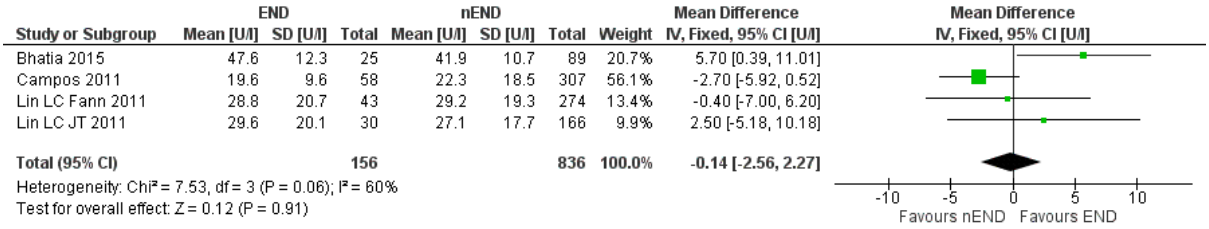
Appendix 13 Triglycerides [mmol/l] (5, 14, 16, 20, 22, 23, 39, 55, 60, 66)



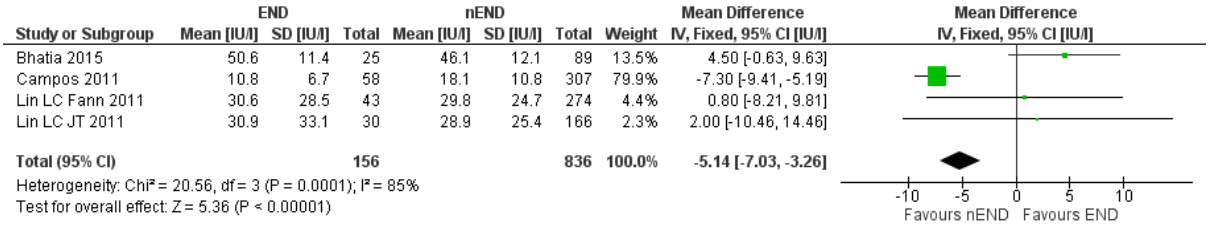
Appendix 14 Albumin [g/dl] (22, 23)



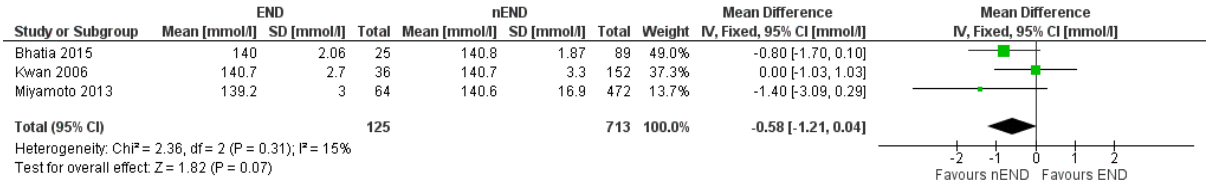
Appendix 15 ALT [U/l] (5, 12, 22, 23)



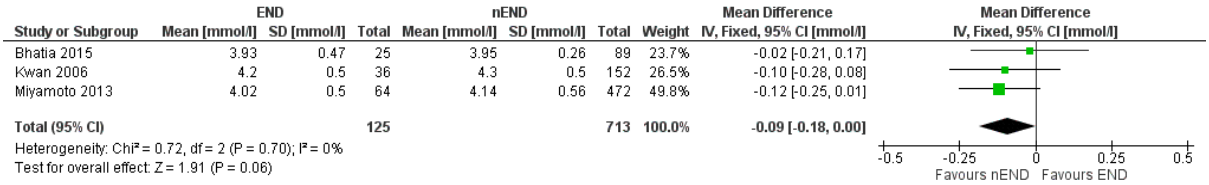
Appendix 16 AST [U/l] (5, 12, 22, 23)



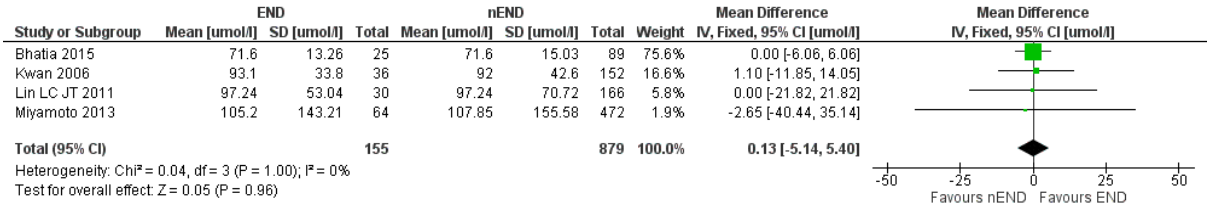
Appendix 17 Sodium [mmol/l] (5, 54, 60)



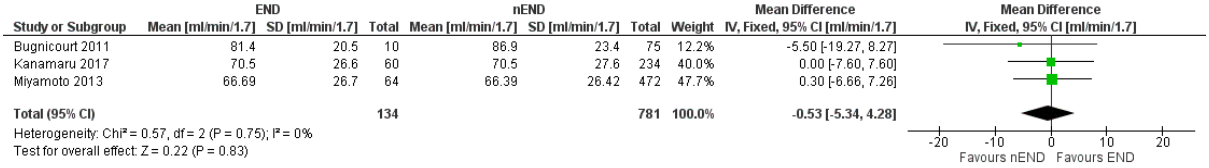
Appendix 18 Potassium [mmol/l] (5, 54, 60)



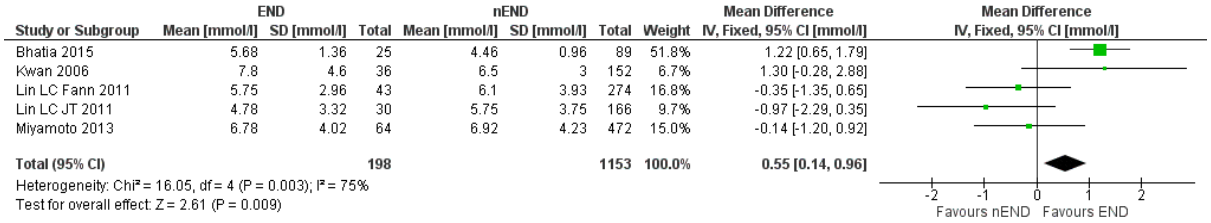
Appendix 19 Creatinine [µmol/l] (5, 23, 54, 60)



