Guideline

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European Stroke Organisation (ESO) guideline on aphasia rehabilitation

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Abstract

Evidence of effective aphasia rehabilitation is emerging, yet intervention and delivery varies widely. This European Stroke Organisation guideline adhered to the guideline development standard procedures and Grading of Recommendations, Assessment, Development and Evaluation (GRADE) methodology. The resulting multi-disciplinary, evidence-based recommendations support the delivery of high-quality stroke-related aphasia rehabilitation. The working group identified 10 clinically relevant aphasia rehabilitation questions and rated outcomes' relevance and importance. Following systematic searching, independent reviewers screened title-abstracts and full-texts for randomised controlled trials of speech-language therapy (SLT) for stroke-related aphasia. Results were profiled using PRISMA. Risk-of-bias was evaluated using the Cochrane Risk-of-Bias 1 tool. We prioritised final-value data. Where possible we conducted meta-analyses (RevMan) using random effects and mean, standardised mean differences (functional communication, quality of life, aphasia severity, auditory comprehension and spoken language outcomes) or odds ratios (adverse events). Using GRADE, we judged quality of the evidence (high-to-very low) and ESO recommendation strength (very strong-to-very weak). Where evidence was insufficient to support recommendations, expert opinions were described. Based on low-quality evidence we recommend the provision of higher total SLT dose (⩾20 h) and suggest higher SLT intensity and frequency to improve outcomes in aphasia rehabilitation. Similarly, we suggest the provision of individually-tailored SLT

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and digital and group therapy delivery models. Very low-level evidence for transcranial direct current stimulation (tDCS) with SLT informed the expert consensus that such interventions should only be provided in the context of high-quality trials. Evidence-based clinical-research priorities to inform SLT aphasia rehabilitation intervention choice and delivery are highlighted.

Keywords
Guideline, systematic review, meta-analysis, stroke, aphasia, speech and language therapy, brain stimulation

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Plain Language Summary

A third of stroke survivors develop aphasia resulting in problems speaking, understanding speech, reading and writing. Aphasia is associated with depression and poorer stroke recovery. This guideline addresses important questions to support optimal speech and language therapy for aphasia rehabilitation. We considered the available evidence and analysed data from 45 trials. We make the following recommendations and multidisciplinary expert consensus statements to support aphasia rehabilitation clinical decisions.

In people with aphasia post-stroke to improve language, communication and quality of life

- we recommend speech and language therapy interventions of $\geq$ 20 hours (**rehabilitation dose**).
- we suggest speech and language therapy $\geq$ 4 days per week (**rehabilitation frequency**).
- we suggest $\geq$ 3 speech and language therapy hours per week (**rehabilitation intensity**).
- we suggest that speech and language therapy can be delivered in-person or digitally (**digital rehabilitation**).
- we suggest using either one-to-one or group speech and language therapy. The decision on the format of the therapy intervention may be made with reference to the health service context and resources available (**rehabilitation context**).
- we suggest that speech and language therapy should be tailored to the person with aphasia so that it is functionally relevant and at the right level of language difficulty for their rehabilitation needs (**tailoring rehabilitation**).
- we suggest that augmentation of in-person speech and language with digital therapy should be offered (**in-person or digital therapy**).

Where research information was lacking, and clinical uncertainties remained we developed the following expert consensus statements to guide clinical decision making

- where access to one-to-one therapy is constrained by resource availability, we suggest that group therapy delivered in addition to one-to-one speech and therapy may facilitate increased therapy time, provide additional opportunities to use language in a social context, and enhance communication confidence. We also suggest that the therapy timing and format should follow other recommendations in this clinical guideline, aiming to enhance language recovery, communication, participation, and quality of life (**augmenting dose**).
- we suggest that in the clinical context, speech and language therapy should be delivered alone rather than with transcranial direct current stimulation. Further evidence is required of the effectiveness of SLT with such brain stimulation. Individualised approaches to the brain stimulation rehabilitation delivery protocol for people with aphasia may be beneficial, but again, further evidence is required (**brain stimulation and speech and language therapy**).

Key recommendations and suggestions of the guideline
People with aphasia after stroke, should have the opportunity to access SLT frequently (we suggest at least four times weekly), intensively (we suggest at least 3 h weekly) and for an overall dose of at least 20 h of therapy to support their language recovery and quality of life.
Alternative approaches to therapy delivery such as digitally-delivered SLT or group-based SLT approaches may augment therapy provision
We suggest that people with aphasia after stroke should be offered individually-tailored SLT by functional relevance and level of language task difficulty.

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Introduction

Aphasia is an acquired impairment associated with stroke (and other neurological damage) that impacts on the ability to speak, write, and understand spoken (auditory comprehension) and written language (reading comprehension). Aphasia (historically also referred to as dysphasia[1]) affects approximately one-third of people after stroke.[2] Across the world, based on the latest stroke incidence figures we estimate that more than 4 million people acquired stroke-related aphasia in 2019 alone.[3] Communication challenges due to impaired speech because of muscular weakness (dysarthria) or co-ordination problems (apraxia of speech) or due to sensory, auditory perceptual or cognitive deficits are excluded from this definition.

People with aphasia experience poorer overall functional,[4] psychosocial,[5] wellbeing,[6] pain[7,8] and economic outcomes[4,9,10] compared to stroke survivors without aphasia, despite having greater access to in-hospital stroke rehabilitation services.[2,11] Effective intervention for language and communication impairment after stroke is a clinical research priority[12,13] that benefits the individual with aphasia and multidisciplinary stroke service provision.

A Cochrane review considered 27 randomised controlled trials ($n = 1620$) and found that speech and language therapy (SLT) benefits language following stroke-related aphasia on measures of everyday language use (functional communication), auditory comprehension, reading, writing and expressive language compared to people with no access to therapy.[14] Direct randomised comparisons of different SLT theoretical approaches were limited. The review concluded that establishing the optimal treatment regimen and approach (e.g. group therapy vs one-to-one therapy, digital vs in-person models of delivery) should be a priority. Building on this evidence base and acknowledging variations in stroke rehabilitation access, the European Stroke Organisation (ESO) published their Action Plan for Stroke in Europe 2018–2030 where improved rehabilitation, cost-effectiveness and evidenced based results relating to timing, level and type of intervention were identified as research and development priorities.[15]

Subsequently, the REhabilitation and recovery of peopLE with Aphasia after StrokE (RELEASE) international collaboration established a database of 5928 individual participants' data (IPD) from 174 aphasia post-stroke research datasets from 28 countries, utilising a systematic review approach. It included demographic, stroke, language impairment, and speech and language therapy intervention data and subsequent outcomes across a range of language outcomes.[16]

Using a systematic review informed, one-stage, IPD network meta-analysis (controlling for participants' baseline language score, age, sex and time since stroke) they explored the importance of different parameters of SLT aphasia rehabilitation; SLT frequency (the number of days therapy was delivered weekly), intensity (the number of therapy hours delivered weekly) and overall dose (total number of therapy hours across the intervention). RELEASE suggested important insights into a critical therapeutic range for SLT frequency, dose, and intensity associated with optimal language gains, though further confirmatory study designs are needed to test the hypotheses generated and to develop more tailored speech and language therapy interventions.[16]

The ESO commissioned this aphasia rehabilitation guideline because of the high epidemiological and societal burden experienced by people with aphasia and their families after stroke; and the associated burden on healthcare professionals and the effective provision of stroke services to people with aphasia. These recommendations are based on findings from randomised controlled trials (RCTs) and RCT meta-analyses. Recommendations were agreed through consensus amongst the members of the guideline working group using the GRADE approach[17] and the ESO standard operating procedure for guideline development,[18] and have the approval of the ESO Guideline and Executive Committees.

The aim of this guideline is to provide recommendations to guide stroke healthcare professionals in the clinical management and decision making relating to aphasia rehabilitation dose, intensity, frequency, the use of brain stimulation, and SLT delivery approaches.

Methods

Composition of the working group

This guideline was initiated by the ESO. Co-chairpersons (MCB, KH) were selected to assemble and coordinate the Guideline Module Working Group (Supplement 1). The final group contained 12 aphasia rehabilitation experts reflecting a broad spectrum of professionals involved in aphasia rehabilitation: SLT (MCB, JI, FC, CJ, KH), speech and hearing sciences (LMTJ), psychology (KH, MM), physical and rehabilitation medicine (KSS, FB), neuropsychology (PM), clinical linguistics (IvdM) and neurology (AF) from 10 European countries. The working group was supported by three methodologists (PC, LH, SH) and three fellows who assisted with abstract and full-text screening, data extraction, quality ratings and drafting the text (CM, HPØ and NN). The group also benefitted from the support of the ESO administrator (YB). The ESO Guideline Board and Executive Committee approved the composition of the group.

Development of the Population, Intervention, Comparator and Outcome (PICO) questions

This guideline was prepared according to the ESO standard operating procedure,[18] and the GRADE framework[17]. The working group developed a list of topics and corresponding questions of greatest clinical interest. Using the

PICO approach (Population, Intervention, Comparator and Outcome), 10 clinically relevant questions were formulated, reviewed by two external reviewers, and approved by members of the ESO Guideline Board and Executive Committee. Outcomes were rated by members of the working group as: critical, important or of limited importance according to GRADE criteria based on a Delphi approach (Table 1). For this guideline, we included data gathered on standardised outcome measurement instruments that captured overall language ability, functional communication, expressive language (and/or naming), auditory comprehension, communicative confidence, psychosocial well-being and quality of life. Safety, reported as adverse events and side effects, was considered in the context of brain stimulation intervention, specifically transcranial direct current stimulation (tDCS). As they were not rated as critical outcomes, reading and writing outcomes were not considered in this guideline (Supplement 2 for PICOs and rating of outcomes per PICO). We excluded qualitative data and data from informal, non-psychometrically tested or unpublished assessment tools, such as discourse analysis or informal tests of naming ability.

Table 1. Rating of outcome importance as part of the Delphi process.

Outcome	Scale	Definitions
of most importance	9 8 7	Critical for decision making (include in evidence profile)
↕	6 5 4	Important, but not critical for decision making (include in evidence profile)
	3 2	Of limited importance for decision making (exclude from evidence profile)
of low importance	1	

Literature search (identification and selection of relevant studies)

Search strategies were developed by the working group and an ESO guideline methodologist (SH) that reflected the scope of literature to inform the 10 approved PICO questions. Existing relevant and validated search strategies (e.g. within a published Cochrane review) were consulted so that our searching overlapped but did not duplicate pre-existing search activities. Where a recent high-quality systematic review addressed our guideline questions, the corresponding search strategy, data, and meta-synthesis results were referred to, extracted, or updated as necessary and appropriate to the objectives and methods of our guideline development procedures. The search strategies are detailed in Supplements 3 and 4.

Two electronic database searches informed this guideline; one relating to SLT intervention evidence base searched the following databases: MEDLINE, EMBASE, CINAHL, PsychInfo, the Cochrane central register of controlled trials, from 2015 to 10/03/2023; the second informed the evidence summary for tDCS delivered alongside SLT for aphasia after stroke and searched the same databases, from 2018 to 10/03/2023. Reference lists of relevant reviews with meta-analyses, included RCTs and working group members' personal reference libraries were also screened for additional relevant records.

Search results were loaded into the web based Covidence platform (Health Innovation, Melbourne, Australia) for working group screening. Two group members were assigned to independently screen each title and abstract. Rating disagreements were resolved by a third reviewer, where necessary. Potentially relevant records were tagged by PICO questions. Two or more group members were subsequently assigned to assess the relevance of full texts retrieved by PICO question.

Studies included were RCTs involving participants that had received SLT for stroke-related aphasia. Where data were limited, we considered high-quality systematic review based individual participant data (IPD) meta-analyses. Specific inclusion/exclusion criteria were applied to the data informing each PICO (Supplement 5). Relevant interventions included all SLT approaches and the use of tDCS, categorised by stimulation location and principles, in conjunction with SLT. Spinal, brain stem and other non-invasive brain stimulation (such as transcranial magnetic stimulation) were excluded.

Data extraction and analysis

We developed and piloted a data extraction form which included categories that support high quality data extraction of complex interventions.[19] We extracted data from all included trials (Supplement 6). All primary dataset reports identified (main publication, additional reports, abstracts, including correspondence with the trialists) informed the data extraction. Where possible, this was supplemented by unpublished data from trialists typically provided to clarify areas of uncertainty in data extraction. Where trials recruited mixed populations, we sought the stroke specific data only, using agreed definitions to categorise participant populations.[20] Some trials randomised participants across several groups (typically two intervention groups compared to a control condition). Meta-analysis was conducted in paired comparisons; each intervention was compared to the control condition with the analysis adjusted to ensure we did not double count participants[21] with trial labels expanded to indicate which intervention was included in that comparison. For all multi-armed RCTs, only the randomised groups that met our eligibility criteria were included. Trial reports emerging from the same research centre (or involving the same

investigators) over a similar publication period, were carefully considered in relation to the trials' design, objectives, and interventions to ensure that we did not double count a single trial reported over two or more publications in any one meta-analysis calculation. We also checked for duplicate representation of participants across such trials. To reduce the risk of any recent SLT trial participation or an associated trial intervention having an impact on the participant's baseline or outcome data in the subsequent trial, wherever possible we excluded duplicate participant's data from the subsequent trial.

