SUPPLEMENTAL MATERIAL

Dosage, intensity and frequency of language therapy for aphasia; a systematic review based, individual participant data network meta-analysis.

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Primary Publication reference	Country	Funder	Participants inclusion and exclusion criteria	IPD	IPD collection time-points contributing to RELEASE	Electronic or Public domain trial
Ciccone (2015)	Australia	Unreported	<u>Inclusion:</u> stroke (less than 5 days); aphasia (score below ceiling of WAB); teaching hospital admission; conscious and medically stable; can maintain alert state for at least 30 minutes <u>Exclusion:</u> previous history of aphasia, mental illness or dementia; non-English speaking background; history of sub- arachnoid and / or subdural haemorrhage or neurosurgical intervention; uncorrected hearing or vision impairment <u>In RELEASE:</u> n=20	20	Baseline; 3 months; 6 months	Electronic
de Jon- Hagelstein (2011)	The Netherlands	Stichting Nuts Ohra (T-07-71)	<u>Inclusion:</u> adult; stroke (less than 3 weeks); aphasia (verbal communication, semantic or phonological disorder, tests and cut- offs defined); life expectancy more than 6 months <u>Exclusion:</u> over 85 years; severe dysarthria; premorbid dementia or aphasia; developmental dyslexia; visual perceptual disorder; recent psychiatric disorder <u>In RELEASE:</u> n=85 (75 completed)	85	Baseline; 3 months; 6 months	Electronic
Doesborgh (2004a)	The Netherlands	Netherlands organisation for Scientific Research	Inclusion: adult (age 20 to 86); stroke (at least 11 months); aphasia (moderate to severe naming deficit BNT); completed intensive impairment- oriented (semantic or phonological) therapy; native speaker (Dutch) <u>Exclusion:</u> global or minimal aphasia; dysarthria; non-native Dutch speaker;	18	Baseline; 2 months	Electronic

Table I. Included randomised controlled trials; location, funding, participants, IPD, data timepoints.

			illiteracy, developmental dyslexia, severe acquired dyslexia; visual perceptual deficit <u>In RELEASE:</u> n= 18			
Doesborgh (2004b)	The Netherlands	Netherlands Organization for Health Research and Development, Chronic Diseases (940-33- 008)	Inclusion: adult; stroke; aphasia (moderate or severe; both semantic and phonological deficit); one of 35 clinical centres; speech and language therapist considered a candidate for intensive treatment (taking into account practical, psychological, physical, cognitive factors); <u>Exclusion:</u> within 3 months of onset; dysarthria; global aphasia; recovered aphasia; non-native speaker; illiteracy; developmental dyslexia; severe acquired dyslexia; visual perceptual deficit In RELEASE: n=58	58	Baseline; 11 months	Electronic
Mattioli (2014)	Italy	Unreported	<u>Inclusion</u> : adult; stroke (first, acute); aphasia with mildly impaired comprehension; native speaker (Italian); suitable for MRI; right- handed; no other neurological or psychiatric disease; no hearing deficit <u>Exclusion</u> : over 80 years; stroke not in middle cerebral artery; aphasia with severely impaired comprehension; not native Italian speaker; unsuitable for MRI (pacemaker; claustrophobia; severe obesity); dementia; psychiatric disorders; deafness In RELEASE; n=12	12	Baseline; 16 days; 190 days	Electronic
Meikle (1979)	UK	Chest, Heart, and Stroke Association	<u>Inclusion:</u> stroke (at least 3 weeks); aphasia (less than 4 th percentile on PICA); previously proficient in English; well enough to attend	31	Baseline; 4, 15, 24, 35, 42, 66, 84 weeks	Public domain

			Exclusion: dementia; lives too far from hospital In RELEASE: n= 31			
Laska (2011)	Sweden	Stockholm County Council Foundation (Expo-95); AFA Insurances; Marianne and Marcus Wallenberg Foundation; Karolinska Institute	Inclusion: stroke (first); aphasia (NGA 0 to 59); able to start SLT within 2 days of onset <u>Exclusion:</u> rapid regression; dementia; drug abuse; severe illness; unable to participate in treatment (as judged by investigator)	125 (plus 2 without group allocation)	Baseline; 3 weeks (16 days); 6 months	Electronic
Rodriguez 2013	Australia	National Health and Medical Rehabilitation Council (NHMRC) Centre for Clinical Research Excellence in Aphasia Rehabilitation (Grant # 569935); DC was funded by an Australia Research Council Future Fellowship and NHMRC Career Development Fellowship	<u>Inclusion:</u> stroke (at least 6 months); aphasia; no other neurological disorders; sufficient vision and hearing to take part <u>Exclusion:</u> concomitant neurological illness	= 11	Baseline; 2 weeks; 4 weeks; 9 weeks;11 weeks	Electronic
Woodhead (2017)	UK	Wellcome Trust and the James S McDonnell Foundation (conducted as part of the Brain Network Recovery Group initiative). APL and ST were supported by personal fellowships from the Wellcome Trust (ME033459MES and 106084/Z/14/Z, respectively).	<u>Inclusion:</u> adult; stroke (3 or more months); aphasia (Wernicke's); competent to consent <u>Exclusion:</u> under 18; significant medical or psychiatric co-morbidity; unable to comply with treatment regime or scanning; significant multifocal cerebral disease; contraindications to cholinesterase inhibitors (sick sinus syndrome; pregnancy; lactation); contraindications to fMRI and MEG (pacemaker; noncompatible metallic implant); severe hearing impairment; unable to provide informed consent <u>In RELEASE:</u> n=20	20	Baseline; 5 weeks; 10 weeks	Electronic
Lincoln (1980a)	UK	Unreported	Inclusion: adult; stroke; no other brain damage; aphasia; referred for SLT by medical staff; able to attend daily (4 days per week) for 8 weeks as in- or out-patient	24	Baseline; week 4; week 8	Public domain

			Exclusion: severely or mildly aphasic			
Lincoln (1980b)	UK	Unreported	<u>Inclusion:</u> adult; stroke; no other brain damage; severe aphasia; referred for SLT by medical staff; able to attend daily (4 days per week) for 8 weeks as in- or out-patient <u>Exclusion:</u> unreported In RELEASE: n=24	24	Baseline; week 4; week 8	Public domain
Szaflarski (2015)	USA	NINDS R01 NS 048281 and by NIH/NCRR UL1-RR026314 (REDCap Database)	<u>Inclusion:</u> stroke (single); aphasia (chronic) <u>Exclusion:</u> more than one stroke; history degenerative or metabolic disorder or supervening illness; history depression or other mental illness; pregnant In RELEASE: n=24	24	Baseline; 2 weeks; 12 weeks	Electronic
Palmer (2012)	UK	NIHR Research for Patient Benefit (RfPB) Programme (Grant Reference Number PB-PG-1207-14097)	Inclusion: stroke; aphasia (predominant word-finding difficulties; able to repeat spoken words); ceased impairment- focused SLT; motor deficits if co- existing; upper limb impairment if computer access addressed by assistive devices <u>Exclusion:</u> severe visual or cognitive difficulties	34	Baseline; 5 months; 8 months	Electronic
Smania (2006) and (2000)	Italy	Ministero Italiano Universita' Ricerca and Finanziamento Italiano Ricerca di Base (FIRB) both awarded to Salvatore M. Aglioti; M.U.R.S.T. and the Consiglio Nazionale delle Ricerche, Italy	Inclusion: stroke; aphasia; limb apraxia (ideational or ideomotor) for at least 2 months Exclusion: history of stroke or other neurological disorders; over 80 years; uncooperativeness; orthopedic or other disabling disorders In RELEASE: n=32	32	Baseline; 10 weeks	Electronic
Breitenstein (2017)	Germany	German Federal Ministry of Education and Research (BMBF); German Society for Aphasia Research and Treatment (GAB)	<u>Inclusion:</u> adult; stroke; aphasia for at least 6 months; native speaker (German); at least basic level of communication and language comprehension	142 (minus14)	Screening; baseline; 3 weeks; 6 weeks (subgroup only); 6 months	Electronic

			<u>Exclusion:</u> severe untreated medical conditions; severe uncorrected vision or hearing impairments; aphasia from traumatic brain injury or neurodegenerative disease; participation in any intensive stroke intervention in previous 4 weeks <u>Not in RELEASE:</u> 14 <u>In RELEASE:</u> n=142			
Godecke (2012)	Australia	Unfunded project	<u>Inclusion:</u> stroke (acute); aphasia (less than 5 days; score of 13 or less on FAST); admitted to teaching hospital; conscious, medically stable, able to maintain alertness for at least 30 minutes <u>Exclusion:</u> previous history subarachnoid/subdural haemorrhage, neurosurgical intervention, aphasia, mental illness, dementia; non-English speaking; uncorrected hearing or vision impairment; already 3 participants in daily therapy group <u>In RELEASE:</u> n=59	59	Baseline; 4 weeks (or acute hospital discharge if sooner); 6 months	Electronic
Kukkonen (unpublished)	Finland	None	<u>Inclusion</u> : older adult (50-64; 65-80); stroke (first); aphasia; right-handed; living in Tampere with someone; no dementia; normal hearing and vision <u>Exclusion</u> : age under 50; two or more, right hemisphere, or haemorrhagic stroke; dementia or other neurological disease; left-handed; living alone; living outside Tampere; problems with hearing or vision	36	Baseline; 4 weeks; 10 weeks; 14 weeks; 20 weeks; 32 weeks; 56 weeks	Unpublished
Martins (2013)	Portugal	None reported	<u>Inclusion:</u> adult (40-80); stroke (single); aphasia (LAAB mild/moderate and severe); native	30	Baseline; 10 weeks; 50 weeks; 62 weeks	Electronic

			speaker (Portuguese); willing to participate <u>Exclusion:</u> more than 3 months since stroke or further stroke; very severe or very mild aphasia; illiteracy; unable to attend on daily basis; evidence of dementia or other severe medical or psychiatric disorder; miss more than 5 consecutive hours of intervention <u>In RELEASE:</u> 30 at baseline; 14 at completion (62 weeks)			
Meinzer (2007)	Germany	Deutsche Forschungsgemeinschaft (DFG, Grant RO 805011-4) and the Kuratorium Zentrales Nervensystem (ZNS, Grant 2001013)	<u>Inclusion:</u> stroke (single); aphasia (at least 6 months; global aphasia if residual expressive language); 1 or more participating relative <u>Exclusion:</u> well-recovered people with minimal aphasia symptoms <u>In RELEASE:</u> n=20	20	Baseline; 10 days	Electronic
Khedr (2014)	Egypt	Unreported	Inclusion: stroke (single); aphasia (non- fluent); subacute hemiplegia <u>Exclusion:</u> head injury or neurological disease other than stroke; unstable cardiac dysrhythmia; fever; infection; hyperglycemia; prior administration of tranquiliser; safety contraindications for rTMS <u>In RELEASE:</u> n=29	29	Baseline; 2 weeks; 6 weeks; 10 weeks	Electronic
van der Meulen (2016)	The Netherlands	Stichting Rotterdams Kinderrevalidatie Fonds Adriaanstichting (grant no. 2007/0168 JKF/07.08.31 KFA).	Inclusion: adult; stroke (more than 1 year); aphasia (candidate for MIT: non- fluent; poor language repetition; poorly articulated speech; moderate to good auditory comprehension) <u>Exclusion:</u> prior stroke resulting in aphasia; bilateral lesion; intensive MIT prior to start of study; severe hearing deficit; relevant psychiatric history In RELEASE: n=17	17	Baseline; 42 days; 82 days	Electronic

Rubi-Fessen (2015)	Germany	Walter and Marga Boll Foundation and the Wolf-Dieter Heiss-Foundation.	<u>Inclusion:</u> 55 to 85 years; stroke (first; up to 16 weeks); aphasia; first language (German); right-handed <u>Exclusion:</u> previous stroke, neurodegenerative or psychiatric disease; epilepsy; auditory or visual deficits that might impair testing <u>In RELEASE:</u> n=30	30	Baseline; 2 weeks	Electronic
Efstratiadou (2019)	Greece	Co-financed by the European Union (European Social Fund—ESF) EFSA aphasia therapy and Greek national funds through the Operational Program 'Education and Lifelong Learning' of the National Strategic Reference Framework (NSRF)—Research Funding Program: THALES UOA—Levels of Impairment in Greek Aphasia: Relationship with Processing Deficits, Brain Region, and Therapeutic Implications	<u>Inclusion:</u> adult; stroke (at least 4 months); aphasia; native speaker (Greek); medically stable; no other neurological or psychiatric history; no considerable cognitive impairment <u>Exclusion:</u> in receipt of other SLT during the project; not living independently at home prior to the stroke <u>Not in RELEASE:</u> 20 received alternative SLT <u>In RELEASE:</u> n=38	38	Baseline; 19 weeks; 32 weeks	Electronic
You (2011)	Korea	Unreported	<u>Inclusion:</u> stroke; not taking pharmacological drugs <u>Exclusion:</u> history of previous stroke, seizure, multiple stroke lesions; metal implants in brain; taking certain medication; uncooperative with SLT <u>In RELEASE:</u> n=21	21	Baseline; 2 weeks	Public domain

IPD Individual participant data

Primary Publication reference	Treatment location	Group	SLT Impairment Target:	SLT Theoretical Approach:	Provided by:	Delivery:	Regimen:	Tailoring:	Home- practice prescribed:
Mattioli (2014)	Hospital, then outpatient	Group 1: n=6	Mixed SLT and Word Finding SLT	Unreported	Speech and language therapist	Face-to-face; 1-to-1	<u>Frequency:</u> 5 days per week. <u>Duration:</u> 2 months. <u>Intensity:</u> 5 hours. <u>Dosage:</u> 10 hours.	Unreported	Unreported
		Group 2: n=6	No SLT						
Hon Meikle (1979) grou reha centr		Group 1: n=16 "Conventional SLT"	Unreported	Unreported	Speech and language therapist	face-to-face; 1-to-1 and group;	<u>Frequency:</u> 3-5 days per week. <u>Duration:</u> IPD. <u>Intensity:</u> between 2 hours 15 minutes and 3 hours 45 minutes. <u>Dosage:</u> IPD	Unreported	Unreported
	Home and groups at rehabilitation centre	Group 2: n=15 "Conventional SLT"	Mixed SLT	Unreported	recruited volunteers.	face-to-face; 1-to-1 and group;	Frequency: 4 home visits per week and a separate group session at rehabilitation centre. <u>Duration:</u> IPD. <u>Intensity:</u> between 2 hours 15 minutes and 3 hours 45 minutes. <u>Dosage:</u> IPD	By difficulty	Unreported
Laska (2011)	Stroke unit, or discharged to (home, rehabilitation clinic, geriatric clinic, nursing home).	<u>Group 1:</u> n=62	Mixed SLT	Unreported	Speech and language therapist	Face-to-face; 1-to-1	Frequency: 3 sessions each day 5 days per week. <u>Duration:</u> 3 weeks. <u>Intensity:</u> 3 hours 45 minutes. <u>Dosage:</u> 11 hours 15 minutes.	By functional relevance	Unreported
		<u>Group 2:</u> n=61 <u>In</u>	tervention type(s): N	lo SLT					

Table II. Included SLT interventions by trial, treatment location, target, approach, provider, delivery, regimen, tailoring and homepractice.

