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Can catastrophes be opportunities? A randomized clinical trial testing a brief mindset intervention for reducing inflammation and depression following COVID-19

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ABSTRACT

Survivors of major catastrophes face significant mental health risks but may also experience growth in meaning, relationships, and self-esteem. Two years after the onset of the Coronavirus disease 2019 (COVID-19) pandemic, we conducted a randomized clinical trial to test the effects of an intervention that promotes the mindset that "catastrophes can be opportunities in the long-term" on mental health and well-being. Adults were randomized to a mindset intervention ($n = 226$) or control group ($n = 153$). The mindset group watched five brief videos that reinforced that "catastrophes can be opportunities in the long-term" and wrote about their mindsets toward the COVID-19 pandemic and how these might encourage or discourage post-traumatic growth. The control group watched videos on the chronology of the pandemic and completed questions reviewing their knowledge. Mindsets regarding catastrophes-as-opportunities, post-traumatic growth, anxiety, depression, and the inflammatory marker C-reactive protein (CRP) were assessed. The mindset intervention significantly reduced CRP ($p = 0.030$) and depressive symptom levels ($p = 0.009$) at 3 months post-intervention. In addition, changes in mindset significantly mediated the effects of the intervention on posttraumatic growth, depressive symptoms, and other domains of mental health and well-being. Brief mindset interventions may thus have beneficial biological and clinical effects for individuals going through major catastrophes.

1. Introduction

The Coronavirus disease 2019 (COVID-19) pandemic has negatively impacted mental health worldwide. Although this effect is difficult to estimate, systematic reviews suggest that the pandemic, caused by SARS-CoV-2, was responsible for a 28 % increase in the prevalence of major depressive disorder (MDD) and a 26 % increase in the prevalence of anxiety disorders globally during 2020 (Santomauro et al., 2021). While much attention has focused on these acute effects, it is also necessary to consider the long-term impacts of the pandemic. Indeed, evidence suggests that large-scale societal disasters can increase rates of posttraumatic stress disorder (PTSD), depression, generalized anxiety disorder, and substance abuse disorder, which can persist for years (Cénat et al., 2021; Maclean et al., 2016). Moreover, infectious disease outbreaks such as COVID-19 often necessitate measures like quarantines and social distancing, which themselves are associated with heightened risk of anxiety and depression, possibly due to reduced social support and disruptions to sleep and exercise habits (Chew et al., 2020; Lee et al., 2024; Slavich, 2022).

Research suggests that alterations in immune processes may serve as one mechanism linking traumatic experiences with adverse mental health outcomes (Slavich, 2020; Slavich and Irwin, 2014; Slavich et al.,

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2023). Acute and chronic stressors can elevate proinflammatory biomarkers such as C-reactive protein (CRP), which has been consistently linked to cognitive and somatic symptoms of Major Depressive Disorder (MDD), as well as reduced effectiveness of antidepressant treatment (Chamberlain et al., 2019; Frank et al., 2021; Tursich et al., 2014). Elevated CRP is also a well-established risk factor for a variety of chronic health conditions, including cardiovascular disease, diabetes, and certain cancers (Kaptoge et al., 2010). Although mindsets are known to influence emotional well-being and coping behaviors (Zion et al., 2023), it remains unclear whether shifts in mindset also affect biological processes such as inflammation. Some theoretical frameworks, such as the "shift and persist" model, suggest that adaptive reframing of adversity may improve mental health outcomes, but evidence for corresponding benefits in physical health is limited and, in some cases, contradictory (Chen et al., 2015; Rudd et al., 2019). Additional research is thus needed to evaluate whether brief mindset interventions can reduce inflammation in addition to mental health problems. Ultimately, this work may shed light on the broader potential of mindset interventions to promote both psychological and biological recovery following major societal stressors.

Paradoxically, while catastrophic events can negatively impact mental and physical health, they can also catalyze positive change, known as post-traumatic growth (Kaptoge et al., 2010; Slavich and Irwin, 2014). Post-traumatic growth has been observed among survivors of various catastrophes, including natural disasters and war (Amiri et al., 2021; Powell et al., 2003). Survivors may report increased appreciation for life, resilience and self-efficacy, improved relationships, strengthened faith or spirituality, and new personal and professional opportunities (Tedeschi and Calhoun, 1996).

At the same time, some self-reports of post-traumatic growth may not indicate actual growth, but rather coping narratives individuals create following traumatic experiences. Meta-analyses have revealed a positive association between self-reported post-traumatic growth and PTSD symptoms (Shakespeare-Finch and Lurie-Beck, 2014). Moreover, Asmundson et al. (2021) found that both real and illusory post-traumatic growth may be widespread among individuals experiencing distress due to the COVID-19 pandemic. Finally, in a sample of American and Canadian adults assessed during the first year of the pandemic, 32 % of participants reported both high levels of post-traumatic growth and reductions in functional impairment, health anxiety, and distress, whereas 17 % reported high levels of post-traumatic growth and increases in the same outcomes. Together, these findings suggest that the COVID-19 pandemic is a source of both significant mental health challenges and genuine growth for many individuals. In addition, the work highlights the importance of assessing growth, alongside mental and physical health challenges, when evaluating post-traumatic growth following a major life stressor.

1.1. Interventions for trauma-exposed individuals

Although various interventions have been developed to support survivors of traumatic life experiences, evidence regarding their efficacy in improving mental health and facilitating post-traumatic growth is mixed. For example, expressive writing has shown effectiveness in reducing depressive symptoms among women with intimate partner violence histories (Koopman et al., 2005). However, recent meta-analyses have found a negligible-to-small effect size on depression (Reinhold et al., 2018). The efficacy of expressive writing in promoting post-traumatic growth is also inconsistent, with a meta-analysis showing little-to-no effect (Pavlacic et al., 2019).

Several cognitive behavior therapy (CBT)-based interventions have also been developed to support survivors of traumatic experiences. For example, exposure therapy, a key component of CBT, has been shown to reduce depressive symptoms in assault survivors and enhance post-traumatic growth in various trauma populations (Foa et al., 1999; Hagenaars and Van Minnen, 2010). Mindfulness-based interventions also show efficacy in lowering depression and promoting post-traumatic growth, with small effect sizes reported among individuals with medical traumas (Shiyko et al., 2017). Psychological interventions play a crucial role in mitigating the psychological burden of the pandemic, potentially offsetting its physical health costs – an aspect particularly relevant given the pandemic's classification as a 'criterion A' traumatic event. However, traditional interventions (e.g., CBT) may not be suitable for the COVID-19 pandemic due to their limited accessibility and scalability.

