Longitudinal Speech Recognition Changes After Cochlear Implant: Systematic Review and Meta-analysis

Cheng Ma, BS ^(D); Jacob Fried, MD; Shaun A. Nguyen, MD ^(D); Kara C. Schvartz-Leyzac, AuD, PhD; Elizabeth L. Camposeo, AuD ^(D); Ted A. Meyer, MD, PhD; Judy R. Dubno, PhD ^(D); Theodore R. McRackan, MD, MSCR ^(D)

Objectives: To examine patterns of change and plateau in speech recognition scores in postlingually hearing impaired adult cochlear implant recipients. The study also examines variations in change patterns for different speech materials and testing conditions.

Study Design: Used systematic review with meta-analysis.

Methods: Articles in English reporting speech recognition scores of adults with postlingual hearing loss at preimplantation and at least two post-implantation time points were included. Statistically significant changes were determined by meta-analysis and the 95% confidence interval.

Results: A total of 22 articles representing 1954 patients were included. Meta-analysis of mean difference demonstrated significant improvements in speech recognition score for words in quiet (37.4%; 95% confidence interval [34.7%, 40.7%]), sentences in quiet (49.4%; 95% confidence interval [44.9%, 53.9%]), and sentences in noise (30.8%; 95% confidence interval [25.2%, 36.4%]) from pre-op to 3 months. Scores continued to increase from 3 to 12 months but did not reach significance. Similarly, significant improvements from pre-op to 3 months were observed for consonant nucleus consonant (CNC) words in quiet (37.1%; 95% confidence interval [33.8%, 40.4%]), hearing in noise test (HINT) sentences in quiet (46.5%; 95% confidence interval [37.0%, 56.0%]), AzBio sentences in quiet (45.9%; 95% confidence interval [44.2%, 47.5%]), and AzBio sentences in noise (26.4%; 95% confidence interval [18.6%, 34.2%]). HINT sentences in noise demonstrated improvement from pre-op to 3 months (35.1%; 95% confidence interval [30.0%, 40.3%]) and from 3 to 12 months (15.5%; 95% confidence interval [7.2%, 23.8%]).

Conclusions: Mean speech recognition scores demonstrate significant improvement within the first 3 months, with no further statistically significant improvement after 3 months. However, large individual variation should be expected and future research is needed to explain the sources of these individual differences.

Key Words: cochlear implants, longitudinal, meta-analysis, postlingual hearing loss, speech recognition, systematic review.

Laryngoscope, 00:1-11, 2022

Check for updates

INTRODUCTION

Cochlear implants (CIs) are Food and Drug Administration approved devices for the treatment of moderateto-profound sensorineural hearing loss in adults.¹ During the CI evaluation process to determine candidacy, patients are counseled regarding the magnitude and progression of communication improvement after implantation. This involves setting realistic expectations on their ability, for example, to understand speech when conversing in noisy listening environments. Patients whose post-

DOI: 10.1002/lary.30354

implantation experiences fall in line with their preimplantation expectations report improved CI-related quality of life (QOL), however, this counseling process is not standardized and research is required to guide informed expectation setting.^{2,3}

Speech recognition is one of the primary outcome measures for cochlear implantation.⁴ In general, speech recognition improves rapidly in the early postimplantation period and stabilizes over time.⁵⁻¹⁰ Following implantation, patients continue to demonstrate performance improvements with improved loudness tolerance, expanded electrical dynamic range, and regular device adjustments.¹¹⁻¹³ Patients must also learn to interpret the degraded auditory signal from the CI and recognize sounds as speech and words. At some time point following implantation, speech recognition no longer improves as the limits of the relatively poor quality of the auditory input provided by the CI are reached.¹⁴ In addition, chronic hearing deprivation weakens the connectivity of central neuronal networks in the auditory cortex. This is especially limiting for older adults with reduced cortical plasticity and a limited capacity to rebuild lost connections.^{15,16}

From the Department of Otolaryngology–Head and Neck Surgery (C.M., J.F., S.A.N., K.C.S.-L., E.L.C., T.A.M., J.R.D., T.R.M.), Medical University of South Carolina, Charleston, South Carolina, U.S.A.

Additional supporting information may be found in the online version of this article.

Triological Society Meeting oral presentation at Coronado, California, U.S.A. on January 22nd, 2022.

Editor's Note: This Manuscript was accepted for publication on July, 26, 2022.

The authors have no funding, financial relationships, or conflicts of interest to disclose.

Send correspondence to Theodore R. McRackan, MD, MSCR, 135 Rutledge Ave, MSC-550, Charleston, SC 29425. E-mail: mcrackan@musc.edu

Patterns of change in speech recognition scores have been studied extensively; however, there is limited agreement on the timing of these changes. In addition, few studies have explored the direction and magnitude of speech recognition scores following cochlear implantation and how early scores impact long-term outcomes. Current studies have noted that speech recognition scores could reach a plateau anywhere from 3 months to over 3 years post-implantation, however, there is much variability in these estimates.^{6,8-10,17} The vast majority of these studies are single-center retrospective studies with small study populations (fewer than 150 participants). In addition, most studies tend to report speech recognition changes based on statistical differences, but fail to consider whether the observed change is beyond the measurement error of the speech recognition test.¹⁸

The aim of this systematic review and meta-analysis is to examine patterns of change and determine the timing of plateau for speech recognition scores in the first 2 years following CI activation in adults with postlingual hearing loss. The study also examines how different speech recognition materials and listening conditions impact patterns of change in speech recognition scores. Systematic review and meta-analysis address the limitations of individual studies and is able to demonstrate associations in a large study population by aggregating data from existing smaller studies to maximize statistical power and more precisely measure intervention effects.^{19,20} In addition, variability in outcome reporting between studies can be analyzed and addressed. With a better understanding of when and to what extent speech recognition scores change after CI, providers can offer better pre-operative counseling and guidance on how much speech recognition might improve after implantation and when patients are likely to achieve these outcomes. These results could also provide clinicians with a more specific timeframe of when to seek additional support for CI users who do not achieve the expected goals.

MATERIALS AND METHODS

Search Criteria

The research objective for this systematic review and metaanalysis was developed in accordance to population, intervention, vomparison, outcome (PICO) criteria.²¹ The study seeks to explore speech recognition score changes (outcome) following cochlear implantation (intervention) across pre- and different post-implantation timepoints (comparison) in adults with postlingual hearing loss (population). To identify studies for inclusion in this review, detailed search strategies were developed for the following three databases: PubMed (U.S. National Library of Medicine, National Institutes of Health), Scopus (Elsevier), and Embase (Elsevier). Databases were searched from the date of inception through January 2022. Search strategies were developed using combinations of subject headings and MeSH terms (e.g., "cochlear implant" [MeSH Terms], "speech recognition" [MeSH Terms], and "postlingual" [MeSH Terms]) for topics related to speech recognition outcomes after CI in adults with postlingual hearing loss. The PubMed search strategy was modified for the other two databases, replacing MeSH terms with appropriate subject headings, when available, and maintaining similar keywords. Detailed search strategies for each database

are listed in Appendix S1. To identify additional articles, the reference lists of relevant articles were hand-searched. References were exported into the review management software, Covidence (Veritas Health Innovation Ltd, Melbourne, Australia), for study selection. Reporting of systematic review and meta-analysis results was performed in accordance with PRISMA reporting guidelines.²²

Selection Criteria

Studies assessing long-term speech recognition outcomes in adults with postlingual hearing loss were included. Studies were considered for inclusion if they were: (1) double- or single-blinded randomized controlled trials, (2) double- or single-blinded randomized comparison trials, (3) non-randomized controlled trials, and (4) prospective or retrospective observational studies with pre-operative and at least two follow-up speech recognition data points at either 3, 6, 12, or 24 months post-implantation. Exclusion criteria included: pediatric study population, non-English language, non-human studies, review articles, case reports, case series (<10 patients), duplicates, inaccessible articles, incomplete or missing statistical data (e.g., did not report mean and standard deviation), articles studying bilaterally implanted patients, participants whose hearing loss occurred prelingually, and nonreporting of pre-operative or post-operative speech recognition outcomes. Abstracts were first independently assessed by two authors (C.M. and J.F.) to identify all articles that met the inclusion criteria. Conflicts were resolved by a third author (S.A.N.).

Included articles were critically appraised to assess the level of evidence using the Oxford Center for Evidence-Based Medicine criteria.²³ The risk of bias was assessed according to the Cochrane Handbook for Systematic Reviews of Interventions version 6.0.24 The Risk of Bias in Non-Randomized Studies-of Interventions tool was used specifically to evaluate nonrandomized studies.²⁵ Two authors (C.M. and J.F.) performed a pilot assessment on three studies to check for consistency of assessment. Both then performed independent risk assessments on the remaining studies. All disagreements were resolved by the way of discussion with a third author (S.A.N.). Risk of bias items included the following: bias due to confounding, bias in the selection of participants into the study, bias in classification of interventions, bias due to deviations from intended interventions, bias due to missing data, bias in the measurement of outcomes, and bias in the selection of the reported results. The risk of bias for each aspect was graded as low, unclear, or high.

Data Extraction

Data extraction was performed by two authors (c.M. and J. F.) independently. Data extracted from studies included: author, year of publication, patient demographics (age, sex), etiology of hearing loss, age at hearing loss onset, duration of hearing loss prior to implantation, age at implantation, history and duration of hearing aid use, follow-up period, and speech recognition outcomes at follow-up. Post-implantation speech recognition scores, including open-set word recognition in quiet and open-set sentence recognition in quiet and in noise, were collected as the primary outcome measures for meta-analysis. In instances of incomplete data, two attempts were made to contact the primary author via email for clarification or sharing of primary data.

Statistical Analysis

Continuous variables were summarized using means and standard deviations. Pre-operative characteristics of the study population were analyzed using a meta-analysis of single proportions for gender and a meta-analysis of single means for age, which were reported as an overall mean with a 95% confidence interval. To produce overall estimates of speech recognition at each time point (pre-op, 3, 6, 12, 24 months), a metaanalysis of single means was performed with Open Meta Analyst (Brown University, 2014). These estimators were used to examine the change over time for each speech recognition measure.

To determine statistically significant differences in speech recognition between two-time points (e.g., pre-op vs. 3 months, 3 vs. 6 months, etc.), the meta-analysis of continuous measures for mean difference was performed using Cochrane Review Manager (RevMan) version 5.4 (The Cochrane Collaboration, 2020). The mean, standard deviation, and sample size of each included study from two separate time points were used for each comparison. A DerSimonian-Laird random-effects model was used, which provides a more conservative estimate compared to a fixed-effects model, but better accounts for between-study variability in subject sampling and heterogeneity. Heterogeneity was assessed using the I^2 -statistic and reported as being absent, mild, moderate, or high. Publication bias of included studies was assessed by examining generated funnel plots for asymmetry and performing Egger's linear regression test. A p-value of <0.05 was considered to indicate a statistically significant difference for all statistical tests.

For the current study, significant changes in speech recognition scores between two time periods were defined as those that demonstrated both (1) statistically significant differences and (2) change beyond the previously established 95% confidence interval for word or sentence recognition tests.^{18,26,27} Each response to an item from a speech recognition test list produces a binomial outcome (correct or incorrect), with the final result expressed as a percentage of correct responses from the list. Based on this, speech recognition scores follow a binomial model with each outcome centered within a 95% confidence interval. Score changes that fall within this measurement error are likely due to chance as opposed to significant improvement in speech recognition ability.²⁶ These comparisons were made using group mean estimates at each timepoint obtained by meta-analysis of single means. A large number of patients in this meta-analysis ensure that changes within the measurement error for word and sentence recognition are not erroneously considered true differences solely based on statistical significance.²⁸

RESULTS

A total of 1544 unique publications were collected in the search. Screening by title and abstract excluded 1263 articles. Full-text review of the remaining articles excluded 259 publications, resulting in 22 articles being included in the final analysis.^{29–50} The search process is summarized in Figure 1. The risk of bias graph is presented as percentages across all included studies and summarized in Figure S1. Bias across all studies ranged from low to high. The included studies were all published between 2001 and 2021 The characteristics of the



Fig. 1. Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) flow diagram. [Color figure can be viewed in the online issue, which is available at www.laryngoscope.com.]

				S	TABLE Study De	E I. esign.			
Author (Year)	Study Design	Patients (n)	Mean Age at CI in Years (SD)	Male (n)	Female (n)	Mean Age at HL Onset in Years (SD)	Mean Duration of HL in Years* (SD)	Speech Instruments Tested	Follow-Up Length in Months
Adunka (2008)	RCo	50	62.3	17	33	52.2	9.9	Words: CNC	12
Bergman (2020)	PCo	40	71 (11.3)	16	24	-	-	Sentences: CUNY, HINT Words: Unspecified	36
Borger (2015)	PCo	10	55.9 (11.1)	4	6	-	3.6 (3.1)	Words: Fournier List	12
Cooper (2020)	RCo	14	61.7 (15.7)	8	6	-	-	Sentences: Unspecified Sentences: HINT	12
Dalbert (2016)	RCo	91	-	41	50	-	22	Words: Freiburger	18
Deep (2021)	RCo	53	53.2 (11.9)	23	30	49.2 (13.1)	4 (7.8)	Words: CNC	24
Firszt (2018)	PCo	47	62.8 (14.6)	27	20	-	-	Words: CNC	12
Friedland (2021)	RCo	50	69.7 (13.7)	33	17	-	-	Sentences: TIMIT Words: CNC	24
Grisel (2021)	RCo	805	-	-	-	-	-	Sentences: AzBio Words: CNC	24
Kelsall (2021)	PCo	100	-	63	37	-	8 (6)	Words: CNC	12
Knopke (2019)	PCo	86	76.2	41	45	-	17.3	Sentences: AzBio Words: Freiburger	12
Knopke (2021)	PCo	49	67.3 (8.7)	20	29	-	22.9 (22.9)	Words: Freiburger	12
Lee (2021)	RCo	18	58.8 (12)	8	10	51.6 (16.2)	7.3 (11.9)	Words: Unspecified	12
Moberly (2020)	PCo	19	67.2 (10.4)	12	7	-	31.3 (18.6)	Sentences: Unspecified Words: CNC	6
Plontke (2020)	PCo	16	55 (14)	10	6	-	7.2 (6)	Sentences: AzBio Words: Freiburger	12
Runge (2016)	PCo	38	63.6	-	-	40.8	22.8	Words: CNC	12
Schramm (2020)	PCo	31	-	19	12	-	8.6	Sentences: AzBio Sentences: HINT	12
Sladen (2017)	PCo	61	67	22	39	-	12.6 (9.2)	Words: CNC	12
Sturm (2021)	RCo	119	-	52	67	-	-	Words: CNC	24
Wang (2010)	RCo	50	45.8	14	36	-	-	Sentences: CUNY, HINT	48
Yang (2016)	RCo	95	48 (14)	58	37	-	13 (13)	Words: Unspecified	36
Zwolan (2001)	PCo	112	57.3	-	-	45.7	11.7	Sentences: Unspecified Words: CNC Sentences: CID, HINT	6

*Duration of hearing loss prior to implantation.

CI = cochlear implant; CID = Central Institute for the Deaf; CNC = Consonant Nucleus Consonant; CUNY = City University of New York; HINT = hearing in noise test; HL = hearing loss; PCo = prospective cohort study; RCo = retrospective cohort study; TIMIT = Texas Instruments and Massachusetts Institute of Technology.

included studies are shown in Table I. Based on the Oxford Center for Evidence-Based Medicine criteria, all studies were considered level 3 evidence.²³

Patient Characteristics

In total, 1954 patients are represented in the included studies. Sex was reported in 19 studies (n = 999) with 488 men and 511 women; based on the meta-analysis of single proportions, the overall proportion of men was 47.6% (95% confidence interval [42.7%, 52.4%]) and of women was 52.4% (95% confidence interval [47.6%, 57.3%]) (Figures S2 and S3). Mean age at implantation was reported in 17 studies (n = 808) and ranges from 45.8 to 76.2 years with an overall mean age of 58.5 years (95% confidence interval [53.9, 63.2]) based on a meta-analysis of single means (Figure S4). The mean age of hearing loss onset was reported by five studies (n = 271) and ranges

from 40.8 to 52.2 years with an overall mean age of 46.8 years (95% confidence interval [43.8, 49.8]) based on a meta-analysis of single means (Figure S5). Mean duration of hearing loss prior to implantation as reported by 15 studies (n = 809) ranged from 3.6 to 31.3 years with an overall mean of 12.3 years (95% confidence interval [9.2, 15.4]) based on a meta-analysis of single means (Figure S6). Hearing aid use was rarely reported; three studies (n = 179) reported that 77.4% (24 of 31 patients), 33% (31 of 95 patients), and 41.5% (22 of 53 patients) had used hearing aids prior to implantation.^{37,40,42} The length of follow-up varied greatly across all studies and ranged from 6 to 48 months post-implantation.

Speech Recognition Score Changes

Mean speech recognition scores were reported for word recognition in quiet (18 studies, n = 1860), sentence

TABLE II. Meta-Analysis of Single Means for Words In Quiet, Sentences In Quiet, and Sentences In Noise at Each Time Point. Words In Quiet Score Sentences In Quiet Score Sentences In Noise Score

ollow-Up	Mean (%)	95% CI (%)	SE (%)	Ν	Mean (%)	95% CI (%)	SE (%)	N	Mean (%)	95% CI (%)	SE (%)	Ν
Pre-op	9.8	(7.6, 12.0)	1.1	1675	18.9	(13.9, 23.8)	2.5	491	14.8	(11.2, 18.4)	1.8	275
3 Months	48.4	(45.5, 51.5)	1.6	1161	70.2	(62.2, 78.1)	4.1	385	46.2	(40.0, 52.4)	3.2	304
6 Months	53.7	(50.5, 56.9)	1.6	1173	74.1	(67.5, 80.6)	3.3	482	50.8	(45.1, 56.6)	2.9	351
12 Months	60.0	(56.4, 63.6)	1.8	1073	80.9	(71.0, 90.9)	5.1	295	62.1	(48.3, 76.0)	7.1	191
24 Months	60.3	(53.9, 66.8)	3.3	529	83.8	(74.9, 92.6)	4.5	185	-	-	-	-

CI = confidence interval: N = sample size: SE = standard error.

recognition in quiet (12 studies, n = 541), and sentence recognition in noise at +10 dB signal-to-noise ratio (SNR) (6 studies, n = 275). Outcomes using sentence recognition in noise at +5 dB SNR were not included as only one study using this measure met inclusion criteria.43 Table II and Figure 2 summarize the mean estimates as determined by a meta-analysis of single means, 95% confidence interval, and pooled standard error for all speech recognition scores at each time point. Forest plots for meta-analysis of single means for words in quiet, sentences in quiet, and sentences in noise are included in Figures S7–S9, respectively. There were no available data on sentence recognition in noise (+10 dB SNR) beyond 12 months. Higher mean speech recognition values (as compared to pre-op) were observed at each subsequent follow-up through the first 2 years for words and sentence recognition in quiet, and through the first 12 months for sentence recognition in noise. The significance of these changes is discussed later.

Meta-Analysis Results

The meta-analysis of continuous measures for mean difference was used to detect significant changes in mean scores between two-time points (Table III). Examination



Fig. 2. Meta-analysis of single means and pooled standard error for words in quiet, sentences in quiet, and sentences in noise for preimplant (0) and various post-implantation time points. [Color figure can be viewed in the online issue, which is available at www. laryngoscope.com.]

of funnel plots showed no evidence of significant publication bias (Figures S10-S12). Forest plots for words in quiet are shown in Figure 3, and for sentences in quiet and sentences in noise in Figures S13 and S14, respectively. Our findings demonstrated that significant improvements in mean words in quiet, sentences in quiet, and sentences in noise scores occurred from pre-op to 3 months post-op. Mean speech recognition scores continued to demonstrate a statistical difference between time points (as defined previously) through 2 years for word recognition, 12 months for sentence recognition in quiet, and 6 months for sentence recognition in noise. However, these changes were not beyond the preceding mean score's 95% confidence interval and thus not considered significant. Further analysis of 3- to 12-month changes in mean score also demonstrated non-significant increases. Thus, based on mean scores, significant improvement in speech recognition occurred within the first 3 months following implantation, with no additional statistically significant improvement after 3 months.

Meta-analysis was also performed on speech recognition scores to determine whether post-implantation score improvement trajectories varied depending on the specific test instrument (Table IV). Forest plots for Consonant Nucleus Consonant (CNC) word recognition are shown in Figure 4 and for Hearing in Noise Test (HINT) in quiet, AzBio sentences in quiet, and HINT sentences in noise in Figures S15-S17, respectively. There were insufficient data to perform similar analyses for AzBio sentences in noise. The post-implantation mean score improvement for all word recognition material and for CNC word recognition was similar with the only significant improvement occurring from pre-op to 3 months post-CI. For sentence recognition in quiet, notable differences were seen between the mean score improvement trajectories as measured by HINT compared to AzBio sentences. Both instruments demonstrated significant improvements from pre-op to 3 months. HINT mean scores continued to show statistical differences from 3 to 6 months, but this was within the measurement error of the speech material. AzBio scores failed to reach statistical significance past 3 months. For sentence recognition in noise at +10 dB SNR, HINT sentences demonstrated significant improvement from 3 to 12 months.

As noted earlier, all instrument scores demonstrated significant improvements from pre-op to 3 months. As

TABLE III. Meta-Analysis of Continuous Measures for Words In Quiet, Sentences In Quiet, and Sentences In Noise.

	Mean Difference of Perc	entage (%) Correct (95%	6 Confidence Interval)		
Speech Recognition Test	Pre-Op to 3 Months	3 to 6 Months	6 to 12 Months	3 to 12 Months	12 Months to 2 Years
Words (in quiet)	37.4 (34.7, 40.7)	4.2 (3.0, 5.5)	4.2 (2.9, 5.5)	7.7 (6.4, 9.1)	2.6 (0.1, 5.0)
Sentences (in quiet)	49.4 (44.9, 53.9)	5.3 (3.5, 7.1)	5.3 (3.4, 7.2)	11.8 (9.7, 13.8)	0.0 (-2.7, 2.7)
Sentences (in noise)	30.8 (25.2, 36.4)	5.4 (1.5, 9.2)	4.6 (-0.3, 9.5)	14.0 (8.5, 19.5)	-

Light shade, Statistically significant change beyond the preceding score's measurement error interval; medium shade, statistically significant change within the preceding score's measurement error interval; dark shade, non-statistically significant change.

A	3-	month		P	ге-ор			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	IV, Random, 95% Cl
1.1.1 Pre-op vs. 3 Mo	nth								
Adunka 2008	42.9	18.6	29	17.9	11.4	29	5.1%	25.00 [17.06, 32.94]	
Deep 2021	50.3	20	53	8.7	15	53	5.7%	41.60 [34.87, 48.33]	
Grisel 2021	49.3	24.3	529	14.8	17.2	805	7.6%	34.50 [32.11, 36.89]	-
Kelsall 2021	56.3	22	96	14.6	11.6	96	6.5%	41.70 [36.72, 46.68]	
Lee 2021	56.1	28.9	18	31.3	25	18	2.1%	24.80 [7.15, 42.45]	
Moberly 2020a	56	16.7	19	19.2	20.4	19	3.5%	36.80 [24.95, 48.65]	·
Moberly 2020b	59.5	23.5	19	17.4	29.7	19	2.2%	42.10 [25.07, 59.13]	· · · · · · · · · · · · · · · · · · ·
Moberly 2020c	66	10.1	19	20	19.9	19	4.2%	46.00 [35.97, 56.03]	
Plontke 2020	56	24	16	7.5	18	16	2.7%	48.50 [33.80, 63.20]	
Runge 2016	49	3.8	37	5.6	1.4	37	7.8%	43.40 [42.10, 44.70]	-
Sturm 2021a	40	16.5	14	2.8	4.7	14	4.6%	37.20 [28.21, 46.19]	
Sturm 2021b	41.3	19.5	16	7.5	11.5	16	3.8%	33.80 [22.71, 44.89]	
Sturm 2021c	42.8	22	16	7	12.4	17	3.4%	35.80 [23.51, 48.09]	
Sturm 2021d	50.9	18.2	16	5.5	8.6	16	4.2%	45.40 [35.54, 55.26]	
Sturm 2021e	49.9	19.9	15	8.5	8.6	18	3.9%	41.40 [30.57, 52.23]	
Sturm 2021f	34.1	16.6	15	4.3	4.9	16	4.7%	29.80 [21.06, 38.54]	
Sturm 2021g	31.4	17.9	22	7.1	11.3	22	4.7%	24.30 [15.45, 33.15]	
Yang 2016a	49.9	30.5	46	9.5	12.9	46	4.4%	40.40 [30.83, 49.97]	
Yang 2016b	53.8	31	19	10	13.8	19	2.6%	43.80 [28.54, 59.06]	
Yang 2016c	59.7	27.2	18	10.6	12.1	18	2.9%	49.10 [35.35, 62.85]	
Yang 2016d	47.8	33.8	12	18.8	13.8	12	1.6%	29.00 [8.34, 49.66]	
Zwolan 2001a	36.2	22.8	53	1.4	2.5	48	5.9%	34.80 [28.62, 40.98]	
Zwolan 2001b	40.3	22.7	54	3.1	5.4	56	5.9%	37.20 [30.98, 43.42]	
Subtotal (95% CI)			1151			1429	100.0%	37.68 [34.70, 40.65]	•
Heterogeneity: $\tau^2 = 2$	8.89;χ ² :	= 93.2	1, <i>df</i> = 1	22 (p < 1	0.0000	01);/²=	76%		
Test for overall effect:	Z= 24.8	34 (p <	0.000	01)					
									-50 -25 0 25 50
									Favours pre-op Favours 3 month
В	6 1	nonth		3 1	nonth			Mean Difference	Mean Difference
Study or Subaroup	Mean	SD	Total	Mean	SD	Total	Weight	IV. Random, 95% Cl	IV. Bandom, 95% Cl
stady of stangioup	mount		. otal	mount	55		. reight	,	Te, rundon, oo // or

Church and Carl and an		00			00		187-1-1-4	D/ Developer 05% Cl	N/ Devidence OFA/ Cl
Study of Subgroup	mean	SD	Total	mean	SD	Total	weight	IV, Random, 95% CI	IV, Random, 95% CI
Adunka 2008	51.4	16.6	29	42.9	18.6	29	2.0%	8.50 [-0.57, 17.57]	<u> </u>
Borger 2015	62	21.5	10	68	19.9	10	0.5%	-6.00 [-24.16, 12.16]	
Grisel 2021	52.7	22.9	399	49.3	24.3	529	17.8%	3.40 [0.34, 6.46]	
Kelsall 2021	60.9	21.1	96	56.3	22	96	4.5%	4.60 [-1.50, 10.70]	+
Lee 2021	64.6	26.4	16	56.1	28.9	18	0.5%	8.50 [-10.09, 27.09]	
Moberly 2020a	59.2	18.7	19	56	16.7	19	1.3%	3.20 [-8.07, 14.47]	
Moberly 2020b	65.4	22.9	19	59.5	23.5	19	0.8%	5.90 [-8.85, 20.65]	
Moberly 2020c	71.7	12.6	19	66	10.1	19	3.1%	5.70 [-1.56, 12.96]	
Plontke 2020	62	27	16	56	24	16	0.5%	6.00 [-11.70, 23.70]	
Runge 2016	52.9	3.8	37	49	3.8	37	55.4%	3.90 [2.17, 5.63]	
Sturm 2021a	50.3	17.7	14	40	16.5	14	1.0%	10.30 [-2.38, 22.98]	
Sturm 2021b	49.7	19.7	15	41.3	19.5	16	0.9%	8.40 [-5.41, 22.21]	
Sturm 2021c	43.3	20	16	42.8	22	16	0.8%	0.50 [-14.07, 15.07]	
Sturm 2021d	58.5	19.5	16	50.9	18.2	16	1.0%	7.60 [-5.47, 20.67]	
Sturm 2021e	48.7	20.5	15	49.9	19.9	15	0.8%	-1.20 [-15.66, 13.26]	
Sturm 2021f	35.5	13.3	15	34.1	16.6	15	1.4%	1.40 [-9.36, 12.16]	
Sturm 2021g	37.5	20.5	19	31.4	17.9	22	1.2%	6.10 [-5.77, 17.97]	
Yang 2016a	54	32.3	46	49.9	30.5	46	1.0%	4.10 [-8.74, 16.94]	
Yang 2016b	57	28.9	19	53.8	31	19	0.5%	3.20 [-15.86, 22.26]	
Yang 2016c	56.9	31.1	18	59.7	27.2	18	0.5%	-2.80 [-21.89, 16.29]	
Yang 2016d	58.6	34.2	12	47.8	33.8	12	0.2%	10.80 [-16.41, 38.01]	
Zwolan 2001a	37.8	22.7	56	36.2	22.8	53	2.3%	1.60 [-6.95, 10.15]	
Zwolan 2001b	56.6	24.3	56	40.3	22.7	54	2.2%	16.30 [7.52, 25.08]	
Total (05% CI)			077			1100	100.0%	4 24 [2 06 5 53]	▲
Total (35% CI)			911			1100	100.0%	4.24 [2.90, 5.55]	· · · · ·
Heterogeneity: $\tau^2 = 0$.	$.00; \chi^2 =$	14.00	dt = 2	2(p = 0)	.90);/*	= 0%			-50 -25 0 25 50
l est for overall effect:	∠ = 6.48	p < (p <	1.0000,	0					Favours 3 month Favours 6 month

Fig. 3. Forest plots for meta-analysis of continuous measures for mean difference of words in quiet from (A) pre-op to 3 months, (B) 3 to 6 months, (C) 6 to 12 months, (D) 3 to 12 months, and (E) 12 months to 2 years. [Color figure can be viewed in the online issue, which is available at www.laryngoscope.com.]