Rodriguez a (2013) 1	Aphasia clinic and other	<u>Group 1:</u> n=4	Word Finding SLT and Mixed SLT	Functional or Pragmatic SLT; Semantic and Phonological SLT	speech and language therapists and students.	face-to-face; 1-to-1 and group;	Frequency: 5 days per week. <u>Duration:</u> 2 weeks. <u>Intensity:</u> 20 hours. <u>Dosage:</u> 40 hours.	By functional relevance and difficulty	Yes
	and other rehabilitation centres.	<u>Group 2:</u> n=7	Word Finding SLT and Mixed SLT	Functional or Pragmatic SLT; Semantic and Phonological SLT	speech and language therapists and students.	face-to-face and computer- based treatment; 2- to-1 and group;	<u>Frequency:</u> 5 days each week. <u>Duration:</u> 4 weeks. <u>Intensity:</u> 25 hours. <u>Dosage:</u> 100 hours.	By functional relevance and difficulty	Yes
Woodhead (2017)	Home	Group 1: n=14 Intervention type(s): SLT intervention	Auditory Comprehension SLT	Phonological SLT plus Co- intervention (Donepezil)	experimental psychologist.	computer- based; self- managed;	Frequency: 7 days a week. <u>Duration</u> : 25 weeks in study, but intervention is over two 5-week blocks. <u>Intensity:</u> 7.3 hours (according to diaries) on average. <u>Dosage:</u> 73 hours (according to diaries).	By difficulty	Yes
		Group 2: n=13 Intervention type(s): SLT intervention Delivery: Location: Regimen: 10 hours of training per week over each 5 week training block.	Auditory Comprehension SLT	Phonological SLT plus Co- intervention (placebo)	experimental psychologist	computer- based; self- managed;	Frequency: 7 days a week. <u>Duration</u> : 25 weeks in study, but intervention is over two 5-week blocks. <u>Intensity:</u> 7.3 hours (according to diaries) on average. <u>Dosage:</u> 73 hours (according to diaries).	By difficulty	Yes
Lincoln (1980a)	Hospital and home	<u>Group 1:</u> 6	Mixed SLT	Unreported	Speech and language therapist	Face-to-face; 1-to-1	Frequency: 4 days per week. <u>Duration:</u> 3.5 weeks. <u>Intensity:</u> 2 hours. <u>Dosage:</u> 7 hours.	Unreported	Unreported
		Group 2: 7 No SLT (operant training) then	Mixed SLT	Unreported	Speech and language therapist	Face-to-face; 1-to-1	hospital and ho <u>Frequency:</u> 4 days per week. <u>Duration:</u>	Unreported	Unreported

		Conventional SLT					3.5 weeks. <u>Intensity:</u> 2 hours. <u>Dosage:</u> 7 hours.		
		Group 3: n=5 Intervention type(s): Social Support then Conventional SLT	Mixed SLT	Unreported	Speech and language therapist	Face-to-face; 1-to-1	<u>Frequency:</u> 4 days per week. <u>Duration:</u> 3.5 weeks. <u>Intensity:</u> 2 hours. <u>Dosage:</u> 7 hours.	Unreported	Unreported
		<u>Group 4:</u> n=6	Mixed SLT	Unreported	Speech and language therapist	Face-to-face; 1-to-1	Frequency: 4 days per week. <u>Duration:</u> 3.5 weeks. <u>Intensity:</u> 2 hours. <u>Dosage:</u> 7 hours.	Unreported	Unreported
Lincoln (1980b)	Hospital	Group 1: n=12	Operant training with SLT then Social Support with SLT	Mixed SLT	Speech and language therapist and psychologist	Face-to-face; 1-to-1	Frequency: IPD between 1.25 and 3.5 days per week. <u>Duration:</u> 8 weeks. <u>Intensity:</u> 2 hours per week. <u>Dosage:</u> IPD.	By difficulty	Unreported
		<u>Group 2:</u> n=12	SLT with Social Support, then operant training with SLT Mixed SLT	Unreported	Speech and language therapist and psychologist	Face-to-face; 1-to-1	Frequency: IPD between 1.25 and 3.5 days per week. <u>Duration:</u> 8 weeks. <u>Intensity:</u> 2 hours per week. <u>Dosage:</u> IPD	By difficulty	Unreported
Szaflarski (2015)	Hospital	Group 1: n=14 Intervention type(s): SLT intervention SLT Impairment Target: SLT Theoretical Approach: Provided by: Delivery: Location: Regimen: 10	Word-finding SLT; Spoken Language SLT	Constraint Induced Aphasia Therapy	Speech and language therapist	face-to-face; groups of 3 to 4;	Frequency: 5 times per week; <u>Duration:</u> 2 weeks; <u>Intensity:</u> 20 hours. <u>Dosage:</u> 40 hours.	By difficulty	Unreported

SUPPLEMENTAL MATERIAL	- Dosage,	intensity and	l frequency	of therapy	for aphasia
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		daily sessions 4 hours per day for 10 consecutive weekdays							
		<u>Group 2:</u> n=10	Intervention type(s): No SLT						
Palmer (2012)		Group 1: n=16	Word-finding SLT and Mixed SLT	Unreported	Self-managed, computer software, supported by speech and language therapist, volunteer.	Home visit plus computer or phone call plus computer; 1- to-1;	<u>Frequency</u> : IPD. <u>Duration</u> : 5 months. <u>Intensity</u> : IPD. <u>Dosage:</u> IPD	By functional relevance	Unreported
		Group 2: n=17	Intervention type	(s): No SLT					
		<u>Group 1:</u> n=17	Intervention type	<u>(s):</u> No SLT (limb apra	axia therapy only)		E 0.1		
Smania (2006) and (2000)	Therapy clinic	<u>Group 2:</u> n= 15	unreported	unreported	Speech and language therapist	unreported;	<u>Frequency:</u> 3 days per week. <u>Duration:</u> 10 weeks. <u>Intensity:</u> 2.5 hours. <u>Dosage:</u> 25 hours.	Unreported	Unreported
Breitenstein	Inpatient and outpatient rehabilitation	<u>Group 1:</u> N=78	Mixed SLT	Functional or Pragmatic SLT	Speech and language therapist	face-to-face; 1-to-1 and group	<u>Frequency:</u> IPD. <u>Duration:</u> IPD. <u>Intensity:</u> IPD. <u>Dosage:</u> IPD.	By difficulty	Yes
(2017)	Outpatient	<u>Group 2:</u> n=78	Unreported (usual care)	Unreported	Speech and language therapist	face-to-face; 1-to-1 and group	<u>Frequency:</u> IPD. <u>Duration:</u> 3 weeks <u>Intensity:</u> IPD. <u>Dosage:</u> IPD.	Unreported	Unreported
Godecke (2012)	Hospital or rehabilitation	<u>Group 1:</u> n=32	Spoken language SLT	Semantic and Phonological SLT	Speech and language therapist	Face-to-face; 1-to-1	Frequency: 5 days per week. <u>Duration:</u> IPD but maximum of 1 month. <u>Intensity:</u> IPD between 2.5 and 7.5 hours per week. <u>Dosage:</u> IPD up to 26.5 hours.	By functional relevance and difficulty	Unreported
		<u>Group 2:</u> n=27	Spoken Language SLT	Semantic and Phonological SLT	Speech and language therapist	Face-to-face; 1-to-1	<u>Frequency:</u> 1 day per week. <u>Duration:</u> IPD up to 1 month.	ву functional relevance	Unreported

							Intensity: up to 1.5 hours per week. Dosage: IPD up to 5.3 hours.	and difficulty	
Ciccone	Hospital,	<u>Group 1:</u> n=8	Word Finding SLT	Phonological and Semantic SLT	Speech and language therapist	Face-to-face; 1-to-1	<u>Frequency:</u> IPD. <u>Duration:</u> 5 weeks. <u>Intensity:</u> IPD. <u>Dosage:</u> IPD.	By functional relevance and difficulty	Unreported
(2015)* renabilitation or home	<u>Group 2:</u> n=12	Word Finding SLT	Phonological and Semantic SLT; Constraint Induced Aphasia Therapy.	Speech and language therapist	face-to-face; group;	<u>Frequency:</u> IPD. <u>Duration:</u> 5 weeks. <u>Intensity:</u> IPD. <u>Dosage:</u> IPD.	By functional relevance and difficulty	Unreported	
		<u>Group 1:</u> n=9	Mixed SLT	Language Enrichment Therapy	Speech and language therapist	Face-to-face; 1-to-1	Frequency: 5 days per week. <u>Duration:</u> 6 weeks + 6 weeks. <u>Intensity:</u> 10 hours. <u>Dosage:</u> 120 hours.	By functional relevance	Unreported
Kukkonen (unpublished)	SLT clinic	<u>Group 2:</u> n=8	Mixed SLT	Language Enrichment Therapy	Speech and language therapist	Face-to-face; 1-to-1	Frequency: 2 days per week. <u>Duration:</u> 6 weeks + 6 weeks. <u>Intensity:</u> 2 hours. <u>Dosage:</u> 48 hours	By functional relevance	Unreported
		<u>Group 3:</u> n=10	Mixed SLT	Language Enrichment Therapy	Speech and language therapist	Face-to-face; 1-to-1	<u>Frequency:</u> 1 day per week. <u>Duration:</u> 6 weeks + 6 weeks. <u>Intensity:</u> 1 hour. <u>Dosage:</u> 24 hours.	By functional relevance	Unreported
		Group 4: n=9	Spouses or caregi and language ther	ver(s) received suppor apists	and information fro	om the speech	Twice, 1 hour per meeting		
Martins	Medical and rehabilitation centres,	Group 1: n=15	Mixed SLT	Multimodal	Speech and language therapist	Face-to-face; 1-to-1	<u>Frequency:</u> 5 days per week. <u>Duration:</u> 10 weeks. <u>Intensity:</u> 10 hours. <u>Dosage:</u> 100 hours.	By functional relevance and difficulty	Yes
(2013)	rehabilitation unit, acute stroke unit.	Group 2: n=15	Mixed SLT	Multimodal Stimulation Approach (MSA) (Duffy 2001)	Speech and language therapist	Face-to-face; 1-to-1	<u>Frequency:</u> 1 day per week. <u>Duration:</u> 50 weeks. <u>Intensity:</u> 2 hours. <u>Dosage:</u> 100 hours.	By functional relevance and difficulty	Yes