Evidence of the benefit of different approaches to SLT (and SLT with tDCS) were sought on a range of language, participation, wellbeing and quality of life outcomes, and in tDCS trials, we also extracted adverse events reports. In cross-over trials, data were extracted up to the point that participants changed intervention. Meta-analysis was performed using the Review Manager (RevMan, Version 5.4 or RevManWeb) Cochrane Collaboration software. For continuous outcomes we calculated the mean difference (MD) or standardised mean difference (SMD). Where the available data were reported using a single outcome measurement instrument, we meta-analysed (or in the context of a single trial's data, presented) the data using MD, representing the mean point difference on that measurement instrument.[21] Where two or more outcome measurement instruments were used to capture a single outcome, the data were meta-analysed using SMD, a statistical value that does not directly reflect a unit of measurement on any of the contributing measurement instruments. We used odds ratios for adverse event data. All data syntheses calculated a 95% confidence interval (CI), used inverse variance and a random effects model.[21] Heterogeneity was checked. Interpretation of the percentage of effect estimate variability that may be due to heterogeneity drew on published guidance; where it may represent substantial ($I^2 \geqslant 50\%$) or considerable heterogeneity ($I^2 \geqslant 75\%$) we highlighted it in the text for the reader.[21]

The working group agreed a-priori to prioritise final value summary scores (post intervention, and where available follow-up as well) over change from baseline scores. Where an RCT only reported change from baseline outcome data, these were reported and presented in the Supplemental Files for information purposes. While meta-analysis of group level summary trial data provides insight into the benefits of an intervention, the guideline working group acknowledged the inherent risk of ecological biases. Thus, where large IPD and network meta-analyses of relevance to a PICO were identified, we considered this evidence alongside the RCT group summary data meta-synthesis conducted in the development of this guideline. IPD meta-analysis may include adjustments which reflect a heterogeneous participant population's baseline performance, individual predictors of recovery and the impact of other participant level covariates on SLT interventions across language outcome measurements. Where data permitted, both approaches informed the development of these guideline recommendations alongside our clinical experience. The group level meta-analysis took precedence where IPD network meta-analysis was exploratory in nature. Where one type of data were available to inform the PICO in the absence of the other, that data underpinned the recommendations made. The working group members considered the number of datasets and the number of participants informing the evidence syntheses in making their recommendations. We took care to avoid any double counting of data in any analysis calculation.

Evaluation of the quality of evidence and formulation of recommendations

With the approval of the European Stroke Organisation's Guideline Committee, the risk of bias for each included RCT was assessed with the Cochrane Risk of Bias (RoB) tool[22] with each RoB domain considered and judged separately, with ratings resolved by a third reviewer, where necessary. As for many rehabilitation interventions, it was considered unfeasible to blind participants or providers to most behavioural SLT interventions for aphasia. Therefore, we considered risk of bias at study level as it related to the RoB domains that could be influenced, and then in aggregate for each of the evidence synthesis comparisons.[17] For each PICO question, and each outcome, the following were considered: risk of bias based on the available evidence (RCTs or IPD meta-analysis); inconsistency of results; indirectness of evidence, imprecision of results, and other possible bias. GRADE (Table 2) evidence profiles were formulated for each PICO.[17]

The working group discussed and agreed the final summaries of the quality and strength of evidence and recommendations for each PICO question. In deciding the strength of the recommendations (Table 3), the group considered the quality of the evidence, in addition to any available data on values and preferences of people with stroke and aphasia, and the balance of desirable and undesirable effects, as recommended by the ESO Guideline standard operating procedure.[18] The working group reviewed and agreed this guideline document. Consensus was required for recommendations. The expert consensus statements were agreed using a Delphi approach. The final draft was subsequently reviewed and approved by two external reviewers, members of the ESO Guidelines Board, the ESO Executive Committee, in addition to the Editor and external peer reviewers of the *European Stroke Journal*.

Sensitivity and subgroup analysis

Sensitivity analyses were conducted to consider the impact of any decisions made in the data synthesis such as choice

of outcome data. For example, where a single RCT reported data from two measurement instruments of relevance to a single outcome, data from either measurement instrument could have been included in the synthesis. In such situations we chose one dataset and then checked whether inclusion of the alternative dataset would have impacted on the meta-synthesis findings. Where data permitted, we planned subgroup analyses to examine time since aphasia onset.

Table 2. GRADE quality of evidence.

Grade	Definition	Symbol
High	Further research is very unlikely to change our confidence in the estimate of effect.	⊕⊕⊕⊕
Moderate	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.	⊕⊕⊕
Low	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.	⊕⊕
Very low	We are very uncertain about the estimate.	⊕

Table 3. Formatting based on strength of recommendations.

Strength of recommendation	Balance of desirable and undesirable consequences	Recommendation formatting
Strong recommendation for intervention	The desirable consequences clearly outweigh the undesirable consequences in most settings	"We recommend"
Strong recommendation against intervention	The undesirable consequences clearly outweigh the desirable consequences in most settings	"We recommend. . .not"
Weak recommendation for intervention	The desirable consequences probably outweigh the undesirable consequences in most settings	"We suggest"
Weak recommendation against intervention	The undesirable consequences probably outweigh the desirable consequences in most settings or when the balance between desirable and undesirable consequences is closely balanced or uncertain	"We suggest. . .not"
Ungraded consensus-based statement	The desirable consequences probably outweigh the undesirable consequences in most settings, but there is little evidence	"We suggest"

Search results

An electronic database search identified 2974 records (after removing 1162 duplicates) of potential relevance to our planned evidence synthesis relating to SLT interventions for aphasia rehabilitation. We reviewed 373 full texts in detail and together with 10 trials drawn from the relevant Cochrane review, 28 trials were included in our subsequent analyses (Supplement 7). A further 668 records (after removing 196 duplicates) were identified in our second electronic search and were screened for evidence relating to the effectiveness of tDCS alongside SLT for aphasia. We reviewed 116 full text records and 17 trials were included in our analyses (Supplement 8). A total of 45 trials across all PICOs were included in our analyses.

Results

Functional communication and quality of life (post-intervention) meta-analyses and associated risk of bias tables are reported below (Figures 1–18) with all other outcome meta-analyses and meta-analysis of data gathered at follow-up timepoints available in Supplemental Files 9–17. The meta-analyses, GRADE evidence profiles (Supplement 18), and risk of bias (below and in Supplement 19) informed our recommendations.

PICO 1 **In people with aphasia after stroke is a higher dose of SLT (⩾20 h) compared to a lower dose of SLT (< 20 h) associated with greater improvements in language, communication, or quality of life?**

Analysis of current evidence

Overall, the evidence is based on five RCTs (randomised $n = 520$ (270 male); RoB Figure 1)[23–27] that compared a high dose SLT (defined for the purposes of this guideline as ⩾20 h of therapy in total) with a low dose SLT (<20 SLT

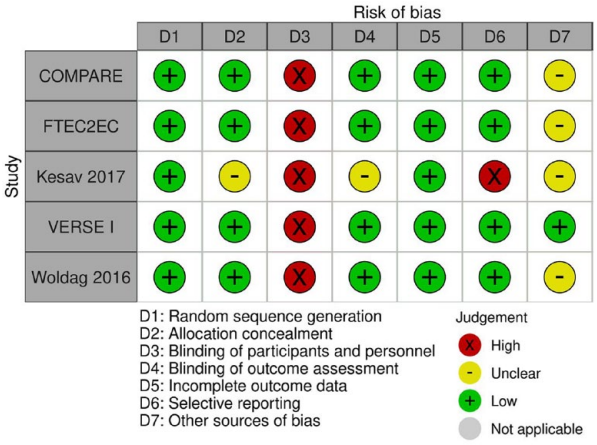

Figure 1. Risk of bias profile for studies included in PICO 1 (immediately postintervention) analysis.

hours) with one to five RCTs per outcome. Included RCTs had small ($n = 24$[23]) to medium sample sizes ($n = 216$[24]). All studies delivered in-person SLT. Participants contributing to our analyses ranged in age from a mean (SD) of 48.7 (11.8)[23] to 71.3 (7.2) years.[27] Average aphasia severity ranged from very severe/severe[25] to severe,[23] and moderate.[24,26,27] Participant time since stroke ranged from on average three[25] to 1290 days post-stroke[26] (Participant characteristics Supplement 20; Table 16). The number of therapy hours in the high dose SLT intervention group ranged from a total of 24 h[23,25] up to 26.5 h[25] to 30 h.[24,26,27] In the low dose intervention group, SLT hours ranged from 4 h,[24–26] up to 5.3 h,[25] 12 h[23] and up to 14 h.[23,27] These high and low dose SLT groups were compared on measures of functional communication, quality of life (Figure 2), overall level of aphasia severity (overall language), naming and auditory comprehension (Supplement 9).

Three RCTs reported on functional communication.[24–26] While two studies favoured high dose intervention,[25,26] there was no difference in the third[24] and no difference overall, though heterogeneity was considerable (Figure 2(a)). We explored the source of the possible statistical heterogeneity. Removing one trial from the analysis resulted in an I^2 of 0%.[24] Synthesis of the remaining data favoured the provision of high dose SLT over lower dose SLT, but this was based on a small number of trials and participants (SMD 0.79, 95% CI [0.51, 1.07], $p < 0.00001$, 2 = RCT, $n = 215$). On measures of quality of life, participants that received high dose SLT benefitted more compared to those that received lower dose SLT (Figure 2(b)).[24,26] In terms of overall language, while one study favoured high dose SLT intervention,[25] there was no differences in the other three studies[23,24,26] and no evidence of a difference overall ($n = 421$, 4 RCTs, $I^2 = 61\%$). In a sensitivity analysis to explore this heterogeneity, we noted that the statistical heterogeneity was reduced following the exclusion of one trial[25] but there remained no difference between the groups (SMD −0.02, 95% CI [−0.23, 0.20], $p = 0.87$, 3 = RCT, $n = 362$). Three RCTs reported on expressive language (specifically naming) but there was no difference between high and low dose SLT intervention.[24,26,27] In terms of auditory comprehension, though one trial's data favoured high dose SLT,[26] following meta-analysis there was no difference between high and low dose SLT interventions ($n = 347$, 2 RCTs)[24,26]). A third trial only reported change scores.[27]

Three RCTs reported data at follow-up (after a period of no treatment post-therapy)[23–25] (Supplement 9; RoB Supplement 18). There was no difference in functional communication at follow up[24,25] though one small trial trended towards favouring high dose intervention at 40 weeks.[25] On measures of quality of life there was no difference between high and low dose at 12 weeks.[24] One trial reported gains in overall language for high dose intervention at 6 months,[25] while two RCTs (follow up at 12 weeks) reported no difference between high and low dose[23,24] and overall, there was no difference in overall language between the two groups. There was no evidence of a difference in expressive language (naming) or auditory comprehension.[24]

Additional information

Additional high-quality evidence relevant to this question was available from the RELEASE network meta-analysis which controlled for baseline age, sex, and time since stroke and drew on IPD from 16 RCTs[28] (the group summaries from two trials also informed the ESO randomised paired comparison meta-analyses described above). The IPD meta-analyses examined individual participants' change from baseline on measures of overall language (480 IPD, 11 RCTs); functional communication (524 IPD, 14 RCTs), auditory comprehension (540 IPD, 16 RCTs) and naming (385 IPD, 13 RCTs). The greatest gains in overall language (18.37 Western Aphasia Battery-Aphasia Quotient (WAB-AQ) points, 95% CI [10.58–26.16], 31 IPD, 4 RCTs) and auditory comprehension (5.23 (Aachen Aphasia Test-Token Test (AAT-TT) points, 95% CI [1.51–8.95], 90 IPD, 7 RCTs) were associated with 20–50 h of SLT. The greatest gains in functional communication (0.94 AAT-Spontaneous Speech Communication (AAT-SSC) points, 95% CI [0.34–1.55], 11 IPD, 3 RCTs) were in the context of a slightly lower SLT dosage of 14–20 h, but this was based on a very small number of IPD and RCTs; the second highest gains occurred in the context of 20–50 h of SLT (0.77 AAT-SSC points, 95% CI [0.43–1.1], 96 IPD, 9 RCTs) and a higher number of IPD and RCTs.

In summary, RELEASE data supported the provision of SLT ⩾ 20 h in relation to overall language, auditory comprehension and potentially functional communication.[28] In our meta-synthesis the total difference in favour of high dose

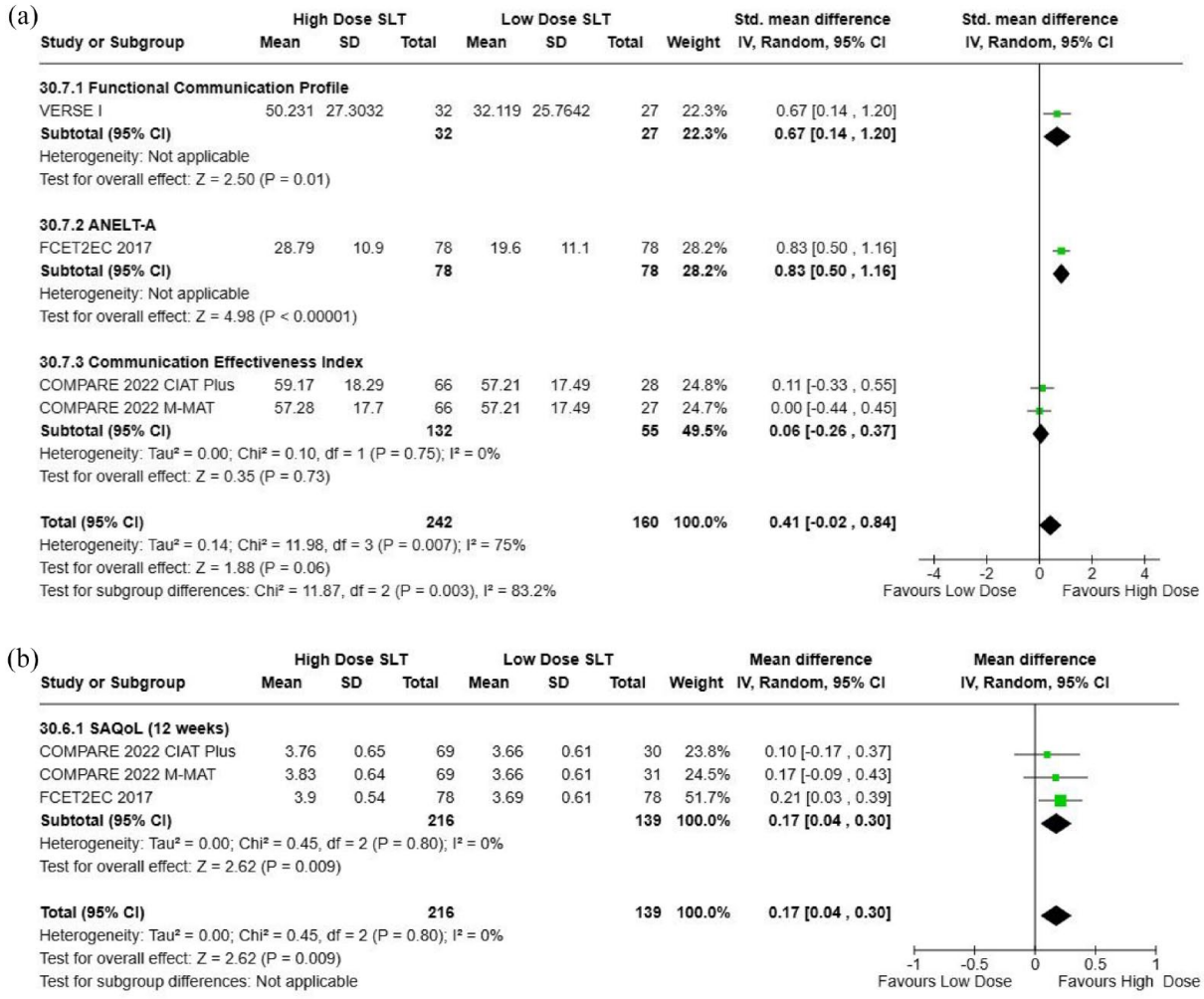

Figure 2. (a) PICO 1 Functional communication and (b) PICO 1 Quality of Life.