С	12	month	1	6-	month			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl
Adunka 2008	59	16.6	29	51.4	16.6	29	2.3%	7.60 [-0.94, 16,14]	
Borger 2015	78	12.3	10	62	21.5	10	0.7%	16.00 (0.65, 31,35)	
Dalbert 2016a	71	25	46	65	25	46	1.6%	6.00 [-4.22, 16.22]	
Dalbert 2016b	79	22	50	67	24	50	2.0%	12.00 [2.98, 21.02]	
Firszt 2018	51	22	39	49	20	39	1.9%	2.00 [-7.33, 11.33]	
Grisel 2021	55.8	23.4	426	52.7	22.9	399	16.6%	3.10 [-0.06, 6.26]	+-
Kelsall 2021	65.2	18.8	91	60.9	21.1	96	5.1%	4.30 [-1.42, 10.02]	+
Knopke 2019a	35.4	25.5	62	35.2	27.3	62	1.9%	0.20 [-9.10, 9.50]	
Knopke 2019b	32.1	25.1	24	34.2	27.2	24	0.8%	-2.10 [-16.91, 12.71]	
Knopke 2021	39.2	28.2	49	36.1	31.3	49	1.2%	3.10 [-8.70, 14.90]	
Lee 2021	61.9	26.8	13	64.6	26.4	16	0.4%	-2.70 [-22.18, 16.78]	
Plontke 2020	75	19	16	62	27	16	0.6%	13.00 [-3.18, 29.18]	
Runge 2016	56.8	3.9	37	52.9	3.8	37	53.8%	3.90 [2.15, 5.65]	
Sladen 2017	67	19	61	56	24	61	2.8%	11.00 [3.32, 18.68]	
Sturm 2021a	53.4	21.3	13	50.3	17.7	14	0.8%	3.10 [-11.73, 17.93]	
Sturm 2021b	48	18.4	8	49.7	19.7	15	0.6%	-1.70 [-17.89, 14.49]	
Sturm 2021c	51.8	23.2	8	43.3	20	16	0.5%	8.50 [-10.33, 27.33]	
Sturm 2021d	59.2	17.4	15	58.5	19.5	16	1.0%	0.70 [-12.29, 13.69]	
Sturm 2021e	51.9	16	13	48.7	20.5	15	0.9%	3.20 [-10.34, 16.74]	
Sturm 2021f	39.1	16.1	13	35.5	13.3	15	1.4%	3.60 [-7.44, 14.64]	
Sturm 2021g	37.8	13.3	9	37.5	20.5	19	1.0%	0.30 [-12.37, 12.97]	
Yang 2016a	61	29.7	46	54	32.3	46	1.0%	7.00 [-5.68, 19.68]	
Yang 2016b	67.2	27.5	19	57	28.9	19	0.5%	10.20 [-7.74, 28.14]	
Yang 2016c	62.1	25.3	18	56.9	31.1	18	0.5%	5.20 [-13.32, 23.72]	
Yang 2016d	58.2	34.9	12	58.6	34.2	12	0.2%	-0.40 [-28.05, 27.25]	
Total (95% CI)			1127			1139	100.0%	4.18 [2.90, 5.47]	•
Heterogeneity: $\tau^2 = 0$.00; χ ² =	14.87,	df = 24	(p = 0.	92);/²	= 0%			
Test for overall effect	Z= 6.37	p < 0	0.00001	1)					Favours 6 month Favours 12 month
D									
_	12	Month		31	Month			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	IV, Random, 95% Cl
Adunka 2008	59	16.6	29	42.9	18.6	29	2.2%	16.10 [7.03, 25.17]	

Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	IV, Random, 95% Cl
Adunka 2008	59	16.6	29	42.9	18.6	29	2.2%	16.10 [7.03, 25.17]	
Borger 2015	78	12.3	10	68	19.9	10	0.9%	10.00 [-4.50, 24.50]	
Deep 2021	54.3	21	41	50.3	20	53	2.6%	4.00 [-4.39, 12.39]	
Grisel 2021	55.8	23.4	426	49.3	24.3	529	19.6%	6.50 [3.46, 9.54]	+
Kelsall 2021	65.2	18.8	91	56.3	22	96	5.3%	8.90 [3.04, 14.76]	
Lee 2021	61.9	26.8	13	56.1	28.9	18	0.5%	5.80 [-13.96, 25.56]	2
Plontke 2020	75	19	16	56	24	16	0.8%	19.00 [4.00, 34.00]	
Runge 2016	56.8	3.9	37	49	3.8	37	58.8%	7.80 [6.05, 9.55]	
Sturm 2021a	53.4	21.3	13	40	16.5	14	0.9%	13.40 [-1.05, 27.85]	
Sturm 2021b	48	18.4	8	41.3	19.5	16	0.7%	6.70 [-9.23, 22.63]	
Sturm 2021c	51.8	23.2	8	42.8	22	16	0.5%	9.00 [-10.36, 28.36]	
Sturm 2021d	59.2	17.4	15	50.9	18.2	16	1.2%	8.30 [-4.23, 20.83]	
Sturm 2021e	51.9	16	13	49.9	19.9	15	1.0%	2.00 [-11.31, 15.31]	
Sturm 2021f	39.1	16.1	13	34.1	16.6	15	1.2%	5.00 [-7.13, 17.13]	
Sturm 2021g	37.8	13.3	9	31.4	17.9	22	1.4%	6.40 [-5.07, 17.87]	
Yang 2016a	61	29.7	46	49.9	30.5	46	1.2%	11.10 [-1.20, 23.40]	
Yang 2016b	67.2	27.5	19	53.8	31	19	0.5%	13.40 [-5.23, 32.03]	
Yang 2016c	62.1	25.3	18	59.7	27.2	18	0.6%	2.40 [-14.76, 19.56]	
Yang 2016d	58.2	34.9	12	47.8	33.8	12	0.2%	10.40 [-17.09, 37.89]	
Total (95% CI)			837			997	100.0%	7.77 [6.42, 9.11]	•
Heterogeneity: $\tau^2 = 0$.	.00; x ² =	9.76, 0	df = 18	(p = 0.9)	94);/ ² =	0%			-50 -25 0 25 50
Test for overall effect:	Z = 11.3	2 (p <	0.0000	01)					Favours 3 month Favours 12 month

Е

_	2	Year		12	Month	1		Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl
Dalbert 2016a	72	25	46	71	25	46	5.8%	1.00 [-9.22, 11.22]	
Dalbert 2016b	83	17	50	79	22	50	10.2%	4.00 [-3.71, 11.71]	
Deep 2021	61.8	20	27	54.3	21	41	6.2%	7.50 [-2.41, 17.41]	
Friedland 2021a	53.1	21.5	30	55.8	22.7	30	4.8%	-2.70 [-13.89, 8.49]	
Friedland 2021b	54.9	14.8	20	53	13.4	20	7.9%	1.90 [-6.85, 10.65]	
Grisel 2021	57.3	22.6	176	55.8	23.4	426	37.7%	1.50 [-2.51, 5.51]	+
Knopke 2021	38.7	24.2	49	39.2	28.2	49	5.6%	-0.50 [-10.90, 9.90]	
Sturm 2021a	60.7	12.8	6	53.4	21.3	13	2.5%	7.30 [-8.16, 22.76]	
Sturm 2021b	58.8	18.4	10	59.2	17.4	15	2.9%	-0.40 [-14.81, 14.01]	
Sturm 2021c	58.8	22.2	10	51.9	16	13	2.3%	6.90 [-9.38, 23.18]	
Sturm 2021d	52.2	12.3	10	39.1	16.1	13	4.5%	13.10 [1.49, 24.71]	
Yang 2016a	63.3	25.7	46	61	29.7	46	4.7%	2.30 [-9.05, 13.65]	
Yang 2016b	70.6	24.8	19	67.2	27.5	19	2.2%	3.40 [-13.25, 20.05]	
Yang 2016c	58.1	29.7	18	62.1	25.3	18	1.9%	-4.00 [-22.02, 14.02]	
Yang 2016d	62.3	32.2	12	58.2	34.9	12	0.8%	4.10 [-22.77, 30.97]	
Total (95% CI)			529			811	100.0%	2.55 [0.09, 5.01]	•
Heterogeneity: $\tau^2 = 0.1$	00; $\chi^2 =$	7.15, (df = 14	(p = 0.9)	3);/ ² =	0%			
Test for overall effect:	Z= 2.03	p = (p = 0)	0.04)						Favours 12 month Favours 2 year

Fig. 3 (Continued)

TABLE IV.
Meta-Analysis of Continuous Measures for Different Speech Recognition Instruments.

	Mean Difference of Percer	ntage (%) Correct (95% Confide	ence Interval)	
Speech Recognition Instrument	Pre-op to 3 Months	3 to 6 Months	6 to 12 Months	3 to 12 Months
CNC words (in quiet)	37.1 (33.8, 40.4)	4.3 (3.0, 5.6)	3.9 (2.6, 5.3)	7.6 (6.2, 9.0)
HINT sentences (in quiet)	46.5 (37.0, 56.0)	5.7 (0.1, 11.4)	4.4 (-1.1, 9.9)	11.5 (4.0, 18.9)
AzBio sentences (in quiet)	45.9 (44.2, 47.5)	3.4 (-1.9, 8.6)	-	-
HINT sentences (in noise)	35.1 (30.0, 40.3)	6.1 (0.1, 12.1)	7.4 (-0.9, 15.6)	15.5 (7.2, 23.8)
AzBio sentences (in noise)	26.4 (18.6, 34.2)	4.9 (-0.2, 9.9)	-	-

Light shade, Statistically significant change beyond the preceding score's measurement error interval; medium shade, statistically significant change within the preceding score's measurement error interval; dark shade, non-statistically significant change.

CNC = Consonant Nucleus Consonant; HINT = hearing in noise test.

expected, this time period also represents the highest degree of between-study heterogeneity. From pre-op to 3 months, all study comparisons demonstrated moderate-to-high degrees of heterogeneity based on the I^2 -statistic (range, 52%–81%) except those examining AzBio sentences in quiet and HINT sentences in quiet, both without heterogeneity ($I^2 = 0\%$). None of the study comparisons demonstrated between-study heterogeneity beyond 3 months ($I^2 = 0\%$) except those examining AzBio sentences in quiet, which demonstrated moderate heterogeneity ($I^2 = 59\%$) from 3 to 12 months. This indicates that there is a wide range of changes in speech recognition scores from pre-op to 3 months, suggesting that although significant improvements are expected based on mean score, individual patient performance varies.

DISCUSSION

In the current study, pre- and post-CI speech recognition data from adults with postlingual hearing loss from multiple studies were analyzed to identify longitudinal patterns of change. When grouped by speech recognition measure, significant improvements in scores were observed only in the immediate post-implantation period from preop to 3 months (Table III). Statistically significant differences were detected beyond 3 months for each speech recognition measure, but these differences were not beyond the measurement error of the speech material and, therefore, were not considered significant changes.^{26,27} No statistically significant changes in speech recognition scores were observed from 3 to 6 months, 6 to 12 months, or 3 to 12 months.

Similar results were found when studies were grouped by the speech recognition material. All tests demonstrated significant improvement from pre-op to 3 months, but no significant changes beyond 3 months on consecutive testing intervals were observed (Table IV). Of note, from 3 to 12 months, only scores for HINT sentences in noise demonstrated significant improvement, whereas scores for HINT sentences in quiet showed no significant change. These differences reflect how the testing environment can impact speech recognition ability and highlight the potential importance of speech recognition testing in multiple settings. In CI users, scores obtained with background noise generally demonstrate more modest improvements compared to scores obtained in quiet.^{51,52} In addition, scores obtained in noise are also known to improve at a slower rate compared to scores obtained in quiet.^{35,37,41} A major motivator for patients pursuing CIs is the desire to improve communication and social independence, especially in challenging listening environments.^{53,54} The present findings support the importance of pre-operative discussions on the maximum speech recognition benefit patients can expect to obtain from CI in noisy settings, which is significantly less when compared to quiet settings. Patients who understand the potential limitation in speech recognition in noise improvements provided by CI prior to implantation may have clearer expectations of their long-term outcome.^{2,3}

Overall, the meta-analysis suggests that the most critical time period for improvements in speech recognition occurs in the early post-implantation period (up to three months). Afterward, scores, on average, might undergo small incremental changes, but are less likely to demonstrate any further significant improvements. These trends are observed regardless of which measures are being analyzed and are consistent with findings from previous studies.⁵⁻¹⁰ In other words, on average, a newly implanted CI user's speech recognition ability at 3 months likely represents a plateau in their abilities and their maximum level of improvement achieved. Similar conclusions have been reported by previous studies. For example, Spivak et al. found that patients with good speech recognition ability in the first 3 months were more likely to demonstrate continued improvement at 12 months compared to patients who performed poorly.⁵⁵ For clinicians, these findings underscore the importance of regular use of the device and repeated evaluation in the early post-operative period. Patients who demonstrate little improvement in speech recognition in the early post-operative period might require additional interventions such as speech-language pathologist-led auditory rehabilitation and computer-based auditory training activities, which have been demonstrated to improve speech recognition in the early post-implantation period. 56-60 Long-term evaluation of speech recognition is necessary for all patients as individual patient outcomes may demonstrate wide variation from group means.^{61,62}

Although speech recognition is considered to be the standard for measuring outcomes in CI users, word and

