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Effects of a Novel, Transdiagnostic Ecological Momentary Intervention for Prevention, and Early Intervention of Severe Mental Disorder in Youth (EMIcompass): Findings From an Exploratory Randomized Controlled Trial

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***Background/Hypothesis*: Digital interventions targeting transdiagnostic mechanisms in daily life may be a promising translational strategy for prevention and early intervention of psychotic and other severe mental disorders. We aimed to investigate the feasibility and initial signals of efficacy of a transdiagnostic, compassion-focused, hybrid ecological momentary intervention for improving resilience (ie, EMIcompass) in youth with early mental health problems. *Study Design*: In an exploratory, assessor-blind randomized controlled trial, youth aged 14–25 with current distress, broad at-risk mental state, or first episode of severe mental disorder were randomly allocated to experimental (EMIcompass+treatment as usual [TAU]) or control condition (TAU). Data on primary (stress reactivity) and secondary candidate mechanisms as well as candidate primary (psychological distress) and secondary outcomes were collected. *Study Results*: Criteria for the feasibility of trial methodology and intervention delivery were met (n = 92 randomized participants). No serious adverse events were observed. Initial outcome signals were evident for reduced momentary stress reactivity (stress×time×condition, B = −0.10 95%CI −0.16–−0.03, d = −0.10), aberrant salience (condition, B = −0.38, 95%CI −0.57–−0.18, d = −0.56) as well as enhanced momentary resilience (condition, B = 0.55, 95%CI 0.18–0.92, d = 0.33) and quality of life (condition, B = 0.82, 95%CI 0.10–1.55, d = 0.60) across post-intervention and 4-week follow-up. No outcome signals were observed for self-reported psychological distress (condition, B = 0.57, 95%CI −1.59–2.72, d = 0.09), but there was suggestive evidence of reduced observer-rated symptoms at the 4-week follow-up (B = −1.41, 95%CI −2.85–0.02, d = −0.41). *Conclusions*: Our findings provide evidence of feasibility and initial signals that EMIcompass may reduce stress reactivity and improve quality of life. A definitive trial is now warranted.**

Key words: digital mobile Health (mHealth) intervention/Just-in-Time Adaptive Intervention (JiTAIs)/Ecological Momentary Assessment (EMA)/clinical staging/stress reactivity/resilience

Introduction

Psychotic and other severe mental disorders have their onset primarily in adolescence and early adulthood and reflect the leading cause of disease burden in this age group.[1] Recent years have seen increasing efforts that quantify psychopathology according to several hierarchical levels, characterize them dimensionally and, thereby, distill transdiagnostic dimensions of psychosis and other severe mental disorders.[2,3] In light of evidence on a pluripotent risk state[4] and extended transdiagnostic phenotype,[5] latest versions of clinical staging models converge on distinguishing three early transdiagnostic stages of nonspecific psychological distress (stage 1a), a broad Clinical High At-Risk Mental State (CHARMS) (stage 1b), and a first episode of severe mental disorder

(stage 2), with psychotic, affective, and anxiety-related conditions as exit syndromes that confer marked risk of enduring disorder (stage 3).[6,7] However, public mental health services remain difficult to access for youth,[8] and we continue to observe a strong need for easily accessible strategies for prevention and early intervention of severe mental disorders.

Recent years have seen rapid advances in mobile health (mHealth) assessment and intervention techniques. Ecological momentary assessment (EMA)[9] and interventions (EMIs)[10,11] use cutting-edge digital technology to facilitate interactive sampling in real-time and target transdiagnostic mechanisms in individuals' living environments (based on EMA data),[11] thereby lowering barriers to care and allowing for ecological translation of prevention and intervention strategies by tailoring them to person, moment and context. Transdiagnostic mechanisms include elevated stress reactivity (ie, more intense emotional reactions to minor stressors in daily life), interpersonal sensitivity, aberrant salience, and threat anticipation, which have been implicated in a range of severe mental health problems.[12–17] In line with the recent shift in focus towards positive mental health (eg, positive affect, well-being, quality of life), EMA studies have further reported emerging evidence on momentary resilience to stress as a protective mechanism in daily life,[18] which may more readily impact indicators of positive mental health. Enhancing emotional resilience through activating emotion regulation systems related to self-compassion, self-acceptance, and positive affect is a primary focus of compassion-focused interventions (CFIs), a third-wave CBT approach.[19] CFIs refer to a wide range of innovative techniques,[19] "…designed to develop compassionate attributes and skills, particularly those that influence affect regulation" (p.199[20]). Indeed, there is experimental evidence that CFI techniques can induce reductions in state negative affect in moments of high stress.[21] Therefore, CFIs are particularly promising for modifying transdiagnostic mechanisms in daily life using principles of EMIs. We have recently developed a transdiagnostic, compassion-focused, hybrid EMI for enhancing resilience in youth with early mental health problems, the EMIcompass intervention.[18] While an uncontrolled pilot study found preliminary evidence on the feasibility, safety, and initial effects of this intervention,[18] evidence from an exploratory trial on feasibility and initial signals of efficacy is pending.

The aim of this exploratory trial was (1) to establish feasibility of conducting a randomized controlled trial (RCT) and delivering the EMIcompass intervention in youth with early mental health problems, and (2) to explore initial signals of efficacy of EMIcompass in reducing psychological distress (candidate primary outcome), reducing momentary stress reactivity (primary candidate mechanism), and on other secondary candidate mechanisms and outcomes as a basis for a future definitive RCT.

