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Richard Norton, MD

Editor-in-Chief, The Lancet

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Dear Dr. Norton,

Please find the manuscript, titled “*Association of Posttraumatic Growth with Covid-19 and Posttraumatic Stress: A Meta-analytic Review,*” uploaded to The Lancet submission site. We hope that itbe considered for review by your editorial board. The manuscript has not been previously published nor is it under consideration at another outlet; furthermore, the findings have not been posted online.

We assume that the finding will be of interest to the readers of The Lancet because this interdisciplinary study provides information on an aggregated outcome, PTG, in populations exposed to the Covid-19 Pandemic, the deadliest global disaster in the 21 century. The under-investigated positive side of the major threat to humanity may have implications for patient-centered preventive and clinical care in coming decades.

All authors have contributed substantively to developing this manuscript and agreed to be a co-author. The authors declare that there are no conflicts of interest. Because this first meta-analysis on this topic in the context of Covid-19 use only published data, the human subject application is not relevant. We do not know which sub-journal under the system of The Lancet will be suitable for this topic. But we trust that you will direct it to the appropriate one.

To make the manuscript short, all subgroup figures are in the Appendix for provision upon request. If you consider that they are acceptable within the desirable length, we can put it back. One more issue, there are more citations than the # in one of the limit instructions. But, our text is several hundred below the word limit. If RR is granted, we are willing to cut more on requests.

Thank you for your attention! We look forward to hearing your editorial decision.

Amy L. Ai, PhD

FSU Distinguished Research Professor

**Association of Posttraumatic Growth with Covid-19 and Posttraumatic Stress:**

**A Meta-analytic Review**

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**(Running Head: Covid-19 and PTG)**

(02/10/2024, in Submission to The Lancet)

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**Abstract: Background**. Posttraumatic growth (PTG), positive gains arising from the struggle with trauma, can be easily assessed and may lead to optimal outcomes of patients, health providers, and general populations affected by Covid-19. This is the first meta-analysis and systematic review of the association between PTG and Covid-19 and posttraumatic stress symptoms (PTSS). **Method.** PubMed (30), PsychINFO (6), Academic Search Complete (4), Ovid MEDLINE (20), electronic databases were systematically searched from May 23, 2023 through January 8, to identify all eligible studies reporting the association between PTG and Covid-19 by suing the following Medical Subject Heading and psychological terms: Covid-19, posttraumatic growth, PTG, stress-related growth, adverse growth, positive outcomes, positive effects, self-growth. Data were screened and extracted independently by 2 investigators. Adjusted effect estimates were employed, and pooled analysis was conducted, using the Hartung-Knapp-Sidik-Jonkman rondom-effects model. Sensitivity and subgroup analyses were conducted to assess the robustness of the findings. The Meta-analysis of Observational Studies in Epidemiology (MOOSE) reporting guideline was followed. **Results.** The search yielded 60 unique publications around the globe, of which 42 qualified for full-text review. **Results.** The final selection involved a composite of 30 studies with data on the COVID-19—PTG association, comprising 42, 386 participants. On pooled analysis, COVID-19 was significantly associated with PTG as determined mostly by Posttraumatic Growth Inventory (PTGI) (*g*=0.75; 95%CI, 0.45-1.05; *p*<.0001), with a high heterogeneity in the analysis (*I*2=99.72%). Subgroup analyses indicated no significant associations between Covid-19 related PTG and risk and protective factors (PTSD, depression, social support, coping, and spirituality). **Conclusion.** The findings indicate that COVID-19 events could be associated with PTG as a potential positive outcome. No test risk and protective factors might moderate this relationship. Future investigation should pursue more prospective design and explore the biobehavioral mechanisms underlying this relationship to promote PTG-related better outcomes in patient-centered care. (300 words + four subtitles).

***Keywords:*** Meta-analysis and systematic review, cardiovascular disease (COVID-19), post-traumatic growth (PTG), myocardial infarction, stroke, cardiac procedures

**Key Points**

**Question** Is Covid-19 potentially associated with posttraumatic growth among patients, health care providers, and general population globally exposed to the deadly pandemic?

**Findings** In this meta-analysis 30 studies including 42, 386. individuals, PTG was associated with individuals exposed to Covid-19 in both medical settings and beyond; the pooled association was consistent with that of findings from studies with diverse populations.

**Meaning** The findings suggest that an optimal outcome, posttraumatic growth, could occur among various populations affected by Covid-19 and that attention to this positive side of this global existential threat may be important for mental and public health during the pandemic.

**Introduction**

Since the World Health Organization declared the 2019 novel coronavirus (Covid-19) as a global emergency(Sohrabi\_et\_al.,2020), the pandemic has created a sweeping impact on mortality and detrimental psychiatric consequences(O’Connor\_et\_al.,2020;Wang\_et\_al.,2022). Unlike other severe diseases (e.g., cardiovascular diseases, cancer), Covid-19’s effect is pervasive and traumatic, influencing many sectors of populations(Krishnamoorthy\_et\_al.,2020) and at all levels (individual, family, community, nation, and the word). In medical settings, its highly contiguous nature also generatYed health and existential threats to both patients and health-care providers(Adjorlolo\_et\_al.,2022;Castiglioni\_et\_al.,2023;Chen\_et\_al.,2021;Khattab\_et\_al.,2020;Lewis\_et\_al.,2022;Yeung\_et\_al.,2022;Zhang\_et\_al.,2021).

Because of exposure to COVID-19, psychiatric stress and alter human cognition (e.g., negative thoughts or views of the world) could rise as do following other traumas(Moreland\_et\_al.,2023). However, positive cognition, such as posttraumatic growth (PTG), can also emerge with struggles as trauma-related psychological gains (e.g., positive mindset changes in cognition and worldview)(Calhoun\_&\_Tedeschi,2006). Most observed domains of PTG involved greater positive changes in personal strength, appreciation of life, and social relationships. PTG is also a kind of better outcomes in patients with life-altering diseases(Ma\_et\_al.,2022;Pięta\_&\_Rzeszutek,2022;Sawyer\_et\_al.,2010;Shand\_et\_al.,2015;Wang\_et\_al.,2022). A few meta-analyses have associated this phenomenon with low mortality in non-pandemic patients(Ma\_et\_al.,2022;Wan\_et\_al.,2023).