1.2. Mindset interventions

Mindset interventions may be one promising approach to reducing pandemic-related distress and promoting growth at scale. Mindsets are core beliefs about a particular domain, such as viewing intelligence as fixed or malleable, or stress as enhancing or debilitating (Crum et al., 2013). Research has shown that mindsets influence health and well-being across various areas, including stress and cancer (Crum et al., 2013; Zion et al., 2023). By acting as mental "lenses," mindsets orient individuals toward specific interpretations of complex and ambiguous information. For example, those with a "stress is enhancing" mindset focus on its benefits, feel less threatened by stress, and display more adaptive physiological responses, leading to self-fulfilling effects on health outcomes (Crum et al., 2013).

Several studies have examined the influence of mindsets in the context of challenging and potentially traumatic situations. Psychosocial interventions that package a mindset-change component with other strategies, such as mindfulness training and goal setting, have been shown to improve resilience among both cancer patients and their caregivers (Rosenberg et al., 2019; Rosenberg et al., 2018). A smaller body of research has attempted to isolate the effect of mindset change from other psychological processes in these contexts by testing brief interventions designed to precisely target a mindset of interest. These brief interventions aimed at shifting particularly high-leverage psychological processes are known as "psychologically-wise" interventions (Walton and Wilson, 2018). For example, Zion et al. (2023) developed a film-based intervention to help recently diagnosed cancer patients view their illness as an opportunity for growth. This intervention significantly improved participants' health-related quality of life and reduced their physical distress. These findings are consistent with a longitudinal study which demonstrated that seeing the COVID-19 pandemic as an opportunity in March 2020 was associated with better quality of life six months later, and that these effects were mediated by increased positive affect and healthy behaviors (Zion et al., 2022).

Taken together, this body of work provides preliminary evidence that mindsets can shape health and well-being outcomes in the context of highly stressful experiences. In particular, the research shows that viewing stressful or traumatic experiences as an opportunity for growth may confer health benefits. At the same time, the benefit of viewing macro societal stressors such as a pandemic as an opportunity to grow is unclear, and to our knowledge, no studies have yet investigated whether a mindset intervention can lead to changes in health-damaging inflammatory biology (Furman et al., 2019; Slavich, 2015).

1.3. Present study

To address these gaps, we assessed the impact of a novel mindset intervention designed to promote the belief that "catastrophes can be opportunities in the long term" following the COVID-19 pandemic. The study was specifically conducted after the acute phase of the pandemic had passed, with a deliberate focus on its aftermath, to mitigate the potential lasting psychological and physiological impacts of the stressor. To accomplish this, we evaluated the intervention's effects on CRP levels, as a key biomarker of inflammation, in addition to post-traumatic growth and a variety of mental health outcomes, including symptoms of anxiety and depression. Based on the research summarized above, we

hypothesized that participants randomized to receive our "catastrophes can be opportunities in the long term" mindset intervention (vs. a control intervention) would exhibit significantly greater increases in this mindset over time. In addition, we hypothesized that the mindset intervention would lead to significantly greater improvements in both inflammation and anxiety and depressive symptoms over time (vs. the control condition), and that these biological and clinical improvements would be mediated by changes in participants' mindsets.

2. Method

2.1. Study design & overview

This study is a double-blind parallel randomized clinical trial, conducted in the United States of America, two years after the start of the COVID-19 pandemic. The data were collected between October 2022 and February 2023. Hypotheses and analyses were pre-registered in early May 2023 prior to data cleaning/pre-analytic processing (https://doi.org/10.17605/OSF.IO/X4C56). The study was pre-approved by the Institutional Review Board at Stanford University (Protocol #65818).

2.2. Participants

Participants were recruited from a U.S.-based longitudinal study that examined the impact of mindsets on health and well-being throughout the pandemic. Recruitment for the original study was conducted via social media (Zion et al., 2022). Individuals who completed all of the surveys and indicated an interest in future research were recruited. Participants were informed about a new study exploring the effects of reflecting on their pandemic experiences on health and well-being, with a link to a survey for more details.

Participants were eligible if they lived in the United States, were 18 years or older, and understood English. Participants were excluded from the physiological branch of the study (i.e., "physio branch") if they reported a major healthcare condition or were treated using systemic

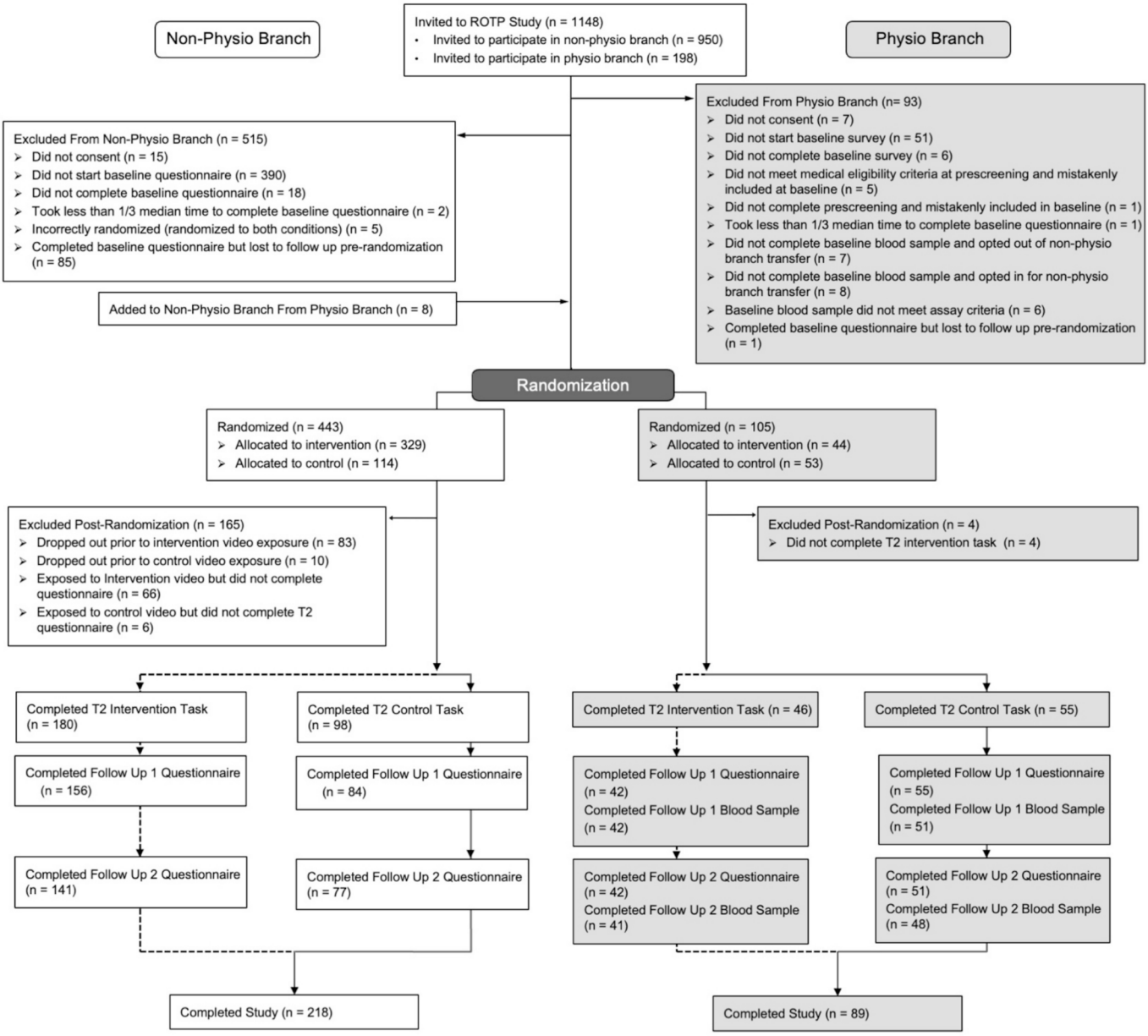

Fig. 1. CONSORT diagram of participants in study visualized separately for physio and non-physio branches.