Meinzer	Unreported	Group 1: n=10	Word Finding SLT	Constraint Induced Aphasia Therapy	trained psychologists	Face-to-face; group	<u>Frequency:</u> 5 days per week. <u>Duration:</u> 10 days. <u>Intensity:</u> 15 hours. <u>Dosage:</u> 30 hours.	By functional relevance and difficulty	Yes
(2007)	emeponed	Group 2: n=10	Word Finding SLT	Constraint Induced Aphasia Therapy	Volunteer relatives with training and supervision	Face-to-face; group	Frequency: 5 days per week. <u>Duration:</u> 10 days. <u>Intensity:</u> 15 hours. <u>Dosage:</u> 30 hours.	By functional relevance and difficulty	Yes
Doesborgh (2004a)	Unreported	Group 1: n=8	Word Finding SLT	Unreported	Speech and language therapist	Computer, supervised by therapist; self- managed;	Frequency: 2 days per week. <u>Duration:</u> 2 months. <u>Intensity:</u> 1 to 1.5 hours weekly. <u>Dosage:</u> 10 to 11 hours.	By difficulty	Unreported
		Group 2: n=10	No SLT						
Khada (2014)	Homital	Group 1: n=10	Mixed SLT	Unreported	Speech and language therapist	Face-to-face; 1-to-1	Frequency: 5 days per week. <u>Duration:</u> 2 weeks. <u>Intensity:</u> 2.5 hours. <u>Dosage:</u> 5 hours.	By difficulty	Unreported
Kneur (2014)	Hospital	Group 2: n=19	Mixed SLT	Unreported	Speech and language therapist	Face-to-face; 1-to-1	<u>Frequency:</u> 5 days per week. <u>Duration:</u> 2 weeks. <u>Intensity:</u> 2.5 hours. <u>Dosage:</u> 5 hours.	By difficulty	Unreported
de Jon- Hagelstein (2011) Hagelstein (2011)	Group 1: n=41	Unreported	Semantic and Phonological SLT	Speech and language therapist	Face-to-face; 1-to-1	Frequency: 3.25 times per week on average. <u>Duration</u> : 6 months (or less if fully recovered). <u>Intensity:</u> 2 to 5 hours. <u>Dosage:</u> 52 hours.	By difficulty	Yes	
-	nursing nome.	<u>Group 2:</u> n=44	Unreported	Functional or Pragmatic SLT	Speech and language therapist	Face-to-face; 1-to-1	<u>Frequency:</u> 3.25 times per week on average. <u>Duration:</u> 6 months (or less if fully recovered).	By difficulty	Yes

							Intensity: 2 to 5 hours. Dosage: 52 hours.		
Doesborgh	Group 1: n=29 Word Finding SLT Speech and Language therapist Face-to-face and therapist Face-to-face and therapist Face-to-face and therapist How were the therapist Buration: Buration: to-1; Buration: Buration: to-1; Buration: Buration: to-1; Buration: Buration: to-1; Buration: Buration: to-1; Buration: Buration: to-1; Buration: Buration: to-1; Buration: to-1; Buration: Buration: to-1; Buration: Buration	By difficulty	Yes						
(2004b)	clinic / home / nursing home.	<u>Group 2:</u> n=29	Word Finding SLT	Phonological SLT	Speech and language therapist	Face-to-face and computer; 1- to-1;	Frequency: 2.25 days a week on average. <u>Duration:</u> 40 weeks. <u>Intensity:</u> 1.5 to 3 hours. <u>Dosage:</u> 40 to 60 hours.	By difficulty	Yes
	Rehabilitation / aphasia centres.	<u>Group 1:</u> n=10	Spoken language SLT	Melodic Intonation Therapy	Speech and language therapist	Face-to-face; 1-to-1	Frequency: 5 days a week. <u>Duration:</u> 12 weeks (6 MIT and 6 no therapy). <u>Intensity:</u> 5 hours a week. <u>Dosage:</u> 30 hours.	By functional relevance and difficulty	Yes
van der Meulen (2016)	Rehabilitation centre / nursing home with rehabilitation facilities.	<u>Group 2:</u> n=7	Auditory Comprehension SLT	unreported (protocol of what was and was not permitted, and manual of practice materials and references; PI helped create tailor-made tasks for a specific participant)	speech and language therapists.	Face-to-face; 1-to-1	Frequency: 5 days a week. <u>Duration:</u> 6 weeks. <u>Intensity:</u> 5 hours a week. <u>Dosage:</u> 30 hours.	By functional relevance and difficulty	Unreported
Rubi-Fessen (2015)	Hospital	Group 1: n=15 SLT intervention with rTMS	Word Finding SLT	Unreported	Speech and language therapist	Face-to-face; 1-to-1	Frequency: 5 days a week. <u>Duration:</u> 2 weeks. <u>Intensity:</u> 3.75 hours. <u>Dosage:</u> 7.5 hours.	By functional relevance and difficulty	Unreported

		Group 2: n=15 SLT intervention with sham rTMS	Word Finding SLT	Unreported	Speech and language therapist	Face-to-face; 1-to-1	Frequency: 5 days a week. <u>Duration:</u> 2 weeks. <u>Intensity:</u> 3.75 hours. <u>Dosage:</u> 7.5 hours.	By functional relevance and difficulty	Unreported
		Group 1: n=18	Word Finding SLT	Semantic SLT	Speech and language therapist	Face-to-face; 1-to-1	<u>Frequency:</u> 3 days a week. <u>Duration:</u> 12 weeks. <u>Intensity:</u> 3 hours. <u>Dosage:</u> 36 hours.	By difficulty	No
Efstratiadou (2019)	Home and hospital	Group 2: n=8	Word Finding SLT	Semantic SLT	Speech and language therapist	Face-to-face; 1-to-1	Frequency: 3 days a week. <u>Duration</u> : 12 weeks. <u>Intensity</u> : 3 hours. <u>Dosage</u> : 36 hours.	By difficulty	No
		Group 3: n=12	No SLT but then	as per Group 1 (n=4) o	r Group 2 (n=6) abo	ove			
		Group 1: n=7	Mixed SLT	Functional or Pragmatic SLT and Co-intervention	Speech and language therapist	Face-to-face; 1-to-1	Frequency: 5 days a week. <u>Duration:</u> 2 weeks. <u>Intensity:</u> 2.5 hours. <u>Dosage:</u> up to 5 hours.	Unreported	Unreported
You (2011)	Hospital rehabilitation department	Group 2: n=7	Mixed SLT	Functional or Pragmatic SLT and Co-intervention	Speech and language therapist	Face-to-face; 1-to-1	Frequency: 5 days a week. <u>Duration:</u> 2 weeks. <u>Intensity:</u> 2.5 hours. <u>Dosage:</u> up to 5 hours.	Unreported	Unreported
		Group 3: n=7	Mixed SLT	Functional or Pragmatic SLT and Co-intervention	Speech and language therapist	Face-to-face; 1-to-1	<u>Frequency:</u> 5 days a week. <u>Duration:</u> 2 weeks. <u>Intensity:</u> 2.5 hours. <u>Dosage:</u> up to 5 hours.	Unreported	Unreported

Speech and Language Therapy	
Defined intervention	593 IPD, 24 trials
Conventional Therapy (no detail)	104 IPD, 3 trials
Therapy with Co-interventions	83 IPD, 5 trials
SLT Theoretical Approach	
Functional or Pragmatic	98 IPD, 3 trials
Phonological	45 IPD, 2 trials
Semantic	27 IPD, 1 trial
Semantic and Phonological	108 IPD, 4 trials
Constraint Induced Aphasia Therapy	44 IPD, 3 trials
Melodic Intonation Therapy	24 IPD, 1 trial
SLT Impairment Target	
Mixed Auditory Comprehension and Spoken Language	249 IPD, 8 trials
Auditory	17 IPD, 2 trials
Spoken Language only	70 IPD, 2 trials
Word finding	224 IPD, 11 trials
Delivery	
Face to face	628 IPD, 21 trials
Computer-based	164 IPD, 6 trials
Self-managed	66 IPD, 1 trial
Phone	9 IPD, 1 trial
Therapy setting	
Healthcare facility	554 IPD, 18 trials
Home	441 IPD, 15 trials
Provider	
Professional (e.g. therapist)	730 IPD, 25 trials
Non-professional (Family member, volunteer)	31 IPD, 3 trials
Personalisation	
Tailoring by functional relevance reported (Y)	346 IPD, 11 trials
Tailoring by level of difficulty reported (Y)	520 IPD, 18 trials
Regimen data	
Frequency	877 IPD, 25 trials
Duration	825 IPD, 24 trials
Intensity	884 IPD, 25 trials
Dosage	875 IPD, 25 trials
Home practice tasks reported (Y/N)	312 IPD, 8 trials
de al manti a mant datas V ana as	

Table III. Characteristics of included SLT interventions Speech and Language Thereau

IPD Individual participant data; Y yes;

	Frequency	Intensity	Dosage	Duration
Overall language ability	0.31	0*	0*	0*
Functional communication	0.24	0*	0.15	0*
Auditory comprehension	0.076	0.097	0*	0.10
Naming	0.11	0.120	0.30	0*

 Table IV. Cluster-effect analysis; p values for within-study clustering effect

*G matrix was not positive definite

I anguaga autaama	RCTs	IPD	Estimate of means
Language outcome	n	n	(95% CI)
Overall language ability – WA	AB-AQ [0-100]		
Mixed	8	245	15.62 (8.82 to 22.43)
Spoken Language	2	70	12.83 (-0.99 to 26.64)
Auditory comprehension	1	6	11.91 (-7.05 to 30.87)
Word Finding	0	0	-
Reference Group	2	65	12.23 (3.75 to 20.70)
Auditory Comprehension - A	AT-TT [0-50]		
Mixed	5	142	3.37 (-1.20 to 7.93)
Spoken Language	0	0	-
Auditory comprehension	2	17	1.25 (-7.58 to 10.09)
Word Finding	7	136	4.46 (0.31 to 8.62)
Reference Group	4	29	2.54 (-2.40 to 7.47)
Naming - BNT [0-60]			
Mixed	4	84	7.33 (0.58 to 14.08)
Auditory comprehension	2	25	0.33 (-11.29 to 11.95)
Word Finding	7	174	8.82 (3.15 to 14.49)
Reference Group	3	27	10.24 (3.56 to 16.92)
Functional Communication -	AAT-SSC [0-5]	
Mixed	3	72	1.05 (0.52 to 1.58)
Spoken Language	1	52	0.68 (-0.40 to 1.77)
Auditory comprehension	8	184	0.72 (0.33 to 1.10)
Word Finding	0	0	-
Reference Group	4	58	0.75 (0.26 to 1.23)

Table V. SLT rehabilitation by impairment target and language outcome

IPD Individual Participant Data

T an and an antionna	RCTs	IPD	Estimate of means
Language outcome	(n)	(n)	(95% CI)
Overall language ability -	- WAB-AQ [0-100]		
Semantic/phonological	2	60	20.39 (1.90 to 38.88)
Phonological	0	0	-
CIAT	1	10	16.11 (-4.87to 37.09)
Functional/pragmatic	2	83	13.50 (-1.48 to 28.47)
Reference group	2	65	23.46 (4.98 to 41.95)
Auditory Comprehension	- AAT-TT [0-50]		
Semantic/phonological	1	35	11.93 (1.44 to 22.43)
Semantic	1	27	3.29 (-4.90 to 11.48)
Phonological	2	45	5.95 (-1.56 to 13.46)
CIAT	2	32	7.46 (0.67 to 14.25)
MIT	1	23	0.26 (-10.08 to 10.59)
Functional/pragmatic	3	98	5.52 (-0.86 to 11.91)
Reference group	4	29	2.33 (-3.53 to 8.20)
Naming - BNT [0-60]			
Semantic/phonological	1	35	19.38 (-13.50 to 52.27)
Semantic	1	26	-2.48 (-35.82 to 30.87)
Phonological	1	25	-1.66 (-34.92 to 31.60)
CIAT	1	13	15.53 (-4.48 to 35.55)
MIT	1	20	-2.25 (-35.04 to 30.53)
Functional/pragmatic	2	32	4.91 (-18.39 to 28.22)
Reference group	3	27	14.78 (-4.60 to 34.15)
Functional Communication	on - AAT-SSC [0-5]		
Semantic/phonological	3	100	0.71 (-0.15 to 1.55)
Semantic	1	26	0.35 (-1.15 to 1.86)
Phonological	1	25	0.37 (-1.11 to 1.84)
CIAT	1	13	0.77 (-0.22 to 1.75)
MIT	1	24	0.20 (-1.11 to 1.50)
Functional/pragmatic	1	8	1.82 (0.36 to 3.28)
Reference group	4	58	0.68 (-0.10 to 1.46)

Table VI. SLT theoretical approach by language outcome

IPD Individual Participant Data

Language outcome	RCTs (n)	IPD (n)	Estimate of means (95% CI)
Overall language ability –	WAB-AQ [0-100]		
Yes	2	87	16.69 (10.01 to 23.37)
No	10	330	13.35 (8.21 to 18.48)
Auditory Comprehension -	· AAT-TT [0-50]		
Yes	7	278	5.28 (2.19 to 8.37)
No	10	217	2.27 (-0.67 to 5.22)
Naming - BNT [0-60]			
Yes	4	167	6.94 (-0.57 to 14.46)
No	9	166	7.08 (1.81 to 12.35)
Functional Communication	n - AAT-SSC [0-5]		
Yes	5	187	0.61 (0.18 to 1.04)
No	10	267	0.74 (0.39 to 1.09)

Table VII. SLT Home-Practice by language domain

IPD Individual Participant Data

Tailoring	Target	RCTs	IPD	Estimate of means (CI 95%)
Overall La	nguage			
Eurotional	Tailored	6	232	16.47 (10.95 to 21.99)
Functional	Not tailored	7	185	12.05 (6.90 to 17.20)
Difficulty	Tailored	7	210	14.46 (8.82 to 20.09)
Difficulty	Not tailored	6	207	13.24 (7.50 to 18.99)
Auditory C	omprehension (A	AT-TT rang	ge 0-50)	
Functional	Tailored	7	194	5.26 (2.05 to 8.47)
Functional	Not tailored	10	301	2.43 (-0.57 to 5.43)
Difficulty	Tailored	10	331	4.57 (1.55 to 7.60)
Difficulty	Not tailored	7	164	1.95 (-1.30 to 5.20)
Naming (Bl	NT range 0 to 60)			
	Tailored	5	113	8.79 (1.95 to 15.63)
Functional	Not tailored	8	220	5.95 (0.57 to 11.32)
Difficulty	Tailored	9	254	5.66 (0.74 to 10.58)
Difficulty	Not tailored	4	79	10.21 (2.75 to 17.67)
Functional	Communication (observer ra	ted AAT	SC range 0 to 5)
Functional	Tailored	6	249	0.74 (0.38 to 1.10)
Functional	Not tailored	8	195	0.71 (0.32 to 1.11)
Difficulty	Tailored	10	313	0.65 (0.32 to 0.98)
Difficulty	Not tailored	5	141	0.81 (0.34 to 1.27)

 Table VIII. Tailoring of SLT interventions (functional relevance and level of difficulty)

 by language domain

Difficulty: Interventions tailored by level of language difficulty;

Functional: Interventions tailored by functional relevance to the participant.

