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#### Kirsten Bibbins-Domingo, PhD, MD, MAS

###### Editor in Chief, Journal of The American Medical Association (JAMA)

Lee Goldman, MD Endowed Professor of Medicine and Professor of Epidemiology and Biostatistics

University of California San Francisco,

San Francisco, California, U.S.A.

Dear Dr. Bibbins-Domingo,

Please find the manuscript, titled “*Association of Posttraumatic Growth with Covid-19 and Posttraumatic Stress: A Meta-analytic Review,*” uploaded to the Journal of The American Medical Association (JAMA) 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 *JAHA* 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 *JAMA* 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.

Finally, congrats for you to be the first woman of color to serve on this honorable position! 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)**

(09/01/2023, In Submission to ……/JAMA)

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

**A Meta-analytic Review**

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**Abstract: Importance** Posttraumatic growth (PTG) can be easily assessed and potentially lead to optimal outcomes of the patients, health providers, and general populations affected by Covid-19. **Objective**To conduct the first meta-analysis and systematic review of the association between PTG and Covid-19 and posttraumatic stress symptoms (PTSS). **DATA SOURCES AND STUDY SELECTION** PubMed, PsychINFO, Academic Search Complete (?), Ovid MEDLINE (?), … and… (Marg) electronic databases were systematically searched from …… through August 20, 2023, (Marg, pls to do one more search) 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, PTG, ….. (Marg). **DATA EXTRACTION AND SYNTHESIS** Data were screened and extracted independently by 2 investigators(A.A. and Q.D.). 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 (QZ). **MAINOUTCOMES AND MEASURES** …. (QZ). PTSS was assessed as a separate outcome with PTG. **RESULTS** The search yielded 24 selected studies comprising 4….. participants of which …?? studies presented data on the COVID-19-PTG association, and …?? presented data on PTSS. On pooled analysis, COVID-19 was significantly associated with PTG (Weighted mean …-…..; 95% Cim 0….-0….; *P* < .001), with a moderate heterogeneity in the analysis(*I*2 = …..%). Subgroup analyses indicated the link between Covid-19 related PTG and PTSS in COVID-19 (QZ???). **Conclusion and Relevance** The findings indicate that COVID-19 events could be associated with PTG as a potential positive outcome. 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. (250 words + four subtitles).

**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 24 studies including 4….. 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.

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

**Introduction**

Since the World Health Organization declaredpr the 2019 novel coronavirus (COVID-19) as a global emergency (Sohrabi et al., 2020), the pandemic has created a sweeping impact on mortalities and detrimental psychiatric consequences (O’Connor et al., 2020; Wang et al., 2022). Unlike other severe diseases (e.g., cardiovascular diseases, cancer), Covid-19 present similar risks to diverse sectors of persons and populations (Krishnamoorthy et al., 2020) and at all levels (individual, family, community, nation, and the word). Traumatic experience can cause psychiatric stress and alter human cognition, such as negative thoughts or views of the self and the world (Moreland et al., 2023). Conversely, posttraumatic growth (PTG) can also emerge with trauma-related struggles as psychological gains (e.g., positive mindset changes in cognition and worldview) (Calhoun & Tedeschi, 2006). PTG is related to better outcomes of patients with life-altering diseases and trauma survivors (Ma et al., 2022; Pięta & Rzeszutek, 2022; Shand et al., 2015; Tsi et al., 2015; Wang et al., 2022).

Given the scope of Covid-19 and similar future pandemics, it is necessary to examine if the existential threat could yield PTG as a broad global phenomenon and a modifiable dimension for both patient-centered care and providers’ self-care. In 2021, a national representative study of US veterans reported moderate to greater levels of PTG of the pandemic-related PTG, especially among those suffering from posttraumatic stress symptoms (PTSD) linked with positive Covid-19 results (Pietrzak et al., 2021). Most observed domains involved greater positive changes in personal strength, appreciation of life, and social relationships. Other small-scale studies on Covid-19 related PTG have also emerged in the United States and beyond. To provide more reliable and robust conclusion on this positive mind-set and worldview gains across different roles (general populations, healthcare providers, and affected patients), we conducted a meta-analytic review. The study employed a systematic approach to synthesize empirical studies examining PTG in COVID-19 in general populations, healthcare providers, and affected patients. 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. The aim is to evaluate the magnitude and consistency of the pandemic-related change in posttraumatic positive cognition.

