

The Reciprocal Relationship Between Alliance and Early Treatment Symptoms: A Two-Stage Individual Participant Data Meta-Analysis

Christoph Flückiger
University of Zurich

Julian Rubel
Justus Liebig University Giessen

A. C. Del Re
University of Zurich

Adam O. Horvath
Simon Fraser University

Bruce E. Wampold
Modum Bad Psychiatric Center, Vikersund, Norway, and
University of Wisconsin–Madison

Paul Crits-Christoph
University of Pennsylvania

Dana Atzil-Slonim
Bar-Ilan University

Angelo Compare
University of Bergamo

Fredrik Falkenström and Annika Ekeblad
Linköping University

Paula Errázuriz
University of Chile

Hadar Fisher
Bar-Ilan University

Asle Hoffart
Modum Bad Psychiatric Center, Vikersund, Norway

Jonathan D. Huppert
Hebrew University of Jerusalem

Yogev Kivity
Bar-Ilan University

Manasi Kumar
University of Nairobi

Wolfgang Lutz
University of Trier

John Christopher Muran
Adelphi University

Daniel R. Strunk
Ohio State University

Giorgio A. Tasca
University of Ottawa

Andreea Vișlă
University of Zurich



Ulrich Voderholzer
University of Munich


Christian A. Webb
Harvard Medical School and McLean Hospital, Boston,
Massachusetts

Hui Xu
Loyola University Chicago

Sigal Zilcha-Mano
University of Haifa

Jacques P. Barber
Adelphi University

 Christoph Flückiger, Department of Psychology, University of Zurich;  Julian Rubel, Department of Psychology, Justus Liebig University Giessen; A. C. Del Re, Department of Psychology, University of Zurich;

 Adam O. Horvath, Faculty of Education, Simon Fraser University; Bruce E. Wampold, Modum Bad Psychiatric Center, Vikersund, Norway, and Department of Counseling Psychology, University of Wisconsin–

continued

Objective: Even though the early alliance has been shown to robustly predict posttreatment outcomes, the question whether alliance leads to symptom reduction or symptom reduction leads to a better alliance remains unresolved. To better understand the relation between alliance and symptoms early in therapy, we meta-analyzed the lagged session-by-session within-patient effects of alliance and symptoms from Sessions 1 to 7. **Method:** We applied a 2-stage individual participant data meta-analytic approach. Based on the data sets of 17 primary studies from 9 countries that comprised 5,350 participants, we first calculated standardized session-by-session within-patient coefficients. Second, we meta-analyzed these coefficients by using random-effects models to calculate omnibus effects across the studies. **Results:** In line with previous meta-analyses, we found that early alliance predicted posttreatment outcome. We identified significant reciprocal within-patient effects between alliance and symptoms within the first 7 sessions. Cross-level interactions indicated that higher alliances and lower symptoms positively impacted the relation between alliance and symptoms in the subsequent session. **Conclusion:** The findings provide empirical evidence that in the early phase of therapy, symptoms and alliance were reciprocally related to one other, often resulting in a positive upward spiral of higher alliance/lower symptoms that predicted higher alliances/lower symptoms in the subsequent sessions. Two-stage individual participant data meta-analyses have the potential to move the field forward by generating and interlinking well-replicable process-based knowledge.

What is the public health significance of this article?

Improvements in the quality of the patient-rated alliance are associated with subsequent symptom reduction early in psychotherapy, and symptom reduction is associated with further improvement in the subsequent alliance. This meta-analysis provides empirical evidence for good clinical wisdom that collaborative qualities within the therapist–patient relationship and early distress remediation go “hand-in-hand.” These results underscore the relevance of respectful, collaborative, and ethically sound care for mental health patients to positively impact therapy outcomes.

Keywords: working alliance, early response, process-based therapy, within-patient effects, individual participant data meta-analysis

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The alliance has been one of the most frequently investigated therapeutic factors associated with psychotherapy success (Norcross & Lambert, 2019). The most recent meta-analytic synthesis of the overall association between the alliance assessed early in treatment and treatment outcome indicated that the early alliance predicted on average 5% of the variance in therapy outcomes

including dropout rates ($k = 295$; Flückiger, Del Re, Wampold, & Horvath, 2018). Flückiger and colleagues found no evidence suggesting that the early alliance and outcome relation was substantially impacted by the patient’s pretreatment severity and/or particular psychotherapy orientation (see also Flückiger et al., 2020), two factors that have been raised as potential confounds for the

Madison; Paul Crits-Christoph, Department of Psychiatry, University of Pennsylvania; Dana Atzil-Slonim, Department of Psychology, Bar-Ilan University; Angelo Compare, Department of Human and Social Science, University of Bergamo; Fredrik Falkenström and Annika Ekeblad, Department of Behavioural Sciences and Learning, Linköping University; Paula Errázuriz, Department of Psychology, University of Chile; Hadar Fisher, Department of Psychology, Bar-Ilan University; Asle Hoffart, Modum Bad Psychiatric Center; Jonathan D. Huppert, Department of Psychology, Hebrew University of Jerusalem; Yogev Kivity, Department of Psychology, Bar-Ilan University; Manasi Kumar, Department of Psychiatry, University of Nairobi; Wolfgang Lutz, Department of Psychology, University of Trier; John Christopher Muran, Gordon F. Derner School of Psychology, Adelphi University; Daniel R. Strunk, Department of Psychology, Ohio State University; Giorgio A. Tasca, School of Psychology, University of Ottawa; Andreea Visla, Department of Psychology, University of Zurich; Ulrich Voderholzer, Department of Psychiatry, University of Munich; Christian A. Webb, Department of Psychiatry, Harvard Medical School, and McLean Hospital, Boston, Massachusetts; Hui Xu, School of Education, Loyola University Chicago; Sigal Zilcha-Mano, Department of Psychology, University of Haifa; Jacques P. Barber, Gordon F. Derner School of Psychology, Adelphi University.

There is no prior manuscript that analyzed this set of data. Furthermore, there is no manuscript submitted or in pipeline that is based on the present dataset. We do not intend to further publish any manuscript with the same set of data. This study was supported by the Swiss National Science Foundation (Grant PP00P1_163702) and the Foundation for Research in Science University of Zurich (Grant: STWF-19-018; Principal investigator: Christoph Flückiger). We are very thankful for the investigators and authors of the primary studies for their contribution to this meta-analysis. The authors’ list and its alphabetic order do not represent the sequence of engagement of the primary study investigators to collect their datasets, and it does not represent the conceptual and methodological innovations of all the authors engaged in the primary manuscripts. More explicit standards are necessary on how to conduct meta-analysis that investigates individual participant datasets, particularly when integrating future open source datasets.

Correspondence concerning this article should be addressed to Christoph Flückiger, Department of Psychology, University of Zurich, Binzmühlestrasse 14/04, 8050 Zurich, Switzerland. E-mail: christoph.flueckiger@uzh.ch

alliance–outcome relation (e.g., Barber, 2009; Crits-Christoph, Connolly Gibbons, & Mukherjee, 2013; DeRubeis, Brotman, & Gibbons, 2005). However, it is less clear whether a stronger alliance relates to subsequent symptom reduction or vice versa (e.g., Barber, Connolly, Crits-Christoph, Gladis, & Siqueland, 2000; Wampold & Imel, 2015; Zilcha-Mano, 2017). Several studies have examined the unfolding of the alliance and symptoms over the course of therapy, but no meta-analytic synthesis of this relation has been conducted.