Study ID	Group	N	Age Median [IQR]	Wilcoxon p	Male Sex N (%)	Chi-Sq p	Aphasia severity WAB AQ median [IQR]	Wilcoxon p	Time since stroke (days) Median [IQR]	Wilcoxon P
1	A	64	75.5 [66, 84]	0.23	33 (53.2)	0.08	57.1 [28.2, 64.4]	0.78	3 [2, 4]	0.19
1.	В	61	79 [72, 85]	0.23	23 (37.7)	0.08	58.0 [28.2, 64.7]	0.78	3 [2, 4]	0.19
2	A	5	55 [47, 66]	0.37	4 (80)	0.49	-	_	1887 [1745, 2092]	0.84
2.	В	5	48 [45, 53]	0.57	3 (60)	0.47	-		2259 [1871, 2478]	0.04
3	A	17	71 [65, 80]	0.30	9 (52.9)	0.29	-	_	2031.5 [1096, 3127]	0.53
5.	В	17	66 [53, 76]	0.50	12 (70.6)	0.29	-		2042 [1761, 3512]	0.55
1	A	15	70 [64, 74]	0.54	5 (83.3)	0.63	-	_	426 [365, 609]	0.36
т.	В	17	67 [56, 73]	0.54	11 (73.3)	0.05	-		183 [91, 914]	0.50
	A	6	45 [28, 57]		5 (83.3)		75.9 [71.4, 81.2]	_	106.5 [30, 244]	
5	B	7	55 [52, 63]	0.29	6 (85.7)	0.43	73.8 [55.9, 80.3]	0.67	61 [30, 61]	0.88
5.	C	5	52 [47, 54]	0.29	3 (60)	0.45	72.1 [58.1, 90.1]	0.07	152 [61, 152]	0.00
	D	6	56 [48, 58]		3 (50)		65.7 [59.2, 72.1]		91 [61, 152]	
6	A	6	55.5 [49, 63]	1.0	5 (83.3)	0.51	39.4 [35.4, 47.8]	0.44	61 [30, 122]	0.48
0.	В	6	53.5 [49, 62]	1.0	4 (66.7)	0.51	48.7 [42.7, 56.3]	0.44	121.5 [30, 335]	0.40
7	A	72	55 [46.5, 60]	0.70	49 (68.1)	0.24	70.4 [40.7, 87.9]	0.80	822.5 [396, 1462]	0.056
/.	В	70	54 [50, 61]		41 (58.6)	0.24	67.2 [44.1, 84.8]	0.80	1263.5 [487, 2071]	0.050
8	A	6	69.5 [63, 75]	0.53	4 (66.7)	0.56	-	_	2.5 [2, 3]	1.00
0.	В	6	61.5 [59, 72]	0.55	3 (50)	0.50	-	_	2 [2, 3]	1.00
0	A	32	72.5 [62.5, 79]	0.52	14 (43.8)	0.37	31 [9.75, 54.5]	0.045	2.5 [2, 4]	0.59
9.	В	27	67 [58, 79]	0.52	15 (55.6)	0.57	9 [0, 34.1]	0.045	3 [2, 4]	0.59
10	A	17	65 [57, 71]	0.23	10 (58.8)	0.10	74.9 [42, 87.3]	0.54	105 [56, 126]	0.28
10.	В	14	69.5 [59, 74]	0.25	12 (85.7)	0.10	55.3 [34.2, 87.7]	0.54	175 [70, 364]	0.20
11	A	14	55.5 [50, 67]	0.11	9 (64.3)	0.48	-	_	1141.5 [426, 2223]	0.75
11.	В	10	51.5 [41, 54]	0.11	5 (50)	0.48	-	_	913.5 [335, 2101]	0.75
	A	9	72 [64, 77]		4 (44.4)		56.3 [0, 81.2]	_	7 [7, 7]	
12	B	8	63 [58.5, 69]	0.23	4 (50)	0.50	60.6 [56.3, 81.2]	0.46	7 [7, 7]	1.00
12.	C	9	64 [61, 72]	0.25	7 (77.8)	0.50	64.9 [56.3, 64.9]	0.40	7 [7, 7]	1.00
	D	10	66.5 [59, 75]		6 (60)		56.3 [0, 64.9]		7 [7, 7]	
13	A	15	57 [51, 72]	0.12	10 (66.7)	0.70	29 [11.5, 67.9]	0.62	56 [42, 70]	0.74
15.	В	15	64 [58, 71]	0.12	9 (60)	0.70	43.1 [16.3, 64.7]	0.02	42 [28, 70]	0.74

Table IX. Trial group comparisons at baseline by age, sex, aphasia severity, time since stroke onset.

SUPPLEMENTAL MATERIAL -	Dosage,	intensity a	and frequen	cy of therap	y for aphasia
			J	J J I I I I	JJ

14	Α	10	65.5 [56, 69]	0.02	9 (90)	0.26	-		1324.5 [1066, 1797]	0.050
14.	В	10	47.5 [43, 61]	0.02	7 (70)	0.20	-	-	913.5 [548, 1035]	0.039
	Α	8	64.3 [56.4, 70]		4 (50)		-		360.5 [345, 383.5]	
15.	В	10	67.4 [56.3,	0.57	5 (50)	1.00	-	-	373.5 [367, 447]	0.19
			74.3]							
16	A	10	56.5 [51, 61]	0.34	5 (50)	0.68	28.2 [0, 56.3]	0.72	28 [14, 35]	0.37
10.	В	19	61 [54, 68]	0.54	8 (42.1)	0.00	0 [0, 56.3]	0.72	28 [14, 56]	0.57
	A	7	68 [56, 77]		5; (71.4)				639 [365, 700]	
17.	В	4	61.5 [37, 67.5]	0.32	2 (50)	0.48	-	-	1020 [441.5,	0.85
									1446.5]	
18	A	38	68 [62, 78]	0.95	14 (36.8)	0.07	-	_	22.5 [17, 26]	0.95
10.	В	42	69.5 [57, 79]	0.75	24 (57.1)	0.07	-		22 [19, 24]	0.75
	A	28	64.9 [58.7,		18 (64.3)		-		116.5 [102.5, 145]	
19			73.9]	0.075		0.34		_		1.00
17.	В	29	58.3 [50.1,	0.075	15 (51.7)	0.54	-	_	115 [101, 147]	1.00
			69.1]							
20	A	18	54 [49, 61]	0.98	11 (61.1)	0.22	-	_	106.5 [61, 1127]	0.71
20.	В	26	55.5 [48, 61]	0.70	11 (42.3)	0.22	-		61 [61, 548]	0.71
21	A	15	67 [65, 73]	0.71	9 (60)	0.14		_	47 [28, 69]	0.37
21.	В	15	70 [59, 47]	0.71	5 (33.3)	0.14	-		38 [24, 56]	0.57
	A	11	63 [61.4; 67.8]		11 (100)				1242 [438, 2703]	
22.	В	9	62.4 [50.2,	0.55	6 (66.7)	0.038	-	-	657 [438, 1863]	0.55
			66.5]							
	A	8	57.5 [53.5,		7 (87.5)		-		853 [365.5, 3014.5]	
23			66.5]	0.97		0.19		_		0.12
23.	В	12	54.5 [49.5, 69]	0.77	6 (50)	0.17	-		213.5 [122, 594	0.12
	C	18	61 [48, 67]		13 (72.2)		-		198 [152, 1248]	
	A	12	74.5 [53, 83.5]		9 (75)		45.5 [14.6, 70.4]		5 [4, 8]	
24.	В	8	76.5 [65.5,	0.76	3 (37.5)	0.09	51.1 [17.7, 68.1]	0.62	6.5 [4.5, 8.5]	0.38
			82.5]							
	A	7	66 [62, 80]		3 (42.9)		48 [9.9, 58.4]		23 [20, 30]	
25.	В	7	65 [49, 78]	0.40	4; 57.1)	0.56	57.8 [19, 58.1]	0.50	23 [20, 35]	0.71
	C	7	64 [55, 72]		5 (71.4)		38.1 [20.7, 48.8]		22 [18, 35]	

Abbreviations ID identification number; N number of participants; IQR interquartile range; Chi-Sq Chi square; * Kruskal-Wallis test

	Significant	result reported
Year of publication	No	Yes
1973-1989	7	4 (37%)
1990-1999	2	13 (87%)
2000-2004	3	16 (84%)
2005-2009	4	28 (88%)
2010-2014	15	53 (78%)
2015-2017	3	12 (80%)

Table X.	Year of	f publication	and report	of significan	t findings
			· · · · · · · · · · · · · · · · · · ·		

We considered risk of publication bias but due to the nature of the dataset a funnel plot was unsuitable. Instead, we considered the historic nature of the data and examined whether there was an association between the age of publication and the reporting of significant findings. Our analysis was restricted to datasets with an associated publication. Using a chi-squared test we found evidence to suggest a publication bias by date of publication (p=0.014). Earlier publications had a higher proportion of non-significant results than findings reported in more recent publications.

Overall language ability	Estimate (95% CI)	IPD	Datasets
2000 and later	15.25 (8.92 to 21.58)	111	4
Before 2000	10.36 (2.75 to 17.97)	371	7
Functional communication			
2000 and later	0.69 (0.39 to 1.00)	103	2
Before 2000	0.54 (-0.15 to 1.23)	430	12
Auditory comprehension			
2000 and later	3.90 (0.73 to 7.06)	82	3
Before 2000	1.84 (-4.45 to 8.14)	458	13
Naming			
2000 and later	7.82 (2.80 to 12.83)	81	3
Before 2000	3.51 (-5.67 to 12.69)	304	10

Table XI. Risk of bias and age of dataset

We considered the risk of bias and the age of included datasets. We took recruitment date as reported by the primary research team and where unavailable we took the date of the first associated publication. Recruitment was grouped as pre-2000 and post-2000. These recruitment groups were added to the basic model of baseline aphasia severity score, sex, time since stroke and age. We found no evidence that recruitment date contributed to the findings.

Table XII. Wu-Hausman test for fixed versus random effects model

Language domain	W	Alt-W	Fixed effect P	Relative variability
Overall language ability	0.13	0.36	< 0.0001	19.3%
Functional communication	3.49	-1.97	< 0.0001	30.8%
Auditory comprehension	3.55	-1.89	< 0.0001	24.3%
Naming	0.37	-0.61	< 0.0001	41.4%

Abbreviations W: Wu-Hausman test; Alt-Wu: Alternative Wu-Hausman Test.

		RCT data	only	
Effect	Number	Denominator	F Value	Р
	DF	DF		value
Frequency of SLT				
Baseline score	1	499	34.78	<.0001
Sex	1	499	4.18	0.042
Age group	3	499	0.97	0.41
Time since stroke group	3	499	4.72	0.0029
Randomisation	-	-	-	-
Frequency group	5	499	1.05	0.39
Duration of SLT				
Baseline score	1	448	41.68	<.0001
Sex	1	448	4.28	0.039
Age group	3	448	0.91	0.43
Time since stroke group	3	448	5.03	0.0019
Randomisation	-	-	-	-
Duration group	5	448	1.15	0.33
Intensity of SLT				
Baseline score	1	506	39.91	<.0001
Sex	1	506	3.72	0.055
Age group	3	506	1.42	0.24
Time since stroke group	3	506	4.50	0.0039
Randomisation	-	-	-	-
Intensity group	5	506	1.16	0.33
Dosage of SLT				
Baseline score	1	497	40.35	<.0001
Sex	1	497	5.70	0.017
Age group	3	497	0.96	0.41
Time since stroke group	3	497	4.11	0.0067
Randomisation	-	-	-	-
Dosage group	5	497	2.74	0.019
Home practice of SLT				
Baseline score	1	431	38.38	<.0001
Sex	1	431	2.83	0.093
Age group	3	431	1.92	0.13
Time since stroke group	3	431	4.24	0.0057
Randomisation	-	-	-	-
Home practice	1	431	0.40	0.53
SLT Target				
Baseline score	1	345	28.00	<.0001
Sex	1	345	4.90	0.028
Age group	3	345	1.68	0.17
Time since stroke group	3	345	2.34	0.07
Randomisation	-	-	-	-
SLT Target	3	345	0.73	0.53
SLT Theoretical Approa	ch			
Baseline score	1	234	17.09	<.0001
Sex	1	234	3.93	0.049
Age group	3	234	2.19	0.09

 Table XIII. Functional communication (observer-rated) data including TOMs participation data

Time since stroke group	3	234	2.16	0.09
Randomisation	-	-	-	-
Theoretical Approach	6	234	0.75	0.61
Expertise-non-professiona	ıl			
Baseline score	1	509	39.51	<.0001
Sex	1	509	3.71	0.055
Age group	3	509	1.42	0.24
Time since stroke group	3	509	3.88	0.0092
Randomisation	-	-	-	-
Expertise-professional	1	509	2.96	0.086
Expertise-non-	1	509	1.56	0.21
professional				
Context of therapy				
Baseline score	1	509	38.36	<.0001
Sex	1	509	3.67	0.056
Age group	3	509	1.27	0.28
Time since stroke group	3	509	5.84	0.0006
Randomisation	-	-	-	-
Inpatient	1	509	1.43	0.23
Outpatient	1	509	2.08	0.15
Mode of therapy				_
Baseline score	1	508	39.41	<.0001
Sex	1	508	3.75	0.05
Age group	3	508	1.52	0.21
Time since stroke group	3	508	2.59	0.05
Randomisation	-	-	-	-
Mode face to face	1	508	3.48	0.063
Mode computer	1	508	0.57	0.45
Functional relevance				
Baseline score	1	422	39.28	<.0001
Sex	1	422	3.02	0.083
Age group	3	422	2.05	0.11
Time since stroke group	3	422	3.25	0.022
Randomisation	-	-	-	-
Functional relevance	1	422	0.00	1.00
Level of difficulty				
Baseline score	1	431	38.43	<.0001
Sex	1	431	2.87	0.091
Age group	3	431	1.89	0.13
Time since stroke group	3	431	4.20	0.006
Randomisation	-	_	-	-
Level of difficulty	1	431	0.35	0.55

Table XIV. Duplicate data, choice of data items and justification

Duplication of language data items by domains and dataset were identified. The language data taken forward to inform our analysis is highlighted together with justification for the choice of dataset.