corticosteroids, deflazacort, immunomodulators, monoclonal antibody therapy, and/or intravenous immunoglobulin treatment (see Supplementary Material). All participants provided informed written consent prior to participating and self-reported their gender as female, male, non-binary, or non-applicable.

This study consisted of two cohorts: the "non-physio" branch, in which participants completed only the intervention/control tasks and questionnaires, and the "physio" branch, in which participants also completed a blood sample collection protocol at three time points. After the baseline survey (Time 1), participants in the non-physio branch were randomized 3:1 into intervention and control groups respectively. A 3:1 randomization ratio was used in the non-physio branch to maximize participant exposure to the intervention's potential benefits while maintaining a sufficient control group for comparison. Participants in the physio branch were randomized 1:1 to each group to ensure sufficient power in physiological analyses (Fig. 1). Simple randomization was completed by the study coordinator using the Qualtrics randomization module, which automatically assigns participants to groups according to a preset schedule. This process ensured allocation concealment by preventing participants from knowing group assignments at the time of allocation. Qualtrics is a secure platform for electronic data capture and the built-in randomization module is a widely used feature (Qualtrics, Provo, Utah; available at https://www.qualtrics.com/).

The research team was aware of participants' condition assignment; however, survey metadata were not accessed until all data collection was complete. Best practices on blinding in behavioral trials were followed (Friedberg et al., 2010; Schulz et al., 2002). Although participants could not be completely blinded to their condition assignment due to the self-evident nature of the intervention, participants were not told their condition assignment; moreover, they were blind to the study hypotheses and to their condition's expected effectiveness. Prior to randomization, participants were told the purpose of the study was to learn about experiences with the COVID-19 pandemic and to provide individuals an opportunity to reflect on the pandemic. Participants were also informed that they would be randomly assigned to one of two equally important programs. Following randomization, both groups completed modules on the pandemic, with the mindset group reflecting on their attitudes and the control group reflecting on facts about the pandemic. This approach aimed to minimize bias by reducing the likelihood of participants inferring their group assignment.

Participants were recruited from October 10th to October 15th, 2022. A total of 525 respondents who indicated interest in the non-physio branch provided informed consent. Of the participants who indicated interest in taking part in the physio branch, 354 respondents met the medical criteria. To achieve a more representative sample, all non-white respondents and a random subset of White respondents were invited, resulting in 134 participants at Time 1 for the physio branch. In total, there were 548 participants who completed the Time 1 assessment and were subsequently randomized to either the mindset intervention condition or control condition (see Fig. 1).

2.3. Procedure

All respondents who indicated interest in the non-physio branch were invited to participate and provided informed consent on Qualtrics. Respondents who indicated interest in participating in the physio branch were emailed an invitation to complete the pre-screening survey with medical eligibility criteria.

Participants completed a baseline survey (Time 1) and three follow-up surveys on Qualtrics: immediately post-intervention/control task (Time 2), 1-month post-intervention/control task (Time 3), and 3-months post-intervention/control task (Time 4) (see Fig. 2). Participants in the physio branch also took blood samples at baseline (Time 1), Time 3, and Time 4 (see Supplementary Material). Blood samples were collected by participants at home using three Tasso M-20 blood sampling kits (Tasso, Inc., Seattle, WA), each of which collects four 17.5 μL whole dried blood spots. Samples were returned using USPS Priority Express overnight shipping and stored in a −80 °C freezer before being transferred to the Stanford Human Immune Monitoring Center for assaying.

Participants in the non-physio branch participated without payment, whereas those in the physio branch were paid $100 to compensate them for the additional time needed to complete the blood samples. Participants in the physio branch who failed to complete the Time 1 survey and/or blood sample were given the option to transfer to the non-physio branch and continue the study without payment. To be included in the present analysis, participants in either branch had to complete the Time 1 survey and their task at Time 2 (a per-protocol rather than an intent-to-treat approach). Participants who were randomized to, but failed to complete the study protocol and assessments were excluded from analysis.

The catastrophes-as-opportunities intervention was developed in line with the psychologically wise intervention framework developed by Walton and Wilson (2018) and was supplemented with reflection questions and saying-is-believing prompts. Participants first watched five videos (each 2 to 4 min) that discussed the self-fulfilling properties

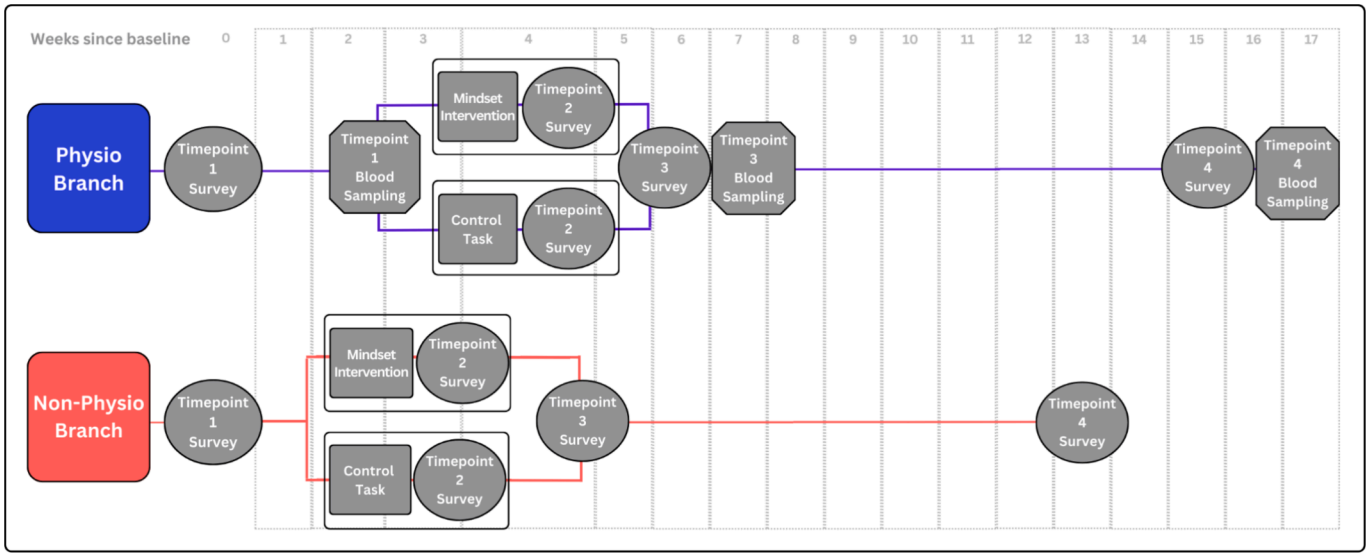

Fig. 2. Study timeline illustrating timing of surveys, intervention/control tasks, and blood samples.