The early alliance and treatment outcome relation suggests that the first phase of therapy is critical to the success of therapy, a conjecture that is widely accepted across theoretical orientations (e.g., Barber et al., 2014; Beard & Delgado, 2019; Gmeinwieser, Hagmayer, Pieh, & Probst, 2019; Kivity, Levy, Kolly, & Kramer, 2020; Norcross & Goldfried, 2019; Spencer, Goode, Penix, Trusty, & Swift, 2019). Some authors have underscored the relevance of particular tasks and related interventions within well-specified disorder-specific treatment approaches to promote symptom reduction (e.g., by behavioral activation or homework; Sasso, Strunk, Braun, DeRubeis, & Brotman, 2016; Strunk, Brotman, & DeRubeis, 2010). Other authors have conceptualized this early treatment phase in a broader context of patients' remoralization, generally characterized by an alleviation of hopelessness and the promotion of (subtle) optimistic expectations about the treatment and the development of the trust in the therapeutic relationship (e.g., Frank & Frank, 1991; Wampold & Imel, 2015). Research across a variety of disorders and orientations has found that early treatment response is predictive of posttreatment outcome (e.g., Delgado et al., 2014; Linardon, Brennan, & de la Piedad Garcia, 2016; Lutz et al., 2013, 2014; Lutz, Stulz, & Köck, 2009; Nazari et al., 2017; Rubel, Lutz, & Schulte, 2015; Shalom et al., 2018; Wucherpfennig, Rubel, Hofmann, & Lutz, 2017). Moreover, a recent meta-analysis found large effect size differences in post-treatment outcomes between patients who showed early treatment response and participants without early improvements ($r = .40$; $g = 0.8$; Beard & Delgado, 2019). Thus, we have evidences from parallel lines of research of two potential early therapy indicators of therapy outcome. In this study we used a meta-analytic approach focused on the session-by-session relation between alliance and symptoms early in therapy to better understand the relation between early symptom reduction and alliance.

The alliance is conceptualized as a primarily pan-theoretical construct (Bordin, 1979; Horvath, 2018). Alliance in the early phase of therapy includes collaboration between therapists and clients in coordinated planning of distress reduction, emphasis of the potential relevance of the patient's belief in the therapist as a potent source of help and a warm, supporting, and caring relationship (e.g., Horvath, 2018; Luborsky, 1976; Norcross & Lambert, 2019; Norcross & Goldfried, 2019). However, theoretical positions on the role of alliance and its relation to early symptoms vary across researchers; for example, in cognitive-behavioral therapy (e.g., Coyne, Constantino, Westra, & Antony, 2019; Sasso et al., 2016; Strunk et al., 2010) as well as in psychodynamic-oriented therapies (e.g., Barber, 2009; Zilcha-Mano, 2017). Thus, more data-based approaches are called for to improve the understanding of how early alliance and early symptoms are connected to each other on a session-by-session basis across theoretical perspectives (e.g., APA Presidential Task Force, 2006; Horvath, 2018).

Most meta-analytic research on the alliance–outcome relation has investigated the impact of alliance on outcome from a between-patient (BP) perspective. Most frequently, one alliance assessment (usually in the early phase of therapy) across many patients predicts between-patient posttreatment outcomes (e.g., Flückiger et al., 2018). The BP effects addresses the question “Do patients with better early alliance ratings have better posttreatment outcomes than patients with lower early alliance ratings?” By contrast, within-patient (WP) effects provide information about the temporal relationship between alliance and outcomes within patients (e.g., Barber et al., 2000; Hawley, Ho, Zuroff, & Blatt, 2006; Klein et al., 2003; Zilcha-Mano, 2017). This session-by-session or WP effect addresses the question, “Is it the case for a particular patient, that sessions with better-than-usual alliance ratings are followed by lower-than-usual symptom ratings, or vice-versa?” Generalizing results from BP effects to WP effects is not warranted because WP effects may be independent of the respective BP effects and different therapeutic factors can play a role on these different levels (e.g., Beltz, Wright, Sprague, & Molenaar, 2016; Curran & Bauer, 2011; Hamaker, Kuiper, & Grasman, 2015; Molenaar, 2004).

One feature of additionally investigating WP effects in parallel to BP effects is the test of the temporal relation between two simultaneously occurring factors (e.g., alliance and symptoms) at a fine-grained, session-by-session level. Given the potential benefits of investigating of WP effects, an increasing number of recent studies have examined the alliance–symptoms link on a session-by-session basis (e.g., Wampold & Imel, 2015; Zilcha-Mano, 2017). However, to summarize or generalize such effects (across studies) is difficult because these studies have tended to use diverse statistical approaches. Furthermore, they have often reported unstandardized coefficients, preventing systematic comparisons across studies.

WP and BP effects of early alliance or symptoms may not be unrelated to each other, that is, BP differences in the alliance or symptoms may impact the session-by-session WP alliance–symptom effects (i.e., cross-level interactions). Preliminary results indicated that patients who rate alliance higher (i.e., BP effects) also report higher alliance–symptom effects (WP effects) compared with patients with lower average alliance ratings (e.g., Hoffart, Øktedalen, Langkaas, & Wampold, 2013; Rubel et al., 2019). Overall, whether BP alliance and symptom scores moderate the WP alliance–symptom relation early in treatment remains unknown.

The primary aim of this study was to examine the WP effects of early alliance and early symptoms on a session-by-session basis. Figure 1 illustrates four different WP effects of alliance and early treatment symptoms. We, a priori, specified a definition of early therapy as comprising Sessions 1 to 7.¹ In our analyses, we used a two-stage individual participant data meta-analysis approach to apply a uniform analysis to all primary data sets and compute standardized WP coefficients to enable the investigation of meta-

¹ There is no uniform definition of early treatment phase in the literature across countries, treatment orientations, and patient populations (e.g., Flückiger et al., 2020; Lutz, Stulz, & Köck, 2009). In the alliance literature early phase is often defined as before Session 6 (e.g., Horvath, Del Re, Flückiger, & Symonds, 2011). In our primary data 14 out of the 17 datasets, treatment duration was more than 14 sessions. For the current analyses, we attempted to balance the statistical requirements (not too few sessions) with definitions of “early phase” used in the literature (i.e., not too many sessions).

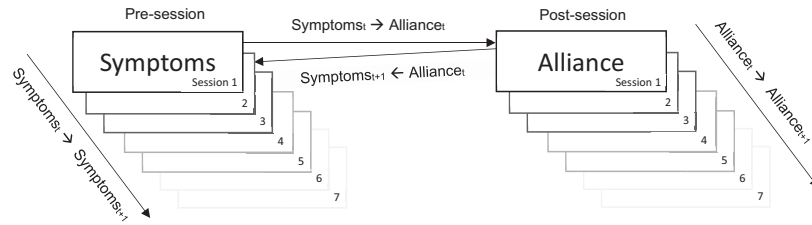


Figure 1. Investigating the impact of alliance in one session on symptoms in a subsequent session and vice versa. Four within-patient effects of early symptoms and early alliance using session-by-session lag models from Sessions 1 to 7.

analytic omnibus effects across particular research questions and study conditions. The first stage comprised WP calculations of alliance–symptoms relations within each study; the second stage comprised integrating these results across patients using standard meta-analytical statistical methods. Based on available prior literature, we derived the following research questions:

Research Question 1 (RQ₁): We investigated the WP effect of the early alliance and early symptoms on a session-by-session basis by examining the relation of alliance on symptoms ($A_t \rightarrow S_{t+1}$) and the relation of symptoms on alliance ($S_t \rightarrow A_t$). We also examined the relation of alliance on the alliance at the next session ($A_t \rightarrow A_{t+1}$) and the relation of symptoms on symptoms at the next session ($S_t \rightarrow S_{t+1}$). We hypothesized that alliance and symptoms were negatively associated with each other (i.e., higher alliance was associated with lower symptoms) in these lagged analyses.

