**Name of Journal:** *World Journal of Psychiatry*

**Manuscript NO:** 85432

**Manuscript Type:** OPINION REVIEW

**Not one thing at a time: When concomitant multiple stressors produce a transdiagnostic clinical picture**

Goldstein Ferber S *et al*. Multiple stressors and transdiagnostic profile

Sari Goldstein Ferber, Gal Shoval, Aron Weller, Gil Zalsman

**Sari Goldstein Ferber,** Department of Psychology and Brain Sciences, University of Delaware, Newark, DE 19716, United States

**Sari Goldstein Ferber, Aron Weller,** Psychology and Gonda Brain Research Center, Bar Ilan University, Ramat Gan 5317000, Israel

**Gal Shoval,** Department of Neuroscience, Princeton University, New Jersey, NJ 08544, United States

**Gal Shoval, Gil Zalsman,** Geha Mental Health Center, Petah Tiqva, Israel and Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv 77096, Israel

**Gil Zalsman,** Department of Psychiatry, Columbia University, New York, NY 10032, United States

**Author contributions:** Goldstein Ferber S led the diagnostic conceptualization and writing of the different versions of this paper and its final version; Shoval G, Weller A, and Zalsman G contributed to the developing versions of this paper.

**Corresponding author: Sari Goldstein Ferber, PhD, Affiliate Associate Professor,** Department of Psychology and Brain Sciences, University of Delaware, 108 Wolf Hall, Newark, DE 19716, United States. sgf@udel.edu

**Received:** April 27, 2023

**Revised:** June 7, 2023

**Accepted:** June 19, 2023

**Published online:** July 19, 2023

**Abstract**

A condition of exposure to multiple stressors resulting in a mixed clinical picture spanning conventional categories without meeting any of them in full, encompasses a risk for a list of comorbidities preventing appropriate prevention and treatment. New transformative transdiagnostic approaches suggest changes spanning conventional categories. They base their systems of classification on biomarkers as well as on brain structural and functional dysregulation as associated with behavioral and emotional symptoms. These new approaches received critiques for not being specific enough and for suggesting a few biomarkers for psychopathology as a whole. Therefore, they put the value of differential diagnosis at risk of avoiding appropriate derived prevention and treatment. Multiplicity of stressors has been considered mostly during and following catastrophes, without considering the resulting mixed clinical picture and life event concomitant stressors. We herewith suggest a new category within the conventional classification systems: The Complex Stress Reaction Syndrome, for a condition of multiplicity of stressors, which showed a mixed clinical picture for daily life in the post coronavirus disease 2019 era, in the general population. We argue that this condition may be relevant to daily, regular life, across the lifespan, and beyond conditions of catastrophes. We further argue that this condition may worsen without professional care and it may develop into a severe mental health disorder, more costly to health systems and the suffering individuals. Means for derived prevention and treatment are discussed.

**Key Words:** Transdiagnostic; Multiple stressors; Clinical picture; Prevention; Treatment; Interpersonal psychotherapy; Cognitive behavioral therapy

**©The** **Author(s) 2023.** Published by Baishideng Publishing Group Inc. All rights reserved.

**Citation**: Goldstein Ferber S, Shoval G, Weller A, Zalsman G. Not one thing at a time: When concomitant multiple stressors produce a transdiagnostic clinical picture. *World J Psychiatry* 2023; 13(7): 402-408

**URL**: https://www.wjgnet.com/2220-3206/full/v13/i7/402.htm

**DOI**: https://dx.doi.org/10.5498/wjp.v13.i7.402

**Core Tip:** Multiplicity of stressors has been considered mostly during and following catastrophes, without considering the resulting mixed clinical picture and life event concomitant stressors. We herewith suggest a new category within the conventional classification systems: The Complex Stress Reaction Syndrome, for a condition of multiplicity of stressors, which showed a mixed clinical picture for daily life in the post coronavirus disease 2019 era, in the general population. We argue that this condition may be relevant to daily, regular life, across the lifespan, and beyond conditions of catastrophes.