of mindsets and the ways in which catastrophic events can open opportunities for growth. By providing education about mindsets in general and evidence for our target mindset, the intervention drew on both traditional and metacognitive approaches to mindset change (Crum et al., 2013). Traditional approaches to mindset change focus on providing factual information to support the target mindset, whereas metacognitive approaches enhance self-awareness and conscious self-regulation of the target mindset. After watching each video, participants were prompted to write about the mindsets that they held towards the COVID-19 pandemic and how these might encourage/discourage growth in the pandemic's aftermath. Finally, participants learned some strategies for mindset change and were encouraged to identify areas of potential growth in their lives. All study procedures were completed remotely. For detailed information on both study conditions and to access the videos, see Supplementary Material.

The control condition also consisted of five videos on Qualtrics (2–4 min each). The videos provided a chronological overview of the major events of the COVID-19 pandemic from late-2019 to mid-2021. They discussed the origins of COVID-19 in China, the virus's spread around the world, and the steps that governments and scientists took to combat it. Unlike the intervention videos, they do not discuss mindsets or post-traumatic growth, nor did they encourage participants to identify ways in which they had already grown or would like to grow as a result of their experiences during the pandemic. As such, they controlled for the intervention task's focus on the COVID-19 pandemic without promoting any given mindset toward the pandemic. After watching each video, participants completed short multiple-choice questions designed to serve as attention checks and to help review the material.

2.4. Study outcomes

Catastrophes-as-Opportunities Mindset. The Catastrophes-as-Opportunities Mindset Measure assesses how participants perceive the long-term effects of living through a catastrophe, either as beneficial or harmful. It includes ten Likert-scale items (1 = *strongly disagree* to 7 = *strongly agree*), with half framed positively (e.g., "Living through a catastrophe makes life more meaningful in the long-term) and half negatively (e.g., "Living through a catastrophe causes long-term harm to your life"; See the Supplementary Material for all items). Negatively framed items are reverse-scored, and a summary score is calculated by averaging all items. The measure was developed for this study and has not been validated, but it demonstrates strong factor reliability, T1: α = 0.86, 95 % CI [0.83, 0.89], T2: α = 0.89, 95 % CI [0.85, 0.91], T3: α = 0.88, 95 % CI [0.85, 0.90] and T4: α = 0.89, 95 % CI [0.86, 0.91]. We also conducted an exploratory factor analysis (EFA). Multiple methods were used to determine the number of factors to retain, specifically the Comparison Data (CD), Empirical Kaiser Criterion, Hull, Parallel Analysis, and scree plot. All factor retention methods except the CD method indicated one factor for the Catastrophes-as-Opportunities Mindset Measure. Consequently, the EFA specified one factor and was carried out using principal axis factor extraction. Factor loadings ranged from moderate-to-high (0.41 – 0.77), and this factor accounted for 44 % of the variance in item scores.

Post-traumatic Growth. Post-traumatic growth was measured using the PTGI – Current Standing (C-PTGI) (Frazier et al., 2009). The original measure (PTGI) consists of 21 items measured on a Likert scale, ranging from 0 (*not at all*) to 5 (*to a very great degree*). The PTGI is divided into five subscales (1) new possibilities, (2) relating to others, (3) spiritual change, (4) personal strength, and (5) appreciation of life. The C-PTGI includes the same items and subscales but asks participants to rate their current levels as opposed to rating them retrospectively. As a result, the C-PTGI is intended to be used at multiple time points to measure genuine growth over time and is shown to be better correlated with other measures of PTG domains than the original PTGI (Frazier et al., 2009). The C-PTGI demonstrated strong factor reliability in this study (α = 0.92, 95 % CI [0.91, 0.93]).

Anxiety and Depression. Anxiety and depressive symptoms were assessed using the PHQ-4 (Kroenke et al., 2009). The PHQ-4 consists of 4 items, two for each subscale, measured on a Likert scale, ranging from 0 (*not at all*) to 3 (*nearly every day*). A total score of 3 or more on the two anxiety items is considered indicative of anxiety, and likewise for depression (Kroenke et al., 2009). Both subscales showed strong factor reliability in this study ($\alpha_{phq_depression}$ = 0.87, 95 % CI [0.85, 0.89], $\alpha_{phq_anxiety}$ = 0.84, 95 % CI [0.81, 0.86]).

Inflammation. Non-specific systemic inflammatory activity levels were assessed with C-reactive protein, an acute phase protein that is commonly used as a key biomarker of inflammation in clinical and research settings (Slavich et al., in press). Increases in circulating CRP predict the onset of depressive symptoms prospectively and individuals with MDD frequently exhibit higher CRP levels compared to non-depressed individuals (Slavich and Irwin, 2014). In brief, CRP levels were quantified in duplicate on a Luminex FlexMap3D Instrument using immunoassay kits purchased from EMD Millipore Corporation (Burlington, MA). Intra-assay variability showed a mean CV of 5.41 %. Inter-assay variability yielded a mean CV of 43.3 %. See the Supplementary Material for more information.

2.5. Statistical analysis

Summary scores were calculated according to scoring instructions for all behavioral variables. Cronbach's alphas were calculated for each measure using the Psych package (Version 2.4.12) (Revelle, 2024) in R to ensure that measures were reliable, and summary scores were computed when warranted. We tested for differences in retention across study-level variables (i.e. condition), demographics, and individual difference variables. Chi-square tests of independence and independent samples t-tests were conducted to examine demographic differences between participants who were retained and those who dropped out of the study (see Results). We then calculated descriptive statistics (e.g., mean, *SD*, range, etc.) for all variables, both overall and separately by study condition and time point.

As described above and in the Supplementary Material, single dry blood spot samples were assayed for CRP using the Luminex Bead Array platform. Detection was shown to be within the immunoassay standard range for most measurements, samples that did not meet this criterion were excluded from further analysis. Each sample underwent duplicate measurements, which were subsequently averaged and normalized using a log2 transformation to mitigate right skewness. In accordance with guidelines provided by the immunoassay manufacturer, we conducted statistical analysis on the mean fluorescent intensity (MFI) values rather than interpolated values (concentrations) for CRP.

