Precision rehabilitation for aphasia by patient age, sex, aphasia severity, and time since stroke? A prespecified, systematic review based, individual participant data, network, subgroup meta-analysis

SUPPLEMENTAL MATERIAL

Supplementary Material A. IPD subgroup network meta-analysis; intervention regimen categories, subgroups and outcomes

	Frequency *SLT days weekly*	**Duration** *total SLT weeks*	**Intensity** *SLT hours weekly*	**Dosage** *total SLT hours*
Network Categories	Up to 2	Up to 2*	Up to 2	Up to 5
	3	3*	>2 to 3	>5 to 14
	4	4-10	>3 to 4	>14 to 20
	5	>10-20	>4 to 9	>20 to <50
	6+	20+	9+	50-100
	Age (years)	**TSO (months)**	**Baseline severity**	**Sex**
Subgroups	≤65	≤3	Mild-moderate	Female
	> 65	>3	Moderate-severe	Male
	Severity	**Overall Language** ***WAB-AQ*** **(n)**	**Auditory Comprehension** ***TT-AAT*** **(n)**	**Functional Communication** ***AAT-SSC*** **(n)**
Outcome (median)	Mild-moderate	≥ 64.9 (163)	≥ 35 (145)	>2 (n=253)
	Moderate-severe	< 64.9 (319)	< 35 (n = 395)	<2 (n=280)

Key: * functional communication categories grouped as "up to 4 weeks". TSO time since aphasia onset; Mild-moderate-severe n = IPD available for base model. SLT speech and language therapy; WAB-AQ Western Aphasia Battery Aphasia Quotient; TT-AAT Token Test from the Aachen Aphasia Test; AAT-SSC Aachen Aphasia Test Spontaneous Speech Communication.

Supplementary Material B

Additional Methodological Detail: Risk of bias

We examined RCT-based and meta-biases, and impact on our findings, including our choice of measures informing language outcomes, a random rather than the fixed-effect model (25), and the inclusion of historical datasets (pre-2000)(22). Included RCTs and IPD were rigorously checked and verified, ensuring data were valid, reliable, consistent, and as complete as possible. The clinical, methodological, and statistical heterogeneity of included trials was reviewed, and methodological differences were recorded as a risk of bias (19). Selection, performance, detection, and attrition bias were rated as low, unclear, or high risk for each RCT. Our data synthesis procedures accommodated between-study outcome differences.

Standard data-synthesis heterogeneity assessments (e.g., I^2) were unsuitable in the context of analysis of unique participant, intervention, and outcome IPD. Instead, variance was considered throughout, comparing variability due to study differences to data variability overall. We reported where it exceeded 25% and checked datasets for undue influence or unbalanced groups. Where it exceeded 50%, we report it for completeness, but the finding was considered unreliable and excluded from our data interpretation.

Dual observer-rated functional communication outcome IPD (Therapy Outcome Measures (TOM, (26) activity and participation subtests) were available. Previously, sensitivity analysis on these data found no indication that the choice of subtest included in the meta-analysis impacted our findings (20). Our subgroup analysis included the TOMs activity data only.

Supplementary Material C

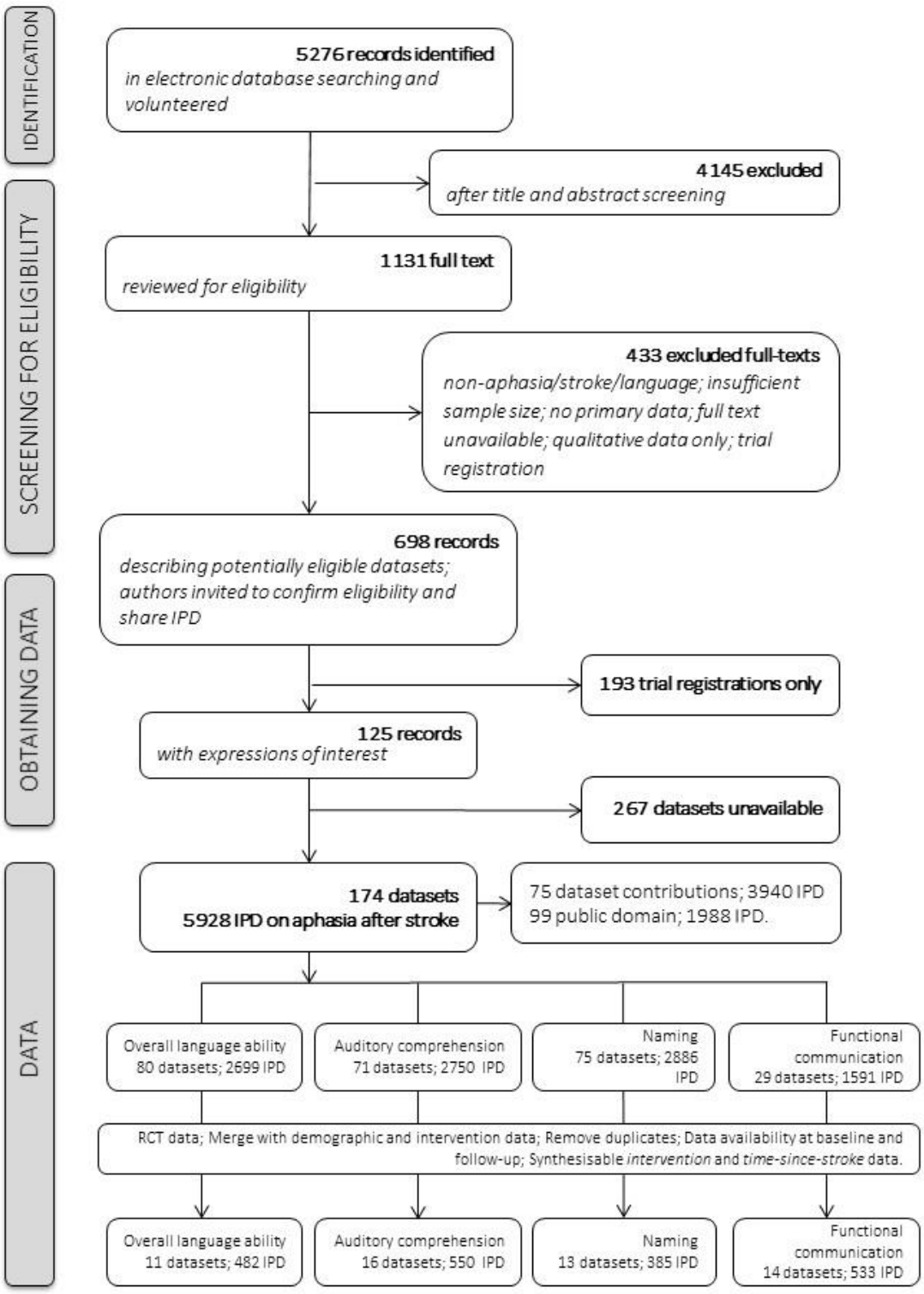

Fig 1. PRISMA flow diagram; data searching and identification

Supplementary Material D

References to included randomised controlled trials

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Supplementary Material E

Characteristics of included randomised controlled trials

Primary Publication reference; Country; Funder	Participants' inclusion and exclusion criteria	IPD; data time-points; electronic or public domain in RELEASE
Ciccone (2015) Australia Funder Unreported	Inclusion: 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 Exclusion: 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	20 IPD Baseline; 3 months; 6 months Electronic
de Jon-Hagelstein (2011) The Netherlands Stichting Nuts Ohra (T-07-71)	Inclusion: adult; stroke (less than 3 weeks); aphasia (verbal communication, semantic or phonological disorder, tests and cut-offs defined); life expectancy more than 6 months Exclusion: over 85 years; severe dysarthria; premorbid dementia or aphasia; developmental dyslexia; visual perceptual disorder; recent psychiatric disorder	85 IPD (75 complete) 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) Exclusion: global or minimal aphasia; dysarthria; non-native Dutch speaker; illiteracy, developmental dyslexia, severe acquired dyslexia; visual perceptual deficit	18 IPD Baseline; 2 months Electronic
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); Exclusion: within 3 months of onset; dysarthria; global aphasia; recovered aphasia; non-native speaker; illiteracy; developmental dyslexia; severe acquired dyslexia; visual perceptual deficit	58 IPD Baseline; 11 months Electronic
Mattioli (2014) Italy Funder Unreported	Inclusion: 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 Exclusion: 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	12 IPD Baseline; 16 days; 190 days Electronic
Meikle (1979) UK Chest, Heart, and Stroke Association	Inclusion: stroke (at least 3 weeks); aphasia (less than 4th percentile on PICA); previously proficient in English; well enough to attend Exclusion: dementia; lives too far from hospital	31 IPD Baseline; 4, 15, 24, 35, 42, 66, 84 weeks

		Public domain
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 Exclusion: rapid regression; dementia; drug abuse; severe illness; unable to participate in treatment (as judged by investigator)	125 IPD (plus 2 without group allocation) Baseline; 3 weeks (16 days); 6 months Electronic
Rodriguez (2013) Australia National Health and Medical Rehabilitation Council 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	Inclusion: stroke (at least 6 months); aphasia; no other neurological disorders; sufficient vision and hearing to take part Exclusion: concomitant neurological illness	11 IPD Baseline; 2 weeks; 4 weeks; 9 weeks;11 weeks Electronic
Woodhead (2017) UK Wellcome Trust and the James S McDonnell Foundation, personal fellowships from the Wellcome Trust (ME033459MES and 106084/Z/14/Z).	Inclusion: adult; stroke (3 or more months); aphasia (Wernicke's); competent to consent Exclusion: 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	20 IPD Baseline; 5 weeks; 10 weeks Electronic
Lincoln (1980a) UK Funder 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 Exclusion: severely or mildly aphasic	24 IPD Baseline; week 4; week 8 Public domain
Lincoln (1980b) UK Funder unreported	Inclusion: 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 Exclusion: unreported	24 IPD Baseline; week 4; week 8 Public domain
Szaflarski (2015) USA NINDS R01 NS 048281 and by NIH/NCRR UL1-RR026314 (REDCap Database)	Inclusion: stroke (single); aphasia (chronic) Exclusion: more than one stroke; history degenerative or metabolic disorder or supervening illness; history depression or other mental illness; pregnant	24 IPD Baseline; 2 weeks; 12 weeks Electronic
Palmer (2012) UK NIHR Research for Patient Benefit (RfPB) Programme (Grant no. 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 Exclusion: severe visual or cognitive difficulties	34 IPD Baseline; 5 months; 8 months Electronic
Smania (2006) and (2000) Italy	Inclusion: stroke; aphasia; limb apraxia (ideational or ideomotor) for at least 2 months	32 IPD

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	Exclusion: history of stroke or other neurological disorders; over 80 years; uncooperativeness; orthopedic or other disabling disorders	Baseline; 10 weeks Electronic
Breitenstein (2017) Germany German Federal Ministry of Education and Research; German Society for Aphasia Research and Treatment	Inclusion: adult; stroke; aphasia for at least 6 months; native speaker (German); at least basic level of communication and language comprehension Exclusion: 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	142 (minus14) Screening; baseline; 3 weeks; 6 weeks (subgroup only); 6 months Electronic
Godecke (2012) Australia Unfunded	Inclusion: 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 Exclusion: 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	59 IPD Baseline; 4 weeks (or acute hospital discharge if sooner); 6 months Electronic
Kukkonen (unpublished) Finland Unfunded	Inclusion: older adult (50-64; 65-80); stroke (first); aphasia; right-handed; living in Tampere with someone; no dementia; normal hearing and vision Exclusion: 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 IPD Baseline; 4 weeks; 10 weeks; 14 weeks; 20 weeks; 32 weeks; 56 weeks Unpublished
Martins (2013) Portugal Funder unreported	Inclusion: adult (40-80); stroke (single); aphasia (LAAB mild/moderate and severe); native speaker (Portuguese); willing to participate Exclusion: 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	30 IPD (14 complete) Baseline; 10 weeks; 50 weeks; 62 weeks Electronic
Meinzer (2007) Germany Deutsche Forschungsgemeinschaft (Grant RO 805011-4), the Kuratorium Zentrales Nervensystem (Grant 2001013)	Inclusion: stroke (single); aphasia (at least 6 months; global aphasia if residual expressive language); 1 or more participating relative Exclusion: well-recovered people with minimal aphasia symptoms	20 IPD Baseline; 10 days Electronic
Khedr (2014) Egypt Funder unreported	Inclusion: stroke (single); aphasia (non-fluent); subacute hemiplegia Exclusion: head injury or neurological disease other than stroke; unstable cardiac dysrhythmia; fever; infection; hyperglycemia; prior administration of tranquiliser; safety contraindications for rTMS	29 IPD Baseline; 2 weeks; 6 weeks; 10 weeks Electronic

van der Meulen (2016) The Netherlands Stichting Rotterdams Kinderrevalidatie Fonds Adriaanstichting (Grant 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) Exclusion: prior stroke resulting in aphasia; bilateral lesion; intensive MIT prior to start of study; severe hearing deficit; relevant psychiatric history	17 IPD Baseline; 42 days; 82 days Electronic
Rubi-Fessen (2015) Germany Walter and Marga Boll Foundation and the Wolf-Dieter Heiss-Foundation	Inclusion: 55 to 85 years; stroke (first; up to 16 weeks); aphasia; first language (German); right-handed Exclusion: previous stroke, neurodegenerative or psychiatric disease; epilepsy; auditory or visual deficits that might impair testing	30 IPD Baseline; 2 weeks Electronic
Efstratiadou (2019) Greece European Social Fund, EFSA, National Strategic Reference Framework — Research Funding Program: THALES UOA.	Inclusion: adult; stroke (at least 4 months); aphasia; native speaker (Greek); medically stable; no other neurological or psychiatric history; no considerable cognitive impairment Exclusion: in receipt of other SLT during the project; not living independently at home prior to the stroke Not in RELEASE: 20 received alternative SLT	38 IPD Baseline; 19 weeks; 32 weeks Electronic
You (2011) Korea Funder unreported	Inclusion: stroke; not taking pharmacological drugs Exclusion: history of previous stroke, seizure, multiple stroke lesions; metal implants in brain; taking certain medication; uncooperative with SLT	21 IPD Baseline; 2 weeks Electronic

Supplementary Material F

Characteristics of included speech and language therapy interventions by randomised controlled trial

Primary Publication reference	Location	Group	Therapy Impairment Target:	Theoretical Approach:	Provided by:	Delivery:	Regimen:	Tailoring:
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	Frequency: 5 days per week. Duration: 2 months. Intensity: 5 hours. Dosage: 10 hours.	Unreported
		Group 2: n=6 No SLT						
Meikle (1979)	Home and groups at rehabilitation centre	**Group 1:** n=16 "Conventional SLT"	Unreported	Unreported	Speech and language therapist	face-to-face; 1-to-1 and group;	Frequency: 3-5 days per week. Duration: IPD. Intensity: between 2 hours 15 minutes and 3 hours 45 minutes. Dosage: IPD	Unreported
		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. Duration: IPD. Intensity: between 2 hours 15 minutes and 3 hours 45 minutes. Dosage: IPD	Difficulty
Laska (2011)	Stroke unit, or discharged to (home, rehabilitation clinic, geriatric clinic, nursing home).	**Group 1:** n=62	Mixed SLT	Unreported	Speech and language therapist	Face-to-face; 1-to-1	Frequency: 3 sessions each day 5 days per week. Duration: 3 weeks. Intensity: 3 hours 45 minutes. Dosage: 11 hours 15 minutes.	Functional relevance
		Group 2: n=61 Intervention type(s): No SLT						
Rodriguez (2013)	Aphasia clinic and other	**Group 1:** n=4	Word Finding SLT and Mixed SLT	Functional or Pragmatic SLT; Semantic and	speech and language	face-to-face; 1-to-1 and group;	Frequency: 5 days per week. Duration: 2 weeks. Intensity: 20 hours. Dosage: 40 hours. Home practice reported.	Functional relevance and difficulty

	rehabilitation centres.			Phonological SLT	therapists and students.			
		Group 2: 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;	Frequency: 5 days each week. Duration: 4 weeks. Intensity: 25 hours. Dosage: 100 hours. Home practice reported.	Functional relevance and difficulty
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. Duration: 25 weeks in study, but intervention is over two 5-week blocks. Intensity: 7.3 hours (according to diaries) on average. Dosage: 73 hours (according to diaries). Home practice reported.	Difficulty
		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. Duration: 25 weeks in study, but intervention is over two 5-week blocks. Intensity: 7.3 hours (according to diaries) on average. Dosage: 73 hours (according to diaries). Home practice reported.	Difficulty
Lincoln (1980a)	Hospital and home	**Group 1:** 6	Mixed SLT	Unreported	Speech and language therapist	Face-to-face; 1-to-1	Frequency: 4 days per week. Duration: 3.5 weeks. Intensity: 2 hours. Dosage: 7 hours.	Unreported
		Group 2: 7	Mixed SLT	Unreported	Speech and language therapist	Face-to-face; 1-to-1	hospital and ho Frequency: 4 days per week. Duration: 3.5 weeks. Intensity: 2 hours. Dosage: 7 hours.	Unreported

		No SLT (operant training) then Conventional SLT						
		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	Frequency: 4 days per week. Duration: 3.5 weeks. Intensity: 2 hours. Dosage: 7 hours.	Unreported
		Group 4: n=6	Mixed SLT	Unreported	Speech and language therapist	Face-to-face; 1-to-1	Frequency: 4 days per week. Duration: 3.5 weeks. Intensity: 2 hours. Dosage: 7 hours.	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. Duration: 8 weeks. Intensity: 2 hours per week. Dosage: IPD.	Difficulty
		Group 2: 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. Duration: 8 weeks. Intensity: 2 hours per week. Dosage: IPD	Difficulty
Szaflarski (2015)	Hospital	**Group 1:** n=14	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; Duration: 2 weeks; Intensity: 20 hours. Dosage: 40 hours.	Difficulty

		Group 2: 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;	Frequency: IPD. Duration**:** 5 months. Intensity: IPD. Dosage: IPD	Functional relevance
		Group 2: n=17	Intervention type(s): No SLT					
Smania (2006) and (2000)	Therapy clinic	**Group 1:** n=17	Intervention type(s): No SLT (limb apraxia therapy only)					
		Group 2: n= 15	unreported	unreported	Speech and language therapist	unreported;	Frequency: 3 days per week. Duration:10 weeks. Intensity: 2.5 hours. Dosage: 25 hours.	Unreported
Breitenstein (2017)	Inpatient and outpatient rehabilitation	**Group 1:** N=78	Mixed SLT	Functional or Pragmatic SLT	Speech and language therapist	face-to-face; 1-to-1 and group	Frequency: IPD. Duration: IPD. Intensity: IPD. Dosage: IPD. Home practice reported.	Difficulty
	Outpatient	**Group 2:** n=78	Unreported (usual care)	Unreported	Speech and language therapist	face-to-face; 1-to-1 and group	Frequency: IPD. Duration: 3 weeks Intensity: IPD. Dosage: IPD.	Unreported
Godecke (2012)	Hospital or rehabilitation	**Group 1:** n=32	Spoken language SLT	Semantic and Phonological SLT	Speech and language therapist	Face-to-face; 1-to-1	Frequency: 5 days per week. Duration: IPD but maximum of 1 month. Intensity: IPD between 2.5 and 7.5	Functional relevance and difficulty

							hours per week. Dosage: IPD up to 26.5 hours.	
		Group 2: n=27	Spoken Language SLT	Semantic and Phonological SLT	Speech and language therapist	Face-to-face; 1-to-1	Frequency: 1 day per week. Duration: IPD up to 1 month. Intensity: up to 1.5 hours per week. Dosage: IPD up to 5.3 hours.	Functional relevance and difficulty
Ciccone (2015)*	Hospital, rehabilitation or home	**Group 1:** n=8	Word Finding SLT	Phonological and Semantic SLT	Speech and language therapist	Face-to-face; 1-to-1	Frequency: IPD. Duration: 5 weeks. Intensity: IPD. Dosage: IPD.	Functional relevance and difficulty
		Group 2: n=12	Word Finding SLT	Phonological and Semantic SLT; Constraint Induced Aphasia Therapy.	Speech and language therapist	face-to-face; group;	Frequency: IPD. Duration: 5 weeks. Intensity: IPD. Dosage: IPD.	Functional relevance and difficulty
Kukkonen (unpublished)	SLT clinic	**Group 1:** n=9	Mixed SLT	Language Enrichment Therapy	Speech and language therapist	Face-to-face; 1-to-1	Frequency: 5 days per week. Duration: 6 weeks + 6 weeks. Intensity: 10 hours. Dosage: 120 hours.	Functional relevance
		Group 2: n=8	Mixed SLT	Language Enrichment Therapy	Speech and language therapist	Face-to-face; 1-to-1	Frequency: 2 days per week. Duration: 6 weeks + 6 weeks. Intensity: 2 hours. Dosage: 48 hours	Functional relevance
		Group 3: n=10	Mixed SLT	Language Enrichment Therapy	Speech and language therapist	Face-to-face; 1-to-1	Frequency: 1 day per week. Duration: 6 weeks + 6 weeks. Intensity: 1 hour. Dosage: 24 hours.	Functional relevance
		Group 4: n=9	Spouses or caregiver(s) received support and information from the speech and language therapists				Twice, 1 hour per meeting	
Martins (2013)	Medical and rehabilitation centres,	**Group 1:** n=15	Mixed SLT	Multimodal	Speech and language therapist	Face-to-face; 1-to-1	Frequency: 5 days per week. Duration: 10 weeks. Intensity: 10 hours. Dosage: 100 hours. Home practice reported.	Functional relevance and difficulty

	outpatient 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	Frequency: 1 day per week. Duration: 50 weeks. Intensity: 2 hours. Dosage: 100 hours. Home practice reported.	Functional relevance and difficulty
Meinzer (2007)	Unreported	**Group 1:** n=10	Word Finding SLT	Constraint Induced Aphasia Therapy	trained psychologists	Face-to-face; group	Frequency: 5 days per week. Duration: 10 days. Intensity: 15 hours. Dosage: 30 hours. Home practice reported.	Functional relevance and difficulty
		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. Duration: 10 days. Intensity: 15 hours. Dosage: 30 hours. Home practice reported.	Functional relevance and difficulty
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. Duration: 2 months. Intensity: 1 to 1.5 hours weekly. Dosage: 10 to 11 hours.	Difficulty
		Group 2: n=10	No SLT					
Khedr (2014)	Hospital	**Group 1:** n=10	Mixed SLT	Unreported	Speech and language therapist	Face-to-face; 1-to-1	Frequency: 5 days per week. Duration: 2 weeks. Intensity: 2.5 hours. Dosage: 5 hours.	Difficulty
		Group 2: n=19	Mixed SLT	Unreported	Speech and language therapist	Face-to-face; 1-to-1	Frequency: 5 days per week. Duration: 2 weeks. Intensity: 2.5 hours. Dosage: 5 hours.	Difficulty
de Jon-Hagelstein (2011)	Hospital, rehabilitation clinic, home, nursing home.	**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. Duration: 6 months (or less if fully recovered). Intensity: 2 to 5 hours. Dosage: 52 hours. Home practice reported.	Difficulty

