Supplementary material

Unguided self-help based on metacognitive training and mindfulness-based interventions targeting auditory verbal hallucinations in persons with psychotic disorders: a randomized controlled trial

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CONSORT Checklist

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	2
Open science			
Trial registration	2	Name of trial registry, identifying number (with URL) and date of registration	6
Protocol and statistical analysis plan	3	Where the trial protocol and statistical analysis plan can be accessed	6
Data sharing	4	Where and how the individual de-identified participant data (including data dictionary), statistical code and any other materials can be accessed	43
Funding and conflicts of interest	5a	Sources of funding and other support (e.g., supply of drugs), and role of funders in the design, conduct, analysis and reporting of the trial	43
	5b	Financial and other conflicts of interest of the manuscript authors	43
Introduction			
Background and rationale	6	Scientific background and rationale	3-6
Objectives	7	Specific objectives related to benefits and harms	3-6
Methods			
Patient and public involvement	8	Details of patient or public involvement in the design, conduct and reporting of the trial	6-9
Trial design	9	Description of trial design including type of trial (e.g., parallel group, crossover), allocation ratio, and framework (e.g., superiority, equivalence, non-inferiority, exploratory)	6-8
Changes to trial protocol	10	Important changes to the trial after it commenced including any outcomes or analyses that were not prespecified, with reason	Supplementary material
Trial setting	11	Settings (e.g., community, hospital) and locations (e.g., countries, sites) where the trial was conducted	6
Eligibility criteria	12a	Eligibility criteria for participants	6-7
	12b	If applicable, eligibility criteria for sites and for individuals delivering the interventions (e.g., surgeons, physiotherapists)	6-7

Intervention and comparator	13	Intervention and comparator with sufficient details to allow replication. If relevant, where additional materials describing the intervention and comparator (e.g., intervention manual) can be accessed	8-10
Outcomes	14	Pre-specified primary and secondary outcomes, including the specific measurement variable (e.g., systolic blood pressure), analysis metric (e.g., change from baseline, final value, time to event), method of aggregation (e.g., median, proportion), and time point for each outcome	10-13
Harms	15	How harms were defined and assessed (e.g., systematically, non-systematically)	13-14
Sample size	16a	How sample size was determined, including all assumptions supporting the sample size calculation	Supplementary material
	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 (e.g., stratification, blocking and block size)	8
Allocation concealment mechanism	18	Mechanism used to implement the random allocation sequence (e.g., central computer/telephone; sequentially numbered, opaque, sealed containers), describing any steps to conceal the sequence until interventions were assigned	8
Implementation	19	Whether the personnel who enrolled and those who assigned participants to the interventions had access to the random allocation sequence	8
Blinding	20a	Who was blinded after assignment to interventions (e.g., participants, care providers, outcome assessors, data analysts)	8
	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	13-14
	21b	Definition of who is included in each analysis (e.g., all randomised participants), and in which group	14, supplementary material
	21c	How missing data were handled in the analysis	14
	21d	Methods for any additional analyses (e.g., subgroup and sensitivity analyses), distinguishing prespecified from post-hoc	13-14
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	16, 17 (Figure 2)
	22b	For each group, losses and exclusions after randomisation, together with reasons	16,17 (Figure 2)
Recruitment	23a	Dates defining the periods of recruitment and follow-up for outcomes of benefits and harms	16

	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 (e.g., where appropriate, who delivered the intervention/comparator, how participants adhered, whether they were delivered as intended [fidelity])	16, 19, 23
	24b	Concomitant care received during the trial for each group	19-21 (Table 1)
Baseline data	25	A table showing baseline demographic and clinical characteristics for each group	19-21 (Table 1)
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	17-30
Harms	27	All harms or unintended events in each group	33-34, supplementary material (Table S1, S2)
Ancillary analyses	28	Any other analyses performed, including subgroup and sensitivity analyses, distinguishing pre-specified from post-hoc	n.a.
Discussion			
Interpretation	29	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	36-40
Limitations	30	Trial limitations, addressing sources of potential bias, imprecision, generalisability, and, if relevant, multiplicity of analyses	40-41

Note. n.a. = not applicable.