SLT was significant for quality of life and, in sensitivity analysis, for functional communication.

Evidence-based Recommendation 1
In people with aphasia post-stroke, we recommend high dose SLT interventions (⩾20 hours) rather than lower dose SLT (<20 hours) should be offered.
Quality of evidence: Low ⊕⊕
Strength of recommendation: Strong for high dose SLT intervention ↑↑

PICO 2 **In people with aphasia after stroke is a higher intensity of SLT (⩾3 h per week) compared to a lower intensity of SLT (< 3 h per week) associated with greater improvements in language, communication or quality of life?**

Analysis of current evidence

The evidence is based on eight RCTs (randomised $n = 863$ (456 male); RoB Figure 3[24–26,29–33] with 1 to 7 RCTs reporting each outcome. Included RCTs had small ($n = 16$)[30] to medium sample sizes ($n = 246$).[33] All SLT interventions were in-person. Participants had a mean (SD) age of 51.25 (10.04)[30] to 76 (15.5)[33] [range 17–92] years. Average aphasia severity ranged from very severe to severe,[25] severe[29,31–33] and moderate.[24,26,30] Participant time since stroke ranged from acute[25] to chronic stages post stroke[26] (Supplement 20 Table 17). With the exception of one trial, high-intensity SLT measured in hours of SLT per week ranged from 4 h,[29] 5 h,[33] up to 7.5 h,[25] 8.4 h,[30] ⩾10 h,[26,31] and 15 h.[24] Delivering a high intensity SLT intervention to a clinically relevant population is challenging; for example one trial aimed to deliver 5 SLT hours weekly to an early

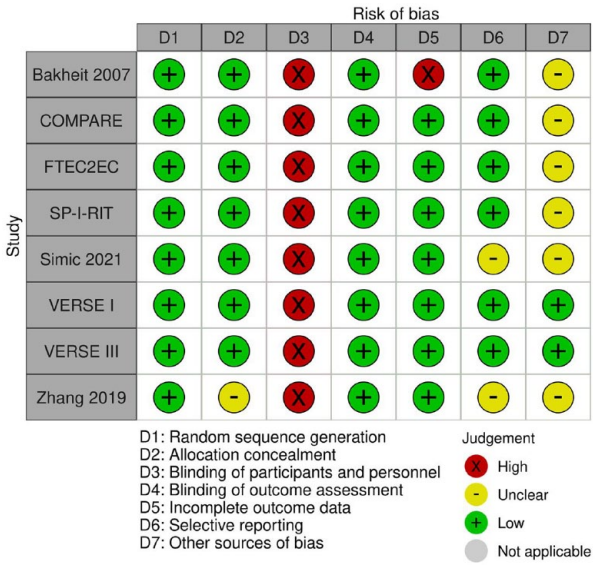

Figure 3. Risk of bias profile for studies included in PICO 2 (immediately postintervention) analysis.

subacute population (mean 34.2 (19.1) days post stroke).[32] Fatigue, treatment refusal and trial dropouts resulted in the high intensity group receiving a mean total of 35.6 (16.4) SLT hours over the 12-week intervention period. While inclusion of this trial's data in the PICO 2 meta-analysis could be questioned (on average 2.97 SLT hours were delivered weekly), we took a pragmatic approach to include the data. Sensitivity analysis explored this decision and is reported below.

The low intensity group (typically a usual care control intervention) had access to SLT ranging from less than an hour,[25] 1.5 h,[26] to 2–2.3 h[29–32] per week. Five RCTs measured functional communication[24–26,29,31] and favoured high intensity SLT though the heterogeneity was substantial (Figure 4(a)). Exploration of the source of the statistical heterogeneity indicated it was reduced on removal of one trial.[24] The benefit of high intensity SLT continued to be observed (SMD 0.76, CI 95% [0.52, 1.01], $p < 0.00001$, $I^2 = 0\%$; 4 RCTs, $n = 280$). Across four trials, there was no evidence that participants that received high intensity SLT benefitted on measures of quality of life though substantial heterogeneity was observed[24,26,30,33] (Figure 4(b)). Removal of one trial[33] resulted in a reduction in heterogeneity and synthesis of the remaining data indicated that high intensity SLT benefitted quality of life (SMD 0.29, 95% CI [0.08, 0.51]), $p = 0.007$, $I^2 = 0\%$; 3 RCTs, $n = 351$). In terms of overall language, two RCTs favoured high intensity SLT,[25,29] with no differences in the other five[24,26,31–33] and no overall evidence of benefit, though heterogeneity was substantial ($I^2 = 51\%$; sensitivity analysis excluding one trial[32] similarly found no evidence of benefit (Supplement 10). On examining the potential sources of heterogeneity, we observed that excluding one trial[25] considerably reduced heterogeneity to a level that might not be important ($I^2 = 27\%$) with no change in our findings. Five RCTs[24,26,29,31,33] reported on expressive language; there were no differences between high and low intensity SLT, though one trial reported high intensity benefit.[29] Four RCTs reported on auditory comprehension ($n = 412$, 4 RCTs, $I^2 = 72\%$) where two trials reported benefits in the context of high intensity SLT[29,31] and a third seemed to favour high intensity[26] but there was no difference overall. Sensitivity analysis did not impact on the statistical heterogeneity observed. Two trials found no difference between the groups on measures of emotional wellbeing[31,33] (Supplement 10).

A smaller number of studies measured outcomes at follow-up (after a period of no treatment post-therapy) (Supplement 10; RoB Supplement 19). Three RCTs followed up on functional communication at 12–40 weeks[24,25,31] ($n = 252$, 3 RCTs) and though one favoured high intensity SLT,[25] there were no overall differences between high and low intensity SLT. Two trials reported on quality of life but found no differences between high and low intensity SLT at 12–26 week follow up.[24,33] Five RCTs looked at overall language[24,25,31–33] with gains maintained in one trial at 6 months[25]; but overall there was no evidence of benefit at follow-up nor in a sensitivity analysis excluding one trial.[32] Three RCTs reported on expressive language[24,31,33] and two on auditory comprehension[24,31] but there were no differences between the SLT groups at follow up. Lastly, two trials reported on emotional wellbeing[31,33] but there was no difference between high and low intensity SLT groups at follow up.

Additional information

The RELEASE IPD network meta-analysis was informed by 16 RCTs (with summary data from three included in the ESO-led paired group-level summary data meta-analyses described above). The IPD meta-analyses drew on individual participants' change from baseline on overall language (482 IPD, 11 RCTs); functional communication (533 IPD, 14 RCTs), auditory comprehension (540 IPD, 16 RCTs) and naming (385 IPD, 13 RCTs). High intensity SLT significantly contributed to auditory comprehension outcomes with peak gains from baseline associated with SLT more than 9 h per week (7.3 AAT-TT points, 95% CI [4.09–10.52], 141 IPD, 6 RCTs).[28] Gains were observed across different SLT intensities for overall language (482 IPD, $n = 11$ RCTs), naming (385 IPD, $n = 13$ RCTs), and functional communication (533 IPD, $n = 14$ RCTs).

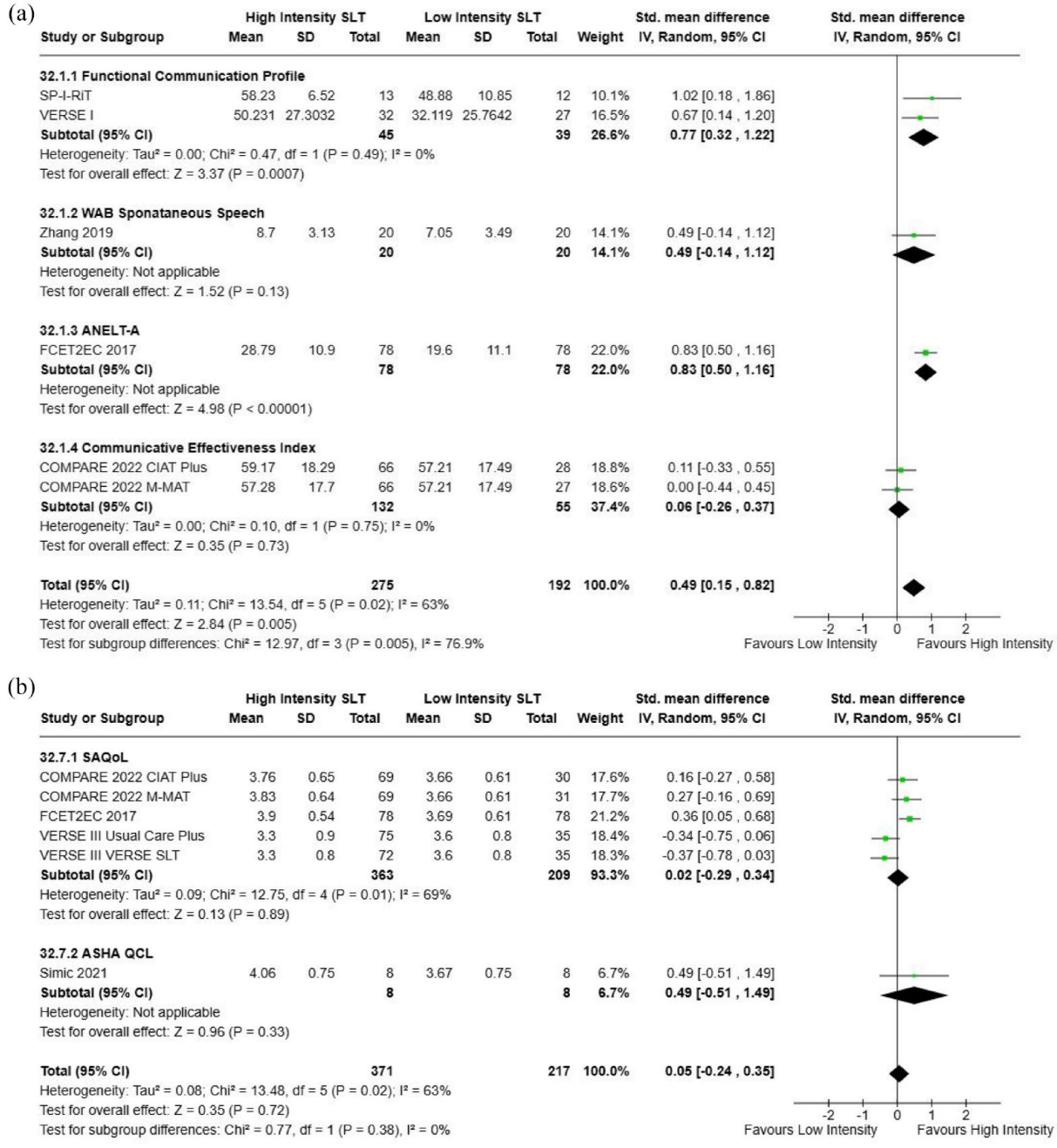

Figure 4. (a) PICO 2 Functional communication and (b) PICO 2 Quality of Life.

In summary, no comparison in our guideline meta-synthesis favoured low intensity usual care SLT interventions. Where significant differences between the high and low intensity SLT groups were observed, these favoured the provision of high intensity SLT. We noted that though our PICO defined high intensity SLT as ⩾3 h per week, high intensity in all but one of the included trials ranged from 4 h weekly[29] to much higher intensities of ⩾10 h[26,31] and 15 h.[24] Nevertheless, individual abilities and preferences should also be considered in planning therapy intensity. Cochrane review evidence identified that participants in the acute-early subacute stages post stroke (within 3 months of aphasia onset) exhibited significant language benefits in the context of higher intensity SLT compared to

participants with access to lower intensity SLT. However, those results were confounded by significantly higher dropouts (and lower adherence) to the higher intensity SLT. These significant gains and the dropout and adherence patterns were not evident amongst participants that were two or more years after aphasia onset.[14]

Evidence-based Recommendation 2
In people with aphasia post-stroke, we suggest high intensity SLT (⩾3 hours per weeks) rather than lower intensity should be offered.
Quality of evidence: Low ⊕⊕
Strength of recommendation: Weak for high intensity SLT intervention ↑?

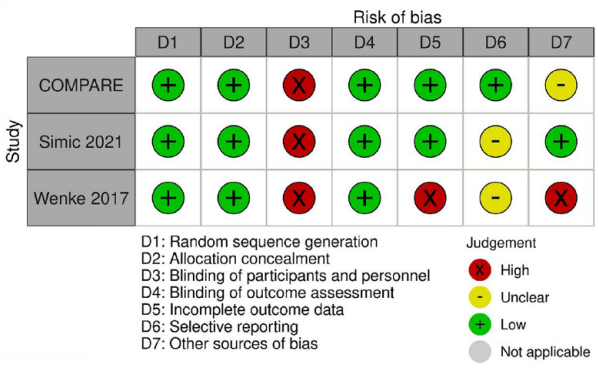

Figure 5. Risk of bias profile for studies included in PICO 3 (immediately postintervention) analysis.

