Supplementary Information

Supplementary table 1: Exclusion criteria.

Exclusion criteria
• Antibiotic use within 14 days of enrolment;
• Severe acute infectious illness or fever above 38.0°C within 14 days before vaccination;
• Present evidence of serious diseases either demanding regular use of oral immunosuppressive medical treatment, like corticosteroids, that might interfere with the results of the study within the last three months or demanding acute use of high-dose oral immunosuppressive that might interfere with the results of the study within the last two weeks;
• Known or suspected allergy to any of the vaccine components (by medical history);
• Occurrence of a serious adverse event after other vaccination by medical history;
• Known or suspected immune deficiency;
• Known or suspected coagulation disorder;
• Oral hormone use, such as postmenopausal hormones, within the last 3 months;
• History of one of the following neurological disorders: multiple sclerosis, Parkinson's disease, or epilepsy;
• Previous administration of plasma-serum products including immunoglobulins within six months before vaccination and blood sampling;
• Major surgery within the last three months;
• Previous meningococcal vaccination;
• Previous confirmed or suspected meningococcal disease;
• Any vaccination within a month before enrolment.

Supplementary table 2: Participant characteristics.

Parameter	All participants *At enrolment*	Primary-only cohort *At 1y (i.e. pre-booster)*	Booster cohort *At 1y (i.e. pre-booster)*
Total n	222	112	104
Age at primary vaccination (median, IQR)	73 (69-76)	73 (69-76)	73 (69-77)
Sex female (number, %)	95 (42,8)	48 (42,9)	46 (44,2)
BMI (median, IQR)	24.7 (22.7-27.5)[&]	24.7 (22.7-27.2)	24.5 (22.6-27.3)[@]
Tilburg Frailty Index (median, IQR)	1 (0-2)	1 (0-2)	1 (0-2)
Self-reported diseases (confirmed by physician and/or for which medication is prescribed; number, %)			
Allergy	10 (4.5)	5 (4.5)	5 (4.8)
Asthma	12 (5.4)	6 (5.4)	5 (4.8)
Diabetes type I	0 (0.0)	0 (0.0)	0 (0.0)
Diabetes type II	18 (8.1)	8 (7.1)	10 (9.6)
Diabetes type unknown	1 (0.5)	1 (0.9)	0 (0.0)
Lung diseases	6 (2.7)	4 (3.6)	2 (1.9)
Gastro-intestinal diseases	9 (4.1)	6 (5.4)	3 (2.9)
Liver diseases	0 (0.0)	0 (0.0)	0 (0.0)
Cancer (currently being treated)	1 (0.5)	0 (0.0)	1 (1.0)
Cancer (in the past; treated)	18 (8.1)	9 (8.0)	8 (7.7)
Cancer (not treated)	2 (0.9)	0 (0.0)	1 (1.0)
Rheumatic diseases	7 (3.2)	5 (4.5)	2 (1.9)
Kidney diseases	0 (0.0)	0 (0.0)	0 (0.0)
Cardiovaculair diseases	86 (38.7)	37 (33.0)	44 (42.3)
Neurological diseases	3 (1.4)	3 (2.7)	0 (0.0)
Skin diseases	7 (3.2)	2 (1.8)	5 (4.8)
Organ or bone marrow transplantation	1 (0.5)	0 (0.0)	1 (1.0)
Other diseases	51 (23.0)	24 (21.4)	26 (25.0)
No disease	69 (30,1)	38 (33.9)	21 (29.8)
Self-reported medication (number, %)			
Antifungal medication	2 (0.9)	1 (0.9)	1 (1,0)
Cholesterol lowering medication	55 (24.8)	27 (24.1)	28 (26.9)
Diabetic medication	14 (6.3)	6 (5.4)	8 (7.7)
Blood pressure lowering medication	75 (33.8)	33 (29.5)	37 (35.6)
Immunosuppressive medication$	20 (9.0)	8 (7.1)	10 (9.6)
Other medication	93 (41.9)	49 (43.8)	40 (38.5)
No medication	85 (38.3)	43 (38.4)	42 (40.4)
Self-reported receipt of vaccines in the last 5 years (number, %)			
COVID-19 vaccination(s)	221 (99.6)	111 (99.1)	104 (100)
Influenza vaccination(s)	210 (94.6)	105 (93.8)	99 (95.2)
Pneumococcal vaccination(s)	113 (50.9)	56 (50.0)	54 (51.9)