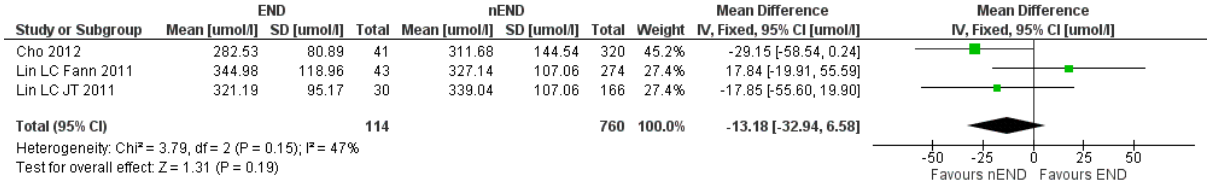
Appendix 20 eGFR [ml/ml/1.7m^3] (11, 49, 60)



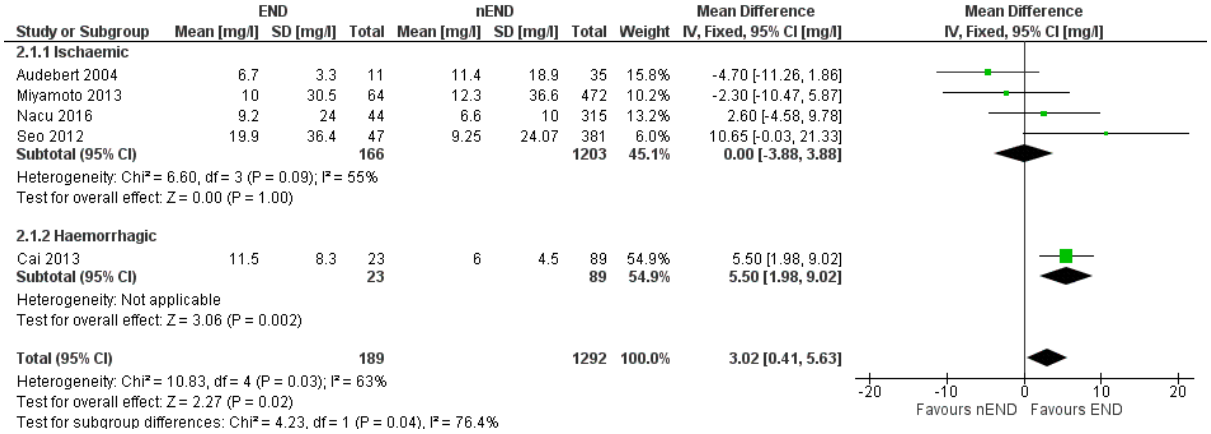
Appendix 21 Urea [mmol/l] (5, 22, 23, 54, 60)



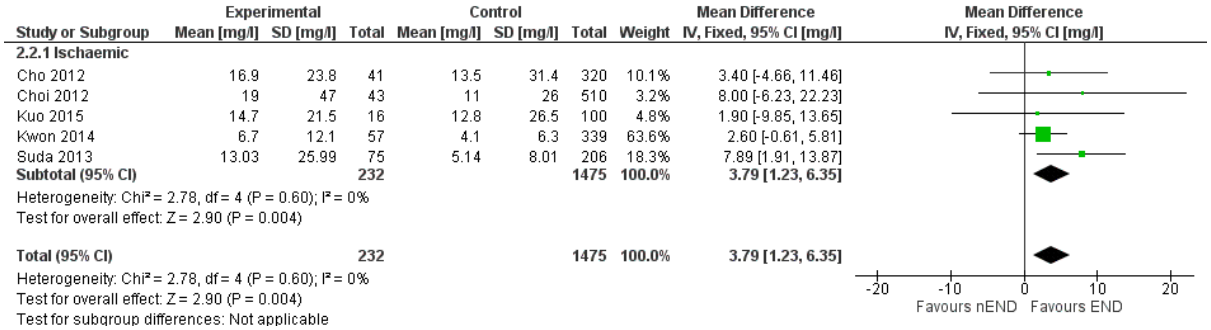
Appendix 22 Uric acid [µmol/l] (15, 22, 23)



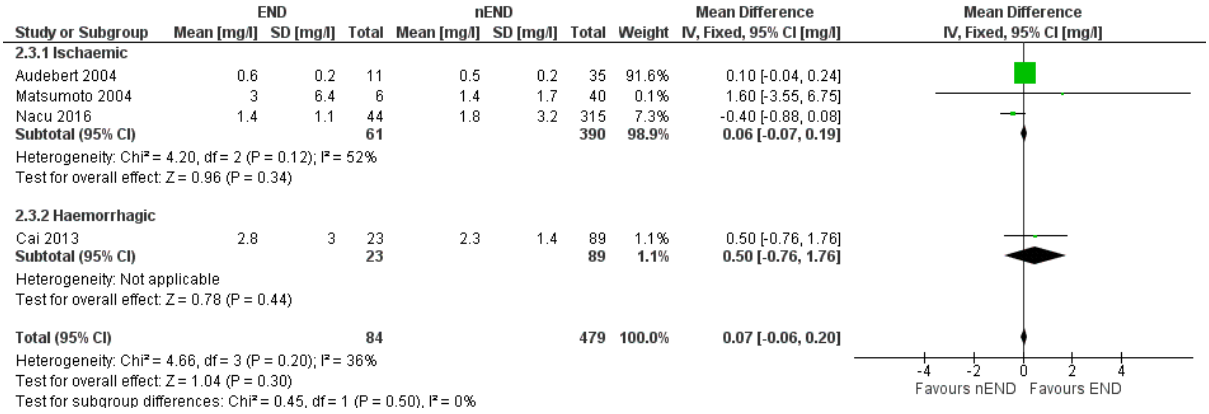
Appendix 23 CRP (28, 38, 60, 66)



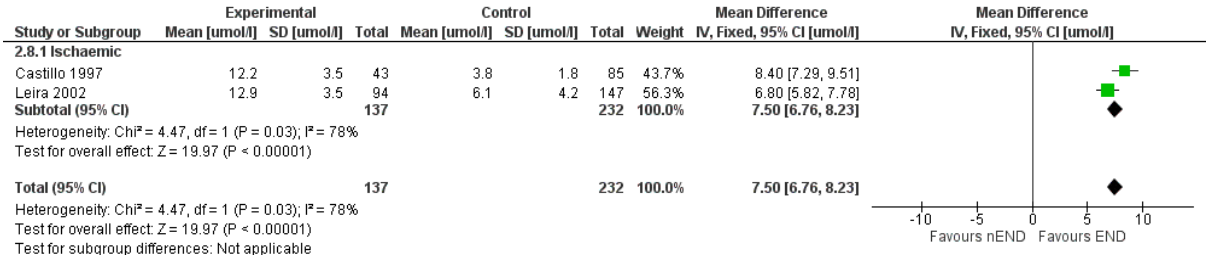
Appendix 24 hsCRP [mg/l] (15, 16, 53, 55, 70)