Study or Subgroup Non- 80 Total Mean Store Negation, 49% Cl Negation, 49% Cl Adm/ab 2006 4.03 1.03 2.03 6.3 7.7 1.4 2.03 2.03 7.7 1.4 2.03 7.7 1.4 1.03 2.03 7.7 1.7 1.4 2.03 7.7 1.7 1.4 2.03 7.7 1.7 1.4 2.03 7.7 1.7	/ \	3	Month		Р	re-op			Mean Difference	Mean Difference						
$ \begin{array}{c} \text{Advalues 2009} & 42.9 & 10.6 & 29 & 17.9 & 11.4 & 29 & 61.5 & 25.00 (17.66, 22.84) \\ \text{Over 30201} & 42.0 & 22.0 & 41.0 & 11.9 & 69 & 67.75 & 41.70 & 12.75 & 68.99 \\ \text{Over 30201} & 42.0 & 22.0 & 41.0 & 11.9 & 69 & 67.75 & 41.70 & 12.75 & 68.99 \\ \text{Over 30201} & 42.0 & 22.0 & 41.0 & 11.9 & 22.8 & 42.0 & 12.57 & 68.99 \\ \text{Over 30201} & 42.0 & 10.5 & 27.4 & 17.4 & 28.7 & 19 & 27.5 & 42.00 (17.67, 66.13) \\ \text{Over 30201} & 42.0 & 10.5 & 77.1 & 17.4 & 25.7 & 47.00 (17.67, 66.13) \\ \text{Sum 30211} & 42.0 & 10.5 & 77.1 & 17.4 & 45.5 & 72.0 (12.74, 48.9) \\ \text{Sum 30211} & 42.0 & 10.5 & 77.1 & 17.4 & 45.5 & 57.0 (17.67, 66.13) \\ \text{Sum 30211} & 42.0 & 10.5 & 17.4 & 17.4 & 17.5 & 15.5 & 16.4 & 64.0 (15.67, 66.13) \\ \text{Sum 30211} & 42.1 & 10.5 & 15.4 & 64.0 & 10.5 & 77.5 & 37.0 (10.68, 33.00) (27.4 & 65.0 & 30.00) (27.4 & 65.0 & 30.00) (27.4 & 65.0 & 30.00) (27.4 & 65.0 & 30.00) (27.4 & 65.0 & 30.00) (27.4 & 65.0 & 30.00) (27.4 & 65.0 & 30.00) (27.4 & 65.0 & 30.00) (27.4 & 65.0 & 30.00) (27.4 & 65.0 & 30.00) (27.4 & 65.0 & 30.00) (27.4 & 65.0 & 30.00) (27.4 & 65.0 & 30.00) (27.4 & 65.0 & 30.00) (27.4 & 65.0 & 30.00) (27.4 & 65.0 & 30.00) (27.4 & 65.0 & 50.0 & 10.0 & 57.6 & 10.0 & 10.0 & 57.6 & 10.0 & 10.0 & 57.6 & 10.0 & 10.0 & 57.6 & 10.0 & 10.0 & 57.6 & 10.0 & 10.0 & 57.6 & 10.0 & 10.0 & 57.6 & 10.0 & 10.0 & 57.6 & 10.0 & 10.0 & 10.0 & 57.6 & 10.0 & 10.0 & 10.0 & 57.6 & 10.0 & $	Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	IV, Random, 95% Cl						
Deep 2021 Compared 2	Adunka 2008	42.9	18.6	29	17.9	11.4	29	6.1%	25.00 [17.06, 32.94]							
$\begin{aligned} \begin{array}{c} \text{Creat} 2021, & 433, 2 & 52, 3 & 148, 17, 2 & 063, 9 & 78, 4130, 1211, 563, 9 & 1430, 1211, 563, 9 & 1430, 1211, 563, 9 & 1430, 1211, 563, 9 & 1430, 1211, 563, 9 & 1430, 1211, 563, 9 & 1430, 1211, 563, 9 & 1430, 1211, 563, 9 & 1430, 1211, 563, 9 & 1430, 1211, 563, 9 & 1430, 1211, 563, 9 & 1430, 1211, 563, 9 & 1430, 1211, 563, 9 & 1430, 1211, 1640, 1211, 1640, 1211, $	Deep 2021	50.3	20	53	8.7	15	53	6.7%	41.60 [34.87, 48.33]							
$ \frac{\text{Models}(2200)}{\text{Models}(2200)} = \frac{1}{6} \frac{1}{2} \frac{1}{$	Grisel 2021	49.3	24.3	529	14.8	17.2	805	8.9%	34.50 [32.11, 36.89]	T						
$ \begin{array}{c} \begin{array}{c} \text{Weak prior 20216} & \text{GB} & G$	Keisali 2021 Mohoriy 2020a	50.3	167	90	14.0	20.4	90	1.1%	41.70 [30.72, 40.08]							
$ \begin{array}{c} \text{Mean 20216} & The set of the set$	Moberly 2020a	59.5	23.5	19	17.4	29.7	19	2.7%	42 10 [25 07 59 13]							
Rung 2016 49 38 37 6. 14 37 9.2% 4.30 [2.1, 0.1, 0.1] Burn 2016 4.31 15. 16 7.6 2.8 3.80 [2.2, 14, 6.19] Burn 2016 4.31 15. 16 7.6 17.5 16 4.5% 3.80 [2.2, 14, 6.19] Burn 2016 4.33 12.5 16 7.14 17.5 16 4.5% 3.80 [2.2, 14, 6.19] Burn 2017 4.33 15.6 6.3 10 4.7% 4.14 [0.55, 5.2.23] Burn 2017 3.1 15.1 5.4 5.6 7.7% 3.80 [2.6, 2.4.3 [1.4] Zwelan 2016 3.2 2.6 3.1 2.5 5.7% 3.90 [0.03, 3.7.4 (0.3)] Heterogenety r= 20.46, r= 4.56 (4, et = 16 (r < 0.0001)/r 2.0 1.00 (0.00, 3.7.7.4 (0.3)] 4.00 [0.5, 17.7.7] Total 5%-CD Dirat Month	Moberly 2020c	66	10.1	19	20	19.9	19	5.0%	46.00 [35.97, 56.03]							
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	Runge 2016	49	3.8	37	5.6	1.4	37	9.2%	43.40 [42.10, 44.70]	+						
Stum 2021b 41.3 19.5 16 7.5 11.5 16 46.8 33.0 12.7.1 44.9 1 14.9 1 14.9 1 14.9 1 14.9 1 14.9 1 14.9 1 14.9 1 14.9 1 14.9 15.9 14.4 15.9 14.4 15.9 14.4 15.9 14.4 15.9 14.4 15.9 14.4 15.9 14.4 15.9 14.4 15.9 14.4 15.9 14.4 15.9 14.4 15.9 14.4 15.9 14.4 15.9 14.4 15.9 14.4 15.9 14.4 15.9 14.4 16.9 14.4 16.9 14.9 16.9 14.9 15.9 14.9 14.9 15.9 14.9 15.9 14.9 15.9 15.9 14.4 16.9 14.9 16.9 14.9 16.9 14.9 16.9 14.9 16.9 14.9 16.9 14.9 16.9 14.9 16.9 14.1 16.9 14.1 16.9 14.1 16.9 14.1 16.9 <td< td=""><td>Sturm 2021a</td><td>40</td><td>16.5</td><td>14</td><td>2.8</td><td>4.7</td><td>14</td><td>5.5%</td><td>37.20 [28.21, 46.19]</td><td></td></td<>	Sturm 2021a	40	16.5	14	2.8	4.7	14	5.5%	37.20 [28.21, 46.19]							
Slum 2011 428 22 16 7 124 17 418 250[251,409] Slum 2016 409 163 15 65 68 14 15 5 68 15 45 46 254 Slum 2016 409 163 15 65 68 14 15 5 68 15 15 44 60[554,4629] Slum 2016 409 222 5 53 14 15 44 25 46 718 340[254,4629] Zwolan 2001 409 22 25 53 14 15 44 25 46 718 340[254,4629] Zwolan 2001 409 22 25 55 14 15 54 42 56 70 58 72.00 98,43.21 Total (95% C) 1022 1300 100.0% 37.08 (33.77,40.39] Hetrographic, r=20 46; r= 86 14, dr= 16 (r= 0.00001); r= 81% Total (95% C) 1022 1300 100.0% 37.08 (33.77,40.39] Hetrographic, r=20 100001 B Slum 2016 514 166 23 422 16 22 218 600001; B Slum 2016 514 166 23 422 16 22 218 600001; B Slum 2016 514 166 19 60 00001; r= 81% Total (95% C) 114 16 56 31 22 66 48 400 150, 1757 Hetrographic, r=20 100001 B Slum 2016 514 166 59 16 50 19 14 19 33% 5018 50.0158 Slum 2016 52 33 32 7 46 33 32 7 758 300 (27,156 12) Slum 2016 62 23 33 27 16 62 8 22 16 088 050 (15,157 150) Slum 2016 65 18 15 65 16 50 9 182 15 18 04 84 00 150, 1750 Slum 2016 65 18 15 54 13 155 14 14 163 15 % 14 104 53 15% 14 00 (15,128) Slum 2016 65 18 53 15 44 116 13 15 % 14 04 150, 1574, 150 1 Slum 2016 65 213 30 21 6 623 227 6 038 501 (45,128) Slum 2016 65 213 30 21 6 629 192 15 08% 100 (54,122) Slum 2016 65 213 54 11 65 15 15 15 14 04 (45,122) Slum 2016 65 213 54 11 65 15 15 15 14 (46,48) 1210 Slum 2016 65 21 35 64 33 227 64 22% 16 01% 77,150 1 Slum 2016 65 21 35 41 16 10 1% 77,050 1 Slum 2016 65 19 15 22 30 14 173 123 15 15% 140 (45,47,129) Slum 2017 65 21 31 31 41 16 13 15 % 14 04 80, 1210 Slum 2017 85 133 14 11 61 15 15% 14 04 150 15% 77,250 1 Slum 2018 65 19 15 22 30 14 07 15 15% 13 300 175,250 80 Slum 2016 65 39 15 27 10 00001 C Slum 2017 65 21 30 57 14 00001 C Slum 2017 65 19 16 22 30 14 07 15 15% 13 300 11 157,150 1 Slum 2017 65 19 16 22 30 14 07 15 15% 13 100 10,22,168 1 Slum 2017 55 13 31 15 15% 140 100 32,250 10 Slum 2017 55 13 31 15 15% 100 100,271 80,140 Slum 2017 50 10,17 12 00 39 25 750 100001 C Slum 2017 50 10 17 12 00 30,77 10 00 30 25 100 10,271 80 14 Slum 2017 50 19 10 72	Sturm 2021b	41.3	19.5	16	7.5	11.5	16	4.6%	33.80 [22.71, 44.89]							
Slum 2021d 60 9 18.2 16 55 8.6 16 51.4 45.0 (25.5, 52.8) Slum 2021f 34 16 15 8.5 8.6 16 51.8 45.0 (25.5, 52.8) Slum 2021f 34.1 16 15 4.5 6.7 75.8 20.0 (21.6, 55.2.2) Slum 2021f 34.2 16.5 7.6 75.8 20.0 (21.6, 55.2.2) Zwolan 2001b 40.3 22.7 54 31.5 54 56 70.8 27.0 (20.8, 34.2) Hetrogene(r, rt= 30.4, 2r=68.1.4, 4r=16 (r - 0.00001), r= 01% Total (95.0) Mean Difference Mean Difference Mean Difference Study of subgroup Mean 21 22.0 15.8 23.0 (15.7, 17.7) Mean Difference Mean Difference Moderly 2020c 71.7 16 55.7 23.0 (15.7, 17.7) Mean Difference Mean Difference Study of subgroup Mean 21 52.8 30.7 75.75 30.9 (15.6, 17.2, 75.9) Mean Difference Mean Difference Study of subgroup 64.7 17.2 16.8 10.9 (15.7, 17.5) Mean Difference Mean Di	Sturm 2021c	42.8	22	16	7	12.4	17	4.1%	35.80 [23.51, 48.09]							
Stum 2021e 49 193 15 15 85 86 118 47 4 41 0[257, 223] Stum 2021e 41 16 5 57 4 280[1016, 834] Zurolas 2001b 42 2 23 43 14 1 2 3 46 57 7 8 340[1016, 834] Zurolas 2001b 40 3 227 54 3 1 5 4 5 6 768 7 20 [088, 434] Zurolas 2001b 40 3 227 54 3 1 5 4 5 6 768 7 20 [088, 434] Total (95: C) 1022 1300 100.04 37 20 [037, 74.39] Hetrogeneity, r= 30.4 6 2 + 23.9 (6 + 0.00001). r= 61% 1022 1300 100.04 37 20 [037, 74.39] B Month Study or study corp Mean Difference Mean Difference Mean Difference Mean Difference Moderly 2020b 64 4 23 4 3 1 8 3 2 21 16 038 7 675 % 300 [037, 74.39] 100 3 37 675 % 300 [037, 74.58] 100 3 38 501 (037, 74.58] Stum 2011 25 2 1 5 7 1 8 6 16 17 7 76 11 9 338 501 (037, 74.58] Mean Difference Mean Difference Mean Difference Moderly 2020b 65 4 123 9 18 6 16 15 7 8 1 40 (180, 128, 228) 100 (03 1 23, 228) 100 (03 1 23, 228) 100 (03 1 23, 228) Sum 2011 25 3 1 3 0 16 4 23 8 21 16 0 18 7 76 10 (18 0 428, 214) 118 10 301 (23 248) 100 (23 248) 100 (23 248) 100 (23 248) 100 (23 248) </td <td>Sturm 2021d</td> <td>50.9</td> <td>18.2</td> <td>16</td> <td>5.5</td> <td>8.6</td> <td>16</td> <td>5.1%</td> <td>45.40 [35.54, 55.26]</td> <td></td>	Sturm 2021d	50.9	18.2	16	5.5	8.6	16	5.1%	45.40 [35.54, 55.26]							
Shum 2021rt 34.1 16 15 43 43 16 57% 2380[14.68, 2316] Shum 2021rt 31.4 17.8 23 57% 2380[14.68, 2316]	Sturm 2021e	49.9	19.9	15	8.5	8.6	18	4.7%	41.40 [30.57, 52.23]							
Shum 2021g 31 17 32 25 X3011245 X3111 Shum 2021g 32 25 14 22 15 56 67 75% X3011245 X33131 Zwain 2021g 60 222 15 16 15 16 16 16 16 17 13 15 15 15 15 16 15 16 <td>Sturm 2021f</td> <td>34.1</td> <td>16.6</td> <td>15</td> <td>4.3</td> <td>4.9</td> <td>16</td> <td>5.7%</td> <td>29.80 [21.06, 38.54]</td> <td></td>	Sturm 2021f	34.1	16.6	15	4.3	4.9	16	5.7%	29.80 [21.06, 38.54]							
$ \begin{array}{c} \begin{array}{c} \mbox{cm} 2016 & 32.22.8 & 3.2 & 13.2.5 & 4.8 & 12.8.2, 4.03.8 \\ \mbox{cm} 2016 & 4.3 & 22.7 & 6.4 & 3.1 & 6.2 & 4.8 & 7.18 & 3.72 & 102.08.8, 4.3.2 \\ \mbox{cm} 1000 & 4.3 & 22.7 & 6.4 & 3.1 & 6.4 & 6.4 & 7.6 & 0.7 & 0.000 \\ \mbox{cm} 1000 & 1.0 & 1022 & 1300 & 100.006 & 37.08 & [3.77, 40.39] \\ \mbox{cm} 1000 & 10000 & 1000 & 100000 & 10000 & 10000 & 100000 & 10000 & 100000 & 100000 & 10000 & $	Sturm 2021g	31.4	17.9	22	7.1	11.3	22	5.6%	24.30 [15.45, 33.15]							
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	Zwolan 2001a Zwolan 2001h	30.2	22.8	53	1.4	2.5	48	7.1%	34.80 [28.62, 40.98]							
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	Zwolali 2001b	40.5	22.0	54	0.1	3.4	50	7.070	37.20 [30.80, 43.42]							
Heterogeneity, $r = 30.46$, $r = 60.40$, $d = 6 (r = 0.00001)$, $r = 81\%$ Test for overall effect. $Z = 21.66$ ($r < 0.00001$), $r = 81\%$ Test for overall effect. $Z = 21.66$ ($r < 0.00001$), $r = 81\%$ Test for overall effect. $Z = 21.66$ ($r < 0.00001$), $r = 81\%$ Test for overall effect. $Z = 21.66$ ($r < 0.00001$), $r = 81\%$ Test for overall effect. $Z = 21.66$ ($r < 0.00001$), $r = 81\%$ Moment Subgroup Momth SD Test Mean SD Test Mean SD Test Mean More mean SS CI Advise 2020 51.7.7 12.6 19 66 53.2 22 66 4.6% (A 0011.60, 10.4, 640) Moherly 2020 65.4 2.12.9 19 65.5 13.2 19 6.5% 5.018.5\% 5.018.5\% 5.019.5\% 5.	Total (95% CI)			1022			1300	100.0%	37.08 [33.77, 40.39]	◆						
Test for overall effect. Z = 21.96 (r < 0.0001) B C Subject Subjection B C Subject Subjecti	Heterogeneity: $\tau^2 = 30$	0.46; χ ² :	= 86.14	4, <i>df</i> = 1	6 (p < 1	0.0000	1);/²=	81%								
B Study of Subgroup Mean SD Total Mean SD Total Weight M Mandon, 95% CL Advines 2006 614 166 29 428 16.6 29 21% 650(157, 17.57) Study of Subgroup Mean SD Total Mean SD Total Weight M Mandon, 95% CL Mean Difference M. Candon, 95% CL Mean Difference Mean Difference Mean Difference M. Candon, 95% CL Mean Difference M. Candon, 95% CL Mean Difference M. Candon, 95% CL Mean Difference Mean Difference M. Candon, 95% CL Mean Difference Mean Difference M. Candon, 95% CL Mean Difference Mean Difference M. Randon, 95% CL Mean Difference Mean Difference	Test for overall effect:	Z= 21.9	36 (p <	0.0000	01)					-50 -25 0 25 50 Favours pre-op Favours 3 month						
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$	D															
	D	6	Month		3	Month			Mean Difference	Mean Difference						
Advise 2009 14 166 29 429 196 29 21% 850 1057,1757 Orise 2021 50 212 393 43 22 43 529 1656 34 30 0136,469 Keisal 2021 60 9 21 1 96 553 22 96 46% 450 150,11570 Moberly 2020 654 229 19 565 235 19 0.8% 520 1665,11470 Moberly 2020 654 229 19 565 235 19 0.8% 520 1645,1290 Runge 2016 52 9 38 37 49 38 37 575% 30 0217,563 Sturm 2021 6 503 17.7 14 40 155 14 11% 103123,232,298 Sturm 2021 6 487 7197 15 413 155 16 0.9% 8.401541,222 11 Sturm 2021 6 487 7197 15 413 155 15 10,98 15 0.08% 6.0015447,2067 Sturm 2021 6 487 7197 15 413 155 15 10,98 15 0.08% 6.0015447,2067 Sturm 2021 6 487 7197 15 414 71 92 21 12% 6.0195477,1797 Zwolan 2010 566 243 32 01 6428 2218 653 12.4% 1.0016454,10151 Zwolan 2011 355 15 49.9 193 14 17.9 22 1 12% 6.019 577,1797 Test for overall effect Z = 6.41 ($p + 0.00001$) C C Test for overall effect Z = 6.41 ($p + 0.00001$) C Test for overall effect Z = 6.41 ($p + 0.00001$) C Test for overall effect Z = 6.41 ($p + 0.00001$) C Test for overall effect Z = 6.41 ($p + 0.00001$) C Test for overall effect Z = 6.41 ($p + 0.00001$) C Test for overall effect Z = 6.41 ($p + 0.00001$) C Test for overall effect Z = 6.41 ($p + 0.00001$) C Test for overall effect Z = 6.41 ($p + 0.00001$) C Test for overall effect Z = 6.41 ($p + 0.00001$) C Test for overall effect Z = 6.41 ($p + 0.00001$) C Test for overall effect Z = 6.41 ($p + 0.00001$) C Test for overall effect Z = 6.41 ($p + 0.00001$) C Test for overall effect Z = 6.41 ($p + 0.00001$) C Test for overall effect Z = 6.41 ($p + 0.00001$) C Test for overall effect Z = 6.41 ($p + 0.00001$) C Test for overall effect Z = 6.41 ($p + 0.00001$) C Test for overall effect Z = 6.41 ($p + 0.00001$) C Test for overall effect Z = 6.41 ($p + 0.00001$) C Test for overall effect Z = 6.41 ($p + 0.00001$) D Test for overall effect Z = 6.41 ($p + 0.00001$) D Test for overall effect Z = 6.41 ($p + 0.00001$) D Test for overall effect Z = 6.41 ($p + 0.00001$) D Test for overall effect Z = 6.41 ($p + 0.00001$) D Test for overall ef	Study or Subaroup	Mean	SD	Total	Mean	SD	Total	Weight	IV. Random, 95% Cl	IV. Bandom, 95% Cl						
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	Adunka 2008	51.4	16.6	29	42.9	18.6	29	2.1%	8.50 (-0.57, 17, 57)							
$ \begin{array}{c} \mbox{kissel} 2021 & 60.9 & 21.1 & 96 & 56.3 & 22 & 96 & 4.058 & 4.60 \mbox{kissel} 14 \mbox{kissel}$	Grisel 2021	52.7	22.9	399	49.3	24.3	529	18.5%	3,40 (0,34, 6,46)							
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	Kelsall 2021	60.9	21.1	96	56.3	22	96	4.6%	4.60 [-1.50, 10.70]	+						
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	Moberly 2020a	59.2	18.7	19	56	16.7	19	1.4%	3.20 [-8.07, 14.47]	<u> </u>						
$ \begin{array}{l c c c c c c c c c c c c c c c c c c c$	Moberly 2020b	65.4	22.9	19	59.5	23.5	19	0.8%	5.90 [-8.85, 20.65]							
Rung 2016 52.9 3.8 37 49 3.8 37 57.5% 3.90[2.17, 5.63] Sturm 2021b 49.7 13.7 14 40.16 14 10.30[2.38, 22.98] Sturm 2021c 43.7 13.7 14 40.8 0.50[14.07, 15.07] Sturm 2021d 68.5 15.6 19.9 15 0.8% 0.50[14.07, 15.07] Sturm 2021d 68.5 15.6 19.9 15 0.8% 1.20[15.65, 12.86] Sturm 2021f 35.5 13.3 15 34.1 16.6 15 1.5% 1.40[9.36, 12.16] Sturm 2021f 35.5 13.3 15 34.1 16.6 1.5% 1.40[9.36, 12.16] Sturm 2021f 37.8 22.7 66 32.27 64 22.26 16.01 Total (95% CI) 840 969 100.0% 4.29 2.92,95.60 4.57 4.50 50 Test for overail effect Z= 6.14 (p < 0.00001) 50 Total (95% CI) Mean Difference Mean Difference Mean Difference Study of Subgroup Mean SD Total (95% C	Moberly 2020c	71.7	12.6	19	66	10.1	19	3.3%	5.70 [-1.56, 12.96]	+						
Sturm 2021a 60.3 17.7 14 40 16.5 14 1.1% 10.30 [2.38, 22.8] Sturm 2021b 49.7 10.7 15 41.3 195 16 0.0% 0.50 [4.4.12.21] Sturm 2021c 43.3 20 16 42.8 22 16 0.0% 0.50 [4.4.07, 15.07] Sturm 2021c 45.8 195 16 5.00 81.82 16 1.0.% 7.60 [5.74, 20.67] Sturm 2021c 45.8 195 16 5.00 81.82 16 1.0.% 7.60 [5.74, 20.67] Sturm 2021c 45.8 7.20.5 11 5 49.9 19.9 15 0.0% -1.20 [5.66, 13.26] Sturm 2021c 37.5 20.5 19 31.4 17.9 22 1.2% 0.10 [5.77, 17.97] Zwolan 2001a 37.5 22.7 56 36.2 22.8 53 2.4% 1.50 [6.957, 17.97] Zwolan 2001b 56.6 24.3 56 40.3 22.7 54 2.2% 15.00 [5.57, 17.97] Zwolan 2001b 56.6 24.3 56 40.3 22.7 54 2.2% 15.00 [5.57, 17.97] Zwolan 2001b 56.6 24.3 56 40.3 22.7 54 2.2% 15.00 [5.7, 17.97] Zwolan 2001b 56.6 24.3 16 40.3 22.7 54 2.2% 15.00 [5.7, 17.97] Zwolan 2001b 56.6 29 51.4 16.6 29 51.4 16.0 [5.7, 17.97] Zwolan 2001b 56.6 29 51.4 16.6 29 51.4 15.0 [7.52, 25.08] Total (95% C) 72.5 11.78, dr = 15 0 Total Weight V, Random, 95% CI Adunka 2000 59 16.6 29 51.4 16.6 29 52.1 % 30 [0.0.0, 6.26] Kelsall 2021 56.5 21.8 91 60.9 21.1 96 5.7% 4.30 [1.42, 10.02] Kelsall 2021 65.2 18.8 91 60.9 21.1 96 5.7% 4.30 [1.42, 10.02] Sturm 2021b 40 18.4 4 84.7 19.7 15 0.7% 4.30 [1.42, 10.02] Sturm 2021b 40 18.4 4 84.7 19.7 15 0.7% 4.30 [1.42, 10.02] Sturm 2021b 40 18.4 4 84.7 19.7 15 0.7% 4.00 [1.5, 6.6] Study or Subgroup Mean SD Total Mean SD Total Weight V, Random, 95% CI Adunka 2008 59 16.5 21.8 91 50.3 17.7 14 0.0% 3.30 [7.44, 14.64] Sturm 2021c 51.8 23.2 8 4.33 20 16 0.5% 8.50 [1.0.3, 2.7.33] Sturm 2021b 40 18.4 4 84.7 19.7 15 0.7% 4.00 [4.3, 12.3, 12.9] Total (95% C) 762 771 100.0% 3.04 [1.2, 7.5.31] Heterogenetic, r*= 0.00, r*= 5.60, dr=12 (p=0.3); r= 0.8 Total (95% C) 762 774 400 [4.3, 12.30] Grieel 2021 55.8 23.4 426 23.2 24.5 10 5.7% 4.00 [4.3, 12.30] Grieel 2021 55.8 23.4 426 43.3 24.3 25.3 20.5 56 (5.0% 8.30 [1.2, 7.5.31] Heterogenetic, r*= 0.00, r, r= 6.50, dr=12 (p=0.5); r= 0.8 Sturm 20216 40 81.8 4 81.3 18.5 16 0.7% 6.00 [7.3, 17.81] Sturm 20217 65.8 23.4 (4.45 20.2 7.76 (4.00, 43.3, 12.30] G	Runge 2016	52.9	3.8	37	49	3.8	37	57.5%	3.90 [2.17, 5.63]	-						
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	Sturm 2021a	50.3	17.7	14	40	16.5	14	1.1%	10.30 [-2.38, 22.98]							
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	Sturm 2021b	49.7	19.7	15	41.3	19.5	16	0.9%	8.40 [-5.41, 22.21]							
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	Sturm 2021c	43.3	20	16	42.8	22	16	0.8%	0.50 [-14.07, 15.07]							
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	Sturm 2021d	58.5	19.5	16	50.9	18.2	16	1.0%	7.60 [-5.47, 20.67]							
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	Sturm 2021e	48.7	20.5	15	49.9	19.9	15	0.8%	-1.20 [-15.66, 13.26]							
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	Sturm 20210	30.0	20.5	10	34.1	17.0	22	1.0%	6 10 [-9.30, 12.10]							
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	Zwolan 2001a	37.8	20.5	56	36.2	22.8	53	7.4%	1 60 66 95 10 15							
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	Zwolan 2001b	56.6	24.3	56	40.3	22.7	54	2.2%	16.30 [7.52, 25.08]							