Method

Study Design

In an exploratory, parallel-group, assessor-blind RCT (DRKS00017265), youth aged 14–25 years were randomly allocated to the EMIcompass intervention in addition to treatment as usual (TAU) (experimental condition) or a control condition of TAU only. Recruitment was from mental health services at the Central Institute of Mental Health (CIMH), online advertisements, social media, and local registries in Mannheim, Germany. The study was approved by the local Ethics Committee (2017-602N-MA), and followed Consolidated Standards of Reporting Trials (CONSORT) reporting guidelines[22] and relevant extensions.[23–26] The full trial protocol has been reported elsewhere.[27]

Participants

We aimed to recruit 92 individuals with current psychological distress (stage 1a), CHARMS (stage 1b), or first episode of severe mental disorder (stage 2).[6] Eligibility was assessed using observer-rated (Structured Clinical Interview for DSM-5 [SCID-5[28]], Comprehensive Assessment of At-Risk Mental State [CAARMS[29]]) and self-report (Kessler Psychological Distress Scale [K10[30,31]]) measures.

The inclusion criteria were: **(1)** aged 14–25 years, **(2)** meeting criteria for stage 1a (K10 score≥20[30,31]), stage 1b (CHARMS), or stage 2 (first episode of psychotic, bipolar, severe depressive, or severe anxiety disorder) based on the staging model by Hartmann et al.[6], **(3)** high-stress reactivity assessed with a 2-item self-report measure ("Please think of the most unpleasant event in the last week: (a) How sad, disappointed, or angry have you been?, (b) Have you been sad, disappointed or angry because of your feelings?") or the CAARMS subscale on impaired tolerance to everyday stress[29], **(4)** reduced positive affect (ie, mean positive affect score<3.19 for men and <3.05 for women) or increased negative affect (ie, mean negative affect score>1.81 for men and >1.75 for women[32]), based on normative scores[32] of the Positive Affect and Negative Affect Scale[33]), **(5)** willingness to participate, and **(6)** ability to provide written informed consent (or consent by parents in case of minors).

Exclusion criteria were: **(1)** primary diagnosis of alcohol/substance abuse/dependence (SCID-5[28]), **2)** symptoms precipitated by an organic disease, **(3)** insufficient German to participate in trial processes, **(4)** diagnoses of a learning disability, and **(5)** acute suicidality (CAARMS score>4[29]).

Randomization and Masking

Participants were randomized (50:50) to the experimental or control condition at the participant level. Block

randomization in blocks of 4 was performed by an independent researcher through a computer-generated sequence, with stratification for the three stages (stages 1a, 1b, and 2). Assessors were masked to allocation. Breaks in masking were documented and another blinded assessor repeated the assessment.

Interventions

Control Condition: TAU. TAU included standard care delivered according to local and national service guidelines and protocols by their general practitioner, psychiatrist, and other providers of (mental) health care (assessed for the trial duration using the Client Service Receipt Inventory[34]). This included all treatment participants received prior to participation (eg, medication, CBT, inpatient, outpatient, and community mental health services, delivered in line with S3 guidelines for unipolar depression, (hypo)manic episodes, psychosis, and anxiety disorders[35–38]) except for treatment using elements of third-wave CBT (e.g., ACT, CFI).[39]

Experimental Condition: EMIcompass + TAU. The EMIcompass intervention was delivered by trained psychologists within a 6-week period in addition to TAU to individuals allocated to the experimental condition. The intervention consisted of a 6-week compassion-focused EMI and 4 biweekly sessions (3 training sessions, and one review session) plus an optional on-demand session with a duration of 45–60 minutes. All sessions were administered face-to-face or using a certified and encrypted video conferencing system. Participants were offered breathing exercises, soothing/compassionate imagery, and compassionate writing techniques. The EMI translated the training from the intervention sessions into individuals' daily lives based on three types of delivery schemes and was administered through a smartphone-based app (movisensXS). The first three sessions and the EMI were based on elements of CFIs[19,20] (online supplement 1 provides further details on the intervention; see Paetzold et al.[40] for the full manual).

Measures

Blinded assessors collected data on candidate mechanisms and outcomes before randomization (at "baseline"), at the end of the 6-week intervention period ("post-intervention"), and at 4-week follow-up ("follow-up"). Detail on all screening and outcome measures is provided in online supplement 2. To screen for clinical stages, data were collected by trained researchers using interviewer-rated and self-report measures.[29,41–46] Clinical feasibility was assessed based on a priori criteria in relation to (1) the trial methodology, and (2) delivering the EMIcompass intervention to youth with early mental health problems using the following three categories (akin to a traffic light system): (1) feasibility fully established (green), (2) feasibility established, but study procedures need modifying (yellow), and (3) feasibility not established (red).

The candidate primary outcome of psychological distress was measured with the sum score of the K10[31,47] selected as a transdiagnostic measure, which has been recommended for capturing clinical outcomes in youth.[47] The K10 is a self-report measure including 10 items rated on a 5-point scale, with higher scores indicating higher levels of psychological distress. Candidate secondary outcomes included general psychopathology (Brief Symptom Inventory)[48]), psychiatric symptoms (Brief Psychiatric Rating Scale (BPRS)[47]), and quality of life (WHOQOL-BREF[49]).