		Group 2: n=44	Unreported	Functional or Pragmatic SLT	Speech and language therapist	Face-to-face; 1-to-1	Frequency: 3.25 times per week on average. Duration: 6 months (or less if fully recovered). Intensity: 2 to 5 hours. Dosage: 52 hours. Home practice reported.	Difficulty
Doesborgh (2004b)	Hospital / rehabilitation clinic / home / nursing home.	**Group 1:** n=29	Word Finding SLT	Semantic SLT	Speech and language therapist	Face-to-face and computer; 1-to-1;	Frequency: 2.25 days a week on average. Duration: 40 weeks. Intensity: 1.5 to 3 hours. Dosage: 40 to 60 hours. Home practice reported.	Difficulty
		Group 2: 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. Duration: 40 weeks. Intensity: 1.5 to 3 hours. Dosage: 40 to 60 hours. Home practice reported.	Difficulty
van der Meulen (2016)	Rehabilitation / aphasia centres.	**Group 1:** n=10	Spoken language SLT	Melodic Intonation Therapy	Speech and language therapist	Face-to-face; 1-to-1	Frequency: 5 days a week. Duration: 12 weeks (6 MIT and 6 no therapy). Intensity: 5 hours a week. Dosage: 30 hours. Home practice reported.	Functional relevance and difficulty
	Rehabilitation centre / nursing home with rehabilitation facilities.	**Group 2:** 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. Duration: 6 weeks. Intensity: 5 hours a week. Dosage: 30 hours.	Functional relevance and difficulty
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. Duration: 2 weeks. Intensity: 3.75 hours. Dosage: 7.5 hours.	Functional relevance and difficulty

		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. Duration: 2 weeks. Intensity: 3.75 hours. Dosage: 7.5 hours.	Functional relevance and difficulty
Efstratiadou (2019)	Home and hospital	**Group 1:** n=18	Word Finding SLT	Semantic SLT	Speech and language therapist	Face-to-face; 1-to-1	Frequency: 3 days a week. Duration: 12 weeks. Intensity: 3 hours. Dosage: 36 hours. No home practice.	Difficulty
		Group 2: n=8	Word Finding SLT	Semantic SLT	Speech and language therapist	Face-to-face; 1-to-1	Frequency: 3 days a week. Duration: 12 weeks. Intensity: 3 hours. Dosage: 36 hours. No home practice.	Difficulty
		Group 3: n=12	No SLT but then as per Group 1 (n=4) or Group 2 (n=6) above					
You (2011)	Hospital rehabilitation department	**Group 1:** n=7	Mixed SLT	Functional or Pragmatic SLT and Co-intervention anodal tDCS)	Speech and language therapist	Face-to-face; 1-to-1	Frequency: 5 days a week. Duration: 2 weeks. Intensity: 2.5 hours. Dosage: up to 5 hours.	Unreported
		Group 2: n=7	Mixed SLT	Functional or Pragmatic SLT and Co-intervention (cathodal tDCS)	Speech and language therapist	Face-to-face; 1-to-1	Frequency: 5 days a week. Duration: 2 weeks. Intensity: 2.5 hours. Dosage: up to 5 hours.	Unreported
		Group 3: n=7	Mixed SLT	Functional or Pragmatic SLT and Co-intervention (sham tDCS)	Speech and language therapist	Face-to-face; 1-to-1	Frequency: 5 days a week. Duration: 2 weeks. Intensity: 2.5 hours. Dosage: up to 5 hours.	Unreported

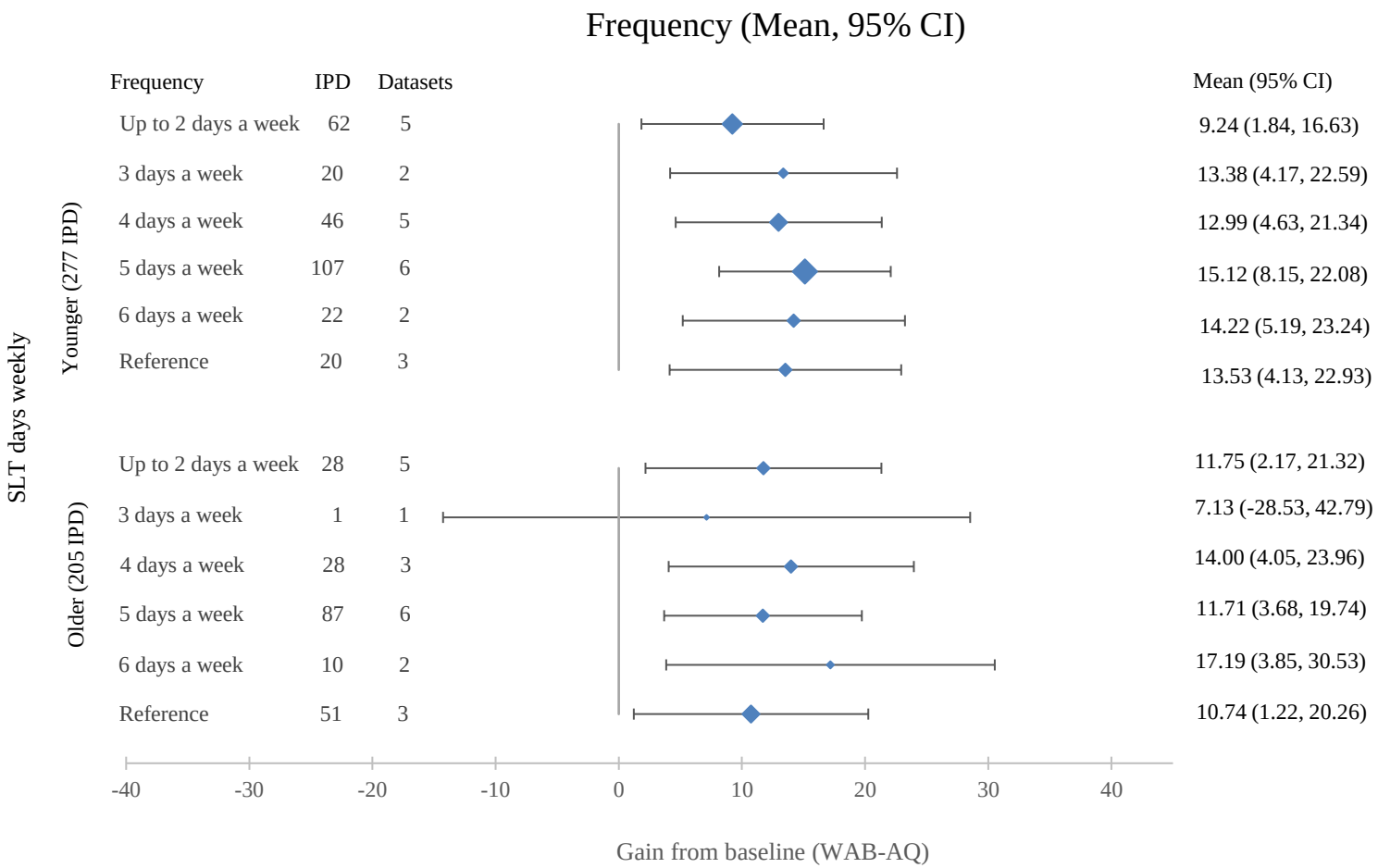
Supplementary Material G. Participant demographics

	IPD (RCTs)		IPD	Median [IQR] (%)		IPD (RCTs)		IPD	Median [IQR] (%)
Age (years)	941 (24)		928	63.0 [54.1, 74.0]	**Hemisphere lesion**	699 (18)	Bilateral	6	(0.9)
							Left	683	(97.7)
							Right	10	(1.4)
Sex	928 (24)	Female	390	(42.0)	**Aphasia onset (days)**	941 (24)		914	61 [7, 487]
		Male	538	(58.0)					
Ethnicity	94 (4)	Black	5	(5.3)	**Stroke Type**	771 (17)	Ischaemic	685	(88.9)
		Caucasian	89	(94.7)			ICH	77	(10.0)
							Subarachnoid Haemorrhage	9	(1.2)
Language	959 (24)	English	255	(26.6)	**Stroke Severity**	298 (4)	NIHSS	298	13 [6, 18]
		Dutch	199	(20.8)		216 (4)	mRS	216	3 [2, 4]
		German	182	(19.0)	**Living context**		Alone	146	(20.8)
		Swedish	125	(13.0)			Formal care	70	(10)
		Italian	38	(4.6)			Living with others	473	(67.5)
		Greek	44	(4.0)			Mixed	12	(1.7)
		Finnish	36	(3.8)	**Handedness**	620 (17)	Ambidextrous	7	(1.1)
		Portuguese	30	(3.1)			Left	21	(3.4)
		Arabic	29	(3.02)			Right	592	(95.5)
		Korean	21	(2.2)					

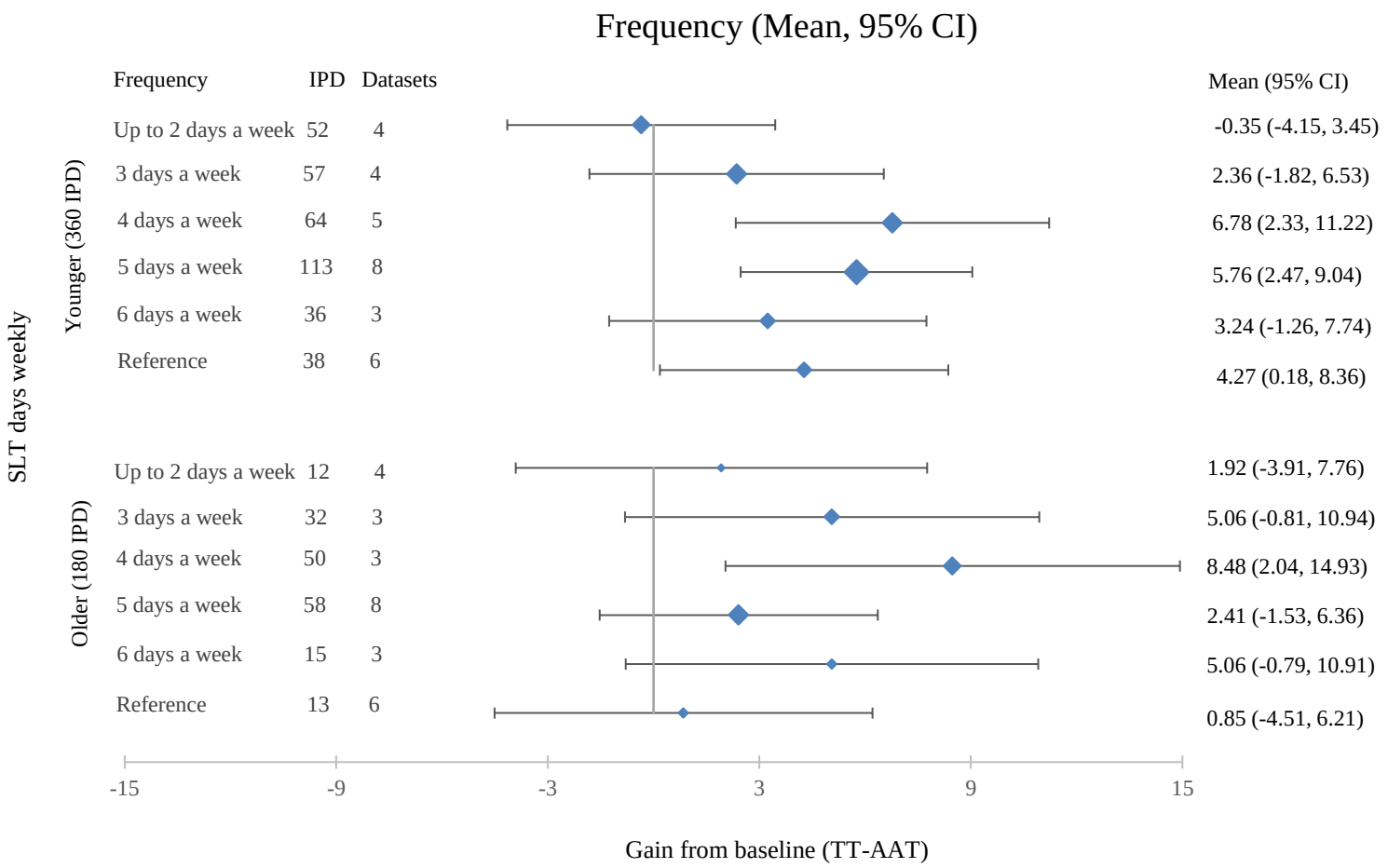
Key: IQR Interquartile range; n (%) or median (IQR); NIHSS = National Institutes of Health Stroke Scale; mRS Modified Rankin Scale

Supplementary Material H: Younger (≤65 years) and Older (>65 years) subgroups by SLT frequency, intensity and dosage and language outcome

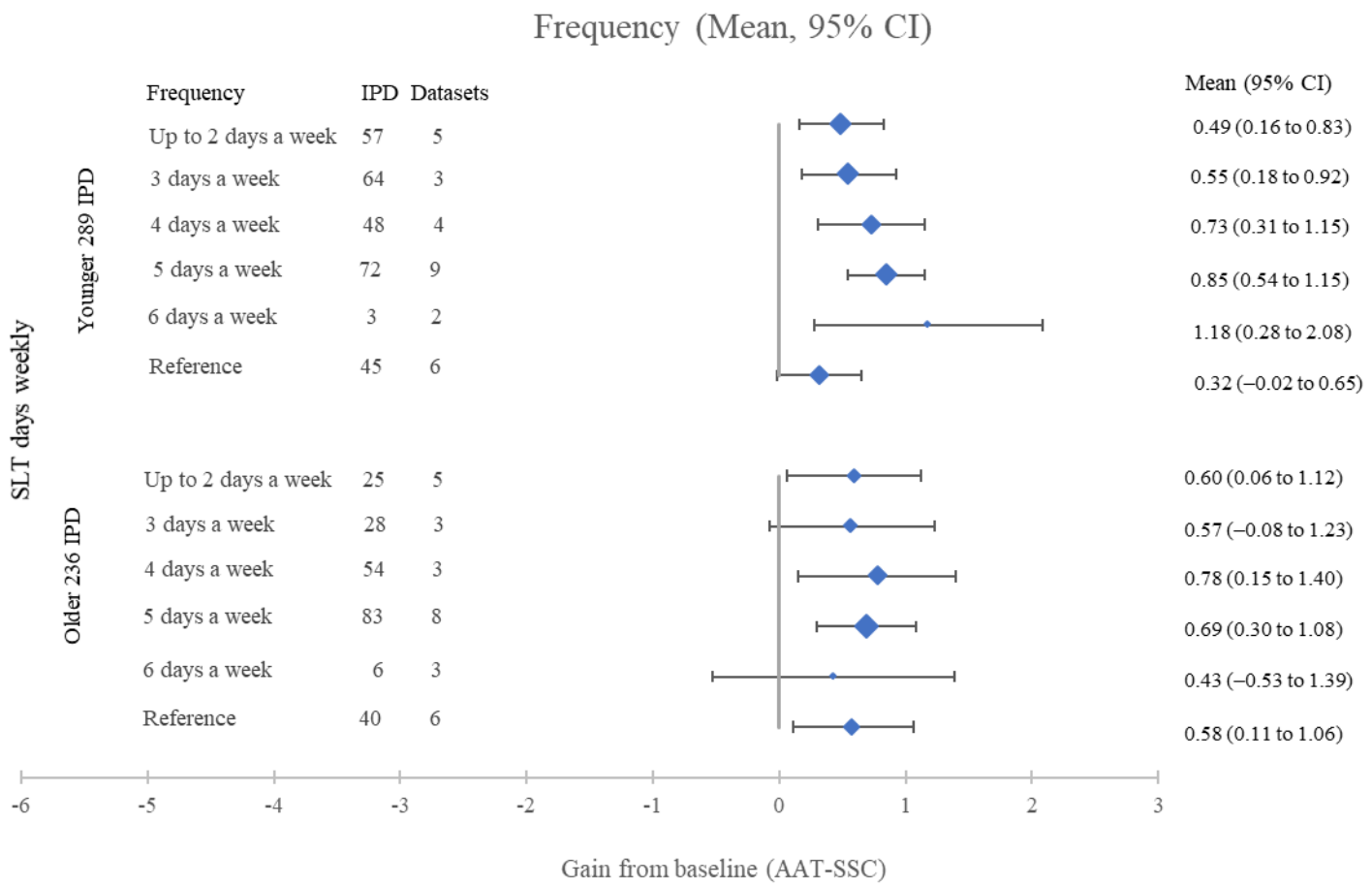
(a) SLT frequency and overall language ability (WAB-AQ 0-100)



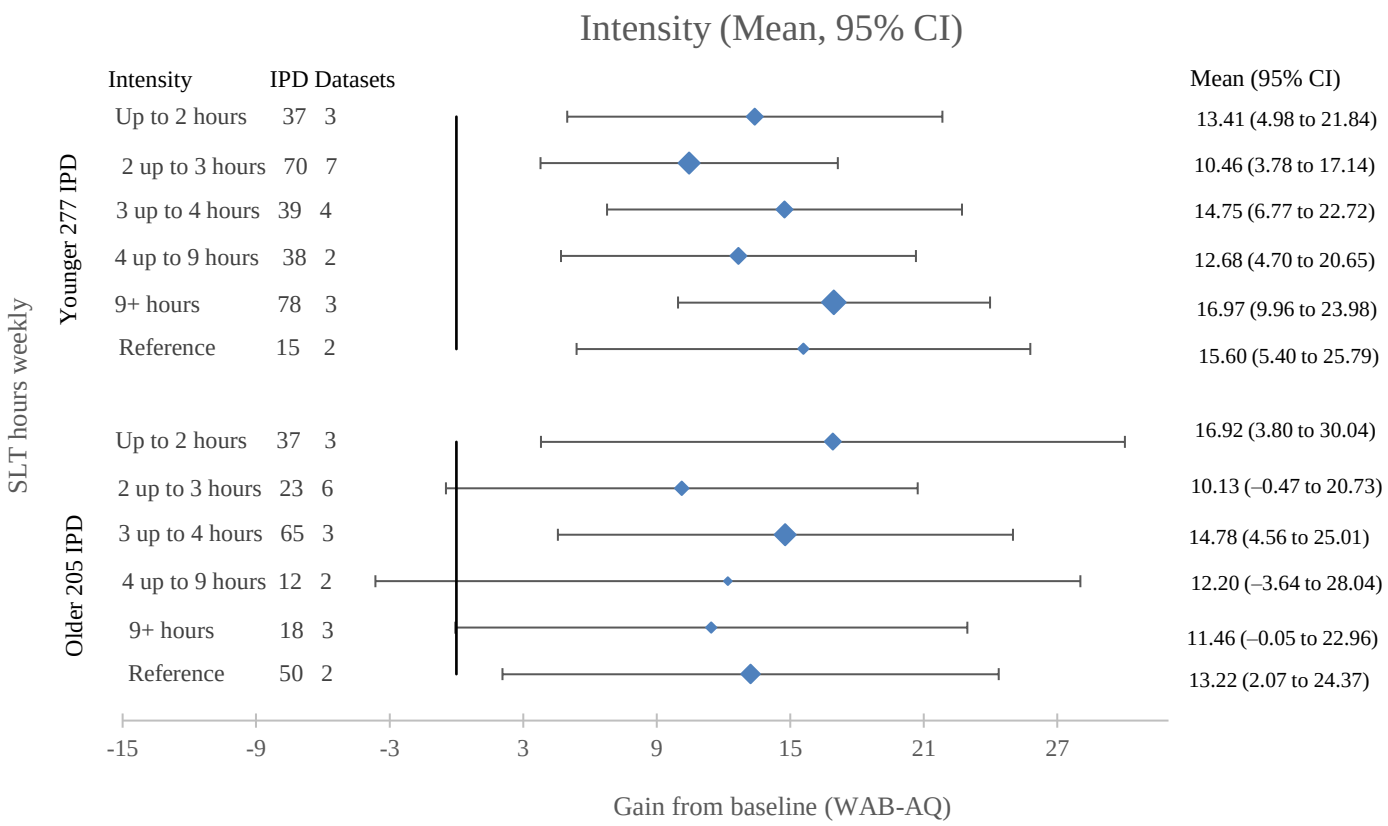
(b) SLT frequency and auditory comprehension (TT-AAT 0-50)



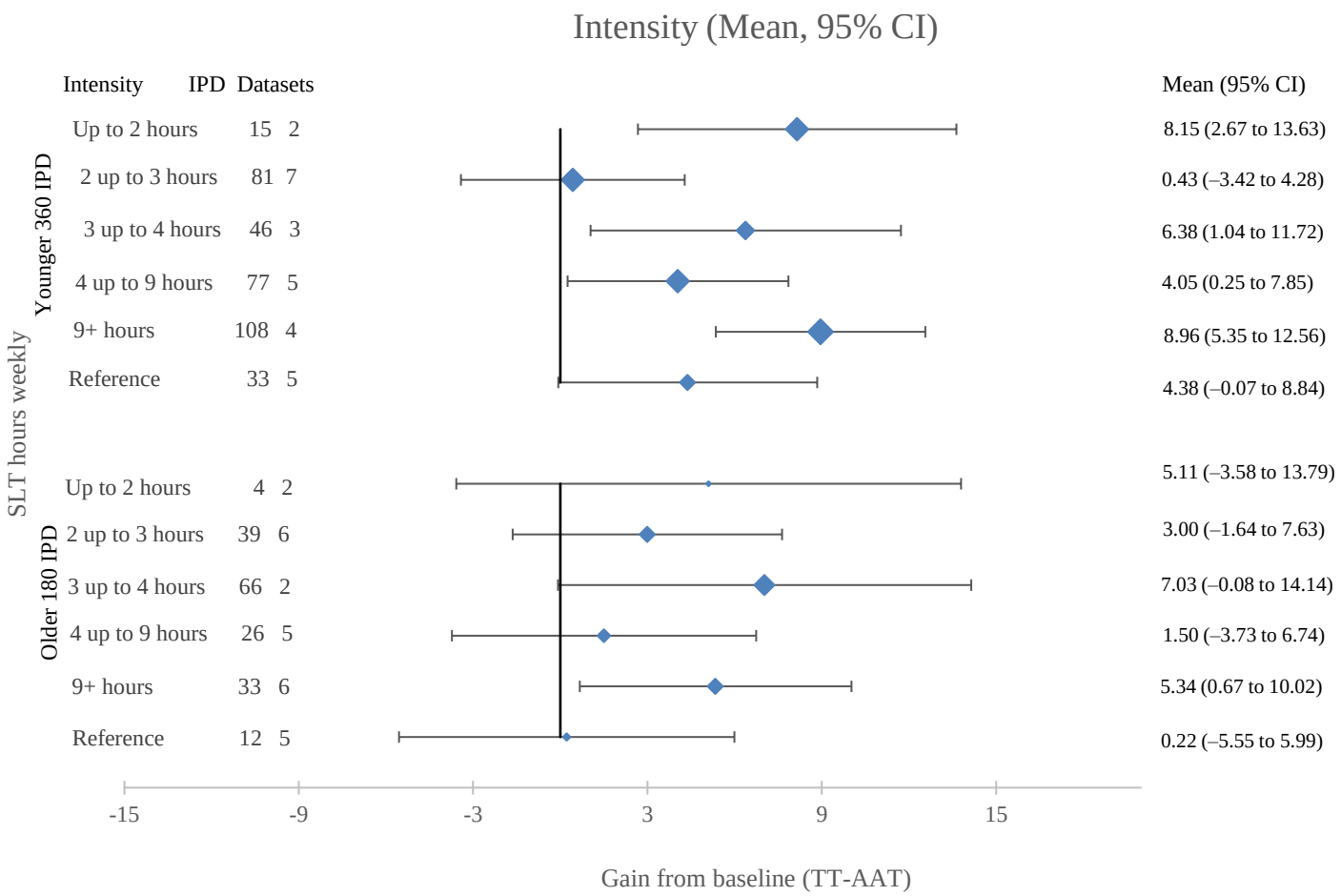
(c) SLT frequency and functional communication (AAT-SSC 0-5)