Given the long-term and vast impact of Covid-19(Emek\_et\_al.,2021;Parums,2021), it is necessary to examine if PTG cooccur with this pandemic as a modifiable dimension of outcomes in the United States and globally. In 2021, a national representative study of US veterans reported moderate to greater levels of PTG resulting from the COVID-19 experience, especially among those suffering from posttraumatic stress symptoms (PTSD) linked with positive Covid-19 results(Pietrzak\_et\_al.,2021). Other studies have also shown the emergence of Covid-19-related PTG in different countries. To provide more reliable and robust conclusion on this positive worldview-based mindset change across different sectors of populations (general populations, health-care providers, and infected patients), we conducted this first meta-analytic review to examining PTG during and post COVID-19.

A meta-analysis on another pandemic has demonstrated the relationship between PTG and adjustment among individuals living with HIV/AIDS(Pięta\_&\_Rzeszutek,2022). Yet, there is a lack of similar pooled analysis on the observed PTG in recent major pandemics. The paucity implies that more meta-analyses will be desirable for this optimal outcome in future medical research. Accordingly, this study employed a systematic approach to synthesize empirical studies in the United States and around the world. We aimed to reach a more creditable conclusion for an urgent question: Whether PTG could be observed globally under the threat of COVID-19 to mankind. More specifically, we evaluated the magnitude and consistency of the pandemic related PTG, as a change in posttraumatic positive cognition. We also conducted subgroup analyses linking PTG with certain risk and protective factors.

# **Methods**

# **Data Sources and Searches**

This systematic meta-analytic review was conducted and presented following the recommendations of the Meta-analysis of Observational Studies in Epidemiology (MOOSE) reporting guideline(Stroup\_et\_al.,2000). A systematic literature search of Ovid MEDLINE, PsycINFO, Academic Search Complete, and PubMed was performed for research articles published from 2000 since the first year of Covid-19, to January, 2024. The following Medical and Psychological Subject Heading terms were used to identify studies that assessed PTG in patients with COVID-19: posttraumatic growth, stress-related growth, adverse growth, COVID-19 MI, positive effects, positive outcome and self-growth. Furthermore, references from selected studies and relevant review articles were reviewed to identify additional publications(Cui\_et\_al.,2021;Feingold\_et\_al.,2022;Finstad\_et\_al.,2021;Hyun\_et\_al.,2021;Kowalski\_et\_al.,2021;Li\_et\_al.,2022;Van der Hallen\_&\_Godor\_et\_al.,2022).

# **Study Selection**

Identified articles were in English, though no language restriction was used to cover publications in both the United States and abroad. Two investigators (A.A., Q.D) independently reviewed the potential candidates for this review. Eligible studies were original empirical research articles that assessed posttraumatic and adulthood growth related terms in different types of people who had various with the global pandemic (e.g., patients, health providers, community dwellers, etc.). Studies on other pandemic only (e.g., Ebola, influenzas) or other disasters were excluded. Then, for the purpose of uniformity of measure, we decided to adopt PTGI(Posttraumatic Growth Inventory;Tedeschi\_&\_Calhoun,1996) as the standard scale for measuring PTG. Any standard variants of PTGI (e.g., PTGI-SF) that could be converted to its scoring style were included. Stated differently, only those with mean scores on PTG with standard deviation or correlates with PTG were included.

Studies using open-ended measures were excluded due to the lack of validation. Studies that did not employ an established and validated scale that specifically focused on PTG, or used other types of measures for gains were excluded. Measures such as Stress-related growth scales(e.g., SRGS, Park,\_Cohen,\_&\_Murch,1996) that were derived from a different set of items, and accesses different aspects of PTG, were excluded. The latter type of exclusion also involved measures on such broader positive changes as Benefit Finding Scale(Mohr\_et\_al.,1999) Perceived Benefit Scale(McMillen\_&\_Fisher.,1998), because certain gains did not pertain to adulthood growth.

**Data Extraction and Quality Assessment**

According to pre-planned protocol and using a standardized form, an assistant investigator (M.R.) reviewed all abstracts first to identify potential studies for inclusion. Full text articles were obtained for all eligible studies and were independently reviewed by two investigators (A.A., Q.D.). Disagreement on the selected studies were then discussed for finalizing the sample. Next, the second reviewer (Q.D.) extracted data from the selected studies. The following data were extracted: study characteristics (e.g., author, year of publication, sample size, study design), patient characteristics (e.g., age, sex, COVID-19 diagnosis), PTG assessment tools, the measures (e.g. PTGI) of PTG, and the standard deviation of the measures for each study. The quality of the selected studies was assessed using Meta-analyses of Observational Studies in Epidemiology Checklist(Zuuren\_&\_Fedorowicz,2016).

**Statistical Analysis**

R (version 4.3.1) was used to conduct the meta-analysis. The current study selected articles that reported the mean and standard deviation (SD) of PTG as assessed by the either PTGI (Tedeschi\_&\_Calhoun,1996) or its variants. The PTG scale used in this study (PTGI) involved summing up ratings across 21 self-reported questions, resulting in a possible score range of 0 to 105. The weighted mean of PTGI was used to identify the level of PTG on COVID-19 patients. To categorize the level of PTG, a cutoff point was established: scores below 45 indicated none to low levels of PTG, while scores of 45 or above indicated medium to high levels of PTG. This cutoff point was chosen based on its frequent usage in existing literature(Mazor\_et\_al.,2016;Naghavi\_et\_al.,2020;Taher\_&\_Allan,2020;Wall\_et\_al.,2023). The PTG scale used in this study (PTGI) involved summing up ratings across 21 self-reported questions, resulting in a possible score range of 0 to 105. The weighted mean of PTGI was used to identify the level of PTG on COVID-19 patients. To categorize the level of PTG, a cutoff point was established: scores below 45 indicated none to low levels of PTG, while scores of 45 or above indicated medium to high levels of PTG. This cutoff point was chosen based on its frequent usage in existing literature(Mazor\_et\_al.,2016;Naghavi\_et\_al.,2020;Taher\_&\_Allan,2020;Wall\_et\_al.,2023).