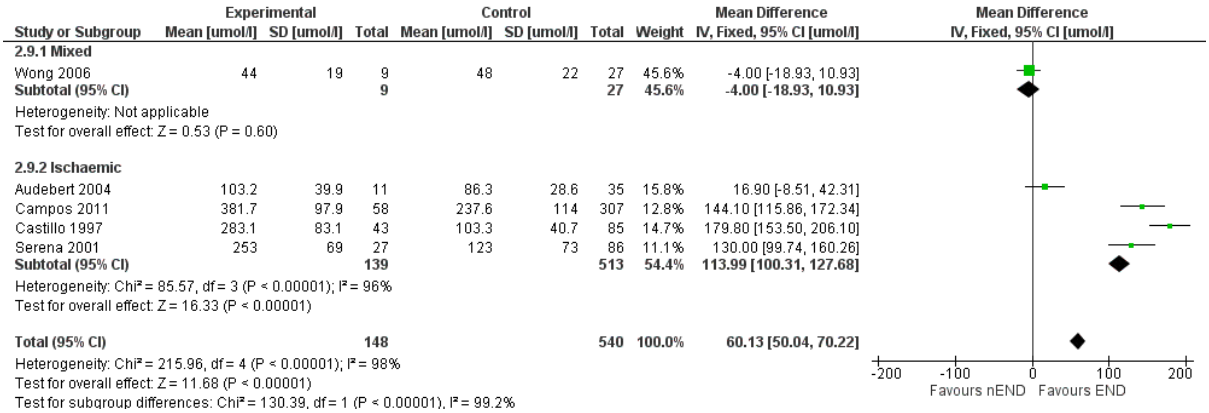
Appendix 25 D-dimer [mg/l] (28, 38, 59)



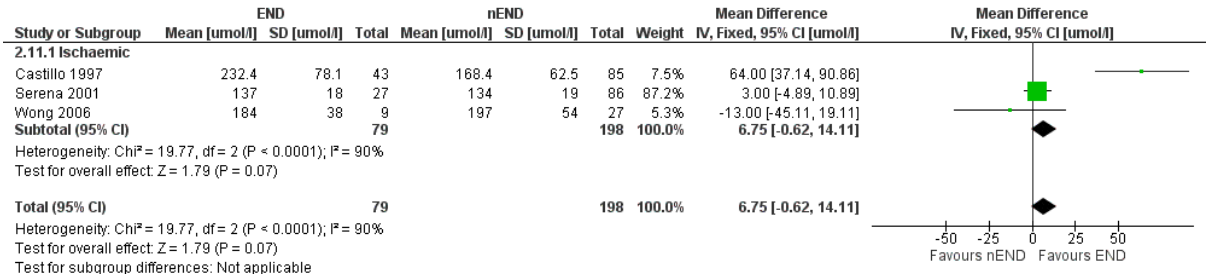
Appendix 26 Glutamate (CSF) [µmol/l] (42)



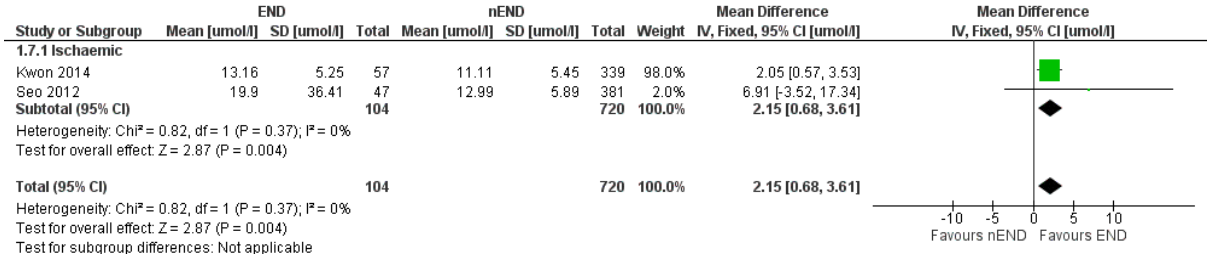
Appendix 27 Glutamate (plasma) (12, 38, 42, 67, 77)



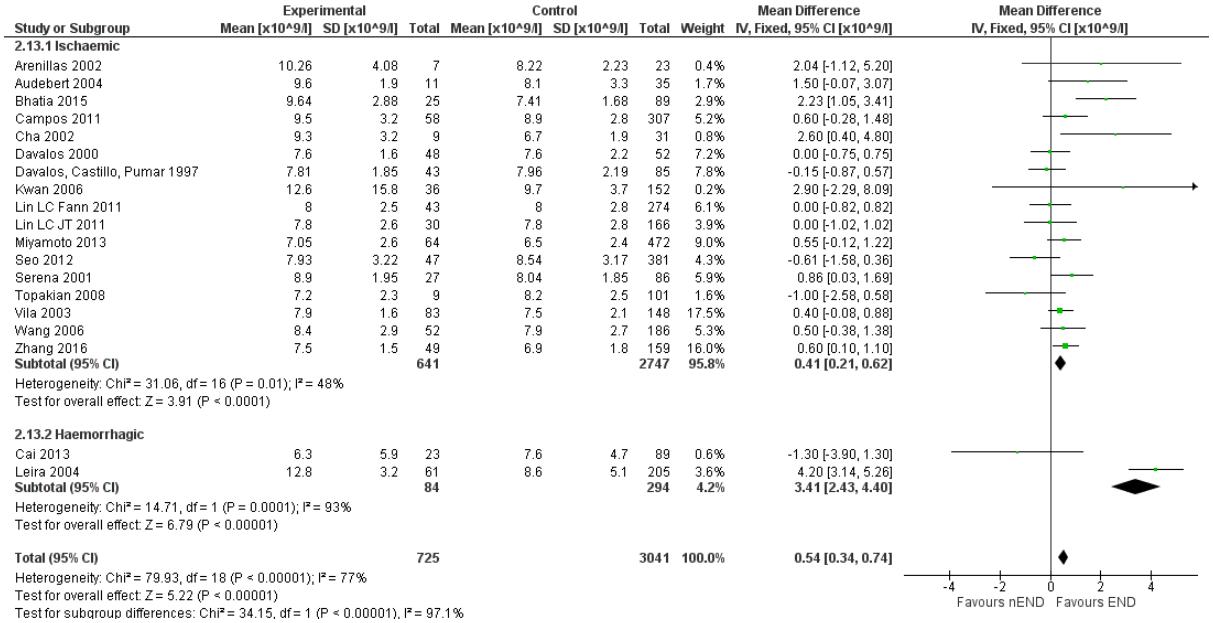
Appendix 28 Glycine (plasma) [µmol/l] (42, 67, 77)