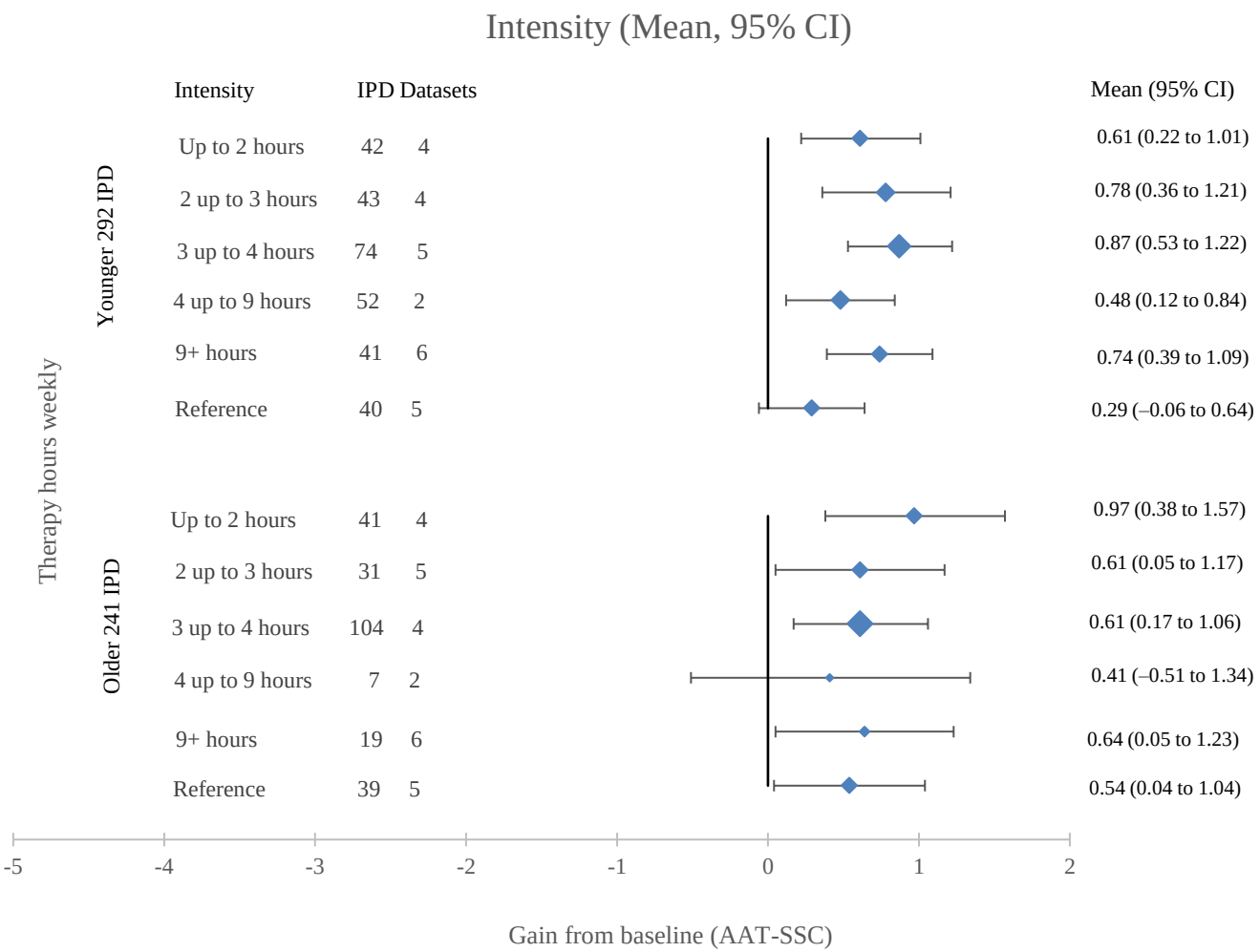
(d) SLT intensity and overall language ability (WAB-AQ 0-100)



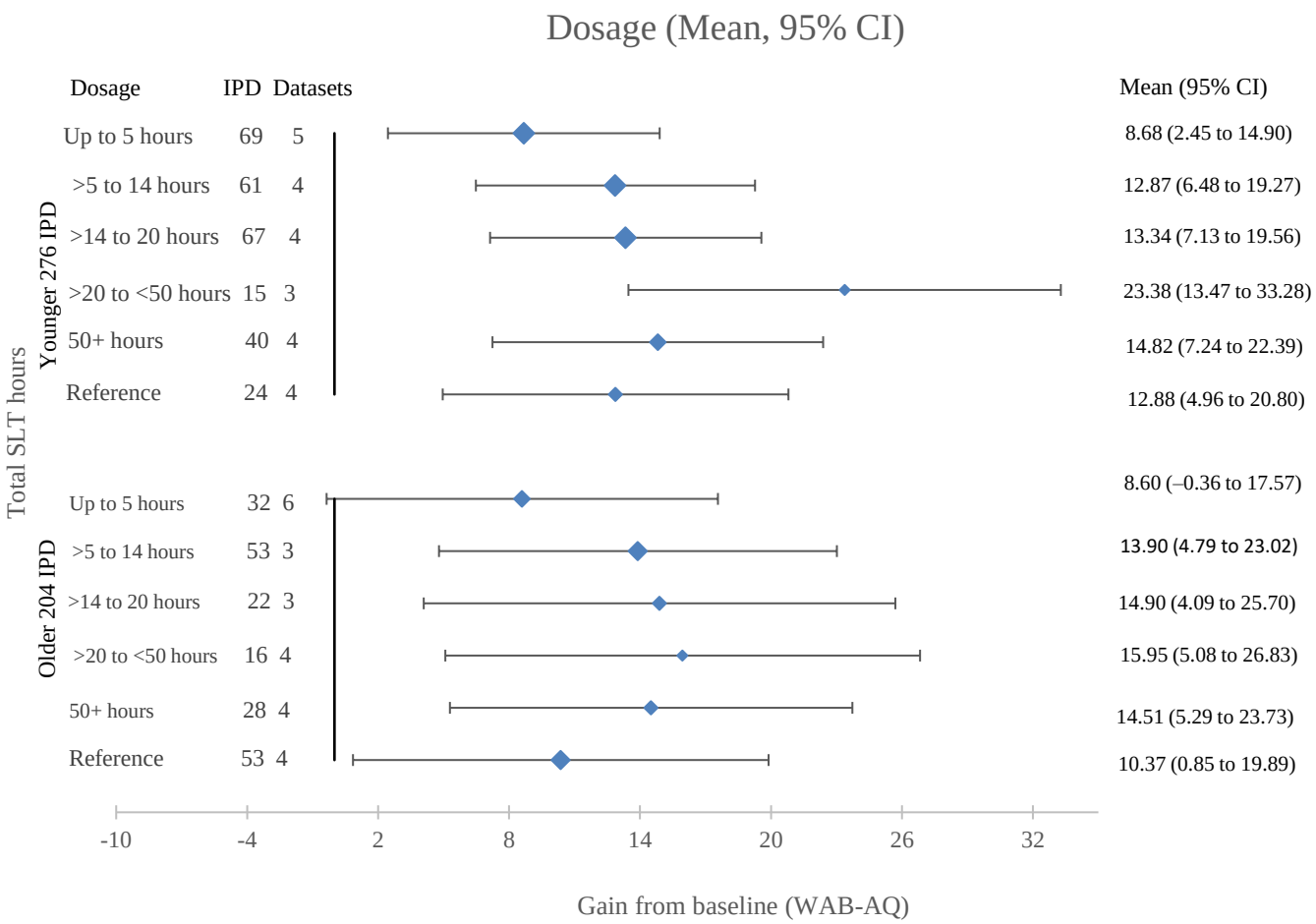
(e) SLT intensity and auditory comprehension (TT-AAT 0-50)



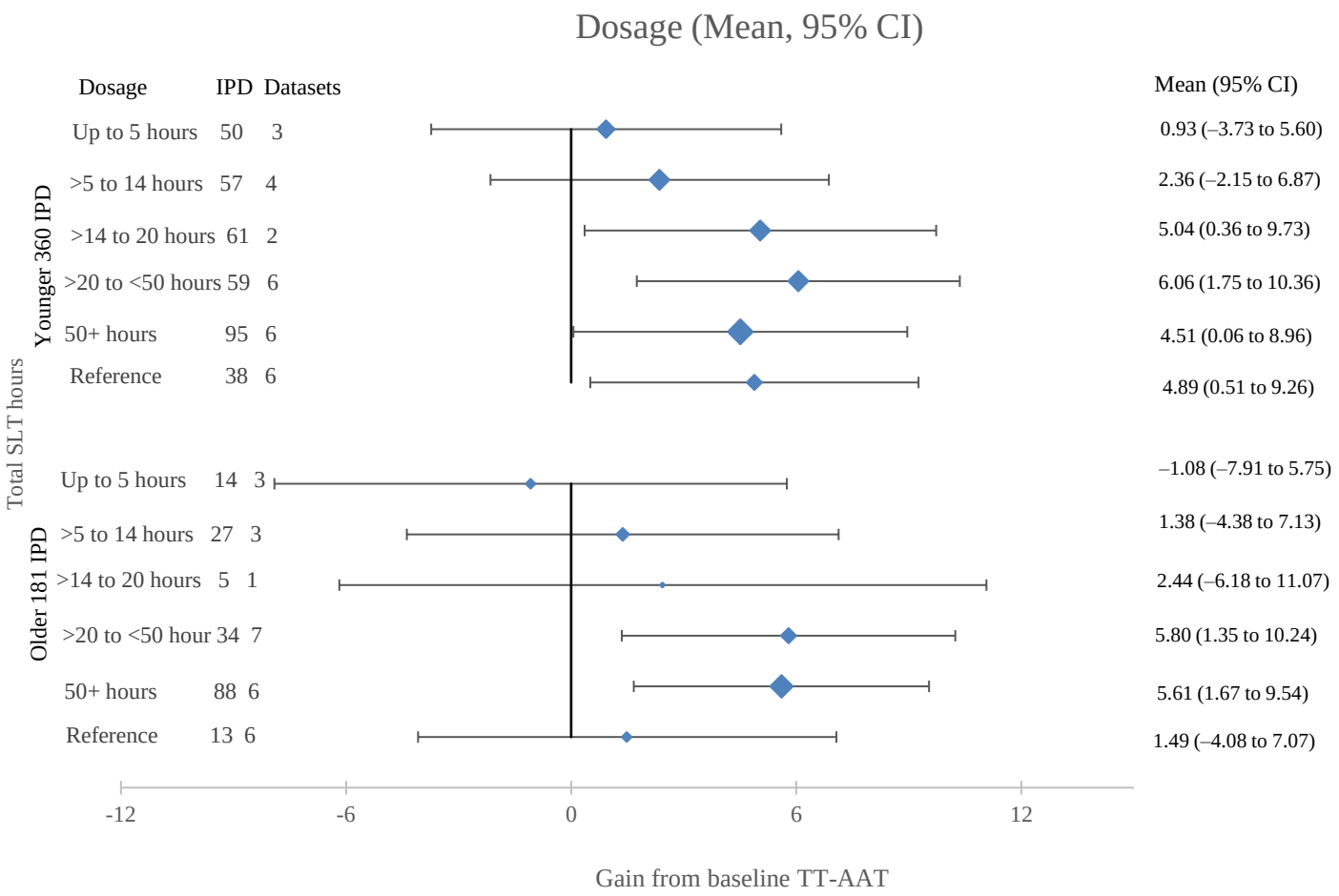
(f) SLT intensity and functional communication (AAT-SSC 0-5)



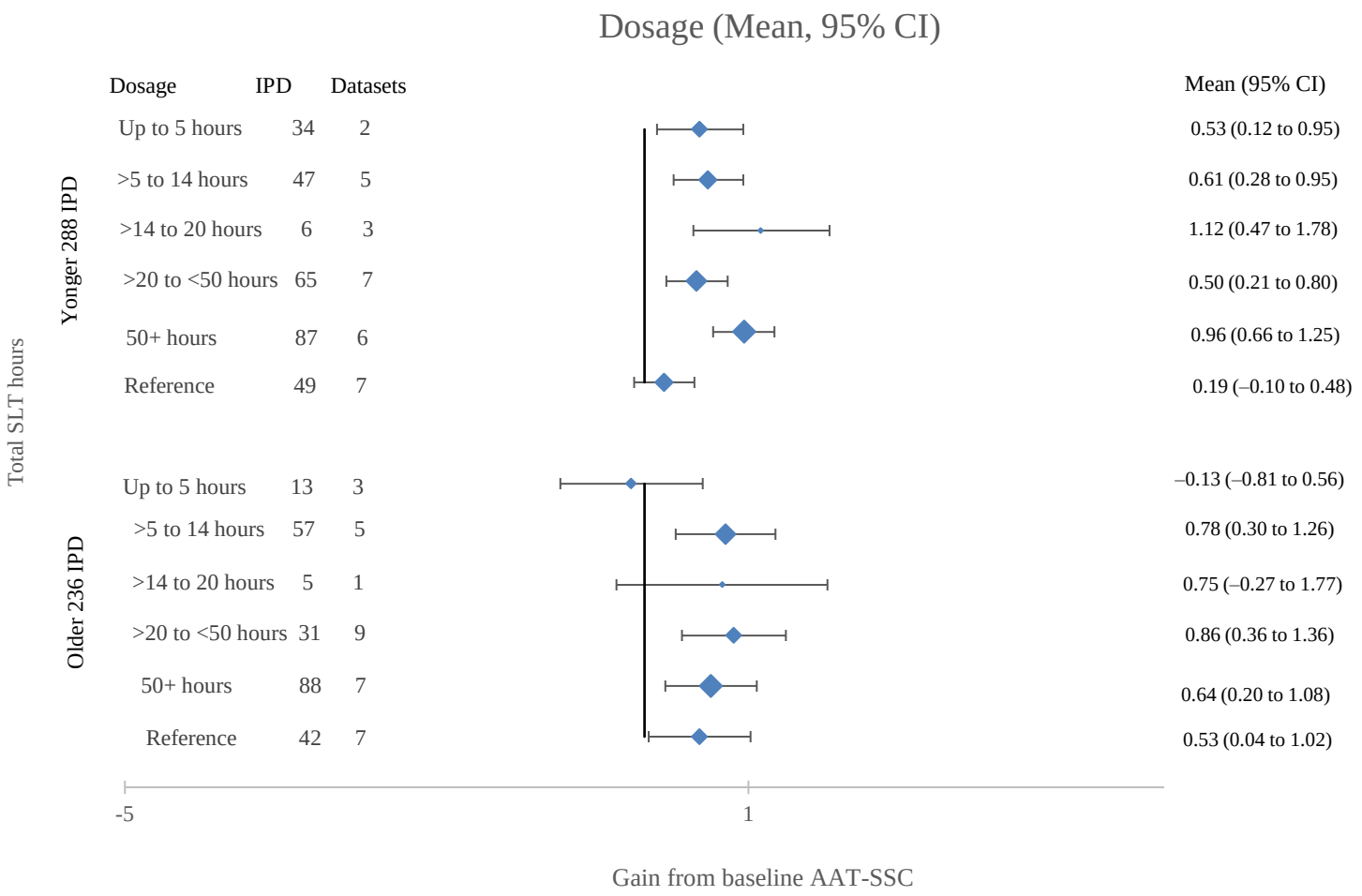
(g) SLT dosage and overall language ability (WAB-AQ 0-100)



(h) SLT dosage and auditory comprehension (TT-AAT 0-50)

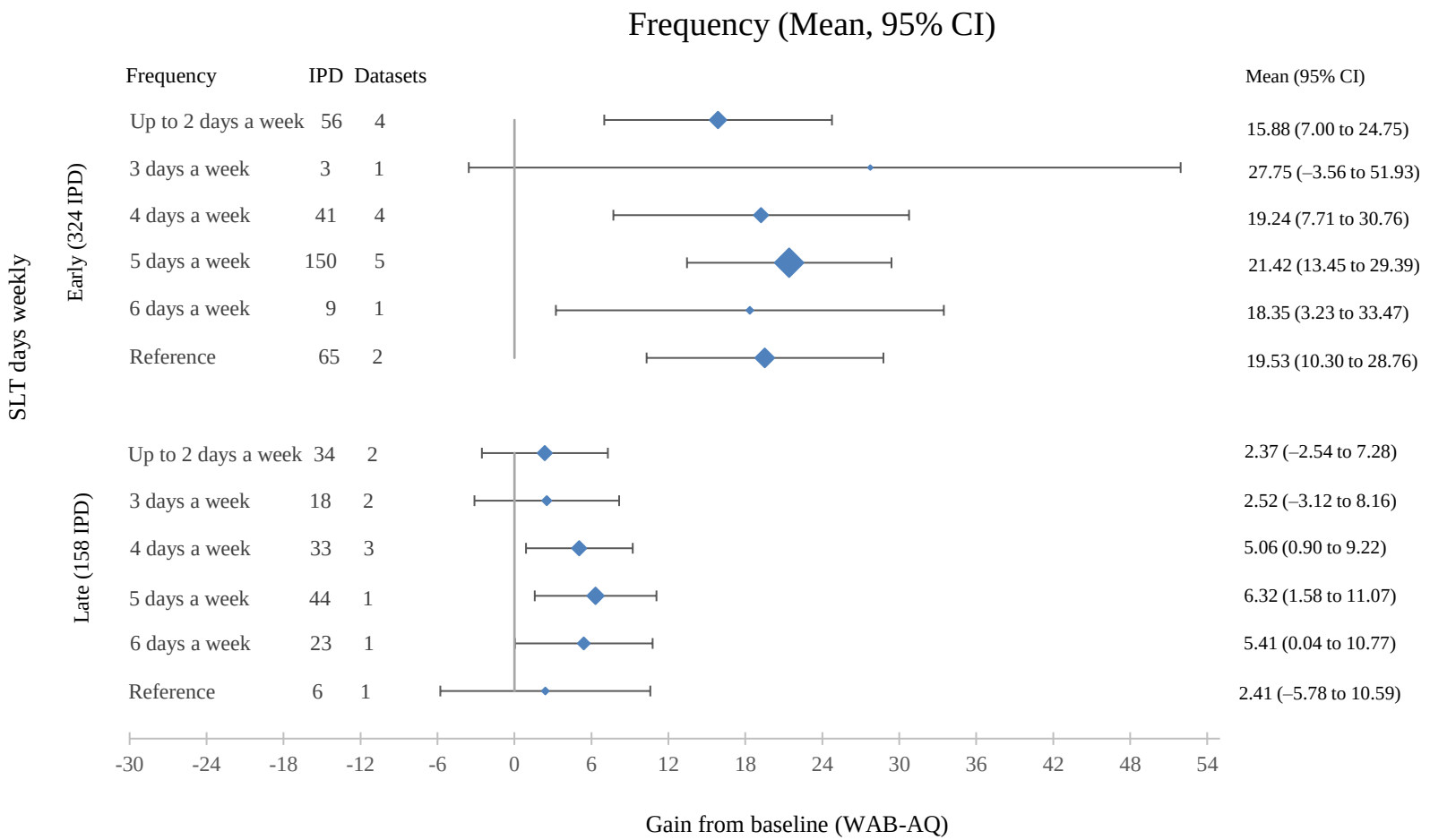


(i) SLT dosage and functional communication AAT-SSC 0-5

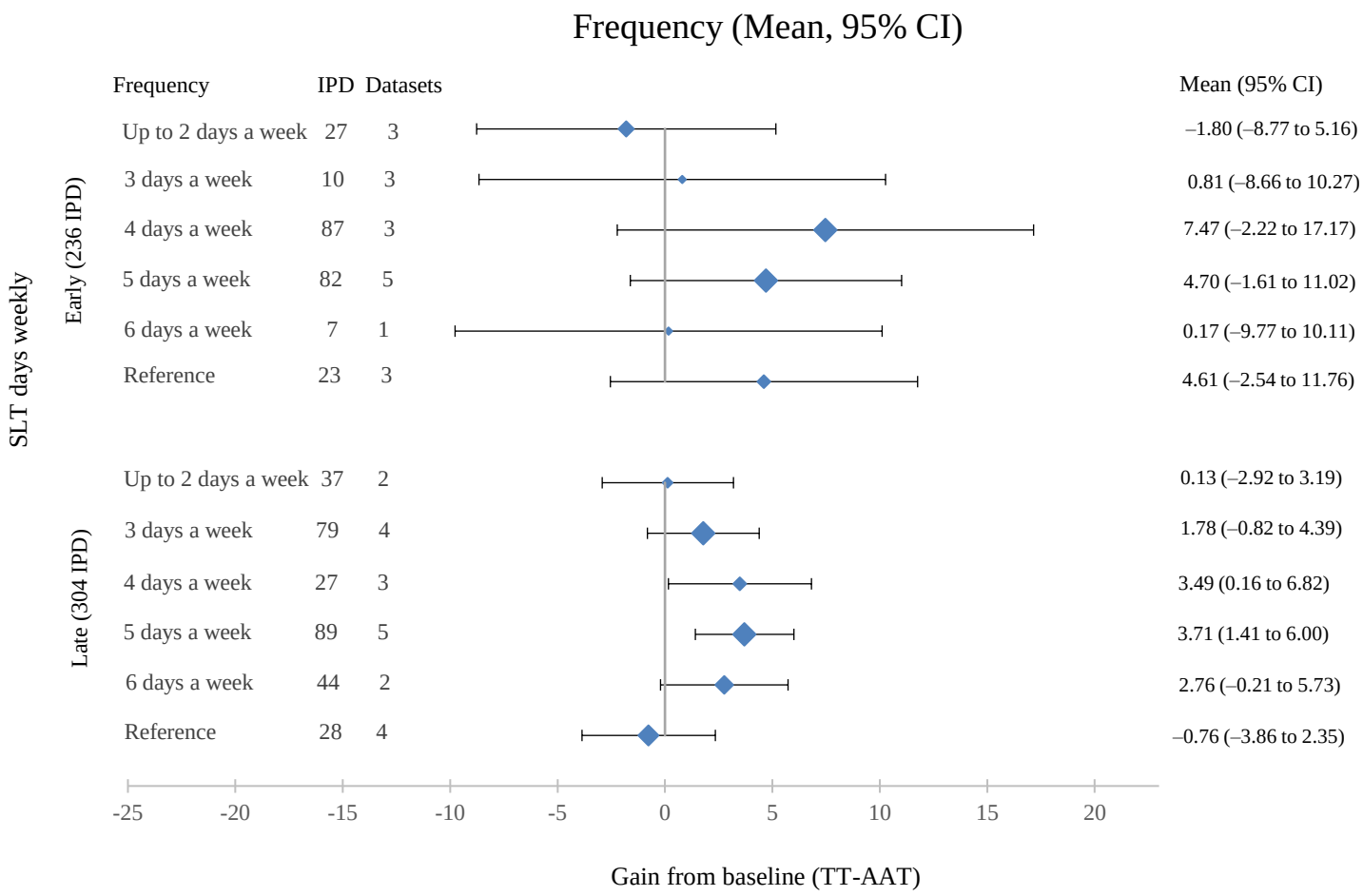


Supplementary Materials I: Early (≤ 3 months) and Later (>3 months) after aphasia onset; subgroups by SLT frequency, intensity and dosage and language outcome