Study ID	Measures (IPD baseline, follow- up)	Choice made with reason
023	WAB (0, 98) WAB-AQ (59, 98)	WAB-AQ – IPD at baseline and follow-up available
027	ASRS (30, 32) WAB-AQ (30, 57)	WAB-AQ – more IPD at follow-up WAB-AQ is also the anchor measure

(i) Overall language ability; Anchor Measure WAB -AQ

(ii) Auditorv comprehension: Anchor Measure AAT

	Measures		
Study ID	(IPD baseline, follow-	Choice made with reason	
	up)		
0110	PICA (24, 24)	TT62 is within the same family as the anchor measure	
011a	TT62 (24, 24)	1102 is wrunn the same ranning as the alichor measure	
	PPVT (12, 24)		
011c	PICA (12, 12)	PPVT has more IPD at follow-up	
	TT62 (12, 12)		
	AAT (140, 0)		
015	SAPS (136, 136)	SAPS has IPD at follow-up	
	TT (141, 0)		
026	PSCT (25, 108)	TT62 has more IDD at hasaling and follow up	
020	TT36 (31, 216)	1102 has more IPD at baseline and follow-up	
027	LAAB (30, 57)	LAAP has more IDD at hasaling and follow up	
027	TT (29, 56)	LAAB has more IFD at baseline and tonow-up	
054	PALPA (80, 0)	TT26 is only one with IDD at follow up	
034	TT36 (76, 155)	1150 is only one with IPD at follow-up	
060	PALPA (57, 51)	TT has marginally more IPD at follow-up and it is also	
000	TT (57, 52)	the anchor measure	
067	AAT (44, 39)	A AT is the only one with IPD at follow up	
007	TT (40, 0)	AAT is the only one with IPD at follow-up	

((iii)	Naming:	Anchor	Measure	BNT
1	222)	1, 4, 1, 1, 1, 1, 2, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1,	11101101	11100000000	

Study ID	Measures (IPD baseline, follow-up)	Choice made and reason			
011a	ONT (24, 48)	ONT has more IPD at follow-up			
0110	ONT (12, 24)	ONT has more IDD at follow, up			
0110	PICA (12, 12)	ONT has more IFD at tonow-up			
041	BNT (11, 22) CAT (11, 22)	BNT is the anchor measure			
054	AAT (72, 0) BNT (71, 152)	BNT has IPD at follow-up			
081	BNT-G (38, 64) Snodgrass (38, 76)	Snodgrass has more IPD at follow-up			

Study ID	Measures (IPD baseline, follow-up)	Choice made and reason
006	AAT (10, 0) CAL (10, 20)	CAL has IPD at follow-up
008	TOMs-activity (34, 49) TOMs-participation (34, 49)	Analysis done on set with activity and set with participation
015	AAT (142, 0) ANELT (72, 142) CETI (71, 129) KOPS (40, 36)	ANELT has more IPD at baseline and follow-up
054	AAT (72, 0) ANELT (80, 160)	ANELT has IPD at follow-up

(iv) Functional communication (observer-rated) Anchor Measure AAT

Effect	Number	Denominator	F Value	P value	
	DF	DF			
Overall language ability					
Baseline score	1	458	79.03	<.0001	
Sex	1	458	1.86	0.17	
Age group	3	458	1.18	0.32	
Time since stroke group	3	458	2.00	0.11	
Randomisation	-	-	-	-	
Frequency group	5	458	0.93	0.46	
Auditory Comprehension					
Baseline score	1	511	83.31	<.0001	
Sex	1	511	0.86	0.35	
Age group	3	511	5.40	0.0012	
Time since stroke group	3	511	1.30	0.28	
Randomisation	-	-	-	-	
Frequency group	5	511	3.10	0.0091	
Naming					
Baseline score	1	360	4.99	0.026	
Sex	1	360	0.06	0.81	
Age group	3	360	2.64	0.049	
Time since stroke group	3	360	2.13	0.097	
Randomisation	-	-	-	-	
Frequency group	4	360	2.70	0.030	
Functional Communication					
Baseline score	1	499	34.09	<.0001	
Sex	1	499	5.54	0.019	
Age group	3	499	0.86	0.46	
Time since stroke group	3	499	4.08	0.0071	
Randomisation	-	-	-	-	
Frequency group	5	499	1.45	0.21	

Table XV SLT frequency and goodness of fit to baseline, sex, age and time; model by language domain

DF = degrees of freedom; F value = F statistic

Effect	Numerator	Denominator	F Value	P value
	DF	DF		
Overall language ability				
Baseline score	1	408	99.39	<.0001
Sex	1	408	2.08	0.15
Age group	3	408	1.38	0.25
Time since stroke group	3	408	3.54	0.01
Randomisation	-	-	-	-
Duration group	1	408	0.96	0.44
Auditory Comprehension				
Baseline score	1	511	82.38	<.0001
Sex	1	511	0.58	0.45
Age group	3	511	5.75	0.0007
Time since stroke group	3	511	1.46	0.22
Randomisation	-	-	-	-
Duration group	5	511	4.04	0.0013
Naming				
Baseline score	1	360	5.38	0.021
Sex	1	360	0.03	0.86
Age group	3	360	2.63	0.05
Time since stroke group	3	360	1.95	0.12
Randomisation	-	-	-	-
Duration group	4	360	0.10	0.98
Functional communication				
Baseline score	1	448	40.69	<.0001
Sex	1	448	5.60	0.018
Age group	3	448	0.67	0.57
Time since stroke group	3	448	4.35	0.0049
Randomisation	-	-	-	-
Duration group	5	448	1.28	0.27

Table XVI. SLT duration and goodness	of fit to baseline	, sex, age and	time; model by
language domain			

DF = degrees of freedom; F value = F statistic

Effect	Numerator	Denominator	F Voluo	D voluo	
	DF	DF	r value		
Overall language ability					
Baseline score	1	458	78.41	<.0001	
Sex	1	458	1.75	0.19	
Age group	3	458	1.41	0.24	
Time since stroke group	3	458	2.27	0.08	
Randomisation	-	-	-	-	
Intensity group	5	458	0.95	0.45	
Auditory Comprehension					
Baseline score	1	511	86.69	<.0001	
Sex	1	511	0.56	0.46	
Age group	3	511	6.16	0.0004	
Time since stroke group	3	511	1.77	0.15	
Randomisation	-	-	-	-	
Intensity group	5	511	4.67	0.0004	
Naming					
Baseline score	1	359	4.94	0.03	
Sex	1	359	0.09	0.76	
Age group	3	359	2.49	0.06	
Time since stroke group	3	359	1.61	0.17	
Randomisation	-	-	-	-	
Intensity group	5	359	1.90	0.09	
Functional Communication					
Baseline score	1	506	35.98	<.0001	
Sex	1	506	5.48	0.02	
Age group	3	506	1.22	0.30	
Time since stroke group	3	506	3.86	0.0095	
Randomisation	-	-	-	-	
Intensity group	5	506	1.13	0.34	

Table XVII: SLT intensity and goodness of fit to baseline, sex, age, time since index stroke; model by language domain

DF = degrees of freedom; F value = F statistic.

Effect	Numerator DF	Denominator DF	F Value	P value
Overall language ability				
Baseline score	1	456	80.20	<.0001
Sex	1	456	2.39	0.12
Age group	3	456	1.32	0.27
Time since stroke group	3	456	2.62	0.05
Randomisation	-	-	-	-
Dosage group	5	456	1.70	0.13
Auditory Comprehension				
Baseline score	1	511	87.74	<.0001
Sex	1	511	0.72	0.40
Age group	3	511	5.52	0.001
Time since stroke group	3	511	1.47	0.22
Randomisation	-	-	-	-
Dosage group	5	511	1.38	0.23
Naming				
Baseline score	1	360	6.31	0.01
Sex	1	360	0.07	0.79
Age group	3	360	2.51	0.06
Time since stroke group	3	360	1.31	0.27
Randomisation	-	-	-	-
Dosage group	5	360	2.36	0.04
Functional Communication				
Baseline score	1	497	38.15	<.0001
Sex	1	497	6.56	0.01
Age group	3	497	0.92	0.43
Time since stroke group	3	497	4.34	0.005
Randomisation	-	-	-	-
Dosage group	5	497	2.76	0.018

Table XVIII: SLT dosage and goodness of fit to baseline, sex, age and time; model by language domain

DF = degrees of freedom; F value = F statistic.

Table XIX. Trials including people with aphasia after stroke, but which did not inform our IPD network meta-analysis: (i) IPD included in RELEASE database but minimum data items for our analysis reported here were unavailable; (ii) Potentially eligible trials invited to contribute IPD, but IPD remained unavailable. Availability of minimum data items was unconfirmed

Citation	Location	Potential IPD	SLT
Table XIX (i). Included trials in RELEASE database with IPD, but minimum database	ta points or	data items rema	uined unavailable
Bowen A, Hesketh A, Patchick E, Young A, Davies L, Vail A, <i>et al.</i> Clinical effectiveness, cost effectiveness and service users' perceptions of early, well-resourced communication therapy following a stroke: a randomised controlled trial (the ACT NoW Study). <i>Health Technology Assessment</i> 2012; 16 (26):1-160. https://doi.org/10.3310/hta16260	UK	153	Eligible language data was unavailable
Baker JM, Rorden C, Fridriksson J. Using transcranial direct-current stimulation to treat stroke patients with aphasia. <i>Stroke</i> 2010; 41 (6):1229-1236. https://doi.org/10.1161/STROKEAHA.109.576785	USA	10	IPD outcomes following intervention unavailable
Barwood CH, Murdoch BE, Whelan BM, Lloyd D, Riek S, O'Sullivan K, <i>et al.</i> The effects of low frequency Repetitive Transcranial Magnetic Stimulation (rTMS) and sham condition rTMS on behavioural language in chronic non-fluent aphasia: short term outcomes. <i>NeuroRehabilitation</i> 2011; 28 (2):113-128. https://doi.org/10.3233/NRE20110640	AU	12	No SLT intervention during study
Berthier ML, Green C, Lara JP, Higueras C, Barbancho MA, Dávila G, et al. Mematine and constraint-induced aphasia therapy in chronic poststroke aphasia. <i>Annals of Neurology</i> 2009; 65 (5):577-585. https://doi.org/10.1002/ana.21597	ES	28	Eligible language data was unavailable
Thomas SA, Walker MF, Macniven JA, Haworth H, Lincoln NB. Communication and Low Mood (CALM): a randomized controlled trial of behavioural therapy for stroke patients with aphasia. <i>Clinical Rehabilitation</i> 2013; 27 (5):398–408. https://doi.org/10.1177/0269215512462227	UK	105	No SLT intervention within study
Rosso C, Perlbarg V, Valabregue R, Arbizu C, Ferrieux S, Alshawan B et al. Broca's area damage is necessary but not sufficient to induce after-effects of cathodal tDCS on the unaffected hemisphere in post-stroke aphasia. <i>Brain Stimulation</i> 2014; 7 (5):627-635.	FR	35	No SLT intervention within study
David RM. A comparison of speech therapists and volunteers in the treatment of acquired aphasia. PhD thesis. London: University of London; 1982.	UK	155	Social support comparison intervention
Elman RJ, Bernstein-Ellis E. The efficacy of group communication treatment in adults with chronic aphasia. <i>Journal of Speech, Language and Hearing Research</i> 1999; 42 (2):411-419. https://doi.org/10.1044/jslhr.4202.411	US	24	SLT intervention delivered but post- intervention IPD language outcome data unavailable