The primary candidate mechanism was stress reactivity, operationalized as the association between momentary stress and negative affect, measured with EMA[15,16,50–58] in 3 independent periods of 6 consecutive days (ie, at baseline, post-intervention, and follow-up) using validated EMA measures.[15,27,59] Secondary candidate mechanisms assessed with EMA included threat anticipation, aberrant salience, interpersonal sensitivity, negative affective appraisals, self-compassion, emotional reactivity, and resilience.[27] Secondary candidate mechanisms assessed using self-report measures included threat anticipation, interpersonal sensitivity, resilience, self-compassion, and emotion regulation.

Statistical Analysis

Statistical analysis was performed blind to random allocation and according to the intention-to-treat principle based on a pre-specified published statistical analysis plan.[60] First, we tested whether feasibility criteria for (1) the trial methodology for conducting a definitive RCT, and (2) delivering the EMIcompass intervention were met based on three categories.[60]

Second, to examine the effect of EMIcompass+TAU compared to TAU on the candidate primary outcome, we fitted a mixed effects regression model with psychological distress at post-intervention and follow-up as dependent variables. We controlled for baseline distress as predictor and, in addition, included the following independent variables in this model: Time, condition, and clinical stage. Please see online supplement 3 for further details on statistical analyses for all candidate outcomes and mechanisms. We constructed 95% CIs (only for the main effect of condition (β_2) on psychological distress, the *P*-value was inspected) and reported these and d-type effect sizes.

Results

The trial was conducted from August 2019 to September 2021. Of the 372 potential participants initially identified, 163 were assessed for eligibility (Supplementary figure 1). Of these, 92 were randomized to EMIcompass + TAU (n = 46) or TAU only (n = 46). Baseline sample characteristics are shown in table 1. Participants were, on average, 21.67 years, mostly female, from the white majority group,

and currently in school, vocational training, or university. At study entry, n = 52 individuals met the criteria for stage 1a, n = 28 for stage 1b, and n = 12 for stage 2.

Feasibility

Table 2 displays findings on feasibility of the trial methodology and show that all targets for (1) recruitment, (2) eligibility assessment, (3) randomization, and (4) retention were met. There were no SAEs and only limited adverse device effects during the trial period (supplementary table 3). Feasibility criteria for intervention delivery indicated, (5) moderate to high satisfaction with the intervention, (6) moderate to strong compliance/adherence, and (7) moderate to high fidelity to intervention protocol (table 2). All targets of feasibility criteria for delivering the EMIcompass intervention were met and indicated progression ("green").

Table 1. Basic Sociodemographic and Clinical Characteristics at Baseline

	Full Sample		Experimental Condition		Control Condition		Experimental vs. Control Condition
		n		*n*		*n*	Effect size (Cohen`s d/ Cramer`s V)
Age (years), mean (S.D.)	21.67 (2.49)	92	21.30 (2.84)	46	22.04 (2.05)	46	−0.28
Gender, *n* (%)		92		46		46	0.07
Female	67 (72.8)		35 (76.1)		32 (69.6)		
Male	25 (27.2)		11 (23.9)		14 (30.4)		
Ethnicity, *n* (%)		92		46		46	0.24
White majority	72 (78.3)		32 (69.6)		40 (87.0)		
Minority							
Mixed white majority/white other	5 (5.4)		3 (6.5)		2 (4.4)		
White other	5 (5.4)		4 (8.7)		1 (2.2)		
Turkish	4 (4.4)		3 (6.5)		1 (2.2)		
Mixed other	3 (3.3)		2 (4.4)		1 (2.2)		
Middle east	2 (2.2)		1 (2.2)		1 (2.2)		
Asian	1 (1.1)		1 (2.2)		0 (0.0)		
Level of education (completed, ongoing)		91		46		45	0.15
School: GCSEs	11 (12.1)		7 (15.22)		4 (8.89)		
Further: A levels	24 (26.4)		14 (30.43)		10 (22.22)		
Higher: university	56 (61.5)		25 (54.35)		31 (68.89)		
Employment status, *n* (%)		91		46		45	0.19
Student	72 (79.1)		39 (84.78)		33 (73.33)		
School	5 (5.5)		4 (8.70)		1 (2.22)		
Vocational training, University	67 (73.6)		35 (76.09)		32 (71.11)		
Employed	11 (12.1)		4 (8.70)		7 (15.56)		
Unemployed	8 (8.8)		3 (6.52)		5 (11.11)		
Medication, *n* (%)	26 (28.3)	92	12 (26.09)	46	14 (30.43)	46	−0.05
Clinical characteristics, mean (S.D.)							
K10	28.08 (5.1)	92	28.20 (5.1)	46	27.96 (5.2)	46	0.05
BSI-18 (GSI score)	23.28 (10.5)	92	24.55 (9.9)	46	22.00 (11.0)	46	0.24
BPRS (total score)	31.40 (5.1)	92	32.00 (5.1)	46	30.80 (5.2)	46	0.25
WHOQOL-BREF, mean score‡	14.12 (1.6)	53	13.92 (1.5)	25	14.30 (1.7)	28	−0.23
CAARMS (total score)	30.74 (12.7)	92	31.61 (14.1)	46	29.87 (11.2)	46	0.14
BDI	17.60 (8.9)	92	17.91 (9.7)	46	17.28 (8.2)	46	0.07
HAM-D	11.50 (5.7)	92	11.33 (6.2)	46	11.67 (5.1)	46	−0.06
HAM-A	13.83 (6.8)	92	14.00 (7.3)	46	13.67 (6.2)	46	0.05
YMRS	1.55 (1.7)	92	1.89 (2.0)	46	1.22 (1.3)	46	0.40
PQ	3.53 (2.9)	88	4.33 (3.5)	43	2.78 (2.0)	45	0.54
SOFAS	70.59 (10.9)	92	71.83 (9.9)	46	69.35 (11.9)	46	0.23
SOFAS (12 months)	73.19 (12.4)	77	72.08 (13.2)	38	74.28 (11.7)	39	−0.17
Stage, *n* (%)		92		46		46	0.07
Stage 1a	52 (56.5)		26 (56.5)		26 (56.5)		
Stage 1b	28 (30.4)		13 (28.3)		15 (32.6)		
Stage 2	12 (13.0)		7 (15.2)		5 (10.9)		