**INTRODUCTION**

Many people with mental health complaints present a mixed clinical picture. Often none of the complaints meet the full criteria of any of the conventional classifications. Possibly, several categories are met (though not completely), leading to a list of comorbidities. This precludes clear diagnosis, prevention and treatment.

There are at least 4 different suggestions to revise classical classifications into transdiagnostic approaches: Hierarchical Taxonomy to Psychopathology[1], Research Domain Criteria[2], Bipolar-Schizophrenia Network on intermediate phenotypes[3,4], and Neuroscience-Based Nomenclature[5]. These suggested new classification systems are based on neuroanatomic findings showing that several brain areas demonstrate similar functionality and structure in various conventional categories[6-9]. However, others have commented on these data that they lack specificity, as the biomarkers show relevance over too many mental disorders[10]. Thus, many current conventional classification categories are gathered in the transformative systems into one pool of psychopathology, preventing consequent application of accurate prevention and treatment per each disorder including the missing clinical attention to individual differences.

Part of the mixed clinical pictures involves the concomitant experience of multiple stressors. As it arises from our literature search using PubMed, Google Scholar and *Reference Citation Analysis* (RCA), the impact of multiple stressors has been discussed by cutting edge papers mostly in the context of disasters such as hurricanes, floods, wars and in drastic conditions experienced by refugees and immigrants including the coronavirus disease 2019 (COVID-19) era, with similarities between the impacts in these types of conditions across the lifespan, *e.g.*,[11-14]. The most common psychiatric outcomes reported are post-traumatic stress disorder (PTSD) and depression[15-20]. There are scarce reports on multiple stressors in daily life as related to the development of psychiatric disorders. Some of these reports relate to stressors in the workplace, economic hardships and the impact of urbanization[21-23]. Surprisingly, here also PTSD and depression are the common outcomes. The diagnosis of these two disorders in such different types of multiple stressors calls for attention and re-evaluation. Thus, the aim of the current paper is to suggest a new potential category for the conventional diagnostic system, which will include conditions of mixed clinical pictures with more than one stressor identified.

As clinicians, we encountered a condition in which many patients showed mixed symptomatology, spanning conventional categories, without fully meeting all the conventional criteria of any of these categories during the multi-stressor COVID-19 outbreak. Our literature review supported our observations[24]. In a following empirical bi-national study, using representative, large samples[25], we further found that combinations of several mental health symptoms studied, PTSD, phobia, depression, anxiety and posttraumatic stress symptoms, were more prevalent than combinations of fewer symptoms, with no majorities-minorities differences in both Italy and Israel[25]. We termed this mixed clinical picture the Complex Stress Reaction Syndrome (CSRS). CSRS includes type A (a psychiatric part) and type B (a neuropsychiatric part for the long-COVID component, excluding systemic symptoms)[24,25]. As more cross-cultural studies of the CSRS are warranted, we are currently conducting such an international study with participants from 8 diverse countries located in the Middle East, Europe, Australia and North America.

In this paper we suggest that the CSRS type A (the psychiatric part, not including type B) may explain mixed clinical pictures in conditions of multiplicity of significant stressful life events in the post-COVID era. Thus, we argue that in the general population, experiencing concomitant multiplicity of life events-related stressors may account for the development of a mixed type of mental health disorder, not only in conditions of catastrophes (see Figure 1).

***Differential diagnosis***

For differential diagnosis, the CSRS (type A) may be compared to: (1) Diagnosis of adjustment disorder rules out PTSD and bereavement, and it displays a short stressor onset-symptoms occurrence latency; (2) PTSD diagnosis includes exposure to one frightening stressor; (3) Obsessional thoughts are ego-syntonic by definition. The behaviors related to extrinsic stressors are clearly not included in the obsessive-compulsive disorder (OCD) conventional category; (4) Diagnosis of acute stress disorder implies a simpler stressor and a specific symptom response; (5) The criteria for defining generalized anxiety disorder list excessive worrying (on diverse issues) and shifting back and forth among them, thus not implying the multiplicity of stressors and a mixed clinical picture; (6) The diagnosis of major depression disorder includes anhedonia, low affect, psychomotor agitation, unfitting guilt feelings, diminished drive and energy, trouble concentrating, and indecisiveness with no other types of symptomatology which are included in a mixed clinical picture; and (7) C-PTSD is described as the result of a series of traumatic events, which is repetitive and hard to escape but does not include a mixed clinical picture beyond the PTSD conventional criteria. It also describes a series of events and not the simultaneous occurrence of multiple stressors as the possible etiological source for psychopathology.