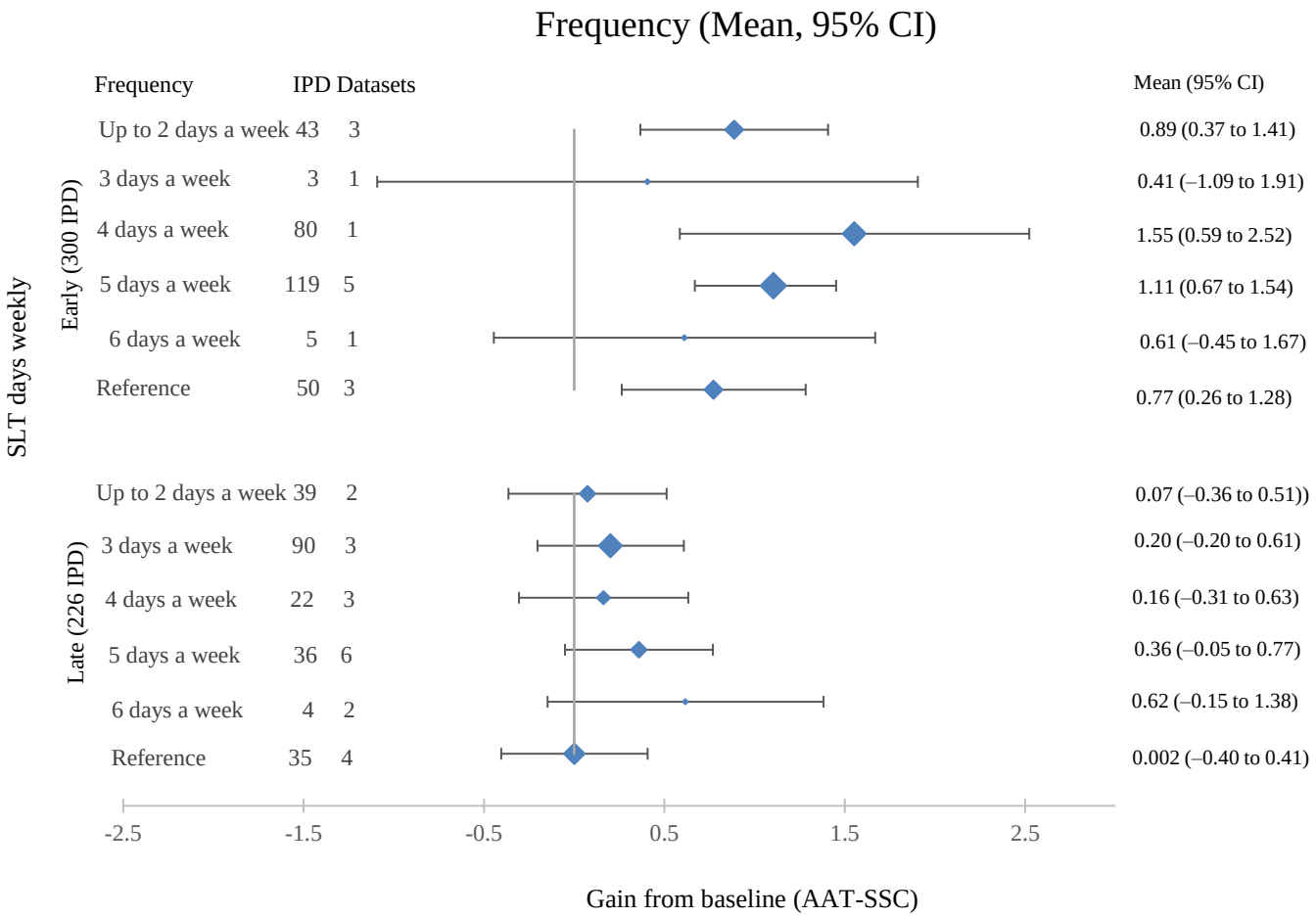
(a) SLT Frequency and Overall Language (WAB 0-100)



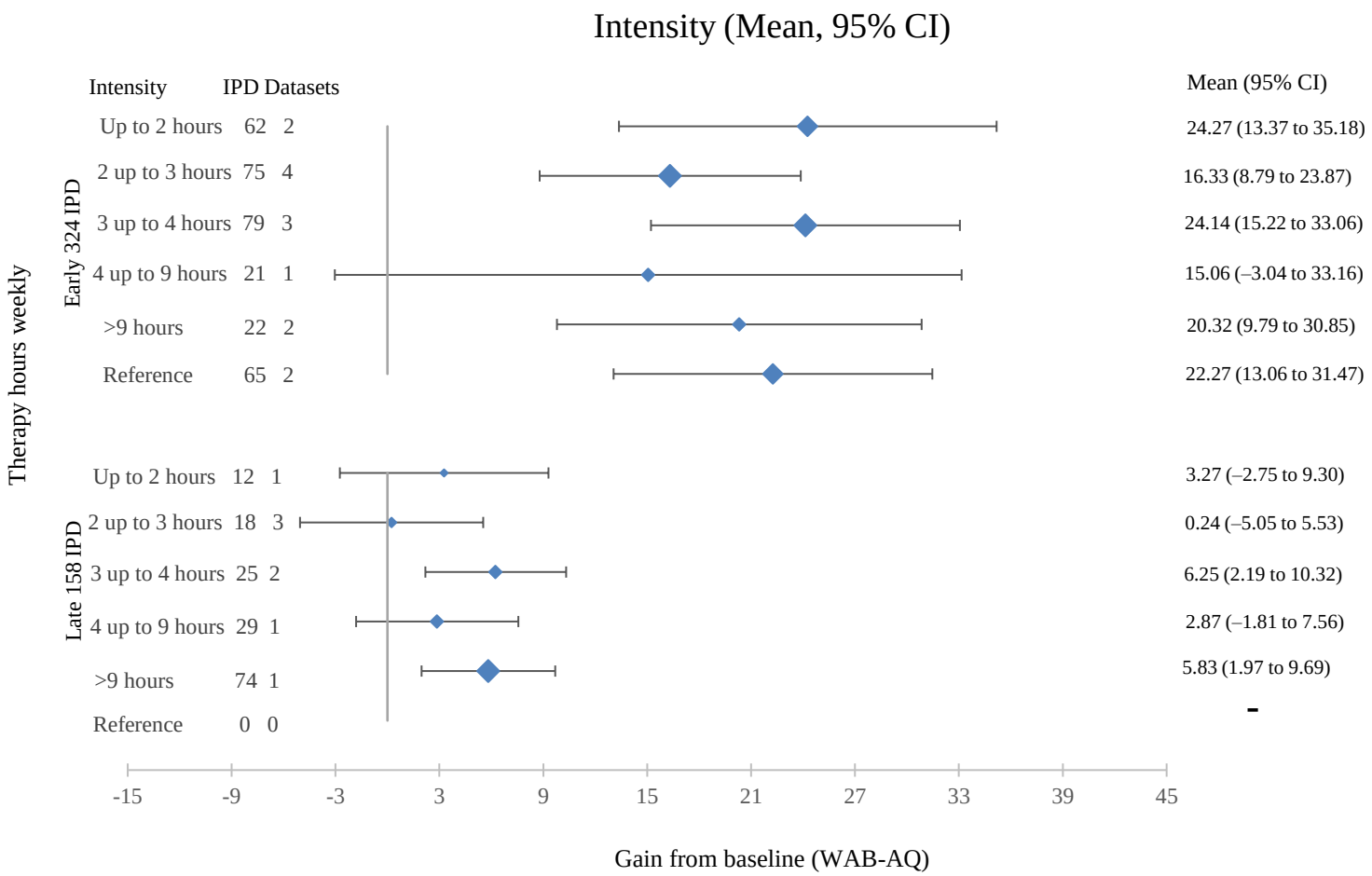
(b) Frequency: Auditory Comprehension (TT-AAT 0-50)



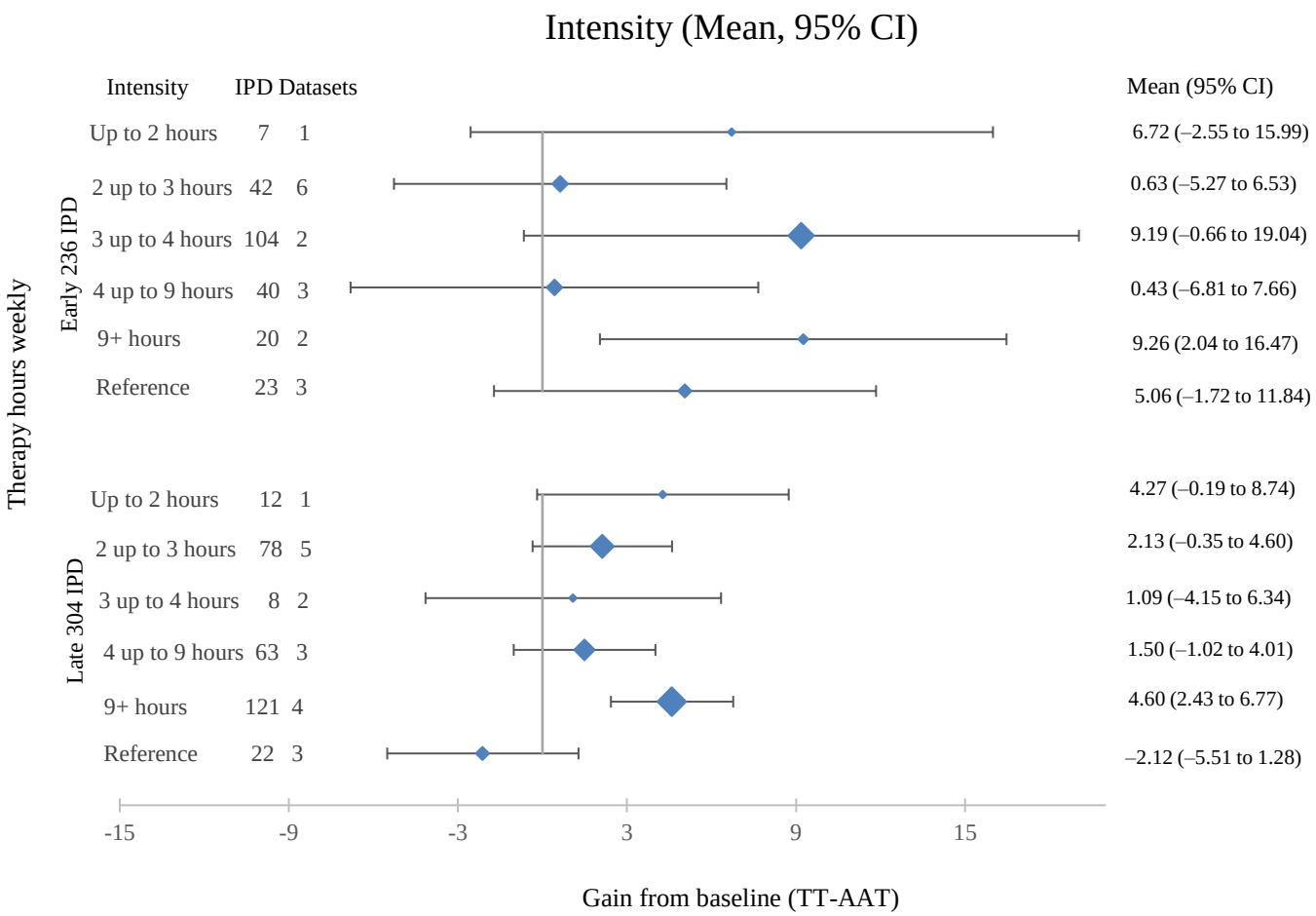
(c) Frequency: Functional Communication (AAT-SSC 0-5)



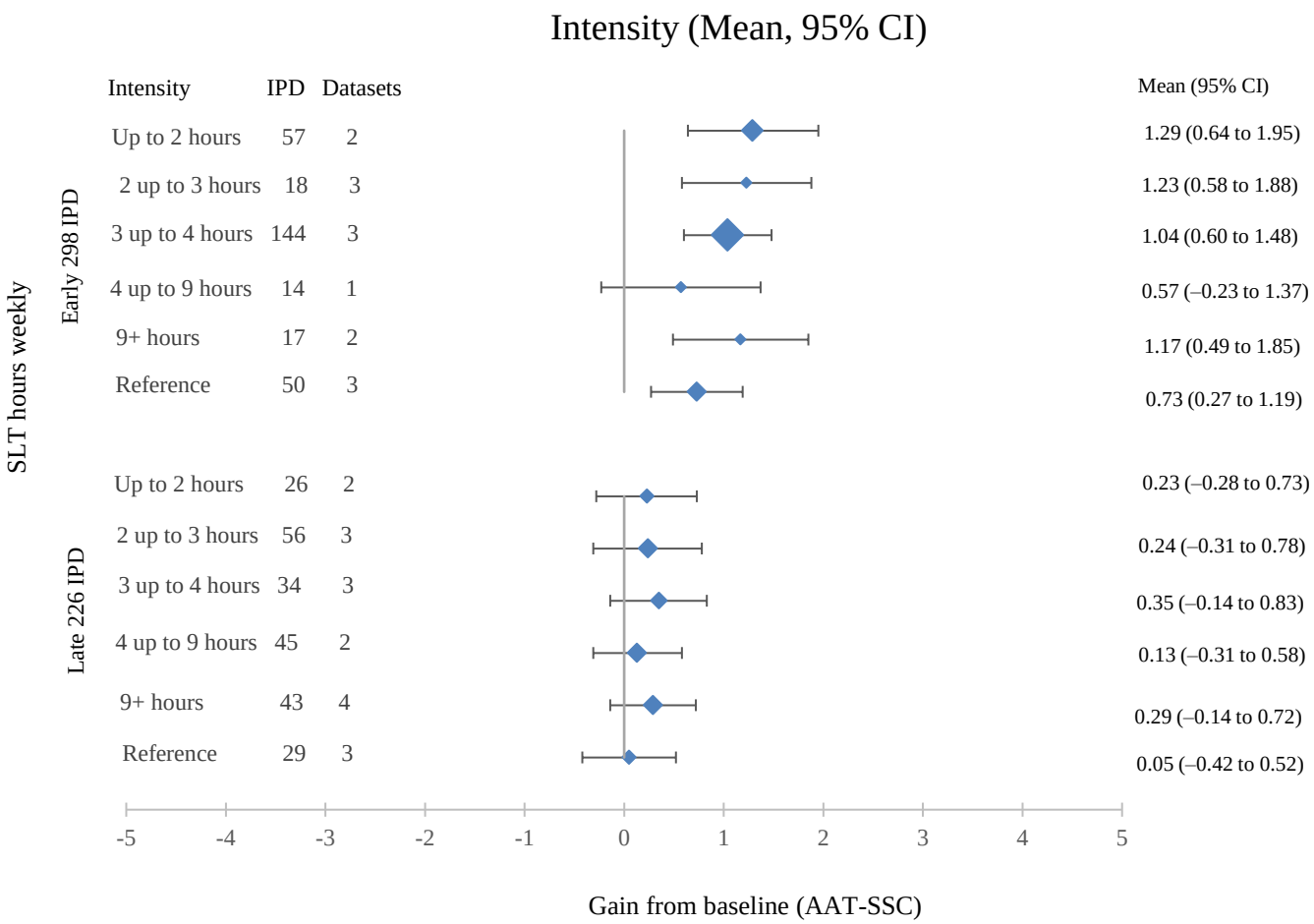
(d) Intensity: Overall Language (WAB 0-100)



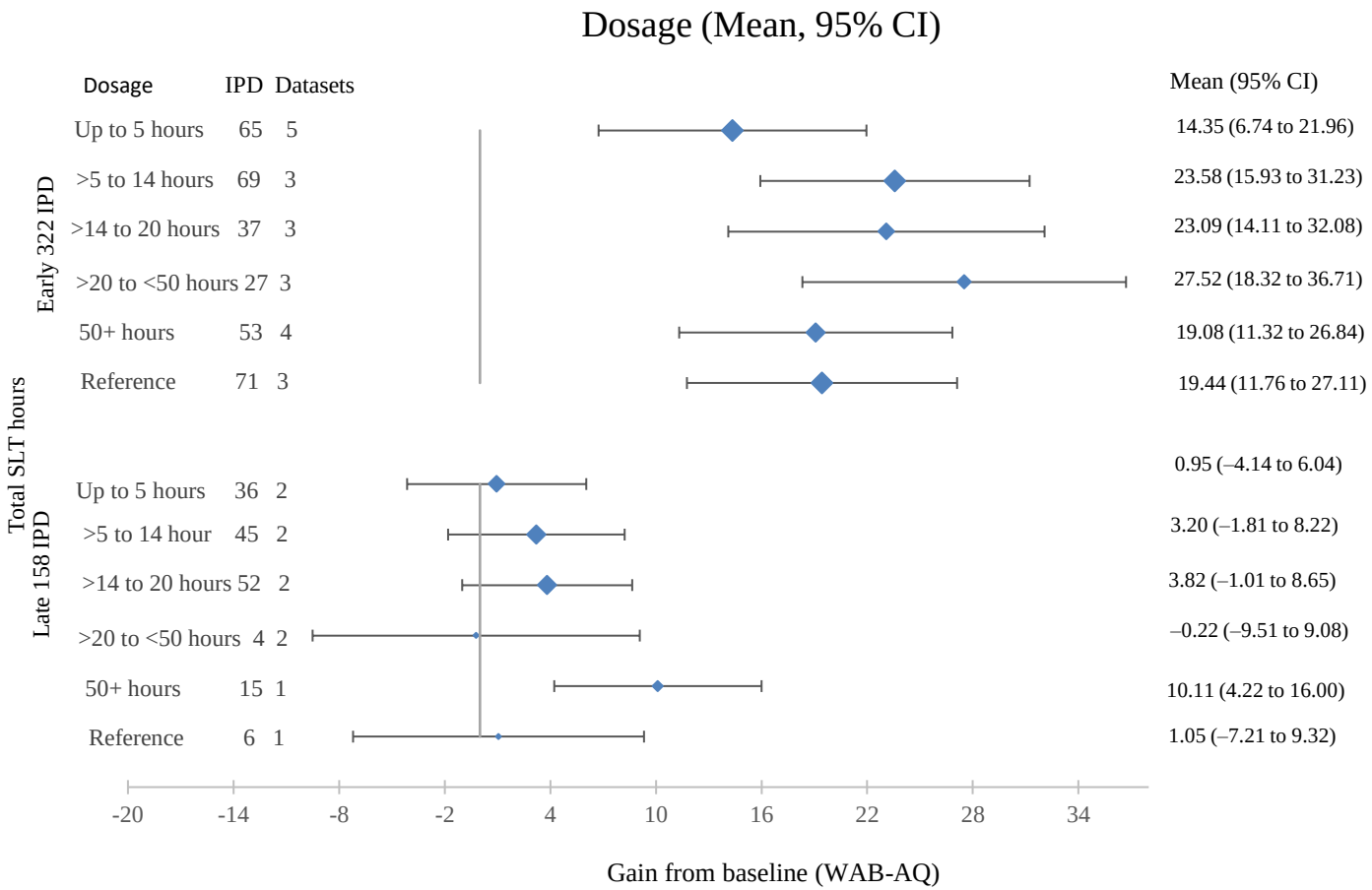
(e) Intensity: Auditory Comprehension (TT-AAT 0-50)



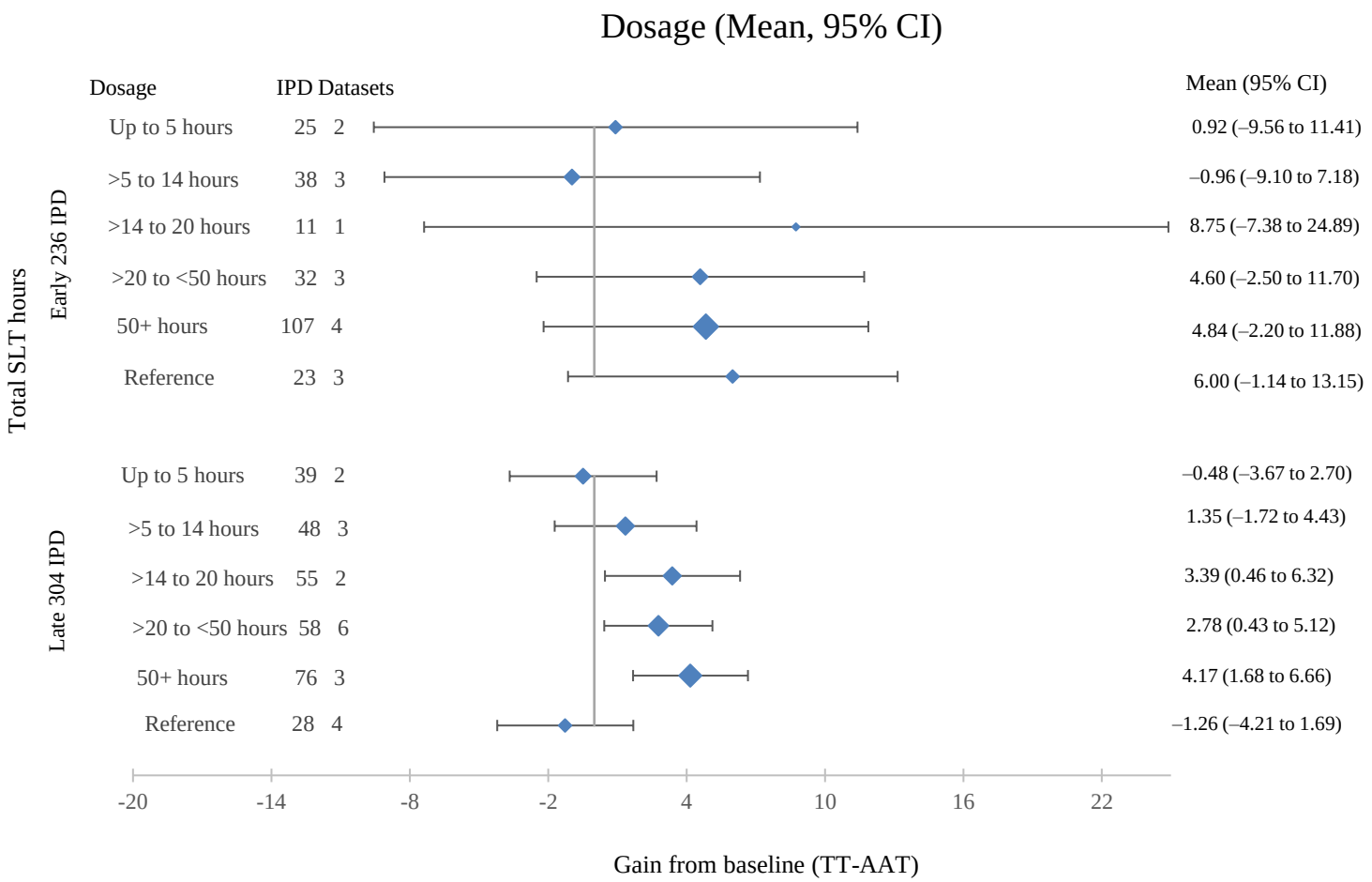
(f) Intensity: Functional Communication (AAT-SSC 0-5)