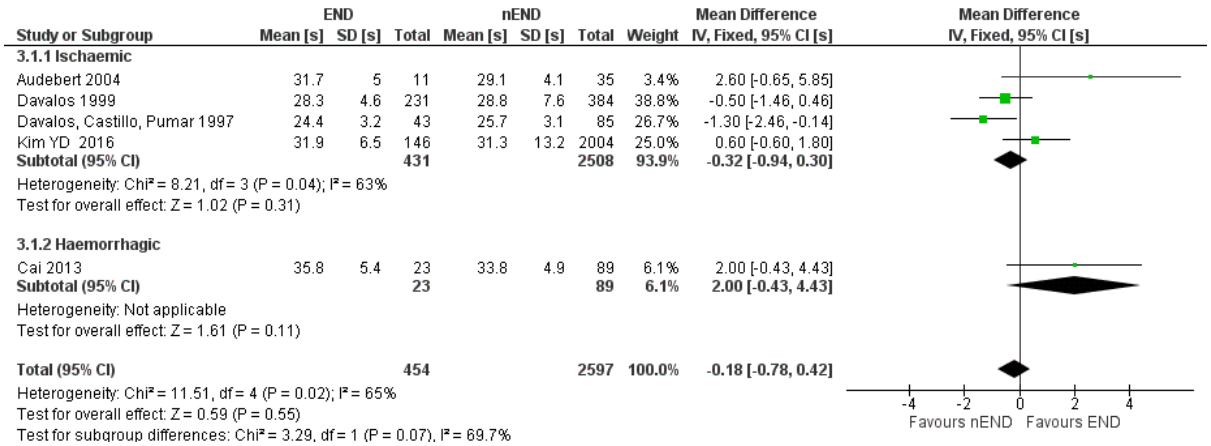
Appendix 29 Homocysteine [µmol/l] (55, 66)



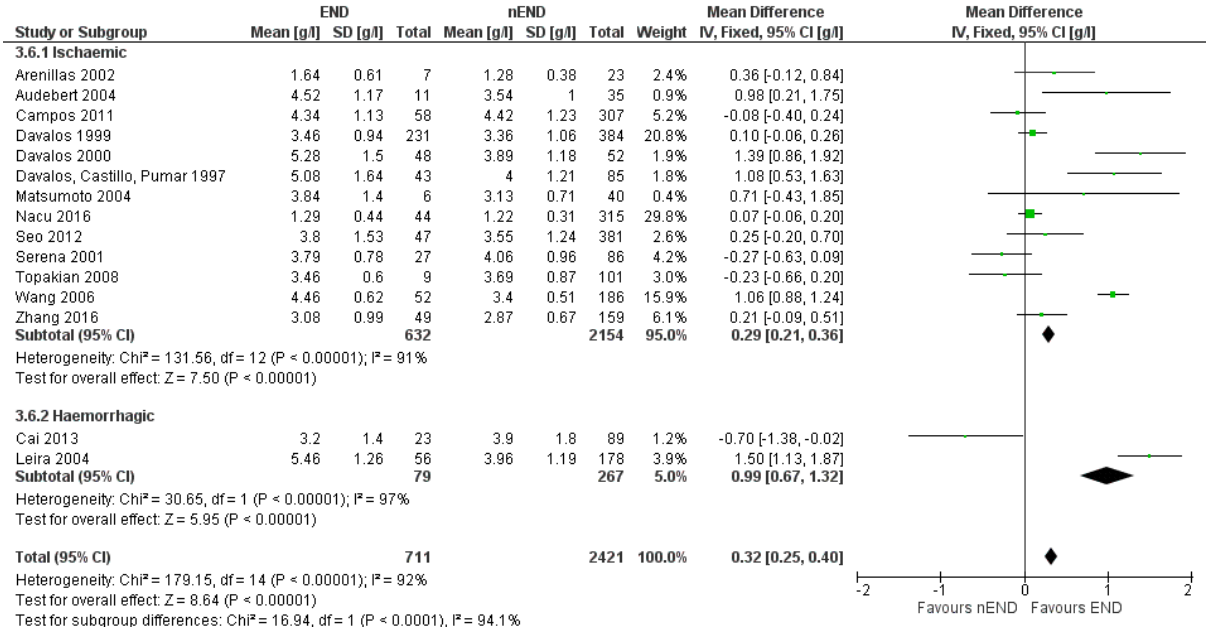
Appendix 30 Leucocyte count [x10^9/l] (3, 5, 12, 14, 22, 23, 32, 38, 46, 47, 54, 60, 66, 67, 74, 75, 78, 81, 84)



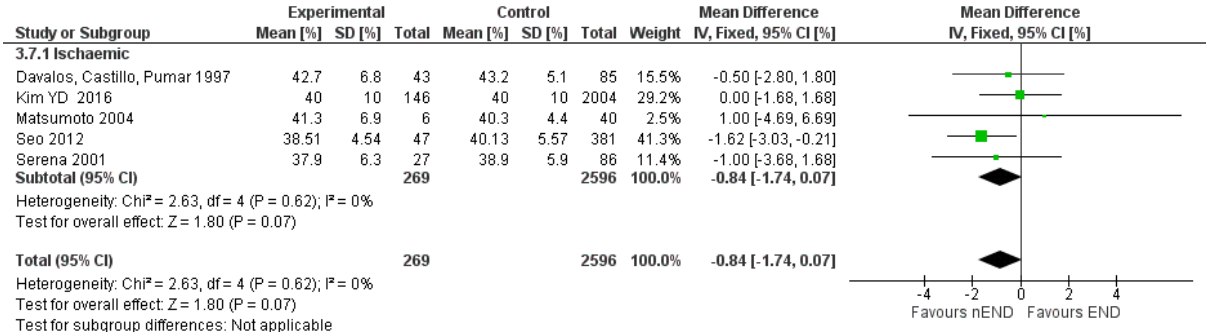
Appendix 31 APTT [s] (20, 38, 47, 84, 86)



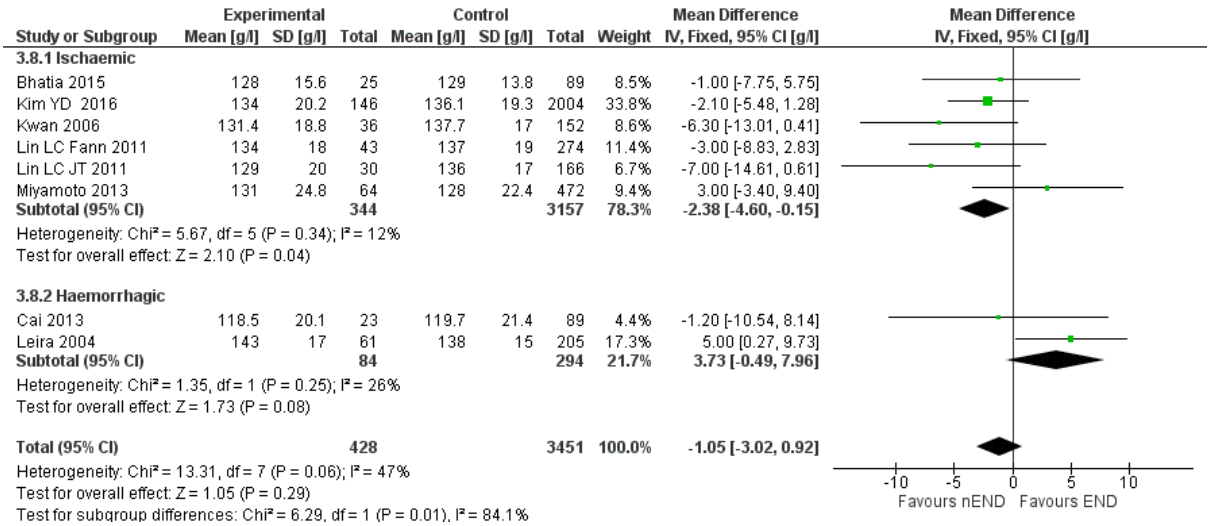
Appendix 32 Fibrinogen [g/l] (2, 12, 28, 32, 38, 46, 47, 59, 66, 67, 75, 78, 81, 84, 86)