PICO 3 **In people with aphasia after stroke is a higher frequency of SLT (⩾4 days per week) compared to a lower frequency of SLT (<4 days per week) associated with greater improvements in language, communication or quality of life?**

Analysis of current evidence

Evidence synthesis for each outcome was based on data from up to three RCTs (randomised $n = 246$ (159 male); RoB Figure 5)[24,30,34] with small ($n = 14$, 16[30,34]) to medium sample sizes ($n = 216$[24]). The groups had a mean (SD) age of 51.3 (10.0)[30] to 75. 7 (10.7)[34] [range 33–86] years, with moderate[24,30] or mild-severe aphasia[34] and were in the early subacute to chronic stages post-stroke (Supplement 20 Table 18). High frequency SLT interventions ranged from 4 days[30,34] to 5 days per week.[24] Low frequency SLT interventions were on average 0.67 days,[24] 2 days,[34] or 3 days each week.[30] All trials delivered in-person therapy. The duration of the high frequency interventions varied from 2 weeks[24] and 2.5 weeks[30] to 8 weeks.[34] Two trials compared high and low SLT frequency by measuring participants' functional communication (Figure 6(a)) and found no difference between the groups.[24,34] Similarly, two RCTs measured participants' quality of life and while there was a consistency in the direction of effect there was no difference between the groups that received high and low frequency SLT[24,30] Figure 6(b)). Two studies found no difference between low and high frequency SLT on overall language and naming (expressive language) though heterogeneity was high in the latter ($I^2 = 57\%$).[24,34] SLT frequency was also compared on measures of auditory comprehension[24] and participants' emotional and social wellbeing,[34] but there was no difference between higher and lower SLT weekly frequency on these measures (Supplement 11).

Two studies reported follow-up outcomes between 4 and 6 weeks[34] and at 12 weeks post-treatment[24] (Supplement 11; RoB Supplement 18). There was no difference between the groups that received high versus low frequency SLT on measures of functional communication,[24,34] quality of life,[24] overall language,[24,34] naming,[24,34] auditory comprehension[24] and emotional well-being.[34]

Additional information

The RELEASE IPD meta-analysis drew from 16 RCTs. None were represented in the ESO-led, paired group-level summary data meta-analyses described above. The IPD meta-analyses drew on individual participants' change from baseline on overall language (482 IPD, 11 RCTs); functional communication (526 IPD, 14 RCTs), auditory comprehension (540 IPD, 16 RCTs) and naming (385 IPD, 13 RCTs). The greatest improvement, observed in overall language, was associated with SLT 5 days per week (14.95 WAB-AQ points, 95% CI [8.67–21.23],194 IPD, 6 RCTs).[28] Numerically lower, but clinically similar gains were observed for three-four and six SLT days per week but based on fewer IPD and RCTs. Significant functional communication gains from baseline were observed (526 IPD,14 RCTs) for SLT ⩽ 5 days per week with the greatest numerical gain associated with SLT 5 days per week (0.78 AAT-SSC points, 95% CI [0.48–1.09],155 IPD, 8 RCTs). On measures of auditory comprehension (540 IPD, 16 RCTs), SLT 4 or 5 days per week was associated with significant clinical gains from baseline, with SLT 4 days per week associated with the greatest numerical gains (5.86 AAT-TT points, 95% CI [1.64–10.01],114 IPD, 5 RCTs). It was notable that no significant gains from baseline were observed in the context of SLT interventions delivered 3 days weekly or less. Overall, the RELEASE data suggested that SLT delivered 4–5 days per

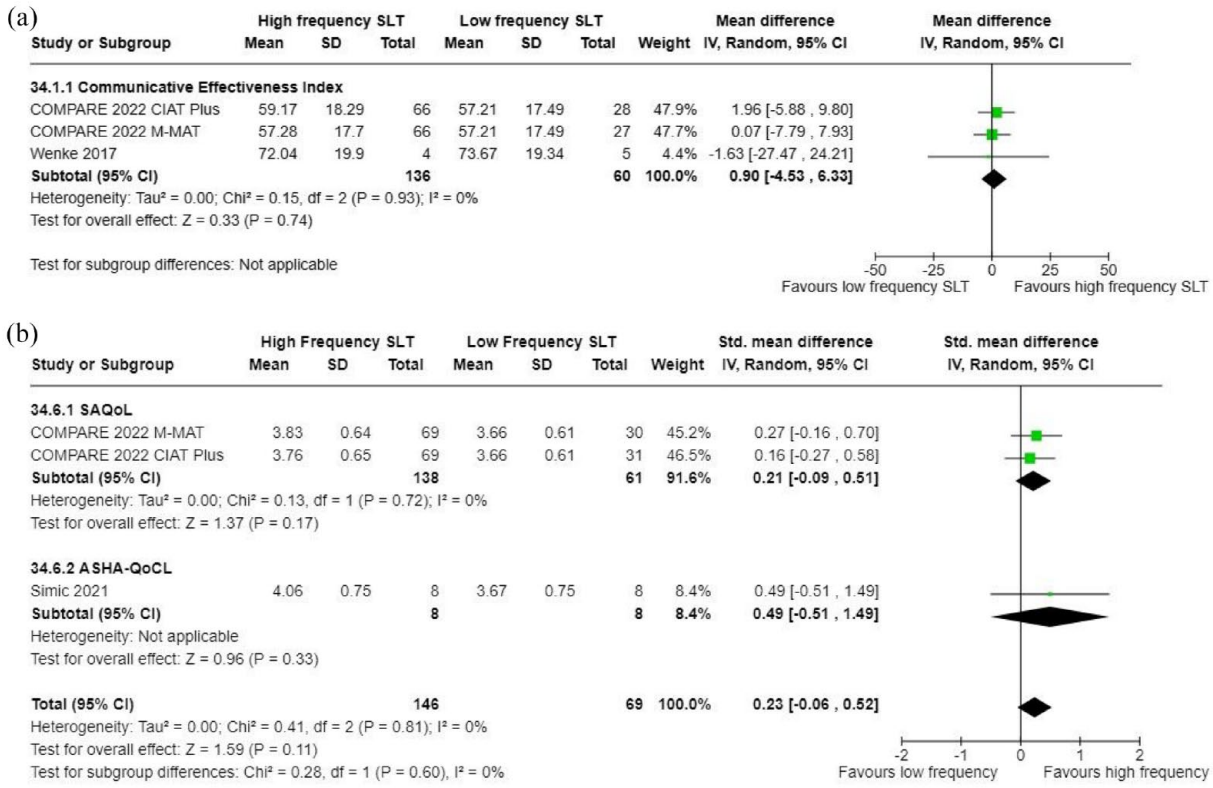

Figure 6. (a) PICO 3 Functional communication and (b) PICO 3 Quality of Life.

week was associated with the greatest overall language, functional communication, and auditory comprehension gains.[28]

Evidence-based Recommendation 3
In people with aphasia post-stroke, we suggest high frequency SLT (⩾4 days per week) should be offered rather than lower frequency SLT (< 4 days per week).
Quality of evidence: Low ⊕⊕
Strength of recommendation: Weak for high frequency SLT intervention ↑?

PICO 4a **In people with aphasia after stroke is digitally delivered SLT (using telerehabilitation, virtual reality therapist or similar) compared to usual in-person SLT associated with similar improvements in language, communication, or quality of life?**

Analysis of current evidence

The search identified 7 RCTs (randomised $n = 157$ (93 male), RoB Figure 7) relevant to this question.[35–41] We included non-inferiority trial designs that explored the equivalence of SLT delivery approaches.[38] Randomised comparisons had small sample sizes, ranging from $n = 10$[41]

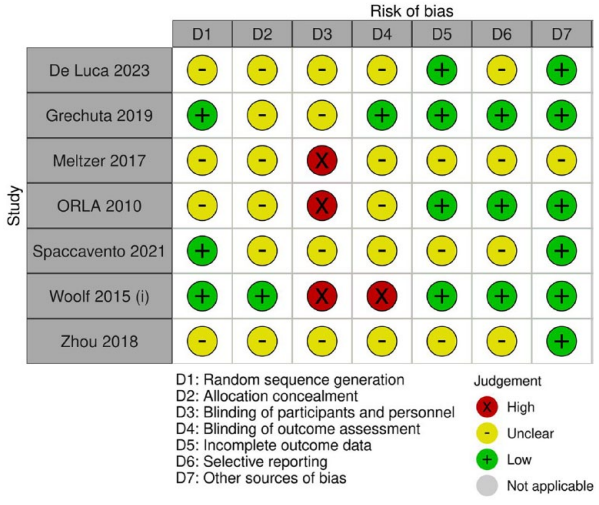

Figure 7. Risk of bias profile for studies included in PICO 4a (immediately postintervention) analysis.

to $n = 33$.[39] Where reported, participants' age ranged from a mean (SD) 51.1 (10.3)[36] to 66.8 (11.2) years[38] and were recruited from early subacute,[37,39] chronic,[35,36,38,40] or across both stages.[41] Where reported, participants aphasia ranged from moderate to severe[35,38,40,41] or on average had severe aphasia[37,39] (Supplement 20 Table 19).

Digital interventions considered varied. They examined the effectiveness of computer-based language exercises targeting specific linguistic components (e.g. word-picture matching, naming),[37,39] remote telerehabilitation,[38,41] or virtual reality and gaming software developed for people with aphasia.[35,36] For example, in one study participants participated in virtual reality training consisting of interactive virtual scenarios.[36]

Four RCTs found no difference between digitally delivered and in-person SLT on measures of functional communication (Figure 8(a))[35,37–39] while one study captured participants' reports of quality of life but similarly found no difference between the groups[37] (Figure 8(b)). Similarly, there was no difference on measures of overall language[35,38–40], auditory comprehension[36–39] or naming.[36–39,41] Communicative confidence was examined in one small study[38] finding that participants that received in-person SLT reported significantly greater communicative confidence than those that received digitally delivered SLT (Supplement 12).

Three studies reported follow-up data after a period without treatment[35,36,41] (Supplement 12; RoB Supplement

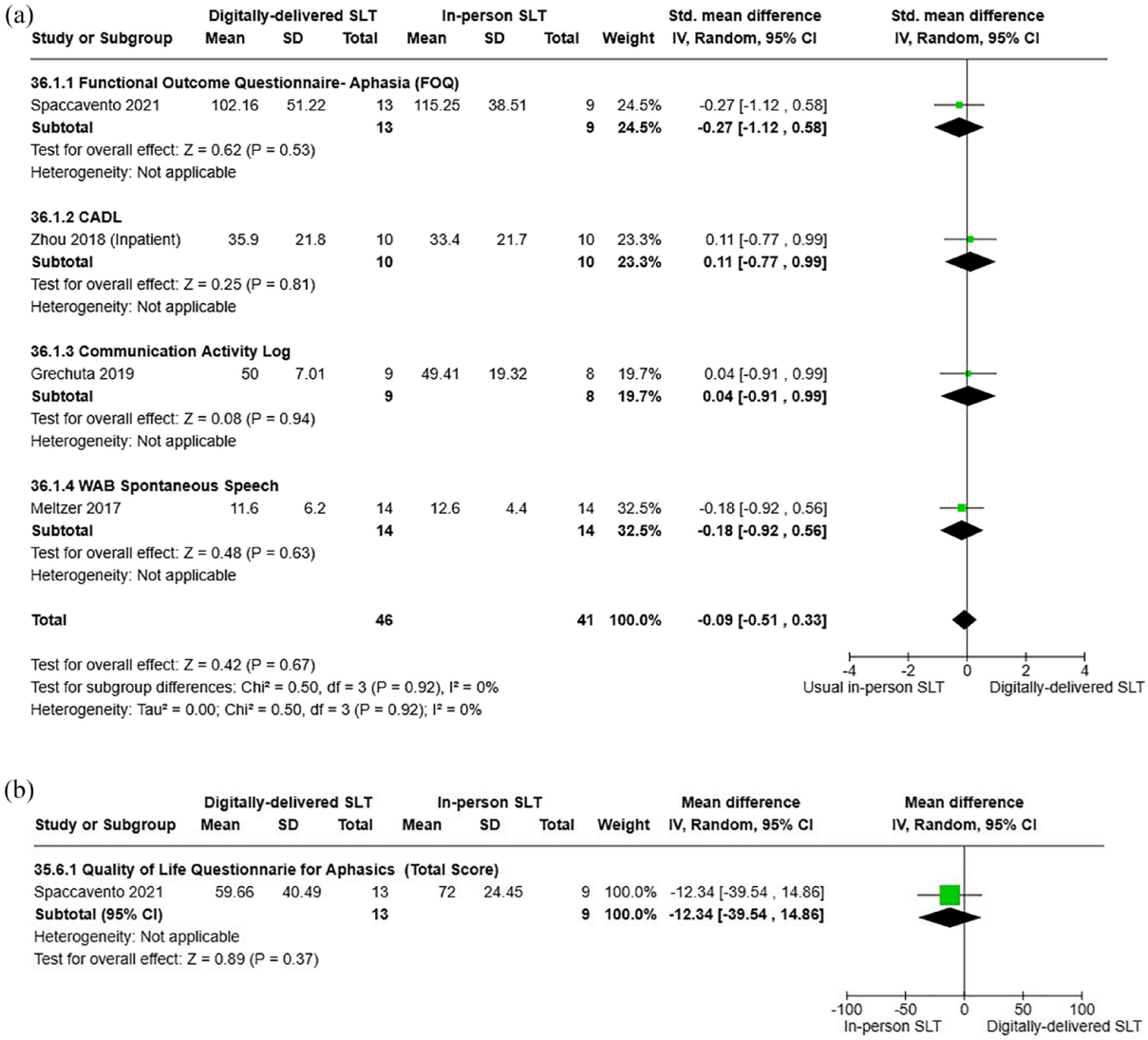

Figure 8. (a) PICO 4a Functional communication and (b) PICO 4a Quality of Life.

18). They reported no difference between participants that received digitally delivered SLT and in-person SLT on measures of functional communication[35] naming[36,41] or auditory comprehension.[36]

Additional information

Evidence from the RELEASE IPD network meta-analysis suggested a slight, but clinically insignificant effect in the direction of in-person SLT.[16] The analysis regarding overall language based on 351 IPD (11 RCTs) found that in-person SLT was associated with mean gains from baseline of 14.13 WAB points (95% CI [8.34–19.91]) compared to gains of 11.06 points (95% CI [2.63–19.49]) associated with digital SLT. There was no overlap between the trials represented in the RELEASE IPD network meta-analyses and the ESO-led, paired group-level summary data meta-analyses described in this PICO.

In summary, current evidence suggests in person and digitally delivered SLT lead to similar gains. Where a difference was observed, based on one small study, that difference favoured a greater increase in communicative confidence after in-person SLT.[38] Other guidelines (e.g. the Australian and New Zealand Living Clinical Guidelines for Stroke Management,[42] National Clinical Guideline for Stroke for the United Kingdom and Ireland[43]) suggest that basic rehabilitation principles should apply to both in-person and digital therapy, such as personalisation to individuals' needs, goals and preferences, and monitoring and adjustment of the intervention by the therapist.