The aforementioned method of using predetermined cutoff point to categorize the level of PTG posits a clear criterion. If the PTG measure collected from the studies were significantly higher than 45 cut-off point, then, the association of PTG with COVID-19 was considered positive.

The current study used a random effect meta-analytical model for main analysis. Random effect model does not assume a single true effect size, but rather assumes a distribution of true effect sizes. This means ensures the flexibility to take the between-study variability/heterogeneity in effect sizes into account in the analysis.

**Results**

**Study Characteristics**

Figure 1 illustrates a flow diagram of the literature and related screening process. The search yielded 60 unique publications, of which 42 qualified for full-text review. In the end, 30 studies(Adjorlolo\_et\_al.,2022;Arnout\_&\_Al-Sufyani,2021;Bai\_et\_al.,2023;Barnicot\_et\_al.,2023;Castiglioni\_et\_al.,2023;Chasson\_et\_al.,2022;Chen\_&\_Tang,2021;Chen\_et\_al.,2020;Das\_et\_al.,2023;El-Khoury Malhame\_et\_al.,2023;Gul\_et\_al.,2023;Kalaitzaki\_et\_al.,2022;Kalaitzaki\_et\_al.,2023;Lan\_et\_al.,2023;Lau\_et\_al.,2021;Lewis\_et\_al.,2022;Lyu\_et\_al.,2021;Morales\_et\_al.,2023;Mo\_et\_al.,2022;Northfield\_&\_Johnston,2021;Tu\_et\_al.,2023;Ulset\_&\_von Soest,2022;Vazquez\_et\_al.,2021;Wang\_et\_al.,2023;Willey\_et\_al.,2022;Yao\_et\_al.,2023;Yeung\_et\_al.,2022;Yildiz, 2021;Zhang\_et\_al.,2021;Zhou\_et\_al.,2020), met the inclusion criteria for the main analysis. 12 studies were selected for subgroup analyses on PTSD citations of them (Arnout\_&\_Al-Sufyani,2021;Chen\_&\_Tang,2021;Chen\_et\_al.,2020;Das\_et\_al.,2023;El-Khoury Malhame\_et\_al.,2023;Lan\_et\_al.,2023;Lau\_et\_al.,2021;Lewis\_et\_al.,2022;Mo\_et\_al.,2022;Vazquez\_et\_al.,2021;Wang\_et\_al.,2023;Zhang\_et\_al.,2021). Of these 12 included in the analysis, all employed PTGI or its variants (e.g. PTGI-SF) to examine PTG. Twenty-Five were cross-sectional studies and 5 were prospective studies. For the selected studies involving a total of 42,386 individuals, table 1 and table 3 present their overall characteristics.

Among the studies included in the analysis, seven studies were performed in the United States(Chen\_et\_al.,2021;Morales\_et\_al., 2023; Northfield\_&\_Johnston,2021; Tu\_et\_al., 2023; Willey et

al.,2022;Zhang\_et\_al.,2021;Zhou\_et\_al.,2020), two in the United Kingdom(Barnicot\_et\_al.,2023;Lewis\_et\_al.,2022), one in Ghana(Adjorlolo\_et\_al.,2022), two from Greece(Kalaitzaki\_et\_al.,2022;Kalaitzaki\_et\_al.,2023) and from the European countries of Norway, Italy and Spain one study was found in each(Castiglioni\_et\_al.,2023;Vazquez\_et\_al.,2021;Ulset\_&\_von Soest,2022) five from the Middle Eastern countries of Turkey, Pakistan and Saudi Arabia, and Israel(Arnout\_&\_Al-Sufyani,2021;Chasson\_et\_al.,2022;Das\_et\_al.,2023;El-Khoury Malhame\_et\_al.,2023;Gul\_et\_al.,2023;Yildiz,2021), nine from China,(Bai\_et\_al.,2023;Chen\_&\_Tang,2021;Lan\_et\_al.,2023;Lau\_et\_al.,2021;Lyu\_et\_al.,2021;Mo\_et\_al.,2022;Wang\_et\_al.,2023;Yao\_et\_al.,2023;Yeung\_et\_al.,2022). Included articles involved a variety of different types of people such as patients and the general population(Adjorlolo\_et\_al.,2022;Arnout\_&\_Al-Sufyani,2021;Castiglioni\_et\_al.,2023;Chen\_&\_Tang,2021;El-Khoury Malhame\_et\_al.,2023;Gul\_et\_al.,2023;Kalaitzaki\_et\_al.,2022;Lau\_et\_al.,2021;Lewis\_et\_al.,2022;Northfield\_&\_Johnston,2021;Ulset\_&\_von Soest,2022;Vazquez\_et\_al.,2021;Willey\_et\_al.,2022;Zhou\_et\_al.,2020), nurses and medical doctors(Bai\_et\_al.,2023;Barnicot\_et\_al.,2023;Chen\_et\_al.,2020;Das\_et\_al.,2023;Kalaitzaki\_et\_al.,2023;Lyu\_et\_al.,2021;Mo\_et\_al.,2022;Yao\_et\_al.,2023;Yeung\_et\_al.,2022;Zhang\_et\_al.,2021), pregnant women(Chasson\_et\_al.,2022), and students(Lan\_et\_al.,2023;Morales\_et\_al.,2023;Tu\_et\_al.,2023;Wang\_et\_al.,2023;Yildiz,2021) most of which centered on the general population during COVID 19.