Research Question 2 (RQ₂): Based on our interest in the WP alliance–symptom coefficient ($A_t \rightarrow S_{t+1}$), we investigated cross-level interactions. We hypothesized that high BP alliance and low BP symptoms will positively affect the WP alliance–symptom coefficient.

Method

Selection of Data

The present study (data selection, inclusion/exclusion criterion, methods, etc.) was preregistered at PROSPERO (CRD420 19133312). A stepwise strategy was used to select the primary studies: First, we identified studies that had investigated the relation between alliance and symptoms on a session-by-session level. Second, the corresponding authors of these studies were contacted to provide more information whether their data fulfill the inclusion and exclusion criteria. Figure 2 provides an overview of the data collection procedure.

Systematic search. To locate studies on the relation between alliance and symptoms on a session-by-session basis we replicated and updated the searches for two meta-analyses on alliance outcome relation (Flückiger et al., 2018; Horvath, Del Re, Flückiger, & Symonds, 2011) on EBSCO for PsycINFO database and PSYNDEX (for German-language articles) in December, 2018. The results of these searches were screened for inclusion in the present study using the following criteria: (a) the article referred to the therapy process variable as *helping alliance*, *working alliance*, or

therapeutic alliance; (b) the articles examined the data of session-by-session alliance and session-by-session symptom improvement; (c) the article reported estimates of the relation session-by-session between alliance and symptoms; (d) the patients were adults (mean age >18 years); and (e) reports were written in English, Italian, German, or French. The exclusion criteria were as follows: (a) use of nonclinical samples (e.g., career counseling), and (b) use of fewer than four patients' self-reported measures at the first seven sessions on the alliance and/or symptoms assessments.

We identified 500 articles (140 articles from Horvath et al., 2011; 201 additional articles from Flückiger et al., 2018, and 159 articles from the updated search). Forty-one out of 500 articles fitted the inclusion criteria based on screening the abstract. These 41 articles were carefully read in full by two of the authors (C.F., A.D). This screening process identified 22 studies potentially fulfilling the inclusion and exclusion criteria. The two authors screened the same number of cases, and marginal cases/decisions were resolved by consensus.

Identifying and contacting corresponding authors. We contacted each corresponding author from the 22 studies to solicit collaboration for the present project. The purpose of the invitation was to obtain standardized coefficients based on a common statistical analysis across all included data sets. The corresponding study authors were provided three options to calculate the standardized coefficients from their primary data sets: (1) the corresponding authors to run an R statistical software command created by our research team on their dataset, (2) the corresponding authors to provide their data sets in a structured form to our research team and we calculate the coefficients, and (3) the corresponding study authors to provide any relevant (unstructured) data sets, which were then restructured analyzed appropriately by us.²

Of the 22 corresponding authors contacted through e-mail, 19 authors responded and agreed to contribute coefficients from their data sets (13 authors selected the aforementioned Options 2 or 3). Of these 19 potential data sets, 15 data sets met all inclusion/exclusion criteria (three data sets were excluded based on having fewer than four alliance/symptom assessments within the first seven sessions, and one did not provide patients' self-reported alliance ratings). Furthermore, each author was asked to provide additional data sets mentioned in submitted papers but not yet

² For the invitation letter please see "For_Authors.pdf" at <http://doi.org/10.17605/OSF.IO/XSTZ2>. The uniform R code is available in the online supplemental materials. This procedure allowed us to integrate datasets where the policies only allowed for inhouse analyses.

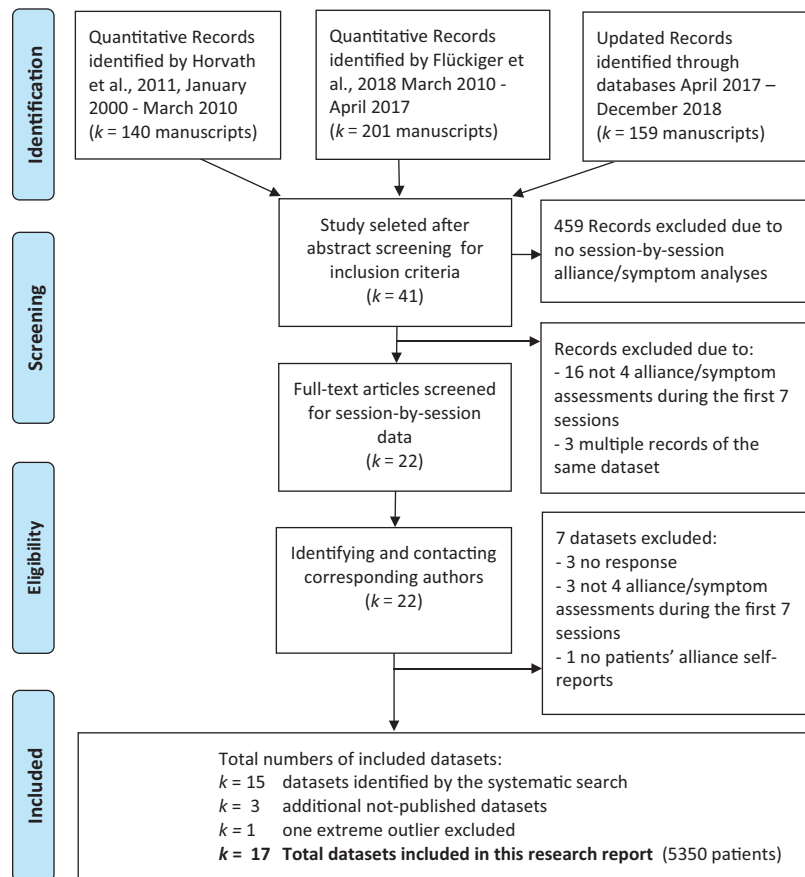


Figure 2. Flowchart of the included and excluded manuscripts. See the online article for the color version of this figure.

published. Three authors provided an additional three data sets (Falkenström, Kuria, Othieno, & Kumar, 2019; Huppert et al., 2018; Rubel et al., 2019). Based on preliminary meta-analytic diagnostics, one dataset (Tasca, Compare, Zarbo, & Brugnera, 2016) was deemed to be an extreme outlier in the session-by-session estimates (up to 8 *SD* from the mean omnibus tests; Viechtbauer & Cheung, 2010) and was therefore excluded from further analyses, resulting in a $k = 17$ included data sets.³

Statistical Analysis and Meta-Analytic Procedure

This analysis followed a two-stage individual participant data meta-analysis approach (e.g., Stewart et al., 2012; Tierney et al., 2015). Accordingly, the coefficients reported in the primary studies were recalculated for this meta-analytic synthesis by using identical statistical models, as described later. The synthesis involved two stages: First, standardized beta-coefficients were generated from the primary study's raw data of each individual patient by applying identical statistical models, and second, standard meta-analytic methods were used to calculate the overall meta-analytic estimates. This approach was used: First, to control heterogeneity that could stem from the use of diverse statistical approaches between studies (e.g., SEM with multiple control variables or a longitudinal MLM with nested random effects). Second,

to generate standardized coefficients for the meta-analytic synthesis, whereas the primary studies' reports have usually provided unstandardized coefficients (e.g., the default of statistical software such as HLM is an unstandardized coefficient; Bryk & Raudenbush, 2002). Third, the two-stage approach integrated standardized coefficients from data sets in cases where the authors were not permitted to share raw data and chose Option 1 (i.e., they ran the R statistical software command by themselves).