In addition, it is crucial to consider how the effect of PTG behaves in different populations based on different categorization criteria. For example, people might experience different levels of PTG based on their demographic information, previous exposure to traumatic events, age group, gender, and different regions in the world. Our current study also aims to address these nuanced aspects of PTG by performing subgroup analysis.

# **Methods**

# **Data Sources and Searches**

This systematic meta-analytic review was conducted and presented according to 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…. (MC!) was performed for research articles published from 2000 since the first year of Covid-19, to 2023. 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, ….. (MC!). Furthermore, references from selected studies and relevant review articles were reviewed to identify additional publications.

# **Study Selection**

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, any studies that did not employ an established and validated scale that specifically focused on PTG (e.g., PTG Inventory/PTGI; Tedeshi & Calhoun, 1996; PTGI-SF, (citation of the scale same as T and Cm 1996???? ) 🡪 the citation is a different one; the short form paper is a 2010 paper by Cann et al.

Excluded studies might use other types of measures on broad positive changes (e.g., Benefit Finding Scale by Mohr et al. 1999; Perceived Benefit Scale by McMillen & Fisher, 1998), because certain gains did not pertain to adulthood growth. In addition, we want to select scales that resemble the factor structure of PTGI as it contains vital components of posttraumatic growth, and consequently scales such as Stress-related growth scales/SRGS, Cohen, & Murch, 1996, Park & Blumberg, 2002) were not included as they are derived from a different sets of items, and accesses different aspects of PTG. Studies using open-ended measures were also excluded due to the lack of validation. In the final selection, only those with mean scores on PTG with standard deviation or correlates with PTG were included.

**Data Extraction and Quality Assessment**

According to preplanned protocol and using a standardized form, an assistant investigator (M.C.) reviewed all abstracts first to identify potential studies for inclusion. Full text articles were obtained for all potentially eligible studies and were independently reviewed by other 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, and estimates of the association between PTG and COVID-19 (e.g., t-value or correlation coefficients MC! QZ!). The quality of the selected studies was assessed using the Cochrane Risk of Bias tool (Higgins JPT, et al., 2016 QZ!).

**Statistical Analysis**

R (version 4.3.1) was used to conduct the meta-analysis. The current study employed a selection criterion such that articles reporting the mean and standard deviation (SD) of Posttraumatic Growth (PTG) as assessed by the Posttraumatic Growth Inventory (PTGI) developed by Tedeschi and Calhoun (1996) or the short form of the PTGI scale were included.

The Posttraumatic Growth (PTG) measure used in this study 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 46 or above indicated medium to high levels of PTG.

The aforementioned method of categorizing the level of PTG based on a predetermined cutoff point allows for a clear distinction between individuals with varying levels of PTG and facilitates the interpretation of study findings.

The current study uses I2 to assess the heterogeneity (Higgins and Thompson, 2002; Higgins et al., 2003). Above 50% of I^2 would be considered as a medium to high level of heterogeneity and a random effect model would be applied. Forest plots were generated to summarize the results of multiple studies and compare the effect size of exposure across different studies.

Given that our I^2 value far exceeds the 50% mark, we proceeded with a Random effects model for our meta-analysis. Once we obtained the random effects model, we then consulted tau^2 for a more accurate representation of the heterogeneity among studies.

In cases where data were available from at least three studies, these analyses were conducted. The final estimated effect size with 95% CI would be reported to assess the association between PTG and different variables.