**Main analysis**

The main analysis included 30 studies involving a total of 42,386 subjects. The sample size of these studies ranged from 100 (Willey\_et\_al.,2022) to 12,586 individuals(Ulset\_&\_von Soest,2022). Among the studies, different proportions of male participants were observed, with the percentage ranging from 4.40%(Chen\_et\_al.,2020) to 74%(Willey\_et\_al.,2022). Mean age of them ranged from age of 24.96(Zhai\_et\_al.,2021) to age of 76.3(Willey\_et\_al.,2022). The mean age of the participants varied with studies, with a few not providing explicit data, but indicating that the participants were adults above 18 years old(Arnout\_&\_Al-Sufyani,2021;Gul\_et\_al.,2023;Morales\_et\_al.,2023).

The mean PTG ranged from 26.54 to 98.30 with varying degrees of standard deviation, indicative of the range and spread of PTG scores in these studies. Table 1 presents overall characteristics of all studies. The main analysis revealed a significant positive effect relative to the cutoff point of 45. The hedges’ g calculated to reflect the deviation from the 45 cutoff points was 0.75 with 95% CI[0.45, 1.05]. Based on the rule of thumb, 0.5 showed a medium effect and 0.8 or above presented a large effect(Taylor\_&\_Alanazi,2023). These results indicated a highly positive relationship of PTG to COVID-19. *I2* value 99.72% in table 3 also showed high heterogeneity among selected studies.

**Subgroup Analyses of PTG and Covariates**

Table 4 shows the summary of subgroup analyses. The studies included in the study considered several factors in conjunction with PTG such as PTSD/PTSS, depression, anxiety, social support, coping, and spirituality.

***PTSD/PTSS***

Twelve selected studies presented the association of PTSD with PTG with a total of 19,774 participants(Arnout\_&\_Al-Sufyani,2021;Chen\_&\_Tang,2021;Chen\_et\_al.,2020;Das\_et\_al.,2023;El-Khoury Malhame\_et\_al.,2023;Lan\_et\_al.,2023;Lau\_et\_al.,2\_&\_021;Lewis\_et\_al.,2022;Mo\_et\_al.,2022;Vazquez\_et\_al.,2021;Wang\_et\_al.,2023;Zhang\_et\_al.,2021). The baseline effect size (the intercept term) was *g*=0.55, and whether the studies investigated PTSD yielded a higher effect with the regression coefficient associated with the PTSD term being *B=*0.49; 95%CI[-0.1, 1.08]; *p*=0.11. However, PTSD as a moderator is not significant (*p*-value=0.11). Thus, there was no significant relationship between PTSD and PTG. but the broad range of effect sizes indicated a considerable amount of uncertainty in the effect estimate (*SE*=0.30). An *I2* value of 99.60% showed substantial heterogeneity across the studies.

***Mental Health* (*Depression, Anxiety*)**

Ten selected studies presented the association of depression with PTG with a total of 17,064 participants(Arnout\_&\_Al-Sufyani,2021; Adjorlolo\_et\_al.,2022;Barnicot\_et\_al.,2023;Castiglioni\_et\_al.,2023;Kalaitzaki\_et\_al.,2022;Tu\_et\_al.,2023;Morales\_et\_al.,2023;Ulset\_&\_Soest,2021;Willey\_et\_al.,2022;Zhou\_et\_al.,2020).The baseline effect size was *g*=0.92, and the regression coefficient for depression is *B*=-0.52; 95%CI[-1.14, 0.09] ; *p*=0.09, indicating that overall, there was an attenuated effect on PTG when one has depression. However, the effect was not significant. The broad range indicated considerable uncertainty in the effect estimate. A high *I2* value of 99.59% showed substantial heterogeneity across these studies.

With regards to Anxiety, there were 11 studies discussed and measured anxiety levels, spanning 7,245 participants. The baseline effect was *g*=0.84, with Anxiety having a regression coefficient of *B*=-0.24 with 95%CI[-0.86, 0.38]; *p*=0.44, indicating a negative trend on PTG if a participant had anxiety symptoms with them. The heterogeneity after considering Anxiety as a moderator was also high with an of 99.71%.

***Social Support***

Seven selected studies discussed social support concerning PTG with a total of 4231 participants(Gul\_et\_al.,2023;Kalaitzaki\_et\_al.,2022;Mo\_et\_al.,2022;Morales\_et\_al.,2023;Northfield\_&\_Johnston,2021;Zhang\_et\_al.,2021;Zhou\_et\_al.,2020). The baseline effect was *g*=0.75, with Social Support having a regression coefficient of *B*=-0.03; 95%CI[-0.74, 0.69]; *p*=0.94. The moderator was not significant indicating that including social support as a moderator did not reduce the heterogeneity in the data. This can be seen from the high of 99.72% for the model that considered social support. Overall, social support did not contribute much to moderating the variability in PTG across studies.

***Coping***

Various types of coping strategies were investigated with PTG in five studies(Kalaitzaki\_et\_al.,2022;Kalaitzaki\_et\_al.,2023;Willey\_et\_al.,2022;Zhang\_et\_al.,2021;Zhou\_et\_al.,2020) with a total of 3,189 participants. The baseline effect size was *g*=0.80, and the regression coefficient for coping was *B*=-0.29; 95%CI[-1.10, 0.51]; *p*=0.47. Coping strategies also was not a significant moderator in explain the high variability in PTG across studies. The for the model that considered coping is 99.72%.

***Spirituality***

Finally, there are 13 studies talked about religion and spirituality with a total of 10,388 participants(Castiglioni\_et\_al.,2023;Das\_et\_al.,2023;El-Khoury Malhame\_et\_al.,2023;Kalaitzaki\_et\_al.,2022;Kalaitzaki\_et\_al.,2023;Morales\_et\_al.,2023;Tu\_et\_al.,2023;Vazquez\_et\_al.,2021;Willey\_et\_al.,2022;Yao\_et\_al.,2023;Yeung\_et\_al.,2022;Zhang\_et\_al.,2021;Zhou\_et\_al.,2020). The baseline effect size was *g*=0.74, and the regression estimate for spirituality was *B*=0.008; 95%CI[-0.60, 0.62]; *p*=0.98. Thus, there was no relation between spirituality and PTG with Consequently, since the regression estimate is not significant, the moderating effect of spirituality was also limited with an of 99.71%.