Evidence-based Recommendation 4a
In people with aphasia after stroke, we suggest using either in-person or digitally delivered SLT
Quality of evidence: Very low ⊕
Strength of recommendation: Weak that digitally delivered and in person SLT interventions lead to similar gains↑?

PICO 4b **In people with aphasia after stroke is in-person SLT plus digital augmentation (using computer or tablet-based software, virtual reality or similar) compared to usual in-person SLT associated with greater improvements in language, communication or quality of life?**

Analysis of current evidence

In this guideline the term 'digital augmentation' was defined as an enrichment of the SLT intervention, where the participants received SLT comprising a digital element in addition to in-person SLT. Our search identified six relevant RCTs (randomised $n=453$ (289 male), RoB Figure 9, relevant to this question.[23,44–48] The included trials had small ($n=24$)[23] to medium sample sizes ($n=278$ of which 198 were relevant to this PICO).[47] Participants had a mean (SD) age of 48.7 (11.8)[23] to 65.0 (12.2)[48] [range 23–89.6] years. Where reported, aphasia was severe,[23,45] ranged from severe to very mild[47] or was moderate to mild.[44] Participants were recruited from the early subacute[23,45,46] and from early subacute to chronic[48] or late subacute to chronic stages post-stroke[44,47] (Supplement 20 Table 20). Digital interventions were diverse ranging from synchronous telerehabilitation of SLT by videoconference[48] to the use of computer-based language therapy software to enhance language recovery.[23,45,47] Computer-based therapy programmes were self-managed and/or supervised by a therapist. In one study, a virtual reality platform provided a social support group to people with aphasia targeting outcomes for language, communication, and quality of life.[44] In three studies, the digital augmentation yielded a larger therapy dose compared to the control group,[23,47,48] while in the remaining RCTs the therapy dose was similar in both groups.[44–46] Usual in-person therapy control conditions differed between trials and were not always described in detail, but all participants in the control groups received some form of SLT.

Five studies compared the groups' functional communication[44–48] (Figure 10). While one study favoured in-person SLT plus digital augmentation ($n=34$),[44] there was no difference in the other RCTs or the overall meta-analysis. No study reported participants' quality of life. There was

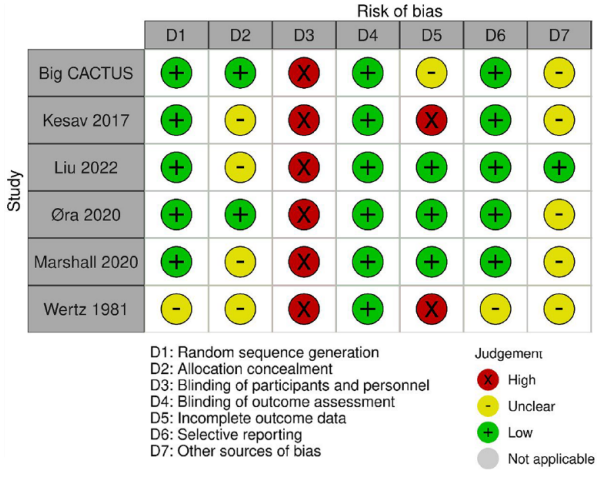

Figure 9. Risk of bias profile for studies included in PICO 4b (immediately postintervention) analysis.

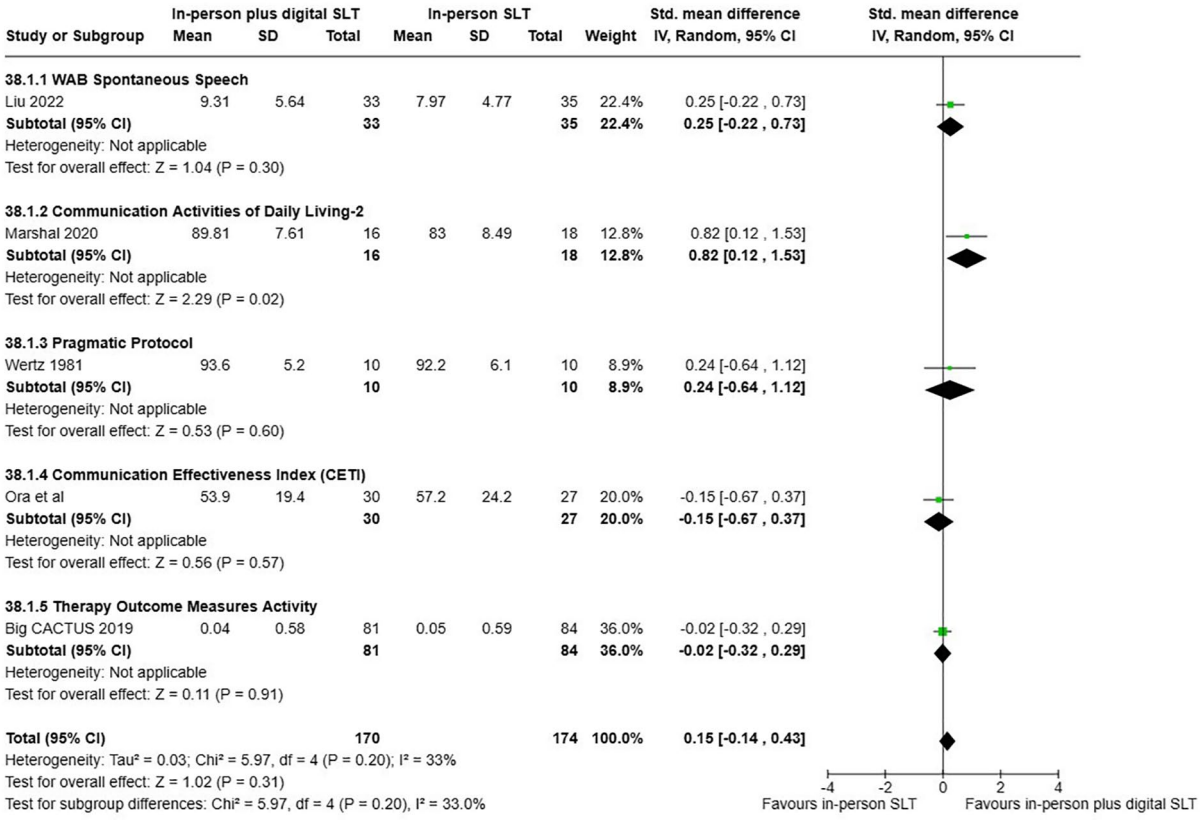

Figure 10. PICO 4b Functional communication.

no difference between the groups' overall language (Supplement 13). Two studies reported higher overall language scores after in-person SLT plus digital augmentation compared to in-person SLT alone ($n = 102$,[44,45]). Meta-analysis of expressive language measures (naming and more general expressive language data) from three trials did not reveal a significant difference between groups.[45,46,48] Nor were there differences when naming[45,48] or sentence production were considered in isolation[48] though the latter reported significant group gains from baseline that favoured the digitally augmented SLT group. Three studies found no auditory comprehension differences between in-person SLT and in-person SLT with digital augmentation though heterogeneity was substantial ($n = 159$, 3 RCTs, $I^2 = 54\%$)[45,46,48]. In exploring the source of heterogeneity, exclusion of either one of two trials removed any indication of heterogeneity.[45,48] The meta-analysis based on the remaining two trials where SLT dosage was similar between the groups,[45,46] found evidence of auditory comprehension benefits in SLT in-person plus digital SLT (SMD 0.66, 95% CI [0.26, 1.06], $p = 0.001$, $I^2 = 0\%$, 2 RCTs, $n = 102$) (Supplement 13).

Three studies reported follow-up data after 3–9 months without treatment[23,47,48] (Supplement 13; RoB Supplement 18). Results showed no difference between in-person SLT and in-person plus digital SLT on functional communication,[47,48] overall language,[23] sentence production,[48] naming[48] or auditory comprehension.[48] In summary, there was limited evidence of the benefit of digital augmentation of in-person SLT. Some digital augmentation approaches may have an additional effect for SLT, as indicated by isolated studies, but more research is needed.

Evidence-based Recommendation 4b
In people with aphasia after stroke, we suggest in-person SLT plus digital augmentation should be offered rather than usual in-person SLT.
Quality of evidence: Very low ⊕
Strength of recommendation: Weak for SLT plus digital augmentation↑?

PICO 5a **In people with aphasia after stroke is group SLT compared to one-to-one SLT associated with similar improvements in language, communication or quality of life?**

Analysis of current evidence

Seven RCTs that compared one-to-one SLT with group SLT for aphasia informed this PICO (randomised $n = 400$ (303 male); RoB Figure 11),[24,35,46,49–52] with small ($n = 9$)[49] to medium sample sizes ($n = 216$).[24] None were non-inferiority trial designs exploring the equivalence of group versus one-to-one SLT. Based on available data, participants' mean (SD) age was between 53.5 (12.1)[35] to 72.6 (14.1)[51] [range 34–81] years, while average aphasia severity was severe,[51] moderate[24,49,50] and ranged from severe to mild. Participants were in the acute,[46,51] chronic[24,35,49] or early subacute to chronic stages after stroke[50] (Supplement 20 Table 21). Though dose, intensity and frequency were the same for one-to-one SLT and group SLT in some studies,[35] in others it was not.[24]

We defined group SLT as therapy involving two or more people with aphasia. SLT approaches delivered included high intensity group therapy (such as constraint induced aphasia therapy or multimodality aphasia therapy)[24] while other group therapy was digitally delivered.[35] No differences were found between the interventions on functional communication which was assessed in four RCTs (Figure 12(a)).[24,35,46,49] Two trials investigated quality of life[24,51] with no differences reported between one-to-one and group SLT (Figure 12(b)). Six RCTs found no difference between one-to-one SLT and group SLT therapy on overall language.[24,35,46,50–52] Similarly, the results showed no differences between one-to-one and group therapy on expressive language (a general measure of expressive language[46] or naming[24,49,50]) or auditory comprehension.[24,46,49,50] (Supplement 14).

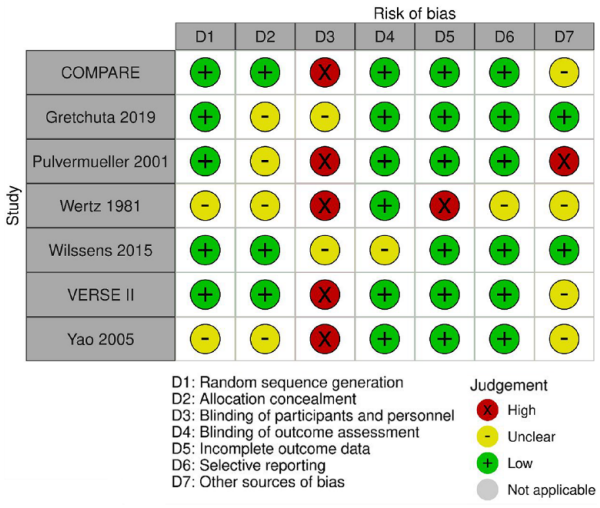

Figure 11. Risk of bias profile for studies included in PICO 5a (immediately postintervention) analysis.

Fewer studies looked at outcomes at follow-up (after a period of no treatment post-therapy) (Supplement 14; RoB Supplement 18). There was no difference between one-to-one and group SLT on 8–12 week follow-up measures of functional communication[24,35] or quality of life.[52] One trial favoured group SLT over one-to-one SLT for overall language[52] while three trials found no difference,[24,35,51] nor was there any difference on meta-synthesis of all four trials' data, though heterogeneity was substantial ($n = 279$, 4 RCTs, $I^2 = 74\%$). In exploring the source of heterogeneity, removal of one trial resulted in a substantial reduction in heterogeneity,[52] $I^2 = 3\%$) but there remained no difference between the groups' overall language at follow up. There was no difference between one-to-one and group SLT on follow-up measures of naming or auditory comprehension.[24]

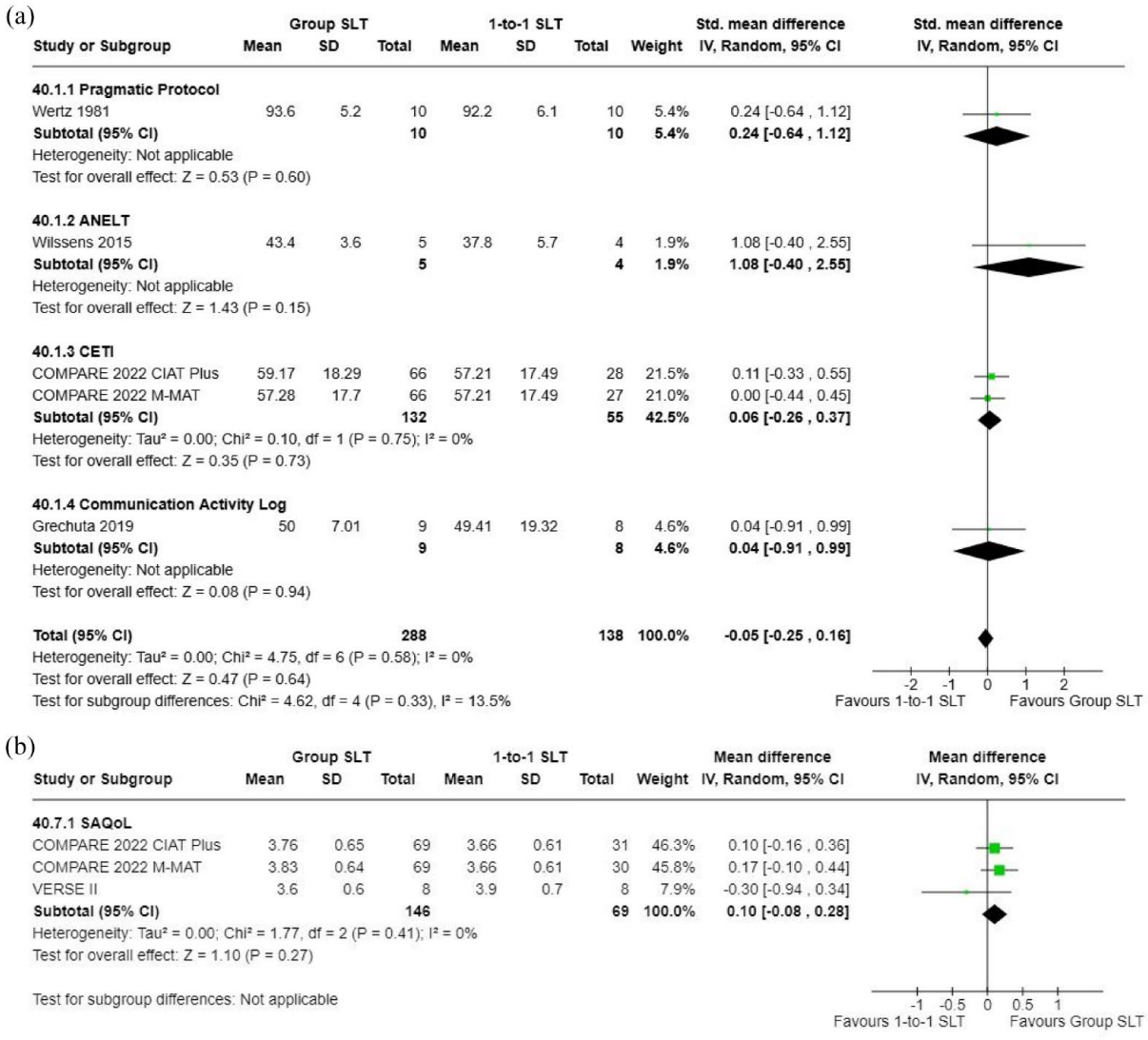

Figure 12. (a) PICO 5a Functional communication and (b) PICO 5a Quality of Life.