Note: *n*, number of participants; CAARMS, Comprehensive Assessment of At-Risk Mental State; BPRS, Brief Psychiatric Rating Scale; BSI-18, Brief Symptom Inventory; GSI, General Index; BDI, Beck Depression Inventory; HAM-D, Hamilton Depression Rating Scale; HAM-A, Hamilton Anxiety Rating Scale; YMRS, Young Mania Rating Scale; PQ, Prodromal Questionnaire; SOFAS, Social and Occupational Functioning Assessment Scale.
‡ WHOQOL-BREF: higher number of missing values due to the scale being administered after approval of an ethics amendment.

Table 2. Feasibility of the Trial Methodology and Delivering the EMIcompass Intervention

	mean (S.D.)/ %	*n* (%)	Target	Evaluation
Feasibility of the trial methodology				
(a) Recruitment, *n*		163	>95	Green
(b) Assessment of eligibility criteria, *n*		163	95%	Green
(c) Randomization, *n* (%)		92 (100%)	92	Green
(d) Retention for outcome assessment at at least one time point (*n*, retention rate in %)		90 (98%)	>85%	Green
Feasibility of delivering the EMIcompass intervention				
(e) Satisfaction with the EMIcompass intervention				Green
Satisfaction rating‡, mean (S.D.)	6.11 (0.99)	44	>4	
MARS quality rating‡‡, mean (S.D.)	3.63 (0.58)	24	>3	
(f) Compliance and adherence				Green
Session attendance, in %	96%	43	≥80%	
Study therapist rating of core components delivered, in %	93%	43	≥80%	
Number of EMI tasks completed per person per week, mean (S.D.), range	14.62 (16.93), 1–55	45	≥1	
(g) Fidelity to session protocol				Green
Independent rating of core components delivered, in %	80%	20	≥80%	
Ability to model and embody the spirit of compassion				
Therapist self-rating‡‡‡‡, mean (S.D.)	4.29 (0.69)	17	≥3	
Independent rating ‡‡‡‡, mean (S.D.)	4.69 (0.48)	16	≥3	
Micro-skills in compassion-focused therapy				
Therapist self-rating‡‡‡‡, mean (S.D.)	3.98 (0.55)	44	≥3	
Independent rating ‡‡‡‡, mean (S.D.)	4.50 (0.69)	20	≥3	

Note: n, number of participants; S.D., standard deviation; MARS, Mobile Application Rating Scale.
‡Satisfaction rating on a 7-point scale;
‡‡MARS quality rating on a 5-point scale (*n* = 24 responses due to the scale being added after approval of an ethics amendment).
‡‡‡Number of EMI tasks completed per person over a 6-month intervention period: mean = 75.84 (SD = 85.09).
‡‡‡‡fidelity rating on a 5-point scale.

Initial Signals of Efficacy

No signals of efficacy of the EMIcompass intervention were evident for self-reported psychological distress as our candidate primary outcome (table 3). Specifically, the 95% CI for the difference in levels of psychological distress between experimental and control conditions across post-intervention and 4-week follow-up was wide and the *P*-value was not statistically significant ($B = 0.57$, 95% CI −1.59–2.72, $P = .93$, $d = 0.09$).

When we next inspected findings for the primary candidate mechanism (table 4), we observed an initial signal of efficacy of the EMIcompass intervention on reduced momentary stress reactivity, which was, on average, lower in the experimental than the control condition ($B = -0.10$, 95% CI −0.16–−0.03, $d = -0.10$). This indicated that, in the experimental condition, a one-unit increase in momentary stress was, on average, associated with a 0.10 lower increase in momentary negative affect in daily life relative to the control condition across post-intervention and follow-up. We also found some evidence suggestive of an initial signal of efficacy on reduced non-EMA stress reactivity, in particular, at follow-up, where a small effect size was observed (B = −0.58, 95% CI, −1.26–0.10, $d = -0.37$).

As can be seen in table 3, findings on secondary outcomes showed signals of efficacy of the EMIcompass intervention on improved quality of life, with an, on average, higher level of quality of life in the experimental than the control condition, a difference in the moderate effect size range ($B = 0.82$, 95% CI 0.10–1.55, $d = 0.60$). There was also some evidence suggestive of an initial signal of efficacy that, compared with the control condition, BPRS total scores were lower at post-intervention in the experimental condition, with the upper limit of the 95% CI being very close to but including zero ($B = -1.41$, 95% CI −2.85–0.02; $d = -0.41$). However, mirroring findings on self-reported psychological distress, no signals of efficacy were evident for self-reported general psychopathology.