Calculation of Standardized Coefficients

For RQ1, we calculated lagged WP beta-coefficients from one time period to another. Alliance was typically measured after a session, and symptoms were usually measured at the beginning of a session (except for Webb, Beard, Auerbach, Menninger, & Björgvinsson, 2014, who analyzed day intervals). Therefore, when predicting symptoms from the alliance ($A_t \rightarrow S_{t+1}$), the lagged WP coefficient mostly reflected the association of the alliance at the end of a session (postsession) with the symptoms measured at

³ Descriptive characteristics are based on the primary study reports and checked by the corresponding authors. There was no traditional meta-analytic data extraction where the coefficients and study characteristics are indirectly extracted from manuscripts.

the beginning of the next session (pre-session). However, when predicting alliance from symptoms ($S_t \rightarrow A_t$), the lagged coefficient reflected the association of the symptoms measured at the beginning of a session with alliance measured at the end of the session (see Figure 1).

As over 80% of the primary studies used a multilevel framework, we a priori defined parsimonious multilevel models that can be applied within an open source software (for studies using a structural equation framework see, e.g., Falkenström, Finkel, Sandell, Rubel, & Holmqvist, 2017; Rubel et al., 2019; Xu & Tracey, 2015). This approach allowed us to estimate the effects of interest with an identical syntax across all data sets. The estimation of a lagged coefficient requires the existence of at least two time points (i.e., t and $t + 1$). Consequently, the WP analyses are based only on those patients that provided at least two time points. WP coefficients were standardized within persons to estimate the strength of the lagged coefficients. WP standardization has recently been illustrated as a better method for enabling meaningful interpretations of lagged coefficients than use of group-based standardization (Schuurman, Ferrer, de Boer-Sonnenschein, & Hamaker, 2016; Wang, Zhang, Maxwell, & Bergeman, 2019). Specifically, before inclusion in the analysis, all variables were centered at the respective person-specific means and standard deviations. To disentangle WP from BP variation, raw scores were person-mean centered based on the recent recommendations of Wang and Maxwell (2015) to obtain a parsimonious model applicable across the included longitudinal data sets. Furthermore, BP estimates were standardized at the overall mean and *SD* to obtain generalizable coefficients across studies. Equation 1 exemplifies the adjusted session-by-session alliance-symptoms model ($A_t \rightarrow S_{t+1}$):

$$WP_S_{t+1i} = \beta_0 + \beta_1(WP_A_{ti}) + \beta_2(WP_S_{ti}) + [u_{0i} + e_{ti}] \quad (1)$$

where WP_S_{t+1i} is a given patient's (i) standardized WP symptom score in session $t + 1$; β_0 is the average intercept, which is allowed to vary between patients (u_{0i}); β_1 is the standardized WP effect of the alliance in session at time t on next session symptoms and is considered fixed between patients (no random effect); and β_2 is the average autoregressive effect of patients' symptom scores at a given session (at time t) on their symptom score at the next session (at time $t + 1$) and is considered fixed between patients (no random effect). We tested if the models improved when this WP effect was allowed to vary between patients (i.e., a random term was included in the model; u_{2i}). Finally, e_{ti} reflected the session-specific error term. These residuals on Level 1 were modeled with a first-order autoregressive (AR[1]) covariance structure, considering that sessions closer together should be more highly correlated than sessions farther apart. We examined models where the autoregressive effects β_2 were included (adjusted models) and models where the autoregressive effects β_2 were excluded (unadjusted models). Both models provided conservative estimates of the fixed autoregressive effects because the residuals at Level 1 were modeled as an AR(1) function for both models and thus accounted for parts of the autoregressive effects (e.g., Hoffman, 2015). To predict the alliance, we used a similar analytic strategy. Models were estimated by software R package "nlme" (Pinheiro,

Bates, DebRoy, Sarkar, & R Core Team, 2019) to generate a transparent statistical approach.

For RQ2, we investigated models that considered cross-level interactions of the average alliance or symptoms scores on the $A_t \rightarrow S_{t+1}$ coefficient. Equation 2 represents one of these adjusted cross-level interaction models:

$$WP_S_{t+1i} = \beta_0 + \beta_1(WP_A_{ti}) + \beta_2(WP_S_{ti}) + \beta_3(BP_A_{ti}) + \beta_4(BP_A_{ti} * WP_A_{ti}) + [u_{0i} + e_{ti}] \quad (2)$$

where the dependent variable and standardized coefficients β_0 to β_2 have the same meaning as in Equation 2. β_3 is the standardized association between the person-specific average alliance score over the first seven sessions and symptoms. β_4 represents the cross-level interaction effect between the average alliance level over the first seven sessions and the WP alliance on outcome. As such, β_4 indicates whether the WP Alliance effect is moderated by the average alliance quality over the first seven sessions.

Meta-Analytic Procedures

To meta-analyze the standardized beta-coefficients we used random effects meta-analysis applying inverse variance method for pooling (e.g., Borenstein, Hedges, Higgins, & Rothstein, 2009). A few studies have reported two measures of primary symptoms (e.g., two measures to assess depression). To avoid favoring these studies (and thus violated the assumption of independent samples), we aggregated within-study coefficients (Del Re & Hoyt, 2010) such that each study finally contributed one coefficient to each model in the meta-analysis. Next, to estimate the overall effects across the study-level coefficients, we calculated overall omnibus tests for each coefficient. To meta-analyze the standardized beta-coefficients from the lag-models (RQ 1, 2), each coefficient was weighted in inverse proportion to its variance (inverse-variance weighting; e.g., Borenstein et al., 2009; Marín-Martínez & Sánchez-Meca, 2010). We used a random-effects model estimator (REML), assuming that the studies in this meta-analysis were sampled from a population of studies. All analyses were conducted using the R software packages for meta-analysis "MAc" (Del Re & Hoyt, 2010) and "metafor" (Viechtbauer, 2017).

Heterogeneity was assessed using the Q and I^2 statistics (Higgins & Thompson, 2002). If the Q statistic was significant, we assumed that the effects aggregated in the analysis were heterogeneous and a moderator analysis might be justified. The statistic I^2 is an index of the degree of heterogeneity computed as a percentage of the observed variability among. In addition, we calculated credibility intervals as a further indicator of heterogeneity (e.g., Wiernik, Kostal, Wilmot, & Dilchert, 2017). We also examined the hypotheses that our search may be biased because we excluded unpublished studies with potentially low or nonsignificant results; we used funnel plots, rank correlation (Begg & Mazumdar, 1994), and regression tests (Egger, Smith, Schneider, & Minder, 1997).