***Prevention***

The impact of multiple concomitant stressors depends on individual subjective perception and stress reaction tendencies[26]. The immediate question is what can prevent the emergence of pathological stress reactions, spanning several conventional categories. In a previous study we found that close relationships may protect the individual across the types of psychopathology investigated, spanning anxiety, depression, PTSD and OCD criteria, in conditions of multiple stressors[27]. The means for illness prevention and enhanced coping are therefore suggested as keeping close relationships active. Public and media educational programs for conditions of multiplicity of life stressful events with transdiagnostic potential consequences, aimed at enhancing individual resilience by utilization of social networks, are herewith suggested, evidence-based[27,28].

***Treatment***

We suggest a combined treatment approach of interpersonal psychotherapy (IPT) and cognitive behavioral therapy (CBT), two evidence-based and cost-effective methods, designed as short-term therapies and found to be equally effective to medications[29] in comparative studies[30,31]. Enhanced close relationships by techniques of problematic interpersonal relations analysis, resolution and role playing adapted from IPT[32], may increase emotional tolerance to accumulating stress emerging from concomitant origins. Our suggested combined psychotherapeutic approach also requires the blending of CBT separate protocols, including techniques for stress reduction and correction of cognitive distortions, rather than following one protocol separately or as recently suggested, one mandatory unified protocol for all types of symptomology[33-36].

We suggested previously that when exposed to multiplicity of stressors, the lack of clear goals implies the diffusion of actions[37]. This could be a risk factor for effective treatment of patients confronted with this type of condensed stressful experience. To overcome this risk and also to respect individual differences, a patient-specific and session-specific therapeutic strategy of assigning clear goals for adaptive coping is warranted, rather than working through a reparation condition or just attempting to eliminate the identified external stressors.

**DISCUSSION**

***The origins of CSRS***

The CSRS emerged from the robust transdiagnostic clinical pictures during and following the pandemic[38]. The World Health Organization indicates a prevalence of 22% of a mixed picture including depression, anxiety, PTSD, and general distress, fatigue, irritability and anger in the general population following the experience of war or natural disaster[39]. Transdiagnostic approaches to classifications were proposed even prior to the COVID-19 pandemic[1-4]. Here we argue that the impact of multiple stressors in daily life is a neglected issue in traditional classifications.

What was probably different about the COVID-19 pandemic compared to previous catastrophes was its global scale and the fact that it was covered extensively by the social, electronic, and print media. This factor may be regarded as an additional stressor in daily life beyond disasters. Whether media use is a source of social support, especially for young people[27,40,41] or a daily life stressor in the form of bombardment of information[42], is still a topic under scientific debate and probably age-related with large inter-individual variance.

Although there is enough evidence to suggest that the mental health of the population deteriorated following the pandemic[43], there are suggestions that the extent of deterioration was less than anticipated[44,45]. In any case, epidemiological studies have shown that anxiety, depression, functional somatic, and even obsessional symptoms can coexist at the population or the community level[38,46,47], supporting our transdiagnostic views and the CSRS.

Inclusion of long COVID symptoms in the CSRS may create the same psychological *vs* physical dispute that we have witnessed with chronic fatigue syndrome or myalgic encephalomyelitis, but we include in the CSRS just neuropsychiatric symptoms, while systemic components of long COVID are excluded. In support of our view, studies that have already started appearing suggest that the long COVID syndrome is more likely to be associated with psychosocial factors rather than the COVID infection itself[48].

Thus, the origins of CSRS are rooted in the multi-faceted stress of the pandemic and its impact on mental health including its residuals in the post COVID era. The relevance of concomitant stressors included in daily life, under regular, non-catastrophic conditions, and their association with a mixed clinical picture, is gradually becoming apparent.