Turning to findings on secondary candidate mechanisms, we observed initial signals of efficacy on enhanced momentary resilience of small effect size (table 4). Specifically, there was, on average, a higher level of momentary resilience in the experimental than the control condition across post-intervention and follow-up ($B = 0.55$, 95% CI 0.18–0.92, $d = 0.33$). This converged with findings on resilience assessed with a non-EMA measure (table 3), which showed a difference in the small effect size range ($d = 0.26$), but the 95% CI included zero ($B = 2.19$, 95% CI −0.78–5.17). Furthermore, we found that levels of momentary aberrant salience were, on average, lower in the experimental condition across post-intervention and follow-up ($B = -0.38$, 95% CI −0.57–−0.18, $d = -0.56$; table 4). There was also some evidence suggestive of an initial signal of reduced momentary negative affect/emotional reactivity ($B = -0.17$, 95% CI −0.40–0.07, $d = -0.20$), in particular, at follow-up ($B = -0.24$, 95% CI −0.48–−0.01, $d = -0.29$). Similarly, some evidence

Table 3. Candidate Primary and Secondary Outcomes and Secondary (non-EMA) Candidate Mechanisms at Post-intervention and 4-Week Follow-up

	Experimental condition			Control condition			Difference between conditions (at time)		
	Mean	SE	*n*	Mean	SE	*n*	Adj. *B*	95% CI	d-type effect size
Candidate primary outcome									
Psychological distress[‡]									
Main effect of condition							0.57	−1.59–2.72	0.09
Time									
Post-intervention	24.14	0.90	45	23.49	0.90	44	0.65	−1.85–3.15	0.11
Follow-up	22.76	0.90	45	22.28	0.91	43	0.48	−2.03 – 2.99	0.08
Candidate secondary outcome									
General psychopathology (BSI-18 GSI)									
Main effect of condition							−0.41	−4.0 –3.19	−0.04
Time									
Post-intervention	17.33	1.43	45	17.59	1.44	45	−0.26	−4.25–3.74	−0.03
Follow-up	15.53	1.43	44	16.09	1.45	43	−0.56	−4.57–3.45	−0.06
BPRS, total score									
Main effect of condition							−0.62	−1.65–0.41	−0.19
Time									
Post-intervention	30.18	0.51	45	31.59	0.52	43	−1.41	−2.85–0.02	−0.41
Follow-up	31.13	0.51	43	30.96	0.54	41	0.17	−1.29–1.63	0.05
Quality of life, total score[‡‡]									
Main effect of condition							0.82	0.10–1.55	0.60
Time									
Post-intervention	15.14	0.32	34	14.34	0.30	34	0.80	−0.05– 1.66	0.58
Follow-up	15.65	0.30	37	14.80	0.30	36	0.84	0.01 –1.67	0.61
Secondary candidate mechanisms (non-EMA)									
Stress reactivity									
Main effect of condition							−0.29	−0.86–0.29	−0.18
Time									
Post-intervention	4.41	0.25	42	4.39	0.25	43	0.02	−0.66–0.70	0.01
Follow-up	3.85	0.24	44	4.43	0.25	43	−0.58	−1.26–0.10	−0.37
Threat anticipation									
Main effect of condition							0.27	−1.11–1.65	0.06
Time									
Post-intervention	11.91	0.67	45	12.46	0.67	45	−0.55	−2.41–1.31	−0.12
Follow-up	12.89	0.67	45	11.78	0.68	43	1.10	−0.77–2.98	0.25
Interpersonal sensitivity									
Main effect of condition							−1.26	−3.91–1.39	−0.16
Time									
Post-intervention	100.09	1.16	45	100.42	1.16	44	−0.33	−3.56–2.90	−0.04
Follow-up	97.64	1.16	45	99.84	1.18	43	−2.20	−5.46–1.05	−0.29
Resilience									
Main effect of condition							2.19	−0.78–5.17	0.26
Time									
Post-intervention	58.34	1.30	45	56.53	1.30	44	1.81	−1.84–5.46	0.21
Follow-up	61.45	1.30	45	58.87	1.31	43	2.58	−1.08–6.24	0.30
Self-compassion									
Main effect of condition							0.24	−0.36–0.84	0.14
Time									
Post-intervention	13.09	0.27	45	12.95	0.27	45	0.14	−0.61–0.89	0.08
Follow-up	13.31	0.27	45	12.96	0.27	43	0.35	−0.40–1.10	0.19

Table 3. Continued

	Experimental condition			Control condition			Difference between conditions (at time)		
	Mean	SE	*n*	Mean	SE	*n*	Adj. *B*	95% CI	d-type effect size
Adaptive emotion regulation									
Main effect of condition							0.09	−0.28–0.45	0.08
Time									
Post-intervention	5.85	0.17	45	5.59	0.17	45	0.26	−0.22–0.74	0.23
Follow-up	5.94	0.17	45	6.03	0.17	43	−0.08	−0.57– 0.34	−0.07
Maladaptive emotion regulation									
Main effect of condition							−0.06	−0.46–0.34	−0.05
Time									
Post-intervention	5.47	0.18	45	5.64	0.18	45	−0.17	−0.67–0.33	−0.14
Follow-up	5.55	0.18	45	5.50	0.18	43	0.04	−0.46–0.55	0.03

Note: S.D., standard deviation; CI, confidence interval. Adjusted for centered baseline values of the respective mechanism/outcome and group status.
‡*P*-value only reported for candidate primary outcome as stated in the statistical analysis plan: Wald test: $\chi^2 = 0.01$ $P = .93$.
‡‡WHOQOL-BREF: higher number of missing values due to the scale being administered after approval of an ethics amendment.

suggestive of an initial signal of reduced momentary threat anticipation was observed ($B = -0.25$, 95% CI −0.58–0.08, $d = -0.20$).