Total (95% C) 840 969 100.0% 4.29 [2.98, 5.60] Heterogeneiky, $r^2 = 0.00$, $r^2 = 11.78$, $dr = 15$ ($p = 0.70$); $r^2 = 0$ % Test for overall effect. $Z = 6.41$ ($p < 0.00001$) C Study or Subgroup Mean SD Total Mean SD Total Weight IV, Random, 95% Cl Adunka 2008 59 16.6 29 51.4 16.6 29 22.6% 7.60 [-0.94, 16.14] First 2018 51 22 39 49 20 39 21.% 2.00 [r ² , 33, 11.3] Grisel 2021 65.8 23.4 426 52.7 22.9 399 18.7% 3.10 [-0.06, 6.26] Kelsal 2021 65.2 18.8 91 60.9 21.1 96 6.7% 4.30 [r ² , 43, 10.10 [3.2, 18.66] Study or Subgroup Mean SD Total Mean SD Total Weight IV, Random, 95% Cl Adunka 2008 59 16.6 29 61.4 11.6 0.92 1.1 96 6.7% 4.30 [r ² , 41.41, 44] Sturm 20216 51.8 23.2 4 43.3 20 16 0.5% 650 [r ² , 17.3 17.3] Sturm 20216 51.8 12.2 18 4 91 60.9 21.1 96 6.7% 4.30 [r ² , 41, 44.8] Sturm 20216 51.8 23.2 4 43.3 20 16 0.5% 650 [r ² , 17.3 17.3] Sturm 20216 51.8 12.2 2 8 4.33 20 16 0.5% 650 [r ² , 17.3 17.3] Sturm 20216 51.8 12.2 2 8 4.33 20 16 0.5% 650 [r ² , 17.3 17.3] Sturm 20216 51.8 12.3 2 15 1.5 1.0% 3.20 [r ² , 17.4 14.64] Sturm 20216 51.8 13.3 9 37.5 20.5 19 1.2% 0.30 [r ² , 12.87, 33] Sturm 20216 51.8 13.3 9 37.5 20.5 19 1.2% 0.30 [r ² , 17.4 14.64] Sturm 20216 39.1 16.1 13 3.55 13.3 15 1.5% 3.60 [r ² , 41, 44.64] Sturm 20216 39.1 16.4 13 3.55 13.3 15 1.5% 3.60 [r ² , 41, 44.64] Sturm 20217 39.1 16.1 13 3.47 20.5 17 1.20 3.94 [r ² , 57.65] Farouus 12 month Favours 6 month D 2tudy or Subgroup Mean Di Total Mean SD Total Weight (W, Random, 95% Cl Adunka 2008 59 16.6 29 42.9 16.8 29 2.28 6 5.5% 8.90 [3.4, 14.76] Sturm 2021 65.8 13.3 14 41.60 13.2 0.5 53 7.7% 4.00 [r ⁴ , 30, 23.517] Deg 2021 65.8 23.4 42.6 49.3 24.3 529 20.6% 6.50 [3.46, 9.56] Sturm 2021 65.8 13.3 7.9 3.1.4 10.9 0.80 (r ⁴ , 10.07% 6.270 [r ³ , 7.8] Sturm 2021 65.8 13.3 7.9 3.1.4 10.6 13.3 20.5 17.7% 4.00 [r ⁴ , 30, 12.39] Favours 12 month Favours 6 month Sturm 2021 65.8 13.4 42.6 49.3 24.3 529 20.6% 6.50 [3.46, 9.56] Sturm 2021 65.8 13.4 42.6 42.8 22 16 0.5% 8.00 [r ⁴ , 13.02, 15.77] Sturm 2021 65.8 13.3 4 91.56																
Heterogeneity: $r^2 = 0.00$; $r^2 = 61.78$, $dr = 15$ ($p = 0.79$); $P = 0\%$ Testfor overall effect. $Z = 6.41$ ($p < 0.00001$) C Study or Subgroup Mean SD Total Keen SD Total Weight N. Random, 95% CI Adunka 2008 59 16.6 29 51.4 16.6 29 2.8% 7.60 [-0.94, 16.14] First 2018 51 22 39 49 20 39 2.1% 2.00 [-7.33, 11.33] Grisel 2021 55.8 23.4 426 52.7 22.9 399 18.7% 310 [-0.06, 6.26] Study or Subgroup 16 56.8 39 37 52.9 3.8 37 60.8% 3.30 [2.15, 56.6] Studm 2017 56.7 19 61 56 24 61 3.2% 11.00 [3.2, 18.66] Sturm 2021 53.8 23.2 8 43.3 20 16 0.5% 8.60 [-1.03, 27.33] Sturm 2021 51.8 23.2 8 43.3 20 16 0.5% 8.60 [-1.03, 27.33] Sturm 2021 51.8 23.2 8 43.3 20 15 0.5% 8.60 [-1.03, 27.33] Sturm 2021 51.9 16 13 48.7 20.5 15 1.0% 3.20 [-1.33, 17.83] Sturm 2021 51.9 16 13 48.7 20.5 15 1.0% 3.20 [-1.33, 17.83] Sturm 2021 51.9 16 13 48.7 20.5 19 12.2% 0.30 [-12.37, 12.97] Total (95% CI) 762 762 771 100.0% 3.94 [2.57, 5.31] Heterogeneity, $r^2 = 0.00$; $r^2 = 568$, $dr = 12 (p = 0.93)$; $p^2 = 0\%$ Testfor overall effect. $Z = 651, p < 0.0001$) D Mean SD Total Mean SD Total Mean SD Total Weight IV, Random, 95% CI Adunka 2008 59 16.6 29 42.3 18.6 29 2.3% 16.10 [7.03, 25.77] Deep 201 54.8 21 Cat 16 3.2 22 0.5 39 7.7% 4.00 [-4.39, 12.9] Grisel 2021 55.8 23.4 426 49.3 24.3 529 20.6% 5.60 [3.46, 9.56] Sturm 2021 55.8 23.4 426 49.3 24.3 529 20.6% 5.60 [3.46, 9.56] Sturm 2021 55.8 23.4 426 49.3 24.3 529 20.6% 5.60 [3.46, 9.56] Sturm 2021 55.8 23.4 426 49.3 24.3 529 20.6% 5.60 [3.46, 9.56] Sturm 2021 55.8 23.4 426 49.3 24.3 529 20.6% 5.60 [1.47, 76] Sturm 2021 55.8 3.34 426 49.3 24.3 529 20.6% 5.60 [-9.23, 22.63] Sturm 2021 55.8 3.34 41.6 16 13 49.9 19.9 15 1.1.1% 2.00 [-1.3, 7.76] Sturm 2021 51.8 91 56.1 3.9 3.7 49 3.8 37 61.7% 7.80 [6.05, 9.56] Sturm 2021 51.9 16 13 49.9 19.9 15 1.1.1% 2.00 [-1.3, 7.76] Sturm 2021 51.8 13.3 9 31.4 17.9 22 1.4% 6.40 [-5.07, 17.37] Fautor s7 month Favours 1 month Sturm 2021 51.9 16 13 49.9 19.9 15 1.1.1% 2.00 [-1.3, 7.73] Sturm 2021 51.9 16 13 49.9 19.9 15 1.1.1% 2.00 [-1.3,	Tetel (OE0/ CI)															
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	Total (95% CI)			840			969	100.0%	4.29 [2.98, 5.60]							
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	Heterogeneity: $\tau^2 = 0$.	00; χ ² =	11.78	840 , <i>df</i> = 15	5 (<i>p</i> = 0	.70);/²	969 = 0%	100.0%	4.29 [2.98, 5.60]	↓ -50 -25 0 25 50						
12 Month Mean SD Total Mean DIFGE N N Total Mean DIFGE N Mean DIFGE N N N N N Mean DIFGE N Mean DIFGE N N N N N N N <t< td=""><td>Heterogeneity: τ² = 0. Test for overall effect:</td><td>00; χ²= Z= 6.41</td><td>11.78 1 (<i>p</i> < (</td><td>840 , <i>df</i> = 15 0.00001</td><td>5 (<i>p</i> = 0)</td><td>.70);/²</td><td>969 = 0%</td><td>100.0%</td><td>4.29 [2.98, 5.60]</td><td>+ -50 -25 0 25 50 Favours 3 month Favours 6 month</td></t<>	Heterogeneity: τ² = 0. Test for overall effect:	00; χ²= Z= 6.41	11.78 1 (<i>p</i> < (840 , <i>df</i> = 15 0.00001	5 (<i>p</i> = 0)	.70);/²	969 = 0%	100.0%	4.29 [2.98, 5.60]	+ -50 -25 0 25 50 Favours 3 month Favours 6 month						
Studproup Mean Studproup Mean Studproup Mean SD Total Mean SD Total Mean SD Total Mean SD Total Mean Difference Adunka 2008 59 16.6 29 2.9 39 2.1% 2.00 [-7.3, 11.33] Grisel 2021 55.8 23.4 42.6 52.7 22.9 39 2.1% 2.00 [-7.3, 11.33] Git 2021 65.8 23.9 37 52.9 38 37 60.8% 3.30 [2.15, 56.5] Studm 2021a 53.4 21.3 150.3 17.7 14 0.9% 3.10 [-10.7, 3, 17.93] Sturm 2021c 51.8 23.2 16 1.3% 2.05 [1-34, 16.74] 16.1 13 35.5 16 1.1% 0.70 [17.29, 13.89] Total (95% CI Mean Difference Mean Difference Study or Subgroup Mean SD To	Heterogeneity: $\tau^2 = 0$. Test for overall effect:	00; χ²= Ζ= 6.41	11.78 1 (<i>p</i> < (840 , <i>df</i> = 15 0.00001	5 (<i>p</i> = 0)	.70);/²	969 = 0%	100.0%	4.29 [2.98, 5.60]	↓ -50 -25 0 25 50 Favours 3 month Favours 6 month						
Adunka 2008 59 16.6 29 51.4 16.6 29 2.6% 7.60 [0.94, 16.14] Firsz 2018 51 22 39 49 20 39 2.1% 2.00 [7.33, 11.33] Grisel 2021 55.8 23.4 426 52.7 22.9 399 18.7% 3.310 [-0.06, 6.26] Kelsall 2021 65.2 18.8 91 60.9 21.1 96 5.7% 4.30 [-1.42, 10.02] Runge 2016 56.8 3.9 37 52.9 3.8 37 60.8% 3.30 [-1.2, 15, 565] Sladen 2017 67 19 61 56 24 61 3.2% 11.00 [3.2, 18.68] Sturm 2021a 53.4 21.3 150.3 17.7 14 0.9% 3.10 [-1.13, 17.93] Sturm 2021b 48 18.4 8 49.7 19.7 15 0.7% -1.70 [-17.89, 14.49] Sturm 2021c 51.8 23.2 8 43.3 20 16 0.5% 8.50 [-10.33, 27.33] Sturm 2021d 59.2 17.4 15 58.5 19.5 16 1.1% 0.70 [-12.2, 13.69] Sturm 2021d 59.2 17.4 15 58.5 19.5 16 1.1% 0.70 [-12.2, 13.69] Sturm 2021d 59.2 17.4 15 58.5 19.5 16 1.1% 0.30 [-12.37, 12.97] Total (95% Cl) 762 771 100.0% 3.94 [2.57, 5.31] Heterogeneity: $r^2 = 0.00; r^2 = 5.68, dr = 12 (p = 0.9); r^2 = 0\%$ Test for overall effect. $r = 5.66 (p < 0.00001)$ D 12 Month 3 Month Mean Difference Study of Subgroup Mean SD Total Mean SD Total Weight M, Random, 95% Cl Adunka 2008 69 16.6 29 42.9 18.6 29 2.3% 16.10 [7.03, 25.17] Deep 2021 56.3 21.4 15 50.3 20 53 2.7% 4.00 [-4.39, 12.39] Grisel 2021 56.8 39.3 7 49 38 37 61.7% 7.80 [6.05, 9.55] Sturm 2021a 56.4 21.3 13 40 16.5 14 0.9% 13.40 [-1.05, 27.85] Sturm 2021a 56.4 21.3 13 40 16.5 14 0.9% 13.40 [-1.05, 27.85] Sturm 2021a 56.4 21.3 13 40 18.5 14 0.9% 13.40 [-1.05, 27.85] Sturm 2021a 56.4 21.3 13 40 18.5 14 0.9% 13.40 [-1.05, 27.85] Sturm 2021a 56.4 21.3 13 40 18.5 14 0.9% 13.40 [-1.05, 27.85] Sturm 2021a 56.4 21.8 91 56.3 222 16 0.55% 8.90 [3.04, 14.76] Sturm 2021a 56.4 21.3 13 40 18.5 14 0.9% 13.40 [-1.05, 27.85] Sturm 2021a 56.4 21.3 13 40 18.5 14 0.9% 13.40 [-1.05, 27.85] Sturm 2021a 56.4 21.3 13 40 18.5 16 1.3% 5.00 [-7.13, 17.13] Sturm 2021b 44 18.4 8 41.13 19.5 16 0.7% 6.70 [-8.23, 20.83] Sturm 2021c 51.8 16 1 13 49.1 19.9 15 1.1% 2.00 [-11.31, 15.31] Sturm 2021c 51.8 16.1 13 34.1 18.6 15 1.3% 5.00 [-7.13, 17.13] Sturm 2021c 51.8 16.1 13 49.1 19.9 15 1.1% 2.00 [-11.31, 15.31] Sturm 2021g 37.8 13.	Heterogeneity: $\tau^2 = 0$. Test for overall effect:	00; $\chi^2 = Z = 6.41$: 11.78 1 (<i>p</i> < (Month	840 , <i>df</i> = 15).00001	5 (p = 0) 6	.70);/² Month	969 = 0%	100.0%	4.29 [2.98, 5.60] Mean Difference	Favours 3 month Favours 6 month Favours 6 month						
First 2018 51 22 39 49 20 39 2.1% 200 [r/3,1], 13] Grisel 2021 55.8 23.4 426 52.7 399 17.8% 310 [r], 142 [10.02] Runge 2016 56.8 3.9 37 52.9 38 37 60.8% 3.90 [2.15, 5.65] Sturm 2021a 53.4 21.3 13 50.3 17.7 14 0.9% 310 [11.73, 17.89] 14.4 0.9% Sturm 2021b 48 18.4 8.4 49.7 15 0.7% 17.0 [17.89] 14.99% 310 [11.73, 17.89] 14 0.9% 310 [11.73, 17.89] 14 0.9% 310 [11.73, 17.89] 14 0.9% 310 [11.73, 17.8] 14 0.9% 310 [11.73, 17.8] 14 0.9% 300 [7.44, 14.64] Sturm 2021c 51.8 23.5 15.5 15.6 15.5% 360 [7.44, 14.64] 15.7% 300 [7.23, 7,12.97] Total (95% CI) Total Mean SD Total Mean SD Total Weight Mean Difference Mean Difference Mean Difference Mean Difference Mean Difference </td <td>Heterogeneity: $\tau^2 = 0$. Test for overall effect: C Study or Subgroup</td> <td>00; χ² = Z = 6.41 12 <u>Mean</u></td> <td>11.78 1 (<i>p</i> < 0 Month SD</td> <td>840 , <i>df</i> = 15 0.00001 <u>Total</u></td> <td>5 (p = 0) 6 I <u>Mean</u></td> <td>.70); /² Month SD</td> <td>969 = 0% Total</td> <td>100.0% Weight</td> <td>4.29 [2.98, 5.60] Mean Difference IV, Random, 95% Cl</td> <td>Favours 3 month Favours 6 month Mean Difference IV, Random, 95% CI</td>	Heterogeneity: $\tau^2 = 0$. Test for overall effect: C Study or Subgroup	00; χ ² = Z = 6.41 12 <u>Mean</u>	11.78 1 (<i>p</i> < 0 Month SD	840 , <i>df</i> = 15 0.00001 <u>Total</u>	5 (p = 0) 6 I <u>Mean</u>	.70); /² Month SD	969 = 0% Total	100.0% Weight	4.29 [2.98, 5.60] Mean Difference IV, Random, 95% Cl	Favours 3 month Favours 6 month Mean Difference IV, Random, 95% CI						
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	$\frac{100}{100} (95\% Cl)$ Heterogeneity: $\tau^2 = 0$. Test for overall effect: C <u>Study or Subgroup</u> Adunka 2008	00; $\chi^2 = Z = 6.41$ 12 Mean 59	11.78 1 (<i>p</i> < 0 Month <u>SD</u> 16.6	840 , <i>df</i> = 15 0.00001 <u>Total</u> 29	5 (p = 0) 6 <u>Mean</u> 51.4	.70);/ ² Month <u>SD</u> 16.6	969 = 0% <u>Total</u> 29	100.0% Weight 2.6%	4.29 [2.98, 5.60] Mean Difference IV, Random, 95% CI 7.60 [-0.94, 16.14]	Favours 3 month Favours 6 month Mean Difference IV, Random, 95% CI						
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$	Hota (95% CI) Heterogeneity: r ² = 0. Test for overall effect: C Study or Subgroup Adunka 2008 Firszt 2018	00; $\chi^2 = Z = 6.41$ 12 Mean 59 51	11.78 (p < 0 Month SD 16.6 22	840 , <i>df</i> = 18 0.00001 <u>Total</u> 29 39	5 (p = 0 l) 6 I <u>Mean</u> 51.4 49	.70); / ² Month SD 16.6 20	969 = 0% <u>Total</u> 29 39	100.0% Weight 2.6% 2.1%	4.29 [2.98, 5.60] Mean Difference IV, Random, 95% CI 7.60 [-0.94, 16.14] 2.00 [-7.33, 11.33]	Favours 3 month Favours 6 month Mean Difference IV, Random, 95% Cl						
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$	Heterogeneity: r ² = 0. Test for overall effect: C <u>Study or Subgroup</u> Adunka 2008 Firszl 2018 Grisel 2021 Kateni 2004	00; $\chi^2 = 6.41$ 12 Mean 59 51 55.8 55.2	11.78 $(p < 0)$ Month SD 16.6 22 23.4	840 , <i>df</i> = 15 0.00001 <u>Total</u> 29 39 426	5 (p = 0) 6 I <u>Mean</u> 51.4 49 52.7	.70); / ² Month SD 16.6 20 22.9	969 = 0% <u>Total</u> 29 39 399	100.0% Weight 2.6% 2.1% 18.7%	4.29 [2.98, 5.60] Mean Difference IV, Random, 95% CI 7.60 [-0.94, 16.14] 2.00 [-7.33, 11.33] 3.10 [-0.06, 6.26]	Favours 3 month Favours 6 month Mean Difference Ⅳ, Random, 95% Cl						
Sturm 2021a 53.4 21.3 13 50.3 17.7 14 0.9% 3.10 [+1.7, 17, 17, 13] Sturm 2021b 48 18.4 8 49.7 19.7 15 0.7% -1.70 [+7.8, 14.49] Sturm 2021c 51.8 23.2 8 43.3 20 16 0.5% 8.50 [+0.33, 27.33] Sturm 2021d 59.2 17.4 15 58.5 19.5 16 1.1% 0.70 [+2.28, 13.69] Sturm 2021f 39.1 16.1 13 35.5 13.3 15 1.5% 3.60 [-7.4, 14.64] Sturm 2021g 37.8 13.3 9 37.5 20.5 19 1.2% 0.30 [+2.37, 12.97] Total (95% CI) 762 771 100.0% 3.94 [2.57, 5.31] Heterogeneily: $r^2 = 0.00$; $r^2 = 5.68$, $df = 12$ ($p = 0.93$); $P = 0\%$ Test for overall effect $Z = 5.65$ ($p < 0.00001$) D 12 Month 3 Month Mean Difference Study or Subgroup 16.6 29 42.9 18.6 29 2.3% 16.10 [7.03, 25.17] D esp 2021 54.3 21 41 50.3 20 53 2.7% 4.00 [+3.9, 12.39] Orisel 2021 65.8 23.4 42.6 49.3 24.3 522 90.6% 6.50 [3.46, 9.54] Kelsall 2021 65.2 18.8 91 56.3 22 96 5.5% 8.90 [3.04, 14.76] Runge 2016 56.8 3.9 37 49 3.8 37 61.7% 7.80 [0.65, 9.55] Sturm 2021a 65.2 18.8 91 56.3 22 96 5.5% 8.90 [3.04, 14.76] Runge 2016 56.8 1.3 4.21.3 13 40 16.5 14 0.9% 13.40 [1.05, 27.85] Sturm 2021a 65.2 18.8 91 56.3 22 96 5.5% 8.90 [3.04, 14.76] Runge 2016 56.8 1.3 4.21.3 13 40 16.5 1.4% 0.90 [-10.3, 15.31] Sturm 2021a 61.9 16 13 49.9 19.9 15 1.1% 2.00 [-11.31, 15.31] Sturm 2021a 51.4 15 50.9 18.2 16 0.7% 6.70 [-9.23, 22.63] Sturm 2021a 51.4 15 30.9 18.2 16 0.5% 9.001 (-10.3, 28.36] Sturm 2021a 51.9 16 13 49.9 19.9 15 1.1% 2.00 [-11.31, 15.31] Sturm 2021a 51.8 d1.4 1.6 15 1.3% 5.00 [-7.13, 17.13] Sturm 2021a 51.9 16 13 49.9 19.9 15 1.1% 2.00 [-11.31, 15.31] Sturm 2021g 37.8 13.3 9 31.4 17.9 22 1.4% 6.40 [-5.07, 17.87] Total (95% CI) 703 858 100.0% 7.62 [6.24, 9.00] Heterogeneity: $r^2 = 0.00$; $r^2 = 6.38$; $df = 11$ ($p = 0.85$); $P = 0\%$ Testfor overall effect $Z = 10.84$ ($p < 0.00001$) Total (95% CI) 703 858 100.0% 7.62 [6.24, 9.00] Heterogeneity: $r^2 = 0.00$; $r^2 = 6.38$; $df = 11$ ($p = 0.85$); $P = 0\%$ Testfor overall effect $Z = 10.8$	Heterogeneity: r ² = 0, Test for overall effect: C Study or Subgroup Adunka 2008 Firszt 2018 Grisel 2021 Kelsall 2021 Punne 2016	00; $\chi^2 = 6.41$ 12 Mean 59 51 55.8 65.2 56.8	11.78 1 (<i>p</i> < 0 Month SD 16.6 22 23.4 18.8 2.9	840 , df = 15 0.00001 <u>Total</u> 29 39 426 91 27	5 (p = 0)) 6 I Mean 51.4 49 52.7 60.9 52.9	.70); / ² Month SD 16.6 20 22.9 21.1 3.8	969 = 0% Total 29 39 399 96 27	100.0% Weight 2.6% 2.1% 18.7% 5.7% 60.9%	4.29 [2.98, 5.60] Mean Difference IV, Random, 95% CI 7.60 [-0.94, 16.14] 2.00 [-7.33, 11.33] 3.10 [-0.06, 6.26] 4.30 [-1.42, 10.02] 2.00 [215 5.65]	Favours 3 month Favours 6 month Mean Difference Ⅳ, Random, 95% CI						
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	Heterogeneity: r ² = 0. Test for overall effect: C <u>Study or Subgroup</u> Adunka 2008 Firszt 2018 Grisel 2021 Kelsall 2021 Runge 2016 Starten 2017	00; $\chi^2 = Z = 6.41$ 12 Mean 59 51 55.8 65.2 56.8 67	Month SD 16.6 22 23.4 18.8 3.9 19	840 , df = 16 0.00001 <u>Total</u> 29 39 426 91 37 61	5 (p = 0)) 6 I Mean 51.4 49 52.7 60.9 52.9 56	.70); / ² Month SD 16.6 20 22.9 21.1 3.8 24	969 = 0% Total 29 39 399 96 37 61	100.0% Weight 2.6% 2.1% 18.7% 5.7% 60.8% 3.2%	4.29 [2.98, 5.60] Mean Difference IV, Random, 95% CI 7.60 [-0.94, 16.14] 2.00 [-7.33, 11.33] 3.10 [-0.06, 6.26] 4.30 [-1.42, 10.02] 3.90 [2.15, 5.65] 1.00 [3.21, 8.68]	Favours 3 month Favours 6 month						
Sturm 2021c 51.8 23.2 8 43.3 20 16 0.5% 8.50 [+0.33, 27.3] Sturm 2021d 59.2 17.4 16 58.5 19.5 16 1.1% 0.70 [+2.29, 13.69] Sturm 2021e 51.9 16 13 48.7 20.5 15 1.0% 3.20 [+0.34, 16.74] Sturm 2021f 39.1 16.1 13 35.5 13.3 15 1.5% $3.00 [-7.44, 14.64]$ Sturm 2021g 37.8 13.3 9 37.5 20.5 19 1.2% $0.30 [+2.37, 12.97]$ Total (95% CI) T62 771 100.0% 3.94 [2.57, 5.31] Heterogeneity, $r^2 = 0.00$; $r^2 = 5.68$, $dr = 12$ ($p = 0.93$); $P = 0\%$ Test for overall effect $Z = 5.65$ ($p < 0.00001$) D 12 Month 3 Month Mean Difference Study or Subgroup Mean SD Total Mean SD Total Weight N. Random, 95% CI Adunka 2008 59 16.6 29 42.9 18.6 29 2.3% 16.10 [7.03, 25.17] Deep 2021 54.3 21 41 50.3 20 53 2.7% 4.00 [4.3, 12.39] Grisel 2021 55.8 23.4 426 49.3 24.3 529 20.6% 6.50 [3.6, 9.54] Kelsall 2021 65.2 18.8 91 56.3 22 96 5.5% 8.90 [3.04, 14.76] Runge 2016 56.8 3.9 37 49 38 37 61.7% 7.80 [6.6, 9.55] Sturm 2021a 53.4 21.3 13 40 18.5 14 0.9% 13.40 [-1.05, 27.85] Sturm 2021a 53.4 21.3 13 40.18.5 14 0.9% (3.30, 14.76) Runge 2016 56.8 3.9 37 49 38 37 61.7% 7.80 [6.6, 9.55] Sturm 2021a 51.8 12.2 8 42.8 22 16 0.5% 9.00 [1.03, 22.83] Sturm 2021a 53.4 21.3 13 40.18.5 11.4 0.9% 13.40 [-1.05, 27.85] Sturm 2021a 51.8 12.2 8 42.8 22 16 0.5% 9.00 [-1.3, 17.31] Sturm 2021a 51.8 12.3 13 40.9 18.9 15 1.1% 2.00 [+1.3, 1, 15.31] Sturm 2021a 51.8 12.3 13 40.9 18.9 15 1.1% 2.00 [+1.3, 1, 15.31] Sturm 2021a 51.8 12.3 2.8 42.8 22 16 0.5% 9.00 [-1.3, 27.85] Sturm 2021a 51.8 13.3 9 31.4 17.9 22 1.4% 6.40 [-5.07, 17.87] Total (95% CI) 703 858 100.0% 7.62 [6.24, 9.00] Heterogeneity, $r^2 = 0.00$; $r^2 = 6.38$, $dr = 11$ ($p = 0.85$); $P = 0\%$ Test for overall effect $Z = 10.84$ ($p < 0.00001$)	Study or Subgroup Adunka 2008 Firszt 2018 Grisel 2021 Kelsall 2021 Runge 2016 Sladen 2017 Sturry 2021a	00; $\chi^2 = Z = 6.41$ 12 Mean 59 51 55.8 65.2 56.8 67 53.4	11.78 1 (<i>p</i> < 0 Month SD 16.6 22 23.4 18.8 3.9 19 21.3	840 , df = 15 0.00001 29 39 426 91 37 61 13	5 (p = 0)) 6 I Mean 51.4 49 52.7 60.9 52.9 56 50.3	.70); / ² Month SD 16.6 20 22.9 21.1 3.8 24 17 7	969 = 0% Total 29 399 96 37 61 14	Weight 2.6% 2.1% 18.7% 5.7% 60.8% 3.2% 0.9%	4.29 [2.98, 5.60] Mean Difference IV, Random, 95% CI 7.60 [-0.94, 16.14] 2.00 [-7.33, 11.33] 3.10 [-0.06, 6.26] 4.30 [-1.42, 10.02] 3.90 [2.15, 5.65] 11.00 [3.32, 18.68] 31.01 [-1.71, 793]	Favours 3 month Favours 6 month Mean Difference IV, Random, 95% Cl						
Sturm 2021d 59.2 17.4 15 10.00 17.4 14.5 18.6 1.1% 0.70 1.2.29, 13.89] Sturm 2021e 51.9 16 1.1% 0.70 1.1% 0.70 1.1% 0.70 1.1% 0.70 1.1% 0.70 1.1% 0.70 1.1% 0.70 1.1% 0.00 1.1% 0.00 1.1% 0.00 1.1% 0.00 1.1% 0.00 1.1% 0.00 1.1% 0.00 1.1% 0.00 1.1% 0.00 1.1% 0.00 1.1% 0.00 1.1% 0.00 1.1% 0.00 1.1% N.0.00 1.1% N.0.00 1.1% N.0.00 N.0.0 <th colspan="6" n"<="" t<="" td=""><td>Heterogeneily: r² = 0. Test for overall effect: C <u>Study or Subgroup</u> Adunka 2008 Firszl 2018 Grisel 2021 Ketsall 2021 Runge 2016 Staden 2017 Sturm 2021b</td><td>00; $\chi^2 = Z = 6.41$ 12 Mean 59 51 55.8 65.2 56.8 67 53.4 48</td><td>Month SD 16.6 22 23.4 18.8 3.9 19 21.3 18.4</td><td>840 , df = 15 0.00001 29 39 426 91 37 61 13 8</td><td>5 (p = 0 1) 6 I Mean 51.4 49 52.7 60.9 52.9 52.9 56 50.3 49.7</td><td>.70); /² Month <u>SD</u> 16.6 20 22.9 21.1 3.8 24 17.7 19.7</td><td>969 = 0% Total 29 399 96 37 61 14 15</td><td>Weight 2.6% 2.1% 18.7% 5.7% 60.8% 3.2% 0.9% 0.7%</td><td>4.29 [2.98, 5.60] Mean Difference <u>IV, Random, 95% CI</u> 7.60 [-0.94, 16.14] 2.00 [-7.33, 11.33] 3.10 [-0.06, 6.26] 4.30 [-1.42, 10.02] 3.90 [2.15, 5.65] 11.00 [3.32, 18.68] 3.10 [-11.73, 17.93] 4.21 [-1.70] [-1.78] 4.49]</td><td>Favours 3 month Favours 6 month Mean Difference IV, Random, 95% Cl</td></th>	<td>Heterogeneily: r² = 0. Test for overall effect: C <u>Study or Subgroup</u> Adunka 2008 Firszl 2018 Grisel 2021 Ketsall 2021 Runge 2016 Staden 2017 Sturm 2021b</td> <td>00; $\chi^2 = Z = 6.41$ 12 Mean 59 51 55.8 65.2 56.8 67 53.4 48</td> <td>Month SD 16.6 22 23.4 18.8 3.9 19 21.3 18.4</td> <td>840 , df = 15 0.00001 29 39 426 91 37 61 13 8</td> <td>5 (p = 0 1) 6 I Mean 51.4 49 52.7 60.9 52.9 52.9 56 50.3 49.7</td> <td>.70); /² Month <u>SD</u> 16.6 20 22.9 21.1 3.8 24 17.7 19.7</td> <td>969 = 0% Total 29 399 96 37 61 14 15</td> <td>Weight 2.6% 2.1% 18.7% 5.7% 60.8% 3.2% 0.9% 0.7%</td> <td>4.29 [2.98, 5.60] Mean Difference <u>IV, Random, 95% CI</u> 7.60 [-0.94, 16.14] 2.00 [-7.33, 11.33] 3.10 [-0.06, 6.26] 4.30 [-1.42, 10.02] 3.90 [2.15, 5.65] 11.00 [3.32, 18.68] 3.10 [-11.73, 17.93] 4.21 [-1.70] [-1.78] 4.49]</td> <td>Favours 3 month Favours 6 month Mean Difference IV, Random, 95% Cl</td>						Heterogeneily: r ² = 0. Test for overall effect: C <u>Study or Subgroup</u> Adunka 2008 Firszl 2018 Grisel 2021 Ketsall 2021 Runge 2016 Staden 2017 Sturm 2021b	00; $\chi^2 = Z = 6.41$ 12 Mean 59 51 55.8 65.2 56.8 67 53.4 48	Month SD 16.6 22 23.4 18.8 3.9 19 21.3 18.4	840 , df = 15 0.00001 29 39 426 91 37 61 13 8	5 (p = 0 1) 6 I Mean 51.4 49 52.7 60.9 52.9 52.9 56 50.3 49.7	.70); / ² Month <u>SD</u> 16.6 20 22.9 21.1 3.8 24 17.7 19.7	969 = 0% Total 29 399 96 37 61 14 15	Weight 2.6% 2.1% 18.7% 5.7% 60.8% 3.2% 0.9% 0.7%	4.29 [2.98, 5.60] Mean Difference <u>IV, Random, 95% CI</u> 7.60 [-0.94, 16.14] 2.00 [-7.33, 11.33] 3.10 [-0.06, 6.26] 4.30 [-1.42, 10.02] 3.90 [2.15, 5.65] 11.00 [3.32, 18.68] 3.10 [-11.73, 17.93] 4.21 [-1.70] [-1.78] 4.49]	Favours 3 month Favours 6 month Mean Difference IV, Random, 95% Cl