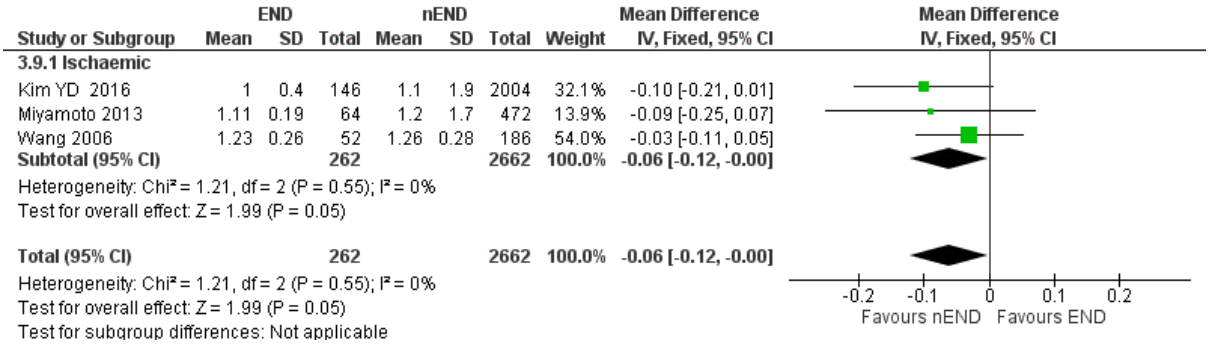
Appendix 33 3.7 Haematocrit [%] (20, 47, 59, 66, 67)



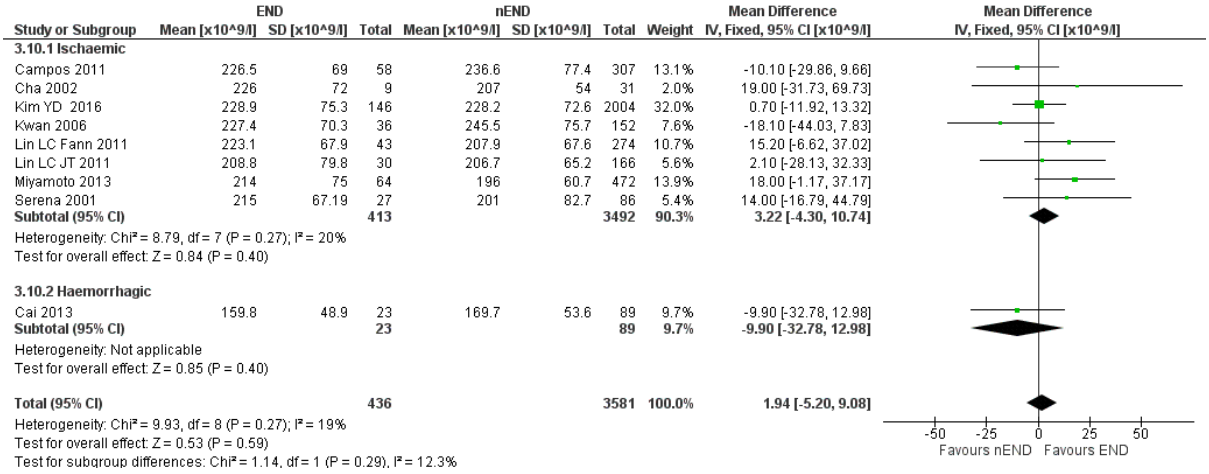
Appendix 34 3.8 Haemoglobin [g/l] (5, 11, 20, 22, 23, 54)



Appendix 35 3.9 INR [ratio] (20, 60, 75)



Appendix 36 3.10 Platelets [x10^9/l] (12, 14, 20, 22, 23, 54, 60, 67, 84)



1. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. BMJ. 2009;339.

2. Alvarez-Sabín J, Molina CA, Montaner J, Arenillas JF, Huertas R, Ribo M, et al. Effects of admission hyperglycemia on stroke outcome in reperfused tissue plasminogen activator–treated patients. Stroke. 2003;34(5):1235-40.

3. Arenillas JF, Rovira A, Molina CA, Grive E, Montaner J, Alvarez-Sabin J. Prediction of early neurological deterioration using diffusion- and perfusion-weighted imaging in hyperacute middle cerebral artery ischemic stroke. Stroke. 2002;33(9):2197-203.

4. Barber M, Langhorne P, Rumley A, Lowe GD, Stott DJ. Hemostatic function and progressing ischemic stroke: D-dimer predicts early clinical progression. Stroke. 2004;35(6):1421-5.

5. Bhatia K, Mohanty S, Tripathi BK, Gupta B, Mittal MK. Predictors of early neurological deterioration in patients with acute ischaemic stroke with special reference to blood urea nitrogen (BUN)/creatinine ratio & urine specific gravity. Indian Journal of Medical Research. 2015;141(3):299-307.

6. Brouns R, Wauters A, Van De Vijver G, De Surgeloose D, Sheorajpanday R, De Deyn PP. Decrease in uric acid in acute ischemic stroke correlates with stroke severity, evolution and outcome. Clinical chemistry and laboratory medicine. 2010;48(3):383-90.

7. Brouns R, Van Hemelrijck A, Drinkenburg WH, Van Dam D, De Surgeloose D, De Deyn PP. Excitatory amino acids and monoaminergic neurotransmitters in cerebrospinal fluid of acute ischemic stroke patients. Neurochemistry International. 2010;56(8):865-70.