Discussion

Main Findings

This study moved beyond previous research by establishing the feasibility of trial methodology and intervention delivery as well as detecting initial signals of efficacy of a novel, transdiagnostic, hybrid ecological momentary intervention using cutting-edge EMA design and sampling principles for interactive sampling in real-time in the living environments of youth with early mental health problems. Consistent with the primary focus of this trial, important criteria for feasibility of trial methodology and intervention delivery were met. No SAEs were observed during the trial period. We found initial signals of efficacy for reduced momentary stress reactivity (primary candidate mechanism) and aberrant salience as well as enhanced momentary resilience and quality of life. No signals of efficacy were evident for self-reported psychological distress (candidate primary outcome) and general psychopathology, but there was suggestive evidence of an initial signal of reduced observer-rated symptoms at post-intervention.

Methodological Considerations

This study was conducted in line with CONSORT reporting guidelines[22] and relevant extensions.[23–26] This allowed us to identify and eliminate important sources of bias and confounding and, hence, to endorse the methodological rigor of an exploratory RCT, which focuses on establishing feasibility and tentative signals of, but not conclusive evidence on efficacy. Hence, caution must be taken in interpreting parameter estimates and 95% CIs.

The evaluation of digital interventions targeting candidate mechanisms across early stages of severe mental disorders faces the challenge of selecting outcome measures that are genuinely transdiagnostic in nature. This applies in particular to clinical outcomes that require measures with sufficient bandwidth cutting across diagnostic entities and capturing relevant variance across clinical stages. While important work to address this challenge is underway (eg, as part of the HiTOP consortium[3]), current studies need to draw on already available and validated scales. The K10 has been recommended for capturing clinical outcomes in youth,[47] which informed our choice as a candidate primary outcome in the current study. However, it has not been designed to cover all relevant domains of early pluripotent or extended transdiagnostic phenotypes. This needs to be carefully considered for a future definitive trial (supplementary table 6 shows recommendations for a future definitive trial).

Although important feasibility criteria for the trial methodology were met, the number of participants included varied markedly across the three clinical stages. This pertained in particular to stage 2, for which the smallest number of participants was included despite our intense efforts to recruit individuals from this stage from a large-scale secondary mental health service. This may have been due to restricting the age range to the upper limit of age 25 years given our focus on youth mental health. In line with the upper age limit of specialist services for people with first-episode psychosis in many countries,[8] this may need to be extended to age 35 years for this specific stage (ie, stage 2). Some individuals from this stage may not have been referred to, or taken part due to the low-intensity nature of the EMIcompass intervention. In fact, it seems plausible that a higher intensity of both EMI components and face-to-face sessions (including more detailed

Table 4. Primary and Secondary Candidate Mechanisms Measured With EMA at Post-intervention and 4-Week Follow-up[§]

	Post-intervention		Follow-Up			
	Adj. *B* (95% CI)	*d*-type effect size	Adj. *B* (95% CI)	*d*-type effect size	Adj. *B* (95% CI)	*d*-type effect size
Primary candidate mechanism: Stress reactivity						
Stress × time × condition[†]					−0.10 (−0.16–−0.03)	−0.10
Condition						
Experimental condition	0.41 (0.37–0.44)	0.42	0.30 (0.26–0.34)	0.30		
Control condition	0.37 (0.34–0.41)	0.38	0.36 (0.32–0.39)	0.37		
Experimental vs. control condition	0.04 (−0.01–0.08)	0.04	−0.06 (−0.11–−0.01)	−0.06		
Secondary candidate mechanism: Threat anticipation						
Condition					−0.25 (−0.58–0.08)	−0.20
Experimental condition	2.13 (1.85–2.42)		2.00 (1.70–2.30)			
Control condition	2.39 (2.11–2.68)		2.23 (1.93–2.54)			
Experimental vs. control condition	−0.26 (−0.61–0.09)	−0.20	−0.24 (−0.6 –0.14)	−0.19		
Time × condition					0.03 (−0.27–0.32)	0.02
Secondary candidate mechanism: Aberrant salience						
Condition					−0.38 (−0.57–−0.18)	−0.56
Experimental condition	1.16 (0.97–1.35)		1.15 (0.99–1.31)			
Control condition	1.61 (1.41–1.80)		1.46 (1.30–1.62)			
Experimental vs. control condition	−0.45 (−0.69–−0.20)	−0.66	−0.30 (−0.50–−0.11)	−0.45		
Time × condition					0.15 (−0.05–0.34)	0.22
Secondary candidate mechanism: Negative affective appraisals						
Condition					0.06 (−0.34–0.45)	0.05
Experimental condition	4.75 (4.46–5.05)		4.80 (4.37–5.23)			
Control condition	4.83 (4.53–5.13)		4.61 (4.19–5.02)			
Experimental vs. control condition	−0.08 (−0.44–0.29)	−0.06	0.19 (−0.37–0.75)	0.16		
Time × condition					0.27 (−0.24–0.78)	0.22
Secondary candidate mechanism: Self-compassion						
Condition					−0.04 (−0.36–0.28)	−0.04
Experimental condition	4.49 (4.22–4.76)		4.62 (4.35–4.90)			
Control condition	4.50 (4.23–4.77)		4.69 (4.41–4.98)			
Experimental vs. control condition	−0.01 (−0.34–0.32)	−0.01	−0.07 (−0.42–0.28)	−0.07		
Time × condition					−0.06 (−0.30–0.18)	−0.06
Secondary candidate mechanism: Interpersonal sensitivity						
Condition					−0.15 (−0.51–0.20)	−0.11