Hinckley JJ, Patterson JP, Carr TH. Differential effects of context- and skill-based treatment approaches: preliminary findings. <i>Aphasiology</i> 2001; 15 (5):463-476. https://doi.org/10.1080/02687040042000340	USA	17	SLT intervention delivered but post- intervention IPD language outcome data unavailable
Kang EK, Kim YK, Sohn HM, Cohen LG, Paik N-J. Improved picture naming in aphasia patients treated with cathodal tDCS to inhibit the right Broca's homologue area. <i>Restorative Neurology and Neuroscience</i> 2011; 29 (3):141-152. https://doi.org/10.3233/RNN-2011-0587	KR	10	SLT intervention delivered but post- intervention IPD language outcome data unavailable
Kendall DL, Oelke M, Brookshire CE, Nadeau SE. The influence of phonomotor treatment on word retrieval abilities in 26 individuals with chronic aphasia: an open trial. <i>Journal of Speech Language and Hearing Research</i> 2015; 58 (3):798-812. https://doi.org/10.1044/2015_JSLHR-L-14-0131	US	26	RCT but reported as cohort. Group allocation code unavailable
Laska AC, von Arbin M, Kahan T, Hellblom A, Murray V. Long-term antidepressant treatment with moclobemide for aphasia in acute stroke patients: a randomised, double-blind, placebo-controlled study. <i>Cerebrovascular Diseases</i> 2005; 19 (2):125-132.	SE	119	No SLT intervention within study
Lyon JG, Cariski D, Keisler L, Rosenbek J, Levine R, Kumpula J, <i>et al.</i> Communication partners: enhancing participation in life and communication for adults with aphasia in natural settings. <i>Aphasiology</i> 1997; 11 (7):693-708. https:// doi.org/10.1080/02687039708249416	US	10	Eligible language data was unavailable
Marangolo P, Fiori V, Calpagnano MA, Campana S, Razzana C, Caltagirone C, <i>et al.</i> tDCS over the left inferior frontal cortex improves speech production in aphasia. <i>Frontiers in Human Neuroscience</i> 2013;7:539. https://doi.org/10.3389/fnhum.2013.00539	IT	12	SLT intervention delivered but post- intervention IPD language outcome data unavailable
Marshall RC, King PS. Effects of fatigue produced by isokinetic exercise on the communication ability of aphasic adults. <i>Journal of Speech Language and Hearing Research</i> 1973; 16 (2):222-230.	US	16	No SLT intervention within study Eligible language data was unavailable
Medina J, Norise C, Faseyitan O, Coslett HB, Turkeltaub PE, Hamilton RH. Finding the right words: transcranial magnetic stimulation improves discourse productivity in non-fluent aphasia after stroke. <i>Aphasiology</i> 2012; 26 (9):1153-1168. https://doi.org/10.1080/02687038.2012.710316	USA	10	No SLT intervention within study
Polanowska KE, Leśniak MM, Seniów JB, Czepiel W, Czlonkowska A. Anodal transcranial direct current stimulation in early rehabilitation of patients with post-stroke non-fluent aphasia: a	PL	26	Post-intervention IPD language outcome data unavailable

randomized, double-blind, sham-controlled pilot study. <i>Restorative Neurology and Neuroscience</i> 2013; 31 (6):761-771. https://doi.org/10.3233/RNN-130333			
Pulvermüller F, Neininger B, Elbert T, Mohr B, Rockstroh B, Koebbel P, et al. Constraint- induced therapy of chronic aphasia after stroke. <i>Stroke</i> 2001; 32 (7):1621-1626. https://doi.org/10.1161/01.STR.32.7.1621	DE	17	Post-intervention IPD language outcome data unavailable
Roberts PM, Le Dorze G. Bilingual aphasia: semantic organization, strategy use, and productivity in semantic verbal fluency. <i>Brain and Language</i> 1998; 65 (2):287-312. https://doi.org/10/1006/brln.1998.1992	CA	16	No SLT intervention within study
Seniów J, Waldowski K, Leśniak M, Iwański S, Czepiel W, Czlonkowska A. Transcranial magnetic stimulation combined with speech and language training in early aphasia rehabilitation: a randomized double-blind controlled pilot study. <i>Topics in Stroke Rehabilitation</i> 2013; 20 (3):250-261. https://doi.org/10.1310/tsr2003-250	PL	40	Post-intervention IPD language outcome data unavailable
Shah-Basak PP, Norise C, Garcia G, Torres J, Faseyitan O, Hamilton RH. Individualized treatment with transcranial direct current stimulation in patients with chronic non-fluent aphasia due to stroke. <i>Frontiers in Human Neuroscience</i> 2015; 9 (201). https://doi.org/10.3389/fnhum.2015.00201	US	12	Post-intervention IPD language outcome data unavailable
Springer L, Willmes K, Haag E. Training in the use of wh-questions and prepositions in dialogues: a comparison of two different approaches in aphasia therapy. <i>Aphasiology</i> 1993;7(3):251-270. https://doi.org./10.1080/02687039308249509	DE	12	Post-intervention IPD language outcome data unavailable

Table XIX (ii) Potentially eligible trials invited to contribute IPD, but IPD remained unavailable. Availability of minimum data items was unconfirmed

Ashtary F, Janghorbani M, Chitsaz A, Reisi M, Bahrami A. A randomized double-blind trial of bromocriptine efficacy in nonfluent aphasia after stroke. <i>Neurology</i> 2006; 66 :914-6.	Iran	38	Usual care - regimen unreported
Bakheit AMO, Shaw S, Barrett L, Wood J, Carrington S, Griffiths S, <i>et al.</i> A prospective, randomized, parallel group, controlled study of the effect of intensity of speech and language therapy on early recovery from poststroke aphasia. <i>Clinical Rehabilitation</i> 2007; 21 :885-94.	UK	97 (plus n=19 non- randomised)	5 hours SLT versus 2 hours SLT

Berthier ML, Green C, Higueras C, Fernandez I, Hinojosa J, Martin MC. A randomized, placebo-controlled study of donepezil in poststroke aphasia. <i>Neurology</i> 2006; 67 :1687-9.	Spain	26	Usual care - regimen unreported
Cherney L. Oral Reading for Language in Aphasia (ORLA): Evaluating the efficacy of computer-delivered therapy in chronic nonfluent aphasia. <i>Topics in Stroke Rehabilitation</i> 2010; 17 :423-31.	USA	25	SLT with virtual therapist versus therapist for 1 hour of therapy, 2 to 3 time weekly for 24 sessions (24 hours in total)
Cherney LB, Babbitt, Cole R, Vuuren S, Hurwitz R, Ngampatipatpong N. Computer treatment for aphasia: efficacy and treatment intensity. <i>Archives of Physical Medicine and Rehabilitation</i> 2006; 87 :E5.	USA	13	4 versus 10 hours SLT weekly for 6 weeks
Conklyn D, Novak E, Boissy A, Bethoux F, Chemali K. The effects of modified melodic intonation therapy on nonfluent aphasia: a pilot study. <i>Journal of Speech, Language and Hearing Research</i> 2012;55:1463-71. http://dx.doi.org/10.1044/1092-4388(2012/11-0105)	USA	30	10 to 15 minutes therapy for up to three sessions. 30-45 minutes total dosage
Crosson B, Fabrizio KS, Singletary F, Cato MA, Wierenga CE, Parkinson RB, <i>et al.</i> Treatment of naming in nonfluent aphasia through manipulation of intention and attention: a phase 1 comparison of two novel treatments. <i>Journal of the International Neuropsychological Society</i> 2007; 13 :582-94.	USA	23	Naming therapy with gesture versus usual care. 1 hour SLT, twice daily, 5 days per week for a total of 30 session. Total dosage 30 hours
Denes G, Perazzolo C, Piani A, Piccione F. Intensive versus regular speech therapy in global aphasia: a controlled study. <i>Aphasiology</i> 1996; 10 :385-94.	Italy	17	45-60 minutes SLT, 5 times weekly for 6 months
Di Carlo LM. Language recovery in aphasia: effect of systematic filmed programmed instruction. <i>Archives of Physical Medicine and Rehabilitation</i> 1980; 61 :41-4.	USA	14	SLT details unreported but at least 80 hours for 5-22 months
Elman RJ, Bernstein-Ellis E. Psychosocial aspects of group communication treatment. Preliminary findings. <i>Seminars in Speech and Language</i> 1999; 20 :65-2.	USA	12 (plus n=12 no SLT)	Group SLT for 150 minutes, twice weekly for 4 months for a total dosage 160 hours

Enderby P, Broeckx J, Hospers W, Schildermans F, Deberdt W. Effect of piracetam on recovery and rehabilitation after stroke: a double-blind, placebo-controlled study. <i>Clinical Neuropharmacology</i> 1994; 17 :320-31.	UK	67	SLT dosage reported in hours at group summary level
Ferro JM, Leal G, Farrajota L, Fonseca J, Guerreiro M, Castro-Caldas A. Speech therapy or home training for stroke aphasics? <i>Journal of neurology</i> 1992; 239 :20.	Portugal	94	SLT over 6 months. Further details unreported
Gonzalez I, Petit H, Muller F, Daviet JC, Trias J, De BX, <i>et al.</i> The workbook of communication C.COM in disclosure alterations of severe vascular aphasia, Le cahier de communication C.COM dans les alterations de la communication de l'aphasie vasculaire severe. <i>Annals of Physical and Rehabilitation Medicine</i> 2012; 55 :e213-e6.	France	29	SLT regimen unreported
Gungor L, Terzi M, Onar MK. Does long term use of piracetam improve speech disturbances due to ischemic cerebrovascular diseases? <i>Brain and Language</i> 2011; 117 :23-7.	Turkey	30	Usual care - regimen unreported
Gupta SR, Mlcoch AG, Scolaro C, Moritz T. Bromocriptine treatment of nonfluent aphasia. <i>Neurology</i> 1995; 45 :2170-3.	USA	20	Usual care - regimen unreported
Hamzei-Moghaddam A, Shafa MA, Nazari M, Akbari M. The effect of priacetam in aphasia due to acute brain ischemic stroke: Clinical trial. <i>Journal of Kerman University of Medical Sciences</i> 2014; 21 :219-29.	Iran	40	Usual care - regimen unreported
Howard D, Patterson K, Franklin S, Orchard-Lisle V, Morton J. Treatment of word retrieval deficits in aphasia. A comparison of two therapy methods. <i>Brain</i> 1985; 108 (Pt 4):817-29.	UK	12	2 versus 4 weeks of semantic or phonological SLT
Huber W, Willmes K, Poeck K, Van Vleymen B, Deberdt W. Piracetam as an adjuvant to language therapy for aphasia: a randomized double-blind placebo-controlled pilot study. <i>Archives of Physical Medicine and</i> <i>Rehabilitation</i> 1997; 78 :245-50.	Germany	66	SLT for 60 minutes, 10 times week (5 individuals; 5 group therapy) for 6 weeks

Katz RC, Wertz RT. The efficacy of computer-provided reading treatment of chronic aphasic adults. <i>Journal of Speech, Language & Hearing Research</i> 1997; 40 :493-507.	USA	21 (of 63)	SLT 3 hours weekly for 26 weeks; 78 hours dosage
Kessler J, Thiel A, Karbe H, Heiss WD. Piracetam improves activated blood flow and facilitates rehabilitation of poststroke aphasic patients. <i>Stroke;</i> 2000; 31 :2112-6.	Germany	24	SLT for 60 minutes, 5 times weekly for 6 weeks. 30 hours total dosage.
Lincoln NB, McGuirk E, Mulley GP. Effectiveness of speech therapy for aphasic stroke patients. A randomised controlled trial. <i>Lancet</i> 1984; 1 :1197-200.	UK	76 (of 327 randomised)	Usual care SLT for 1 hour, twice weekly, for 24 weeks. 48 hours total dosage
Liu Y, Zhang L. The TCM-combined treatment for aphasia due to cerebrovascular disorders. <i>Journal of traditional Chinese medicine / Chung i tsa chih ying wen pan</i> 2006; 26 :19-21.	Peoples Republic of China	19 (of 36 randomised)	SLT details unreported
Ma L. Cognitive function training for patients with thalamic aphasia. <i>Chinese Journal of Clinical Rehabilitation</i> 2005; 9 :160-1.	China	30	SLT details unreported
MacKay S, Holmes DW, Gersumky AT. Methods to assess aphasic stroke patients. <i>Geriatric Nursing (New York, NY)</i> 1988; 9 :177-9.	USA	95 but SLT versus no SLT allocation unreported	SLT for 3 to 6 hours weekly, for 1 year. Up to 312 hours dosage.
Marshall RC, Wertz RT, Weiss DG, Aten JL, Brookshire RH, Garcia- Bunuel L, <i>et al.</i> Home treatment for aphasic patients by trained nonprofessionals. <i>Journal of Speech and Hearing Disorders</i> 1989; 54 :462-			Usual care SLT (n=38); 8-10 hours weekly, for 12 weeks. Up to 120 hours dosage
70.	USA	81 (of 121 randomised)	versus
			Volunteer-facilitated SLT (n=43) for 8 to 10 hours weekly, for 12 weeks. 120 hours total dosage
Nobis-Bosch R, Springer L, Radermacher I, Huber W. Supervised Home Training in Aphasia: Language Learning in Dialogues. <i>Forum Logopadie</i> 2010; 24 :6-13.	Germany	9 (of 18 randomised)	SLT (n=9) for 1 hour, twice daily, four days each week for 4 week plus 1 hour individual SLT session versus (no SLT) n=9