Results

Preliminary Analyses

A description of the included data sets and their characteristics are presented in Table 1. The number of patients per dataset ranged from 29 to 1,550 patients; the number of sessions ranged from 2 to 7, $M = 5.07$ per patient. The gender distribution was 27 to 100% female ($M = 62\%$ female), and the mean patients age ranged from 26.1 to 46.7 years ($M = 37.3$). There were 10 disorder-specific data sets (four depression, four anxiety, one posttraumatic stress disorder, and one eating disorder samples) and seven data sets with mixed diagnoses (usually in the depression-anxiety cluster). Treatment orientations included cognitive-behavioral therapy ($k = 8$), psychodynamic therapies ($k = 2$), and eclectic/various orientations ($k = 6$). One study provided a contrast between cognitive-behavioral therapy and alliance-focused therapy. Seven data sets were gathered under randomized controlled trial conditions, and 10 data sets were sourced from routine clinical practice. Geographical distribution of the data: United States ($k = 4$), Israel ($k = 3$) Germany, Sweden, Switzerland (each $k = 2$), Canada, Chile, Kenya, and Norway (each $k = 1$). Patient-rated alliance was primarily assessed by a short form of the Working Alliance Inventory (WAI, $k = 11$), Bern Post-Session Report (BPSR, $k = 3$), California Psychotherapy Alliance Scale ($k = 2$), and Session Report Scale (SRS, $k = 1$). In nine data sets, patients' self-reported session symptoms and posttreatment outcome were assessed by a disorder-specific measure, and eight data sets provided a more general distress measure. Two studies had reported positive mental health measures and were reversely coded for this study. The original articles had been published in the *Journal of Consulting and Clinical Psychology* ($k = 7$), *Journal of Counseling Psychology* ($k = 5$), *Behavior Research and Therapy* ($k = 2$), *Psychotherapy Research*, *Journal of Anxiety Disorders*, and *Psychotherapy* (each $k = 1$).

To test whether the prior large-scale meta-analytic findings of the positive relation between early alliance and outcome can be replicated within the present set of data, we ran several BP alliance-outcome correlations. The overall BP effect ($k = 17$) of the correlation between early alliance_{Session 1-7} and posttreatment symptoms was $r_{unadjusted} = -.274$ (95% CI [-.212, -.327]; $p < .0001$; $Q_{unadjusted} = 27.1$, $p < .03$; $I^2 = 43\%$). When adjusted for baseline symptoms the correlations were $r_{adjusted} = -.219$ (95% CI [-.160, -.279]; $p < .0001$, $Q_{adjusted} = 40.2$, $p < .0004$; $I^2 = 64\%$). The BP effect between session alliance_{Session 1-7} and dropout rates ($k = 11$) was $r_{unadjusted} = .244$ (95% CI [.152, .337]; $p < .0001$, $Q_{unadjusted} = 17.5$, $p < .06$; $I^2 = 0\%$) and $r_{adjusted} = .232$ (95% CI [.136, .329]; $p < .0001$, $Q_{adjusted} = 14.3$, $p < .16$; $I^2 = 0\%$). Overall, these findings were in line with the estimates reported in Flückiger et al. (2018).

Session-by-Session Lag Models (RQ1)

A summary of the session-by-session lag models is presented in Table 2. The standardized beta-coefficients were interpreted as the magnitude of relations between two sequential observations. For example, for the $A_t \rightarrow S_{t+1}$ beta-coefficient: for every 1-point *SD* increase in WP alliance, there was a corresponding WP 1-point *SD* decrease in symptoms at the next time point.

Alliance_t → Alliance_{t+1}. The overall WP effect ($k = 17$) of the lag models between A_t and A_{t+1} was $\beta = .044$ (95% CI [-.002, .089]; $p < .06$), indicating a statistical trend in the direction that high alliance at time t was positively related to high alliance at time $t + 1$; however, this trend did not reach statistical significance. Note; we observed significant heterogeneity in these effects ($Q = 112.5$, $p < .0001$; $I^2 = 89\%$). Inspection of the funnel plots indicated no substantial asymmetry (rank correlations and regression tests, $p > .52$), suggesting that publication bias was likely absent.

Alliance_t → Symptoms_{t+1}. The overall WP effect ($k = 17$) of the relation between A_t and S_{t+1} was $\beta_{unadjusted} = -.072$ (95% CI [-.101, -.042]; $p < .0001$) and $\beta_{adjusted} = -.065$ (95% CI [-.092, -.038]; $p < .0001$), indicating that high alliance at time t was related to low symptoms at time $t + 1$. We observed significant heterogeneity in these effects ($Q_{unadjusted} = 52.2$, $p < .0001$; $I^2 = 71\%$; $Q_{adjusted} = 41.4$, $p < .001$; $I^2 = 63\%$). The funnel plots indicated no substantial asymmetry (rank correlations and regression tests, $p > .18$).

Symptoms_t → Alliance_{t+1}. The overall WP effect ($k = 17$) of the lag models between S_t and S_{t+1} was $\beta = .082$ (95% CI [.034, .130]; $p < .0001$) in the direction high symptoms at time t were positively related to high symptoms at time $t + 1$. There was significant heterogeneity in these effects ($Q = 15.4$, $p < .0001$; $I^2 = 90\%$). The funnel plots indicated no substantial asymmetry (rank correlations and regression tests, $p > .79$).

Symptoms_t → Alliance_t. The overall WP effect ($k = 17$) of the relation between S_t and A_t was $\beta_{unadjusted} = -.194$ (95% CI [-.260, -.127]; $p < .0001$) and $\beta_{adjusted} = -.148$ (95% CI [-.215, -.081]; $p < .0001$) in direction that high pre-session symptoms were related with low post-session alliance. We observed significant heterogeneity in these effects ($Q_{unadjusted} = 329.7$, $p < .0001$; $I^2 = 95\%$; $Q_{adjusted} = 41.4$, $p < .001$; $I^2 = 63\%$). The funnel plots indicated no substantial asymmetry (rank correlations and regression tests, $p > .54$).

Cross-Level Interactions on $A_t \rightarrow S_{t+1}$ (RQ2)

Cross-level interaction alliance₁₋₇. The overall effect of the cross-level interaction of the BP alliance₁₋₇ on the $A_t \rightarrow S_{t+1}$ WP coefficient ($k = 17$) was $\beta_{unadjusted} = -.028$ (95% CI [-.042, -.014]; $p < .0001$) and $\beta_{adjusted} = -.025$ (95% CI [-.038, -.012]; $p < .0002$), indicating that the association $A_t \rightarrow S_{t+1}$ was stronger in individuals with generally high alliances (see Table 3). We observed low heterogeneity in these effects ($Q_{unadjusted} = 20.7$, $p > .19$, $I^2 = 4\%$; $Q_{adjusted} = 18.7$, $p > .28$, $I^2 = 1\%$). The funnel plots indicated no substantial asymmetries (rank correlations and regression tests, $p > .26$).

Cross-level interaction symptoms₁₋₇. The overall effect of the cross-level interaction of the BP symptoms₁₋₇ on the $A_t \rightarrow S_{t+1}$ WP coefficient ($k = 17$) was $\beta_{unadjusted} = .030$ (95% CI [.008, .051]; $p < .007$) and $\beta_{adjusted} = .027$ (95% CI [.004, .051]; $p < .02$), indicating that the $A_t \rightarrow S_{t+1}$ coefficient was weaker for individuals with high symptoms compared to individuals with low symptoms (see Table 3). We observed considerable heterogeneity in these effects ($Q_{unadjusted} = 31.6$, $p > .01$, $I^2 = 36\%$; $Q_{adjusted} =$