8. Brouns R, Heylen E, Willemse JL, Sheorajpanday R, De Surgeloose D, Verkerk R, et al. The decrease in procarboxypeptidase U (TAFI) concentration in acute ischemic stroke correlates with stroke severity, evolution and outcome. Journal of Thrombosis & Haemostasis. 2010;8(1):75-80.
9. Brouns R, Wauters A, De Surgeloose D, Marien P, De Deyn PP. Biochemical markers for blood-brain barrier dysfunction in acute ischemic stroke correlate with evolution and outcome. European Neurology. 2011;65(1):23-31.
10. Brouns R, Sheorajpanday R, Wauters A, De Surgeloose D, Marien P, De Deyn PP. Evaluation of lactate as a marker of metabolic stress and cause of secondary damage in acute ischemic stroke or TIA. Clinica Chimica Acta. 2008;397(1):27-31.
11. Bugnicourt JM, Roussel B, Garcia PY, Canaple S, Lamy C, Godefroy O. Aspirin non-responder status and early neurological deterioration: a prospective study. Clinical Neurology & Neurosurgery. 2011;113(3):196-201.
12. Campos F, Rodriguez-Yanez M, Castellanos M, Arias S, Perez-Mato M, Sobrino T, et al. Blood levels of glutamate oxaloacetate transaminase are more strongly associated with good outcome in acute ischaemic stroke than glutamate pyruvate transaminase levels. Clinical Science. 2011;121(1):11-7.
13. Castellanos M, Sobrino T, Pedraza S, Moldes O, Pumar JM, Silva Y, et al. High plasma glutamate concentrations are associated with infarct growth in acute ischemic stroke. Neurology. 2008;71(23):1862-8.
14. Cha JK, Jeong MH, Kim EK, Lim YJ, Ha BR, Kim SH, et al. Surface expression of P-selectin on platelets is related with clinical worsening in acute ischemic stroke. Journal of Korean Medical Science. 2002;17(6):811-6.
15. Cho BH, Kim JT, Chang J, Choi KH, Nam TS, Choi SM, et al. Early clinical implications of microalbuminuria in patients with acute ischaemic stroke. Postgrad Med J. 2012;88(1045):632-8.
16. Choi KH, Park MS, Kim JT, Chang J, Nam TS, Choi SM, et al. Serum triglyceride level is an important predictor of early prognosis in patients with acute ischemic stroke. Journal of the Neurological Sciences. 2012;319(1):111-6.
17. Cuadrado-Godia E, Jimena S, Ois A, Rodriguez-Campello A, Giralt-Steinhauer E, Soriano-Tarraga C, et al. Factors associated with early outcome in patients with large-vessel carotid strokes. Journal of Neurology, Neurosurgery & Psychiatry. 2013;84(3):305-9.
18. Garcia-Berrocoso T, Giralt D, Bustamante A, Llombart V, Rubiera M, Penalba A, et al. Role of beta-defensin 2 and interleukin-4 receptor as stroke outcome biomarkers. Journal of Neurochemistry. 2014;129(3):463-72.
19. Kim JT, Kim HJ, Yoo SH, Park MS, Kwon SU, Cho KH, et al. MRI findings may predict early neurologic deterioration in acute minor stroke or transient ischemic attack due to intracranial atherosclerosis. European Neurology. 2010;64(2):95-100.
20. Kim YD, Choi HY, Jung YH, Yoo J, Nam HS, Song D, et al. The Ischemic Stroke Predictive Risk Score Predicts Early Neurological Deterioration. Journal of Stroke & Cerebrovascular Diseases. 2016;25(4):819-24.
21. Krarup LH, Sandset EC, Sandset PM, Berge E. D-dimer levels and stroke progression in patients with acute ischemic stroke and atrial fibrillation. Acta Neurologica Scandinavica. 2011;124(1):40-4.
22. Lin LC, Fann WC, Chou MH, Chen HW, Su YC, Chen JC. Urine specific gravity as a predictor of early neurological deterioration in acute ischemic stroke. Medical Hypotheses. 2011;77(1):11-4.
23. Lin LC, Yang JT, Weng HH, Hsiao CT, Lai SL, Fann WC. Predictors of early clinical deterioration after acute ischemic stroke. American Journal of Emergency Medicine. 2011;29(6):577-81.
24. Llombart V, Dominguez C, Bustamante A, Rodriguez-Sureda V, Martin-Gallan P, Vilches A, et al. Fluorescent molecular peroxidation products: a prognostic biomarker of early neurologic deterioration after thrombolysis. Stroke. 2014;45(2):432-7.
25. Marousi S, Ellul J, Antonacopoulou A, Gogos C, Papathanasopoulos P, Karakantza M. Functional polymorphisms of interleukin 4 and interleukin 10 may predict evolution and functional outcome of an ischaemic stroke. European Journal of Neurology. 2011;18(4):637-43.

26. Marousi SG, Theodorou GL, Karakantza M, Zampakis P, Papathanasopoulos P, Ellul J. Acute post-stroke adiponectin in relation to stroke severity, progression and 6 month functional outcome. Neurological Research. 2010;32(8):841-4.
27. Mori M, Naganuma M, Okada Y, Hasegawa Y, Shiokawa Y, Nakagawara J, et al. Early neurological deterioration within 24 hours after intravenous rt-PA therapy for stroke patients: the Stroke Acute Management with Urgent Risk Factor Assessment and Improvement rt-PA Registry. Cerebrovascular Diseases. 2012;34(2):140-6.
28. Nacu A, Bringeland GH, Khanevski A, Thomassen L, Waje-Andreassen U, Naess H. Early neurological worsening in acute ischaemic stroke patients. Acta Neurologica Scandinavica. 2016;133(1):25-9.
29. Roquer J, Rodriguez-Campello A, Gomis M, Jimenez-Conde J, Cuadrado-Godia E, Vivanco R, et al. Acute stroke unit care and early neurological deterioration in ischemic stroke. Journal of Neurology. 2008;255(7):1012-7.
30. Saqqur M, Molina CA, Salam A, Siddiqui M, Ribo M, Uchino K, et al. Clinical deterioration after intravenous recombinant tissue plasminogen activator treatment. Stroke. 2007;38(1):69-74.
31. Seners P, Hurford R, Tisserand M, Turc G, Legrand L, Naggara O, et al. Is Unexplained Early Neurological Deterioration after Intravenous Thrombolysis Associated with Thrombus Extension? Stroke. 2017;48(2):348-52.
32. Topakian R, Strasak AM, Nussbaumer K, Haring HP, Aichner FT. Prognostic value of admission C-reactive protein in stroke patients undergoing iv thrombolysis. Journal of neurology. 2008;255(8):1190-6.
33. Urra X, Villamor N, Amaro S, Gomez-Choco M, Obach V, Oleaga L, et al. Monocyte subtypes predict clinical course and prognosis in human stroke. Journal of Cerebral Blood Flow & Metabolism. 2009;29(5):994-1002.
34. Wang CL, Lin HY, Xu JW, Jiang FF, Yang M, Wang JH, et al. Blood levels of adrenomedullin on admission predict outcomes after acute intracerebral hemorrhage. Peptides. 2014;54.
35. Yang SS, Teng D, You DY, Su ZQ, Li F, Zhao JY. Association between fifteen risk factors and progressing ischemic stroke in the Han population of northeast China. Chinese Medical Journal. 2010;123(11):1392-6.
36. Alvarez FJ, Segura T, Castellanos M, Leira R, Blanco M, Castillo J, et al. Cerebral hemodynamic reserve and early neurologic deterioration in acute ischemic stroke. Journal of Cerebral Blood Flow & Metabolism. 2004;24(11):1267-71.
37. Armengou A, Hurtado O, Leira R, Obon M, Pascual C, Moro MA, et al. L-arginine levels in blood as a marker of nitric oxide-mediated brain damage in acute stroke: a clinical and experimental study. Journal of Cerebral Blood Flow & Metabolism. 2003;23(8):978-84.
38. Audebert HJ, Pellkofer TS, Wimmer ML, Haberl RL. Progression in lacunar stroke is related to elevated acute phase parameters. European Neurology. 2004;51(3):125-31.
39. Bharosay A, Bharosay VV, Bandyopadhyay D, Sodani A, Varma M, Baruah H. Effect of lipid profile upon prognosis in ischemic and haemorrhagic cerebrovascular stroke. Indian Journal of Clinical Biochemistry. 2014;29(3):372-6.
40. Blanco M, Moro MA, Davalos A, Leira R, Castellanos M, Serena J, et al. Increased plasma levels of 15-deoxyDelta prostaglandin J2 are associated with good outcome in acute atherothrombotic ischemic stroke. Stroke. 2005;36(6):1189-94.
41. Castellanos M, Castillo J, Garcia MM, Leira R, Serena J, Chamorro A, et al. Inflammation-mediated damage in progressing lacunar infarctions: a potential therapeutic target. Stroke. 2002;33(4):982-7.
42. Castillo J, Davalos A, Noya M. Progression of ischaemic stroke and excitotoxic aminoacids. Lancet. 1997;349(9045):79-83.
43. Castillo J, Rama R, Davalos A. Nitric oxide-related brain damage in acute ischemic stroke. Stroke. 2000;31(4):852-7.