Sturm 2021e 51.9 16 13 48.7 20.5 15 1.0% 3.20 [-10.34, 16.74] Sturm 2021f 39.1 16.1 13 35.5 13.3 15 1.5% 3.60 [-7.44, 14.64] Sturm 2021g 37.8 13.3 9 37.5 20.5 19 1.2% 0.30 [-12.37, 12.97] Total (95% Cl) 762 771 100.0% 3.94 [2.57, 5.31]	Heterogeneity: r ² = 0. Test for overall effect: C <u>Study or Subgroup</u> Adunka 2008 Firszt 2018 Grisel 2021 Kelsall 2021 Runge 2016 Sladen 2017 Sturm 2021a Sturm 2021c	00; $\chi^2 = Z = 6.41$ 12 Mean 59 51. 55.8 65.2 56.8 67 53.4 48 51.8	Month SD 16.6 22 23.4 18.8 3.9 19 21.3 18.4 23.2	840 , df = 15 0.00001 29 39 426 91 37 61 13 8 8	5 (p = 0 1) 6 I Mean 51.4 49 52.7 60.9 52.9 56 50.3 49.7 43.3	.70); / ² Month SD 16.6 20 22.9 21.1 3.8 24 17.7 19.7 20	969 = 0% Total 29 39 399 96 37 61 14 15 16	Weight 2.6% 2.1% 18.7% 5.7% 60.8% 3.2% 0.7% 0.5%	4.29 [2.98, 5.60] Mean Difference IV, Random, 95% CI 7.60 [-0.94, 16.14] 2.00 [-7.33, 11.33] 3.10 [-10.06, 6.26] 4.30 [-1.42, 10.02] 3.90 [2.15, 5.65] 11.00 [3.32, 18.68] 3.10 [-11.73, 17.93] 1.70 [-17.89, 14.49] 8.50 [-10.32, 27.33]	Favours 3 month Favours 6 month Mean Difference IV, Random, 95% Cl						
Sturm 2021f 39.1 16.1 13 35.5 13.3 19 1.2% 3.00 [-7.44, 14.64] Sturm 2021g 37.8 13.3 9 37.5 20.5 19 1.2% 0.30 [-7.24, 71, 12.97] Total (95% CI) 762 771 100.0% 3.94 [2.57, 5.31] Heterogeneity: $r^2 = 0.00$; $\chi^2 = 5.68$, $df = 12$ ($p = 0.93$); $l^2 = 0.\%$ 3.90 Total Weight V, Random, 95% CI Mean Difference Mean Difference Mean Difference N. Random, 95% CI Adunka 2008 59 16.6 29 6.55% 8.90 [10.10 [7.03 25.17] Geadea	Heterogeneity: r ² = 0. Test for overall effect: C Adunka 2008 Firszt 2018 Grisel 2021 Kelsall 2021 Runge 2016 Sladen 2017 Sturm 2021a Sturm 2021b Sturm 2021c Sturm 2021d	00; $\chi^2 = 2$ Z = 6.41 12 Mean 59 51 55.8 65.2 56.8 65.2 56.8 65.2 56.8 65.2 56.8 65.2 56.8 65.4 48 51.8 59.4 59.5 53.4 48 59.5 53.4 55.8	Month SD 16.6 22 3.4 18.8 3.9 19 21.3 18.4 23.2 17.4	840 , df = 15 0.00001 29 39 426 91 37 61 13 8 8 15	5 (<i>p</i> = 0 1) 6 I Mean 51.4 49 52.7 60.9 52.9 56 50.3 49.7 43.3 58.5	.70); / ² Month <u>SD</u> 16.6 20 22.9 21.1 3.8 24 17.7 19.7 20 19.5	969 = 0% 29 399 96 37 61 14 15 16 16	Weight 2.6% 2.1% 18.7% 5.7% 60.8% 3.2% 0.9% 0.7% 0.5% 1.1%	4.29 [2.98, 5.60] Mean Difference IV, Random, 95% CI 7.60 [-0.94, 16.14] 2.00 [-7.33, 11.33] 3.10 [-10.06, 6.26] 4.30 [-1.42, 10.02] 3.90 [2.15, 5.65] 1.100 [13.32, 18.68] 3.10 [-11.73, 17.93] -1.70 [-17.89, 14.49] 8.50 [-10.33, 27.33] 0.70 [-12.29, 13.68]	Favours 3 month Favours 6 month Mean Difference IV, Random, 95% CI						
sturm 2021g 37.8 13.3 9 37.5 20.5 19 1.2% 0.30 [-12.37, 12.97] Total (95% CI) 762 771 100.0% 3.94 [2.57, 5.31] Heterogeneity: $r^2 = 0.00; r^2 = 5.68, df = 12 (p = 0.93); l^2 = 0% 3.94 [2.57, 5.31] D 12 Month 3 Month Mean Difference Mean Difference Mean Difference Mean Difference Mean Difference Study or Subgroup Mean SD Total Mean SD Total Weight Mean Difference Study or Subgroup Mean SD Total Weight Mean Difference Study or Subgroup Mean SD Total Weight Mean Difference Mean Difference Mean Difference SUT Mean Difference Mean Difference Runge 2$	Study or Subgroup Adunka 2008 Firszt 2018 Grisel 2021 Kelsail 2021 Runge 2016 Sladen 2017 Sturm 2021a Sturm 2021b Sturm 2021c Sturm 2021b	00; $\chi^2 = 2$ Z = 6.41 12 Mean 59 51 55.8 65.2 56.8 56.8 57.5 56.8 57.5 56.8 57.5 56.8 57.5 56.8 57.5 56.8 57.5 56.8 57.5 56.8 57.5 56.8 57.5 57.5 57.5 57.5 57.4 57.5 57	Month SD 16.6 23.4 18.8 3.9 21.3 18.4 23.2 17.4 16	840 , df = 15 0.00001 29 39 426 91 37 61 13 8 8 15 13	5 (<i>p</i> = 0 1) 6 I Mean 51.4 49 52.7 60.9 56 50.3 49.7 43.3 58.5 48.7	.70); / ² Month SD 16.6 20 22.9 21.1 3.8 24 17.7 19.7 20 19.5 20.5	969 = 0% 29 399 96 37 61 14 15 16 16 15	Weight 2.6% 2.1% 5.7% 60.8% 3.2% 0.9% 0.5% 1.1% 1.0%	4.29 [2.98, 5.60] Mean Difference IV, Random, 95% CI 7.60 [-0.94, 16.14] 2.00 [-7.33, 11.33] 3.10 [-0.6, 6.26] 4.30 [-1.42, 10.02] 3.30 [2.15, 5.65] 11.00 [3.32, 18.68] 3.10 [-11.73, 17.93] -1.70 [-17.89, 14.49] 8.50 [-10.33, 27.33] 3.20 [-10.34, 16.74]	Favours 3 month Favours 6 month Mean Difference IV, Random, 95% CI						
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	Heterogeneily: r ² = 0. Test for overall effect: C Adunka 2008 Firszt 2018 Grisel 2021 Kelsall 2021 Runge 2016 Sladen 2017 Sturm 2021a Sturm 2021b Sturm 2021b Sturm 2021c Sturm 2021c Sturm 2021c	00; $\chi^2 = 6.41$ 12 Mean 59 51. 55.8 65.2 56.8 67 53.4 48 51.8 59.2 51.9 39.1	Month SD 16.6 23.4 18.8 3.9 21.3 18.4 23.2 17.4 16 16.1	840 , df = 15 0.00001 29 39 426 91 37 61 13 8 8 15 13 13	5 (p = 0) 6 I Mean 51.4 49 52.7 60.9 52.9 56 50.3 49.7 43.3 58.5 48.7 35.5	.70); /* Month SD 16.6 20 22.9 21.1 3.8 24 17.7 19.7 20 19.5 20.5 13.3	969 = 0% 29 399 96 37 61 14 15 16 16 15 15	Weight 2.6% 2.1% 18.7% 5.7% 60.8% 0.9% 0.7% 0.5% 1.0% 1.5%	4.29 [2.98, 5.60] Mean Difference <u>IV, Random, 95% CI</u> 7.60 [0.94, 16.14] 2.00 [7.33, 11.33] 3.10 [0.06, 6.26] 4.30 [1.42, 10.02] 3.90 [215, 5.65] 11.00 [3.32, 18.68] 3.10 [11.7, 17.93] 4.10 [11.73, 17.93] 3.00 [1.42, 9], 14.84] 9.20 [10.33, 27.33] 0.70 [12.29, 13.68] 3.20 [10.34, 16.74] 3.60 [7.44, 14.64]	Favours 3 month Favours 6 month Mean Difference N, Random, 95% Cl						
Note: The first or overall effect $Z = 5.68$, $df = 12$ ($p = 0.93$); $l^2 = 0\%$ Test for overall effect $Z = 5.65$ ($p < 0.00001$) D 12 Month Mean SD Total Mean SD Total Weight IV, Random, 95% CI Mean SD Total Mean SD Total Weight IV, Random, 95% CI Mean Difference Mean SD Total Mean SD Total Weight IV, Random, 95% CI Mean Difference Mean Difference Adunka 2008 S9 16.6 29 2.3% 16.10 [7.03, 25.17] Deep 2021 54.3 21 44.3529 2.06% 6.50(3.49, 9.54) Keisall 2021 65.2 8.8 91 56.3 2.7% 4.00 [4.39, 12.39] Git S5 Notice 10.5% 9.00 [6.05, 9.55] Sturm 20216 56.8 3.00 [4.10.5, 27.85] Sturm 2021c 51.8 8 42.2 16 1.2% 8.30 [4.2,3,20.8] Imo	Heterogeneity: r ² = 0. Testfor overall effect: C <u>Study or Subgroup</u> Adunka 2008 Firszt 2018 Grisel 2021 Kelsall 2021 Runge 2016 Sladen 2017 Sturm 2021a Sturm 2021b Sturm 2021b Sturm 2021b Sturm 2021f Sturm 2021f Sturm 2021g	00; $\chi^2 = 6.41$ 12 Mean 59 51 55.8 65.2 56.8 67 53.4 48 51.8 59.2 51.9 39.1 37.8	Month SD 16.6 22 23.4 18.8 3.9 21.3 18.4 23.2 17.4 16.1 13.3	840 , <i>df</i> = 15 0.00001 29 39 426 91 37 61 13 8 8 15 13 13 9	5 (p = 0) 6 I Mean 51.4 49 52.7 60.9 52.9 56 50.3 49.7 43.3 58.5 48.7 35.5 37.5	70); /* Month <u>SD</u> 16.6 20.9 21.1 3.8 24 17.7 19.7 20.5 13.3 20.5	969 = 0% 29 399 96 37 61 14 15 16 16 16 15 15 19	Weight 2.6% 2.1% 18.7% 5.7% 60.8% 0.9% 0.7% 0.5% 1.1% 1.0% 1.5% 1.2%	4.29 [2.98, 5.60] Mean Difference IV, Random, 95% CI 7.60 [0.94, 16.14] 2.00 [7.33, 11.33] 3.10 [-0.06, 6.26] 4.30 [-1.42, 10.02] 3.90 [2.15, 5.65] 11.00 [3.32, 18.68] 3.10 [-11.73, 17.93] 1.70 [-17.89, 14.49] 8.50 [-10.34, 27.33] 0.70 [-12.29, 13.68] 3.20 [-10.34, 16.74] 3.60 [-7.44, 14.64] 0.30 [-12.37, 12.97]	Favours 3 month Favours 8 month Mean Difference IV, Random, 95% Cl						
-25 -25 -25 50 -25 25 50 -25 25 50 Favours 12 month Favours 2 60 25 50 D 12 Month 3 Month Mean Difference Mean Difference </td <td>Heterogeneity: r² = 0. Test for overall effect: C Study or Subgroup Adunka 2008 Firszt 2018 Grisel 2021 Kelsall 2021 Runge 2016 Sladen 2017 Sturm 2021a Sturm 2021b Sturm 2021c Sturm 2021c Sturm 2021e Sturm 2021g Total (95% CD)</td> <td>00; $\chi^2 = 6.41$ 12 Mean 59 51 55.8 65.2 56.8 67 53.4 48 51.8 57.4 48 51.9 39.1 37.8</td> <td>11.78 ((p < (Month SD 16.6 22 23.4 18.8 3.9 21.3 18.4 23.2 17.4 16.1 13.3</td> <td>840 , df = 15 0.00001 29 39 426 91 37 61 13 8 8 15 13 13 9 762</td> <td>5 (p = 0) $6 I$ $Mean$ 51.4 49 52.9 56 50.3 49.7 43.3 58.5 48.7 35.6 37.5</td> <td>70); /* Month SD 16.6 20 22.9 21.1 3.8 24 17.7 20 19.5 20.5 13.3 20.5</td> <td>969 = 0% Total 29 399 96 37 61 15 16 15 16 15 19 771</td> <td>Weight 2.6% 2.1% 18.7% 60.8% 3.2% 0.5% 1.1% 1.0% 1.5% 1.2% 100.0%</td> <td>4.29 [2.98, 5.60] Mean Difference IV, Random, 95% CI 7.60 [-0.94, 16.14] 2.00 [-7.33, 11.33] 3.10 [-10.06, 6.26] 4.30 [-14.2, 10.02] 3.90 [2.15, 56.65] 11.00 [3.32, 18.68] 3.10 [-11.73, 17.93] -1.70 [-17.98, 14.64] 3.20 [-10.34, 16.74] 3.60 [-7.44, 14.64] 0.30 [-12.37, 12.97] 3.94 [2.57, 5.31]</td> <td>Favours 3 month Favours 6 month Mean Difference IV, Random, 95% CI</td>	Heterogeneity: r ² = 0. Test for overall effect: C Study or Subgroup Adunka 2008 Firszt 2018 Grisel 2021 Kelsall 2021 Runge 2016 Sladen 2017 Sturm 2021a Sturm 2021b Sturm 2021c Sturm 2021c Sturm 2021e Sturm 2021g Total (95% CD)	00; $\chi^2 = 6.41$ 12 Mean 59 51 55.8 65.2 56.8 67 53.4 48 51.8 57.4 48 51.9 39.1 37.8	11.78 ((p < (Month SD 16.6 22 23.4 18.8 3.9 21.3 18.4 23.2 17.4 16.1 13.3	840 , df = 15 0.00001 29 39 426 91 37 61 13 8 8 15 13 13 9 762	5 (p = 0) $6 I$ $Mean$ 51.4 49 52.9 56 50.3 49.7 43.3 58.5 48.7 35.6 37.5	70); /* Month SD 16.6 20 22.9 21.1 3.8 24 17.7 20 19.5 20.5 13.3 20.5	969 = 0% Total 29 399 96 37 61 15 16 15 16 15 19 771	Weight 2.6% 2.1% 18.7% 60.8% 3.2% 0.5% 1.1% 1.0% 1.5% 1.2% 100.0%	4.29 [2.98, 5.60] Mean Difference IV, Random, 95% CI 7.60 [-0.94, 16.14] 2.00 [-7.33, 11.33] 3.10 [-10.06, 6.26] 4.30 [-14.2, 10.02] 3.90 [2.15, 56.65] 11.00 [3.32, 18.68] 3.10 [-11.73, 17.93] -1.70 [-17.98, 14.64] 3.20 [-10.34, 16.74] 3.60 [-7.44, 14.64] 0.30 [-12.37, 12.97] 3.94 [2.57, 5.31]	Favours 3 month Favours 6 month Mean Difference IV, Random, 95% CI						
D 12 Month 3 Month Mean Difference Mean Difference Adunka 2008 59 Total Mean 50 Total Weight N, Random, 95% CI Adunka 2008 59 16.6 29 42.9 18.6 29 2.3% 16.10 [7.03, 25.17] Deep 2021 54.3 21 41 50.3 22 96 55% 8.90 [3.04, 14.76] Ketsall 2021 65.8 23.4 42.6 49.3 24.3 529 20.6% 6.50 [3.46, 9.54] ++ Ketsall 2021 65.8 23.4 42.6 49.3 24.3 529 20.6% 6.50 [3.46, 9.54] ++ Kunge 2016 56.8 3.9 3.7 8.90 [1.05, 0.57, 8.5] ++ <td>Heterogeneity: $r^{2} = 0$. Test for overall effect: C Study or Subgroup Adunka 2008 Firszt 2018 Grisel 2021 Kelsall 2021 Runge 2016 Sladen 2017 Sturm 2021a Sturm 2021b Sturm 2021c Sturm 2021c Sturm 2021c Sturm 2021f Sturm 2021g Total (95% CI) Heterogeneity: $r^{2} = 0.0$</td> <td>00; $\chi^2 = 6.41$ 12 Mean 59 51 55.8 65.2 56.8 67 53.4 48 51.8 57.4 48 51.8 59.2 51.8 59.2 51.8 59.2 51.8 59.2 51.9 39.1 37.8 20: $\chi^2 = 20$</td> <td>11.78 1 (p < 0 Month SD 16.6 22 23.4 18.8 3.9 19 21.3 18.4 23.2 17.4 16.1 13.3 5.68 a</td> <td>840 , df = 19 0.00001 29 39 426 91 37 61 13 8 8 8 15 13 13 9 762 4762 4762</td> <td>5 (p = 0)) 6 F Mean 51.4 49 52.7 60.9 52.9 56 50.3 49.7 43.3 548.7 35.5 37.5</td> <td>70); /* Month SD 16.6 20 22.9 21.1 3.8 24 17.7 19.7 20.5 13.3 20.5 13.3 20.5 3); /* =</td> <td>969 = 0% Total 29 399 96 37 61 14 15 16 15 15 19 771 0%</td> <td>Weight 2.6% 2.1% 18.7% 5.7% 60.8% 0.5% 0.5% 1.1% 1.0% 1.2% 100.0%</td> <td>4.29 [2.98, 5.60] Mean Difference <u>IV, Random, 95% CI</u> 7.60 [-0.94, 16.14] 2.00 [-7.33, 11.33] 3.10 [-10.06, 6.26] 4.30 [-1.42, 10.02] 3.30 [2.15, 5.65] 1.100 [33, 21,868] 3.10 [-11.73, 17.93] -1.70 [-17.89, 14.49] 8.50 [-10.33, 27.33] 0.70 [-12.29, 13.68] 3.20 [-10.34, 16.74] 3.60 [-7.44, 14.64] 0.30 [-12.37, 12.97] 3.94 [2.57, 5.31]</td> <td>Favours 3 month Favours 6 month Mean Difference IV, Random, 95% CI</td>	Heterogeneity: $r^{2} = 0$. Test for overall effect: C Study or Subgroup Adunka 2008 Firszt 2018 Grisel 2021 Kelsall 2021 Runge 2016 Sladen 2017 Sturm 2021a Sturm 2021b Sturm 2021c Sturm 2021c Sturm 2021c Sturm 2021f Sturm 2021g Total (95% CI) Heterogeneity: $r^{2} = 0.0$	00; $\chi^2 = 6.41$ 12 Mean 59 51 55.8 65.2 56.8 67 53.4 48 51.8 57.4 48 51.8 59.2 51.8 59.2 51.8 59.2 51.8 59.2 51.9 39.1 37.8 20: $\chi^2 = 20$	11.78 1 (p < 0 Month SD 16.6 22 23.4 18.8 3.9 19 21.3 18.4 23.2 17.4 16.1 13.3 5.68 a	840 , df = 19 0.00001 29 39 426 91 37 61 13 8 8 8 15 13 13 9 762 4762 4762	5 (p = 0)) 6 F Mean 51.4 49 52.7 60.9 52.9 56 50.3 49.7 43.3 548.7 35.5 37.5	70); /* Month SD 16.6 20 22.9 21.1 3.8 24 17.7 19.7 20.5 13.3 20.5 13.3 20.5 3); /* =	969 = 0% Total 29 399 96 37 61 14 15 16 15 15 19 771 0%	Weight 2.6% 2.1% 18.7% 5.7% 60.8% 0.5% 0.5% 1.1% 1.0% 1.2% 100.0%	4.29 [2.98, 5.60] Mean Difference <u>IV, Random, 95% CI</u> 7.60 [-0.94, 16.14] 2.00 [-7.33, 11.33] 3.10 [-10.06, 6.26] 4.30 [-1.42, 10.02] 3.30 [2.15, 5.65] 1.100 [33, 21,868] 3.10 [-11.73, 17.93] -1.70 [-17.89, 14.49] 8.50 [-10.33, 27.33] 0.70 [-12.29, 13.68] 3.20 [-10.34, 16.74] 3.60 [-7.44, 14.64] 0.30 [-12.37, 12.97] 3.94 [2.57, 5.31]	Favours 3 month Favours 6 month Mean Difference IV, Random, 95% CI						
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$	Study or Subgroup Adunka 2008 Firszt 2018 Grisel 2021 Kelsall 2021 Runge 2016 Sladen 2017 Sturm 2021a Sturm 2021b Sturm 2021c Sturm 2021d Sturm 2021d Sturm 2021d Sturm 2021d Sturm 2021f Sturm 2021g Total (95% CI) Heterogeneity: :* = 0.0	00; $\chi^2 = 6.41$ 12 Mean 59 51 55.8 67 53.4 59.2 51.9 39.1 37.8 20; $\chi^2 = 2$ Z = 5.65	11.78 1 (p < 0 Month SD 16.6 22 23.4 18.8 3.9 19 21.3 18.4 23.2 17.4 16.1 13.3 5.68, a (p < 0	840 , df = 19 0.00001 29 39 426 91 37 61 13 8 8 15 13 13 9 762 <i>ff</i> = 12 (0.0001	5 (p = 0 Mean 51.4 49 52.7 60.9 56.3 49.7 43.3 58.5 36.5 37.5 (p = 0.9)	70); /² Month <u>SD</u> 16.6 20.9 21.1 3.8 24 17.7 19.7 20.5 13.3 20.5 20.5 13.3 20.5 13.5 13.5 13.5 13.5 13.5 13.5 13.5 13.5 13.5 15.5	969 = 0% Total 29 399 96 37 61 14 15 16 15 15 19 771 0%	Weight 2.6% 2.1% 5.7% 60.8% 3.2% 0.9% 0.7% 0.5% 1.1% 1.0% 1.5% 1.2%	4.29 [2.98, 5.60] Mean Difference IV, Random, 95% CI 7.60 [-0.94, 16.14] 2.00 [-7.33, 11.33] 3.10 [-0.06, 6.26] 4.30 [-1.42, 10.02] 3.30 [2.15, 5.65] 11.00 [3.32, 18.68] 3.10 [-11.73, 17.93] -1.70 [-17.88, 14.48] 8.50 [-10.33, 27.33] 0.70 [-12.29, 13.68] 3.20 [-10.34, 16.74] 3.60 [-7.44, 14.64] 0.30 [-12.37, 12.97] 3.94 [2.57, 5.31]	A constraint of the second sec						
Study or Subgroup Mean SD Total Mean SD Total Weight IV, Random, 95% CI NV, Random, 95% CI Adunka 2008 59 16.6 29 42.9 18.6 29 2.3% 16.10 [7.03, 25.17] Deep 2021 54.3 21 41 50.3 20 53 2.7% 4.00 [4.39, 12.39] Orisel 2021 65.2 18.8 91 56.3 22 96 6.56% 8.90 [3.04, 14.76] Runge 2016 56.8 3.9 37 49 3.8 37 61.7% 7.80 [60.5, 9.55] Sturm 2021a 53.4 21.3 13 40 16.5 1.4 0.9% 13.40 [-1.05, 27.85] Sturm 2021b 48 18.4 41.3 19.5 16 0.7% 6.70 [-9.23, 22.63] Sturm 2021d 59.2 17.4 15 50.9 18.2 16 1.2% 8.30 [-4.23, 20.83] Sturm 2021d 39.3 14.1 1.8 1.1% 2.00 [-11.31, 15.31]	Heterogeneity: r ² = 0. Test for overall effect: C Study of Subgroup Adunka 2008 Firszl 2018 Grisel 2021 Kelsall 2021 Sturm 2021a Sturm 2021a Sturm 2021b Sturm 2021b Sturm 2021c Sturm 2021c Sturm 2021c Sturm 2021f Sturm 20	00; $\chi^{2} = 6.41$ 12 Mean 59 51 55.8 65.2 56.8 67 53.4 48 69.2 51.9 39.1 37.8 00; $\chi^{2} = 2.5.65$	11.78 (1 (7 < 0) 1 (7 < 0) 1 (7 < 0) 16.6 22 23.4 18.8 3.9 19 21.3 18.4 23.2 17.4 16.1 13.3 5.68, aa (p < 0)	840 , df = 15 0.00001 29 39 426 91 37 61 13 77 61 13 13 8 8 8 5 13 13 9 762 762 17 (2) 0.00001	5 (p = 0 6 F Mean 51.4 49 52.7 50.3 52.9 56 50.3 49.7 35.5 48.7 35.5 48.7 37.5 (p = 0.9)	70); / ² Month <u>SD</u> 16.6 20.9 21.1 3.8 24 17.7 19.5 20.5 13.3 20.5 13.3 20.5 13.3 20.5 13.3 20.5 13.3 20.5 13.3 20.5 13.3 20.5 13.5 20.5 13.5 20.	969 = 0% Total 29 399 96 37 61 15 16 15 15 15 19 771 0%	100.0% Weight 2.6% 2.1% 18.7% 5.7% 60.8% 0.5% 0.5% 0.5% 1.1% 1.0% 1.5% 1.2% 100.0%	4.29 [2.98, 5.60] Mean Difference <u>IV, Random, 95% CI</u> 7.60 [0.94, 16.14] 2.00 [-7.3, 11.33] 3.10 [-0.06, 6.26] 4.30 [-1.42, 10.02] 3.90 [21.5, 5.65] 11.00 [3.32, 18.68] 3.10 [-11.73, 17.93] 4.50 [-10.33, 27.33] 0.70 [-12.29, 13.68] 3.20 [-10.34, 16.74] 3.60 [-7.44, 14.64] 0.30 [-12.37, 12.97] 3.94 [2.57, 5.31]	A constraint of the second sec						
Adunka 2008 59 16.6 29 42.9 18.6 29 2.3% 16.10 [7.03, 25.17] Deep 2021 54.3 21 41 50.3 20 53 2.7% 4.00 [4.39, 12.39] Grisel 2021 55.8 23.4 426 49.3 24.3 529 20.6% 6.50 [3.46, 9.54] Ketsall 2021 65.2 18.8 91 56.3 22 96 5.5% 8.90 [3.04, 14.76] Runge 2016 56.8 3.9 37 49 3.8 37 61.7% 7.80 [6.05, 9.55] Sturm 2021a 53.4 21.3 13 40 16.5 14 0.9% 13.40 [1.05, 27.85] Sturm 2021b 48 18.4 8 41.3 19.5 16 0.7% 6.70 [-9.23, 22.63] Sturm 2021c 51.8 23.2 8 42.8 22 16 1.2% 8.30 [4.23, 20.83] Sturm 2021d 59.2 17.4 15 50.9 18.2 16 1.3% 50.0 [7.13, 17, 13] Sturm 2021g 37.8 13.3 9 31	Heterogeneity: r ² = 0. Testfor overall effect: C Study of Subgroup Adunka 2008 Firszt 2018 Grisel 2021 Kelsall 2021 Runge 2016 Sladen 2017 Sturm 2021a Sturm 2021b Sturm 2021	00; $\chi^{2} = 6.41$ 12 Mean 59 51 55.8 65.2 56.8 67 53.4 48 59.2 51.9 39.1 37.8 20; $\chi^{2} = 5.65$	11.78 (1 (<i>p</i> < 0) Month SD 16.6 22 23.4 18.8 3.9 19 21.3 18.4 23.2 17.4 16.1 13.3 5.68, <i>a</i> (<i>p</i> < 0) Month	840 , df = 19 0.00001 29 39 426 91 13 37 61 13 37 61 13 37 61 13 37 61 13 37 61 13 9 762 47 92 12 9 10 91 93 9 94 10 90 91 93 9 94 10 90 90 91 90 94 10 90 90 94 10 90 90 94 10 90 94 10 90 94 10 90 94 10 90 94 10 90 94 10 90 94 10 90 94 10 90 94 10 90 94 10 90 94 10 90 94 10 90 94 10 90 94 10 90 94 10 90 94 10 90 94 10 97 94 10 97 94 10 97 94 10 97 94 10 97 94 10 97 94 10 97 97 97 97 97 97 97 97 97 97 97 97 97	5 (p = 0)) 6 F Mean 51.4 49 52.7 60.9 52.9 56 50.3 49.7 43.3 58.5 48.7 35.5 37.5 (p = 0.9)	70); /* Month SD 16.6 20 22.9 21.1 3.8 24 17.7 19.7 20.5 13.3 20.5 3); /* = Month	969 = 0% Total 29 39 96 37 61 15 16 15 16 15 15 19 771 0%	Weight 2.6% 2.1% 5.7% 60.8% 0.5% 0.5% 1.1% 1.5% 1.5% 1.2% 100.0%	4.29 [2.98, 5.60] Mean Difference <u>IV, Random, 95% CI</u> 7.60 [-0.94, 16.14] 2.00 [-7.33, 11.33] 3.10 [-0.06, 6.26] 4.30 [-1.42, 10.02] 4.30 [-1.42, 10.02] 3.10 [-10.06, 6.26] 4.30 [-1.42, 10.02] 3.10 [-1.32, 18.68] 3.10 [-1.73, 17.93] 3.20 [-1.34, 14.68] 3.20 [-1.34, 14.674] 3.20 [-1.24, 14.64] 0.30 [-12.37, 12.97] 3.94 [2.57, 5.31] Mean Difference	Favours 3 month Favours 6 month Mean Difference IV. Random, 95% CI -50 -50 -25 Favours 12 month Favours 6 month Mean Difference						
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	Heterogeneity: r ² = 0. Test for overall effect: C Study or Subgroup Adunka 2008 Firszt 2018 Grisel 2021 Kelsall 2021 Runge 2016 Sladen 2017 Sturm 2021a Sturm 2021b Sturm 2021c Sturm 2021c Sturm 2021g Total (95% CI) Heterogeneity: r ² = 0.0 Test for overall effect. D Study or Subgroup	00; $\chi^{2} = 6.41$ 12 Mean 59 51 56.8 65.2 56.8 67 53.4 48 51.8 59.2 51.9 37.8 00; $\chi^{2} = 2.655$ 12 Mean	11.78 (1 (7 < 0) Month SD 16.6 22 23.4 18.8 9 9 21.3 18.4 23.2 17.4 16.1 13.3 5.68, <i>a</i> (<i>p</i> < 0) Month SD 5.0 Month SD 19 21.3 18.4 19 21.3 19 21.3 19 21.3 18.4 10 20 20 20 20 20 20 20 20 20 2	840 , df = 19 0.00001 70001 29 39 426 91 13 37 61 13 8 8 5 13 13 9 762 762 12 (0.0001] 7021	5 (p = 0) 6 I Mean 51.4 49 52.7 50.3 50.3 49.7 43.3 58.5 50.3 49.7 43.3 58.5 37.5 (p = 0.9) 3 I M Mean	70); /² Month SD 16.6 20 22.9 21.1 3.8 24 17.7 20 19.5 20.5 3); /² = Month SD	969 = 0% Total 29 399 96 14 15 16 16 15 15 19 771 0% Total	100.0% Weight 2.6% 2.1% 5.7% 60.8% 0.9% 0.9% 0.9% 0.9% 0.9% 1.1% 1.0% 1.5% 1.2% 100.0% Weight	4.29 [2.98, 5.60] Mean Difference IV, Random, 95% CI 7.60 [-0.94, 16.14] 2.00 [-7.33, 11.33] 3.10 [-10.06, 6.26] 4.30 [-14.2, 10.02] 3.90 [2.15, 65] 1.100 [3.32, 18.68] 3.10 [-11.73, 17.93] -1.70 [-17.89, 14.64] 3.20 [-10.34, 16.74] 3.20 [-10.34, 16.74] 3.20 [-10.34, 16.74] 3.20 [-10.34, 16.74] 3.394 [2.57, 5.31] Mean Difference IV, Random, 95% Cl	Favours 3 month Favours 6 month Mean Difference IV, Random, 95% CI -50 -25 Favours 12 month Favours 6 month Mean Difference IV, Random, 95% CI						