**Discussion**

To our knowledge, this study is the first meta-analysis to estimate the relationship between Covid-19 and PTG. The weighted mean PTGI score of the selected studies demonstrates a moderate level of PTG in patients reporting growth after facing the global pandemic that could lead to traumatic experiences. This meta-analysis consisted of 30 studies(Adjorlolo\_et\_al.,2022;Arnout\_&\_Al-Sufyani.,2021;Bai\_et\_al.,2023;Barnicot\_et\_al.,2023;Castiglioni\_et\_al.,2023;Chasson\_et\_al.,2022;Chen\_&\_Tang.,2021;Das\_et\_al.,2023;El-Khoury Malhame\_et\_al.,2023;Gul\_et\_al.,2023;Kalaitzaki\_et\_al.,2022;Kalaitzaki\_et\_al.,2023;Lan\_et\_al.,2023;Lau\_et\_al.,2021;Lewis\_et\_al.,2022;Lyu\_et\_al.,2021;Morales\_et\_al.,2023;Mo\_et\_al.,2022;Northfield\_&\_Johnston,2021;Tu\_et\_al.,2023;Ulset\_&\_von Soest,2022;Vazquez\_et\_al.,2022;Wang\_et\_al.,2023;Willey\_et\_al.,2022;Yao\_et\_al.,2023;Yeung\_et\_al.,2022;Yildiz,2021;Zhang\_et\_al.,2021;Zhou\_et\_al.,2020) involving 42,386 participants. The finding of main analysis indicates that the positive result could derive from the catastrophic event that imposed existential crisis despite heterogeneity (*I* statistic of 99.72%).

Selected studies cover research being conducted in the United States and beyond with high and low incomes, coming across diverse populations in four post-popularized continents, and involving patients, health care providers, students, veterans, and general populations from four continents. The current review thus provides compelling evidence for Covid-19-associated PTG over three years since late 2019. The affected global populations could become stronger after experiencing the deadly challenge of a pandemic diseases, as was shown in other chronic ailments with certain life risks (Ma\_et\_al.,2022;Pięta\_&\_Rzeszutek,2022;Sawyer\_et\_al.,2010;Shand\_et\_al.,2015;Wang\_et\_al.,2022). Different from those previously evident diseases, Covid-19 took lives of nurses and physicians who provided direct or indirect services of patients who were infected.

Nevertheless, the meta-analysis found no significant association between PTG and five risk/protective factors (Anxiety, Depression, Social Support, and Religion). This surprise result suggests that more concise analysis should be done to identify these relationships across diverse populations or roles during the pandemic so as to facilitate better intervention and prevention in the future. Twenty-two of selected study has demonstrated the mental health damage of Covid 19 in this analysis (Adjorlolo\_et\_al., 2022; Arnout\_&\_Al‐Sufyani, 2021; Barnicot\_et\_al, 2023; Castiglioni\_et.\_al, 2023; Chasson\_et\_al., 2022; Chen\_&\_Tang, 2021; Chen\_et\_al., 2020; Das\_et\_al., 2023; El-Khoury\_Malhame\_et\_al., 2023; Kalaitzaki\_et\_al., 2022; Lan\_et\_al, 2023; Lau\_et\_al., 2021; Lewis\_et\_al. ,2022; Mo ,2022; Morales\_et\_al, 2023; Tu\_et\_al., 2023; Ulset\_&\_Soest ,2022; Vazquez\_et\_al., 2021; Wang\_et.\_al, 2023; Willey\_et\_al., 2022; Zhang\_et\_al., 2021; Zhou\_et\_al., 2020). Observed PTG indicates the renewal of worldview, including restoration of meaning and purpose. Individuals high in growth could possess other unrevealed psychosocial strengths or traits, motivationally, behaviorally, and affectively. This negative finding does not end but calls for a new level of clinical awareness and investigation after the Covid-19 survival.

**Clinical Significance**

The pooled international evidence on Covid-based PTG points to three potential directions for future pandemic health care and investigation. First, this systematic review involves considerable variability in study samples, global locations, age range, and cultural diversity. The consistent growth phenomenon, however, suggest that the PTGI may be a suitable instrument for assessing the positive outcome following Covid-19 and similar pandemics. Further longitudinal research might provide more information for its application as a tool (e.g., its short form) in clinical settings.

Second, Covid-19 and similar deadly pandemics may cause catastrophe in the public and long-term health damage in certain proportions of large populations (e.g., long-Covid). Whether PTG will be related to the better prognosis of pathological process and a survival benefit for victims of long Covid-19 remains unknown. However, meta-analyses showed its association with low mortality in non-pandemic patients (Ma\_et\_al.,2022; Wan\_et\_al.,2023). If this is the case for people affected by pandemics, the development of PTG-enhancing interventions may benefit patients and high-risk care providers.

Finally, PTG and pathology (e.g., depression, PTSD) belong to two different paradigms in posttraumatic human wellbeing, *hedonic* versus *eudaemonic well-being* (Ai\_et\_al.,2013; 2021), while PTG and PTSD are both related to struggle as two sides for one coin, trauma. Beyond PTG-related psycho-behavioral theories, a new study also suggested the complicated mechanisms involving many domains (e.g., physiological, biochemical, immunological, neuronal, and genetic alteration (Dell’Osso\_et\_al.,2023). More interdisciplinary studies are warranted in this regard to better inform clinical medicine for both sides.