The preprocessed biomarker data were then merged into a single dataset with the behavioral data. After careful consideration, we adjusted our original preregistered plan to exclude participants from the physio branch who reported specific medications/medical conditions at Time 3 or Time 4. Instead, given the small sample size in the physio branch, we opted to retain these participants and create a dummy-coded variable to indicate whether participants reported a medication or condition at Time 3/Time 4 that could influence CRP levels. Mixed effects models evaluating the effect of time and condition on CRP were run both with and without this covariate, with no difference in findings between the two models.

All analyses were conducted in R. The manipulation check and primary outcome analyses consisted of multilevel models (MLMs) carried out with the lme4 package (Version 1.1–36) (Bates et al., 2015). The MLMs included fixed effects for condition and timepoint, a condition × timepoint interaction effect, and a random effect for each participant. For the manipulation check, timepoint was specified as a categorical variable with four levels, given that catastrophes-as-opportunities mindset was measured at all four timepoints. For all other MLMs, timepoint was specified as a categorical variable with three levels (Time 1, Time 3, and Time 4), since most outcome variables were not measured at Time 2.

Mediation analyses were carried out using the Lavaan package (Version 0.6–19) (Rosseel, 2012), with study condition serving as the independent variable, catastrophes-as-opportunities mindset measured at Time 3 as the mediating variable, and the outcome of interest measured at Time 4 as the dependent variable. Participants' scores on catastrophes-as-opportunities mindset and the outcome of interest at Time 1 were included as covariates to control for baseline levels of these variables.

3. Results

3.1. Sample characteristics

The final analytic sample included 379 participants who were randomized and completed their assigned task at Timepoint 2 (Table 1). Participants had an average age of 51 years ($SD = 14.4$) and were primarily female (75 %), White (81 %), and educated beyond high school (77 %). Between-group comparisons showed no significant differences for the demographic variables. Descriptive statistics for the behavioral and physiological measures at baseline, Timepoint 3, and Timepoint 4 are presented in the Supplementary Material, along with correlations between variables. Retention was assessed at each time point (see Fig. 1). At Time 2, dropout rates were significantly higher in the non-physio branch, with 45 % of participants in the mindset intervention condition dropping out, compared to 14 % in the control condition. Notably, 55 % of those who dropped out in the intervention group did so while reading the pre-task instructions. In contrast, attrition in the physio branch was much lower, with only 7 % of the intervention group failing to complete the task, compared to 0 % in the control group. Post-hoc analyses testing for possible differences between participants who were retained and those who dropped out revealed no significant differences in gender or political affiliation ($ps > 0.05$). There was a significant difference in retention-by-age ($p = 0.039$). Specifically, participants who were retained past the intervention/control task (T2) were on average three years older (50.5 years old) than those who dropped out (47.6 years old).

Table 1
Participant demographics (*n*, [%]).

Baseline characteristic	Intervention $n = 226$		Control $n = 153$		Full sample $n = 379$	
	n	%	*n*	%	*n*	%
Gender						
Female	168	74.6	117	76.5	285	75.4
Male	30	13.3	22	14.4	52	13.8
Non-Binary	1	0.4	3	2.0	4	1.0
N/A	26	11.6	11	7.2	37	9.8
Race/Ethnicity						
Asian	6	2.7	5	3.3	11	2.9
Hispanic	7	3.1	3	2.0	10	2.6
Multiracial	2	0.9	3	2.0	5	1.3
Native American	0	0	1	0.7	1	0.3
White	181	80.1	125	81.7	306	80.7
N/A	29	13.3	16	10.5	46	12.1
Highest educational level						
High School or Less	26	11.5	25	16.3	51	13.5
More than High School	174	77.0	118	77.1	292	77.0
N/A	26	11.5	10	6.5	36	9.5
Political Party						
Democrat	120	53.1	89	58.2	209	55.1
Independent	52	23.0	27	17.6	79	20.8
Other	13	5.8	15	9.8	28	7.4
Republican	15	6.6	12	7.8	27	7.1
N/A	26	11.5	10	6.5	36	9.5
Income						
$0 – $50,000	8	3.5	13	8.5	21	5.5
$50,000 – $150,000	27	11.9	31	20.3	58	15.3
Greater than $150,000	10	4.4	10	6.5	20	5.3
Prefer not to answer	1	0.4	1	0.7	2	0.5
N/A	180	79.6	98	64.0	278	73.4
Age (Mean, *SD*)	52 (14.7)		49 (13.8)		51 (14.4)	

3.2. Manipulation check

As hypothesized, across the full sample ($N = 379$) significant differences in the catastrophes-as-opportunities mindset were observed by condition at all three timepoints: baseline to Time 2 ($B = 0.35$, 95 % CI [0.21, 0.49], $p < 0.001$), baseline to Time 3 ($B = 0.27$, 95 % CI [0.14, 0.40], $p < 0.001$), and baseline to Time 4 ($B = 0.23$, 95 % CI [0.10, 0.37], $p = 0.001$) (see Fig. 3). This indicates that the intervention had a significant effect on enhancing participants' beliefs that catastrophes can be opportunities for growth, and that this effect was sustained at all three follow-up timepoints.

3.3. Mental health outcomes

As hypothesized, across the full sample ($N = 379$) a significant difference in the trajectory of depressive symptoms across time was observed by condition, from baseline to Time 4 ($B = -0.34$, 95 % CI [-0.60, -0.09], $p = 0.009$), but not from baseline to Time 3 (see Fig. 4a). This finding suggests that the effect of the intervention on depressive symptoms may have been mediated by behavioral changes that unfolded over a period of weeks or months. In contrast, no significant Time × Condition differences were observed for post-traumatic growth, meaning, resilience, or anxiety (all $ps > 0.05$).

3.4. Inflammatory outcome

As hypothesized, among participants in the physio branch ($n = 101$), a significant difference in the trajectory of CRP levels was observed by condition, from baseline to Time 4 ($B = -0.69$, 95 % CI [-1.32, -0.07], $p = 0.030$) (Fig. 4b). Similar results were found when including a covariate indicating a reported medical issue/medication at Time 3 and/or Time 4 ($B = -0.70$, 95 % CI [-1.33, -0.07], $p = 0.029$). Similarly to the depressive symptoms analysis described above, no significant Time × Condition differences were observed from baseline to Time 3. This finding provides further indication that effects of the intervention emerged slowly, despite the immediate and sustained changes in catastrophes-as-opportunities mindset that were observed.