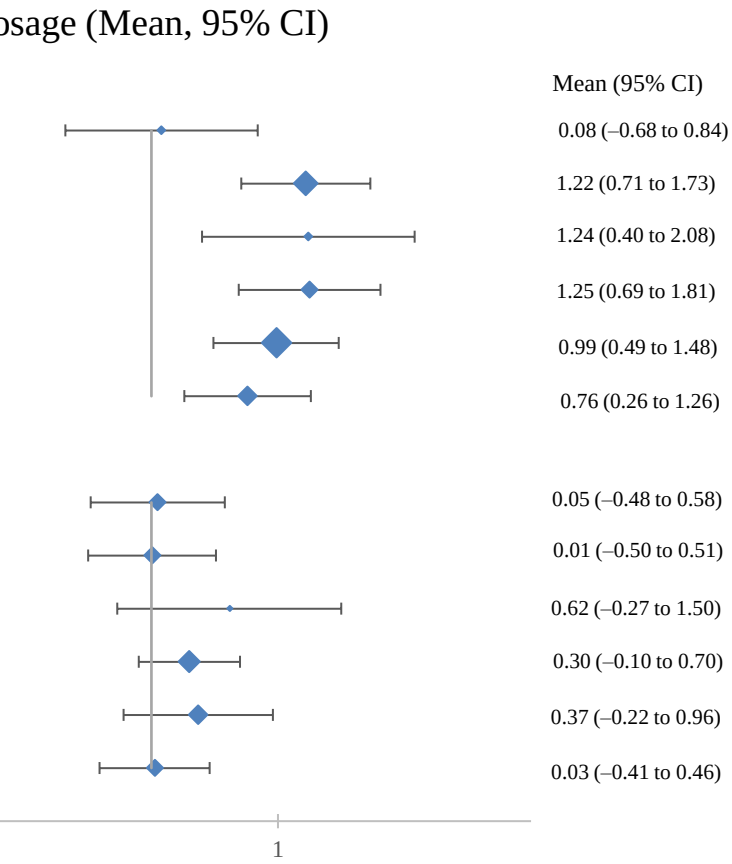
(g) Dosage: Overall Language (WAB 0-100)



(h) Dosage: Auditory Comprehension TT-AAT (0-50)

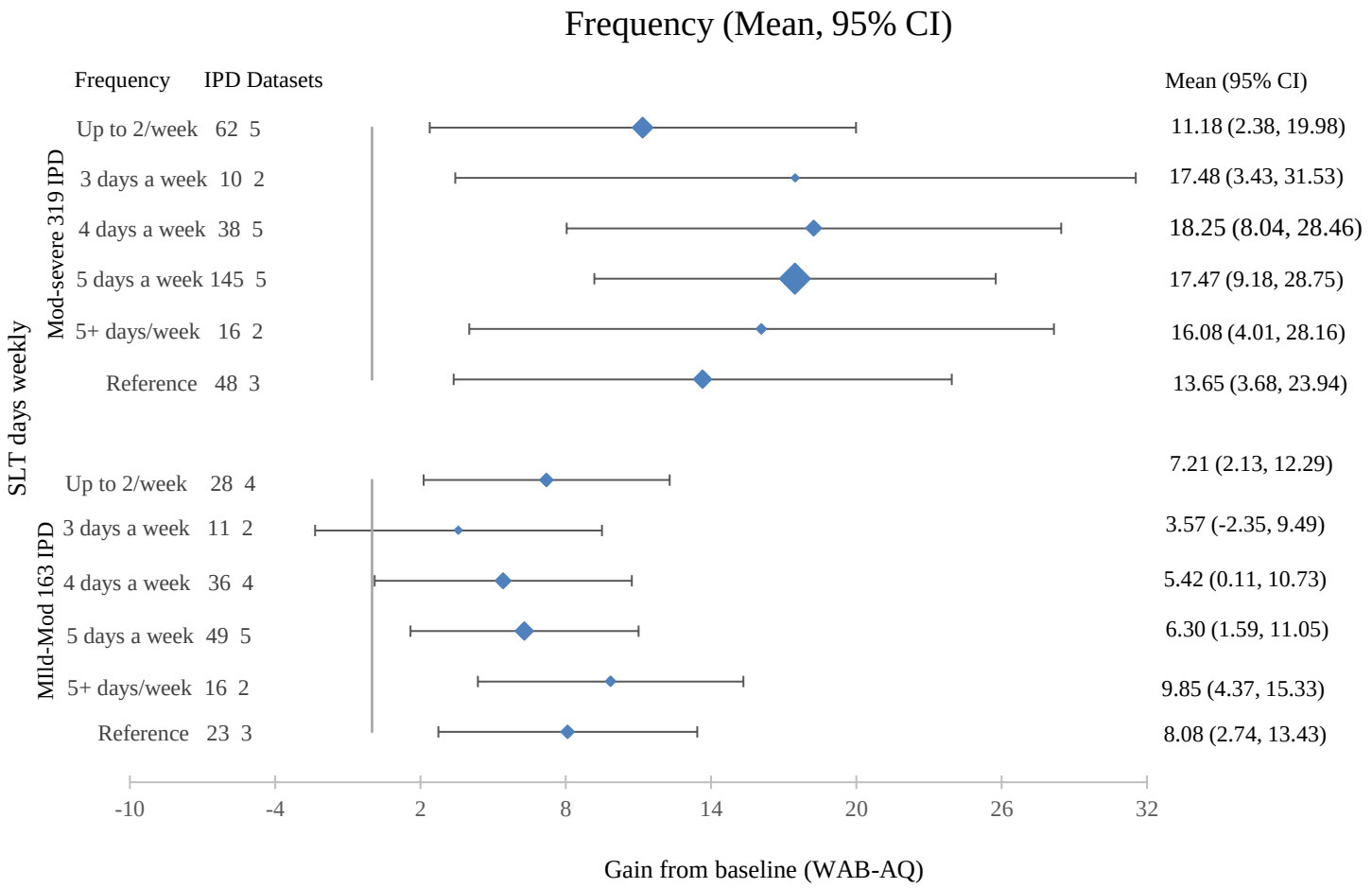


(i) Dosage: Functional Communication (AAT-SSC 0-5)

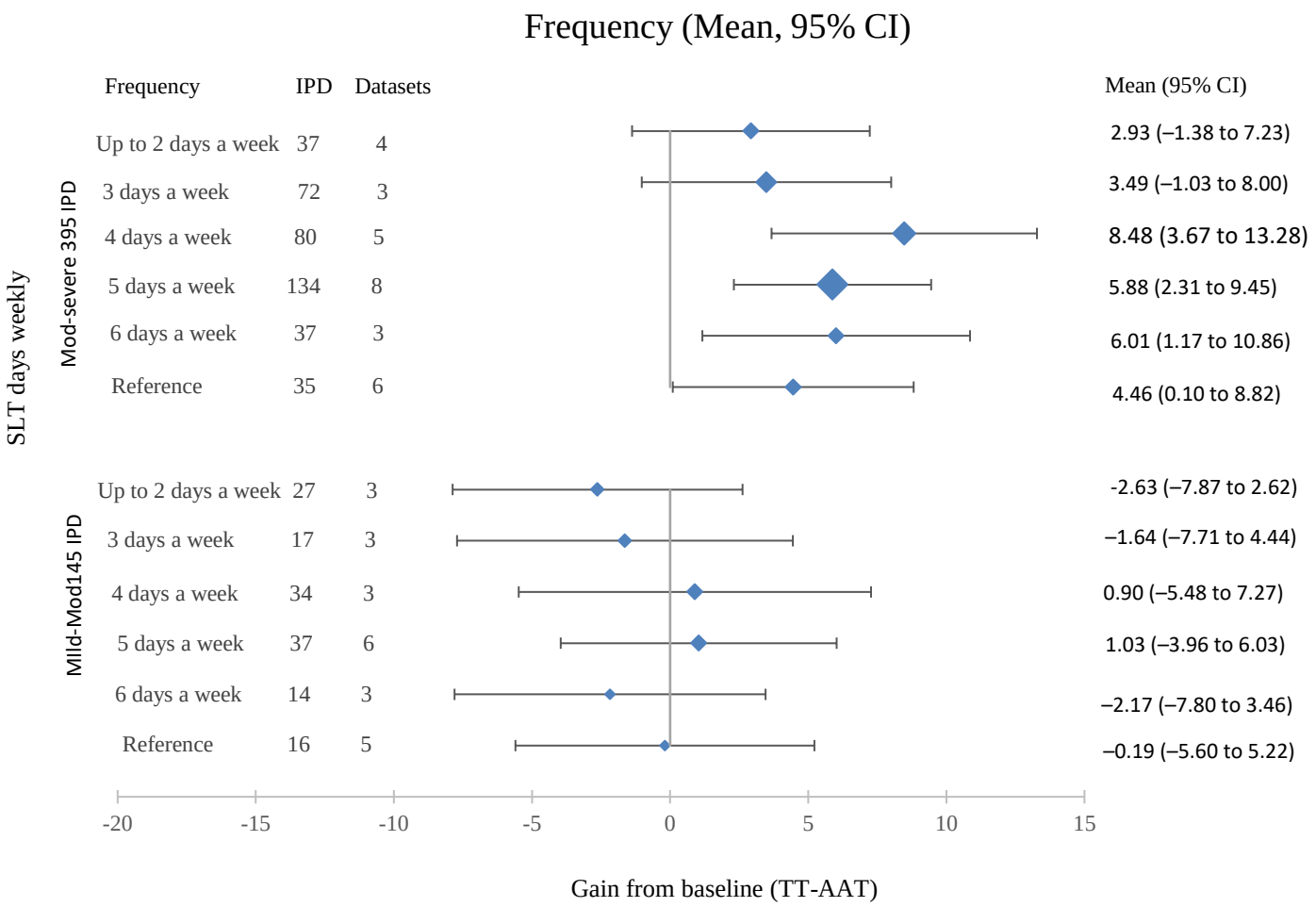


Supplementary Material J: Aphasia Severity; Below the median (Moderate-Severe) v above the median (Mild-Moderate): subgroups by SLT frequency, intensity and dosage and language outcome

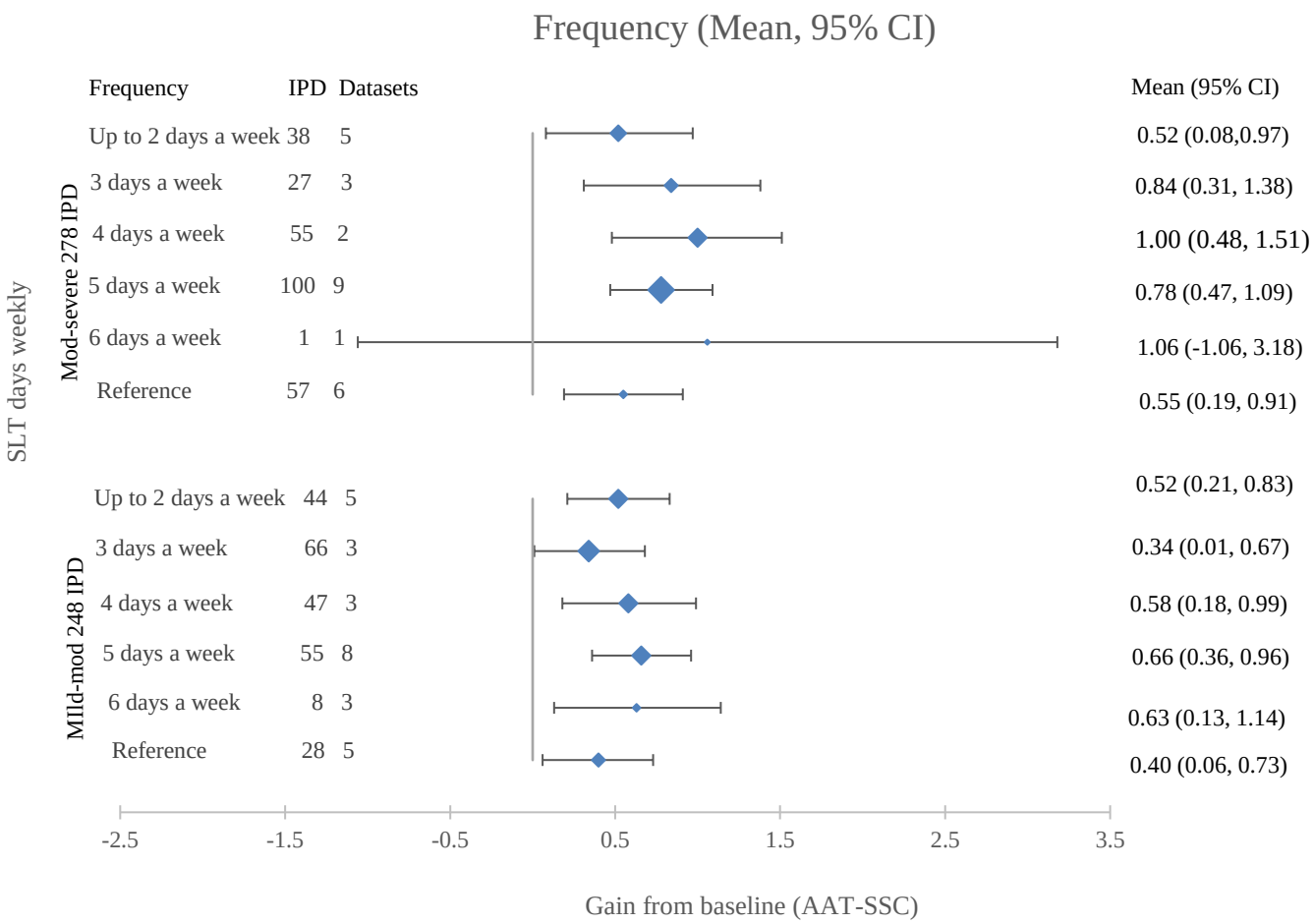
(a) SLT frequency and overall language ability (WAB-AQ 0-100)



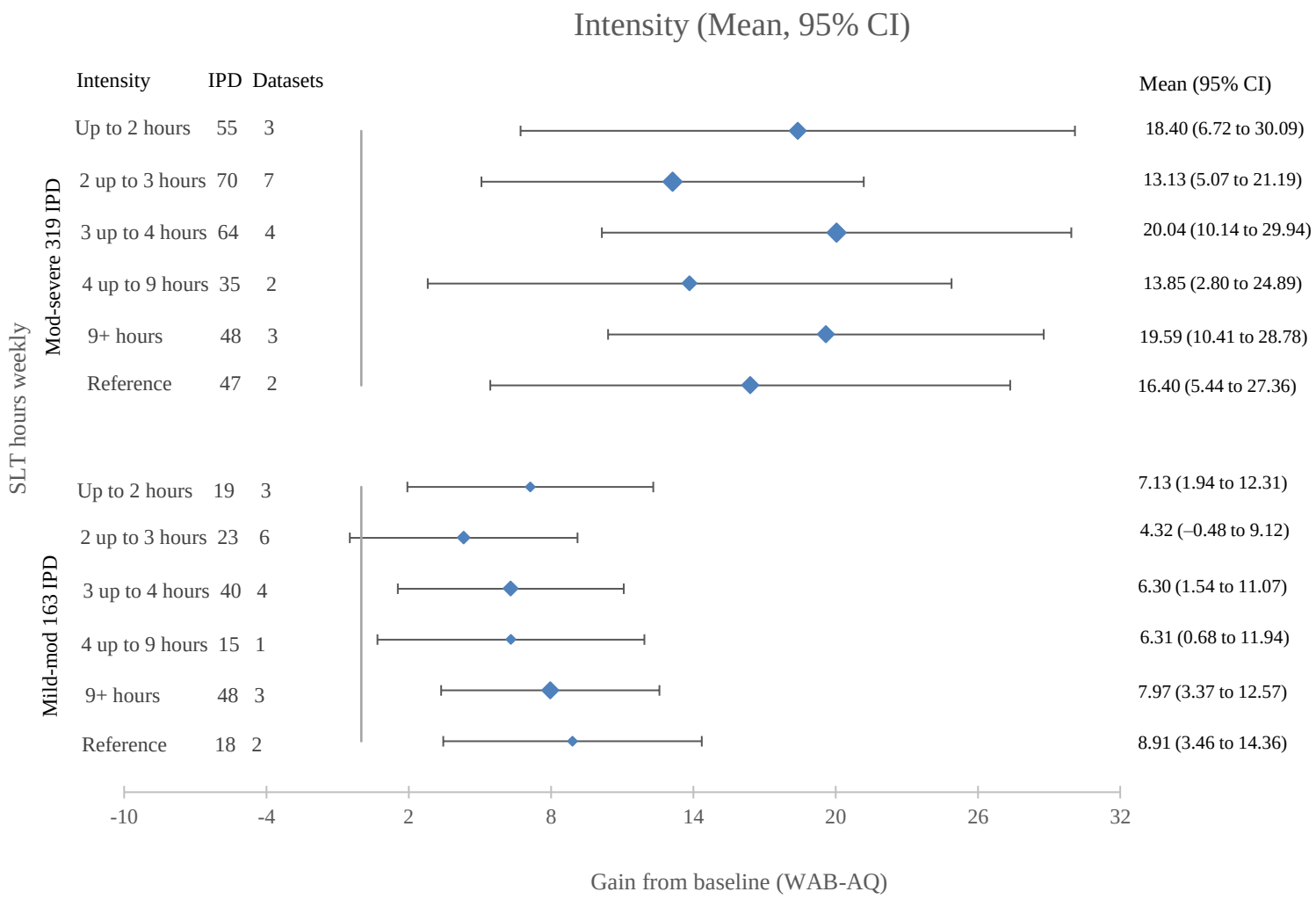
(b) SLT frequency and auditory comprehension (TT-AAT 0-50)



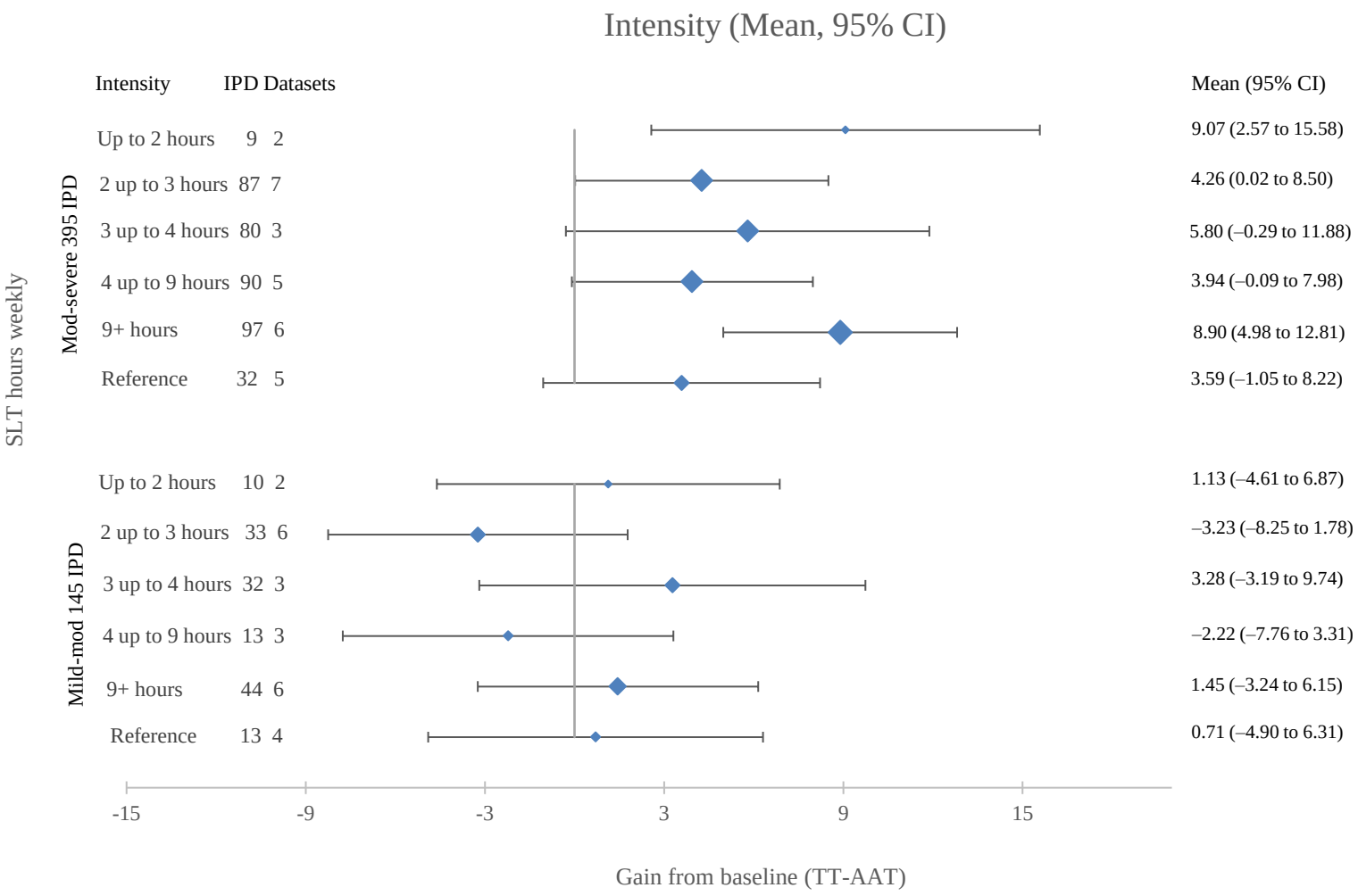
(c) SLT frequency and functional communication (AAT-SSC 0-5)