Evidence-based Recommendation 5a
In people with aphasia post-stroke, we suggest using either one-to-one or group therapy.
Quality of evidence: Low ⊕⊕
Strength of recommendation: Weak that one-to-one and group SLT interventions lead to similar gains ↑?

Expert consensus statement
The decision on the format of the intervention may be made with reference to the health service context and resources available.

PICO 5b **In people with aphasia after stroke is one-to-one plus group SLT compared to one-to-one SLT alone associated with greater improvements in language, communication, or quality of life?**

Analysis of current evidence

Meta-synthesis was not conducted for this PICO question. Two potentially eligible trials were identified in our search, but suitable outcome data were unavailable from one unpublished trial,[53] leaving one small trial eligible for inclusion (randomised $n = 36$ (24 male), RoB Figure 13) relevant to this question.[54] Participants ranged from 38 to 84 years of age, had mild to severe aphasia and were in the late subacute to chronic stage post stroke (Supplement 20 Table 22). The trial randomly allocated participants to one of two interventions or a usual care control group.[54] No difference was found on functional communication (Figure 14(a)), quality of life (Figure 14(b)), expressive language (naming) or wellbeing between people that received one-to-one plus group SLT compared to those that only received one-to-one SLT (Supplement 15). No suitable

follow-up data was available. Both groups received the same dose, intensity and frequency of SLT. The clinical relevance of the question remains, particularly considering the findings in PICO 5a, and in clinical contexts characterised by constrained resources. Because of limited evidence to support recommendations in this PICO, expert consensus statements were developed, which were agreed by 12/12 voting members of the working group.

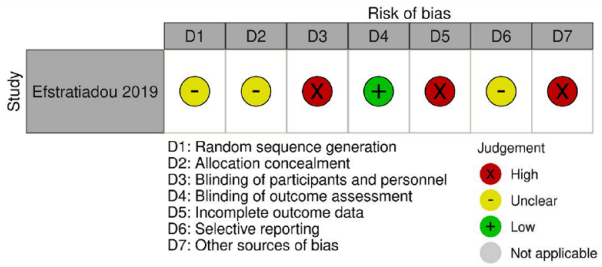

Figure 13. PICO 5b Risk of bias profile for studies (immediately post intervention) analysis.

Evidence-based Recommendation 5b
In people with aphasia post-stroke, the benefits of providing one-to-one plus group SLT compared to one-to-one SLT alone are uncertain and therefore we cannot make a recommendation.
Quality of evidence: Very low ⊕
Strength of recommendation: -

Expert consensus statement 5b
In people with aphasia following stroke where access to one-to-one therapy is constrained by resource availability, we suggest that group therapy delivered in addition to one-to-one SLT may facilitate increased therapy time, provide additional opportunities to use language in a social context and enhance communication confidence.

We also suggest that the therapy timing and format should follow other recommendations in this clinical guideline, aiming to enhance language recovery, communication, participation, and quality of life.

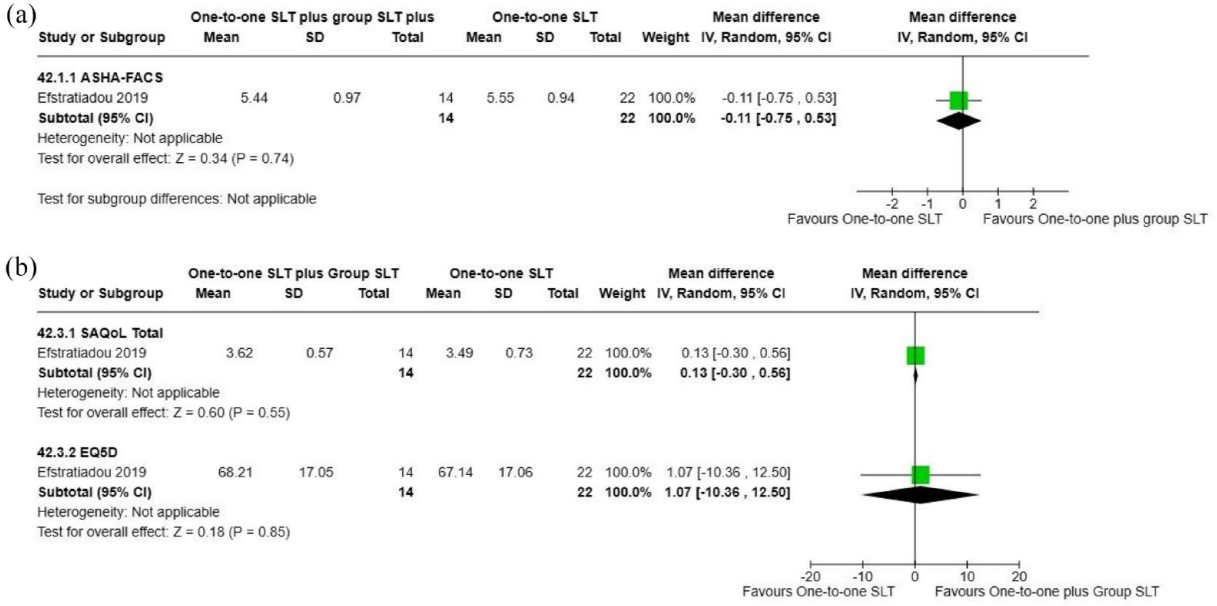

Figure 14. (a) PICO 5b Functional communication and (b) PICO 5b Quality of Life.

PICO 6 **In people with aphasia after stroke is SLT plus tDCS compared to SLT plus sham tDCS associated with greater improvements in language and communication with no changes to safety?**

Analysis of current evidence

The evidence for tDCS alongside SLT for aphasia is based on data from 17 RCTs (randomised $n = 412$ (268 male) that recruited relatively small samples from $n = 6$[55,56] to $n = 74$.[57] Participants had a left hemisphere stroke (93.6% ischaemic strokes data from 10 RCTs). Where reported, participants' mean (SD) age was between 49.9 (4.7)[58] to 73.3 (5.8)[55] [range 34–82] years. Aphasia was on average very severe[59] severe,[60,61] severe to moderate,[62] moderate,[57,58,63–68] moderate to mild[55,69] and mild.[56,70,71] Time since stroke spanned acute to chronic stages after stroke (informed by 11 RCTs) (Supplement 20 Table 23). Eleven RCTs employed parallel group designs,[55,57–60,62–65,68,69] six studies treated participants in cross-over designs.[56,61,66,67,70,71] As in all PICOs in

this guideline, only the first-phase data of cross-over trials was included to avoid potential carry-over effects of treatment and/or tDCS effects. Intervention comparisons were grouped based on tDCS location (e.g. left or right hemisphere) and polarity (anodal or cathodal). Thus, we considered the following comparisons in this PICO:

a. Left Hemisphere anodal tDCS plus SLT versus sham tDCS plus SLT
b. Left Hemisphere cathodal tDCS plus SLT versus sham tDCS plus SLT
c. Right Hemisphere anodal tDCS plus SLT versus sham tDCS plus SLT
d. Right Hemisphere cathodal tDCS plus SLT versus sham tDCS plus SLT
e. Cerebellar (anodal or cathodal) tDCS plus SLT versus sham tDCS plus SLT
f. Individualised Left Hemisphere (anodal or cathodal) tDCS plus SLT versus sham tDCS plus SLT

PICO 6 (a) Left Hemisphere anodal tDCS plus SLT versus sham tDCS plus SLT. Twelve RCTs (randomised $n = 317$, RoB Figure 15) compared the use of left hemispheric anodal tDCS to sham tDCS with SLT.[55,57–60,63–65,68–71] Immediately after intervention there was no difference in functional communication or quality of life (Figure 16(a) and (b)), overall language or naming (nouns 7 RCTs, $n = 165$; verbs 2 RCTs, $n = 14$) (Supplement 16). One trial reported naming using two outcome measurement instruments.[68] Following a sensitivity analysis, we found that the choice of naming outcome data included in the analysis did not alter our findings. Similarly, there was no difference between those that received tDCS alongside SLT for aphasia compared to those that did not on auditory comprehension, in reported adverse events (pain) or side effects[57,58,60,64,69] (Supplement 16).

A further small study also compared anodal left hemisphere tDCS administered to the left primary motor cortex during a 2-week computerised SLT naming therapy intervention to sham tDCS plus SLT ($n = 26$) but only reported functional communication change from baseline data,[63] preventing meta-synthesis with the other available data in this comparison. Participants' functional communication gains from baseline were significantly greater amongst those who had received anodal tDCS alongside SLT than those that had received sham tDCS post intervention (Supplement 16).

Similarly, in the studies above, there was no difference between the interventions at follow-up timepoints (ranging from 1 week to 6 months post treatment) on functional communication, quality of life, overall language, naming (nouns or verbs) or auditory comprehension (Supplement 16; RoB Supplement 18). Sensitivity analyses were conducted which confirmed that the inclusion of alternative auditory comprehension data from a second outcome measurement used by one trial made no difference to these findings.[69] At 6 months follow-up, the additional change from baseline functional communication data continued to favour the group that received anodal tDCS compared to the sham intervention[63] (Supplement 16).

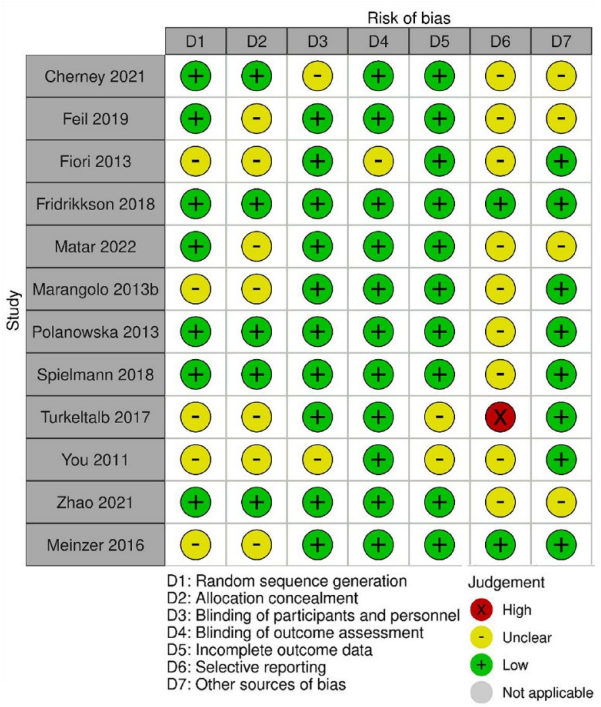

Figure 15. PICO 6a Risk of bias profile for studies included (immediately post intervention) analysis.

PICO 6 (b) Left Hemisphere cathodal tDCS plus SLT versus sham tDCS plus SLT. Left hemispheric cathodal tDCS plus SLT was compared with sham tDCS plus SLT by one very small trial[58] which found that functional communication measures favoured cathodal tDCS compared to the sham tDCS with SLT (Figure 16(c)). However, there was no between group difference in overall language immediately after treatment (Supplement 16; RoB Supplement 18).

No adverse events were reported and there was no difference in the reported side effects between the groups.[58] At 6 weeks follow-up on measures of functional communication, the participants that had received tDCS continued to gain higher scores than those that had received the sham intervention (Supplement 16). There remained no difference between the groups on measures of overall language (Supplement 16; RoB Supplement 18).