Grisel 2021 558 23.4 426 49.3 24.3 529 20.6% 6.50 [3.46, 9.54] Ketsall 2021 65.2 18.8 91 56.3 22 96 5.5% 8.90 [3.04, 14.76] Runge 2016 56.8 39 37 49 3.8 37 61.7% 7.80 [6.05, 9.55] Sturm 2021a 53.4 21.3 13 40 16.5 14 0.9% 13.40 [-1.05, 27.85] Sturm 2021b 48 18.4 8 41.3 19.5 16 0.7% 6.70 [-9.23, 22.63] Sturm 2021c 51.8 23.2 8 42.2 16 1.2% 9.00 [-10.36, 28.36]	Study or Subgroup Adunka 2008 Firszt 2018 Grisel 2021 Kelsall 2021 Runge 2016 Sladen 2017 Sturm 2021a Sturm 2021b Sturm 2021c Sturm 2021b Sturm 2021c Sturm 2021d Sturm 2021d Sturm 2021d Sturm 2021f Sturm 2021g Total (95% CI) Heterogeneity: r² = 0.0 Test for overall effect. D Study or Subgroup Adunka 2008	00; $\chi^{2} = 6.41$ 12 Mean 59 51 55.8 65.2 56.8 67 53.4 48 59.2 51.9 39.1 37.8 50.2 51.9 39.1 37.8 50.2 51.9 39.1 37.8 50.2 51.9 39.1 37.8 50.2 51.9 39.1 37.8 50.2 51.9 5	11.78 (p < 0 Monthh SD 16.6 22 23.4 18.8 3.9 19 21.3 18.4 23.2 17.4 16.1 13.3 5.68, a (p < 0 Monthh SD 18.6 19 21.3 18.4 19 21.3 18.4 19 21.3 18.4 19 21.3 18.4 19 21.3 18.4 19 21.3 18.4 19 21.3 18.4 19 21.3 18.4 19 21.3 18.4 16.6 19 21.3 18.4 16.6 19 21.3 18.4 16.6 19 21.3 18.4 16.6 19 21.3 18.4 16.6 17.4 16.6 16.6 17.4 16.6 16.7 17.4 16.6 16.6 17.4 16.6 16.7 17.4 16.6 16.7 17.4 16.6 16.7 17.4 16.6 16.7 17.4 16.6 16.7 17.4 16.6 16.7 17.4 16.6 16.7 17.4 16.6 16.7 17.4 16.6 16.7 17.4 16.6 16.7 17.4 16.7 15.6 16.8 16.7 17.4 16.8 16.7 17.4 16.8 16.7 17.4 16.8 16.7 17.4 16.8 16.8 16.7 17.4 16.8 16.7 16.8 16.7 16.8 1	840 , df = 19 .00001 29 39 426 91 37 61 13 37 61 13 38 8 5 13 39 762 tf = 12 (.00001) 762 tf = 12 (.00001)	5 (p = 0 6 f Mean 51.4 49 52.7 50.3 52.9 563 50.3 58.5 37.5 (p = 0.9) 3 f Mean 42.9	70); / ² Month SD 16.6 22.9 21.1 3.8 24 17.7 19.5 20.5 13.3 20.5 3); / ² = Month SD 18.6	969 = 0% Total 29 399 61 15 16 15 15 15 19 771 0% Total 29	100.0% Weight 2.6% 2.1% 5.7% 60.8% 0.9% 0.7% 0.5% 1.1% 1.0% 1.5% 1.2% 100.0% Weight 2.3%	4.29 [2.98, 5.60] Mean Difference IV, Random, 95% CI 7.60 [-0.94, 16, 14] 2.00 [-7.33, 11.33] 3.10 [-10.06, 6.26] 4.30 [-1.42, 10.02] 3.90 [2.15, 5.65] 1.100 [3.32, 18.68] 3.10 [-11.73, 17.93] -1.70 [-17.89, 14.49] 8.50 [-10.33, 27.33] 0.70 [-12.29, 13.68] 3.20 [-10.34, 16.74] 3.60 [-7.44, 14.64] 0.30 [-12.37, 12.97] 3.94 [2.57, 5.31] Mean Difference IV, Random, 95% CI 16.10 [7.03, 25.17]	Favours 3 month Favours 6 month Mean Difference IV, Random, 95% CI -50 -25 0 25 50 Favours 12 month Favours 6 month Mean Difference IV, Random, 95% CI -50 -25 0 25 50 Favours 12 month Favours 6 month Mean Difference IV, Random, 95% CI						
Kelsall 2021 65.2 18.8 91 56.3 2.2 96 5.5% 8.90 [3.0, 14.76] Runge 2016 56.8 3.9 3.7 49 3.8 37 61.7% 7.80 [6.05, 9.56] Sturm 2021a 53.4 21.3 13 40 16.5 14 0.9% 1.340 [-10.5, 27.86] Sturm 2021b 48 18.4 8 41.3 19.5 16 0.7% 6.70 [-9.23, 22.63] Sturm 2021c 51.8 23.2 8 23.2 16 0.5% 9.00 [-10.5, 27.86] Sturm 2021d 59.2 17.4 15 50.9 18.2 16 1.2% 8.30 [-4.23, 20.83] Sturm 2021e 51.9 16 13 49.9 19.9 15 1.1% 2.00 [-11.31, 15.31] Sturm 2021g 37.8 13.3 9 31.4 17.9 22 16 6.40 [-5.07, 17.87] Total (95% CI) 703 858 100.0% 7.62 [6.24, 9.00]	Study or Subgroup Adunka 2008 Firszt 2018 Grisel 2021 Kelsall 2021 Kalden 2016 Sladen 2017 Sturm 2021a Sturm 2021b Sturm 2021c Sturm 2021b Sturm 2021c Sturm 2021c Sturm 2021b Sturm 2021c Sturm 2021g Total (95% CI) Heterogeneity: = = 0.0 Test for overall effect. D Study or Subgroup Adunka 2008 Deep 2021	$00; x^{2} = 4$ $\frac{12}{Z} = 6.41$ $\frac{12}{Mean}$ 59 55.8 65.2 55.8 67 $75.3.4$ 48 51.8 59.2 51.9 39.1 37.8 $00; x^{2} = 5.65$ $\frac{12}{Mean}$ $\frac{12}{Mean}$	11.78 () (p < () () () () () () () () () () () () ()	840 , df = 1 29 39 426 91 37 61 13 8 8 5 13 13 13 13 13 13 13 27 62 762 772 762 772 762 41	5 (p = 0 Mean 51.4 4 99 52.7 60.9 52.7 60.9 52.9 56 50.3 49.7 43.3 58.5 48.7 37.5 (p = 0.9) 3 I Mean 42.9 50.3 45.3 50.3 58.5 59.5 58.5 59.5 50.5	70); / ² Month SD 16.6 22.9 21.1 3.8 24 17.7 19.7 20.5 13.3 20.5 13.3 20.5 3); / ² = Month SD 18.6 20 22.9 19.5 19.5 20.5 13.3 20.5 19.5 20.5 13.3 20.5 20.5 19.5 20.5 19.5 20.5 19.5 20.5 19.5 20.5 19.5 20.5 19.5 20.5 19.5 20.5 19.5 20.5 19.5 20.5 19.5 20.5 19.5 20.5 19.5 20.5 20.5 19.5 20.5	969 = 0% <u>Total</u> 29 39 39 96 14 15 16 15 15 19 771 0% <u>Total</u> 29 53	Weight 2.6% 2.1% 18.7% 5.7% 60.8% 0.9% 0.5% 1.1% 1.0% 1.5% 1.2% 100.0% Weight 2.3% 2.7%	4.29 [2.98, 5.60] Mean Difference <u>N, Random, 95% CI</u> 7.60 [0.94, 16.14] 2.00 [7.33, 11.33] 3.10 [0.06, 6.26] 3.30 [1.42, 10.02] 3.90 [2.15, 5.65] 11.00 [3.32, 18.68] 3.10 [1.17, 17.93] 3.01 [1.17, 17.93] 3.01 [1.17, 17.93] 3.01 [1.17, 17.93] 3.01 [1.17, 17.93] 3.01 [1.17, 17.93] 3.01 [1.22, 13.68] 3.20 [1.03, 27.33] 0.70 [1.2, 29, 13.68] 3.20 [1.03, 27.33] 3.20 [1.03, 12.37] Mean Difference <u>N, Random, 95% CI</u> 16.10 [7.03, 25.71] 4.00 [4.38, 12.38]							
Runge 2016 56.8 3.9 37 49 3.8 37 61.7% 7.80 [6.05, 9.55] Sturm 2021a 53.4 21.3 13 40 16.5 14 0.9% 13.40 [1.05, 27.85] Sturm 2021b 48 18.4 8 41.3 19.5 16 0.7% 6.70 [9.23, 22.63] Sturm 2021c 51.8 23.2 8 42.8 22 16 0.5% 9.00 [-10.36, 28.36] Sturm 2021c 51.8 23.2 8 42.8 22 16 1.2% 8.30 [4.23, 20.83] Sturm 2021c 51.9 16 1.3 49.9 19.9 15 1.1% 2.00 [-11.31, 15.31] Sturm 2021g 37.8 13.3 9 31.4 17.9 22 1.4% 6.40 [-5.07, 17.87] Total (95% CI) 703 858 100.0% 7.62 [6.24, 9.00]	Heterogeneily: r ² = 0. Test for overall effect: C Study or Subgroup Adunka 2008 Firszt 2018 Grisel 2021 Kelsall 2021 Runge 2016 Sladen 2017 Sturm 2021a Sturm 2021b Sturm 2021b Sturm 2021b Sturm 2021c Sturm 2021c Sturm 2021f Sturm 2021f Sturm 2021g Total (95% CI) Heterogeneity: r ² = 0.1 Test for overall effect. D Study or Subgroup Adunka 2008 Deep 2021 Grisel 2021	00; $\chi^{*} = \frac{1}{Z} = 6.41$ 12 Mean 59 51 55.8 65.2 56.8 67 53.4 48 51.8 59.2 51.9 39.1 37.8 00; $\chi^{*} = \frac{2}{S} = 5.65$ 12 Mean 59 54.3 55.8 55.8 55.8 55.8 55.8 55.8 55.8 55.8 55.8 55.8 55.8 55.8 55.8 55.8 55.9 55.8	$\begin{array}{c} 11.78\\ 1 \ (p < 0 \\ \hline \\ \textbf{Month} \\ \textbf{SD} \\ 16.6\\ 22\\ 23.4\\ 18.8\\ 3.9\\ 19\\ 21.3\\ 18.4\\ 23.2\\ 17.4\\ 16\\ 16.1\\ 13.3\\ \hline \\ 5.68, a \\ (p < 0 \\ \hline \\ \textbf{Month} \\ \textbf{SD} \\ 116.6\\ 21\\ 23.4\\ \end{array}$	840 , df = 19 29 39 426 91 37 61 13 8 8 8 5 13 13 13 9 762 df = 12 (.00001) 764 41 426	5 (p = 0 Mean 51.4 49 52.7 60.9 52.9 56.3 49.7 43.3 58.5 37.5 (p = 0.9 31 Mean 42.9 50.3 49.7 34.7 35.5 37.5 (p = 0.9) 31 49.7 40.9 40.9 40.9 50.9 50.9 50.9 50.9 50.9 50.9 50.9 50.9 50.9 50.9 50.9 50.9 50.9 50.9 50.3 50.3 50.3 50.3 50.5 50.3 50.5 50.3 50.5 50.3 50.5	$(70); l^2$ North SD 16.6 20 22.9 21.1 3.8 24 17.7 19.5 20.5 13.3 20.5 3); l^2 = Month SD 18.6 20 24.3 18.6 20 24.4 3.8 20.5 3.5 20.5 3.5 20.5 3.5 20.5	969 = 0% Total 29 39 96 37 61 14 15 16 15 15 19 771 0% Total 29 37 61 14 15 15 19 771 0%	100.0% Weight 2.6% 2.1% 5.7% 60.8% 0.9% 0.5% 1.1% 1.0% 1.5% 1.2% 100.0% Weight 2.3% 2.7% 2.6%	4.29 [2.98, 5.60] Mean Difference <u>IV, Random, 95% CI</u> 7.60 [0.94, 16.14] 2.00 [-7.3, 11.33] 3.10 [-0.06, 6.26] 4.30 [-1.42, 10.02] 3.90 [2.15, 5.65] 11.00 [3.32, 18.68] 3.10 [-1.73, 17.93] 4.70 [-17.89, 14.49] 5.05 [-1.03, 27.33] 0.70 [-12.29, 13.68] 3.20 [-1.34, 16.74] 3.20 [-1.34, 16.74] 3.20 [-1.34, 16.74] 3.20 [-1.34, 16.74] 3.20 [-1.34, 16.74] 3.20 [-1.34, 12.97] 3.94 [2.57, 5.31] Mean Difference <u>IV, Random, 95% CI</u> 16.10 [7.03, 25.17] 4.00 [-4.39, 12.39] 6.50 [3.46, 9.54]	50 -25 0 25 50 Favours 3 month Favours 6 month Mean Difference IV, Random, 95% CI -50 -25 0 25 50 Favours 12 month Favours 6 month Mean Difference IV, Random, 95% CI						
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	Total (95% CI) Heterogeneity: r ² = 0. Testfor overall effect: C Adunka 2008 Adunka 2008 Firszt 2018 Grisel 2021 Kelsall 2021 Runge 2016 Sturm 2021a Sturm 2021b Sturm 2021c Sturm 2021c Sturm 2021g Total (95% CI) Heterogeneity: r ² = 0.0 Total (95% CI) Heterogeneity: r ² = 0.0 Study or Subgroup Adunka 2008 Dep 2021 Grisel 2021 Grisel 2021 Kelsall 2021	00; $\chi^{2} = 6.41$ 12 Mean 59 51 55.8 65.2 56.8 67 53.4 48 69.2 51.9 69.2 51.9 69.2 51.9 69.2 51.9 60.2 51.9 60.2 60.5 60.2 60.5 60.2 60.5	$\begin{array}{c} 11.78\\ 1 \ (p < 0 \\ \hline \\ \textbf{Month} \\ \textbf{SD} \\ 16.6\\ 22\\ 23.4\\ 18.8\\ 3.9\\ 19\\ 21.3\\ 18.4\\ 23.2\\ 17.4\\ 16\\ 16.1\\ 13.3\\ \hline \\ 5.68, a\\ (p < 0 \\ \hline \\ \textbf{Month} \\ \textbf{SD} \\ 16.6\\ 21\\ 13.4\\ 18.8 \end{array}$	840 , df = 19 29 38 426 91 37 61 13 8 8 5 13 13 13 9 762 <i>tf</i> = 12 (.00001) 762 <i>tf</i> = 12 (.00001) 762 41 426 91 99 41 426 91 91 91 91 91 91 91 91 91 91 91 91 91	5 (p = 0 Mean 51.4 499 56.5 50.3 56.5 50.3 56.5 50.3 56.5 50.3 56.5 50.3 56.5 50.9 56.5 50.9 56.5 50.9 56.7 50.9 56.7 50.9 56.7 50.9 56.7 56.9 56.5 56.	70); /² Month SD 16.6 20.0 22.9 24.1 19.5 13.3 20.5 13.3 20.5 3); /² = Month SD 18.6 20 24.3 22.3 24.3 22.3 24.3 22.3 24.3 22.3 24.3 22.3 24.3 22.3 24.3 22.3 24.3 22.3 24.3 24.3 24.3 24.3 24.3 24.3 24.3 24.3 24.3 24.3 24.3 24.3 24.3 24.3 24.3 24.5 24	969 = 0% Total 29 39 96 37 61 14 15 16 15 15 19 771 0% Total 29 53 529 96	100.0% Weight 2.6% 2.1% 5.7% 60.8% 0.9% 0.9% 0.9% 0.9% 1.1% 1.0% 1.5% 100.0% Weight 2.3% 2.7% 20.6% 5.5%	4.29 [2.98, 5.60] Mean Difference IV, Random, 95% CI 7.60 [-0.94, 16.14] 2.00 [-7.33, 11.33] 3.10 [-10.06, 6.26] 4.30 [-14.2, 10.02] 3.90 [2.15, 65, 626] 4.30 [-14.2, 10.02] 3.90 [2.16, 16, 026] 3.10 [-11.73, 17.93] -1.70 [-17.98, 14.64] 3.20 [-10.34, 16.74] 3.20 [-10.34, 16.74] 3.20 [-10.34, 16.74] 3.60 [-7.44, 14.64] 0.30 [-12.37, 12.97] 3.94 [2.57, 5.31] Mean Difference IV, Random, 95% CI 16.10 [7.03, 25.17] 4.00 [-4.39, 12.39] 6.50 [3.46, 9.54] 8.90 [3.04, 14.76]	Favours 3 month Favours 6 month Mean Difference IV, Random, 95% CI -50 -25 0 25 50 Favours 3 month Favours 6 month Mean Difference IV, Random, 95% CI Favours 12 month Favours 6 month Mean Difference IV, Random, 95% CI						
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	Study or Subgroup Adunka 2008 Firszt 2018 Grisel 2021 Kelsall 2021 Runge 2016 Sladen 2017 Sturm 2021a Sturm 2021b Sturm 2021d Sturm 2021d Sturm 2021d Sturm 2021d Sturm 2021d Sturm 2021d Sturm 2021g Total (95% Cl) Heterogeneity: ** = 0.0 Test for overall effect. D Study or Subgroup Adunka 2008 Deep 2021 Grisel 2021 Kelsall 2021 Runge 2016	$00; z^{*} = \frac{1}{Z} = 6.41$ 12 Mean 59 51 55.8 65.2 55.8 67.7 53.4 48 51.8 57.3 48 51.2 51.9 51.2	11.78 (1 (<i>p</i> < (Month SD 16.6 22 23.4 18.8 3.9 21.3 18.4 23.2 17.4 16.1 13.3 5.68, <i>a</i> 6 (<i>p</i> < 0 Month SD 10.6 21.3 17.4 16.5 13.3 3.9 3.9 3.9 3.9 3.9 3.9 3.9	840 , df = 18 0.00001 29 33 426 91 33 426 91 33 761 13 37 61 13 37 61 13 37 762 tf = 12 (0.00001) 762 tf = 12 0 13 37 762 41 426 91 37 37 37 37 37 38 9 762 41 42 9 9 39 9 41 42 9 9 41 42 9 9 41 42 9 9 42 9 42	5 (p = 0 Mean 51.4 49 52.7 60.9 56.5 58.5 48.7 37.5 (p = 0.9) 31 Mean 42.9 50.3 42.9 50.3 37.5 (p = 0.9) 31 42.9 50.3 48.7 35.5 37.5 (p = 0.9) 31 42.9 (p = 0.9) 31 49.3 (p = 0.9) 31 49.3 32 (p = 0.9) 31 49.3 32 (p = 0.9) 31 49.3 33 (p = 0.9) 31 49.3 34 49.3 34 49.3 49.3 49.3 49.3 49.3 49.3 49.3 49.3 49.3 49.3 49.3 49.3 49.3 49.3 49.3 49.3 49.3 49.3 49.3 40.3	70); / ² Month SD 16.6 20 22.9 24.1 3.8 24.4 17.7 20.5 13.3 20.5 3); / ² = Month SD 18.6 20 24.3 3.3; / ² = 3.8 3); / ² = 3.8 3.8 3.8 3.9 3.8 3.9 3.8 3.8 3.8 3.8 3.8 3.8 3.8 3.8	969 = 0% Total 29 399 96 37 61 14 15 16 16 15 15 19 771 0% Total 29 53 529 96 37	100.0% Weight 2.6% 2.1% 5.7% 60.8% 0.9% 0.7% 0.5% 1.1% 1.0% 1.5% 1.0% 1.5% 100.0% Weight 2.3% 2.7% 20.6% 5.5% 61.7%	4.29 [2.98, 5.60] Mean Difference IV, Random, 95% CI 7.60 [-0.94, 16, 14] 2.00 [-7.33, 11.33] 3.10 [-10.06, 6.26] 4.30 [-1.42, 10.02] 3.90 [2.15, 5.65] 1.100 [3.32, 18.68] 3.10 [-11.73, 17.93] -1.70 [-17.89, 14.49] 8.50 [-10.33, 27.33] 0.70 [-12.29, 13.68] 3.20 [-10.34, 16.74] 3.60 [-7.44, 14.64] 0.30 [-12.37, 12.97] 3.94 [2.57, 5.31] Mean Difference IV, Random, 95% CI 1.6.10 [7.03, 25.17] 4.00 [-4.39, 12.39] 6.50 [3.46, 9.54] 7.80 [6.05, 9.55]	Favours 3 month Mean Difference N, Random, 95% CI -50 -25 0 25 50 Favours 3 month Mean Difference N, Random, 95% CI -50 -25 0 25 50 Favours 12 month Mean Difference N, Random, 95% CI -50 -25 0 25 50 Favours 12 month Mean Difference N, Random, 95% CI						
Sturm 2021c 51.8 23.2 8 42.8 22 16 0.5% 9.00 [-10.36, 28.36] Sturm 2021d 59.2 17.4 15 50.9 18.2 16 1.2% 8.30 [-4.23, 20.83] Sturm 2021e 51.9 16 13 49.9 19.9 15 1.1% 200 [-11.31, 15.31] Sturm 2021g 37.8 13.3 9 31.4 17.9 22 1.4% 6.40 [-5.07, 17.87] Total (95% Cl) 703 858 100.0% 7.62 [6.24, 9.00]	Study or Subgroup Adunka 2008 Firszt 2018 Grisel 2021 Kelsall 2021 Runge 2016 Sladen 2017 Sturm 2021a Sturm 2021b Sturm 2021c Sturm 2021b Sturm 2021c Sturm 2021g Total (95% CI) Heterogeneity: r ^a = 0.0 Adunka 2008 Deep 2021 Grisel 2021 Keisall 2021 Runge 2016 Sturm 2021a	$00; x^{2} = 6.41$ 12 Mean 59 51 55.8 65.2 56.8 67 53.4 48 51.9 37.8 00; $x^{2} = 5.65$ 12 Mean 59 00; $x^{2} = 5.65$ 12 Mean 59 1 1 1 1 1 1 1 1	11.78 ((p < (Month SD 16.6 22 23.4 18.8 3.9 21.3 18.4 23.2 17.4 16.1 13.3 5.68, a (p < 0 Month SD 11.4 23.4 18.8 3.9 21.3 18.4 23.4 18.8 21.2 23.4 18.8 21.2 23.4 23.5	840 , df = 18).00001 29 339 426 91 13 37 61 13 37 61 13 37 61 13 37 61 13 37 762 tf = 12 (00001) 762 tf = 12 (13 41 426 91 13 77 13 77 13	5 (p = 0 6 I Mean 51.4 40.9 52.7 60.9 52.7 60.9 52.9 66 50.3 43.3 58.5 37.5 (p = 0.9) 3 I Mean 42.9 50.3 49.3 50.3 49.3 49.3 50.3 49.3 49.3 50.3 49.3 50.3 49.3 50.3 49.3 50.5 50.3 50.5 50.3 50.5 50.3 50.5 50.3 50.5	70); / ² Month SD 16.6 20.9 21.1 3.8 24 17.7 19.5 20.5 13.3 20.5 18.6 20 21.1 19.5 20.5 13.3 20.5 18.6 20 21.1 20.5 13.3 20.5 18.6 20 21.1 20.5 13.3 20.5 18.6 20 21.1 20.5 13.3 20.5 18.6 20 21.1 20.5 13.3 20.5 18.6 20 21.1 20.5 18.5 20.5 18.6 20 21.1 20.5 20.5 18.6 20.5 20.5 20.5 18.6 20.5	969 = 0% Total 29 399 96 14 15 16 16 15 15 19 771 0% Total 29 96 53 529 96 53 771 14	100.0% Weight 2.6% 2.1% 18.7% 5.7% 60.8% 0.5% 1.5% 1.5% 1.2% 100.0% Weight 2.3% 20.6% 5.5% 61.7% 0.9%	4.29 [2.98, 5.60] Mean Difference IV, Random, 95% CI 7.60 [0.94, 16, 14] 2.00 [7.33, 11.33] 3.10 [0.06, 6.26] 4.30 [1.42, 10.02] 3.90 [2.16, 5.65] 11.00 [3.32, 18.68] 3.10 [11.73, 17.93] 4.70 [-17.89, 14.49] 3.20 [-10.34, 16, 74] 3.20 [-10.34, 16, 74] 3.20 [-10.34, 16, 74] 3.20 [-10.34, 16, 74] 3.20 [-2.97] 3.94 [2.57, 5.31] Mean Difference IV, Random, 95% CI 16.10 [7.03, 25, 17] 4.00 [-4.39, 12.39] 6.50 [3.46, 9.54] 8.90 [3.04, 14, 76] 9.70 [3.04, 9.54] 13.40 [-105, 27.85]							
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	Heterogeneily: $r^2 = 0$. Testfor overall effect: C Study or Subgroup Adunka 2008 Firszt 2018 Grisel 2021 Kelsall 2021 Runge 2016 Sladen 2017 Sturm 2021a Sturm 2021b Sturm 2021b Sturm 2021c Sturm 2021c Sturm 2021b Sturm 2021b Sturm 2021b Total (95% CI) Heterogeneity: $r^2 = 0.0$ Test for overall effect. D Study or Subgroup Adunka 2008 Deep 2021 Grisel 2021 Kelsall 2021 Runge 2016 Sturm 2021a Sturm 2021a	00; $\chi^{2} = 4$ 12 Mean 59 51 55.8 65.2 56.8 67 53.4 48 59.2 51.9 39.1 37.8 00; $\chi^{2} = 5.65$ 12 Mean 59 54.3 55.8 65.2 54.8 59.2 54.8 55.8	11.78 (p < (Month SD 12 23.4 18.8 3.9 19 21.3 18.4 16.1 13.3 5.68, a (p < 0 Month SD 16.6 21 23.4 18.8 3.9 21.3 18.4 18.8 21.3 18.6 21 21.4 18.8 21.3 18.6 21.5	840 , df = 1;).00001 29 39 426 91 37 61 13 8 8 8 5 13 13 9 762 762 762 762 762 762 41 426 91 37 37 429 41 426 91 37 8 8 8 8 8 8 8 8 8 9 762 77 12 9 9 762 77 12 9 9 762 77 762 762 763 763 763 763 763 763 763 763 763 763	5 (p = 0 6 I Mean 51.4 43.3 52.9 56 50.3 49.7 56.5 37.5 (p = 0.9) 3 I Mean 42.9 50.3 56.3 49.3 56.3 49.3 56.3 49.3 56.3 49.3 56.3 49.3 56.3 49.3 56.3 49.3 56.3 49.3 56.3 49.3 56.3 49.3 56.3 49.3 56.3 49.3 56.3 49.3 56.3 49.3 56.3 49.3 56.5 56.3 56.5 57.5 56.5 57.5 56.5 57.5 56.5 57.5 56.5 57.5 56.5 57.5 56.5 57.5 56.5 57.5 56.5 57.5 56.5 57.5 56.5 57.5 57.5 56.5 57.5 57.5 57.5 56.5 57.5 5	70); / ² Month SD 16.6 20.9 22.9 24 17.7 19.5 20.5 13.3 20.5 13.3 20.5 33); / ² = Month SD 20 24.3 22 3.8 20 24.3 22 3.8 20 24.3 20 20 24.3 20 24.3 20 25.3 20 24.3 25.5	969 = 0% 29 389 96 37 61 14 15 16 16 15 15 15 19 771 0% Total 29 53 529 96 37 31 4	100.0% Weight 2.6% 2.1% 5.7% 60.8% 0.5% 1.2% 100.0% Weight 2.3% 2.7% 5.5% 61.7% 2.6% 5.5% 61.7% 0.9% 0.9% 0.7%	4.29 [2.98, 5.60] Mean Difference <u>IV, Random, 95% CI</u> 7.60 [-0.94, 16, 14] 2.00 [-7.33, 11.33] 3.10 [-10.06, 6.26] 4.30 [-1.42, 10.02] 9.10 [-1.32, 11.33] 3.10 [-10.06, 6.26] 1.00 [3.32, 18.68] 3.10 [-11.73, 17, 93] 3.20 [-1.34, 14, 64] 3.20 [-1.34, 14, 64] 3.20 [-1.34, 16, 74] 3.60 [-7.44, 14, 64] 0.30 [-12.37, 12.97] 3.94 [2.57, 5.31] Mean Difference <u>IV, Random, 95% CI</u> 16.10 [7.03, 25.17] 4.00 [-4.39, 12.39] 6.50 [3.46, 9.54] 8.90 [3.04, 14.76] 7.80 [6.05, 9.54] 8.90 [3.90, 14.8, 15] 8.90 [3.90, 14.8, 15] 8.90 [3.90, 15] 9.90 [3.90, 15] 9.	Favours 3 month Favours 6 month Mean Difference IV, Random, 95% CI -50 -25 Favours 12 month Favours 6 month Mean Difference IV, Random, 95% CI -50 -25 Favours 12 month Favours 6 month Mean Difference IV, Random, 95% CI						
Sturm 2021e 51.9 15 13 49.9 19.9 15 1.1% 2.00 [+11.3], 15.31] Sturm 2021f 39.1 16.1 13 34.1 16.6 15 1.3% 5.00 [-7.13, 17.13] Sturm 2021g 37.8 13.3 9 31.4 17.9 22 1.4% 6.40 [-507, 17.87] Total (95% CI) 703 858 100.0% 7.62 [6.24, 9.00]	Heterogeneity: $r^2 = 0$. Test for overall effect: C Study or Subgroup Adunka 2008 Firszt 2018 Grisel 2021 Kelsall 2021 Runge 2016 Sladen 2017 Sturm 2021a Sturm 2021a Sturm 2021d Sturm 2021d Sturm 2021d Sturm 2021d Sturm 2021f Sturm 2021g Total (95% Cl) Heterogeneity: $r^2 = 0.0$ Test for overall effect. D Study or Subgroup Adunka 2008 Deep 2021 Grisel 2021 Kelsall 2021 Runge 2016 Sturm 2021a Sturm 2021b Sturm 2021g Total (95% Cl) Heterogeneity: $r^2 = 0.0$ Test for overall effect.	00; $\chi^{2} = 6.4$ 12 $Z = 6.4$ Mean 59 51 55.8 66.2 56.8 67 53.4 48 59.2 51.9 39.1 59.2 51.9 39.1 39.2 51.9 51.9 5	$\begin{array}{c} 11.78\\ 1 \ (p < 0 \\ \hline \textbf{Month} \\ \textbf{SD} \\ 16.6\\ 22\\ 23.4\\ 18.8\\ 3.9\\ 19\\ 21.3\\ 18.4\\ 16\\ 16.1\\ 13.3\\ \hline \textbf{SD} \\ 16.6\\ 21\\ 23.4\\ 16.1\\ 13.3\\ \hline \textbf{Month} \\ \textbf{SD} \\ 16.6\\ 21\\ 23.4\\ 18.8\\ 3.9\\ 21.3\\ 18.4\\ 23.2\\ \hline \textbf{SD} \\ 18.4\\ 18.4\\ 23.2\\ \hline \textbf{SD} \\ 18.4\\ 18.4\\ 23.2\\ 24.2\\ 18.4\\ 18.$	840 , df = 19 0.00001 29 39 426 91 37 61 13 8 8 5 13 13 13 13 13 13 13 13 13 13 13 13 13	5 (p = 0 Mean 51.4 499 56.5 50.3 56.5 50.3 56.5 57.7 56.5 50.3 56.5 57.7 56.5 57.7 56.5 57.7 56.5 57.7 56.7 56.9 56.3 56.5 56.3 56.3 56.3 56.3 56.3 56.3 49.9 49.3 49.3 49.3 49.3 49.3 49.4 49.9 56.3 49.4 49.9 56.3 49.4 49.4 40.9 56.3 49.4 40.9 40.9 56.3 40.9 40.	.70); / ² Month SD 16.6 20 22.9 21.1 3.8 24 17.7 19.5 20.5 13.3 20.5 33); / ² = Month SD 18.6 20 24.3 22.3 88 16.5 20 24.3 22.3 18.6 20 24.3 22.3 18.6 20 24.3 22.3 18.6 20 24.3 22.3 18.6 20 24.3 22.3 18.6 20 24.3 22.5 18.6 20 24.3 24.5 25.5 26.5 26.5 27.5 26.5 27.5	969 = 0% Total 29 399 96 14 15 16 16 16 16 16 16 19 771 0% Total 29 53 529 96 37 71 10%	100.0% Weight 2.6% 2.1% 5.7% 60.8% 0.9% 0.5% 1.1% 1.0% 1.2% 100.0% Weight 2.3% 2.7% 20.6% 61.7% 0.5% 61.7%	4.29 [2.98, 5.60] Mean Difference IV, Random, 95% CI 7.60 [-0.94, 16, 14] 2.00 [-7.33, 11.33] 3.10 [-10.06, 6.26] 4.30 [-14.2, 10.02] 3.30 [2.15, 56] 1.00 [3.32, 18.68] 3.10 [-11.73, 17.93] -1.70 [-17.89, 14.48] 3.20 [-10.34, 16, 74] 3.60 [-7.44, 14.64] 3.00 [-7.44, 14.64] 3.00 [-7.44, 14.64] 3.04 [-2.57, 5.31] Mean Difference IV, Random, 95% CI 16.10 [7.03, 25.17] 4.00 [-4.39, 12.39] 6.50 [3.46, 9.54] 8.90 [3.04, 14.76] 7.80 [6.05, 9.55] 13.40 [-1.05, 27.85] 13.40 [-1.05, 27.85] 9.00 [-10.38, 28.86] 9.00 [-10.38, 28.86] 9.00 [-10.38, 28.86]	Favours 3 month Favours 6 month Mean Difference IV, Random, 95% CI -50 -25 Favours 12 month Mean Difference IV, Random, 95% CI -50 -25 Favours 6 month Mean Difference IV, Random, 95% CI -50 -25 -50 -25 -50 -25 -50 -25 -50 -50 -25 -50 -50 -25 -50 -50 -25 -50 -50 -25 -50 -50 -25 -50 -50 -50 -50 -50 -50 -50 -5						