Table 1
Study Characteristics of the Included Datasets

First author, (Publication year)	N	% Females	Age	Primary diagnosis	SUD	Type	Duration	Design	Country	Alliance measure	Symptom measure	Disorder- specific	Period of time	Alliance _t → Symptoms _{t+1} β (SE)	Symptoms _t → Alliance _t β (SE)
Cris-Christoph et al. (2006, 2011)	45	0.56	42.8	MDD	excluded	PsyDyn	16 w	RCT	USA	CALPAS	HAM-D*, BDI-II	yes	1-7 w	-0.190 (0.056)	-0.127 (0.057)
Falkenström et al. (2013)	645	0.74	37.3	Transd.	not ex.	various	1-37 s	other	Sweden	WAI	CORE-OM	no	1-7 s	-0.148 (0.019)	-0.343 (0.017)
Falkenström et al. (2016)	96	0.69	33.8	MDD	excluded	various	14 s	RCT	Sweden	WAI	BDI-II	yes	1-7 s	-0.067 (0.043)	-0.157 (0.042)
Falkenström et al. (2019)	345	0.27	28.9	Transd.	not ex.	various	1-8 s	other	Kenya	WAI	CORE-OM	no	1-7 s	-0.007 (0.058)	-0.121 (0.058)
Fisher et al. (2016)	101	0.62	39.8	Transd.	not ex.	PsyDyn	4-49 s	other	Israel	SRS	ORS	no	2-7 s	-0.001 (0.050)	-0.163 (0.044)
Flückiger et al. (2013)	430	0.62	37	Transd.	excluded	CBT	1-169 s	other	Switzerland	BPSR	OC*, Improv.	no	1-7 s	-0.022 (0.022)	-0.076 (0.219)
Hoffart et al. (2013)	65	0.58	45.2	PTSD	not ex.	CBT	10 s	RCT	Norway	WAI	PSS-SR*, GSI	yes/no	1-7 s	-0.171 (0.054)	-0.014 (0.053)
Huppert et al. (2018)	29	0.44	29	SAD	excluded	CBT	20 s	RCT	Israel	WAI	SPIN	yes	1-7 s	-0.113 (0.070)	-0.124 (0.070)
Rübel et al. (2017)	1550	0.63	36	Transd.	not ex.	CBT	1-109 s	other	Germany	BPSR	GSI	no	1-7 s	-0.039 (0.010)	-0.084 (0.010)
Rübel et al. (2019)	55	0.75	43.9	GAD	not ex.	CBT	14 s	RCT	Switzerland	WAI	BAI	yes	1-7 s	-0.116 (0.055)	-0.132 (0.053)
Schwartz et al. (2018)	193	0.53	46.7	MDD	not ex.	CBT	22-111d	other	Germany	BPSR	BDI-II	yes	1-7 w	-0.057 (0.054)	-0.490 (0.045)
Tasca & Lampard (2012)	238	1.00	26.1	ED	not ex.	various	14 w	other	Canada	CALPAS	Utr	yes	1-7 w	0.015 (0.036)	-0.100 (0.035)
Webb et al. (2014)	103	0.64	36	MDD	not ex.	CBT	2-26 d	other	USA	WAI	CESD-10	yes	1-4 d	-0.004 (0.086)	-0.423 (0.075)
Weiss et al. (2014)	29	0.58	31	Panic	excluded	CBT	12 s	other	Israel	WAI	PDSS-SR	yes	1-7 s	-0.208 (0.068)	-0.213 (0.066)
Xu & Tracey (2015)	638	0.46	—	Transd.	not ex.	various	3-14 s	other	USA	WAI	OQ	no	3-7 s	-0.081 (0.035)	-0.119 (0.034)
Zilcha-Mano & Errázuriz (2017)	547	0.74	41.3	Transd.	not ex.	various	1-55 s	RCT	Chile	WAI	OQ, Life satis.	no	1-7 s	-0.063 (0.025)	-0.123 (0.023)
Zilcha-Mano et al. (2016)	241	0.65	42	MDD	excluded	CBT/AFT	30 s	RCT	USA	WAI	GSI*, Probl.solv.	no	1-7 s	-0.054 (0.028)	-0.398 (0.026)

Note. N = patient sample size of the session-by-session analyses; MDD = major depressive episode; Transd. = transdiagnostic samples; PTSD = posttraumatic stress disorder; ED = eating disorder; GAD = generalized anxiety disorder; SAD = social anxiety disorder; SUD = substance use disorder; excluded = SUD excluded from the primary study; not ex. = SUD not excluded from the primary study; PsyDyn = psychodynamic therapy; CBT = cognitive behavioral therapy; AFT = alliance focused therapy; various = multiple therapy approaches. Duration: Prescriptive duration of a therapy; w = weeks, s = sessions, d = days. RCT = randomized clinical trial; other = other design than RCT under naturalistic conditions; CALPAS = California Psychotherapy Alliance Scale; WAI = Working Alliance Inventory-Short Version; BPSR = Bern Post-Session Report; SRS = Session Report Scale; HAM-D = Hamilton Depression Rating Scale (patient self-report); BDI-II = Beck Depression Inventory II; CORE-OM = Clinical Outcomes in Routine Evaluation-Outcome Measure; ORS = Reliable Change Chart; PSS-SR = PTSD Symptom Scale-Self-report; GSI = Global Severity Index; Utr = Urge to Restrict; CESD-10 = Center of Epidemiologic Studies Depression Scale 10; SPDSS-SR = Panic Disorder Severity Scale-Self-report; OQ = Outcome Questionnaire; Life satis. = Life Satisfaction Scale; OC = outcome composite of seven outcome measures; Improv. = weekly symptom improvement items; BAI = Beck Anxiety Inventory; SPIN = Social Phobia Inventory; Period of time = Analyzed session range (assessed in the primary studies).

* only at posttreatment assessment.

Table 2
Omnibus Test Results of the Session-by-Session Lag Models ($k = 17$)

Lag model	$\beta_{unadjusted}$ [95% CI]	τ^2	80% CrIn	$\beta_{adjusted}$ [95% CI]	τ^2	80% CrIn
Alliance _t → Alliance _{t+1}	.044 [−.002, .130] [†]	.007	−.064, .152			
Alliance _t → Symptoms _{t+1}	−.072 [−.101, −.042] ^{***}	.002	−.131, −.034	−.065 [−.092, −.038] ^{***}	.002	−.115, −.015
Symptoms _t → Symptoms _{t+1}	.082 [.034, .130] ^{***}	.008	−.034, .198			
Symptoms _t → Alliance _t	−.194 [−.260, −.127] ^{***}	.017	−.359, −.029	−.148 [−.215, −.081] ^{***}	.017	−.313, .017

Note. β = meta-analytic estimates of the standardized WP beta-coefficients; adjusted beta-coefficients are adjusted for prior symptoms (at t) or alliance (at t-1) respectively; CI = confidence interval; τ^2 = absolute value of the true variance (heterogeneity); CrIn = credibility interval; WP = within-patient. [†] $p < .010$. ^{***} $p < .0001$.

33.1, $p > .007$, $I^2 = 46\%$). The funnel plots indicated no substantial asymmetries (rank correlations and regression tests, $p > .32$).⁴

Discussion

Although the relation between the alliance and outcome has been a primary interest of psychotherapy researchers for several decades, the underlying dynamics of this association can be difficult to interpret (Hofmann & Hayes, 2019; Muran & Barber, 2010; Norcross & Goldfried, 2019; Norcross & Lambert, 2019; Wampold & Imel, 2015). One major unresolved question is how symptoms and the alliance interact over the course of treatment, particularly in the critical early portion of therapy (e.g., DeRubeis et al., 2005). The primary purpose of this meta-analysis was to estimate the session-by-session effects of alliance on symptoms and the impact of symptoms on the subsequent alliance in the early phase of treatment. Using data sets from 17 independent studies from nine countries, we first calculated the alliance–outcome relation and the standardized session-by-session lagged WP estimates for each of the first seven sessions. Second, we meta-analyzed these estimates using random-effects models to calculate omnibus effects across the studies.