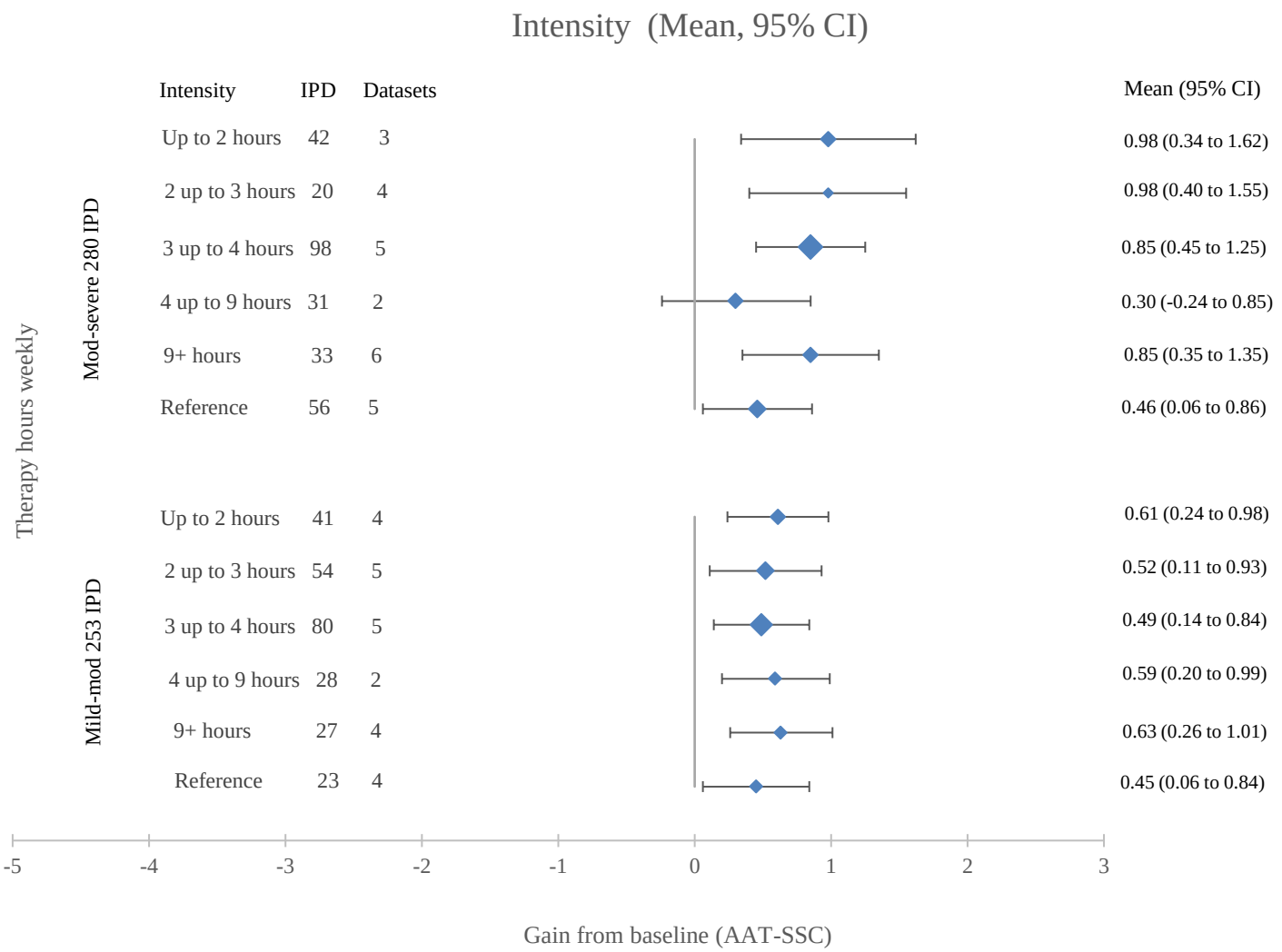
(d) SLT intensity and overall language (WAB-AQ 0-100)



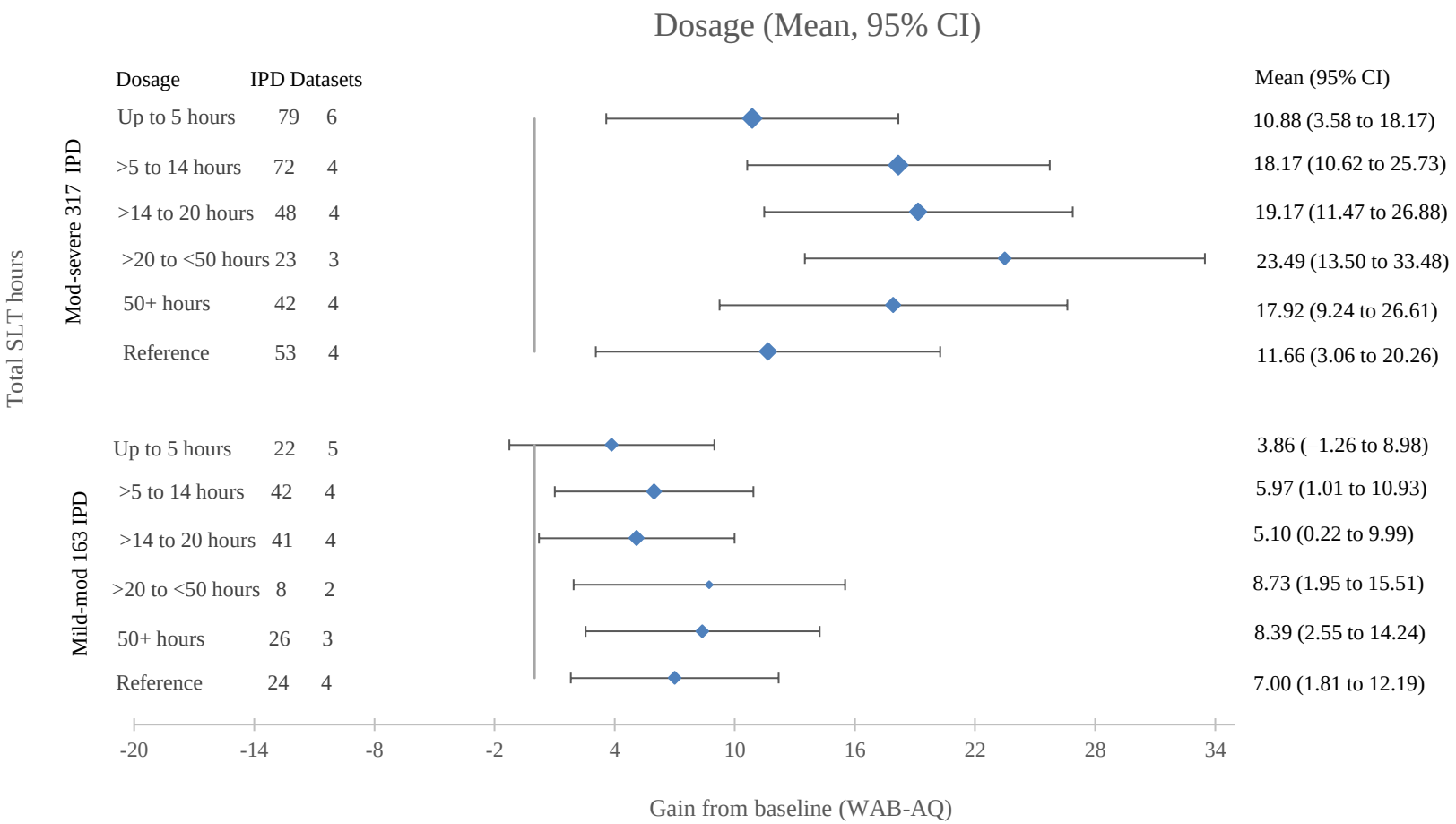
(e) SLT intensity and auditory Comprehension (TT-AAT 0-50)



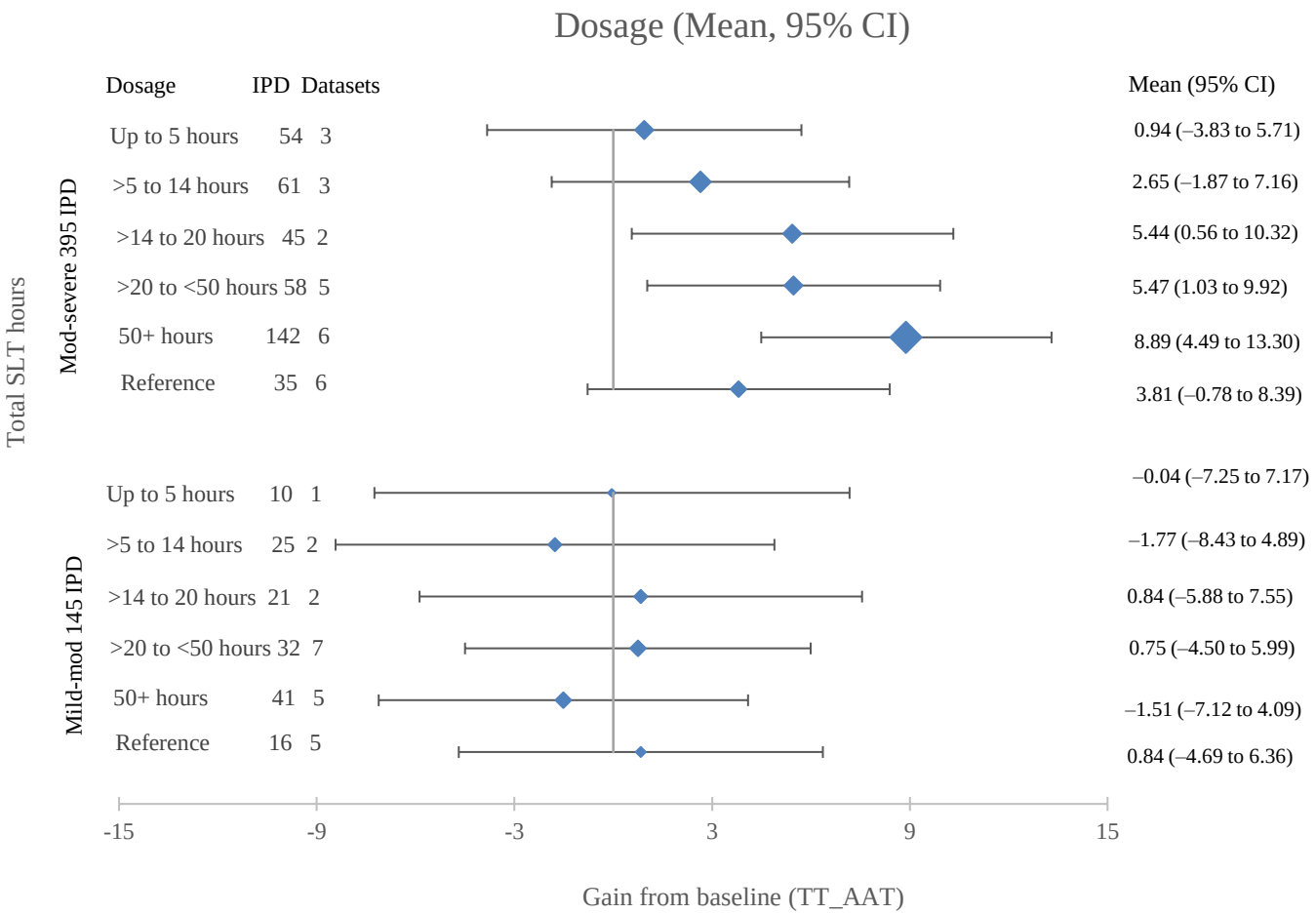
(f) SLT intensity and functional communication (AAT-SSC 0-5)



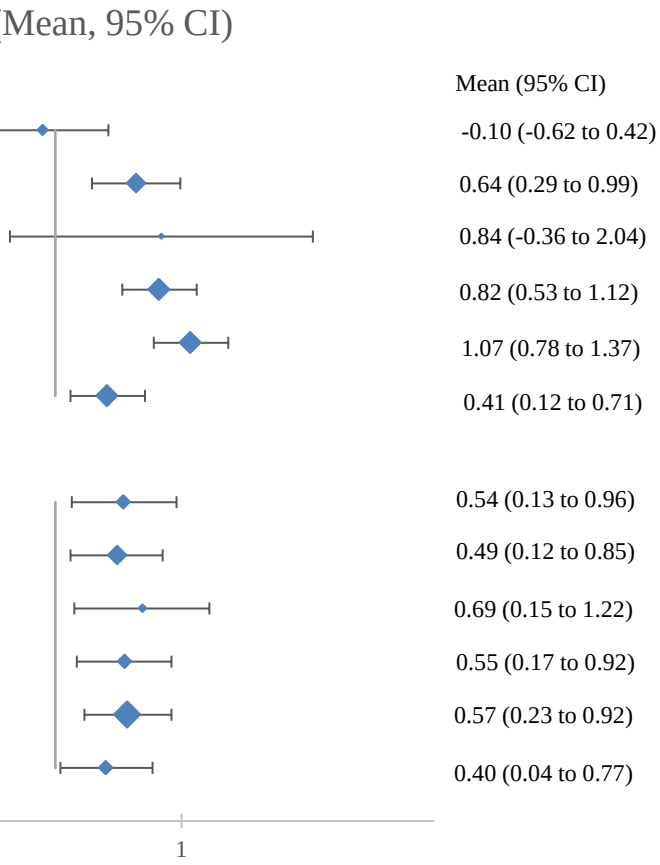
(g) SLT dosage and overall language ability (WAB-AQ 0-100)



(h) SLT dosage and auditory comprehension TT-AAT (0-50)

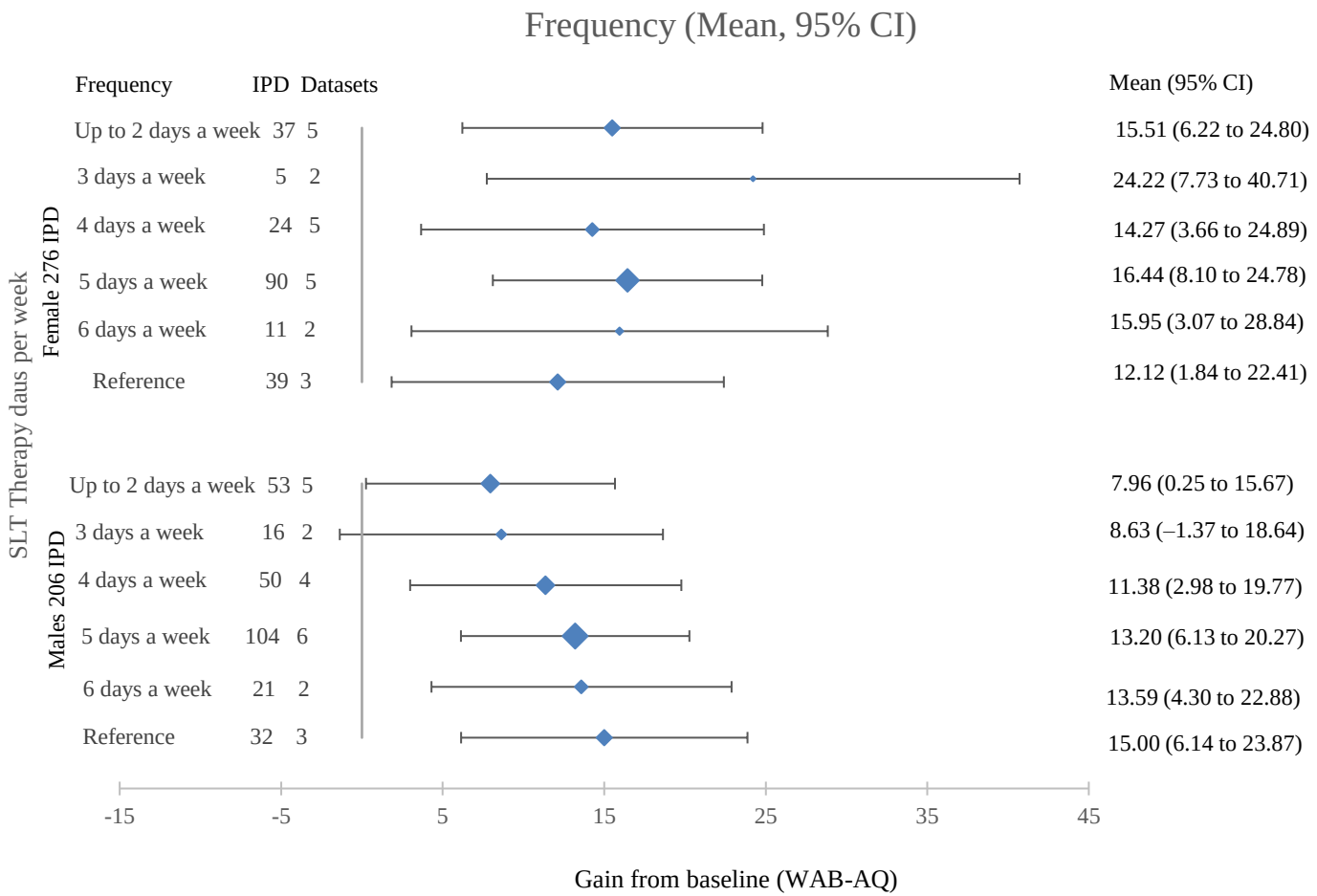


(i) SLT dosage and functional communication AAT-SSC (0-5)

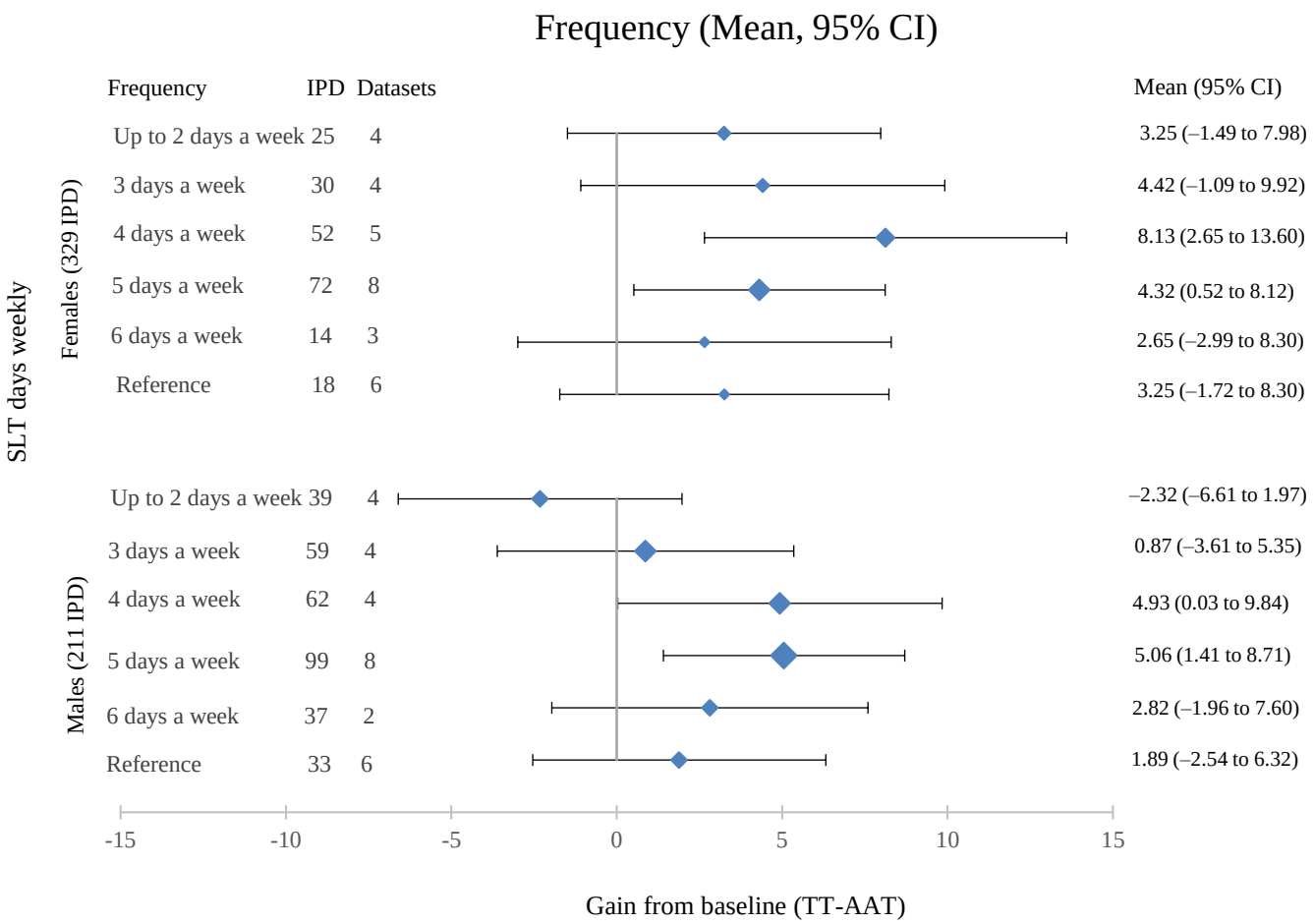


Supplementary Material K: Male and Female subgroups by SLT frequency, intensity and dosage and language outcome

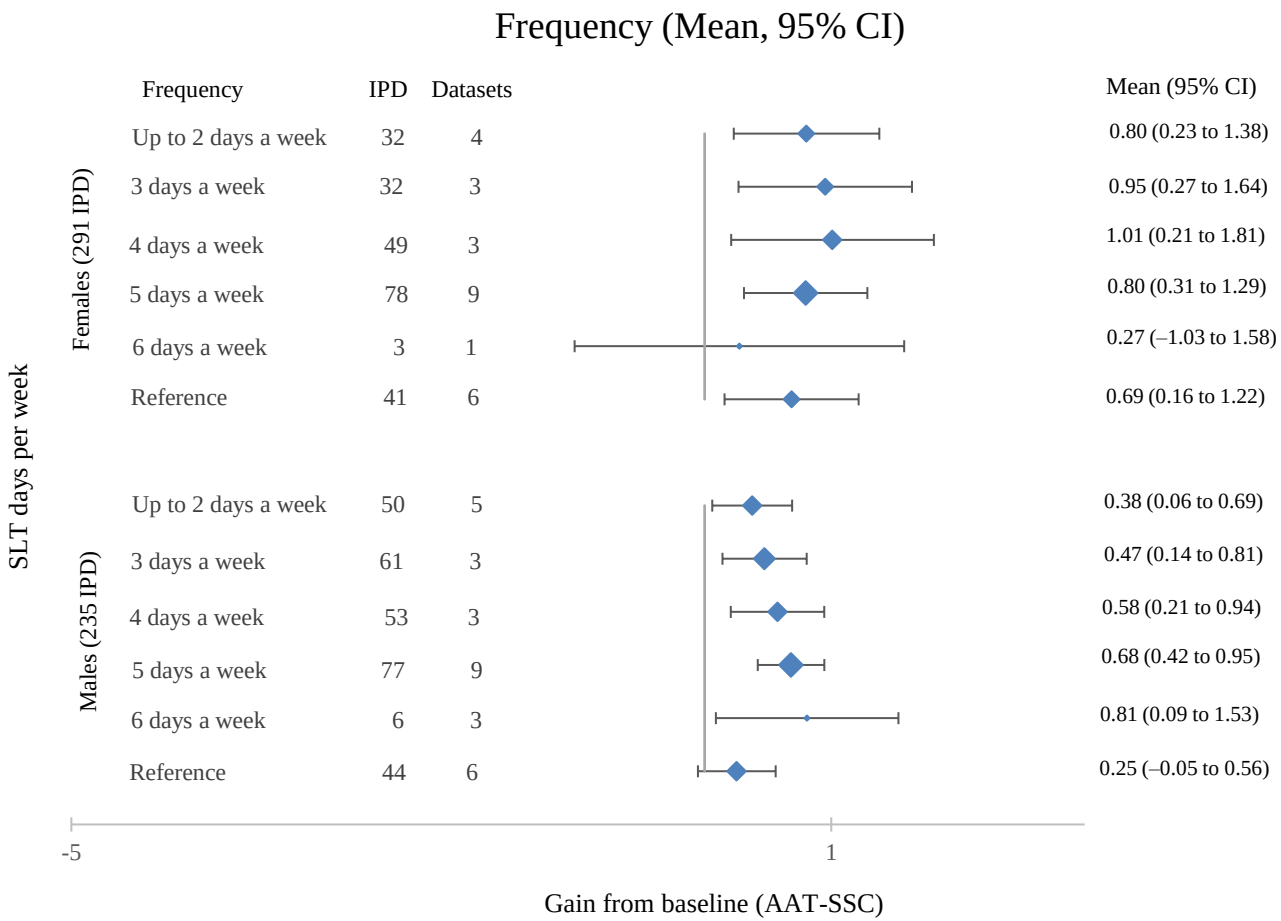
(a) SLT Frequency and overall language ability (WAB-AQ 0-100)