**Results**

**Study Characteristics**

Identified articles were in English, though no language restriction was used to cover publications in both the United States and abroad. Figure 1 illustrates a flow diagram of the literature and related screening process. The search yielded 35 unique publications, of which 24 ( QZ! - yes) qualified for full-text review. In the end, 24 (QZ???? Double check below! potentially exclude 2 studies whose scales that are neither PTGI nor PTGI-SF, so 22 studies) studies (Adjorlolo et al., 2022); (Arnout & Al-Sufyani, 2021); (Chasson et al., 2022); (Chen & Tang, 2021); (Chen et al., 2020); (Dominick & Elam, 2023); (Gul et al., 2023); (Kalaitzaki, Tsouvelas & Tamiolaki, 2022); (Lau, Chan & Ng, 2021); (Lewis et al., 2022); (Lyu et al., 2021); (Mo et al., 2022); (Northfield & Johnston, 2021); (Pietrzak, Tsai & Southwick, 2021); (Prieto-Ursua & Rafael, 2020);(Ulset & von Soest, 2022); (Vazquez et al., 2021); (Willey et al., 2022); (Yeung et al., 2022); (Yildiz, 2021); (Zhai et al., 2021); (Zhang et al., 2021); (Zhou, MacGeorge & Myrick, 2020), met the inclusion criteria for the main analysis. #? (QZ!) studies were selected for subgroup analyses on PTSD citations of them (….. QZ! MC! -- ) . Of these 24 included in the analysis, all employed PTGI to examine PTG with the exception of two, ((…..QZ! MC!). ?? were cross-sectional studies and seven were prospective studies (#??….QZ!). For the selected studies involving a total of 40,000+ 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); (Dominick & Elam, 2023); (Northfield & Johnston, 2021); (Pietrzak, Tsai & Southwick, 2021);(Willey et al., 2022); (Zhang et al., 2021); (Zhou, MacGeorge & Myrick, 2020), one in the United Kingdom (Lewis et al., 2022), one in Ghana (Adjorlolo et al., 2022), one from Greece, two from Spain, one from Norway and one from the Netherlands (Kalaitzaki, Tsouvelas & Tamiolaki, 2022); (Prieto-Ursua & Rafael, 2020); (Vazquez et al., 2021); (Ulset & von Soest, 2022); (Garnefski et al., 2008), four from the Middle Eastern countries of Turkey, Pakistan and Saudi Arabia, and Israel (Arnout &Al‐Sufyani, 2021); (Gul et al., 2023), (Javed & Dawood, 2016); (Chasson et al., 2022), six in China, (Chen & Tang, 2021); (Lau et al., 2021); (Lyu et al., 2021); (Mo et al., 2022); (Yeung et al., 2022); (Zhai et al. 2021). 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); (Chen & Tang, 2021); (Dominick & Elam, 2023); (Gul et al.,2023); (Kalaitzaki, Tsouvelas & Tamiolaki, 2022); (Lau, Chan & Ng, 2021); (Lewis et al., 2022); (Northfield & Johnston, 2021); (Prieto-Ursua & Rafael, 2020);(Vazquez et al., 2021); (Willey et al., 2022); (Zhai et al., 2021); (Zhou et al., 2020), nurses (Chen et al., 2020); (Lyu et al., 2021); (Mo et al., 2022); (Yeung et al., 2022); (Zhang et al., 2021), pregnant women (Chasson et al., 2022), veterans (Pietrzak, Tsai & Southwick, 2021) and students (Ulset & von Soest, 2022); (Yildiz, 2021); most of which centered on a single condition or event. → this need to be extracted from the paper by MC!!!!

**Main analysis**

The main included a total of 24 studies, involving a total of 40k…. individuals. The sample size of these studies ranged from 176 (Willey et al., 2022) to 12,596 individuals (Ulset & von Soest, 2022). Most of the studies had a significant proportion of male participants, with the percentage ranging from 4.40% (Chen et al., 2020) to 91.60%% (Pietrzak, Tsai & Southwick, 2021). Mean age of them ranged from 24.96 (Zhai et al., 2021) to 63.3 (Pietrzak, Tsai & Southwick, 2021) years. 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 (….). The mean PTG ranged from ??.? (….) to ??.? (….QZ?), 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 meta-analysis was conducted using a fixed-effects model instead of the presupposed random-effect model due to low heterogeneity. …. (….QZ?)

**Subgroup Analyses**

Table 4 shows the summary of subgroup analysis on PTSD???? , ….(….QZ?)

***Age***

The influence of age on PTG was examined across five studies, involving a total of ?? participants (….). The pooled effect size yielded a value of 0.0? shown in Figure 7, indicating a small positive correlation between age and PTG. The 95% confidence interval, ranging from -0.12 to 0.20, suggests that age could have a slightly favorable impact on the experience of PTG. However, the I2 statistic of ??.??% indicated a significant level of heterogeneity among the selected studies.

***Gender***

The relationship between gender and PTG was analyzed in four studies, with a total of ?? participants (….) reveal. The pooled effect size revealed a small positive correlation shown in Figure ?, with a value of 0.??, indicating that gender might played a slightly positive role in the degree of PTG. The 95% confidence interval, ranging from 0.0? to 0.??, suggests a relatively consistent effect across the studies. However, the ?? statistic of ??.??% indicated a low level of heterogeneity among the examined studies, indicating a certain degree of consistency in the relationship.