The preliminary analyses indicated that better average early alliance scores had a significant positive association with patients' posttreatment outcome and dropout rate, confirming that these studies are representative, given the well-established relationship between early alliance and outcome (Flückiger et al., 2018). Of note, that the positive associations with posttreatment outcome indicated some heterogeneity (within the positive associations). The primary studies included in the meta-analysis reported a variety of outcome measures across different disorders and populations. This lack of uniformity likely contributed to the observed heterogeneity in some of the analyses. The observed associations were independent of the severity of symptoms at baseline, in line with previous results of a meta-analysis on the alliance–outcome partial correlations that adjusted for a broad range of pretreatment characteristics ($k = 60$; Flückiger et al., 2020; Sharf, Primavera, & Diener, 2010).

In respect to the session-by-session lag models, higher-than-usual alliance scores in one session were followed by lower-than-usual symptoms in the following session, adjusting for previous session symptoms. Notably, however, the reverse effects ($S_t \rightarrow A_t$) were significant as well. Namely, higher-than-usual symptoms ratings reported at the beginning of a session were followed by lower-than-usual alliance ratings in that session, adjusting for previous session alliance. Several considerations may have affected the reciprocal but also heterogeneous relation between time-

specific changes in alliance and symptoms early in therapy. First, the associations observed suggest that the assessment of alliance and symptom improvement go hand in hand (e.g., Hatcher, 2010; Huppert, Fabbro, & Barlow, 2006). These early pre- and postsession evaluations may go along with many further evaluations that must be monitored and coordinated simultaneously, such as gaining a comprehensive overview of a patient's distress and overall situation, setting an overall psychotherapy schedule, creating positive expectations for change, eliciting remoralization, and detecting potential fluctuations in early progress, for example, in symptom severity, well-being, or psychosocial functioning (e.g., Flückiger, Grosse Holtforth, Del Re, & Lutz, 2013; Luborsky, 1976; Wampold & Imel, 2015; Wucherpennig et al., 2017). Significant reciprocal relations between the alliance and symptoms were found from session to session. Notably, these associations are characterized by different time intervals (see Figure 2): The symptom–alliance coefficient typically indicated a time period of approximately 50 min pre- to postsession, and the alliance–symptom coefficient usually covered a time period of 1 week between the alliance at time t and subsequent symptoms at time t + 1. Thus, differences in the magnitude of various coefficients must be interpreted cautiously (even adjusted for prior assessments) and might be a consequence of the differences in assessment time intervals and particular assessment times. Weiss, Kivity, and Huppert (2014) made a critical innovation when they assessed alliance pre- and postsession in a cognitive–behavioral therapy for panic disorder. Using this assessment plan, the authors observed a constant pattern of within-session alliance improvements followed by decreases between sessions (i.e., a “sawtooth pattern” of the alliance across assessments). Clearly, more research is necessary to improve the understanding of the potential impact of particular assessment times (i.e., at pre- and postsession).

A second consideration of the reciprocal relation between alliance and symptoms may regard the overlap between symptom and alliance self-reports since both measures are evaluated from the patient perspective. Such a monomethod assessment is limited, and it would have been interesting to investigate other perspectives such as observer- and/or therapist rating for both concepts, alliance and symptoms (e.g., Horvath et al., 2011; for a notable inclusion of

⁴ We further explored the moderating effects of psychotherapy orientations (i. e., cognitive behavioral therapy, psychodynamic therapy, and others) for all WP coefficients (RQ 1, 2). The results of meta-analytic moderator analyses indicated no moderating effect of the treatment orientation at study level (for all moderator analyses: $Q < 2.99$, $p > .23$, no correction for multiple testing).

Table 3
Omnibus Test Results of the Cross-Level Interaction Alliance_t → Symptoms_{t+1}

Cross-level interaction	$\beta_{unadjusted}$ [95% CI]	τ^2	80% CrIn	$\beta_{adjusted}$ [95% CI]	τ^2	80% CrIn
Alliance ₁₋₇	-.028 [-.042, -.014]***	<.0001	-.036, -.020	-.025 [-.038, -.012]***	<.0001	-.029, -.022
Symptoms ₁₋₇	.030 [.008, .051]**	.0005	.000, .059	.027 [.004, .051]*	.0008	-.010, .065

Note. β = meta-analytic estimates of the standardized WP beta-coefficients; adjusted beta-coefficients are adjusted for prior symptoms (at t); CI = confidence interval; τ^2 = absolute value of the true variance (heterogeneity); CrIn = credibility interval; WP = within-patient.

* $p < .01$. ** $p < .001$. *** $p < .0001$.

a therapist alliance rating see, e.g., Falkenström, Ekeblad, & Holmqvist, 2016 and alliance observer rating see Strunk et al., 2010).

Third, the findings of pre-session and post-session assessments may represent a generalized overall evaluation of the entire session-by-session process rather than an assessment of specific interventions and behaviors (e.g., Ogles, 2013). Consequently, attention should be exercised regarding conclusion of the pre-session and post-session evaluations to in-session behaviors. For example, patients who perceive themselves as “too friendly” may report socially desirable strong alliances with their therapists (e.g., Coyne et al., 2019; Dinger, Strack, Sachsse, & Schauenburg, 2009; Gómez Penedo et al., 2020) and they may be more cautious in reporting negative events in the relationship, such as immediate ruptures during the sessions (e.g., Eubanks, Muran, & Safran, 2018; Rubel, Zilcha-Mano, Feils-Klaus, & Lutz, 2018). There is growing evidence that ruptures (i.e., negative disruptions in alliance levels) are common occurrences in treatments and if these negative events go unresolved, they may be followed by less positive outcomes (Eubanks et al., 2018). Consequently, pre- and post-session evaluations may provide clinically relevant information of how patients process the many tasks related to the early phase of therapy.

Compared with the considerable heterogeneous findings observed with respect to RQ_1 (i.e., relatively large heterogeneity of the overall effects), the results of the cross-level interactions (RQ_2) were much more homogeneous: For patients who generally reported better alliances, the fluctuations in the alliance significantly related to a higher subsequent decrease in symptoms compared to lower BP alliance scores. Similarly, for patients who were less severely distressed during the first seven sessions, larger improvements in the alliance was related significantly to larger subsequent symptom reduction compared to patients with higher symptom severity scores. This pattern was similar to what Hoffart and colleagues (2013) reported for the task component of the WAI in individuals with a posttraumatic stress disorder and Rubel and colleagues (2019) report in a generalized anxiety disorder population. Thus, the results of this study (across $RQs_{1, 2}$) support a positive upward spiral of higher alliance/lower symptoms that facilitates higher alliances and lower symptoms in the subsequent sessions early in therapy (Flückiger, Del Re, et al., 2013; Grawe, 2004; Wucherpfennig et al., 2017). Moreover, the directions of the WP effects were consistent with those of the BP effects.

Although the moderator analyses of this meta-analysis were exploratory in nature given the relatively small number of primary studies, our results are in line with previous meta-analytic findings that have suggested nonsignificant differences between treatment orientations ($p > .23$ for all analyses). Overall, these results may best be understood as evidence that the relation between alliance

and outcome, and the interactive dynamics between alliance and session level outcome are reasonably uniform across treatment methods and diagnostic classifications in early phases of therapy: The growth in the alliance and decreases in symptoms are imbedded in the patients' engagement, treatment acceptance, and related remoralization early in treatment (Frank & Frank, 1991; Howard, Moras, Brill, Martinovich, & Lutz, 1996; Luborsky, 1976; Wampold & Imel, 2015). Clearly, further research should focus on improved detection and understanding of (at risk) patients with high symptoms and low alliances that do not show a positive upward spiral early in treatment (e.g., Brattland et al., 2018; Lambert, Whipple, & Kleinstäuber, 2018; Wucherpfennig et al., 2017).