Changes to the pre-registration

This study was preregistered on clinical trials (NCT06186570) and included a pre-defined study plan. We additionally reported outcomes for retention, adherence and adverse events according to recommendations, although this was not specifically mentioned in the pre-registration. The statistical plan was implemented in the pre-submitted ethics approval. According to this, we additionally defined significant deviations from the study and treatment protocol when participants stated that they did not truthfully answer the post-assessment or could not remember applying the manual. This was added as specific exclusion reasons for the per-protocol (PP) sample since adherence to treatment or trial procedures could not be ensured in these cases which corresponds to our pre-definition of PP criteria (at least 50% of manual done and post-assessment data). Besides, we conducted within-group analyses to examine potential changes in symptoms within groups. No other changes to the *a-priori* criteria and plans were made.

Additional information on medication

Medication was calculated as dose equivalents based on defined daily doses (DDD-method) according to Leucht et al. (2016)[1]. Since all measures were self-reported and the participation was fully online to allow for a low-threshold access, participants had to state their medication, including substance, doses, regular or irregular intake, and long-acting injection (LAI) or oral intake. Medication was calculated to Chlorpromazine equivalents according to Leucht et al. (2016)[1]. LAIs were converted into a 30-days (for 100 and 150mg Paliperidone, and 400mg Aripiprazole) or 90-days (for 350mg Paliperidone) administration according to treatment recommendations on medication.

Additional information on data safety and monitoring

The generated data of the participants were restricted to safeguard their personal rights and respect guidelines for clinical practice. The study was implemented in accordance with the Declaration of Helsinki, data protection laws and Good Clinical Practice (GCP) guidelines. Identifying characteristics of participants were secured in separate password-protected clinical notes that were stored on secure data servers of the Charité – Universitätsmedizin Berlin, to which solely study personal had access. Moreover, data protection was ensured using pseudonymous identification codes for data collection and management. All assessments were carried out by electronic case report forms (eCRF) using the database management application RedCap[2]. Prior to the first data entry, a structured training by an experienced scientist was conducted for all researchers that were involved in the data assessment and management.

Additional methods

To evaluate whether baseline medication dosage as an additional covariate improves model fit, we compared the two models (*post-value ~ group + baseline-value + gender* vs. *post-value ~ group + baseline-value + gender + baseline-medication*) in each outcome using *F*-tests in PP-data that indicated no significant improvements in model fit except for resistance, social withdrawal, and positive affect. However, there were no changes in between-group results and interpretation of findings. We, therefore, used the initial models with baseline values and gender as covariates.

Additional information on recruitment, retention, and adherence

Retrospective exclusion of participants. Two participants were retrospectively identified as ineligible for the study since they did not fulfill the predefined inclusion criteria and/or fulfilled the exclusion criteria. One person from the intervention group had to be excluded retrospectively because the symptoms of the person did not occur within a diagnosis of the psychosis spectrum (F2X.X) according to ICD-10 (exclusion due to a wrong diagnosis). The person was, however, randomized and completed the study and was therefore retrospectively excluded from the data set for not fulfilling the inclusion criteria. Another person from the control group had to be excluded retrospectively since the person stated in the baseline assessment to not hear voices at least once a week (exclusion due to hearing voices < once a week). The person only participated in the baseline assessment and was randomized, but was also retrospectively excluded from the data set for not fulfilling the inclusion criteria. Since the two exclusions appeared both in the intervention and control group, randomization was balanced.

Reasons for drop-out. From $n = 8$ dropouts in the intervention group, one person experienced a Pre-Treatment Emergent Event (PTEE) unrelated to the intervention or trial procedures and dropped out of the study, referring to a hospitalization one day after T_0 to avoid homelessness. Another person from the intervention group reported an adverse event (AE) which was temporarily related to trial procedures, causing an inner conflict and distress of the participant that omitted after stopping the participation (transient, non-harmful, mild without consequences; see Table S1); this person also stopped the participation and dropped out. A third person from the intervention group refused to participate after three weeks due to time capacities and dropped out of the study. The remaining $n = 4$ participants could not be reached anymore and dropped out. Only one person from the control group dropped out of the study due to an AE unrelated to treatment (*death of relative*; see Table S1) and could not be reached

anymore. The person participated in the post-assessment 15 weeks after baseline, leading to unusable data.