44. Christensen H, Boysen G, Johannesen HH, Christensen E, Bendtzen K. Deteriorating ischaemic stroke. cytokines, soluble cytokine receptors, ferritin, systemic blood pressure, body temperature, blood glucose, diabetes, stroke severity, and CT infarction-volume as predictors of deteriorating ischaemic stroke. Journal of the Neurological Sciences. 2002;201(1):1-7.
45. Chung JW, Kim N, Kang J, Park SH, Kim WJ, Ko Y, et al. Blood pressure variability and the development of early neurological deterioration following acute ischemic stroke. Journal of Hypertension. 2015;33(10):2099-106.
46. Davalos A, Castillo J, Marrugat J, Fernandez-Real JM, Armengou A, Cacabelos P, et al. Body iron stores and early neurologic deterioration in acute cerebral infarction. Neurology. 2000;54(8):1568-74.
47. Davalos A, Castillo J, Pumar JM, Noya M. Body temperature and fibrinogen are related to early neurological deterioration in acute ischemic stroke. Cerebrovascular Diseases. 1997;7(2):64-9.
48. Davalos A, Castillo J, Serena J, Noya M. Duration of glutamate release after acute ischemic stroke. Stroke. 1997;28(4):708-10.
49. Kanamaru T, Suda S, Muraga K, Okubo S, Watanabe Y, Tsuruoka S, et al. Albuminuria predicts early neurological deterioration in patients with acute ischemic stoke. Stroke. 2017;0:American Heart Association/American Stroke Association 2016 International Stroke Conference and State-of-the-Science Stroke Nursing Symposium. Los Angeles, CA United States. Conference Start: 20160216. Conference End: 9. Conference Publication: (var.pagings). 47 (no pagination).
50. Kawano T, Miyashita K, Takeuchi M, Metoki N, Akaiwa Y, Yamamoto Y, et al. The importance of blood biomarkers in penetrating artery territory infarction; a prospective multicenter observational study. Stroke. 2016;0:American Heart Association/American Stroke Association 2015 International Stroke Conference and State-of-the-Science Stroke Nursing Symposium. Nashville, TN United States. Conference Start: 20150211. Conference End: 3. Conference Publication: (var.pagings). 46 (no pagination).
51. Kehoe K, Brouns R, Verkerk R, Engelborghs S, De Deyn PP, Hendriks D, et al. Prolyl carboxypeptidase activity decline correlates with severity and short-term outcome in acute ischemic stroke. Neurochemical Research. 2015;40(1):81-8.
52. Kim JM, Moon J, Ahn SW, Shin HW, Jung KH, Park KY. The Etiologies of Early Neurological Deterioration after Thrombolysis and Risk Factors of Ischemia Progression. Journal of Stroke & Cerebrovascular Diseases. 2016;25(2):383-8.
53. Kuo CY, Lin CH, Kuo YW, Hsu HL, Lin YH, Wu CY, et al. Factor VIII levels are associated with ischemic stroke, stroke subtypes and neurological worsening. Current Neurovascular Research. 2015;12(1):85-90.
54. Kwan J, Hand P. Early neurological deterioration in acute stroke: clinical characteristics and impact on outcome. Qjm. 2006;99(9):625-33.
55. Kwon HM, Lee YS, Bae HJ, Kang DW. Homocysteine as a predictor of early neurological deterioration in acute ischemic stroke. Stroke. 2014;45(3):871-3.
56. Leira R, Davalos A, Aneiros A, Serena J, Pumar JM, Castillo J. Headache as a surrogate marker of the molecular mechanisms implicated in progressing stroke. Cephalalgia. 2002;22(4):303-8.
57. Lin CH, Kuo YW, Kuo CY, Hsu CY, Hsu HL, Lin YH, et al. Shortened Activated Partial Thromboplastin Time is Associated with Acute Ischemic Stroke, Stroke Severity, and Neurological Worsening. Journal of Stroke and Cerebrovascular Diseases. 2015;24(10):2270-6.
58. Liu D, Sun W, Scalzo F, Xiong Y, Zhang X, Qiu Z, et al. Early Magnetic Resonance Imaging Predicts Early Neurological Deterioration in Acute Middle Cerebral Artery Minor Stroke. Journal of stroke and cerebrovascular diseases : the official journal of National Stroke Association. 2016;25(2):469-74.
59. Matsumoto N, Kimura K, Yokota C, Yonemura K, Wada K, Uchino M, et al. Early neurological deterioration represents recurrent attack in acute small non-lacunar stroke. Journal of the Neurological Sciences. 2004;217(2):151-5.