The results of this meta-analysis have notable clinical implications. Past literature has tended to contrast early symptoms and early alliances, emphasizing a priori either early symptoms (e.g., DeRubeis et al., 2005) or alliance (e.g., Barber et al., 2000). In contrast, this meta-analysis highlights the reciprocal, dialectical nature of both early symptoms and early alliance, and does not support an “either-or” hypothesis. Moreover, our results support “hand-in-hand” processes that might affect, for example, decisions regarding the assessment of routine outcome monitoring, clinical supervision, and daily practice. More specifically, this meta-analysis provides further empirical evidence for good clinical wisdom that collaborative qualities within the therapist–patient relationship and early distress remediation do not play off each other, but rather, they complement each other early in therapy (e.g., APA Presidential Task Force, 2006; Ribeiro, Ribeiro, Gonçalves, Horvath, & Stiles, 2013). Moreover, the results support the importance of active patient involvement in therapist–patient collaboration early in therapy (e.g., Ryan, Lynch, Vansteenkiste, & Deci, 2011; Scheel, 2011; Pope & Vasquez, 2016).

This meta-analysis integrated samples from nine countries including a sample from Sub-Saharan Africa, representing a broad range of professional training and mental health contexts. Global mental health researchers may be encouraged by the present results to generate patient-centered public health awareness that highlights collaborative qualities between the health providers and their patients (e.g., Ogden, Barr, & Greenfield, 2017; Stewart, 2001).

Overall, our findings provide additional support for the growing body of research showing temporal reciprocity of alliance and symptoms on a session-by-session basis. By focusing on WP associations, potentially confounding effects of more stable person-specific characteristics were controlled for, which may allow a firmer conclusion regarding the bidirectional or interactive nature of these variables (e.g., Falkenström et al., 2017).

There are several questions raised, but not yet answered, by this investigation: A limitation of this meta-analysis is the relatively lim-

ited size of primary studies ($k = 17$), which may not accurately reflect the diverse universe of psychotherapy approaches; thus, an investigation of potential differential effects across particular treatment orientations was limited. Time-specific and outside-therapy confounds, for example, intersession processes, could have impact the results (see, e.g., Hartmann, Orlinsky, & Zeeck, 2011; Kaiser & Laireiter, 2019; Quirk, Smith, & Owen, 2018; Strunk et al., 2010).

Based on our decision to include data sets where the alliance and symptoms were measured from Session 1 to 7 to predict posttreatment outcome, we cannot draw conclusions regarding later phases of therapy. Notably, this restriction has some advantages because research has shown that the time of the alliance assessment affects the overall alliance–outcome association (e.g., Flückiger et al., 2018) and that later alliance may partly reflect the general growth of changes in treatment perceived by each patient (Horvath et al., 2011). Furthermore, the alliance assessed early in treatment may provide the best opportunity for making adjustments in treatment, if necessary. Additionally, from a meta-analytic perspective, concentrating on the early phase allowed us to investigate the omnibus effects across short-term, long-term, and time-unlimited treatments.

We relied on computing standardized WP beta-coefficients across data sets based on one statistical method using a uniform syntax. There are emerging alternate approaches for cross-lagged models (e.g., Asparouhov, Hamaker, & Muthén, 2018; Hamaker et al., 2015). Each of these approaches have some benefits and costs and no consensus has been reached as to the best approach. In the future, alternative statistical methods should be explored to find the most useful methodological routes (e.g., Falkenström et al., 2017).

We investigated the average WP alliance–outcome association across patients. Consequently, our overall beta-coefficients of the WP alliance–outcome association may obscure potentially important heterogeneity that might be present between subgroups of patients (e.g., Lorenzo-Luaces, DeRubeis, & Webb, 2014; Zilcha-Mano & Errázuriz, 2015). This variation could have been separately modeled in the first stage of this two-stage analysis by including a random effect for the WP alliance–outcome estimate. This would have allowed the WP alliance–outcome association to vary between patients (i.e., different alliance–outcome associations per patient) and would have produced an estimate of this variability. We decided to not explicitly model this potential variability for several reasons. Most importantly, models with an additional random slope for the WP alliance–outcome association have a higher probability for nonconvergence in small samples. In order to be able to include as many studies in our analysis as possible, we chose a parsimonious model that estimates our effect of interest (i.e., the beta-coefficient of the WP alliance–outcome association) and has a high likelihood to converge in a range of different circumstances. Future research may usefully investigate the questions if between-patient variability in WP alliance–outcome effects is significantly different from zero when pooled across studies and which study characteristics moderate the amount of variability.

Possible therapist effects were not considered in this meta-analysis (e.g., Del Re, Flückiger, Horvath, Symonds, & Wampold, 2012). This decision was primarily based on the methodological consideration that for WP effects, the exclusion of higher-order effects would generally not result in substantial changes in the lower-level estimates (e.g., Falkenström, Solomonov, & Rubel, 2020; Van Landeghem, De Fraigne, & Van Damme, 2005). Additionally, not all data sets had information on the treating therapists,

which would have resulted in an exclusion of several studies. Nonetheless, particular therapists may be more sensitive to early changes and fluctuations in alliance and symptoms compared to other therapists, which may potentially impact the overall unfolding of the early phase of therapy (e.g., Eubanks et al., 2018; Safran & Muran, 2000).

We observed a general lack of assessing and reporting various symptoms and outcome measures simultaneously, somewhat neglecting further outcome components within the broad definition of the World Health Organization such as well-being or psychosocial functioning (Howard, Lueger, Maling, & Martinovich, 1993; WHO, 2019 for exceptions see Huppert et al., 2018 and Weiss et al., 2014). Further research is necessary to better understand to what extent the outcome definition and assessment method may affect the association between process-based psychotherapy factors such as the alliance and outcome (e.g., Flückiger et al., 2019).

Although this meta-analysis integrated studies conducted across nine countries, our results may primarily summarize investigations from westernized contexts in line with other meta-analyses in the field (e.g., Norcross & Lambert, 2019). Clearly, further research is necessary to better understand the potential generalizability of effects across (sub-) cultural contexts (e.g., Errázuriz & Zilcha-Mano, 2018; Flückiger, Del Re, et al., 2013; Kumar, Kuria, Othieno, & Falkenström, 2018; Vasquez, 2007).

To conclude, this meta-analysis is a step in developing a rigorous empirical foundation of process-based psychotherapy across many theoretical considerations (e.g., Crits-Christoph, Gallop, Gaines, Rieger, & Connolly Gibbons, 2020; Hofmann & Hayes, 2019; Muran & Barber, 2010; Norcross & Goldfried, 2019; Norcross & Lambert, 2019; Wampold & Imel, 2015), particularly, early in therapy (e.g., Beard & Delgadillo, 2019; Howard et al., 1993; Spencer et al., 2019; Wucherpfennig et al., 2017). More specifically, this meta-analysis is the first to investigate WP effects on a session-by-session basis suggesting that the alliance and symptoms influence each other early in therapy (Wampold & Imel, 2015; Zilcha-Mano, 2017). Moreover, there is no evidence of a replication problem in the alliance–outcome literature, in contrast, this rigorous meta-analysis provides a practical example of how to investigate the robustness of psychological effects across populations and treatments by taking coordinated advantage of advanced statistical models (e.g., Muthukrishna & Henrich, 2019). This meta-analysis is a first step toward exploring the practicability and applicability of two-stage individual participant data meta-analysis in process-based psychotherapy summarizing WP effects.

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