**Mechanisms**

Most studies in this meta-analysis did not involve basic science investigation, but evidence has emerged in the past decade. In the neuroendocrine and immunological area, research has assorted higher levels of PTG with low levels of cortisol in patients suffering from PTSD and women with breast c­­ancer, respectively (Smyth\_et\_al.,2008; Diaz\_et\_al.,2014). In studies on brain function and structures, PTG was linked with the frontocentral EEG alpha asymmetry in survivors of motor vehicle accidents, controlling for trait positive affect (Rabe\_et\_al.,2006), and was was negatively correlated with grey matter volume in left dorsolateral prefrontal cortex during Covid-19(Lan\_et\_al.,2023). However, PTSS was positively associated with grey matter volume in medial prefrontal cortex/dorsal anterior singular cortex in structured magnetic resonance imaging data acquired before the pandemic(Lan\_et\_al.,2023). PTG.

In (Dunn\_et\_al.,2014) A pioneer work in the genomic area found a relation of PTG to the gene-environment (GxE) interaction study using a New Orleans sample of low-income non-Hispanic Black individuals who exposed to Hurricane Katrina. Among the identified ten common variants in seven genes, the presence of homozygotes rs4606 variants of RGS2 gene was strongly associated with greater PTG after multiple testing, which appeared to be driven by a GxE interaction. Finally, a cardiac physiology study revealed that, in posttraumatic individuals who responded to positive images, the low and high frequency components of HRV were significantly higher in PTG group than in control and PTSD group (Wei\_et\_al.,2017). Accordingly, basic science research of PTG in Covid-19 may assist better understanding of its medical implications.

**Limitations**

The limitations of this meta-analysis should be acknowledged. First, methodological heterogeneous exist across studies and contributed to divergent findings of studies included. The diverse populations, concerning age, race, cultural, geographic location, and roles in the pandemic (e.g., patients, health providers, general populations), may also lead to heterogeneous findings. This divergency suggests the need for further subgroup analysis (e.g., roles). The link between Covid-19 and PTG was nevertheless evident across these studies. Second, to be conceptually sound, we excluded studies with scales without specific foci on growth and those with only unvalidated, single-item measures. This decision could exclude potentially valuable information. Third, important medical indices are missing in most studies; thus, we could not systematically assess their associations with PTG. Fourth, covariates included in studies vary wildly, which may account for the heterogeneity in our subgroup analysis. Finally, due to the emergent pandemic, studies in this meta-analysis were published in a close period (2020-2022) with few were conducted in a prospective design. The increased overtime growth has been observed by a new Covid-19(Kalaitzaki\_et\_al.,2023) and a few non-Covid(Ai\_et\_al.,2021;Hu\_et\_al.,2020;Kelly\_et\_al.,2018) prospective studies, a fact underscoring the need to follow-up post-pandemic PTG.

**Conclusions**

Over the past two decades, burgeoning research has shown PTG as a promising endpoint after trauma and disasters. The findings from this first meta-analysis suggest that the optimal outcome could occur among patients, health care providers, and general populations who were all exposed to the Covid-19 threat globally. PTG includes a posttraumatic outlook change in varied domains, or positive outlook, that could lead to optimal behavioral changes. The worldview-based gain is consistent with psychiatrist Frankl’s (2004; p. XIII) survival tenon: “when we are no longer able to change a situation, we are challenged to change ourselves.” Future research should employ prospective designs to reveal its health benefit in long-term survival and quality of life. Investigation should also address important medical questions (e.g., What could be behavioral and salutogenic bio-psycho-behavioral mechanism to inform clinical practices.

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**Figure 1: Flowchart of Study Selection**

Studies from databases/registers (n=60)

**Identification**

Duplicates removed. (n=10)

Records screened.

(n=42)

Records excluded\*\*

(n=30)

Reports not retrieved.

(n =0)

Reports sought for retrieval.

(n=35)

**Screening**

Reports excluded:

(n=30)

Wrong scale: (n= 10)

Reports assessed for eligibility.

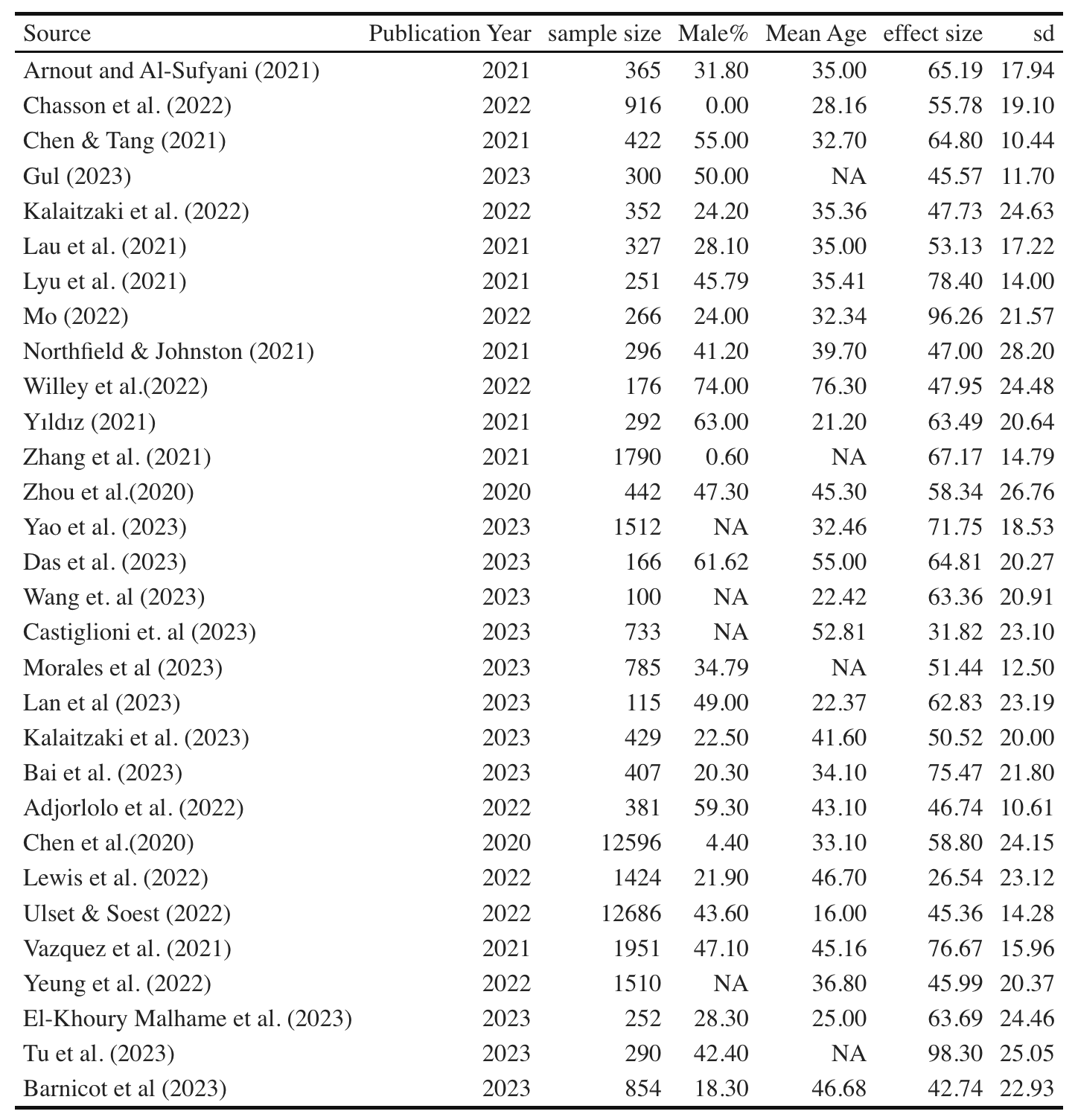
(n=35)