60. Miyamoto N, Tanaka Y, Ueno Y, Kawamura M, Shimada Y, Tanaka R, et al. Demographic, clinical, and radiologic predictors of neurologic deterioration in patients with acute ischemic stroke. Journal of Stroke & Cerebrovascular Diseases. 2013;22(3):205-10.
61. Nam KW, Kim CK, Kim TJ, An SJ, Demchuk AM, Kim Y, et al. D-dimer as a predictor of early neurologic deterioration in cryptogenic stroke with active cancer. European Journal of Neurology. 2017;24(1):205-11.
62. Ogata T, Yasaka M, Wakugawa Y, Ibayashi S, Okada Y. Predisposing factors for acute deterioration of minor ischemic stroke. Journal of the Neurological Sciences. 2009;287(1):147-50.
63. Ong CT, Wu CS. Neurological deterioration in patients with first-ever ischemic stroke. Acta Neurologica Taiwanica. 2007;16(3):143-9.
64. Protti GG, Gagliardi RJ, Forte WC, Sprovieri SR. Interleukin-10 may protect against progressing injury during the acute phase of ischemic stroke. Arquivos de Neuro-Psiquiatria. 2013;71(11):846-51.
65. Saji N, Kimura K, Kawarai T, Shimizu H, Kita Y. Arterial stiffness and progressive neurological deficit in patients with acute deep subcortical infarction. Stroke. 2012;43(11):3088-90.
66. Seo WK, Seok HY, Kim JH, Park MH, Yu SW, Oh K, et al. C-reactive protein is a predictor of early neurologic deterioration in acute ischemic stroke. Journal of Stroke & Cerebrovascular Diseases. 2012;21(3):181-6.
67. Serena J, Leira R, Castillo J, Pumar JM, Castellanos M, Davalos A. Neurological deterioration in acute lacunar infarctions: the role of excitatory and inhibitory neurotransmitters. Stroke. 2001;32(5):1154-61.
68. Siegler JE, Boehme AK, Albright KC, Bdeir S, Kar AK, Myers L, et al. Acute decrease in serum magnesium level after ischemic stroke may not predict decrease in neurologic function. Journal of Stroke & Cerebrovascular Diseases. 2013;22(8):e516-21.
69. Siegler JE, Boehme AK, Albright KC, George AJ, Monlezun DJ, Beasley TM, et al. A proposal for the classification of etiologies of neurologic deterioration after acute ischemic stroke. Journal of Stroke & Cerebrovascular Diseases. 2013;22(8):e549-56.
70. Suda S, Katsumata T, Okubo S, Kanamaru T, Suzuki K, Watanabe Y, et al. Low serum n-3 polyunsaturated fatty acid/n-6 polyunsaturated fatty acid ratio predicts neurological deterioration in Japanese patients with acute ischemic stroke. Cerebrovascular Diseases. 2013;36(5):388-93.
71. Thampy A, Pais CC. Early Clinical Implications of Microalbuminuria in Patients with Acute Ischaemic Stroke. Journal of clinical and diagnostic research : JCDR. 2016;10(9):Oc29-oc31.
72. Umemura T, Senda J, Fukami Y, Mashita S, Kawamura T, Sakakibara T, et al. Impact of albuminuria on early neurological deterioration and lesion volume expansion in lenticulostriate small infarcts. Stroke. 2014;45(2):587-90.
73. Vila N, Castillo J, Davalos A, Chamorro A. Proinflammatory cytokines and early neurological worsening in ischemic stroke. Stroke. 2000;31(10):2325-9.
74. Vila N, Castillo J, Davalos A, Esteve A, Planas AM, Chamorro A. Levels of anti-inflammatory cytokines and neurological worsening in acute ischemic stroke. Stroke. 2003;34(3):671-5.
75. Wang JY, Zhou DH, Li J, Zhang M, Deng J, Gao C, et al. Association of soluble intercellular adhesion molecule 1 with neurological deterioration of ischemic stroke: The Chongqing Stroke Study. Cerebrovascular Diseases. 2006;21(1):67-73.
76. Weimar C, Mieck T, Buchthal J, Ehrenfeld CE, Schmid E, Diener H-C. Neurologic worsening during the acute phase of ischemic stroke. Archives of neurology. 2005;62(3):393-7.
77. Wong PT, Qu K, Chimon GN, Seah AB, Chang HM, Wong MC, et al. High plasma cyst(e)ine level may indicate poor clinical outcome in patients with acute stroke: possible involvement of hydrogen sulfide. Journal of Neuropathology & Experimental Neurology. 2006;65(2):109-15.
78. Zhang X, Sun Z, Ding C, Tang Y, Jiang X, Xie Y, et al. Metabolic Syndrome Augments the Risk of Early Neurological Deterioration in Acute Ischemic Stroke Patients Independent of Inflammatory Mediators: A Hospital-Based Prospective Study. Oxidative medicine & cellular longevity. 2016;2016:8346301.

79. Castillo J, Leira R, Garcia MM, Serena J, Blanco M, Davalos A. Blood pressure decrease during the acute phase of ischemic stroke is associated with brain injury and poor stroke outcome. Stroke. 2004;35(2):520-6.
80. Barber M, Wright F, Stott DJ, Langhorne P. Predictors of early neurological deterioration after ischaemic stroke: a case-control study. Gerontology. 2004;50(2):102-9.
81. Leira R, Davalos A, Silva Y, Gil-Peralta A, Tejada J, Garcia M, et al. Early neurologic deterioration in intracerebral hemorrhage: predictors and associated factors. Neurology. 2004;63(3):461-7.
82. Miyagi T, Koga M, Yamagami H, Okuda S, Okada Y, Kimura K, et al. Reduced estimated glomerular filtration rate affects outcomes 3 months after intracerebral hemorrhage: the stroke acute management with urgent risk-factor assessment and improvement-intracerebral hemorrhage study. Journal of Stroke & Cerebrovascular Diseases. 2015;24(1):176-82.
83. Sun W, Peacock A, Becker J, Phillips-Bute B, Laskowitz DT, James ML. Correlation of leukocytosis with early neurological deterioration following supratentorial intracerebral hemorrhage. Journal of clinical neuroscience : official journal of the Neurosurgical Society of Australasia. 2012;19(8):1096-100.
84. Cai JY, Lu C, Chen MH, Ba HJ, Chen XD, Lin JH, et al. Predictive value of phosphorylated axonal neurofilament subunit H for clinical outcome in patients with acute intracerebral hemorrhage. Clinica Chimica Acta. 2013;424.
85. Kim JT, Heo SH, Choi KH, Nam TS, Choi SM, Lee SH, et al. Clinical Implications of Changes in Individual Platelet Reactivity to Aspirin Over Time in Acute Ischemic Stroke. Stroke. 2015;46(9):2534-40.
86. Davalos A, Toni D, Iweins F, Lesaffre E, Bastianello S, Castillo J. Neurological deterioration in acute ischemic stroke: potential predictors and associated factors in the European cooperative acute stroke study (ECASS) I. Stroke. 1999;30(12):2631-6.
87. Seners P, Turc G, Tisserand M, Legrand L, Labeyrie MA, Calvet D, et al. Unexplained early neurological deterioration after intravenous thrombolysis: incidence, predictors, and associated factors. Stroke. 2014;45(7):2004-9.