**Discussion**

The current review has provided compelling findings for PTG, associated with the Covid-19 pandemic that imposed existential crisis around the world over three years since late 2019. Selected studies cover strong evidence from research conducted the United States and beyond, which involving patients, health care providers, students, veterans, and general populations from four continents. Our findings suggest that a positive outcome can emerge from deadly diseases with a global scope, 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 conditions, Covid-19 did take lives of nurses and physicians who provided direct or indirect services of patients who were infected (QZ).

This meta-analysis consisted of 23 studies (citations…. MR) involving …. Participants. All of them associated PTG with Covid-19. # of studies also associated PTG with ..???? (QZ). Despite the heterogeneity in sample characteristics (e.g., age, country of origin, culture, position in the pandemic), the result among studies were consistent. An overall pooled risk ratio of….. suggests…….(QZ). Of 23 studies, ??# of them showed whatever….(need just key # here to make your statement! (QZ)

**Methodological Heterogeneity across Studies**

In the final sample of studies, most studies used PTGI or its variations (e.g., SF, CPTGI), except one used SRGS-SF (Zhai et al., 2021). Despite the discrepancy in assessments, the link between CVD and PTG were compatible among studies. Thus, both scales on adulthood growth should be seen as usable in Covid-19 research. Given its wide usage in international studies, PTGI should be considered as a better choice in future clinical studies. Furthermore, the heterogeneous findings from this meta-analysis may also be related to diverse populations in these studies concerning age, race, cultural, and roles in the pandemic (e.g., patients, health providers, general populations). For example, mean age of Chasson et al.’s (2022) study was 28.16, whereas Pietrzak et al.’ (2021) was 63.3. Both groups showed moderate or moderately high-level PTG (this may be modified based on subgroup analysis of age effects).

Finally, there was also the variation in when PTG was observed across 24 studies. The assessment time ranged from ?? month (?? et al., 202?) to?? years (?? et al., 202?). The link between Covid-19 and PTG was nevertheless evident across these studies. Understandably, due to the emergent pandemic, studies in this meta-analysis were published in a close time period (2020-2022) with few were conducted in a prospective design. Although not involved in these studies, non-Covid prospective study have observed the increased level of growth over the post-event time (Ai et al., 2021; Hu et al., 2020; Kelly et al., 2018). The finding suggests that the need to assess the follow-up time after pandemic in future investigation.

**Subgroup Analyses of PTG and Covariates**

PTSS….

**Comparison with Other Studies of PTG and Other Medical Conditions**

To our knowledge, this study is the first meta-analysis to estimate the relationship between Covid-19 and PTG. Findings resembled emerging meta-analyses that assessed the relationship between PTG and other medical conditions, including a few on other pandemics. These include studies that demonstrated an association between PTG and adjustment among individuals living with HIV/AIDS (Pięta & Rzeszutek, 2022) and/or cancer (Ma et al., 2022; Sawyer et al., 2010; Shand et al., 2015; Wang et al., 2022). However, there is a lack of similar pooled analysis on the observed PTG in recent major pandemics. The paucity suggests that more meta-analyses will be desirable for this optimal outcome in future medical research.

**Mechanisms**

None of the studies in this meta-analysis has involved clinical factors in basic science (QZ??). Nevertheless, bourgeoning studies on PTG have provided valuable information in an interdisciplinary knowledge base for PTG, which may suggest mechanisms in several domains involving physiological, biochemical, immunological, neuronal, and genetic alteration (Dell’Osso et al., 2023). In the neuroendocrine and immunological area, Smyth et al. (2008) and Diaz et al. (2014) have associated higher levels of PTG with low levels of cortisol in patients suffering from PTSD and women with breast cancer, respectively. In the more established area, brain function and structures, Rabe et al. (2006) showed the association between PTG and the frontocentral EEG alpha asymmetry in survivors of motor vehicle accidents, after controlling for trait positive affect.

In the genomic area, Dunn et al. (2014) pioneered the gene-environment (GxE) interaction study in relation to PTG 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, in the cardiac physiology area, Wei et al. (2017) found 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. Taken together, more interdisciplinary research on the mechanism PTG may assist better clinical Covid-19 care through enhancement on pademic-related PTG in the future.

**Clinical Significance**

Over the past two decades, burgeoning research has shown PTG as a promising endpoint after trauma and disasters. The findings of the present study 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. The pooled international evidence made PTG a compelling arena for study within broad areas of preventive medicine, behavioral was associated with medicine, and public health. The consistent finding from this meta-analysis pointed to three dimensions for future investigation in the patient-centered care era.