Polanowska KE, Lesniak M, Seniow JB, Czlonkowska A. No effects of anodal transcranial direct stimulation on language abilities in early rehabilitation of post-stroke aphasic patients. <i>Neurologia i neurochirurgia polska</i> 2013; 47 :414-22.	Poland	37	SLT 45 minutes daily, five times weekly, for three weeks. 11 hours total dosage.
Prins RS, Schoonen R, Vermeulen J. Efficacy of Two Different Types of Speech Therapy for Aphasic Stroke Patients. <i>Applied Psycholinguistics</i> 1989; 10 :85-123.	Netherlands	21	SLT twice weekly for 5 months. Dosage unreported
Seniow J, Litwin M, Litwin T, Lesniak M, Czlonkowska A. New approach to the rehabilitation of post-stroke focal cognitive syndrome: effect of levodopa combined with speech and language therapy on functional recovery from aphasia. <i>Journal of the neurological sciences</i> 2009; 283 :214- 8.	Poland	39	SLT 45 minutes, 5 times weekly, for 3 weeks. 11 hours total dosage.
Shewan CM, Kertesz A. Effects of speech and language treatment on recovery from aphasia. <i>Brain and Language</i> 1984; 23 :272-99.	Canada	52 (of 77 randomised)	Language oriented SLT (n=28) 1 hour, 3 times weekly for 12 months. 156 hours total dosage. Usual care SLT (n=24) 1 hour, 3 times weekly for 12 months. 156 hours
Sickert A, Anders LC, Münte T, Sailer M. Constraint-induced aphasia therapy following sub-acute stroke: a single-blind, randomised clinical trial of a modified therapy schedule. <i>Journal of Neurology, Neurosurgery &</i> <i>Psychiatry</i> 2014; 85 :51-5.	Germany	100	Constraint-induced aphasia therapy (n=50) 2 hours SLT daily, for 15 days. Total dosage 30 hours. Usual care SLT (n=50) 2 hours SLT daily, for 15 days. Total dosage 30 hours.
Spielmann K, Van De Sandt-Koenderman MWME, Ribbers GM. Transcranial direct current stimulation (tDCS) to enhance treatment effects in aphasia. <i>Archives of Physical Medicine and Rehabilitation</i> 2014; 95 :e21.	Netherlands	58	SLT for 2 weeks.
Tsai PY, Wang CP, Ko JS, Chung YM, Chang YW, Wang JX. The persistent and broadly modulating effect of inhibitory rTMS in nonfluent	Taiwan	56	SLT for 1 hour in addition to usual care

aphasic patients: a sham-controlled, double-blind study. Neurorehabilitation and Neural Repair 2014;28:779-87. http://dx.doi.org/10.1177/1545968314522710			
Waldowski K, Seniow J, Lesniak M, Iwanski S, Czlonkowska A. Effect of low-frequency repetitive transcranial magnetic stimulation on naming abilities in early-stroke aphasic patients: a prospective, randomized, double- blind sham-controlled study. <i>Scientific World Journal</i> 2012; 2012 :518568	Poland	26	SLT for 45 minutes, 5 days a week for 3 weeks. Total dosage 11 hours.
Walker-Batson D, Unwin H, Ford J, Curtis S, Porch B. A double-blind controlled study of the use of amphetamine in the treatment of aphasia. <i>Stroke</i> 2001; 32 :2093-2098.	USA	21	SLT for 1 hour, for 10 sessions over 5 weeks
Wang L, Liu SM, Liu M, Li BJ, Hui ZL, Gao X. [Post-stroke speech disorder treated with acupuncture and psychological intervention combined with rehabilitation training: a randomized controlled trial]. <i>Zhongguo Zhen Jiu</i> 2011; 31 :481-6.	People's Republic of China	120	SLT details unreported
Weiduschat N, Thiel A, Rubi-Fessen I, Hartmann A, Kessler J, Merl P, <i>et al.</i> Effects of Repetitive Transcranial Magnetic Stimulation in Aphasic Stroke. A Randomized Controlled Pilot Study. <i>Stroke</i> 2011; 42 :409-15.	Germany	10	SLT for 45 minutes
Wu XJ. Analysis of the effect of "two-step method" on aphasia in patients with acute cerebrovascular disease. <i>Chinese Journal of Clinical Rehabilitation</i> 2004; 8 :4422-3.	People's Republic of China	120 (of 236 randomised)	SLT details unreported over 6 months SLT duration
Xie SL, Zhu MG, Zhang XL, Xue ZJ. The role of community nursing in family rehabilitation of stroke patients with impaired spoken language. <i>Chinese Journal of Clinical Rehabilitation</i> 2002; 6 :3289.	People's Republic of China	17 (of 34 randomised)	SLT for 1 hour, 6 times weekly, over 12 months. 312 hours total dosage
Yao J, Xue Y, Li F. Clinical application research on collective language strengthened training in rehabilitation nursing of cerebral apoplexy patients with aphasia. <i>Chinese Nursing Research</i> 2005; 19 :482-4.	People's Republic of China	54	SLT (n=30) daily for 28 days. Usual care SLT (n=24) daily. Further details unreported
Zhang HM. [Clinical treatment of apoplectic aphemia with multi-needle puncture of scalp-points in combination with visual-listening-speech training]. <i>Zhen ci yan jiu [Acupuncture research]</i> 2007; 32 :190-4.	People's Republic of China	19 (of 36 randomised)	SLT details unreported

Zhang SH, Lu XM. Nursing care of the patient with cerebral infarction and aphasia receiving carotid internal drug injection and early speech training. <i>Journal of Nursing Science</i> 1997; 12 :34-5.	People's Republic of China	16 (of 35 randomised)	SLT for 30 minutes, 3 to 5 times daily. Duration unreported
Zhao H, Ying B, Shen C. Clinical Study on the Effect of Combined Therapy of Medicine, Acupuncture and Speech Training on Aphasia from Ischemic Apoplexy. <i>Henan Traditional Chinese Medicine Henan Zhong yi</i> 2000; 20 :31-2.	People's Republic of China	98 (of 138 randomised)	SLT details unreported
IPD Individual participant data			

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Table XX. Unavailable potentially eligible randomised controlled trial IPD

Ref	Study References*	IPD
1.	Ashtary F, Janghorbani M, Chitsaz A, Reisi M, Bahrami A. A randomized double-blind trial of bromocriptine efficacy in nonfluent aphasia after stroke. <i>Neurology</i> 2006; 66 :914-6.	38
2.	Bakheit AM, Carrington S, Griffiths S, Searle K. High scores on the Western Aphasia Battery correlate with good functional communication skills (as measured with the Communicative Effectiveness Index) in aphasic stroke patients. <i>Disability and Rehabilitation</i> 2005; 27 :287-91.	67
3.	Bakheit AMO, Shaw S, Barrett L, Wood J, Carrington S, Griffiths S, <i>et al.</i> A prospective, randomized, parallel group, controlled study of the effect of intensity of speech and language therapy on early recovery from poststroke aphasia. <i>Clinical Rehabilitation</i> 2007; 21 :885-94.	116
4.	Berthier ML, Green C, Higueras C, Fernandez I, Hinojosa J, Martin MC. A randomized, placebo-controlled study of donepezil in poststroke aphasia. <i>Neurology</i> 2006; 67 :1687-9.	28
5.	Cherney L. Oral Reading for Language in Aphasia (ORLA): Evaluating the efficacy of computer-delivered therapy in chronic nonfluent aphasia. <i>Topics in Stroke Rehabilitation</i> 2010; 17 :423-31.	25
6.	Cherney LB, Babbitt, Cole R, Vuuren S, Hurwitz R, Ngampatipatpong N. Computer treatment for aphasia: efficacy and treatment intensity. <i>Archives of Physical Medicine and Rehabilitation</i> 2006; 87 :E5.	13
7.	Conklyn D, Novak E, Boissy A, Bethoux F, Chemali K. The effects of modified melodic intonation therapy on nonfluent aphasia: a pilot study. <i>Journal of Speech, Language and Hearing Research</i> 2012;55:1463-71. http://dx.doi.org/10.1044/1092-4388(2012/11-0105)	30
8.	Crosson B, Fabrizio KS, Singletary F, Cato MA, Wierenga CE, Parkinson RB, <i>et al.</i> Treatment of naming in nonfluent aphasia through manipulation of intention and attention: a phase 1 comparison of two novel treatments. <i>Journal of the International</i> <i>Neuropsychological Society</i> 2007; 13 :582-94.	23
9.	Denes G, Perazzolo C, Piani A, Piccione F. Intensive versus regular speech therapy in global aphasia: a controlled study. <i>Aphasiology</i> 1996; 10 :385-94.	17
10.	Di Carlo LM. Language recovery in aphasia: effect of systematic filmed programmed instruction. <i>Archives of Physical Medicine and Rehabilitation</i> 1980; 61 :41-4.	14
11.	Elman RJ, Bernstein-Ellis E. Psychosocial aspects of group communication treatment. Preliminary findings. <i>Seminars in Speech and Language</i> 1999; 20 :65-2.	12
12.	Enderby P, Broeckx J, Hospers W, Schildermans F, Deberdt W. Effect of piracetam on recovery and rehabilitation after stroke: a double-blind, placebo-controlled study. <i>Clinical Neuropharmacology</i> 1994; 17 :320-31.	67

13.	Ferro JM, Leal G, Farrajota L, Fonseca J, Guerreiro M, Castro-Caldas A. Speech therapy or home training for stroke aphasics? <i>Journal of neurology</i> 1992; 239 :20.	94
14.	Gonzalez I, Petit H, Muller F, Daviet JC, Trias J, De BX, <i>et al.</i> The workbook of communication C.COM in disclosure alterations of severe vascular aphasia, Le cahier de communication C.COM dans les alterations de la communication de l'aphasie vasculaire severe. <i>Annals of Physical and Rehabilitation Medicine</i> 2012; 55 :e213-e6.	29
15.	Gungor L, Terzi M, Onar MK. Does long term use of piracetam improve speech disturbances due to ischemic cerebrovascular diseases? <i>Brain and Language</i> 2011; 117 :23-7.	30
16.	Gupta SR, Mlcoch AG, Scolaro C, Moritz T. Bromocriptine treatment of nonfluent aphasia. <i>Neurology</i> 1995; 45 :2170-3.	20
17.	Hamzei-Moghaddam A, Shafa MA, Nazari M, Akbari M. The effect of priacetam in aphasia due to acute brain ischemic stroke: Clinical trial. <i>Journal of Kerman University of Medical Sciences</i> 2014; 21 :219-29.	40
18.	Howard D, Patterson K, Franklin S, Orchard-Lisle V, Morton J. Treatment of word retrieval deficits in aphasia. A comparison of two therapy methods. <i>Brain</i> 1985; 108 (Pt 4):817-29.	12
19.	Huber W, Willmes K, Poeck K, Van Vleymen B, Deberdt W. Piracetam as an adjuvant to language therapy for aphasia: a randomized double-blind placebo-controlled pilot study. <i>Archives of Physical Medicine and Rehabilitation</i> 1997; 78 :245-50.	66
20.	Katz RC, Wertz RT. The efficacy of computer-provided reading treatment of chronic aphasic adults. <i>Journal of Speech, Language & Hearing Research</i> 1997; 40 :493-507.	55
21.	Kessler J, Thiel A, Karbe H, Heiss WD. Piracetam improves activated blood flow and facilitates rehabilitation of poststroke aphasic patients. <i>Stroke;</i> 2000; 31 :2112-6.	24
22.	Lincoln NB, McGuirk E, Mulley GP. Effectiveness of speech therapy for aphasic stroke patients. A randomised controlled trial. <i>Lancet</i> 1984; 1 :1197-200.	191
23.	Liu Y, Zhang L. The TCM-combined treatment for aphasia due to cerebrovascular disorders. <i>Journal of traditional Chinese medicine / Chung i tsa chih ying wen pan</i> 2006; 26 :19-21.	36
24.	Ma L. Cognitive function training for patients with thalamic aphasia. <i>Chinese Journal of Clinical Rehabilitation</i> 2005; 9 :160-1.	30
25.	MacKay S, Holmes DW, Gersumky AT. Methods to assess aphasic stroke patients. <i>Geriatric Nursing (New York, NY)</i> 1988; 9 :177-9.	95
26.	Marshall RC, Wertz RT, Weiss DG, Aten JL, Brookshire RH, Garcia-Bunuel L, <i>et al.</i> Home treatment for aphasic patients by trained nonprofessionals. <i>Journal of Speech and</i> <i>Hearing Disorders</i> 1989; 54 :462-70.	121