Additional results

Table S1. *(Serious) Adverse Events during participation, differentiated according to Linden [3] (2013)*

Present	Classification	Context	Relation	Severity	Side effect
Non-compliance in the intervention group: $SH_{MBI-MCT}$ (n = 1)	Adverse Event (AE)	Participant experienced distress due to a perceived inner conflict between study participation and a pre-existing "pact" (belief system) with the voices not to discuss their experiences. Consequently, the participant withdrew from the study, and study procedures were discontinued.	• Probably related to study procedures. • Treatment correctly applied. • Distress omitted after stopping the participation.	Mild: without consequences.	no
Hospitalization in the intervention group (n = 1)	Serious Pre-Treatment Emergent Event (PTEE)	Serious adverse event unrelated to treatment: hospitalization one day after T_0 to avoid homelessness; participant never used the manual.	• Unrelated to treatment.	Very severe: hospitalization.	no
Hospitalization in the control group (n = 2)	Serious Adverse Event (SAE)	Serious adverse event unrelated to treatment: control group; hospitalization during the six-week waiting list period.	• Unrelated to treatment.	Very severe: hospitalization.	no
Strains in family relation in the control group (n = 1)	Adverse Event (AE)	Adverse event unrelated to treatment: control group; death of a relative.	• Unrelated to treatment.	Moderate to severe: distressing, death of a relative.	no
Unwanted event, not classified as an (S)AE					
Cognitive difficulties in the intervention group (n = 1)	Unwanted event (UE)	Participant experienced cognitive difficulties that led to insufficient verification of manual use, which was rated as not related to treatment.	• Unrelated to treatment.	Mild: without consequences.	no

Note. $SH_{MBI-MCT}$ = self-help intervention, WL = waiting list, (S)AE = (serious) adverse event.

Table S2. *Unwanted events, side effects, and adverse treatment reactions in the intervention group reported at post-treatment (T_1)*

VP	Unwanted Event				Additional description from participants	Satisfaction with $SH_{MBI-MCT}$	Classification according to Linden (2013)		Side effect of $SH_{MBI-MCT}$
	Cognitive	Emotional	Somatic	Others	Stated at T_1	*Mean (SD)*	Side effect and relation to treatment	Severity	yes / no
1	moderate	severe	mild	none	Intense exposure to voices caused excessive demand and emotional distress. Participant needed support from their outpatient psychotherapist and social worker. The distress decreased over time, and it was increasingly possible for the person to be confronted with the analysis of voices.	3.6 (0.55)	Adverse treatment reaction (ATR), related to treatment, transient, distressing.	Moderate to severe: distressing, causing support from professionals.	yes
2	moderate	moderate	moderate	none	The voices “get angry” when the person confronts themself with the symptoms which caused somatic side effects.	3.0 (1.00)	Adverse treatment reaction (ATR), related to treatment, transient, non-harmful, expectable side effect.	Mild to moderate: probably distressing.	yes
3	moderate	moderate	moderate	none	-	3.4 (0.89)	Unwanted event (UE), possibly related to treatment, not specified.	Moderate: distressing (*as stated*)	Possibly

4	mild	moderate	none	none	Person had to deal with symptoms and “wrong assumptions”.	3.6 (0.55)	Adverse treatment reaction (ATR), related to treatment, transient, non-harmful, expectable side effect.	Mild: without consequences	yes
5	Severe	mild	none	none	Manual was helpful to reduce voices but did not help to identify the causes.	3.2 (0.84)	Dissatisfaction with one aspect of the manual, non-harmful.	Mild: without consequences	no
6	moderate	none	none	Hearing voices.	-	2.8 (0.84)	Unwanted event (UE), possibly related to treatment, not specified.	Moderate: distressing (*as stated*)	Possibly
7	none	severe	mild	none	Person felt angry and parallelly guilty since the manual did not help so much. This caused an inner conflict.	2.2 (1.30)	Dissatisfaction with the manual, non-harmful.	Mild: without consequences	no
8	mild	mild	mild	none	Mild nervosity due to becoming aware of the voices.	3.0 (1.00)	Adverse treatment reaction (ATR), related to treatment, transient, non-harmful, expectable side effect.	Mild: without consequences	yes
9	mild	severe	severe	none	During audio files (mindfulness exercise) that focused on the body the person experienced panic attacks that was something	2.8 (0.45)	Adverse treatment reaction (ATR), related to treatment, transient, non-harmful, expectable side effect.	Mild to moderate: distressing but without consequences.	yes

					the person always had problems with and knew about it when using mindfulness.				
10	mild	moderate	none	none	Unwanted events during the participation were not related to the manual.	2.4 (0.89)	Unwanted event (UE), unrelated to treatment.	Not related to treatment.	no
11	moderate	severe	moderate	none	During and after work the voices were very distressing. The person stopped working due to the voices. However, the person did not relate this event and the increase in voices to the intervention, specifically stating that the difficulties in work and with voices were related to personal matters and not the study or treatment.	2.8 (0.84)	Unwanted event (UE), changes in the work situation, unrelated to treatment.	Moderate: voices caused distress at work.	no
12	none	none	none	none	Voices were more intense in the beginning of the intervention which got milder after the voices were used to the manual.	3.8 (0.45)	Adverse treatment reaction (ATR), related to treatment, transient, non-harmful, expectable side effect.	Mild: without consequences	yes