Studies included in review.

(n=30)

**Included**

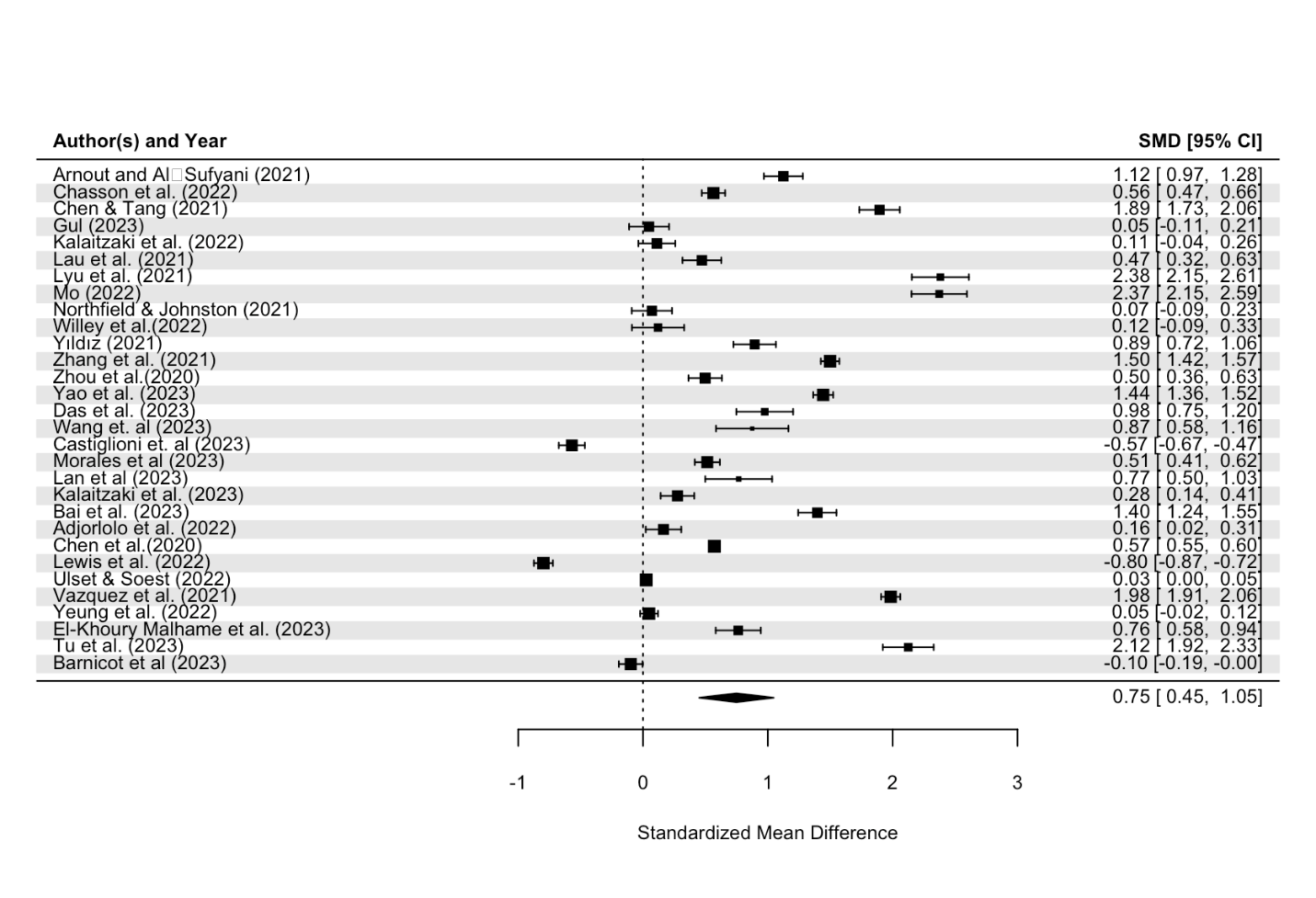
**Table 1: Overview of the selected studies (k=30) for main analysis**