Table 4. Continued

	Post-intervention		Follow-Up			
	Adj. *B* (95% CI)	*d*-type effect size	Adj. *B* (95% CI)	*d*-type effect size	Adj. *B* (95% CI)	*d*-type effect size
Experimental condition	4.45 (4.15–4.76)		4.74 (4.41–5.07)			
Control condition	4.60 (4.3 –4.91)		4.90 (4.56–5.23)			
Experimental vs. control condition	−0.15 (−0.5 0.23)	−0.11	−0.16 (−0.5 0.26)	−0.12		
Time × condition					−0.01 (−0.37–0.35)	−0.01
Secondary candidate mechanism: Negative affect/Emotional reactivity						
Condition					−0.17 (−0.40–0.07)	−0.20
Experimental condition	2.05 (1.84–2.25)		1.86 (1.66–2.05)			
Control condition	2.13 (1.92–2.35)		2.10 (1.90–2.30)			
Experimental vs. control condition	−0.09 (−0.35– 0.17)	−0.11	−0.24 (−0.48–−0.01)	−0.29		
Time × condition					−0.15 (−0.33–0.03)	−0.18
Secondary candidate mechanism: Resilience item‡						
Condition					0.55 (0.18–0.92)	0.33
Experimental condition	4.23 (3.85–4.62)		4.39 (4.02–4.77)			
Control condition	3.69 (3.33–4.05)		3.84 (3.47–4.21)			
Experimental vs. control condition	0.54 (0.06–1.02)	0.33	0.56 (0.07–1.04)	0.34		
Time × condition					0.02 (−0.58–0.61)	0.01
Secondary candidate mechanism: Second resilience measure (positive affect)						
Condition					−0.12 (−0.38–0.15)	0.11
Experimental condition	4.11 (3.89–4.33)		4.24 (4.02–4.47)			
Control condition	4.26 (4.03–4.49)		4.32 (4.09–4.55)			
Experimental vs. control condition	−0.16 (−0.43– .12)	−0.15	−0.08 (−0.36–0.21)	−0.07		
Time × condition					0.08 (−0.13–0.28)	0.07

Note: §All models are adjusted for the centered baseline values of the respective mechanism/outcome and group status; †Coefficient for highest-level interaction term; ‡This model did not converge with the full random effects specification, which was likely due to the low number of observations within some individuals and, hence, the random effect for the regression coefficient "time" (post-intervention vs. follow-up) was removed, assuming the same slope across individuals.

counseling and support for the EMI components) and, hence, evaluation of efficacy of such a high-intensity version of EMIcompass may need to be separately investigated (supplementary table 6). As it stands, we see the scope of the current version of EMIcompass, which will be refined based on detailed quantitative and qualitative process data, primarily for stage 1a and 1b individuals aged 14–25 years. Recruitment and randomization in a future definitive trial will need to stratify for clinical stage to prevent imbalance between conditions (supplementary table 6).

Concerns have been raised that digital interventions may create new barriers to care.[61] However, in designing the EMIcompass intervention, we paid careful attention to ensure acceptance, accessibility, and reach, including vulnerable populations that face social and ethnic inequalities in health. This is in part reflected in meeting feasibility criteria for recruitment and a proportion of 22% from migrant and minority ethnic groups, which reflects a higher proportion than the proportion currently living in the CIMH catchment area (i.e., 18%) according to population register data.[62] Girls/women were

over-represented and, hence, randomization in a future definitive trial may need to stratify by gender to rule out potential confounding by this factor. We will continue to scrutinize the reach for a future definitive trial (supplementary table 6), including for populations exposed to emerging vulnerabilities, such as those resulting from the COVID-19 pandemic. This will be informed by additional process data from the current study, which suggest that insecurity, doubt, loss of structure, and loneliness associated with the COVID-19 pandemic were echoed by descriptively increasing recruitment numbers.[63,64] Also, the shift from on-site contact to video calls in sessions to comply with infection control measures may have lowered barriers to, and reduced burden of both accessing help and translating skills to everyday life.[63] Findings further indicate the reach of participants by the intervention independently from key sociodemographic, clinical, and functional characteristics and highlight intervention delivery based on principles of EMIs as important aspects to lower barriers to care.[40,63] Finally, while we cannot rule out that, eg, compliance was lower in moments of high stress, overall, compliance with EMA was high (online supplement 3).[11] Similarly, compliance with EMI tasks (ie, 76 completed tasks, on average, over the 6-week intervention period) was, overall, high and may reflect an important marker of ecological translation of intervention techniques and principles to daily living environments.