3.5. Mediation analyses

Finally, as hypothesized, across the full sample ($N = 379$) the effect of condition on change in PHQ-Depression levels from baseline to Time 4 was significantly mediated by change in catastrophes-as-opportunities mindset from baseline to Time 3 (ab = − 0.049, 95 % CI [-0.089, -0.009], $p = 0.017$) (Fig. 5b). There were also significant mediation effects of catastrophes-as-opportunities mindset (measured at Time 3, controlling for baseline) on the association between condition and a range of outcome variables (measured at Time 4, controlling for baseline), including post-traumatic growth, presence of meaning, anxiety, and negative affect (See Supplementary Material). In other words, to the extent that the intervention increased catastrophes-as-opportunities mindset, there was a significant downstream effect on each of these mental health outcomes of interest.

4. Discussion

To our knowledge, this is the first study to investigate whether promoting the mindset that "catastrophes can be opportunities in the long-term" influences inflammation and mental health. As hypothesized, the results demonstrate that a brief mindset intervention effectively reduced both CRP and depressive symptom levels two years after the onset of a large-scale societal catastrophe. Specifically, compared to the control group, participants who received the mindset intervention reported significant reductions in both CRP, our marker of systematic inflammation, and depression by three months. This decrease in depression was significantly mediated by greater endorsement that

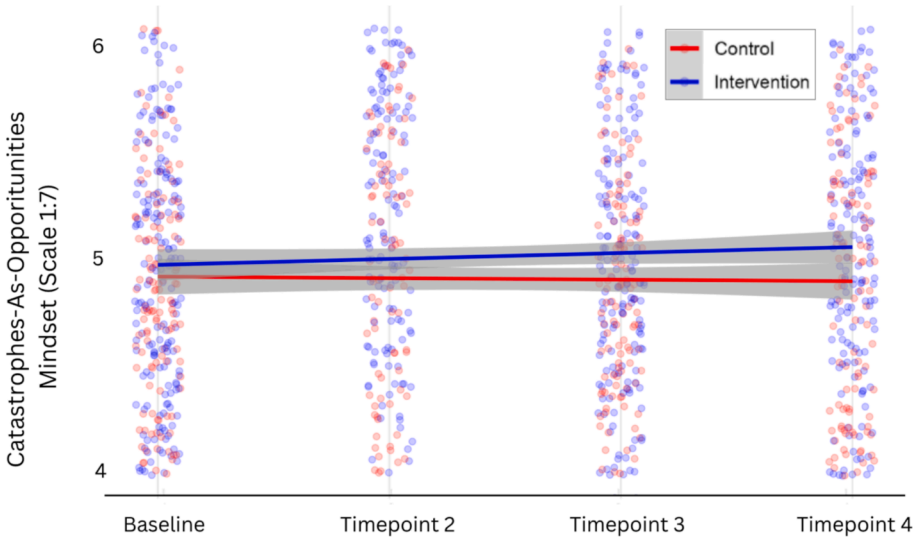

Fig. 3. Change in catastrophes-as-opportunities mindset over time, across conditions. The gray shaded regions flanking the regression slopes visually denote the standard error in the linear model, which incorporates both sampling variation and model fit to capture the inherent variability in catastrophes-as-opportunities mindset across conditions at each timepoint. The figure includes observations from both branches of the study (n = 1,050) and distinguishes the intervention and control groups with blue and red color schemes, respectively.

catastrophes can be opportunities in the long-term. Therefore, fostering a catastrophes-as-opportunities mindset may be a useful approach to promoting adaptive coping in the aftermath of large-scale events like the COVID-19 pandemic.

The findings highlight the self-fulfilling impact of mindsets on health and well-being. This is consistent with prior research on individuals newly diagnosed with cancer and those navigating the early months of the COVID-19 pandemic (Zion et al., 2022; Zion et al., 2023). Specifically, viewing challenging or traumatic events as opportunities can enhance quality of life and promote adaptive coping. Additionally, our results support the effectiveness of psychologically wise interventions—brief strategies that target core psychological processes—in alleviating mental health symptoms during periods of distress (Walton and Wilson, 2018). These scalable interventions can benefit all populations, particularly those in communities with limited access to high-quality mental health care, who are often the most affected by catastrophic events.

The present data also demonstrate that the intervention led to significant decreases in CRP levels over time, whereas the control group showed a slight upward trend. This divergence suggests that the intervention may have helped reduce systemic inflammation but also potentially prevented stress-induced increases in inflammatory activity that are frequently observed (Alley et al., 2025; Gillespie et al., 2022). These results are especially significant as research shows an increased rate of depression during the pandemic, which is associated with higher levels of CRP (Yuan et al., 2020). Intervention-related reductions in inflammation have also been found for psychosocial interventions (Shields et al., 2020). However, other traditional approaches typically require 8 to 12 one-hour sessions, making them resource-intensive and very difficult to scale (Shields et al., 2020). In contrast, our digital intervention is designed to be completed in just one hour, offering a highly scalable, cost-effective alternative for reducing inflammation. Although definitive evidence linking CRP to clinical outcomes such as depression is still needed, CRP is a well-studied mechanism underlying a wide variety of mental and physical health outcomes (see Furman et al., 2019). Given its accessibility and efficiency, this mindset intervention could thus be a potentially valuable tool in both public health campaigns and clinical practice, particularly for helping to manage inflammation-related conditions and enhancing overall disease management strategies.

Although there was no main effect of condition on post-traumatic growth, we observed significant mediation effects of the catastrophes-as-opportunities mindset on the association between condition and overall post-traumatic growth, CRP, depression, presence of meaning, anxiety, and negative affect. These findings indicate that to the degree to which the intervention did alter catastrophes-as-opportunities mindset, those changes led to statistically significant improvements in post-traumatic growth and other important mental health outcomes. However, the intervention did not produce a strong enough increase in this mindset to generate a significant main effect. Therefore, the mediation analyses support our theoretical model, indicating that shifts in the catastrophes-as-opportunities mindset facilitate post-traumatic growth and broader improvements in psychological health.

4.1. *Strengths and weaknesses*

This study has several strengths. First, we tested an intervention that could be a scalable and effective response to large-scale stressors like pandemics, disasters, and economic crises. Second, the study was conducted in the post-acute phase of the COVID-19 pandemic, a time when many immediate public health measures in the United States had been lifted, but when individuals continued to experience residual psychological and physiological effects. Intervening at this stage is critical, as the aftermath of large-scale crises often involves prolonged stress, disrupted routines, and lasting uncertainty. Our findings in this context suggest that brief mindset interventions can alleviate enduring psychological and physiological effects of the crisis. Importantly, the timing of the intervention also aligns with windows for psychological change, when people are not in the acute phase of the crisis but are still navigating the ambiguity of a "new normal." As highlighted in the wise interventions framework (Walton and Wilson, 2018), the effectiveness of mindset interventions is dependent on both what is delivered and when, making timing a key component of impact. Finally, we focused on inflammation as a key outcome of interest. This focus on inflammation is notable for at least two reasons. First, inflammation has been implicated in the pathophysiology of a wide variety of diseases, making the present findings both clinically relevant and consistent with prior work linking psychosocial interventions and inflammatory activity (e.g., Black and Slavich, 2016; Shields et al., 2020). Second, unlike the psychological outcomes assessed, inflammatory levels are not subject to potential self-report or social desirability biases, thus providing a degree of certainty in effect not afforded by the other outcomes.