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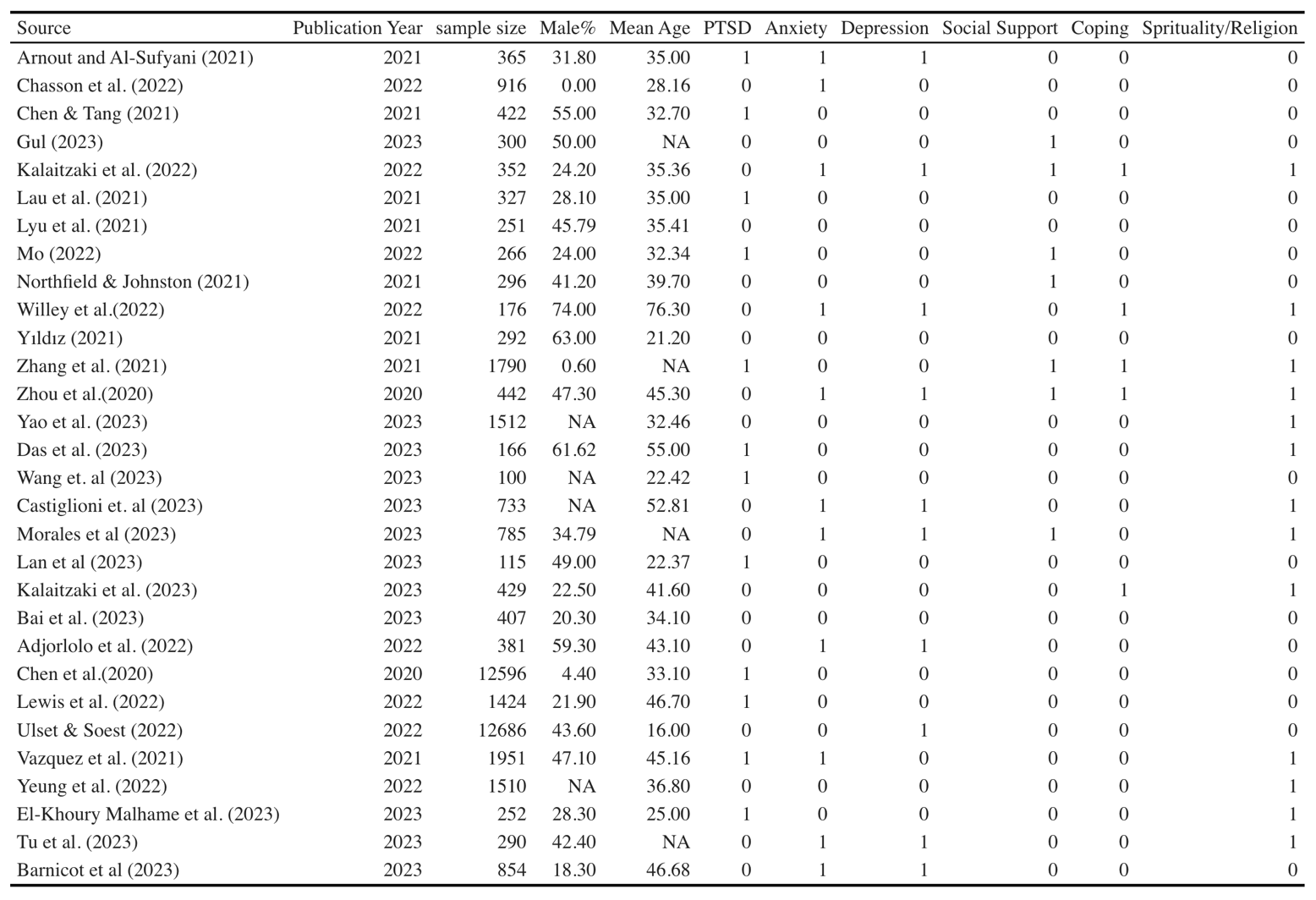
**Table 2: Statistical result of Main Analysis**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Random Effects Model (k=30)** | |  |  |  |  |  |  |
|  | Estimate | se | Z | p | CI Lower Bound | CI Upper Bound |  |
| Intercept | 0.75 | 0.15 | 4.92 | <.0001 | 0.45 | 1.05 |  |
| Heterogeneity Statistics | |  |  |  |  |  |  |
|  | Tau | Tau^2 | I^2 | H^2 | df | Q | p |
|  | 0.83 | 0.69 | 99.72% | 352.96 | 29 | 6174.90 | <.0001 |

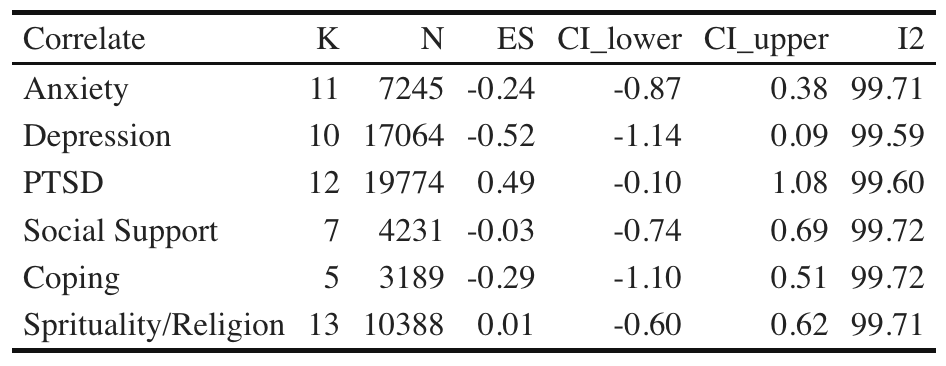
**Figure 2 : Forest Plot of Main Analysis**

****

**Table 3:** Overview of the selected studies for subgroup analysis

****

**Table 4: Results Summary of subgroup analysis**



**Appendix**

**Figure 3: Forest plot for Depression related PTG among COVID-19 people**

A graph with numbers and a line

Description automatically generated