Sturm 2021g 37.8 13.3 9 31.4 17.9 22 1.4% 6.40 [-5.07, 17.87] Total (95% CI) 703 858 100.0% 7.62 [6.24, 9.00] -50 -25 0 25 50 Heterogeneity: $r^2 = 0.00; \chi^2 = 6.38, df = 11 (p = 0.85); l^2 = 0\%$ 7.62 [6.24, 9.00] -50 -25 0 25 50 Test for overall effect: $Z = 10.84 (p < 0.00001)$ Favours 12 month Favours 12 month Favours 12 month Favours 12 month	Study or Subgroup Heterogeneily: r ² = 0. Test for overall effect: C Adunka 2008 Firszt 2018 Grisel 2021 Kelsall 2021 Runge 2016 Sladen 2017 Sturm 2021a Sturm 2021b Sturm 2021d Sturm 2021d Sturm 2021d Sturm 2021d Sturm 2021d Sturm 2021g Total (95% CI) Heterogeneity: r ² = 0.0 Test for overall effect: D Study or Subgroup Adunka 2008 Deep 2021 Grisel 2021 Krisel 2021 Keisall 2021 Sturm 2021a Sturm 2021a Sturm 2021a Sturm 2021a Sturm 2021a Sturm 2021b Sturm 2021c Sturm 2021c Sturm 2021c	$00; x^{*} = x^{*}$ Mean 12 Mean 59 51 55.8 65.2 55.8 65.2 55.8 65.2 51.9	11.78 (1 ($p < 0$) Month SD 16.6 22 23.4 18.8 21.3 18.4 23.2 17.4 16.1 13.3 5.68, a ($p < 0$) Month SD 21.3 18.4 23.2 17.4 18.3 18.4 23.2 17.4 18.3 18.4 23.2 17.4 18.4 19.2 21.3 18.4 21.3 21.3 18.4 21.3 21.3 18.4 21.3 21.5 21.	8400 , df = 18 0.00001 29 33 426 91 13 37 61 13 37 61 13 37 61 13 37 61 13 37 61 13 37 61 13 37 61 13 37 762 tf = 18 0.00001 91 13 8 8 762 tf = 18 0.00001 1 37 9 426 91 13 37 9 762 tf = 18 13 37 9 762 tf = 18 13 37 761 13 38 9 762 tf = 18 13 37 761 13 38 8 8 8 13 37 762 tf = 18 13 37 761 13 38 8 8 8 13 37 761 13 38 9 77 61 13 38 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8	5 (p = 0 6 I Mean 51.4 49 52.7 60.9 52.7 43.3 58.5 5 37.5 (p = 0.9) 3 I Mean 42.9 50.3 49.3 56.3 49.3 56.3 49.9 40.4 42.8 50.9 42.9 40.9 50.3 49.9 40.9 50.7 50.3 49.9 40.9 50.7 50.3 49.9 40.9 50.7 50.3 49.7 50.3 49.7 50.7 50.3 49.7 50.7 50.7 50.3 50.7 50.3 50.7 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.5 50.3 50.7 50.3 50.7 50.3 50.7 50.3 50.7 50.7 50.7 50.7 50.7 50.7 50.7 50.7 50.7 50.7 50.3 50.7 50.3 50.5 50.3 49.7 50.3 49.7 50.3 49.7 50.3 49.7 40.7 50.3 49.7 40.7 50.3 49.7 40.7 50.3 49.7 40.7 50.3 49.7 40.7 50.3 49.7 40.7 50.3 40.7 50.3 40.7 50.3 40.7 50.3 40.7 50.3 40.7 50.3 40.7 40.7 50.3 40.7 40.	Month SD 22.9 21.1 20 21.3 24 17.7 20 13.3 20.5 33);/² = Month SD 24 19.7 20.5 33);/² = Month SD 24.3 3.8 16.5 19.5 22 3.8 16.5 22 3.8 16.5 22 3.8 16.5 22 3.8 16.5 21 22 3.8 16.5 22 3.8 16.5 22 23.8 30.7	969 = 0% Total 29 399 96 14 14 15 15 15 15 15 15 19 771 0% Total 29 96 53 529 96 53 529 96 14 16 16 15 15 15 19 771 0%	100.0% Weight 2.6% 2.1% 18.7% 5.7% 60.8% 0.9% 0.5% 1.0% 0.5% 1.2% 100.0% Weight 2.3% 20.6% 5.5% 5.5% 0.9% 0.5% 1.2% 20.6% 5.5% 2.1% 2.5% 2.1% 2.5%	4.29 [2.98, 5.60] Mean Difference <u>N, Random, 95% C1</u> 7.60 [-0.94, 16.14] 2.00 [-7.3, 11.33] 3.10 [-0.06, 6.26] 3.30 [-1.42, 10.02] 3.90 [2.15, 5.65] 11.00 [3.32, 18.68] 3.10 [-11.73, 17.93] 3.00 [-12.29, 13.68] 3.20 [-10.33, 27.33] 0.70 [-12.29, 13.68] 3.20 [-10.33, 27.33] 0.70 [-12.29, 13.68] 3.20 [-10.33, 27.33] 3.20 [-10.34, 14.64] 0.30 [-7.44, 14.64] 0.30 [-7.44, 14.64] 0.30 [-7.44, 14.64] 0.30 [-7.44, 14.64] 0.30 [-7.43, 12.37] Mean Difference <u>IV, Random, 95% C1</u> 16.10 [7.03, 25.71] 4.00 [-4.39, 12.39] 6.50 [3.46, 9.54] 13.40 [-1.05, 27.85] 6.70 [-9.23, 22.63] 9.00 [-10.36, 28.38] 8.30 [-4.23, 20.83]	Favours 3 month Favours 6 month Mean Difference N, Random, 95% CI -50 -25 0 25 50 Favours 12 month Favours 6 month Mean Difference N, Random, 95% CI -50 -25 -25 0 -25 -25 0 -25 -25 0 -25 -25 0 -25						
Total (95% Cl) 703 858 100.0% 7.62 [6.24, 9.00] Heterogeneity: τ² = 0.00; χ² = 6.38, df = 11 (p = 0.85); /² = 0% -50 -25 0 25 50 Test for overall effect: Z = 10.84 (p < 0.00001)	Total (95% CI) Heterogeneity: r ² = 0. Test for overall effect: C Adunka 2008 Firszt 2018 Grisel 2021 Kelsall 2021 Runge 2016 Sladen 2017 Sturm 2021a Sturm 2021b Sturm 2021c Sturm 2021d Sturm 2021d Sturm 2021d Sturm 2021f Sturm 2021g Total (95% CI) Heterogeneity: r ² = 0.0 Test for overall effect: D Study or Subgroup Adunka 2008 Deep 2021 Grisel 2021 Keisall 2021 Runge 2016 Sturm 2021a Sturm 2021b<	00; $\chi^{2} = 4$ 12 $Z = 6.4$ Mean 59 51 55.8 65.2 56.8 67 53.4 48 51.8 51.9 37.8 00; $\chi^{2} = 5.65$ 12 Mean 59.2 54.3 55.8 65.2 54.3 55.8 65.2 54.8 54.9 55.8 54.3 55.8 55.8 55.8 55.8 55.8 55.8 55.8 55.8 55.8 55.8 55.8 55.9 55.8 55.9 55.8	11.78 ($p < 0$ Month SD 16.6 22 23.4 18.8 9 19 21.3 18.4 23.2 17.4 16.1 13.3 5.68, a ($p < 0$ Month SD 16.4 18.4 23.2 17.4 16.2 23.2 17.4 18.4 23.2 17.4 18.4 23.2 17.4 18.4 23.2 17.4 18.4 16.5 17.4 16.5 16.5 17.4 16.5 16.5 17.4 16.5 16.5 17.4 16.5 16.5 17.4 16.5 16.5 17.4 17.4 16.5 17.4 17.4 16.5 17.4 17.4 16.5 17.4 17.4 16.5 17.4 17.4 16.5 17.4 17.4 16.5 17.4 17.4 16.5 17.4 17.4 16.5 17.4 17.4 16.5 17.4 17.4 16.5 17.4 17.4 16.5 17.4 17.4 16.5 17.4 16.5 17.4 17.4 16.5 17.4 17.4 16.5 17.4 17.4 16.5 17.4 16.5 17.4 17.4 16.5 17.4 17.4 16.5 17.4 16.5 17.4 16.5 17.4 16.5 17.4 16.5 17.4 16.5 17.4 16.5 17.4 16.5 17.4 16.5 17.4 16.5 16.5 16.5 17.4 16.5 17.4 16.5 16.5 16.5 16.5 16.5 16.5 17.4 16.5 16.5 16.5 17.4 16.5 16.5 16.5 17.4 16.5 16.5 17.4 16.5 16.5 17.4 16.5 16.5 17.4 16.5 17.4 16.5 17.4 16.5 17.4 16.5 17.4 16.5 17.4 16.5 17.4 16.5 17.4 16.5 17.4 16.5 17.4 16.5 17.4 16.5 17.4 16.5 17.4 16.5 17.4 16.5 17.4 16.5 17.4 16.5 17.4 16.5 17.4 17.4 16.5 17.4 17	840 , df = 19).00001 29 339 426 91 13 37 61 13 37 61 13 37 61 13 37 762 762 762 77 29 9 77 20 9 77 20 9 77 20 9 77 20 9 77 20 9 77 20 9 77 20 9 77 20 70 20 9 70 20 9 70 20 9 70 20 9 70 20 70 20 9 70 20 70 70 70 70 70 70 70 70 70 70 70 70 70	5 (p = 0 6 (P = 0 1) 6 (P = 0 6 (P = 0 6 (P = 0 6 (P = 0 7	<pre>/// // // // // // // // // // // // //</pre>	969 969 29 399 96 61 14 15 16 16 15 15 15 15 15 19 771 0% Total 29 529 96 37 14 16 16 15 15 15 15 15 15 15 15 15 15 15 15 15	100.0% Weight 2.6% 2.1% 18.7% 5.7% 60.8% 0.9% 0.5% 1.1% 1.0% 1.5% 1.2% 100.0% Weight 2.3% 2.7% 20.6% 5.5% 61.7% 20.6% 5.5% 61.7% 2.7% 2.6% 1.2% 2.7% 2.7% 2.6% 2.7% 2.6% 2.7% 2.7% 2.6% 2.7%	4.29 [2.98, 5.60] Mean Difference IV, Random, 95% CI 7.60 [0.94, 16.14] 2.00 [-7.33, 11.33] 3.10 [-0.06, 6.26] 4.30 [-1.42, 10.02] 3.90 [2.15, 5.65] 11.00 [3.32, 18.68] 3.10 [-1.73, 17.93] 4.70 [-17.89, 14.49] 5.00 [-10.32, 27.33] 0.70 [-12.29, 13.68] 3.20 [-10.34, 16.74] 3.20 [-10.34, 16.74] 3.20 [-10.34, 16.74] 3.20 [-10.34, 16.74] 3.20 [-10.34, 16.74] 3.20 [-10.34, 12.97] 3.94 [2.57, 5.31] Mean Difference IV, Random, 95% CI 16.10 [7.03, 25.17] 4.00 [-4.39, 12.39] 6.50 [3.46, 9.54] 8.90 [3.04, 14.76] 9.00 [-10.36, 28.36] 8.30 [-4.23, 20.83] 2.00 [-11.31, 15.31]	Favours 3 month Favours 6 month Mean Difference V, Random, 95% CI Favours 12 month Favours 6 month Mean Difference N, Random, 95% CI Favours 12 month Favours 6 month Mean Difference N, Random, 95% CI Favours 12 month Favours 6 month						
Total (95% Cl) 703 858 100.0% 7.62 [6.24, 9.00] Heterogeneity: τ² = 0.00; χ² = 6.38, df = 11 (p = 0.85); /² = 0% 7.62 [6.24, 9.00] -50 -25 0 25 50 Test for overall effect: Z = 10.84 (p < 0.00001)	Total (95% CI) Heterogeneily: r ² = 0. Test for overall effect: C Adunka 2008 Firszt 2018 Grisel 2021 Kelsall 2021 Runge 2016 Sladen 2017 Sturm 2021a Sturm 2021b Sturm 2021c Sturm 2021c Sturm 2021b Sturm 2021f Sturm 2021g Total (95% CI) Heterogeneity: r ² = 0.1 Test for overall effect. D Study or Subgroup Adunka 2008 Deep 2021 Grisel 2021 Kelsall 2021 Runge 2016 Sturm 2021a Sturm 2021a Sturm 2021a Sturm 2021d	00; $\chi^{*} = \frac{1}{2}$ Mean 59 51 55.8 65.2 56.8 67 53.4 4 51.8 55.2 51.8 67 53.4 51.8 51.2 51.9 39.1 37.8 00; $\chi^{*} = \frac{1}{2}$ Mean 59 54.3 55.8 65.2 56.8 67 53.4 48 59.2 54.8 55.9 54.8 55.9 55.8 55.9 55.8 55.8 55.8 55.8 55.8 55.8 55.8 55.8 55.8 55.8 55.8 55.8 55.8 55.9 55.8 55.9 55.8 55.9 55.8 55.9 55	$\begin{array}{c} \text{11.78}\\ 1 \ (p < 0 \\ \textbf{Month}\\ \textbf{SD}\\ 12 \\ 22 \\ 3.4 \\ 18.8 \\ 3.9 \\ 19 \\ 21.3 \\ 18.4 \\ 23.2 \\ 17.4 \\ 16.1 \\ 13.3 \\ \textbf{SD}\\ 16.6 \\ 21 \\ 23.4 \\ 18.8 \\ 3.9 \\ 21.3 \\ 18.4 \\ 23.2 \\ 21.3 \\ 18.4 \\ 23.2 \\ 17.4 \\ 16 \\ 16 \\ 16 \\ 11 \\ 3.3 \\ 18.4 \\ 23.2 \\ 17.4 \\ 16 \\ 16 \\ 11 \\ 3.3 \\ 16 \\ 16 \\ 11 \\ 3.3 \\ 16 \\ 16 \\ 16 \\ 16 \\ 16 \\ 16 \\ 16 \\ 1$	840 , df = 19).00001 701 29 39 426 91 33 426 91 13 8 8 5 13 13 9 762 762 762 762 761 13 8 8 762 762 762 763 763 8 8 8 91 33 9 762 763 763 763 763 763 763 763 763 763 763	5 (p = 0 Mean 51.4 52.9 56.0 52.9 56.5 50.3 56.5 37.5 (p = 0.9) Mean 42.9 50.3 56.3 49.7 36.5 37.5 (p = 0.9) 31 Mean 42.9 50.3 49.3 40	70); / ² Month SD 22,9 21,1 3,8 24 17,7 19,7 20,5 20,5 20,5 20,5 20,5 20,5 20,5 20,5 20,5 20,5 20,7 20,7 20,9 20,9 21,1 20,9 20,9 21,1 20,9 20,9 21,1 20,9 20,9 21,1 20,9 20,5	969 = 0% Total 29 389 96 37 61 14 15 16 16 15 19 771 0% Total 29 529 96 37 14 15 529 96 371 0%	100.0% Weight 2.6% 2.1% 5.7% 60.8% 0.9% 0.5% 1.1% 1.0% 1.2% 100.0% Weight 2.3% 2.7% 60.8% 5.5% 61.7% 0.5% 1.2% 1.1% 1.2% 1.1% 1.2% 1.1% 1.2% 1.1% 1.2% 1	4.29 [2.98, 5.60] Mean Difference <u>N, Random, 95% CI</u> 7.60 [-0.94, 16, 14] 2.00 [-7.33, 11.33] 3.10 [-10.06, 6.26] 4.30 [-1.42, 10.02] 9.10 [-1.32, 11.33] 3.10 [-10.32, 12.56] 1.100 [3.32, 11.68] 3.10 [-11.73, 17, 93] 3.20 [-1.34, 14, 64] 3.20 [-1.34, 14, 64] 0.30 [-12.29, 13.66] 3.20 [-10.34, 16, 74] 3.60 [-7.4, 14, 64] 0.30 [-12.37, 12.97] 3.94 [2.57, 5.31] Mean Difference <u>V, Random, 95% CI</u> 16.10 [7.03, 25.17] 4.00 [-4.39, 12.39] 6.50 [3.46, 9.54] 8.90 [3.04, 14, 76] 7.80 [6.05, 9.54] 8.90 [3.04, 14, 76] 7.80 [7.90 [7.90 [7.90 [7.90 [7.90 [7.90 [7.90 [7.90 [7.90 [7.90 [50 -25 0 25 50 Favours 3 month Favours 6 month Mean Difference IV, Random, 95% CI						
Heterogeneity: $\tau^2 = 0.00; \ \chi^2 = 6.38, df = 11 \ (p = 0.85); l^2 = 0\%$ Test for overall effect: Z = 10.84 (p < 0.00001) Favours 3 month Favours 12 month	$\label{eq:second} \begin{array}{l} \label{eq:second} \end{tabular} \\ \mbox{Heterogeneity: } r^2 = 0. \\ \mbox{Test for overall effect:} \\ \mbox{C} \\ \mbox{Adunka 2008} \\ \mbox{Firszt 2018} \\ \mbox{Grisel 2021} \\ \mbox{Kelsall 2021} \\ \mbox{Kelsall 2021} \\ \mbox{Kelsall 2021} \\ \mbox{Sturm 20216} \\ \mbox{Sturm 2021a} \\ \mbox{Sturm 2021d} \\ \mbox{Sturm 2021d} \\ \mbox{Sturm 2021d} \\ \mbox{Sturm 2021d} \\ \mbox{Sturm 2021f} \\ Sturm 202$	00; $\chi^{2} = 4$ 12 $Z = 6.41$ 13 14 15 15 15 15 15 15 15 16 17 17 17 18 17 18 18 19 19 11 15 15 17 17 18 18 17 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 18 	$\begin{array}{c} 11.78\\ 1 \ (p < (\\ \textbf{Month}\\ \textbf{SD}\\ 11 \ (p < \\ 12 \ 23.4\\ 18.8\\ 3.9\\ 19\\ 21.3\\ 18.4\\ 16\\ 16.1\\ 13.3\\ \hline \textbf{SD}\\ 16.6\\ 21\\ 16.6\\ 21\\ 16.6\\ 21\\ 18.8\\ 3.9\\ 21.3\\ 18.4\\ 23.2\\ 17.4\\ 18.8\\ 3.9\\ 21.3\\ 18.4\\ 18.2\\ 3.4\\ 16.1\\ 13.3\\ \hline \end{array}$	840 , df = 1;).00001 701 939 39 426 91 37 61 13 8 8 5 13 13 9 762 762 762 762 762 762 91 37 762 91 41 426 91 37 762 12 (.00001 13 8 8 8 13 37 8 8 13 9 9 762 71 8 12 9 12 9 13 9 9 762 763 763 763 763 763 763 763 764 764 765 765 765 765 765 765 765 765 765 765	5 (p = 0 Mean 51.4 49 52.7 60.9 52.9 56 50.3 49.7 44.7 35.5 58.5 48.7 35.5 (p = 0.9) 311 Mean 42.9 56.3 49.9 31.5 56.3 49.7 42.9 56.3 49.7 42.9 56.3 49.7 42.9 56.3 49.7 42.9 56.3 49.7 42.9 56.3 49.7 42.9 56.5 31.4 42.9 56.3 49.7 42.9 56.5 31.5 42.7 56.5 48.7 35.5 56.3 49.7 42.9 56.3 49.7 42.9 56.3 49.7 42.9 56.3 49.7 42.9 56.3 49.7 42.9 56.3 49.7 42.9 56.3 49.7 42.9 56.3 49.7 42.9 56.3 49.7 42.9 56.3 49.7 42.9 56.3 49.7 42.9 56.3 49.3 40.3 49.3 40.4 40	Month SD 16.6 20 21.1 3.8 24 17.7 19.5 20.5 33); /² = Month SD 18.6 20.5 33); /² = 18.6 20.5 18.2 18.5 19.5 22.1 18.2 18.2 18.2 18.9 16.6 17.9	969 = 0% Total 29 393 96 11 14 15 16 16 16 16 15 19 771 0% Total 29 53 399 96 61 16 16 15 19 771 0% Total 29 53 97 61 16 16 16 16 16 16 16 16 16	100.0% Weight 2.6% 2.1% 5.7% 60.8% 0.9% 0.9% 0.9% 0.5% 1.1% 1.0% 1.2% 100.0% Weight 2.3% 2.7% 20.6% 5.5% 61.7% 0.9% 0.5% 1.1% 1.3% 1.4%	4.29 [2.98, 5.60] Mean Difference IV, Random, 95% CI 7.60 [-0.94, 16, 14] 2.00 [-7.33, 11.33] 3.10 [-10.06, 6.26] 4.30 [-14.2, 10.02] 3.90 [2.15, 6.63] 1.1.00 [3.32, 18.68] 3.10 [-11.73, 17.93] -1.70 [-17.89, 14.64] 3.20 [-10.34, 16.74] 3.20 [-10.34, 16.74] 3.20 [-10.34, 16.74] 3.20 [-10.34, 16.74] 3.394 [2.57, 5.31] Mean Difference IV, Random, 95% CI 16.10 [7.03, 25.17] 4.00 [-4.39, 12.39] 6.50 [3.46, 9.54] 8.90 [3.46, 9.54] 8.90 [3.46, 9.54] 8.90 [3.46, 9.54] 8.90 [-10.32, 22.63] 9.00 [-10.36, 22.83] 2.00 [-11.31, 15.31] 5.00 [-7.13, 17.13] 6.40 [-5.07, 17.87]	Favours 3 month Favours 6 month Mean Difference IV, Random, 95% CI -50 -25 Favours 12 month Mean Difference IV, Random, 95% CI -50 -25 Favours 12 month Mean Difference IV, Random, 95% CI -50 -25 Favours 12 month Mean Difference IV, Random, 95% CI						
Test for overall effect: Z = 10.84 (p < 0.00001) Favours 3 month Favours 12 month Favours 3	Study or Subgroup Heterogeneily: r ² = 0. Test for overall effect: C Adunka 2008 Firszt 2018 Grisel 2021 Keisall 2021 Runge 2016 Sladen 2017 Sturm 2021a Sturm 2021a Sturm 2021d Sturm 2021d Sturm 2021d Sturm 2021g Total (95% CI) Heterogeneity: r ² = 0.0 Test for overall effect: D Study or Subgroup Adunka 2008 Deep 2021 Grisel 2021 Kelsall 2021 Runge 2016 Sturm 2021a Sturm 2021b Sturm 2021c Sturm 2021c Sturm 2021g Total (95% CI)	$00; x^{*} = X$ Z = 6.41 Mean 59 51 55.8 65.2 55.8 65.2 57.3 48 51.2 57.3 48 51.2 51.2 51.9 39.1 37.8 00; $x^{*} = \frac{1}{2}$ Mean 59 39.1 37.8 55.3 55.8 65.2 55.8 67.2 57.4 48 59.2 56.8 56.8 57.4 59.2 56.8 56.8 57.4 59.2 56.8 57.4 59.2 56.8 57.4 59.2 56.8 57.4 59.2 56.8 57.4 59.2 56.8 57.4 59.2 56.8 57.4 59.2 56.8 57.4 59.2 56.8 57.4 59.2 56.8 57.4 59.2 56.8 57.4 59.2 56.8 57.4 59.2 56.8 57.4 57.4 59.2 56.8 57.4 57.4 57.4 59.2 56.8 57.4 57.	11.78 ($(p < 0$ Month SD 16.6 22 23.4 18.8 19 21.3 18.4 23.2 17.4 16.1 13.3 5.68, a ($(p < 0$ Month SD 21.3 18.4 21.3 18.4 21.3 18.4 21.3 18.4 21.3 18.4 21.3 18.4 21.3 18.4 19 21.3 18.4 10.5 10	8400 , df = 18).000011 29 33 426 91 13 37 61 13 8 8 8 5 5 13 13 9 762 07 12 9 17 12 9 17 12 9 17 12 9 17 13 8 8 8 13 9 7 7 62 17 17 18 19 19 19 19 19 19 19 19 19 19 19 19 19	5 (p = 0 6 I Mean 51.4 49 52.7 60.9 52.7 60.9 52.7 43.3 58.5 37.5 (p = 0.9) 3 I Mean 42.9 40.3 49.3 56.3 37.5 (p = 0.9) 3 I 42.9 40.3 56.3 49.7 42.9 40.3 56.3 49.7 42.9 40.3 56.3 49.7 42.9 40.3 49.7 40.3 49.7 40.9	70); / ² Month SD 22.9 21.1 19.7 20 19.5 13.3 20.5 13.3 20.5 13.3 20.5 13.3 20.5 13.3 20.5 18.6 19.5 20 24.3 20.5 18.6 19.7 20 24.9 18.7 19.7 20.5 18.6 19.7 20.5 18.6 19.7 20.5 18.6 19.7 20.5 18.6 19.7 20.5 18.6 19.7 20.5 18.6 19.7 20.5 18.6 19.7 20.5 18.6 19.7 20.5 18.6 19.7 20.5 18.6 19.7 20.5 18.6 19.7 20.5 18.6 19.7 20.5 19.7 18.6 19.7 20.5 19.7 20.5 2	969 = 0% Total 29 96 14 14 15 15 15 15 15 15 15 15 15 15	100.0% Weight 2.6% 2.1% 18.7% 5.7% 60.8% 0.9% 0.5% 1.0% 0.5% 1.0% 1.0% 1.0% 1.0% 1.0% 0.5% 1.2% 100.0%	4.29 [2.98, 5.60] Mean Difference <u>N, Random, 95% C1</u> 7.60 [0.94, 16.14] 2.00 [7.33, 11.33] 3.10 [0.06, 6.26] 3.30 [1.42, 10.02] 3.90 [2.15, 5.65] 11.00 [3.32, 18.68] 3.10 [1.17, 17.93] 3.91 [1.23, 14.94] 8.50 [10.33, 27.33] 0.70 [12.29, 13.68] 3.20 [10.33, 27.33] 0.70 [12.29, 13.68] 3.20 [10.33, 27.33] 3.20 [10.34, 16.74] 3.60 [7.44, 14.64] 0.30 [12.37, 12.97] 3.94 [2.57, 5.31] Mean Difference <u>IV, Random, 95% C1</u> 16.10 [7.03, 25.17] 4.00 [-4.39, 12.39] 6.50 [3.46, 9.54] 13.40 [-1.05, 27.85] 6.70 [9.23, 22.63] 8.30 [-4.23, 20.83] 8.30 [-4.23, 20.83] 9.30 [-11.31, 15.31] 5.00 [-7.13, 17.13] 6.40 [-5.07, 17.87]	Favours 3 month Favours 6 month Mean Difference IV, Random, 95% CI						
	Study or Subgroup Adunka 2008 Firszl 2018 Grisel 2021 Kelsall 2021 Runge 2016 Sladen 2017 Sturm 2021a Sturm 2021b Sturm 2021c Sturm 2021g Total (95% CI) Heterogeneity: r² = 0.0 Grisel 2021 Grisel 2021 Grisel 2021 Grisel 2021 Runge 2016 Sturm 2021a Sturm 2021b Sturm 2021c Sturm 2021d Sturm 2021d Sturm 2021d Sturm 2021d Sturm 2021d Sturm 2021g Total (95% CI) Heterogeneity: r² = 0.0	$00; x^{2} = 4$ $\frac{12}{Z} = 6.41$ $\frac{12}{59}$ $\frac{12}{56.8}$ $\frac{56.8}{66.2}$ $\frac{56.8}{66.2}$ $\frac{56.2}{56.8}$ $\frac{56.2}{56.8}$ $\frac{59.2}{51.9}$ $\frac{12}{37.8}$ $\frac{12}{56.8}$ $\frac{66.2}{56.8}$ $\frac{56.8}{56.4}$ $\frac{56.8}{56.8}$ $\frac{56.4}{56.8}$ $\frac{56.8}{56.8}$ 56	Month SD 16.6 22 3.4 18.4 23.2 17.4 16.1 13.3 5.68, a (p < 0)	840 , df = 18).00001 29 38 426 91 13 37 61 13 37 61 13 37 61 13 37 61 13 37 61 13 37 61 13 29 762 41 426 91 426 91 41 426 91 13 8 8 8 8 8 8 8 8 8 8 9 7 7 62 7 7 8 9 7 7 61 13 9 7 7 61 13 9 7 7 61 13 8 8 8 8 8 8 8 8 8 8 8 9 7 7 61 13 8 9 7 7 61 13 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 9 7 7 7 61 13 8 9 7 7 7 61 13 8 8 8 8 8 8 7 7 7 61 13 8 8 8 8 8 8 7 7 7 61 13 8 8 8 8 8 7 7 7 61 13 8 8 8 8 8 8 7 7 7 7 61 13 8 8 8 8 8 8 7 7 7 7 61 13 8 8 8 8 8 7 7 7 7 61 13 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8	5 (p = 0 6 (P = 0 1) 6 (P = 0 6 (P = 0 5 (P = 0 7	.70); l^2 Month SD 16.6 20 22.9 21.1 3.8 24 17.7 19.7 20.5 20.5 20.5 20.5 3.3; $l^2 =$ Month SD 20.5 13.3 20.5 3.3; $l^2 =$ 18.6 SD 22.9 24.3 22.5 18.2 19.5 21.1 3.8 20.5	969 = 0% Total 29 399 96 14 15 16 16 15 15 19 771 0% Total 29 96 53 529 53 529 96 53 529 53 53 54 54 54 54 54 55 54 54 54 54	100.0% Weight 2.6% 2.1% 18.7% 5.7% 60.8% 0.9% 0.5% 1.1% 1.0% 1.2% 100.0% Weight 2.3% 20.6% 5.5% 61.7% 0.9% 0.7% 0.9% 0.7% 1.2%	4.29 [2.98, 5.60] Mean Difference IV, Random, 95% CI 7.60 [0.94, 16, 14] 2.00 [7.3, 11.33] 3.10 [0.06, 6.26] 4.30 [1.42, 10.02] 3.90 [2.16, 5.65] 11.00 [3.32, 18.68] 3.10 [11.73, 17.93] 4.70 [-17.83, 14.49] 5.00 [10.33, 27.33] 0.70 [-12.29, 13.68] 3.20 [-10.34, 16, 74] 3.20 [-10.34, 16, 74] 3.20 [-10.34, 16, 74] 3.20 [-12.37, 12.97] 3.94 [2.57, 5.31] Mean Difference IV, Random, 95% CI 16.10 [7.03, 25, 17] 4.00 [-4.33, 12.39] 6.50 [3.46, 9.54] 8.90 [3.04, 14.76] 9.00 [10.32, 82.86] 6.70 [9.23, 22.63] 9.00 [10.32, 82.86] 6.30 [-4.23, 20.83] 2.00 [-11.31, 15.31] 5.00 [-7.13, 17.13] 6.40 [-5.07, 17.87] 7.62 [6.24, 9.00]							