***The CSRS within the debate on psychiatric nosology***

Our opinion goes beyond conventional approaches for construction of psychiatric taxonomy. Alternative concepts of psychiatric validity include controversies between validation of nosological structures (typical for medicine) as compared to prototype, cluster and dimensional diagnosis of mental disorders[49]. While the field of psychiatry moved towards more medically oriented nomothetic knowledge, alternative groups which we follow in our empirical and review papers, suggest that the field has to move away from this type of knowledge towards a more ideographic and subjective approach to psychopathology[49].

The main differences between the validity of dimensional diagnostics and that of traditional nosology are apparent in several aspects: (1) In traditional approaches, mental pathology is regarded as a strict drift from acceptable norms while the transdiagnostic views, similar to ours, suggest an axis between normal and psychopathological conditions; (2) In dimensional approaches co-existing psychopathological states appear in parallel along with personal strengths and capacities for resilience, unlike traditional nomenclature; (3) Dimensional approaches to the convergent and divergent validity of a cluster or co-existence of different pathologies without meeting a full criteria of any category in the conventional systems, such as the CSRS, do justice to the patient and the entire individual clinical picture he or she describes to the clinician, while traditional approaches prefer multiple comorbidities; and (4) The dimensional approaches such as the CSRS, unlike conventional systems, emphasize subjective complaints of the patient (symptoms) rather than signs judged by the clinician. By that, these dimensional approaches are shifting the focus from the powerful societies of professionals towards the patient’s subjectivity, and they recognize that professionals too, have their own subjective perspectives to consider before endorsing a diagnosis based only on signs.

Specifically, the CSRS has shown high reliability, as in two different countries and with two different methodologies similar results were found[25]. Additionally, the CSRS has shown high convergent and divergent validity as a combination of several identified stress symptoms, without meeting any full conventional category. These findings suggest a complex and unique type of reactivity to multiplicity of stressors. Other combinations suggested earlier, as complex anxiety and depression[50] or complex post traumatic stress disorder, showed validity for inclusion of just two conventional categories[51] while others showed a too wide range of inclusion, ruling out the potential judgement of divergent validly[10].

We acknowledge the importance of biological validation of psychiatric illness, but this still cannot be utilized for a treatment per any specified condition until the field of neuropsychiatric science advances considerably. The CSRS implies symptoms more than signs and subjectivity more than objectivity. The treatment derived from the CSRS would be patient-specific and session-specific, as human experience may go back and forth on the axis of elevated symptomology *vs* resilience and adaptive coping. Therefore, the notion of session-specific treatment requires the clinician’s diagnostic effort at every given session to reevaluate the patient’s symptomology for progression *vs* regression and to offer treatment accordingly. We propose that the human experience transits along time that elapses and a condition may be judged for a given patient, in a given environment at a given moment, considering how the observed syndrome has been individually experience-shaped[52-55].

It was noted earlier that the empirical validation used as the basis of conventional categories has been mostly regression statistical analyses with a weak basis for causality[49]. Contrary to any etiological arguments, we argue that the CSRS represents an association between multiplicity of stressors and a mixed clinical picture, which is worth treating to avoid further increase in the patient’s stress reactivity and future limitations of his or her resilience capacities.

We locate CSRS within the blend of the biopsychosocial model (BPS)[56] and the person-centered medicine (PCM) approach[57], as the novel CSRS is related to exogenic stressors (BPS) and occurs as a subjective complex stress reaction of the patient (PCM). Thus, as outlined here and according to our bi-national research design and findings[25], the CSRS falls within the post-modern dimensional approaches more than within any strict nosology, for better prevention and treatment. CSRS was designed and investigated from a humanistic perspective, arguing that mental health is not represented by the lack of psychopathology, while psychopathology, in turn, is a condition with an indication to treat and may be reversible.