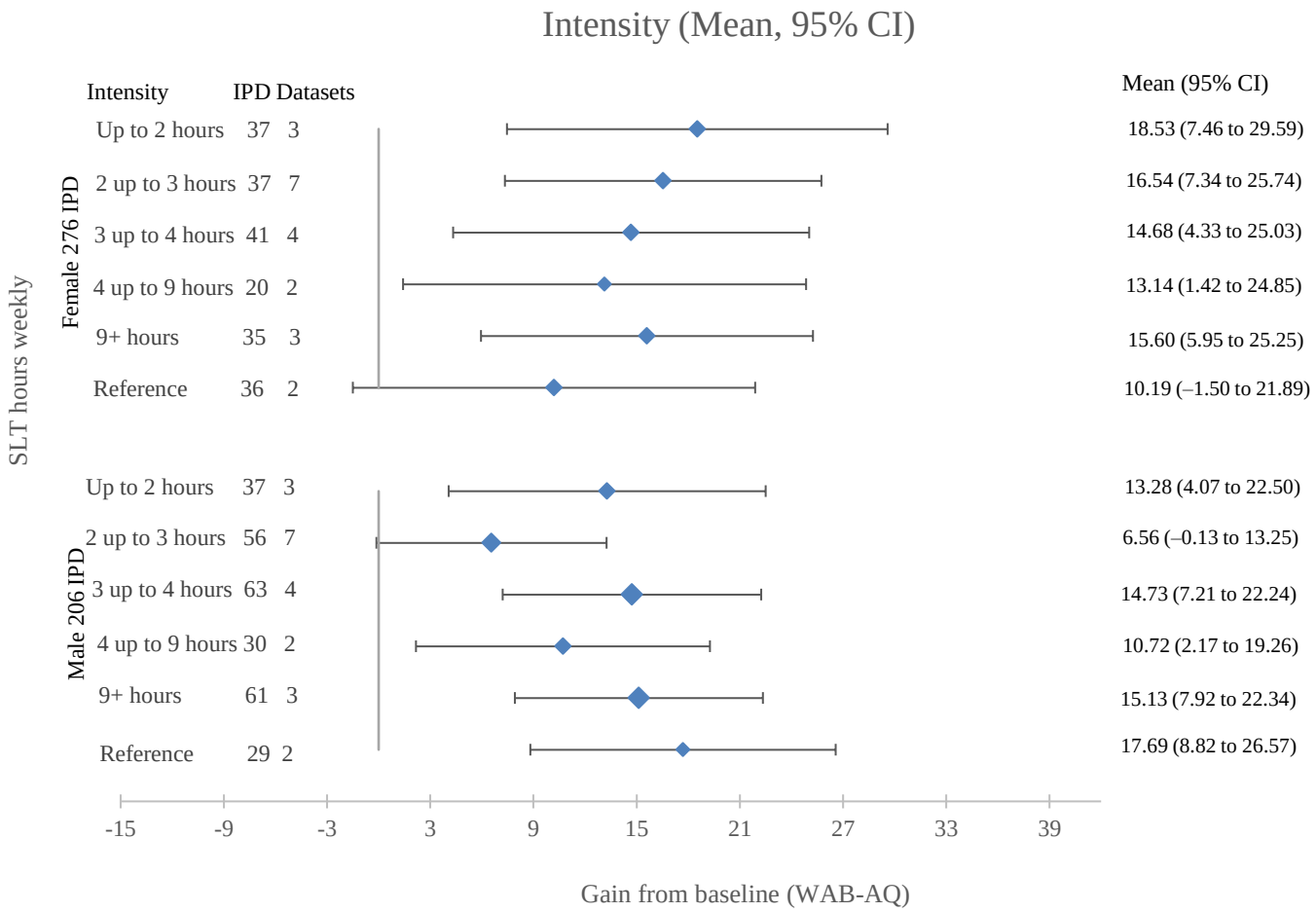
(b) SLT Frequency and auditory comprehension (TT-AAT 0-50)



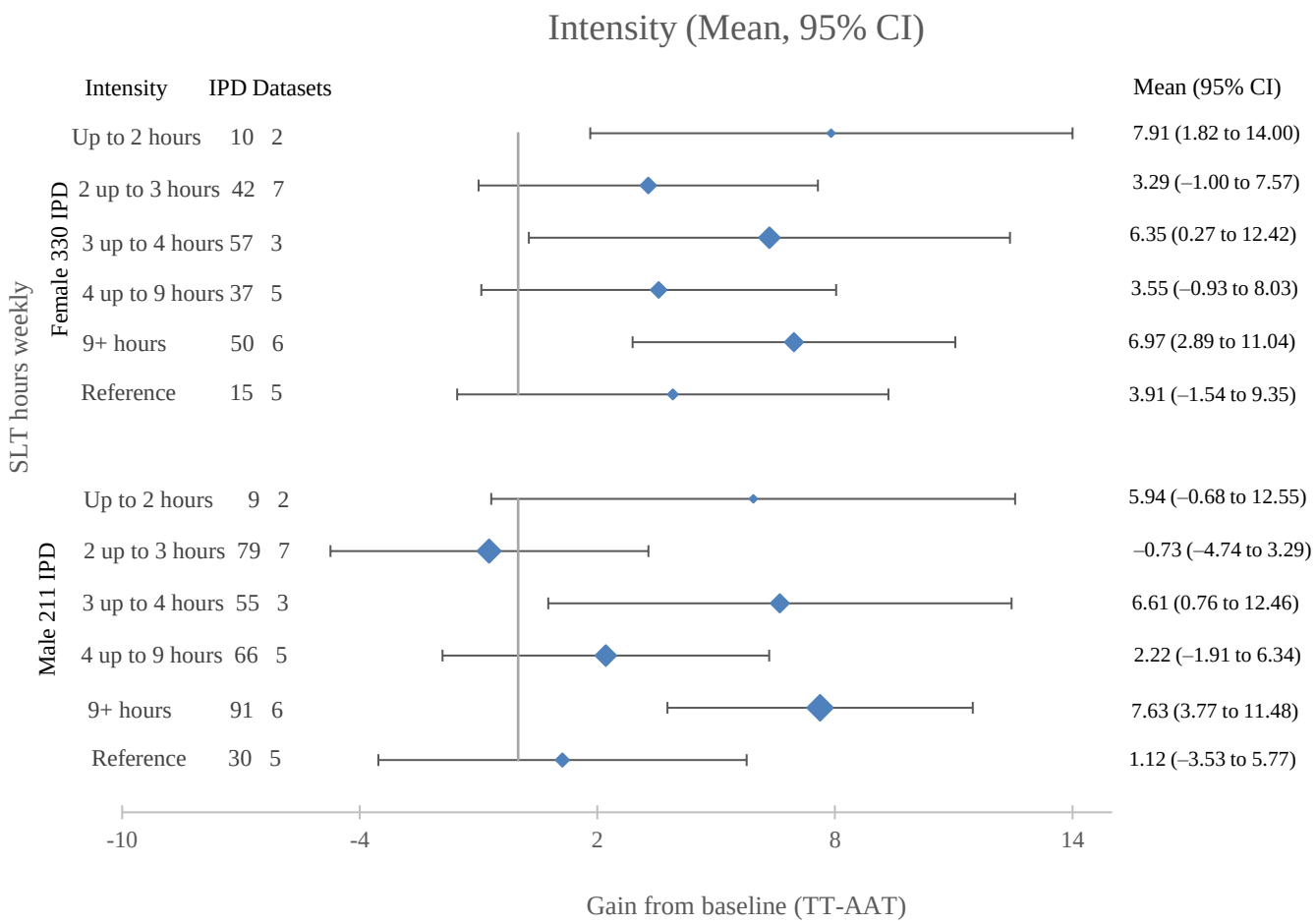
(c) SLT Frequency and functional communication (AAT-SSC 0-5)



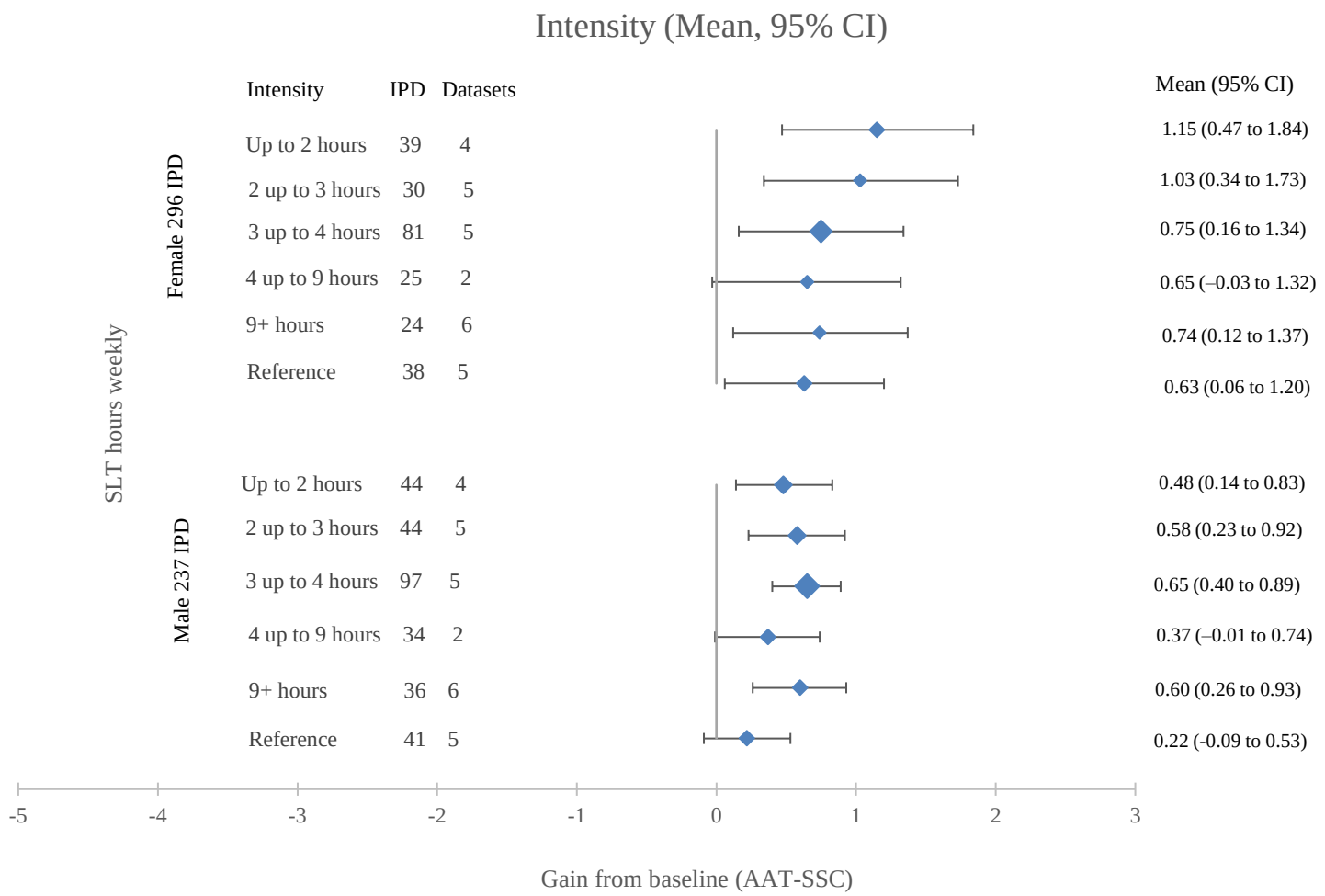
(d) SLT Intensity and overall language ability (WAB-AQ 0-100)



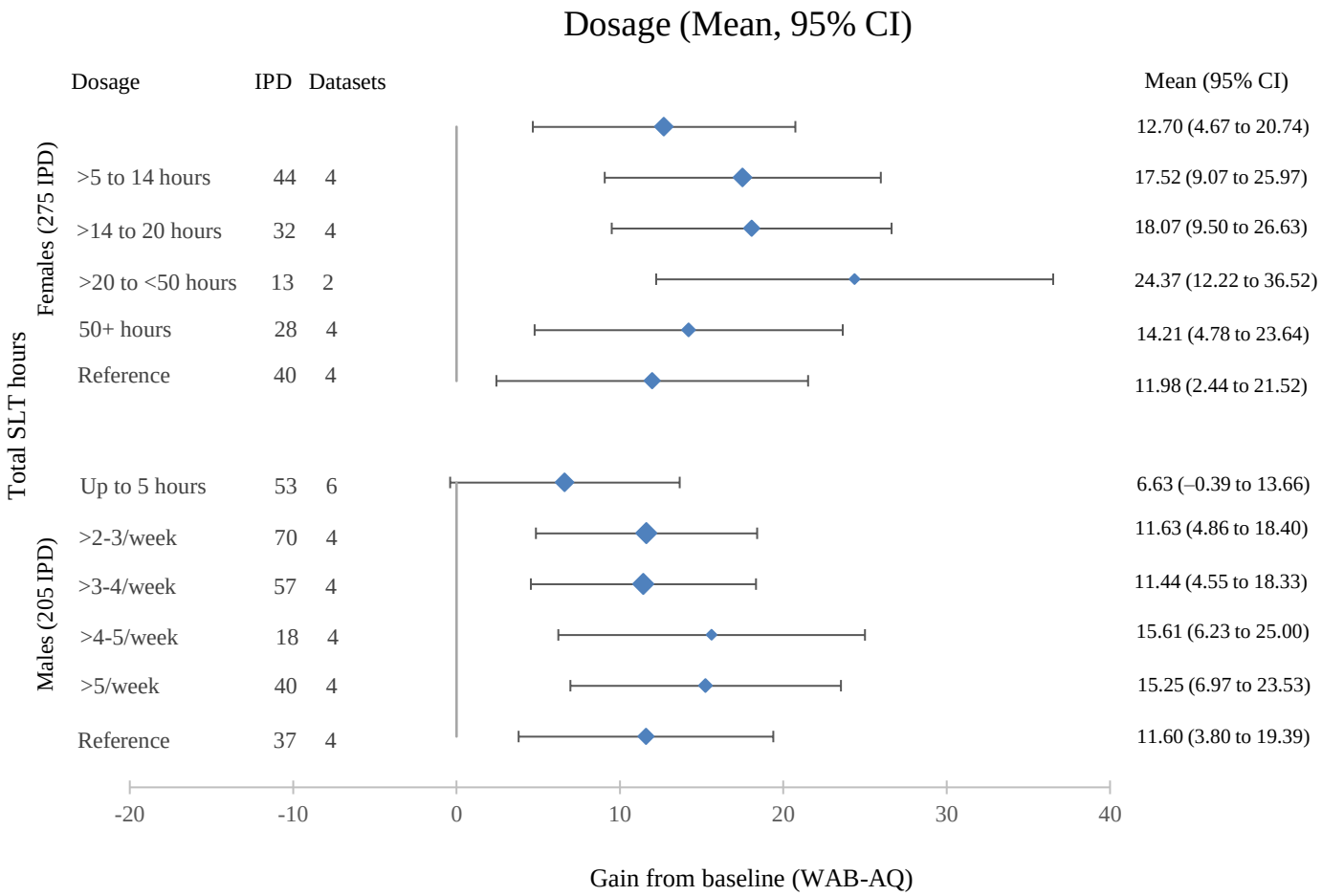
(e) SLT intensity and auditory comprehension (TT-AAT 0-50)



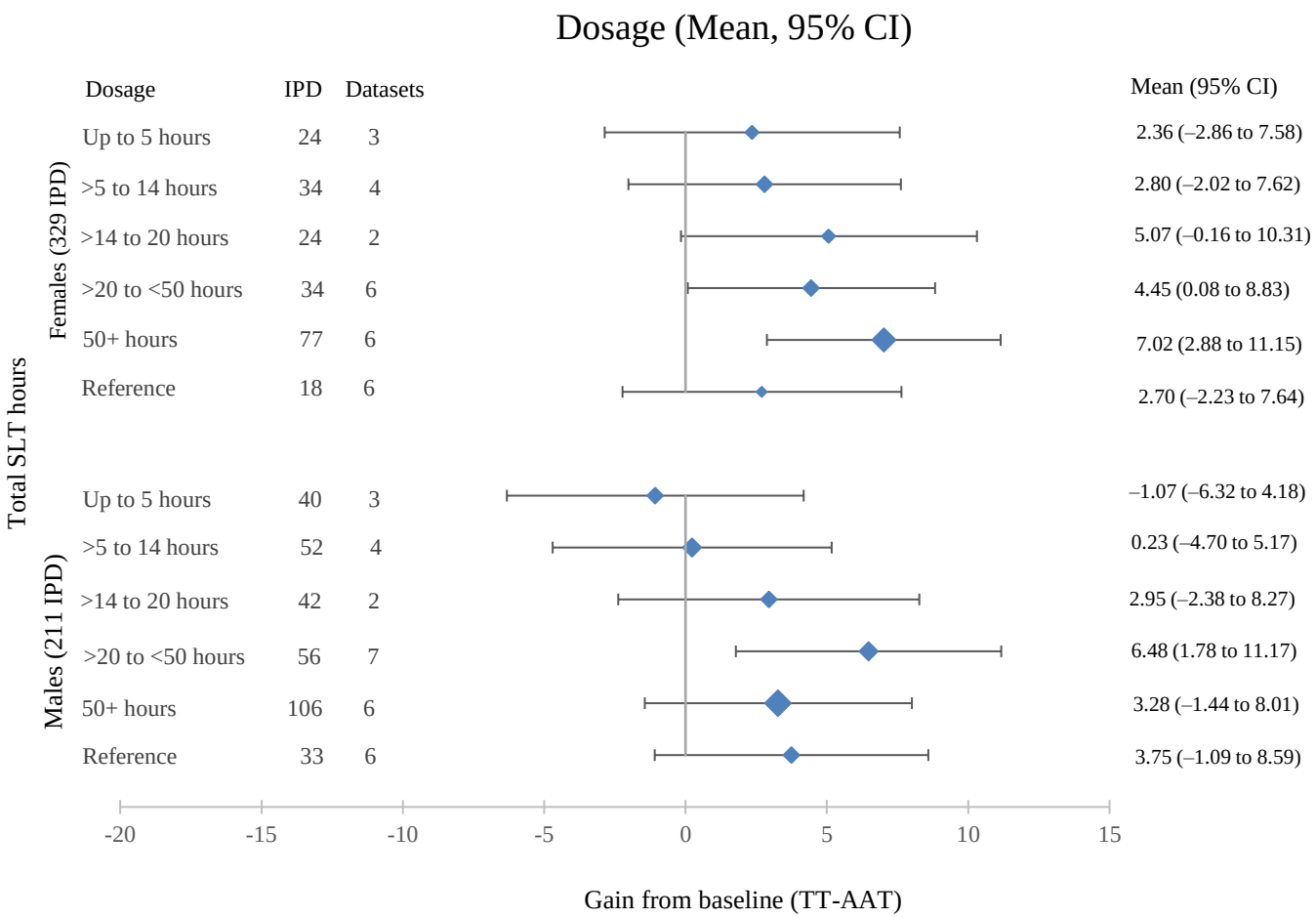
(f) SLT intensity and functional communication (AAT-SSC 0-5)



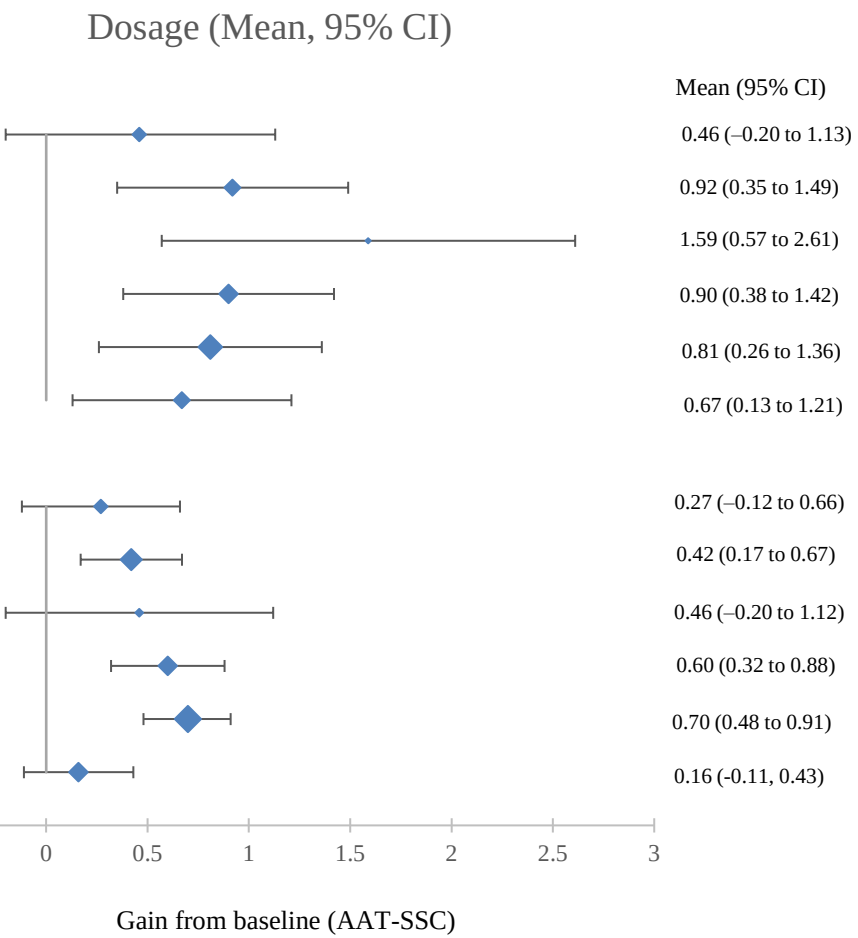
(g) SLT dosage and overall language (WAB-AQ 0-100)



(h) SLT dosage and auditory comprehension (TT-AAT 0-50)



(i) SLT dosage and functional communication (AAT-SSC 0-5)



Supplementary Material L.

Subgroups by language outcome and median SLT frequency, intensity and dosage.