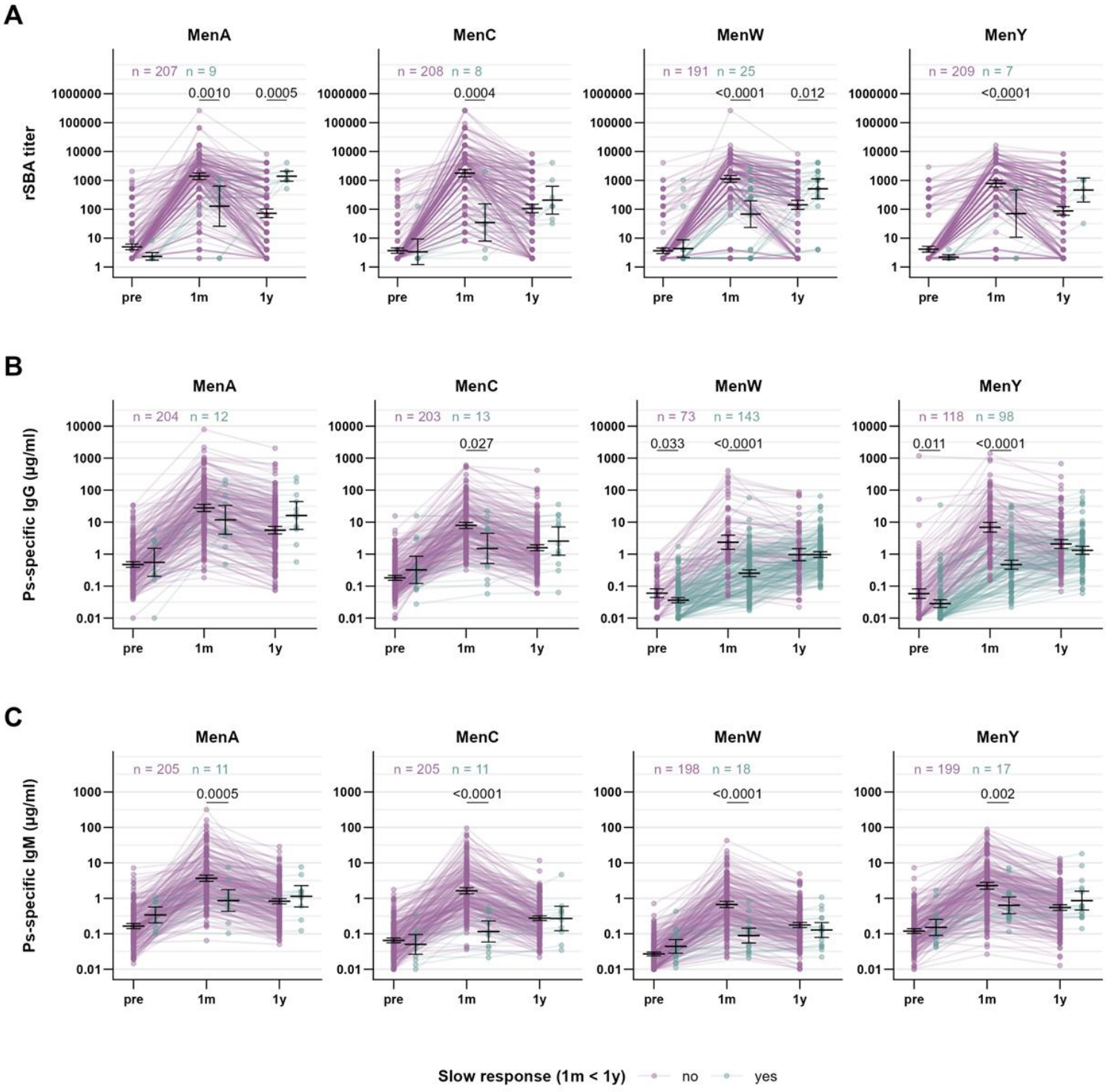
Detailed characteristics for all participants at enrolment, as well as separated by vaccination cohort (i.e. primary-only and booster cohort). $ either topically, inhaled or longer than 3 months ago; & n=221; @ n=103.

Supplementary table 3: Effect of age and sex on post-vaccination MenACWY-specific rSBA responses.