PICO 6 (c) Right Hemisphere anodal tDCS plus SLT versus sham tDCS plus SLT. A very small study compared right

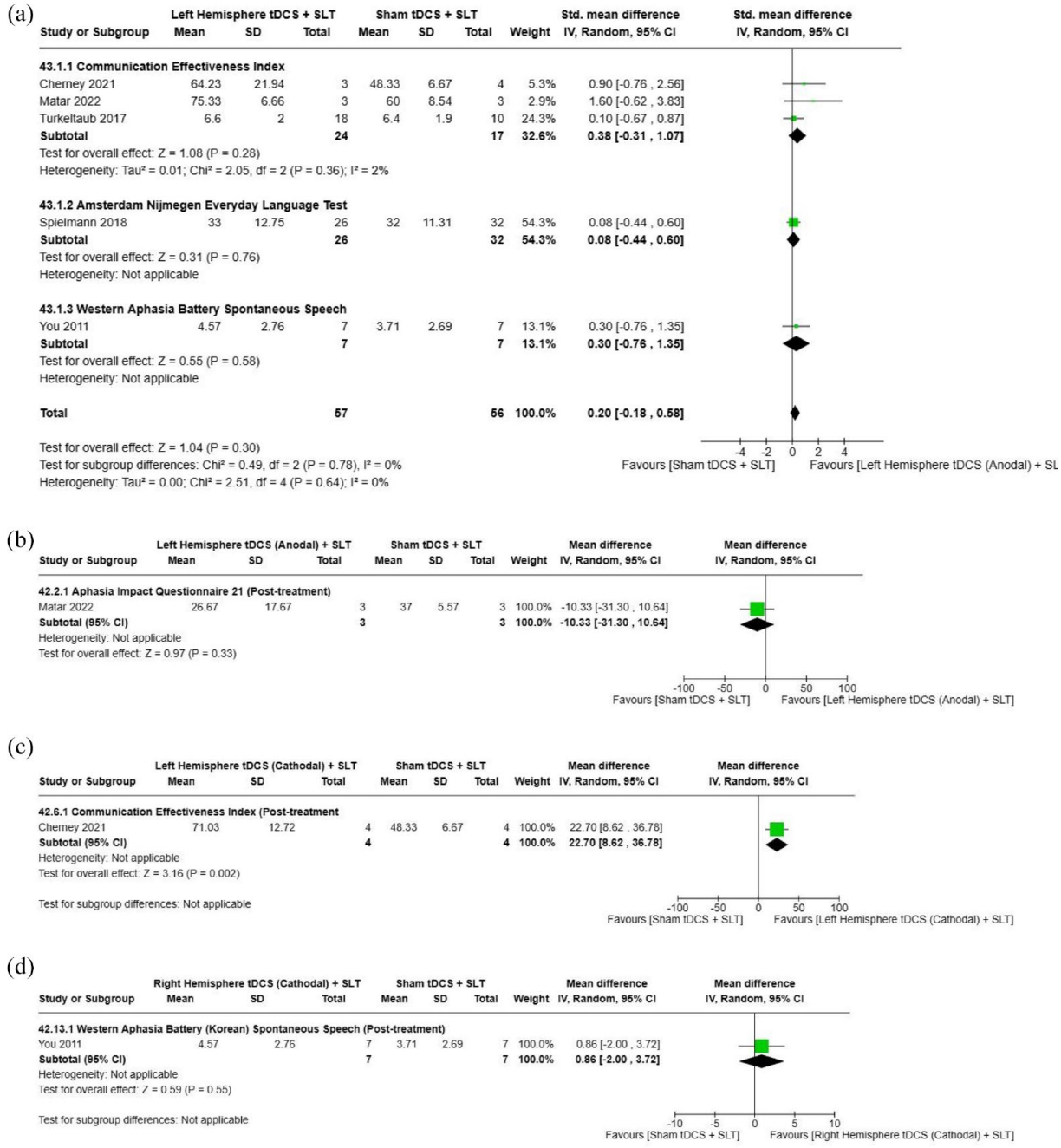

Figure 16. (a) PICO 6a Functional communication, (b) PICO 6a Quality of Life, (c) PICO 6b Functional communication, and (d) PICO 6d Functional communication.

hemispheric anodal tDCS with a reference electrode on the contra-lateral frontopolar cortex delivered alongside SLT to a sham tDCS intervention and SLT.[56] Outcomes immediately after treatment favoured the provision of right hemispheric anodal tDCS with SLT for naming nouns (MD 46.66, 95% CI [25.00, 68.32], $p < 0.0001$, 1 RCT, $n = 6$) and verbs (MD 51.67, 95% CI [28.12, 75.22], $p < 0.0001$ RCT, $n = 6$) (Supplement 16; RoB Supplement 18).

PICO 6 (d) Right Hemisphere cathodal tDCS plus SLT versus sham tDCS plus SLT. Two RCTs ($n = 24$)[59,61] found there was no difference, between the groups that received right

hemisphere cathodal tDCS plus SLT and those that received the sham intervention on functional communication (Figure 16(d)), overall language or expressive language (naming) (Supplement 16; RoB Supplement 18). The auditory comprehension data however trended towards favouring the right hemisphere cathodal tDCS plus SLT group (MD 32.85, 95% CI [0.15, 65.55], $p = 0.05$, 1 RCT, $n = 14$). Data on reported adverse events (pain) and side effects (headache and dysaesthesia) were available from a further study,[62] which indicated no between group differences.

PICO 6 (e) Cerebellum anodal or cathodal tDCS plus SLT versus sham tDCS plus SLT. One study compared effects of right cerebellar anodal or cathodal tDCS alongside a computerised picture-word matching SLT intervention to sham tDCS and SLT but found no differences in expressive language (naming nouns) between the groups immediately post treatment or at 2-month follow-up ($n = 21$).[66] Adverse events were recorded as the number of sessions where pain was reported; there was no significant difference between the groups (Supplement 16; RoB Supplement 18).

PICO 6 (f) Individualised left hemisphere anodal or cathodal tDCS plus SLT versus sham tDCS plus SLT. One small trial (randomised $n = 6$) adopted an individualised approach to tDCS brain stimulation.[67] Participants initially completed four matched 80-picture naming tasks with different active tDCS montages (left or right; anodal or cathodal prefrontal tDCS) to identify the most effective stimulation site for each participant. They were then randomised to receive the active optimal tDCS montage (specifically, left hemisphere anodal $n = 1$; left hemisphere cathodal $n = 2$) or sham tDCS ($n = 3$) alongside 2 weeks of naming tasks. No overall language differences were observed immediately after treatment or at 2-month follow-up (Supplement 16; RoB Supplement 18).

Additional information. Previous systematic reviews and meta-analyses of RCTs investigated potential short- or long-term benefits of anodal or cathodal tDCS in combination with different types of SLT interventions.[72–74] Inclusion criteria and meta-syntheses varied substantially across reviews, results were based on a small number of trials and participants, low to very low-quality evidence, and results were inconclusive. Hence, there is an urgent need for larger multi-centre trials of tDCS alongside SLT for aphasia using validated outcome measures and improved reporting of individual participant characteristics (e.g. time since stroke), interventions and adverse events. Owing to the large heterogeneity of lesion and symptom patterns across studies, exploration of individually tailored tDCS approaches (e.g. optimisation of current flow to intended target regions based on computational modelling) is warranted.[75] Notably, the absence of serious adverse effects reports associated with tDCS is a common finding so far, suggesting that tDCS may be a safe non-invasive brain stimulation approach for people with stroke-related aphasia, while abiding with current safety guidelines.[76]

Evidence-based Recommendation 6 a-f
In people with aphasia post-stroke, the benefits of SLT plus tDCS compared to SLT plus sham tDCS are uncertain and therefore we cannot make a recommendation.
Quality of evidence: Very low ⊕
Strength of recommendation: -

The expert consensus statement below was developed. All members agreed that left- or right-sided cortical or cerebellar tDCS (anodal or cathodal) should only be delivered alongside SLT in a high-quality trial context, where validated outcome measurement instruments are used, participant demographics are fully described and adverse events (even if none are observed) are reported. For the expert consensus statement below, of the 12 voting members of the working group, 10 agreed with the first statement, and 12 agreed with the remaining statement.

Expert consensus statement 6 a-f
In people with aphasia following stroke, we suggest that in the clinical context, SLT should be delivered alone, rather than SLT alongside tDCS. Individualised tDCS protocols for post-stroke aphasia may be beneficial, but further evidence is required.

PICO 7a **In people with aphasia after stroke, is individually-tailored SLT by functional relevance compared to non-tailored SLT associated with greater improvements in language, communication or quality of life?**

Analysis of current evidence

We identified no trials that specifically compared individually-tailored SLT by functional relevance to non-tailored SLT interventions. Future studies should consider tailoring treatment to individual needs by functional relevance to inform the evidence in this area.

Additional information

The RELEASE study extracted data on whether individual trial participants' therapy interventions were tailored by functional relevance. Using IPD network meta-analysis and controlling for participants' baseline age, sex and time since stroke, they found that SLT that was individually-tailored for functional relevance significantly contributed to auditory comprehension outcomes.[28]

Significant gains on measures of auditory comprehension were only associated with functionally relevant SLT (5.26 AAT-TT points, 95% CI [2.05–8.47], 194 IPD, 7 RCTs).[28] On other outcomes, when significant changes from baseline were observed, higher gains occurred in the context of functionally relevant SLT for overall language ability (16.47 WAB-AQ points, 95% CI [10.95–21.99], 232 IPD, 6 RCTs), naming (8.79 Boston Naming Test (BNT) points, 95% CI [1.95–15.63], 113 IPD, 5 RCTs), and functional communication (0.74 AAT-SSC points, 95% CI [0.38–1.10], 249 IPD, 6 RCTs) than with non-tailored SLT interventions.

Evidence-based Recommendation 7a
In people with aphasia post-stroke, we suggest tailored SLT by functional relevance rather than non-tailored SLT by functional relevance should be offered.
Quality of evidence: Very low ⊕
Strength of recommendation: Weak for SLT tailored by functional relevance intervention ↑?

PICO 7b **In people with aphasia after stroke is individually-tailored SLT by level of language task difficulty, compared to non-tailored SLT associated with greater improvements in language, communication or quality of life?**

Analysis of current evidence

One small RCT ($n = 36$ (18 male), RoB Figure 17) compared individually-tailored SLT by level of language task difficulty on a computer-based SLT app (Constant Therapy-Research™) to non-tailored SLT workbooks.[77] Participants were between 43 and 84 years of age, were in the late subacute to chronic stages post stroke and had mild-severe aphasia (Supplement 20 Table 24). Individually-tailored SLT was reported as 3 h per week while adherence to the non-tailored therapy treatment schedule was reported by the participant. We found no difference between participants that received individually-tailored and non-tailored SLT by language task difficulty on quality of life (Figure 18), overall language, naming or auditory comprehension (Supplement 17). Future studies should consider tailoring treatment by level of language difficulty to provide more evidence in this area.

Additional information

In the RELEASE network meta-analysis involving 495 IPD from an additional 17 RCTs, individually-tailored SLT by level of language task difficulty significantly contributed to auditory comprehension.[28] Significant auditory comprehension gains from baseline were only evident when SLT was tailored by level of language difficulty (4.57 TT-AAT points, 95% CI [1.55–7.60], 331 IPD, 10 RCTs). In contrast, SLT that was not tailored by level of language difficulty was associated with greater gains from baseline on measures of naming (10.21 BNT points, 95% CI [2.75–17.67], 79 IPD, 4 RCTs) and functional communication (0.81 AAT-SSC points, 95% CI [0.34–1.27], 141 IPD, 5 RCTs) compared to interventions tailored for level of language task difficulty. Similar overall language gains from baseline occurred in SLT tailored and non-tailored by level of language task difficulty.

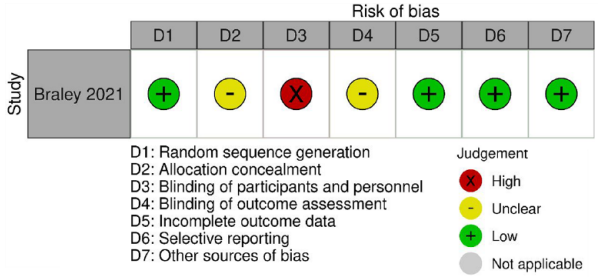

Figure 17. Risk of bias profile for studies included in PICO 7b (immediately post intervention analysis).

Evidence-based Recommendation 7b
In people with aphasia post-stroke, we suggest that SLT individually-tailored by level of language task difficulty should be offered.
Quality of evidence: Very low ⊕
Strength of recommendation: Weak for SLT tailored by language task difficulty intervention ↑?

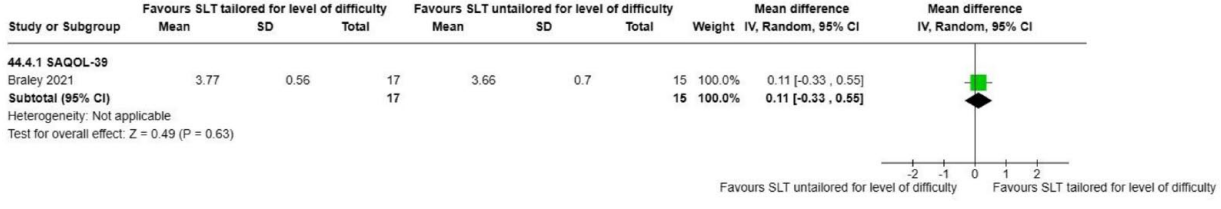

Figure 18. PICO 7b Quality of Life.

Table 4. Synoptic table of all recommendations and expert consensus statements.

Recommendation	Expert consensus statement
PICO 1: In people with aphasia after stroke is a higher dose of SLT (⩾20 hours) compared to a lower dose of SLT (<20 hours) associated with greater improvements in language, communication, or quality of life?	
In people with aphasia post-stroke, we recommend high dose SLT interventions (⩾20 hours) rather than lower dose SLT (<20 hours) should be offered. Quality of the evidence: **Low** ⊕⊕ Strength of the recommendation: **Strong for high dose SLT intervention** ↑↑	
PICO 2: In people with aphasia after stroke is a higher intensity of SLT (⩾3 hours per week) compared to a lower intensity of SLT (<3 hours per week) associated with greater improvements in language, communication or quality of life?	
In people with aphasia post-stroke, we suggest high intensity SLT (⩾3 hours per week) rather than lower intensity should be offered. Quality of evidence: **Low** ⊕⊕ Strength of recommendation: **Weak for high intensity SLT intervention** ↑?	
PICO 3: In people with aphasia after stroke is a higher frequency of SLT (⩾4 days per week) compared to a lower frequency of SLT (<4 days per week) associated with greater improvements in language, communication or quality of life?	
In people with aphasia post-stroke, we suggest high frequency SLT (⩾4 days per week) should be offered rather than lower frequency SLT (<4 days per week). Quality of the evidence: **Low** ⊕⊕ Strength of the recommendation: **Weak for high frequency SLT intervention** ↑?	
PICO 4a: In people with aphasia after stroke is digitally-delivered SLT (using telerehabilitation, virtual reality therapist or similar) compared to usual in-person SLT associated with similar improvements in language, communication or quality of life?	
In people with aphasia after stroke, we suggest using either in-person or digitally-delivered SLT Quality of the evidence: **Very low** ⊕ Strength of the recommendation: **Weak that digitally delivered and in-person SLT interventions lead to similar gains** ↑?	
PICO 4b: In people with aphasia after stroke is in-person SLT plus digital augmentation (using computer or tablet-based software, virtual reality or similar) compared to usual in-person SLT associated with greater improvements in language, communication or quality of life?	
In people with aphasia after stroke, we suggest in-person SLT plus digital augmentation should be offered rather than usual in-person SLT. Quality of the evidence: **Very low** ⊕ Strength of the recommendation: **Weak for SLT plus digital intervention** ↑?	