First, the present meta-analysis was associated with considerable variability in study samples, areas of origins, age range, cultural diversity, and the cut points that were applied to PTG (QZ??). The consistent global evidence in this systematic review suggests that the PTGI may be an suitable instrument for assessing this positive outcome following a deadly pandemic in epidemiological studies. Further longitudinal studies may provide more information for its usage as a clinical tool in medical settings. Second, more interdisciplinary and longitudinal research is warranted to reveal how PTG is related to medical, biophysical, and behavioral mechanisms as well as the prognosis of pathological process of Covid-19 and the like. A complicated relation therein can be expected, because PTG and pathology belong to two differenty paradigms in human wellbeing (Ai et al., 2013; 2021). However, PTG and PTSD as two sides for one coin, trauma, are also correlated given that both related to struggle.

Finally, PTG involves a new worldview after trauma in varied domains or positive outlook that could lead to optimal behavioral changes. For example, a meta-analysis showed its association with low mortality in cancer patients (?? Marg). Covid-19, and likely similar pandemics in the future, causes remarkable population impact and certain long-term health damage in certain proportions of patients (e.g., long-Covid). The findings from this first meta-analysis on a growth phenomenon may support development of interventions that could enhance real growth and related optimal outcomes in patients and benefit health care providers at high risks. Taken together, future investigation should address important medical questions such as: Whether PTG has a survival benefit for victims of Covid-19? What could be behavioral and salutogenic mechanism of adulthood growth aligned with such medical struggles?

**Limitations**

The limitations of our meta-analysis should be acknowledged. Firstly, the sample sizes of many studies are small, which suggests the need for more rigorous design in future investigation. Second, important medical indices are missing in most studies; thus, we could not systematically assess their associations with PTG. Third, most studies are cross-sectional in nature, hindering the statement of causality, even though and a cross-sectional design was included in previous meta-analyses (e.g., Stroup et al., 2000). Fourth, covariates included in studies vary wildly, which may account for the heterogeneity in our subgroup analysis. Fifth, some studies did not specify the gender positively related to PTG. Sixth, 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. Finally, we do not have enough effect size to test a PTG-PTSD relationship in PTG. Given the complicated relationship of PTG with PTSD and depression, two CVD mortality risks, it should be interesting to explore the likely intertwining trajectory of the three constructs in patients with CVD prognosis.

**Conclusions**

Our findings suggest that after the global pandemic Covid-19, the PTG phenomena can occur in various populations, including patients, health providers, and general populations. Future investigation should employ prospective design with large samples to reveal its health benefit in long-term survival and quality of life, as well as the biobehavioral mechanisms underlying this optimal outcome and the potential intervention for future pandemics.

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**Figure 1: Flowchart of Study Selection**

A screenshot of a flowchart

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**Table 1: Overview of the selected studies (k=21) for main analysis**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Source | Year | Sample size | Male,% | Age (mean) | End Point | Follow up, y | PTG Mean | PTG SD |
| Bluvstein et al. | 2013 | 82 | 60 % | 63.70 | Coronary heart disease | 6 months | 41.3 | 27.3 |
| Hu et al. | 2020 | 65 | 70.80% | N/A (>18) | Stroke | 3 months | 56.94 | 9.11 |
| Kearns et al. | 2020 | 304 | 65.5% | 65.5 | Cardiovascular diseases | ~12 months | 55.5 | 33.0 |
| Kelly et al. | 2017 | 43 | 58% | 74.53 | Stroke | 6 months | 51.53 | 26.25 |
| Leung et al. | 2012 | 2636 | 75% | 65.49 | Coronary artery disease | 1 year | 47.3 | 8.5 |
| Leung et al. | 2010 | 1497 | 71.30% | 65.98 | Coronary artery disease | 9 months | 50.3 | 27.2 |
| Losiak & Nikiel | 2014 | 53 | 60.37% | 57.30 | Myocardial infarction | ~5.5 weeks | 47.28 | 21.83 |
| Magid et al. | 2019 | 52 | 69.20% | 64.80 | Cardiac disease | 43 months | 35.25 | 15.93 |
| Maria et al. | 2021 | 44 | 100% | 63.26 | Myocardial infarction | N/A | 18.77 | 7.01 |
| Overbaugh et al. | 2017 | 103 | 76% | 74 | Heart failure | N/A | 48.6 | 28.6 |
| Rahimi et al. | 2016 | 166 | 84.9% | 55.3 | Myocardial infarction | ~7.78 months | 68.39 | 19.40 |
| Sheikh | 2004 | 110 | 79% | 63.5 | Heart disease | ~5 years | 55.85 | 24.19 |
| Aydındoğmuş, A., & Savaşan, A. | 2022 | 25 | 88% | 54.84 | Myocardial infarction | 3 months | 76.24 | 17.80 |
| De Oliveria et al. | 2023 | 63 | 65% | 65 | Heart failure |  | 67.02 | 13.26 |
| Gangstad & Norman et al. | 2009 | 60 | 56.67% | 71.67 | Stroke |  | 50.33 | 19.92 |
| Huang et al. | 2021 | 158 |  |  | Stroke | 3 months | 54.89 | 23.08 |
| Karagiorgou & Cullen | 2016 | 47 | 79% | 66.4 | Myocardial infarction |  | 54.6 | 23.6 |
| Kuenemund et al. | 2014 | 42 | 64% | 52.83 | Stroke | ~ 21 months | 57.69 | 19.28 |
| Ogińska-Bulik, N | 2014 | 86 | 72.10% | 60.50 | Myocardial infarction |  | 61.54 | 16.75 |
| Oginska-Bulik, N., & Gurowiec, P. J. | 2020 | 63 | 61.90% | 67 | Myocardial infarction |  | 37.05 | 17.67 |
| Peng, Z. Y., & Wan, L. H. | 2018 | 115 | 70.4% | 62.43 | Stroke | 6 months | 61.12 | 25.41 |