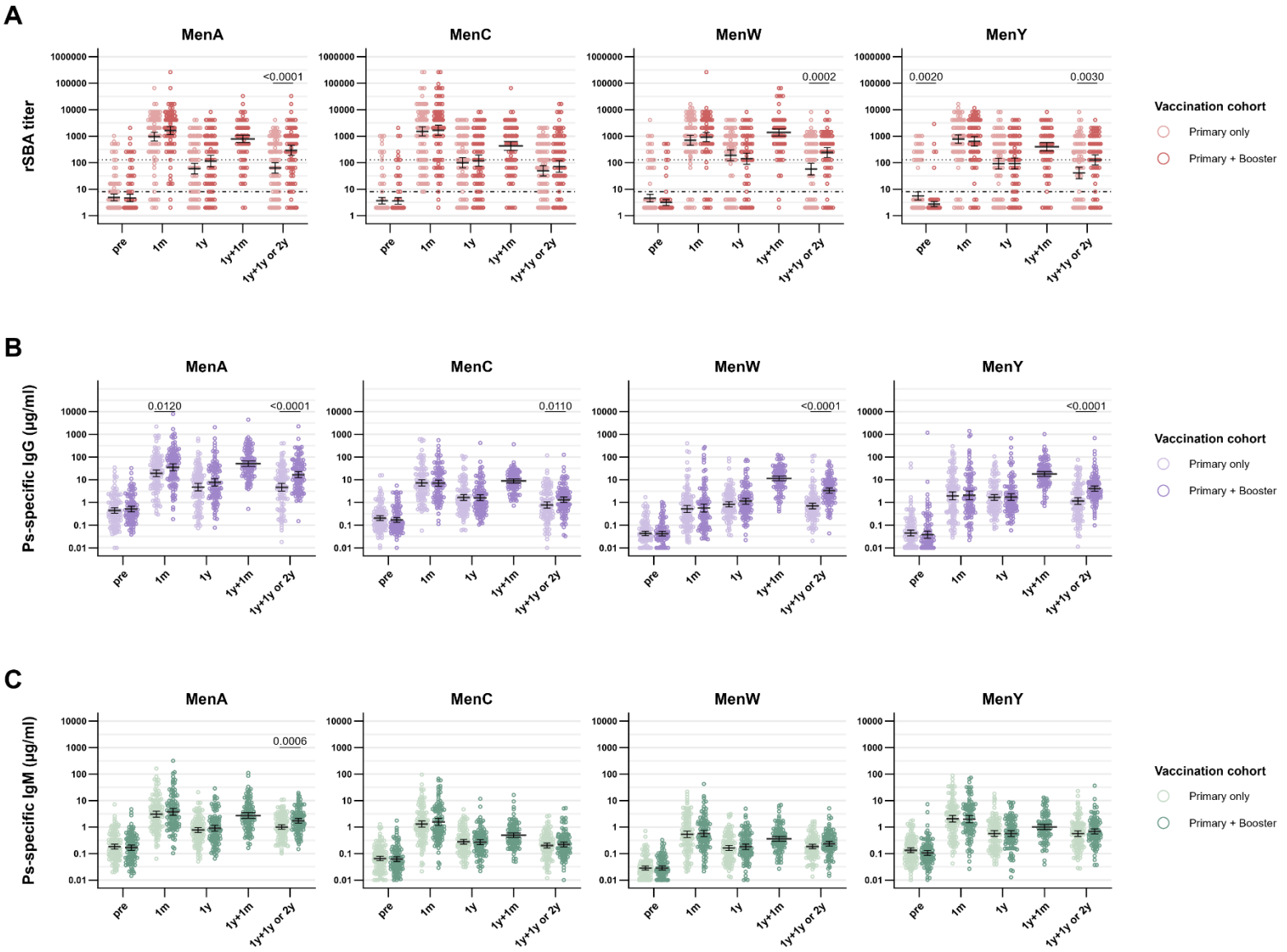
		1m post-vaccination (n = 222)		*1y post-vaccination (n = 216)*		*1m post-booster vaccination (n = 104)*		*1y post-booster vaccination (n = 103)*	
Serogroup		**Estimate**	**Adjusted p-value**	**Estimate**	**Adjusted p-value**	**Estimate**	**Adjusted p-value**	**Estimate**	**Adjusted p-value**
MenA	baseline rSBA titer	**0,280**	**0,002**	**0,348**	**0,004**	**0,364**	**0,000**	**0,663**	**0,000**
	Age at vaccination	-0,021	0,233	0,016	1,000	-0,012	1,000	-0,008	1,000
	Sex (female)	**0,333**	**0,014**	0,215	0,584	0,084	1,000	-0,044	1,000
MenC	baseline rSBA titer	0,196	0,165	**0,458**	**0,000**	**0,602**	**0,000**	**0,867**	**0,000**
	Age at vaccination	0,015	0,985	0,032	0,073	-0,015	0,810	0,004	1,000
	Sex (female)	**0,507**	**0,000**	0,242	0,327	0,088	1,000	-0,048	1,000
MenW	baseline rSBA titer	**0,282**	**0,011**	**0,451**	**0,000**	**0,352**	**0,000**	**0,586**	**0,000**
	Age at vaccination	0,004	1,000	0,018	0,883	0,004	1,000	0,015	0,964
	Sex (female)	0,197	0,530	-0,014	1,000	0,206	0,305	0,213	0,468
MenY	baseline rSBA titer	**0,273**	**0,005**	**0,508**	**0,000**	**0,450**	**0,000**	**0,593**	**0,000**
	Age at vaccination	-0,010	1,000	0,000	1,000	0,007	1,000	0,016	1,000
	Sex (female)	0,108	1,000	0,094	1,000	0,237	0,264	0,041	1,000