**CONCLUSION**

Transdiagnostic considerations towards a change in the classification of mental disorders can be accomplished within the existing systems without ruling out the importance of differential diagnosis if these conventional systems will start to include transdiagnostic phenomena as legitimate conditions for treatment and care. This reduces the risk of diagnosing too many comorbidities and by that precluding appropriate prevention and treatment. We argue that the syndrome termed as CSRS better identifies those patients reacting in a manner that spans several conventional diagnostic categories following exposure to concomitant multiple stressors. Unlike approaches that argue for complete transformation of conventional classifications[1-5], we claim that that a specific diagnosis concerning multiplicity of stressors that result in a mixed clinical picture, is a potential contribution to the revised Diagnostic and Statistical Manual of Mental Disorders and the International Classification of Diseases for more accurate derived prevention and treatment. The future will tell if the openness to include post-modern transdiagnostic approaches to accurately serve more patients in need and to facilitate clinical practice of each individual psychiatrist, will be part of the discussions on the next revisions of the Diagnostic and Statistical Manual of Mental Disorders and the International Classification of Diseases or whether the debate and crisis in psychiatry[58] will continue.

**REFERENCES**

1 **Kotov R**, Krueger RF, Watson D, Achenbach TM, Althoff RR, Bagby RM, Brown TA, Carpenter WT, Caspi A, Clark LA, Eaton NR, Forbes MK, Forbush KT, Goldberg D, Hasin D, Hyman SE, Ivanova MY, Lynam DR, Markon K, Miller JD, Moffitt TE, Morey LC, Mullins-Sweatt SN, Ormel J, Patrick CJ, Regier DA, Rescorla L, Ruggero CJ, Samuel DB, Sellbom M, Simms LJ, Skodol AE, Slade T, South SC, Tackett JL, Waldman ID, Waszczuk MA, Widiger TA, Wright AGC, Zimmerman M. The Hierarchical Taxonomy of Psychopathology (HiTOP): A dimensional alternative to traditional nosologies. *J Abnorm Psychol* 2017; **126**: 454-477 [PMID: 28333488 DOI: 10.1037/abn0000258]

2 **Casey BJ**, Craddock N, Cuthbert BN, Hyman SE, Lee FS, Ressler KJ. DSM-5 and RDoC: progress in psychiatry research? *Nat Rev Neurosci* 2013; **14**: 810-814 [PMID: 24135697 DOI: 10.1038/nrn3621]

3 **Clementz BA**, Sweeney JA, Hamm JP, Ivleva EI, Ethridge LE, Pearlson GD, Keshavan MS, Tamminga CA. Identification of Distinct Psychosis Biotypes Using Brain-Based Biomarkers. *Am J Psychiatry* 2016; **173**: 373-384 [PMID: 26651391 DOI: 10.1176/appi.ajp.2015.14091200]

4 **Reininghaus U**, Böhnke JR, Chavez-Baldini U, Gibbons R, Ivleva E, Clementz BA, Pearlson GD, Keshavan MS, Sweeney JA, Tamminga CA. Transdiagnostic dimensions of psychosis in the Bipolar-Schizophrenia Network on Intermediate Phenotypes (B-SNIP). *World Psychiatry* 2019; **18**: 67-76 [PMID: 30600629 DOI: 10.1002/wps.20607]

5 **Caraci F**, Enna SJ, Zohar J, Racagni G, Zalsman G, van den Brink W, Kasper S, Koob GF, Pariante CM, Piazza PV, Yamada K, Spedding M, Drago F. A new nomenclature for classifying psychotropic drugs. *Br J Clin Pharmacol* 2017; **83**: 1614-1616 [PMID: 28401576 DOI: 10.1111/bcp.13302]

6 **Nasrallah HA**. Re-inventing the DSM as a transdiagnostic model: Psychiatric disorders are extensively interconnected. *Ann Clin Psychiatry* 2021; **33**: 148-150 [PMID: 34398730 DOI: 10.12788/acp.0037]

7 **Sambuco N**, Bradley MM, Lang PJ. Hippocampal and amygdala volumes vary with transdiagnostic psychopathological dimensions of distress, anxious arousal, and trauma. *Biol Psychol* 2023; **177**: 108501 [PMID: 36646300 DOI: 10.1016/j.biopsycho.2023.108501]