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

A table with numbers and symbols

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

A graph with numbers and lines

Description automatically generated

**Table 3 :** Overview of the selected studies (k=13) for subgroup analysis

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Source | Year | Sample size | Male,% | Age (mean) | End Point | Follow up, y | Determinant |
| Ai et al. | 2013 | 262 | 60% | 62.4 | Cardiovascular diseases | 2.5 years | Depression, Coping, Spirituality, Social Support, Age, Gender |
| Garnesfski et al. | 2008 | 139 | 82% | 35-70 | Myocardial infarction | 3~12 months | Depression, Coping, Spirituality, Age, Gender |
| Hu et al. | 2020 | 65 | 70.80% | N/A (>18) | Stroke | 1 month | Depression, Spirituality, Social Support |
| Javed & Dawood | 2016 | 90 | 58% | 45-65 | Myocardial infarction | 1 month – 3 years | Coping, Social Support |
| Kelly et al. | 2017 | 43 | 58% | 74.53 | Stroke | 6 months | Coping, Social Support |
| Losiak & Nikiel | 2014 | 53 | 60.37% | 57.30 | Myocardial infarction | ~5.5 weeks | Coping, Spirituality |
| Magid et al. | 2019 | 52 | 69.20% | 64.80 | Cardiac disease | 43 months | Coping, Age |
| Overbaugh et al. | 2014 | 103 | 76% | 74 | Heart failure | N/A | Age, Gender |
| Rahimi et al. | 2016 | 166 | 84.9% | 55.3 | Myocardial infarction | ~7.78 months | Social support |
| Sheikh | 2004 | 110 | 79% | 63.5 | Heart disease | ~5 years | Coping. Social Support |
| Senol-Durak & Ayvasik | 2010 | 132 | 11.4% | 52.04 | Myocardial infarction | N/A | Depression, Coping, Social Support, Age, Gender |
| Gangstad & Norman et al. | 2009 | 60 | 56.67% | 71.67 | Stroke |  | Depression, Coping |
| Peng, Z. Y., & Wan, L. H. | 2018 | 115 | 70.4% | 62.43 | Stroke | 6 months | Social Support |

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

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Correlate** | **K** | **N** | **ES** | **95% CI lower** | **95% CI upper** | **I2** |
| Depression | 5 | 658 | -0.15 | -0.41 | 0.11 | 91.96% |
| Coping Strategies | 9 | 941 | 0.50 | 0.33 | 0.66 | 93.04% |
| Spirituality | 4 | 519 | 0.56 | 0.38 | 0.75 | 89.38% |
| Social Support | 8 | 983 | 0.29 | -0.05 | 0.62 | 98.25% |
| Age | 5 | 688 | 0.04 | -0.12 | 0.20 | 78.49% |
| Gender | 4 | 636 | 0.10 | 0.03 | 0.18 | 11.01% |

**Appendix**

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

A graph with numbers and a line

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