At the same time, several limitations should be noted. First, there were significant differences in dropout rates between the non-physio

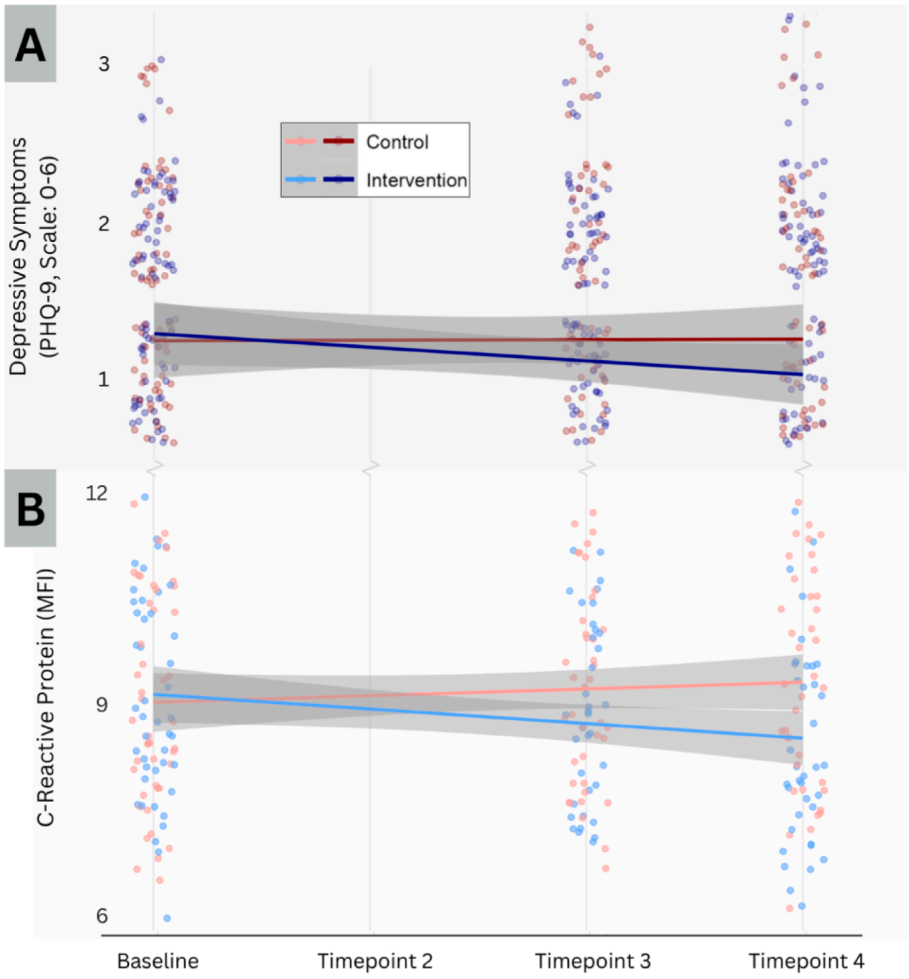

Fig. 4. Changes in (A) Depressive Symptoms (PHQ-Depression) and (B) C-reactive protein (Mean Fluorescence Intensity) across timepoints and conditions. The gray shaded regions flanking the regression slopes represent the standard error in the linear model, which encompasses both sampling variation and model fit to capture the inherent variability in (B) PHQ-Depression scores and (A) C-reactive protein levels at each timepoint across conditions. The figure distinguishes intervention groups with a blue color scheme and control groups with varying shades of red. Y-axis break denotes a change in scale. (B) PHQ-9 Depression includes both branches of the study ($n = 1{,}035$), whereas (A) C-reactive protein is based exclusively on physio branch observations ($n = 277$). A PHQ-9 Score ≥ 3 on the two depression items suggests depression. MFI = mean fluorescent intensity.

and physio branches, particularly during the pre-task instructions. Specifically, participants in the physio branch had notably lower dropout rates. This discrepancy may be attributed to differences in task length and content. The intervention was advertised as lasting 60–90 min, which may have deterred participants who were not receiving payment. Therefore, the accuracy and generalizability of our findings should be interpreted cautiously. Second, some participants may have taken issue with the intervention videos' message. Indeed, a few expressed that adopting the mindset of viewing "catastrophes as opportunities" felt insensitive given the suffering caused by the COVID-19 pandemic. Although the intervention aimed to convey that acknowledging trauma can coexist with growth, some participants may have disagreed. Additionally, a small subset viewed the pandemic as exaggerated by mainstream media, which may have led to negative reactions.

Third, despite our best efforts to recruit a highly diverse sample, our participants were disproportionately White and highly educated, potentially limiting the generalizability of the findings. In the U.S., this demographic faced lower rates of COVID-19 infection, hospitalization, and mortality compared to people of color and those from lower socioeconomic backgrounds (Magesh et al., 2021). Fourth, we relied on self-rated measures of well-being (e.g., PHQ-4) rather than clinician-administered assessments, which would have enhanced diagnostic accuracy. Fifth, although participants with a history of certain medical conditions (e.g., autoimmune disorders) and those taking specific medications were excluded, we did not conduct an extensive screening for supplement (e.g., omega-3) or antidepressant medication use, which could have improved the precision of our models. Sixth, although this study is the first that we know of to show that a brief mindset intervention significantly reduces inflammation, the mechanisms linking inflammation and depression have yet to be fully described, and a single biomarker of inflammatory activity provides only a limited view of immune system functioning. Therefore, caution is warranted in drawing causal conclusions about the relation between mindsets, depression, and inflammation.