(Continued)

Table 4. (Continued)

Recommendation	Expert consensus statement
PICO 5a: In people with aphasia after stroke is group SLT compared to one-to-one SLT associated with similar improvements in language, communication or quality of life?	
In people with aphasia post-stroke, we suggest using either one-to-one or group therapy. Quality of the evidence: **Low** ⊕⊕ Strength of the recommendation: **Weak that one-to-one and group SLT interventions lead to similar gains ↑?**	
PICO 5b: In people with aphasia after stroke is one-to-one plus group SLT compared to one-to-one SLT alone associated with greater improvements in language, communication, or quality of life?	
In people with aphasia post-stroke, the benefits of providing one-to-one plus group SLT compared to one-to-one SLT alone are uncertain and therefore we cannot make a recommendation. Quality of the evidence: **Very low** ⊕ Strength of recommendation: -	In people with aphasia following stroke where access to one-to-one therapy is constrained by resource availability, we suggest that group therapy delivered in addition to one-to-one SLT may facilitate increased therapy time, provide additional opportunities to use language in a social context and enhance communication confidence. We also suggest that the therapy timing and format should follow other recommendations in this clinical guideline, aiming to enhance language recovery, communication, participation, and quality of life. 12/12 (100%) writing group members agreed? (Supplement 21).
PICO 6 (a)-(f): In people with aphasia after stroke is SLT plus tDCS compared to SLT plus sham tDCS associated with greater improvements in language and communication with no changes to safety?	
In people with aphasia post-stroke, the benefits of SLT plus tDCS compared to SLT plus sham tDCS are uncertain and therefore we cannot make a recommendation Quality of the evidence: **Very low** ⊕ Strength of recommendation: -	In people with aphasia following stroke, we suggest that in the clinical context, SLT should be delivered alone, rather than SLT alongside tDCS. Individualised tDCS protocols for post-stroke aphasia may be beneficial, but further evidence is required.
PICO 7a: In people with aphasia after stroke, is individually-tailored SLT by functional relevance compared to non-tailored SLT associated with greater improvements in language, communication or quality of life?	
In people with aphasia post-stroke, we suggest tailored SLT by functional relevance rather than non-tailored SLT by functional relevance should be offered. Quality of the evidence: **Very low** ⊕ Strength of the recommendation: **Weak for SLT tailored by functional relevance intervention ↑?**	
PICO 7b: In people with aphasia after stroke is individually-tailored SLT by level of language task difficulty, compared to non-tailored SLT associated with greater improvements in language, communication or quality of life?	
In people with aphasia post-stroke, we suggest that SLT individually-tailored by level of language task difficulty should be offered Quality of the evidence: **Very low** ⊕ Strength of the recommendation: **Weak for SLT tailored by level of language task difficulty intervention ↑?**	

Discussion

The ESO Aphasia Rehabilitation guideline offers a rigorous, in-depth and up-to-date evidence synthesis of the effectiveness of interventions for stroke-related aphasia where language (overall ability, expressive and receptive language), functional ability and quality of life benefits were considered. This evidence synthesis reflects significant updates on existing reviews of SLT and non-invasive tDCS for aphasia after stroke.[14] Where our pre-specified clinically relevant questions could not be informed by the available group-level syntheses, the findings of a recent IPD network meta-analysis informed our guideline recommendations.[28] The guideline aims to support multidisciplinary stroke rehabilitation team members' clinical decision-making for the benefit of people with aphasia after stroke.

Aphasia has a profound impact on people's lives, affecting their language, their ability to communicate and interact with their environment (functional communication) and their overall quality of life. People with aphasia have lower quality of life than those with stroke but without aphasia.[78] SLT benefits language recovery after stroke[14] and earlier intervention is associated with greater language gains (which may be achieved through a variety of mechanisms) and notable gains may continue to be made in the long term.[16,79,88] The priority clinical question of 'how' therapy is delivered and the impact on language, quality of life and safety of brain stimulation were considered. Existing SLT guideline recommendations for aphasia typically stop short of quantifying specific therapeutic dose, intensity, or frequency.[80] Consequently, the standard dosage of SLT for aphasia varies widely across and within countries[81–84] with some reported levels considered to be so low as to be of questionable benefit to language recovery, a problem that extends across stroke rehabilitation disciplinary areas.[85]

Following ESO guideline and meta-analysis processes we made a strong recommendation for interventions of ⩾20 SLT hours. Our confidence is based on the balance of the current evidence syntheses (including[28]) and the lack of possible risks. We made weak recommendations for higher weekly SLT intensity (⩾3 h; noting intensity was ⩾4 h in all but one of the eight included RCTs), frequency (⩾4 days) and tailored SLT approaches. Our positive suggestions for intensity and frequency were made in the context of a therapeutic intervention which was highly unlikely to result in harm and thus outweighed any associated risks. Tailored SLT approaches are often mentioned as best practice recommendations, while our recommendation is based on best available evidence.

We identified fewer trials that compared standard in-person, one-to-one SLT with alternative therapy delivery models such as digital or group therapy, or augmentation of more traditional delivery models with digital therapy. We confidently suggest these alternative models can be used to augment traditional SLT dosage in resource constrained contexts, being unlikely to cause harm and outweighing any associated risks.

In the absence of evidence supporting the use of tDCS brain stimulation alongside SLT, such interventions should be considered experimental and should only be delivered in the context of a well-regulated clinical trial where potential adverse events and side effects are fully reported. Synthesis of tDCS trials was based on stimulation site and principles rather than a broad lumping approach. Several trials ($n = 8$) were excluded from our meta-analysis due to an absence of validated outcome measurement instruments (i.e. only non-validated measures were reported), tDCS intervention in the absence of SLT or use of a non-sham tDCS control. We also noted seven tDCS trials that made no report on the presence or absence of adverse events; thus, use of validated outcome measurement instruments and transparent reporting of all data is vital. It is promising that trial evidence continues to emerge in this area. Zheng et al.'s[86] recent double-blind RCT ($n = 50$) comparing left anodal tDCS alongside SLT to SLT plus sham reported significant improvements for the SLT plus tDCS group over time as opposed to the SLT plus sham group (group × time interaction) on overall language and auditory comprehension, using validated outcome measures and in the absence of adverse events.

Our recommendations (summarised in Table 4) were informed by trials that recruited participants across the post-stroke trajectory; from acute to chronic stages of recovery.[20] The data identified was insufficient to support our planned subgroup analysis based on post-stroke timepoints. While insights continue to emerge from trial-level and large aphasia-specific IPD subgroup meta-analyses, to date these have been insufficiently powered to support definitive conclusions relating to the language recovery gains at specific timepoints.[79,87–89] Evidence from the wider stroke rehabilitation literature highlights the importance of early access to stroke rehabilitation[90] and specifically aphasia rehabilitation.[91] New evidence suggests that with personalised, intensive and high dose speech and language therapy [6–7 weeks of intensive therapy (10 h per week, median (IQR) dosage = 68[61–76]], young people (46–62 years) in the chronic stages post-stroke may (after adjusting for spontaneous recovery) make similar gains across language modalities to those in subacute stages (early $n = 52$ and late $n = 65$).[88] Alternative meta-analysis (unadjusted for spontaneous recovery) suggests that early interventions (within 1 month of onset) may be associated with greater absolute and relative gains from baseline with diminishing gains at later timepoints post stroke (>3 months).[79] Thus, the ESO Aphasia Rehabilitation Guideline recommendations are not specific to a particular post-stroke timepoint but instead reflect the evidence to date which is based on trial participants recruited from days to several years after aphasia onset. Ideally, people with aphasia should have the opportunity to benefit from aphasia rehabilitation across

their recovery trajectory. Further evidence on whether this approach is beneficial is required.

A recent systematic synthesis of stroke guidelines referring to aphasia therapy drew recommendations from 200 international stroke guidelines[91] and recommended aphasia treatment starts within 1 month of onset. Another systematic stroke guideline synthesis considered guidelines rated as high quality from Australia, Canada, UK and US and recommended offering people with aphasia 'early, frequent, intensive treatment, as tolerated'.[92] Our recommendations extend those by adding specificity and important guidance on overall dose and regime. For some settings, offering SLT as recommended in this guideline may require an increase in current service provision; and alternative models of therapy delivery including for example group therapy and augmenting SLT with digital content. For others, usual care may be in excess of these recommended levels ($\geqslant$20 h of therapy, $\geqslant$3 h weekly) and in such contexts, we highlight that our recommendations indicate *minimum* SLT levels to achieve gains. Recent evidence strongly indicates that very high levels of therapy (intensity for example) may be required for optimal gains in specific aspects of language recovery such as auditory comprehension, while there is also some suggestion that specific subgroups may benefit from more intensive interventions, including working-aged participants and those several months after onset.[16,87] Though aphasia rehabilitation guidelines exist across Europe (e.g. from the Netherlands,[93] Finland[94] and emerging guidelines in Germany[95]), to the best of our knowledge and based on the literature[92] this is the first English-language based clinical guideline developed specifically for aphasia rehabilitation.

Our large multidisciplinary expert working group supported detailed and accurate data extraction, and clinically relevant comparisons and syntheses which prioritised a-priori the analysis of final value scores. To date, the evidence base for aphasia rehabilitation is predominantly based on a relatively small number of small-medium scaled studies, as is the case for much of the stroke rehabilitation interventions. Meta-analysis of trials' average or group-level outcome summary scores offers an improvement on isolated trial reports from multiple small-medium scale studies by providing an evidence synthesis which considers the study size, precision and risk of bias. More recently, IPD meta-analysis has been undertaken, based on individual performance records, important individual characteristics (e.g. time post stroke or baseline aphasia severity) and where relevant, their specific treatment profile.[16,88,89] We drew on the findings from both meta-synthesis approaches in developing this guideline. While there was a small overlap in the individual participant data informing these different meta-analysis approaches for two of the 10 PICOs addressed in this guideline (215 IPD in total), we have carefully highlighted where, and the degree to which this overlap occurred. While our preference would always be for many large-scaled trials in this field, such trials are just beginning to emerge. We hope that these clinical guidelines and consensus statements by experts in the field and associated evidence syntheses will not only contribute to improved clinical practice but also research developments (including larger trials evaluating more specific therapy comparisons and meta-analyses of such trials) in the future.

Our brain stimulation comparisons and evidence syntheses were carefully constructed to ensure meaningful comparisons. They were based on target hemisphere (left or right) and tDCS polarity (anodal or cathodal) resulting in six separate meta-syntheses. We carefully extracted data on standardised outcome measurement instruments, at study level (where relevant across multiple published reports of a single trial), and up to the point of intervention cross-over to avoid carry over effects. We also performed a detailed review of IPD across brain stimulation trials and removed any overlapping or duplication of trial participants in our analyses.

Our recommendations are based on a narrow approach focussed on 10 PICOs. Additional clinically relevant SLT and brain stimulation review questions (such as the effectiveness of transcranial magnetic stimulation[96]) and outcomes (such as reading and writing) could have been included in this review but for feasibility reasons were postponed for future guideline updates. Similarly, we relied on published reports of patient preferences and priorities. Due to limited direct trial-based comparisons in the literature,[16] examination of the effectiveness of different SLT approaches was not within the scope of this guideline.

Methodologically, two of our PICO questions would have been best addressed in non-inferiority trial designs. Moreover, blinding of participants to rehabilitation interventions is always problematic. Though brain stimulation can be compared to a placebo (sham) condition, it is difficult to blind participants to differences in SLT provision or delivery models. Lack of participant blinding contributes to risk of bias, lower GRADE ratings, and lower confidence in the evidence synthesis, thus reducing the strength of rehabilitation recommendations and potentially the impact of guidelines on clinical services. Lastly, future guidelines may revisit our a-priori decision to prioritise the meta-analysis of final value scores over change scores which may better reflect treatment response in a heterogeneous clinical population, though such a decision would carry the inherent risk that change score data may not be available for older trials.

Future research

Our review highlighted clinical-evidence gaps, small sample sizes (within trials and meta-analysis comparisons), use of non-validated outcome measurement instruments, and limited follow-up data with short timelines. More specific trial comparisons, evaluated within adequately funded

studies of sufficient size and power that employ the highest quality methodologies (including use of the aphasia core outcome set[97,98]), detailed description of SLT interventions and home practice to support intervention comparisons and routinely captured follow-up data (up to a year post-intervention) are required to further the evidence base and in turn clinical guidelines. Greater insight is also required into the contribution social support for people with aphasia makes to measures of quality of life. While non-inferiority trials may inform clinical decision making, such trials are not without their own methodological challenges.[99,100] We recognise the challenges of applying these requirements in the context of aphasia trials. Multicentred trials are becoming more common across settings with similar language, healthcare contexts and resources. The multilingual global population needs language-specific and culturally relevant outcome measurement instruments to capture language abilities and deficits. In turn, language-specific versions of outcome measurement instruments should be treated as separate outcome measurements within meta-analyses. While trials of language-based interventions will always require outcome measurement instruments that reflect the linguistic and cultural variations across global languages, adoption of the consensus core outcome set would improve trial quality and relevant secondary data analyses.[97,101] Moreover, transparent and complete reporting of participant descriptors, social support, data and trials which address areas of priority would advance our field of research for the benefit of people with aphasia and the healthcare professionals that work with them.[12,13,15,102,103]

Conclusion

Although a third of stroke survivors experience aphasia, high quality trial data on the impact of SLT and brain stimulation on important aphasia outcomes is limited to a relatively small number of trials. For some clinically relevant research questions such as the benefit of tailoring in-person SLT interventions by functional relevance or level of language difficulty, we were unable to identify a trial-level comparison. This ESO aphasia rehabilitation clinical guideline not only supports clinical management and decision making relating to aphasia but also informs the development and design of future aphasia rehabilitation trials.

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Ethical approval was unnecessary for the work reported in this paper.

Informed consent

Not applicable.

Guarantor

MCB and KH

Contributorship

All authors contributed to conceptualisation of the work and drafted and refined the PICO questions. SH conducted the literature search. All authors screened and reviewed the search results, conducted the data extraction, interpreted the data, drafted various sections of the manuscript. MCB and LH performed the meta-analyses. PC, HPØ and NN reviewed the RoB; PC drafted the GRADE tables. All authors reviewed and edited the manuscript critically for important intellectual content and approved the final version of the manuscript.

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Supplemental material

Supplemental material for this article is available online.

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