Note. SD = standard deviation, $SH_{MBI\text{-}MCT}$ = self-help intervention. The questionnaire assessing unwanted cognitive, emotional, and somatic experiences during the participation was rated on a Likert-scale ranging from 0 = “none”, 1 = “mild”, 2 = “moderate”, to 3 = “severe”. The satisfaction scale is ranging from 1 to 4, with higher scores indicating higher satisfaction a maximum mean of 4.

Table S3. *Schedule of the applied study instruments across each measurement time point*

Time point	Intervention group		Control group	
	Baseline, T_0	Post intervention, T_1	Baseline, T_0	Post intervention, T_1
WEEK	0	6	0	6
Demographics	x		x	
Current (psychological) treatment and medication	x	x	x	x
General characteristics of AVH	x	x	x	x
The Hallucination Subscale of the Psychotic-Symptom Rating Scale (PSYRATS)	x	x	x	x
Believes About Voices Questionnaire – Revised (BAVQ-R)	x	x	x	x
The Revised Launay-Slade Hallucination Scale (LSHS-R)	x	x	x	x
Positive and Negative Affect Schedule (PANAS)	x	x	x	x
Self-assessment of Negative Symptoms (SNS)	x	x	x	x
Thinking Scale (TS)	x	x	x	x
The Patient Satisfaction Questionnaire (ZUF-8)		x		
Additional questions regarding the satisfaction with the manual		x		

Note. AVH = auditory verbal hallucinations. Measurements are presented in consideration of the applied chronological order during the trial.

Table S4. *Associations between voice hearing, intrusions, and thoughts (Thinking Scale)*

		$SH_{MBI-MCT}$		WL	
		Pre	Post	Pre	Post
Domain	Item	*n* (%)	*n* (%)[1]	*n* (%)	*n* (%)[1]
Loudness	*The perceived or "inner" voices are just as loud as real voices.*	18 (41.9%)	16 (37.2%)	15 (43.9%)	15 (43.9%)
	The perceived voices are louder than real voices.	4 (9.3%)	1 (2.3%)	3 (7.0%)	3 (7.0%)
	The perceived voices are quieter than real voices.	17 (39.5%)	15 (43.9%)	21 (48.8%)	20 (46.5%)
	The perceived voices are actually audible in the real world.	4 (9.3%)	4 (9.3%)	4 (9.3%)	4 (9.3%)
Ego-Boundness	*The voices I hear reflect my own thoughts.*	8 (18.6%)	11 (25.6%)	6 (14.0%)	7 (16.3%)
	The voices I hear say things that I would never think or feel myself.	17 (39.5%)	14 (32.6%)	16 (37.2%)	14 (32.6%)
	The voices I hear are just as uncontrollable as real voices.	18 (41.9%)	11 (25.6%)	21 (48.8%)	21 (48.8%)
Reality	*The voices I hear do not seem particularly real.*	11 (23.3%)	10 (23.3%)	11 (25.6%)	11 (25.6%)
	The voices I hear are almost like real voices.	19 (44.2%)	17 (39.5%)	22 (51.2%)	23 (53.5%)
	The voices I hear are completely indistinguishable from real voices.	13 (30.2%)	9 (20.9%)	10 (23.3%)	8 (18.6%)

Note. $SH_{MBI-MCT}$ = self-help intervention, WL = waiting list. Seven missing in the $SH_{MBI-MCT}$ group and one missing in the control group at post-assessment.

[1]Missing were excluded since imputation is not valid for the subjective description of voice characteristics.

References for supplementary material

1. Leucht S, Samara M, Heres S, Davis JM. Dose equivalents for antipsychotic drugs: the DDD method. *Schizophrenia bulletin*. 2016;42(suppl_1):S90-S94. doi:10.1093/schbul/sbv167

2. Harris PA, Taylor R, Minor BL, et al. The REDCap consortium: building an international community of software platform partners. *J Biomed Inform*. 2019;95:103208. doi:10.1016/j.jbi.2019.103208

3. Linden M. How to define, find and classify side effects in psychotherapy: from unwanted events to adverse treatment reactions. *Clinical psychology & psychotherapy*. 2013;20(4):286-296. doi:10.1002/cpp.1765