Generalized linear models were used to determine the effect of age at vaccination and sex on rSBA responses at 1 month and 1 year following primary and booster MenACWY-TT vaccination. The effects of age and sex on primary and booster rSBA responses were adjusted for pre-primary- ("pre"; n =222) and pre-booster vaccination (1y; n = 104) rSBA titers. Bonferroni corrections were applied to correct for multiple testing. Significant effects are indicated in bold.

Supplementary figure 1. Slow MenW and MenY ps-specific IgG responses following primary MenACWY-TT vaccination. MenACWY-specific rSBA titers, IgG, and IgM concentrations before (pre) and after primary vaccination are shown, stratified by response type. A slow response is defined as rSBA titers or antibody concentrations at one year post primary vaccination (1y) exceeding those at one month post vaccination (1m), whereas a normal response is defined as 1y ≤ 1m. In each figure, the number of participants with a normal response is indicated in purple, while those with a slow response are shown in cyan. Geometric mean titers (GMTs) and geometric mean concentrations (GMCs) are depicted in black, with error bars representing 95% confidence intervals. rSBA titers and antibody concentrations were compared between participants with a slow and normal response using the Mann-Whitney U test with Bonferroni correction.



Supplementary figure 2. MenACWY-specific rSBA, IgG, and IgM responses up to two years following primary MenACWY-TT vaccination, stratified by vaccination cohort. MenACWY-specific rSBA titers, IgG, and IgM concentrations were assessed over two years in two cohorts: one that received only the primary MenACWY-TT vaccination and one that received a booster vaccination at one year post-primary vaccination (1y, i.e., pre-booster). Geometric mean titers (GMTs) and geometric mean concentrations (GMCs) are shown in black, with error bars representing 95% confidence intervals. Responses were compared between vaccination cohorts at each timepoint using the Mann-Whitney U test with Bonferroni correction for multiple comparisons. Timepoints: Pre = pre-vaccination; 1m = one month post primary vaccination; 1y = one year post primary and pre-booster vaccination; 1y+1m = one month post booster vaccination; 1y+1y = one year post booster vaccination (i.e. two years post primary vaccination); 2y = two years post primary vaccination.