27.	Nobis-Bosch R, Springer L, Radermacher I, Huber W. Supervised Home Training in Aphasia: Language Learning in Dialogues. <i>Forum Logopadie</i> 2010; 24 :6-13.	18
28.	Polanowska KE, Lesniak M, Seniow JB, Czlonkowska A. No effects of anodal transcranial direct stimulation on language abilities in early rehabilitation of post-stroke aphasic patients. <i>Neurologia i neurochirurgia polska</i> 2013; 47 :414-22.	37
29.	Prins RS, Schoonen R, Vermeulen J. Efficacy of Two Different Types of Speech Therapy for Aphasic Stroke Patients. <i>Applied Psycholinguistics</i> 1989; 10 :85-123.	32
30.	Seniow J, Litwin M, Litwin T, Lesniak M, Czlonkowska A. New approach to the rehabilitation of post-stroke focal cognitive syndrome: effect of levodopa combined with speech and language therapy on functional recovery from aphasia. <i>Journal of the neurological sciences</i> 2009; 283 :214-8.	39
31.	Shewan CM, Kertesz A. Effects of speech and language treatment on recovery from aphasia. <i>Brain and Language</i> 1984; 23 :272-99.	100
32.	Sickert A, Anders LC, M«"nte T, Sailer M. Constraint-induced aphasia therapy following sub-acute stroke: a single-blind, randomised clinical trial of a modified therapy schedule. <i>Journal of Neurology, Neurosurgery & Psychiatry</i> 2014; 85 :51-5.	100
33.	Spielmann K, Van De Sandt-Koenderman MWME, Ribbers GM. Transcranial direct current stimulation (tDCS) to enhance treatment effects in aphasia. <i>Archives of Physical Medicine and Rehabilitation</i> 2014; 95 :e21.	58
34.	Tsai PY, Wang CP, Ko JS, Chung YM, Chang YW, Wang JX. The persistent and broadly modulating effect of inhibitory rTMS in nonfluent aphasic patients: a sham-controlled, double-blind study. <i>Neurorehabilitation and Neural Repair</i> 2014;28:779-87. http://dx.doi.org/10.1177/1545968314522710	56
35.	Waldowski K, Seniow J, Lesniak M, Iwanski S, Czlonkowska A. Effect of low-frequency repetitive transcranial magnetic stimulation on naming abilities in early-stroke aphasic patients: a prospective, randomized, double-blind sham-controlled study. <i>Scientific World Journal</i> 2012; 2012 :518568	26
36.	Walker-Batson D, Unwin H, Ford J, Curtis S, Porch B. A double-blind controlled study of the use of amphetamine in the treatment of aphasia. <i>Stroke</i> 2001; 32 :2093-2098.	21
37.	Wang L, Liu SM, Liu M, Li BJ, Hui ZL, Gao X. [Post-stroke speech disorder treated with acupuncture and psychological intervention combined with rehabilitation training: a randomized controlled trial]. <i>Zhongguo Zhen Jiu</i> 2011; 31 :481-6.	120
38.	Weiduschat N, Thiel A, Rubi-Fessen I, Hartmann A, Kessler J, Merl P, <i>et al.</i> Effects of Repetitive Transcranial Magnetic Stimulation in Aphasic Stroke. A Randomized Controlled Pilot Study. <i>Stroke</i> 2011; 42 :409-15.	10
39.	Wu XJ. Analysis of the effect of "two-step method" on aphasia in patients with acute cerebrovascular disease. <i>Chinese Journal of Clinical Rehabilitation</i> 2004; 8 :4422-3.	236

40.	Xie SL, Zhu MG, Zhang XL, Xue ZJ. The role of community nursing in family rehabilitation of stroke patients with impaired spoken language. <i>Chinese Journal of Clinical Rehabilitation</i> 2002; 6 :3289.	34
41.	Yao J, Xue Y, Li F. Clinical application research on collective language strengthened training in rehabilitation nursing of cerebral apoplexy patients with aphasia. <i>Chinese Nursing Research</i> 2005; 19 :482-4.	60
42.	Zhang HM. [Clinical treatment of apoplectic aphemia with multi-needle puncture of scalp- points in combination with visual-listening-speech training]. <i>Zhen ci yan jiu [Acupuncture research]</i> 2007; 32 :190-4.	36
43.	Zhang SH, Lu XM. Nursing care of the patient with cerebral infarction and aphasia receiving carotid internal drug injection and early speech training. <i>Journal of Nursing Science</i> 1997; 12 :34-5.	35
44.	Zhao C, Zhen Y, Zhang Y. Observations on the effect of acupuncture for treatment of 46 patients with apoplectic aphasia. Shanghai Journal of <i>Acupuncture and Moxibustion</i> 2004; 23 :13-4.	81
45.	Zhao H, Ying B, Shen C. Clinical Study on the Effect of Combined Therapy of Medicine, Acupuncture and Speech Training on Aphasia from Ischemic Apoplexy. <i>Henan Traditional Chinese Medicine Henan Zhong yi</i> 2000; 20 :31-2.	138

* = primary reference identified. Secondary references available on request. IPD = Individual participant data

Fig I. Data searching and identification



Fig II. SLT Frequency Networks (days per week)













Fig III. SLT Frequency (by days/weekly) and associated gains from baseline (mean; 95% CI)



A. Overall Language - WAB-AQ [0-100]; 482 IPD 11 RCTs)

B. Functional Communication - AAT-SSC [0-5]; 526 IPD (14 RCTs)



50







Fig IV. SLT Duration (total weeks) networks



Fig. V Duration (weeks of SLT) and associated language gains from baseline (mean; 95% CI)



A. Overall Language - WAB-AQ [0-100]; 430 IPD (10 RCTs)

B. Functional Communication - AAT-SSC [0-5]; 474 IPD (13 RCTs)





C. Auditory Comprehension - AAT Token Test [0-50]; 540 IPD (16 RCTs)

SUPPLEMENTAL MATERIAL - Dosage, intensity and frequency of therapy for aphasia

D. Naming - BNT [0-60]; 385 IPD (13 RCTs)



Fig. VI. Risk of bias by RCT dataset



PRISMA-IPD Section/topic	ltem No	Checklist item	Reported on page
Title	•		
Title	1	Identify the report as a systematic review and meta-analysis of individual participant data.	1
Abstract			
Structured	2	Provide a structured summary including as applicable:	2-3
summary		Background : state research question and main objectives, with information on participants, interventions, comparators and outcomes.	(Registration page 3; funding page 19)
		Methods : report eligibility criteria; data sources including dates of last bibliographic search or elicitation, noting that IPD were sought; methods of assessing risk of bias.	
		Results : provide number and type of studies and participants identified and number (%) obtained; summary effect estimates for main outcomes (benefits and harms) with confidence intervals and measures of statistical heterogeneity. Describe the direction and size of summary effects in terms meaningful to those who would put findings into practice.	
		Discussion: state main strengths and limitations of the evidence, general interpretation of the results and any important implications.	
		Other: report primary funding source, registration number and registry name for the systematic review and IPD meta-analysis.	
Introduction			
Rationale	3	Describe the rationale for the review in the context of what is already known.	5-6
Objectives	4	Provide an explicit statement of the questions being addressed with reference, as applicable, to participants, interventions, comparisons, outcomes and study design (PICOS). Include any hypotheses that relate to particular types of participant-level subgroups.	6
Methods			
Protocol and registration	5	Indicate if a protocol exists and where it can be accessed. If available, provide registration information including registration number and registry name. Provide publication details, if applicable.	Several mentions but first on pages 3 & 7
Eligibility criteria	6	Specify inclusion and exclusion criteria including those relating to participants, interventions, comparisons, outcomes, study design and characteristics (e.g. years when conducted, required minimum follow-up). Note whether these were applied at the study or individual level i.e. whether eligible participants were included (and ineligible participants excluded) from a study that included a wider population than specified by the review	6-7

PRISMA-IPD Checklist of items to include when reporting a systematic review and meta-analysis of individual participant data (IPD)

		inclusion criteria. The rationale for criteria should be stated.	
Identifying studies - information sources	7	Describe all methods of identifying published and unpublished studies including, as applicable: which bibliographic databases were searched with dates of coverage; details of any hand searching including of conference proceedings; use of study registers and agency or company databases; contact with the original research team and experts in the field; open adverts and surveys. Give the date of last search or elicitation.	pages 2, 7 and in cited protocol publication Ref 18 and
Identifying studies - search	8	Present the full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	In cited protocol publication Ref 18
Study selection processes	9	State the process for determining which studies were eligible for inclusion.	pages 2, 7-8 and in more detail in cited protocol publication Ref 18
Data collection processes	10	Describe how IPD were requested, collected and managed, including any processes for querying and confirming data with investigators. If IPD were not sought from any eligible study, the reason for this should be stated (for each such study).	pages 7-8 and in more detail in cited protocol publication Ref 18 and supplementary materials.
		If applicable, describe how any studies for which IPD were not available were dealt with. This should include whether, how and what aggregate data were sought or extracted from study reports and publications (such as extracting data independently in duplicate) and any processes for obtaining and confirming these data with investigators.	
Data items	11	Describe how the information and variables to be collected were chosen. List and define all study level and participant level data that were sought, including baseline and follow-up information. If applicable, describe methods of standardising or translating variables within the IPD datasets to ensure common scales or measurements across studies.	pages 7-8 and in more detail in cited protocol publication Ref 18
IPD integrity	A1	Describe what aspects of IPD were subject to data checking (such as sequence generation, data consistency and completeness, baseline imbalance) and how this was done.	pages 8-10 and in more detail in cited protocol publication Ref 18
Risk of bias assessment in individual studies.	12	Describe methods used to assess risk of bias in the individual studies and whether this was applied separately for each outcome. If applicable, describe how findings of IPD checking were used to inform the assessment. Report if and how risk of bias assessment was used in any data synthesis.	10-11
Specification of outcomes and effect measures	13	State all treatment comparisons of interests. State all outcomes addressed and define them in detail. State whether they were pre-specified for the review and, if applicable, whether they were primary/main or secondary/additional outcomes. Give the principal measures of effect (such as risk ratio, hazard ratio, difference in means) used for each outcome.	2, 7-9
Synthesis	14	Describe the meta-analysis methods used to synthesise IPD. Specify any statistical methods and models used. Issues should include (but are not restricted to):	9-10

methods		 Use of a one-stage or two-stage approach. How effect estimates were generated separately within each study and combined across studies (where applicable). Specification of one-stage models (where applicable) including how clustering of patients within studies was accounted for. Use of fixed or random effects models and any other model assumptions, such as proportional hazards. How (summary) survival curves were generated (where applicable). Methods for quantifying statistical heterogeneity (such as l² and τ²). How studies providing IPD and not providing IPD were analysed together (where applicable). How missing data within the IPD were dealt with (where applicable). 	
Exploration of variation in effects	A2	If applicable, describe any methods used to explore variation in effects by study or participant level characteristics (such as estimation of interactions between effect and covariates). State all participant-level characteristics that were analysed as potential effect modifiers, and whether these were pre-specified.	10
Risk of bias across studies	15	Specify any assessment of risk of bias relating to the accumulated body of evidence, including any pertaining to not obtaining IPD for particular studies, outcomes or other variables.	10-11
Additional analyses	16	Describe methods of any additional analyses, including sensitivity analyses. State which of these were pre-specified.	9-11
Results			
Study selection and IPD obtained	17	Give numbers of studies screened, assessed for eligibility, and included in the systematic review with reasons for exclusions at each stage. Indicate the number of studies and participants for which IPD were sought and for which IPD were obtained. For those studies where IPD were not available, give the numbers of studies and participants for which aggregate data were available. Report reasons for non-availability of IPD. Include a flow diagram.	Fig 1, Supplementary Materials (Fig I) and reported in more detail in cited companion paper Ref 18
Study characteristics	18	For each study, present information on key study and participant characteristics (such as description of interventions, numbers of participants, demographic data, unavailability of outcomes, funding source, and if applicable duration of follow-up). Provide (main) citations for each study. Where applicable, also report similar study characteristics for any studies not providing IPD.	Supplementary Materials and pages 20-29 for citations for each study included.
IPD integrity	A3	Report any important issues identified in checking IPD or state that there were none.	11
Risk of bias within studies	19	Present data on risk of bias assessments. If applicable, describe whether data checking led to the up-weighting or down-weighting of these assessments. Consider how any potential bias impacts on the robustness of meta-analysis conclusions.	15 and Supplementary Materials
Results of individual	20	For each comparison and for each main outcome (benefit or harm), for each individual study report the number of eligible participants for which data were obtained and show simple summary data for each intervention group (including, where applicable, the number of events), effect estimates and confidence intervals. These may be	Figs 1-5 network diagrams and plots in Supplementary Materials

studies		tabulated or included on a forest plot.	and includes overview of each study IPD contribution to the study.			
Results of syntheses	21	Present summary effects for each meta-analysis undertaken, including confidence intervals and measures of statistical heterogeneity. State whether the analysis was pre-specified, and report the numbers of studies and participants and, where applicable, the number of events on which it is based.	12-15 Figs 1-5 network diagrams and plots with additional items in Supplementary materials			
		When exploring variation in effects due to patient or study characteristics, present summary interaction estimates for each characteristic examined, including confidence intervals and measures of statistical heterogeneity. State whether the analysis was pre-specified. State whether any interaction is consistent across trials.				
		Provide a description of the direction and size of effect in terms meaningful to those who would put findings into practice.				
Risk of bias across studies	22	Present results of any assessment of risk of bias relating to the accumulated body of evidence, including any pertaining to the availability and representativeness of available studies, outcomes or other variables.	15			
Additional analyses	23	Give results of any additional analyses (e.g. sensitivity analyses). If applicable, this should also include any analyses that incorporate aggregate data for studies that do not have IPD. If applicable, summarise the main meta-analysis results following the inclusion or exclusion of studies for which IPD were not available.	17 and reported separately (manuscript submitted)			
Discussion						
Summary of evidence	24	Summarise the main findings, including the strength of evidence for each main outcome.	15-17			
Strengths and limitations	25	Discuss any important strengths and limitations of the evidence including the benefits of access to IPD and any limitations arising from IPD that were not available.	16-17			
Conclusions	26	Provide a general interpretation of the findings in the context of other evidence.	17-18			
Implications	A4	Consider relevance to key groups (such as policy makers, service providers and service users). Consider implications for future research.	17-18			
Funding	•		·			
Funding	27	Describe sources of funding and other support (such as supply of IPD), and the role in the systematic review of those providing such support.	19			

A1 – A3 denote new items that are additional to standard PRISMA items. A4 has been created as a result of re-arranging content of the standard PRISMA statement to suit the way that systematic review IPD meta-analyses are reported.

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