Comparison With Previous Research

The current exploratory RCT sought to document feasibility and initial signals of efficacy and, thereby, to support the development of a future definitive trial. In addressing the primary focus of this exploratory trial, we found strong evidence of the feasibility of our trial methodology and delivery of the EMIcompass intervention. This is in line with previous work on the feasibility of RCTs that aim to investigate the efficacy of EMIs narrowly defined,[10,11] and digital interventions broadly coined.[61]

There were no signals of efficacy of the EMIcompass intervention in reducing self-reported psychological distress as our candidate primary outcome. This may at least in part be accounted for by the methodological issues discussed in relation to measuring symptom outcomes across clinical stages. It is also broadly in line with findings from our recent multi-center INTERACT RCT across 2 clinical stages of early psychosis (ie, ultra-high-risk state, first episode),[65] but may have been even more pronounced given the transdiagnostic focus of the current study. While this finding was echoed in findings on self-reported general psychopathology, there was suggestive evidence of reduced observer-rated symptoms of small effect size at post-intervention using the BPRS. This is consistent with a review of clinical outcome measures in youth,[47] in which the BPRS was identified as appropriate for capturing change. Hence, this might be the better measure to capture clinical outcomes across transdiagnostic clinical stages in a definitive trial.

For more than 2 decades, we have seen strong evidence to accrue on stress reactivity as a transdiagnostic momentary mechanism underlying a range of mental health outcomes.[15,16,50–58] Our setting out to design the EMIcompass intervention was strongly informed by this evidence, which motivated the targeting of this momentary mechanism in daily life.[18,27] Transdiagnostic CFI techniques were deemed particularly appealing for this endeavor given the evidence that these can induce reductions in stress reactivity.[21] Ecological translation of these findings from the lab to individuals' living environments was our goal. Intriguingly, an initial signal of efficacy of the EMIcompass intervention on reduced momentary stress reactivity was evident. While the effect size for this was small, it may be considered clinically important, as a marked increase in stress (ie, by 6 points on the EMA stress measure) was associated with a notably lower increase in momentary negative affect *in daily life* (ie, a 0.6-point lower increase in negative affect). It has long been noted that such small effects can have a large impact at population level,[66] which holds in particular for digital EMIs because, first, they impact directly individuals' daily life, and, second, they are readily scalable to large numbers of users at population level.[61]

Findings on secondary outcomes showed an initial signal of efficacy of EMIcompass on improved quality of life in the moderate effect size range, although the number of missing values were higher for this candidate outcome. Hence, this requires careful corroboration from an adequately powered definitive trial. It is, nonetheless, tempting to speculate whether EMIcompass, as a compassion-focused EMI, might more readily impact dimensions of positive mental health,[19,20] and, only at a later point, clinical outcome. While, in line with the former, initial signals of efficacy of EMIcompass on enhanced momentary resilience of small effect size were evident in the current study, the – potentially later – impact on clinical outcome remains to be established in longer periods of follow-up. It would, though, be in line with propositions that shifting the (population) mean of positive mental health even to a limited extent, may yield substantial gains for reducing the prevalence (or even incidence) of mental health outcomes (at the population level),[66] a complex claim that requires further scrutiny.[66]

Overall, further signals of efficacy of EMIcompass on secondary candidate mechanisms were primarily evident in daily life, for momentary aberrant salience and, tentatively, for momentary negative affect. Given the key role aberrant salience has been posited to play in the occurrence of paranoia, this is broadly in line with evidence on experimentally induced reductions in negative affect and paranoia by CFI techniques.[21,67] Given, further, the primary goal of EMIs is ecological translation

to individuals' daily life, the primary impact on putative *momentary* mechanisms was in line with expectations.

Conclusions

Transdiagnostic mechanisms implicated in the origins of severe mental disorders are important targets for prevention and early intervention. Ecological translation of innovative preventive and therapeutic principles to individuals' daily life through EMIs offers new opportunities for tangible prevention and early intervention strategies involving real-world and real-time adaptive interventions tailored to person, moment, and context. Our findings provide evidence of the feasibility and safety of our trial methodology and intervention delivery. Evidence from this exploratory RCT further suggests initial signals that EMIcompass may reduce stress reactivity and enhance both resilience in daily life and quality of life in youth as priority target population. A definitive multi-center RCT is now warranted as an important next step with appropriate design elements and strategies for implementation in routine public mental health services. This will provide the basis for addressing the long-recognized but still often neglected research-to-practice gap[68] for this novel EMI at an early stage, with the goal of transfer, uptake, and scale-up of EMIcompass as an evidence-based innovation generated along the translational chain from risk and protective mechanisms to improving population mental health.

Supplementary Material

Supplementary material is available at https://academic.oup.com/schizophreniabulletin/.

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Conflict of Interests

TB served in an advisory or consultancy role for ADHS digital, Infectopharm, Lundbeck, Medice, Neurim Pharmaceuticals, Oberberg GmbH, Roche, and Takeda. He received conference support or speaker's fee from Medice and Takeda. He received royalties from Hogrefe, Kohlhammer, CIP Medien, and Oxford University Press; this work is unrelated to these relationships. The other authors declare that they have no competing interests.

Authors' Contributions

UR designed the study, is PI and had managerial responsibility for the successful completion of the study. UR, BB, IP, and CR contributed to the development of the intervention. JRB is the trial statistician. BB provided supervision for trial therapists delivering the intervention. DH, TB, and AML supported the recruitment of study participants. UR and AS drafted the manuscript. All authors were involved in the writing, and have read, and approved the final manuscript.

Ethics Approval and Consent to Participate

The study has received ethical approval by the local Ethics Committee of the Medical Faculty Mannheim of Heidelberg University (2017-602N-MA). All participants provided written informed consent before inclusion to the study.

Data Availability

Data acquired during this trial will not be publicly available. The data, protocol, and statistical code are available from the corresponding author upon reasonable request.

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