Section/topic	No	CONSORT 2025 checklist item description	Reported on page no.
Title and abstract			
Title and structured abstract	1a	Identification as a randomised trial	1
	1b	Structured summary of the trial design, methods, results, and conclusions	1
Open science			
Trial registration	2	Name of trial registry, identifying number (with URL) and date of registration	8
Protocol and statistical analysis plan	3	Where the trial protocol and statistical analysis plan can be accessed	8
Data sharing	4	Where and how the individual de-identified participant data (including data dictionary), statistical code and any other materials can be accessed	10
Funding and conflicts of interest	5a	Sources of funding and other support (eg, supply of drugs), and role of funders in the design, conduct, analysis and reporting of the trial	10
	5b	Financial and other conflicts of interest of the manuscript authors	10
Introduction			
Background and rationale	6	Scientific background and rationale	2
Objectives	7	Specific objectives related to benefits and harms	2
Methods			
Patient and public involvement	8	Details of patient or public involvement in the design, conduct and reporting of the trial	8
Trial design	9	Description of trial design including type of trial (eg, parallel group, crossover), allocation ratio, and framework (eg, superiority, equivalence, non-inferiority, exploratory)	8
Changes to trial protocol	10	Important changes to the trial after it commenced including any outcomes or analyses that were not prespecified, with reason	8
Trial setting	11	Settings (eg, community, hospital) and locations (eg, countries, sites) where the trial was conducted	8
Eligibility criteria	12a	Eligibility criteria for participants	Supplement pg. 1
	12b	If applicable, eligibility criteria for sites and for individuals delivering the interventions (eg, surgeons, physiotherapists)	N.A.
Intervention and comparator	13	Intervention and comparator with sufficient details to allow replication. If relevant, where additional materials describing the intervention and comparator (eg, intervention manual) can be accessed	8
Outcomes	14	Prespecified primary and secondary outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome	8
Harms	15	How harms were defined and assessed (eg, systematically, non-systematically)	8
Sample size	16a	How sample size was determined, including all assumptions supporting the sample size calculation	8
	16b	Explanation of any interim analyses and stopping guidelines	N.A.
Randomisation:			
Sequence generation	17a	Who generated the random allocation sequence and the method used	8
	17b	Type of randomisation and details of any restriction (eg, stratification, blocking and block size)	8
			Reported on page no.

Allocation concealment mechanism	18	Mechanism used to implement the random allocation sequence (eg, central computer/telephone; sequentially numbered, opaque, sealed containers), describing any steps to conceal the sequence until interventions were assigned	N.A.
Implementation	19	Whether the personnel who enrolled and those who assigned participants to the interventions had access to the random allocation sequence	N.A.
Blinding	20a	Who was blinded after assignment to interventions (eg, participants, care providers, outcome assessors, data analysts)	N.A.
	20b	If blinded, how blinding was achieved and description of the similarity of interventions	N.A.
Statistical methods	21a	Statistical methods used to compare groups for primary and secondary outcomes, including harms	9
	21b	Definition of who is included in each analysis (eg, all randomised participants), and in which group	8-9
	21c	How missing data were handled in the analysis	8-9
	21d	Methods for any additional analyses (eg, subgroup and sensitivity analyses), distinguishing prespecified from post hoc	9
Results			
Participant flow, including flow diagram	22a	For each group, the numbers of participants who were randomly assigned, received intended intervention, and were analysed for the primary outcome	3
	22b	For each group, losses and exclusions after randomisation, together with reasons	3
Recruitment	23a	Dates defining the periods of recruitment and follow-up for outcomes of benefits and harms	8
	23b	If relevant, why the trial ended or was stopped	N.A.
Intervention and comparator delivery	24a	Intervention and comparator as they were actually administered (eg, where appropriate, who delivered the intervention/comparator, how participants adhered, whether they were delivered as intended (fidelity))	3-5
	24b	Concomitant care received during the trial for each group	N.A.
Baseline data	25	A table showing baseline demographic and clinical characteristics for each group	Supplement pg. 2
Numbers analysed, outcomes and estimation	26	For each primary and secondary outcome, by group: ● the number of participants included in the analysis ● the number of participants with available data at the outcome time point ● result for each group, and the estimated effect size and its precision (such as 95% confidence interval) ● for binary outcomes, presentation of both absolute and relative effect size	3-5
Harms	27	All harms or unintended events in each group	N.A.
Ancillary analyses	28	Any other analyses performed, including subgroup and sensitivity analyses, distinguishing pre-specified from post hoc	3-5
Discussion			
Interpretation	29	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	6-7
Limitations	30	Trial limitations, addressing sources of potential bias, imprecision, generalisability, and, if relevant, multiplicity of analyses	7

Citation: Hopewell S, Chan AW, Collins GS, Hróbjartsson A, Moher D, Schulz KF, et al. CONSORT 2025 Statement: updated guideline for reporting randomised trials. BMJ. 2025; 388:e081123. https://dx.doi.org/10.1136/bmj-2024-081123

*We strongly recommend reading this statement in conjunction with the CONSORT 2025 Explanation and Elaboration and/or the CONSORT 2025 Expanded Checklist for important clarifications on all the items. We also recommend reading relevant CONSORT extensions. See www.consort-spirit.org.