Subgroups	SLT Frequency (days/week)		SLT Intensity (hours/week)		SLT Dosage (total hours)	
	Median [IQR]	n	Median [IQR]	n	Median [IQR]	n
Overall-Language						
Moderate-severe	4.7 [1-5]	319	3 [2-5]	274	9.3 [4.5-17.2]	317
Mild-moderate	4 [1.3-5]	163	3.8 [2-10]	156	14.0 [4.5-16]	163
Female	4 [1-5]	206	3 [1.5-5]	180	9.3 [3.6-16]	205
Male	4 [1.5-5]	276	3.8 [2-6.8]	250	11.3 [5-175]	275
<65 years	4 [2-5]	277	3.8 [2-10]	256	12.5 [5-16]	276
≥65 years	4 [1-5]	205	3 [0-3.8]	174	9.5 [0-19.7]	205
Early SLT [≤3 mths]	4 [1-5]	324	2.5 [1-3.8]	272	9.7 [3.8-20]	322
Late SLT [>3 mths]	4 [2-5]	158	6.8 [3-10]	158	14 [4.5-15]	158
Auditory comprehension						
Moderate-severe	3.3 [2.3-5]	404	3.8 [2.3-7.3]	404	17 [5.5-50]	404
Mild-moderate	3.3 [2-5]	146	3.5 [2-10]	146	19.3 [7.5-50]	146
Female	3.3 [2.3-5]	211	3.5 [2.3-7.3]	211	25 [7.5-52]	211
Male	3.3 [2.3-5]	329	2.8 [2.3-10]	329	16 [6.8-50]	329
<65 years	4 [2.1-5]	360	4.5 [2.3-10]	360	15 [5.4-50]	360
≥65 years	3.3 [2.3-5]	180	3.5 [2.3-5]	180	48 [7.5-52]	180
Early SLT [≤3 mths]	3.3 [3-5]	236	3.5 [2-5]	236	30 [7.5-52]	236
Late SLT [>3 mths]	4 [2.3-5]	304	6 [2.3-10]	304	15 [6.8-45]	304
Functional communication						
Moderate-severe	3.3 [1-5]	280	3.5 [2-4.5],	245	30 [3.8-50]	278
Mild-moderate	3.0 [2-4.9]	251	3.5 [2.3-3.8]	234	24 [6-50]	251
Female	3.3 [1-5]	237	3.5 [2-3.8]	211	30 [4.5-52]	236
Male	3 [1-5]	294	3.5 [2.3-4.5]	268	22.6 [4.5-50]	293
<65 years	3 [1-4]	291	3.5 [2-5]	270	30 [4.5-50]	290
≥65 years	3.3 [1.1-5]	240	3.5 [2.3-3.8]	209	24.0 [6.8-52]	239
Early SLT [≤3 mths]	3.3 [1-5]	300	3.5 [2-3.8]	248	24.0 [7.5-52]	298
Late SLT [>3 mths]	2.3 [2-4]	226	3.0 [2.3-6]	226	30 [4.5-40]	226

Supplementary Materials M:

Base Models by age, time since aphasia onset, aphasia severity and sex.

Base Model	RCT	IPD	Estimate of means (CI 95%)	RCT	IPD	Estimate of means (CI 95%)
Younger (≤ 65 years) versus Older (>65 years) subgroups						
Overall language ability on WAB-AQ; range 0-100						
Female	11	97	13.97 (7.98, 19.97)	9	109	13.86 (6.92, 20.79)
Male	11	180	12.21 (6.53, 17.89)	10	96	11.74 (5.02, 18.45)
0 to 1 month	8	97	17.89 (11.84, 23.95)	8	163	22.36 (16.78, 27.95)
>1 to 3 months	6	45	16.44 (9.77, 23.11)	5	19	11.71 (2.60, 20.82)
>3 to 6 months	3	10	9.52 (-1.33, 20.36)	1	6	11.18 (-5.05, 27.41)
6+ months	4	125	8.53 (-0.33, 17.39)	2	17	5.94 (-6.00, 17.88)
Auditory Comprehension on TT-AAT; range 0-50						
Female	16	135	4.63 (1.73, 7.53)	13	76	4.50 (1.09, 7.92)
Male	16	225	3.95 (1.20, 6.69)	15	104	3.22 (0.05, 6.38)
0 to 1 month	6	62	7.66 (3.49, 11.82)	6	77	4.77 (0.70, 8.83)
>1 to 3 months	9	70	3.91 (0.54, 7.27)	8	27	6.63 (2.22, 11.05)
>3 to 6 months	5	37	3.80 (-1.48, 9.08)	3	24	2.54 (-3.95, 9.03)
6+ months	9	191	1.79 (-1.65, 5.23)	7	52	1.50 (-2.48, 5.48)
Naming on BNT; range 0-60						
Female	13	87	9.85 (5.30, 14.40)	11	78	4.01 **(**-0.96**,** 8.98**)**
Male	13	140	7.21 (2.87, 11.54)	12	80	7.44 (2.61, 12.27)
0 to 1 month	5	55	14.61 (8.33, 20.88)	5	74	11.56 (5.29, 17.83)
>1 to 3 months	8	65	9.15 (4.16, 14.14)	7	28	6.68 (0.26, 13.10)
>3 to 6 months	5	44	5.21 (-1.06, 11.47)	3	26	1.91 (-6.48, 10.31)
6+ months	7	63	5.15 (-0.22, 10.52)	5	30	2.74 (-4.02, 9.50)
Functional Communication on the AAT-SSC; range 0 to 5						
Female	14	109	0.79 (0.52, 1.06)	14	127	0.69 (0.41, 0.97)
Male	14	183	0.55 (0.29, 0.81)	13	113	0.57 (0.30, 0.83)
0 to 1 month	6	78	1.19 (0.83, 1.55)	6	154	1.11 (0.82, 1.39)
>1 to 3 months	5	46	0.86 (0.50, 1.22)	5	22	0.87(0.37, 1.36)
>3 to 6 months	3	38	0.27 (-0.20, 0.75)	3	24	0.28 (-0.27, 0.84)
6+ months	7	130	0.36 (0.05, 0.67)	7	40	0.25 (-0.13, 0.63)
Early SLT (≤ 3 months) versus Late SLT (> 3 months since onset) subgroups						
Overall language ability on WAB-AQ; range 0-100						
Female	10	150	21.54 (15.70, 27.38)	4	56	13.86 (6.92, 20.79)
Male	10	174	17.99 (12.35, 23.64)	4	102	11.74 (5.02, 18.45)
55+ years	10	55	21.13 (14.30, 27.96)	4	81	6.98 (4.30, 9.65)
56 to 65 years	10	87	18.98 (12.73, 25.23)	3	54	4.13 (1.06, 7.19)
66 to 75 years	9	76	18.60 (12.15, 25.05)	2	20	2.70 (-1.67, 7.06)
75+ years	6	106	20.35 (13.86, 26.85)	1	3	5.33 (-5.08, 15.73)
Auditory Comprehension on TT-AAT; range 0-50						
Female	11	112	4.00 (-0.78, 8.79)	10	99	2.58 (0.50, 4.66)
Male	11	124	3.36 (-1.41, 8.12)	11	205	1.93 (0.11, 3.75)
55+ years	10	53	7.12 (1.93, 12.30)	9	125	4.03 (2.06, 6.01)
56 to 65 years	11	79	2.51 (-2.37, 7.39)	9	103	1.80 (-0.27, 3.86)
66 to 75 years	9	59	4.12 (-1.05, 9.29)	9	57	1.37 (-0.95, 3.70)
75+ years	7	45	0.97 (-4.41, 6.35)	6	19	1.82 (-1.70, 5.33)
Naming on BNT; range 0-60						

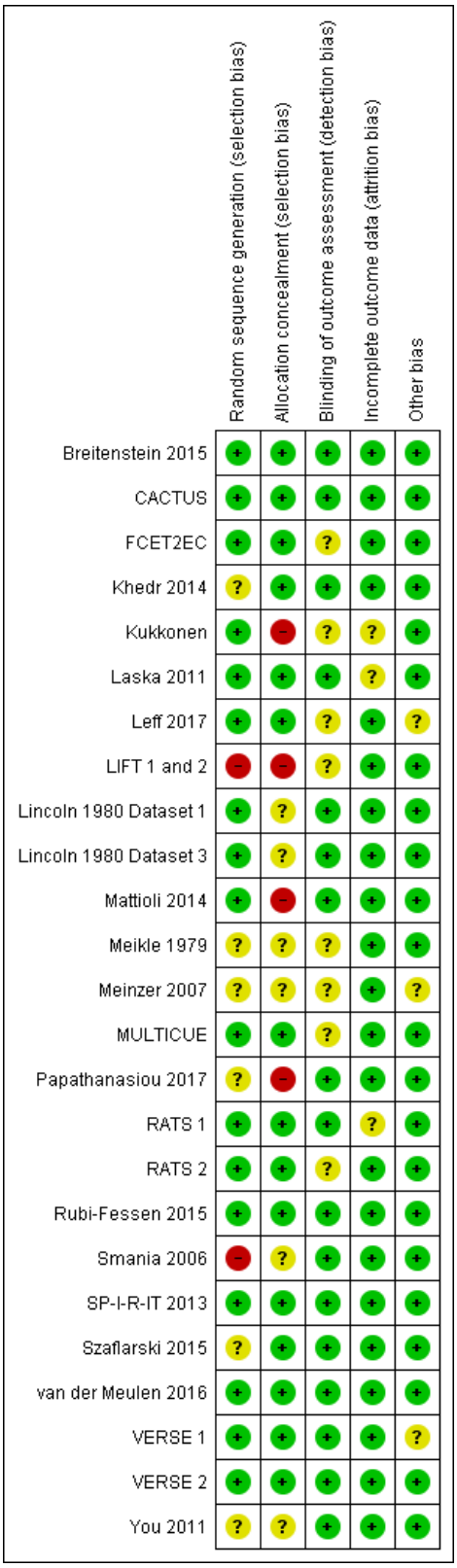
Female	9	104	9.29 (1.49, 17.09)	8	61	2.20 (0.58, 3.82)
Male	9	118	9.35 (1.60, 17.10)	9	102	1.26 (-0.20, 2.73)
55+ years	8	44	13.30 (4.93, 21.66)	8	59	3.28 (1.68, 4.88)
56 to 65 years	9	76	9.20 (1.33, 17.07)	7	48	2.23 (0.41, 4.05)
66 to 75 years	7	58	8.18 (-0.06, 16.41)	7	39	1.17 (-0.71, 3.05)
75+ years	6	44	6.60 (-1.87, 15.08)	6	17	0.24 (-2.44, -2.92)
Functional Communication on AAT-SSC; range 0 to 5						
Female	8	151	1.12 (0.77, 1.48)	8	86	0.37 (-0.06, 0.69)
Male	8	149	0.93 (0.57, 1.29)	9	147	0.14 (-0.23, 0.51)
55+ years	7	53	1.15 (0.73, 1.58)	8	94	0.29 (-0.09, 0.67)
56 to 65 years	8	71	1.05 (0.65, 1.44)	7	74	0.25 (-0.14, 0.64)
66 to 75 years	7	79	0.89 (0.49, 1.28)	9	43	0.14 (-0.26, 0.54)
75+ years	7	97	1.02 (0.63, 1.42)	6	22	0.23 (-0.23, 0.69)
Moderate-severe aphasia versus mild-moderate aphasia subgroups by language outcome						
Overall language ability on the WAB-AQ; range 0-100:						
Moderate-severe (below the median: <64.9 (n=319))				**Mild-moderate (≥ 64.9 (n=163))**		
Female	11	138	17.81 (11.13, 24.50)	9	68	5.95 (1.36, 10.55)
Male	11	181	14.66 (8.17, 21.15)	10	95	6.87 (2.34, 11.40)
55+years	11	76	19.60 (12.49, 26.71)	9	60	7.50 (2.8, 12.19)
56 to 65 years	11	91	13.99 (6.93, 21.06)	6	50	8.36 (3.61, 13.12)
66 to 75 years	10	71	14.23 (6.94, 21.53)	7	25	5.66 (0.52, 10.80)
75+years	7	81	17.13 (9.33, 24.93)	6	28	4.11 (-1.04, 9.26)
0 to 1 month	7	199	24.10 (17.62, 30.59)	7	61	10.95 (6.18, 15.73)
>1 to 3 months	6	46	22.15 (14.43, 29.86)	3	18	5.21 (-0.68, 11.10)
>3 to 6 months	3	10	9.25 (-4.43, 22.93)	2	6	5.54 (-1.71, 12.79)
6+ months	4	64	9.45 (-2.25, 21.16)	4	78	3.94 (-2.19, 10.06)
Auditory Comprehension on the TT-AAT; range 0-50						
Moderate-severe (below median <35 (n=395))				**Mild-moderate (≥ 35 (n=145))**		
Female	16	155	5.40 (2.11, 8.69)	12	56	0.65 (-3.83, 5.13)
Male	16	240	5.59 (2.37, 8.83)	12	89	-1.24 (-5.61, 3.13)
55+years	15	133	8.22 (4.90, 11.56)	9	45	1.50 (-3.24, 6.22)
56 to 65 years	16	132	5.33 (1.99, 8.68)	13	50	-1.24 (-5.75, 3.28)
66 to 75 years	15	88	5.21 (1.70, 8.73)	9	28	-0.46 (-5.28, 4.37)
75+years	11	42	3.20 (-0.80, 7.20)	8	22	-0.98 (-5.94, 3.97)
0 to 1 month	6	88	8.63 (4.51, 12.75)	5	51	-0.12 (-5.82, 5.59)
>1 to 3 months	9	80	6.72 (3.11, 10.32)	5	17	0.21 (-5.52, 5.93)
>3 to 6 months	4	50	4.37 (-1.43, 10.17)	4	11	-1.77 (-8.08, 4.54)
6+ months	9	177	2.25 (-1.49, 5.99)	8	66	0.50 (-4.79, 5.79)
Naming on BNT; range 0-60;						
Moderate-severe (below the median <23 (n=304))				**Mild-moderate (≥ 23 (n=81))**		
Female	12	130	6.84 (1.98, 11.71)	8	35	7.59 (3.79, 11.38)
Male	13	174	6.99 (2.27, 11.70)	8	46	8.36 (4.57, 12.14)
55+years	12	79	9.53 (4.50, 14.56)	7	24	8.79 (4.59, 13.00)
56 to 65 years	12	97	7.39 (2.38, 12.39)	7	27	8.13 (4.05, 12.21)
66 to 75 years	12	84	6.76 (1.67, 11.84)	6	13	6.74 (1.66, 11.82)
75+years	9	44	3.98 (-1.59, 9.56)	6	17	8.22 (3.43, 13.02)
0 to 1 month	5	99	12.22 (6.35, 18.09)	3	30	11.61 (6.25, 16.97)
>1 to 3 months	8	78	7.99 (2.67, 13.30)	3	15	9.37 (3.76, 14.97)
>3 to 6 months	6	62	3.56 (-3.10, 10.21)	2	8	6.83 (0.32, 13.33)
6+ months	7	65	3.89 (-1.81, 9.59)	5	28	4.08 (-0.37, 8.54)
Functional Communication on the AAT-SSC; range 0 to 5						
Moderate-severe (below the median: <3.7 (n=433))				**Mild-moderate (≥3.7 (n=100))**		
Female	14	189	0.93 (0.65, 1.22)	9	48	-0.01 (-0.24, 0.21)
Male	14	244	0.70 (0.42, 0.98)	10	52	0.03 (-0.16, 0.23)

55+years	13	118	0.88 (0.58, 1.18)	7	29	0.03 (-0.22, 0.29)
56 to 65 years	13	120	0.90 (0.60, 1.21)	9	25	-0.19 (-0.42, 0.04)
66 to 75 years	14	101	0.66 (0.35, 0.98)	7	21	0.11 (-0.15, 0.37)
75+years	12	94	0.82 (0.49, 1.14)	6	25	0.09 (-0.17, 0.36)
0 to 1 month	6	183	1.33 (0.95, 1.70)	6	49	0.33 (0.19, 0.47)
>1 to 3 months	5	62	0.96 (0.58, 1.33)	3	6	0.32 (-0.04, 0.68)
>3 to 6 months	4	61	0.55 (0.06, 1.03)	2	2	-0.56 (-1.19, 0.08)
6+ months	7	127	0.44 (0.10, 0.77)	4	43	-0.05 (-0.21, 0.11)
Male (IPD 329) versus female (IPD 211) subgroups						
Overall language ability WAB-AQ range 0-100						
55 years	11	81	14.08 (7.70, 20.46)	10	55	16.28 (8.84, 23.72)
56 to 65 years	11	99	10.92 (4.70, 17.14)	10	42	13.68 (6.01, 21.36)
66 to 75 years	10	55	8.86 (2.03, 15.68)	9	41	15.07 (7.15, 22.99)
75+ years	7	41	12.17 (4.75, 19.59)	6	68	16.63 (8.38, 24.89)
0 to 1 month	8	133	16.07 (9.99, 22.16)	7	127	22.86 (16.17, 29.55)
>1 to 3 months	6	41	14.58 (7.56, 21.59)	5	23	18.46 (9.78, 27.13)
>3 to 6 months	3	9	8.29 (-3.37, 19.95)	3	7	11.15 (-3.24, 25.54)
6+ months	4	93	7.09 (-2.10, 16.27)	3	49	9.20 (-3.52, 21.93)
Auditory Comprehension on TT-AAT range 0-50						
55+ years	15	103	6.05 (2.72, 9.39)	13	75	6.27 (2.95, 9.59)
56 to 65 years	16	122	2.36 (-0.90, 5.61)	15	60	3.98 (0.58, 7.38)
66 to 75 years	15	74	2.47 (-1.00, 5.94)	13	42	5.87 (2.15, 9.59)
75+ years	10	30	1.13 (-3.16, 5.42)	8	34	2.93 (-1.06, 6.91)
0 to 1 month	6	72	6.00 (1.58, 10.41)	6	67	5.53 (1.55, 9.51)
>1 to 3 months	9	52	4.19 (0.30, 8.09)	9	45	5.13 (1.36, 8.90)
>3 to 6 months	6	39	1.43 (-4.12, 6.97)	3	22	5.70 (-0.84, 12.24)
6+ months	8	166	0.39 (-3.34, 4.12)	8	77	2.69 (-1.41, 6.80)
Naming on BNT range 0-60						
55+ years	12	55	7.88 (3.32, 12.44)	11	48	10.35 (4.35, 16.34)
56 to 65 years	13	85	6.42 (2.13, 10.71)	13	39	9.44 (3.33, 15.54)
66 to 75 years	12	56	6.68 (2.10, 11.25)	11	41	6.69 (0.46, 12.91)
75+ years	8	24	7.72 (2.03, 13.42)	10	37	3.59 (-2.70, 9.89)
0 to 1 month	5	66	15.93 (10.23, 21.63)	5	63	8.54 (1.45, 15.63)
>1 to 3 months	7	52	7.62 (2.75, 12.52)	8	41	8.86 (2.34, 15.39)
>3 to 6 months	6	44	2.10 (-4.03, 8.24)	4	26	7.46 (-0.85, 15.76)
6+ months	7	58	3.05 (-2.08, 8.18)	6	35	5.21 (-2.15, 12.57)
Functional Communication AAT-SSC* range 0 to 5 (Male n=296; Female n=237)						
55+ years	13	77	0.49 (0.25, 0.72)	12	70	1.01 (0.56, 1.46)
56 to 65 years	13	106	0.56 (0.35, 0.76)	12	39	0.81 (0.33, 1.30)
66 to 75 years	13	70	0.44 (0.20, 0.67)	14	52	0.74 (0.27, 1.21)
75+ years	10	43	0.60 (0.30, 0.91)	12	76	0.77 (0.31, 1.23)
0 to 1 month	6	117	1.15 (0.93, 1.38)	6	115	1.07 (0.54, 1.60)
>1 to 3 months	5	32	0.65 (0.31, 0.99)	5	36	1.05 (0.51, 1.59)
>3 to 6 months	4	40	0.11 (-0.25, 0.47)	2	23	0.80 (0.01, 1.59)
6+ months	7	107	0.17 (-0.07, 0.40)	7	63	0.41 (-0.10, 0.93)

Key: RCT randomised controlled trial; IPD individual participant data;

Supplementary Material N:

*Risk of Bias by included trial dataset**



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Additional Results - Heterogeneity

Collaborators confirmed that included interventions were SLT, and these were categorised through consensus (19). Therapy regimen, delivery, and content differences were examined in an a-priori analysis and reported elsewhere (20). Our analyses revealed 10-25% relative variance in most instances. Risk of primary and meta-biases was moderate to low; random sequence generation (17 RCTs; 68%) and concealment of allocation was adequate (15 RCTs; 60%); 68% (17 RCTs) reported outcome assessor blinding(20). Participants were retained, or dropouts and non-adherence were fully reported. Most groups were comparable by age, sex, time since stroke, and aphasia severity (where available) at baseline (20). We found no evidence in sensitivity analyses that fixed versus random-effects model, historic dataset exclusion, publication date, or outcome measure choice would have altered the findings (20).

Supplementary Materials O

Author contributions

Author contributions are listed by contribution, followed by the order of authors as they appear in the authorship list. First, middle and last name initials are used. Where duplicates exist, abbreviations are used: MA1 Myzoon Ali; MA2 Mashiro Abo; CB1 Caitlin Brandenburg; CB2 Caterina Breitenstein.

MCB conceived, designed, and led the study, assessed the risk of bias, drafted and finalised the manuscript. MB, KVB, LRW screened records, abstracts, and full titles, extracted data, checked data extraction and risk of bias. KVB, LRW Retrieved papers. MA2, FB, AB, CB1, CB2, SB, DAC, TBC, MdiP-B, PE, JF, FLG, MG, BG, EG, KH, JH, SH, PJ, EJ, LMTJ, MK, EYK, EMK, AP-HK, TK, ML, MALP, ACL, BL, APL, RRL, AL, BMacW, RSM, FM, IM, MM, RN, EN, N-JP, RP, IP, BFP, IPM, CP, TPJ, ER, MLR, CR, IR-F, MBR, CS, BS, JPS, SAT, MvdS-K, IvdM, EV-B, LW, HHW contributed IPD primary data. LJW and MA analysed the data. NH Advised on the statistical analysis SH Co-ordinated and Facilitated Patient and Public Involvement in the study. All authors were involved in the interpretation of the results, reviewing and approving of this manuscript.

Declaration of interests

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Role of the funders

The RELEASE funders had no role in the study design, data collection, analysis or interpretation, reporting, or publication processes. The methodological decision making, and analysis data were shared with co-authors. The corresponding author had final responsibility for the decision to submit for publication. The views and opinions expressed herein are those of the authors and do not necessarily reflect those of the NIHR, NHS, or the Department of Health, UK or the CSO and the Department of Health and Social Care, Scotland. All members of the RELEASE collaboration had the opportunity to review and critically appraise the final draft of the report.

Data Availability

To ensure adherence to primary and meta-dataset ethical approvals and minimize the risk of unintentionally sharing information that can be used to re-identify personal information, a subset of the data utilized in this study is available via the Collaboration of Aphasia Trialists www.aphasiatrials.org.

Supplementary Materials P

Acknowledgements

- We acknowledge the time and effort of people aphasia to inform the primary dataset activities and whose data has in turn informed this IPD meta-analysis.

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