Finally, the timing of the study is worth noting. As described above, the study was conducted between October 2022 and February 2023, several years after the height of the COVID-19 pandemic. Consequently, many individuals may have already reflected on their experiences or undergone post-traumatic growth, which could have minimized our ability to find effects for post-traumatic growth. Relatedly, some participants may have simply preferred to "move on" from their experiences

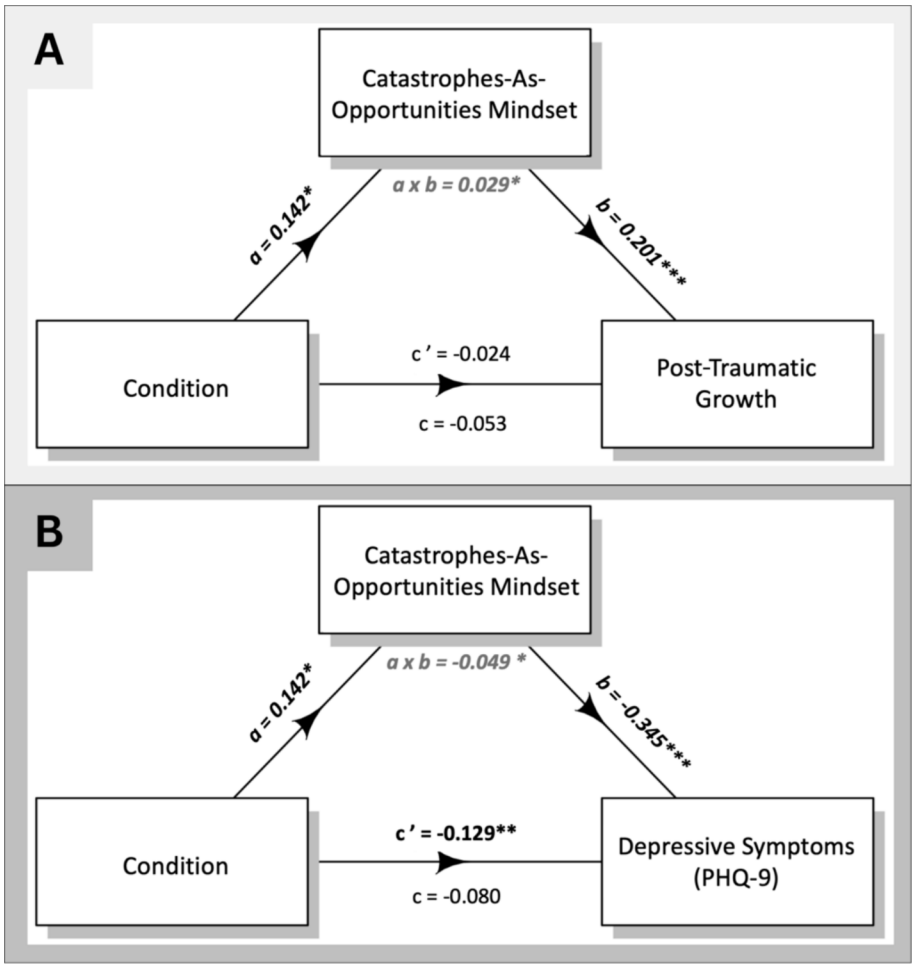

Fig. 5. Path diagrams depicting the mediating effect of catastrophes-as-opportunities mindset on the association between condition (Intervention vs. Control) and outcomes of interest. (A) Represents the mediating effect of catastrophes-as-opportunities mindset (measured at Time 3, controlling for Time 1) on the association between condition and Post-Traumatic Growth (measured at Time 4, controlling for Time 1) (SE = 0.013, 95 % CI [0.003, 0.054]). (B) Depicts the mediating effect of catastrophes-as-opportunities mindset (measured at Time 3, controlling for Time 1) on the association between condition and PHQ-Depression (measured at Time 4, controlling for Time 1) (SE = 0.02, 95 % CI = [-0.089, −0.009]). The path diagram significance levels are indicated as follows: *$p < 0.05$; **$p < 0.01$; ***$p < 0.001$.

during the pandemic rather than engage in additional reflection, which may have limited their engagement with the intervention materials.

4.2. Future directions

Despite these limitations, the mindset intervention we used still significantly reduced circulating levels of CRP and depressive symptoms. Future research should thus investigate the potential benefits of this intervention in other contexts, such as natural or technological disasters, and among populations with acute life event or trauma exposure. Additionally, given that the mediation models indicated that shifts in the catastrophes-as-opportunities mindset were associated with adaptive changes across a range of post-traumatic growth domains, future studies should explore more effective strategies for enhancing this mindset. Lastly, more research is needed to understand the biopsychosocial mechanisms by which this mindset impacts immune functioning, including studies on a wider range of inflammatory and other biomarkers (Mengelkoch et al., 2024; Mengelkoch et al., 2023).

4.3. Conclusion

In conclusion, the COVID-19 pandemic will likely be a watershed moment in the lives of many individuals, causing both significant distress and potential for transformative growth. It is thus crucial for researchers to identify factors that promote growth in the aftermath of such stressors, and to develop effective, scalable, and accessible interventions for reducing stress and enhancing resilience. The present data suggest that individuals' mindsets about the long-term effects of catastrophes can be modified through traditional and metacognitive approaches, which is an important advancement in this line of work. Furthermore, we showed that fostering a perspective that views catastrophes as opportunities may enhance not just mental health but also immune health, which has implications for a wide variety of other conditions. We hope future research will clarify the connections between mindsets, the immune system, and mental health, and ultimately help individuals better navigate the immense challenges and opportunities posed by both the COVID-19 pandemic and future catastrophes.

Role of the funding source

The funders had no role in the conceptualization, design, data collection, analysis, preparation of, or decision to publish the manuscript.

Artificial intelligence

No artificial intelligence-assisted technologies were used in this research or the creation of this article.

Ethics

This research was pre-approved by the Institutional Review Board at Stanford University (Protocol #65818).

Preregistration

Hypotheses and the data analysis plan were pre-registered in May 2023 prior to data cleaning and pre-analytic processing (https://doi.org/10.17605/OSF.IO/X4C56).

Materials

The materials are available upon request to the corresponding author.

CRediT authorship contribution statement

Jesse A. Barrera: Writing – original draft, Methodology, Data curation, Investigation, Resources, Writing – review & editing, Project administration, Formal analysis, Conceptualization. **Lexi D. Straube:** Writing – original draft, Methodology, Data curation, Resources, Investigation, Conceptualization, Writing – review & editing, Visualization, Project administration, Formal analysis. **Zoë Huml:** Investigation, Project administration, Writing – review & editing. **Rachael M. Yielder:** Investigation, Writing – review & editing, Project administration. **Sean R. Zion:** Conceptualization, Writing – original draft, Formal analysis, Resources, Supervision, Methodology. **Kristopher M. Evans:** Writing – review & editing, Conceptualization, Resources, Methodology. **Kengthsagn Louis:** Resources, Writing – review & editing, Conceptualization. **Daniel P. Moriarity:** Writing – review & editing, Methodology, Conceptualization, Resources. **Chiara Gasteiger:** Writing – original draft, Investigation, Writing – review & editing. **George M. Slavich:** Writing – original draft, Conceptualization, Supervision, Writing – review & editing, Methodology. **Alia J. Crum:** Writing – original draft, Methodology, Supervision, Funding acquisition, Writing – review & editing, Resources, Conceptualization.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data for this article can be found online at https://doi.org/10.1016/j.bbi.2025.07.011.

Data availability

The data can be accessed on the Health and Medical Care Archive (HMCA) and on OSF https://osf.io/s6fa2/.

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