Fig. 4. Forest plots for meta-analysis of continuous measures for mean difference of Consonant-Nucleus-Consonant (CNC) word recognition in quiet from (A) pre-op to 3 months, (B) 3 to 6 months, (C) 6 to 12 months, and (D) 3 to 12 months. [Color figure can be viewed in the online issue, which is available at www.laryngoscope.com.]

sentence recognition measured in a controlled environment does not assess communication abilities in more complex environments and, therefore, does not reflect CI users' abilities in real-world listening situations.^{63–66} Multiple studies show that QOL, as assessed by patientreported outcome measures (PROMs), improves significantly after CI and that there is a poor correlation between speech recognition and patient-reported functional abilities across multiple domains.^{63,65–67} However, very few studies have reported longitudinal changes in PROM scores and the extent to which changes in PROM scores mirror changes in speech recognition.^{67–69} Given that PROMs are more direct measures of the functional abilities of CI patients, additional studies of post-CI patterns of change in PROMs are necessary to determine when and how much QOL improvement occurs following cochlear implantation.

LIMITATIONS

These meta-analysis results reflect the trends in mean scores observed in a large cohort of CI users. However, the results of previous studies demonstrate that for a sizeable group of CI users, individual speech recognition scores can fall within a wide range of outcomes that are very different from the mean.^{17,70} As such, our findings cannot capture the wide range of individual CI outcomes and might not be representative of every CI user's experience. This limits the utility of using mean speech recognition scores to guide pre-operative counseling discussions. In practice, patients should be made aware of this variability and group mean scores should only be used as a general guideline of expected post-implantation speech recognition change. Future studies focusing on changes in speech recognition by individual CI users can be helpful in personalized counseling and setting expectations for patients whose performance deviates from those of the average patient.

Being a systematic review, data are drawn from previously published studies. As such, there is an inherent risk of bias associated with such data. For example, we are unable to control for pre-operative factors or testing conditions in our included studies. In addition, several relevant studies were excluded from quantitative analysis due to missing key data metrics (e.g., standard deviation values), being unavailable for full-text review, or being published in a language other than English. Our analysis of overall mean scores features multiple different speech recognition measures including CNC, HINT, and AzBio. The current standard for speech testing includes CNC and AzBio due to known ceiling effects associated with the HINT, which is part of an older battery of tests.^{71,72} Given this, our aggregate results likely include a subset of CI users from earlier time periods assessed with a speech recognition measure no longer widely used. Finally, our analysis of significant changes in speech recognition is limited to the first 12 months post-CI. A previous study confirmed that speech recognition could continue to improve beyond 12 months.⁶ While the included studies reported some speech recognition data after 12 months, meta-analysis was not possible due to

the low number of contributing studies and limited quantitative data. Future studies are necessary to better understand whether any significant changes occur beyond 12 months.

CONCLUSIONS

Cochlear implantation has established benefits for speech recognition ability in adults with severe to profound hearing loss. Mean scores demonstrate rapid and significant improvement within the first 3 months, with no further statistically significant improvement for the average patient after 3 months. Longitudinal changes in average scores are important discussion points that can facilitate pre-operative counseling and setting of expectations, but large individual variation in scores should be anticipated. Future research that focuses on explaining the sources of these individual differences is warranted to develop a more complete understanding of longitudinal changes in speech recognition outcomes for individual patients.

BIBLIOGRAPHY

- Naples JG, Ruckenstein MJ. Cochlear implant. Otolaryngol Clin North Am. 2020;53(1):87-102.
- McRackan TR, Reddy P, Costello MS, Dubno JR. Role of preoperative patient expectations in adult cochlear implant outcomes. *Otol Neurotol.* 2021;42(2):e130-e136.
- Harris MS, Capretta NR, Henning SC, Feeney L, Pitt MA, Moberly AC. Postoperative rehabilitation strategies used by adults with cochlear implants: a pilot study. *Laryngoscope Investig Otolaryngol*. 2016;1(3): 42-48.
- Messersmith JJ, Entwisle L, Warren S, Scott M. Clinical practice guidelines: cochlear implants. J Am Acad Audiol. 2019;30(10):827-844.
- Carlson ML. Cochlear implantation in adults. N Engl J Med. 2020;382(16): 1531-1542.
- Cusumano C, Friedmann DR, Fang Y, Wang B, Roland JTJ, Waltzman SB. Performance plateau in prelingually and postlingually deafened adult cochlear implant recipients. *Otol Neurotol.* 2017;38(3):334-338.
- Lenarz M, Sönmez H, Joseph G, Büchner A, Lenarz T. Long-term performance of cochlear implants in postlingually deafened adults. *Otolaryngol Head Neck Surg.* 2012;147(1):112-118.
- Massa ST, Ruckenstein MJ. Comparing the performance plateau in adult cochlear implant patients using HINT and AzBio. Otol Neurotol. 2014; 35(4):598-604.
- Rak K, Schraven SP, Schendzielorz P, et al. Stable longitudinal performance of adult cochlear implant users for more than 10 years. *Otol Neurotol.* 2017;38(9):e315-e319.
- Ruffin CV, Tyler RS, Witt SA, Dunn CC, Gantz BJ, Rubinstein JT. Longterm performance of Clarion 1.0 cochlear implant users. *Laryngoscope*. 2007;117(7):1183-1190.
- Henkin Y, Kaplan-Neeman R, Kronenberg J, Migirov L, Hildesheimer M, Muchnik C. A longitudinal study of electrical stimulation levels and electrode impedance in children using the Clarion cochlear implant. Acta Otolaryngol. 2006;126(6):581-586.
- Hughes ML, Vander Werff KR, Brown CJ, et al. A longitudinal study of electrode impedance, the electrically evoked compound action potential, and behavioral measures in nucleus 24 cochlear implant users. *Ear Hear*. 2001;22(6):471-486.
- Vargas JL, Sainz M, Roldan C, Alvarez I, de la Torre A. Analysis of electrical thresholds and maximum comfortable levels in cochlear implant patients. *Auris Nasus Larynx*. 2013;40(3):260-265.
- Eisenberg LS. Perceptual capabilities with the cochlear implant: implications for aural rehabilitation. *Ear Hear.* 1985;6(3 Suppl):60s-69s.
- Moore DR, Shannon RV. Beyond cochlear implants: awakening the deafened brain. Nat Neurosci. 2009;12(6):686-691.
- Yusuf PA, Hubka P, Tillein J, Vinck M, Kral A. Deafness weakens interareal couplings in the auditory cortex. *Front Neurosci.* 2020;14:625721.
- Oh SH, Kim CS, Kang EJ, et al. Speech perception after cochlear implantation over a 4-year time period. Acta Otolaryngol. 2003;123(2):148-153.
 Dornhoffer JR, Reddy P, Meyer TA, Schvartz-Leyzac KC, Dubno JR,
- Dornhoffer JR, Reddy P, Meyer TA, Schvartz-Leyzac KC, Dubno JR, McRackan TR. Individual differences in speech recognition changes after cochlear implantation. JAMA Otolaryngol Head Neck Surg. 2021;147(3): 280-286.
- Fokkens WJ. The advantage of systematic reviews and meta-analysis. *Rhinology*. 2019;57(6):401.

- 20. Stone DL, Rosopa PJ. The advantages and limitations of using metaanalysis in human resource management research. Hum Resour Manag Rev. 2017:27(1):1-7
- 21. Methley AM, Campbell S, Chew-Graham C, McNally R, Cheraghi-Sohi S. PICO, PICOS and SPIDER: a comparison study of specificity and sensitivity in three search tools for qualitative systematic reviews. BMC Health Serv Res. 2014;14:579.
- 22. Moher D, Altman DG, Liberati A, Tetzlaff J. PRISMA statement. Epidemiology. 2011;22(1):128 author reply 128.
- 23. Oxford Centre for Evidence-Based Medicine. The Oxford levels of evidence 2. 2016. Accessed September 6, 2020. https://www.cebm.net/2016/05/ ocebm-levels-of-evidence/
- 24. Higgins JP, Thomas J, Chandler J, et al. Cochrane handbook for systematic reviews of interventions version 6.0. 2019. Accessed September 6, 2020.
- 25. Sterne JA, Hernán MA, Reeves BC, et al. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. BMJ. 2016;355: i4919.
- 26. Thornton AR, Raffin MJ. Speech-discrimination scores modeled as a bino-
- mial variable. J Speech Hear Res. 1978;21(3):507-518.
 27. Spahr AJ, Dorman MF, Litvak LM, et al. Development and validation of the AzBio sentence lists. Ear Hear. 2012;33(1):112-117.
- 28. Piccirillo JF. Improving the quality of the reporting of research results. JAMA Otolaryngol Head Neck Surg. 2016;142(10):937-939.
- 29. Adunka OF, Buss E, Clark MS, Pillsbury HC, Buchman CA. Effect of preoperative residual hearing on speech perception after cochlear implantation. Laryngoscope. 2008;118(11):2044-2049.
- 30. Bergman P, Lyxell B, Harder H, Mäki-Torkko E. The outcome of unilateral cochlear implantation in adults: speech recognition, health-related quality of life and level of anxiety and depression: a one- and three-year follow-up study. *Int Arch Otorhinolaryngol.* 2020;24(3):e338-e346.
- 31. Borger D, Lina-Granade G, Verneyre S, et al. One-year follow up of auditory performance in post-lingually deafened adults implanted with the Neurelec Digisonic(®) SP/Saphyr(®) neo cochlear implant system. Audiol Res. 2015;5(2):139.
- 32. Cooper T, Melder KL, Hyre R, Hobson CE, McCall AA, Hirsch BE. Cochlear implant performance in adult patients with absent intraoperative electri-cally evoked compound action potentials. Otolaryngol Head Neck Surg. 2020;162(5):725-730.
- 33. Dalbert A, Huber A, Baumann N, Veraguth D, Roosli C, Pfiffner F. Hearing preservation after cochlear implantation may improve long-term word perception in the electric-only condition. Otol Neurotol. 2016;37(9):1314-1319.
- 34. Firszt JB, Reeder RM, Holden LK, Dwyer NY, Asymmetric Hearing Study Team. Results in adult cochlear implant recipients with varied asymmetric hearing: a prospective longitudinal study of speech recognition, localization, and participant report. Ear Hear. 2018;39(5):845-862.
- 35. Moberly AC, Vasil K, Baxter J, Klamer B, Kline D, Ray C. Comprehensive auditory rehabilitation in adults receiving cochlear implants: a pilot study. Laryngoscope Investig Otolaryngol. 2020;5(5):911-918.
- 36. Runge CL, Henion K, Tarima S, Beiter A, Zwolan TA. Clinical outcomes of Kenige Cochlear™ Nucleus[®] 5 Cochlear implant system and SmartSound™ 2 signal processing. J Am Acad Audiol. 2016;27(6):425-440.
 Schramm D, Chen J, Morris DP, et al. Clinical efficiency and safety of the oticon medical neuro cochlear implant system: a multicenter prospective
- longitudinal study. Expert Rev Med Devices. 2020;17(9):959-967.
- 38. Sladen DP, Peterson A, Schmitt M, et al. Health-related quality of life outcomes following adult cochlear implantation: a prospective cohort study. Cochlear Implants Int. 2017;18(3):130-135.
- 39. Wang JR, Yuen HW, Shipp DB, et al. Cochlear implantation in patients with autoimmune inner er disease including Cogan syndrome: a comparison with age- and sex-matched controls. Laryngoscope. 2010;120(12):2478-2483.
- 40. Yang CJ, Lee JY, Ahn JH, Lee K-S. Value of pre-operative caloric test in predicting speech perception after cochlear implantation in adults with post-lingual hearing loss. Acta Otolaryngol. 2016;136(9):912-918.
- 41. Zwolan T, Kileny PR, Smith S, Mills D, Koch D, Osberger MJ. Adult cochlear implant patient performance with evolving electrode technology. Otol Neurotol. 2001;22(6):844-849.
- Deep NL, Spitzer ER, Shapiro WH, Waltzman SB, Roland JT Jr, Friedmann DR. Cochlear implantation in adults with single-sided deaf-ness: outcomes and device use. *Otol Neurotol.* 2021;42(3):414-423.
- 43. Kelsall D, Lupo J, Biever A. Longitudinal outcomes of cochlear implantation and bimodal hearing in a large group of adults: a multicenter clinical study. Am J Otolaryngol. 2021;42(1):102773.
- 44. Lee SY, Choe G, Lee SY, et al. Outcome of cochlear implantation in the worse ear of post-lingual asymmetric hearing loss: elucidation of prognos-
- tic markers. Acta Otolaryngol. 2021;141(5):495-501. 45. Sturm JJ, Patel V, Dibelius G, Kuhlmey M, Kim AH. Comparative performance of lateral wall and perimodiolar cochlear implant arrays. Otol Neurotol. 2021;42(4):532-539.
- 46. Grisel J, Miller S, Schafer EC. A novel performance-based paradigm of care for cochlear implant follow-up. Laryngoscope. 2021;132:S1-S10.

- 47. Friedland DR, Kozlowski K, Runge CL. Cochlear implant performance in candidates with moderate hearing loss qualifying in noise. Otol Neurotol. 2021:42(10):1484-1491
- 48. Knopke S, Bauknecht HC, Gräbel S, Häußler SM, Szczepek AJ, Olze H. White matter lesions as possible predictors of audiological performance in adults after cochlear implantation. Brain Sci. 2021;11(5):600.
- 49. Knopke S, Häussler S, Gräbel S, et al. Age-dependent psychological factors influencing the outcome of cochlear implantation in elderly patients. Otol Neurotol. 2019;40(4):e441-e453.
- 50. Plontke SK, Fröhlich L, Wagner L, et al. How much cochlear do you need for cochlear implantation? *Otol Neurotol.* 2020;41(5):694-703.
 Gifford RH, Revit LJ. Speech perception for adult cochlear implant recipi-
- ents in a realistic background noise: effectiveness of preprocessing strategies and external options for improving speech recognition in noise. J Am Acad Audiol. 2010;21(7):441-451. quiz 487-448.
- 52. Fetterman BL, Domico EH. Speech recognition in background noise of cochlear implant patients. Otolaryngol Head Neck Surg. 2002;126(3): 257-263
- 53. Bierbaum M, McMahon CM, Hughes S, et al. Barriers and facilitators to cochlear implant uptake in Australia and the United Kingdom. Ear Hear. 2020;41(2):374-385
- 54. Ebrahimi-Madiseh A, Eikelboom RH, Bennett RJ, et al. What influences decision-making for cochlear implantation in adults? Exploring barriers and drivers from a multistakeholder perspective. Ear Hear. 2020;41(6): 1752-1763.
- 55. Spivak LG, Waltzman SB. Performance of cochlear implant patients as a function of time. J Speech Hear Res. 1990;33(3):511-519. 56. Schvartz-Leyzac KC, Conrad CA, Zwolan TA. Datalogging statistics and
- speech recognition during the first year of use in adult cochlear implant recipients. Otol Neurotol. 2019;40(7):e686-e693.
- 57. Moberly AC, Vasil K, Baxter J, Ray C. What to do when cochlear implant users plateau in performance: a pilot study of clinician-guided aural rehabilitation. Otol Neurotol. 2018;39(9):e794-e802.
- 58. Bernstein CM, Brewer DM, Bakke MH, et al. Maximizing cochlear implant outcomes with short-term aural rehabilitation. J Am Acad Audiol. 2021; $32(3) \cdot 144 - 156$
- 59. Schumann A, Hast A, Hoppe U. Speech performance and training effects in the cochlear implant elderly. Audiol Neurootol. 2014;19(Suppl 1):45-48. 60. Dornhoffer JR, Reddy P, Ma C, Schvartz-Leyzac KC, Dubno JR,
- McRackan TR. Use of auditory training and its influence on early cochlear implant outcomes in adults. Otol Neurotol. 2021;43(2):e165-e173.
 61. Heutink F, Verbist BM, van der Woude WJ, et al. Factors influencing
- speech perception in adults with a cochlear implant. *Ear Hear.* 2021; 42(4):949-960.
- 62. Plant K, McDermott H, van Hoesel R, Dawson P, Cowan R. Factors predicting postoperative unilateral and bilateral speech recognition in adult cochlear implant recipients with acoustic hearing. Ear Hear. 2016; 37(2):153-163.
- 63. Vasil KJ, Lewis J, Tamati T, Ray C, Moberly AC. How does quality of life relate to auditory abilities? A subitem analysis of the Nijmegen Cochlear Implant Questionnaire. J Am Acad Audiol. 2020;31(4):292-301.
 64. Brungart DS, Sheffield BM, Kubli LR. Development of a test battery for
- evaluating speech perception in complex listening environments. J Acoust Soc Am. 2014;136(2):777-790.
- 65. Capretta NR, Moberly AC. Does quality of life depend on speech recognition performance for adult cochlear implant users? Laryngoscope. 2016;126(3): 699-706
- 66. McRackan TR, Bauschard M, Hatch JL, et al. Meta-analysis of quality-oflife improvement after cochlear implantation and associations with speech recognition abilities. Laryngoscope. 2018;128(4):982-990.
- 67. Arnoldner C, Lin VY, Bresler R, et al. Quality of life in cochlear implantees: comparing utility values obtained through the Medical Outcome Study Short-Form Survey-6D and the Health Utility Index Mark 3. Laryngoscope. 2014;124(11):2586-2590.
- 68. Damen GW, Beynon AJ, Krabbe PF, Mulder JJ, Mylanus EA. Cochlear implantation and quality of life in postlingually deaf adults: long-term follow-up. Otolaryngol Head Neck Surg. 2007;136(4):597-604.
- 69. Távora-Vieira D, Marino R, Acharya A, Rajan GP. The impact of cochlear implantation on speech understanding, subjective hearing performance, and tinnitus perception in patients with unilateral severe to profound hearing loss. *Otol Neurotol.* 2015;36(3):430-436.
- 70. Bodmer D, Shipp DB, Ostroff JM, et al. A comparison of postcochlear implantation speech scores in an adult population. Laryngoscope. 2007; 117(8):1408-1411.
- 71. Gifford RH, Shallop JK, Peterson AM. Speech recognition materials and ceiling effects: considerations for cochlear implant programs. Audiol Neurootol, 2008:13(3):193-205.
- 72. Minimal speech test battery. Auditory potential. 2011. Accessed 2022. https://www.auditorypotential.com/MSTBfiles/MSTBManual2011-06-20% 20.pdf.