8 **Gudmundsson OO**, Walters GB, Ingason A, Johansson S, Zayats T, Athanasiu L, Sonderby IE, Gustafsson O, Nawaz MS, Jonsson GF, Jonsson L, Knappskog PM, Ingvarsdottir E, Davidsdottir K, Djurovic S, Knudsen GPS, Askeland RB, Haraldsdottir GS, Baldursson G, Magnusson P, Sigurdsson E, Gudbjartsson DF, Stefansson H, Andreassen OA, Haavik J, Reichborn-Kjennerud T, Stefansson K. Attention-deficit hyperactivity disorder shares copy number variant risk with schizophrenia and autism spectrum disorder. *Transl Psychiatry* 2019; **9**: 258 [PMID: 31624239 DOI: 10.1038/s41398-019-0599-y]

9 **Gong Q**, Scarpazza C, Dai J, He M, Xu X, Shi Y, Zhou B, Vieira S, McCrory E, Ai Y, Yang C, Zhang F, Lui S, Mechelli A. A transdiagnostic neuroanatomical signature of psychiatric illness. *Neuropsychopharmacology* 2019; **44**: 869-875 [PMID: 30127342 DOI: 10.1038/s41386-018-0175-9]

10 **Parkes L**, Satterthwaite TD, Bassett DS. Towards precise resting-state fMRI biomarkers in psychiatry: synthesizing developments in transdiagnostic research, dimensional models of psychopathology, and normative neurodevelopment. *Curr Opin Neurobiol* 2020; **65**: 120-128 [PMID: 33242721 DOI: 10.1016/j.conb.2020.10.016]

11 **Vardi N**, Zalsman G, Madjar N, Weizman A, Shoval G. COVID-19 pandemic: Impacts on mothers' and infants' mental health during pregnancy and shortly thereafter. *Clin Child Psychol Psychiatry* 2022; **27**: 82-88 [PMID: 33855857 DOI: 10.1177/13591045211009297]

12 **Corley SS**, Ornstein KA, Rasul R, Lieberman-Cribbin W, Maisel H, Taioli E, Schwartz RM. Mental Health Effects of Hurricane Sandy on Older Adults. *J Appl Gerontol* 2022; **41**: 1131-1142 [PMID: 34752154 DOI: 10.1177/07334648211052992]

13 **Ettman CK**, Cohen GH, Abdalla SM, Sampson L, Trinquart L, Castrucci BC, Bork RH, Clark MA, Wilson I, Vivier PM, Galea S. Persistent depressive symptoms during COVID-19: a national, population-representative, longitudinal study of U.S. adults. *Lancet Reg Health Am* 2022; **5**: 100091 [PMID: 34635882 DOI: 10.1016/j.lana.2021.100091]

14 **Stephenson T**, Pinto Pereira SM, Shafran R, de Stavola BL, Rojas N, McOwat K, Simmons R, Zavala M, O'Mahoney L, Chalder T, Crawley E, Ford TJ, Harnden A, Heyman I, Swann O, Whittaker E; CLoCk Consortium, Ladhani SN. Physical and mental health 3 months after SARS-CoV-2 infection (long COVID) among adolescents in England (CLoCk): a national matched cohort study. *Lancet Child Adolesc Health* 2022; **6**: 230-239 [PMID: 35143770 DOI: 10.1016/S2352-4642(22)00022-0]

15 **Cherry KE**, De Vito AN, Calamia MR, Elliott EM, Yu S, Sampson L, Galea S, Mansoor M, McKneely KJ, Nguyen QP. Disaster stressors and psychological well-being in older adults after a flood. *Psychol Aging* 2021; **36**: 660-666 [PMID: 33856820 DOI: 10.1037/pag0000602]

16 **Waddell SL**, Jayaweera DT, Mirsaeidi M, Beier JC, Kumar N. Perspectives on the Health Effects of Hurricanes: A Review and Challenges. *Int J Environ Res Public Health* 2021; **18** [PMID: 33803162 DOI: 10.3390/ijerph18052756]

17 **Fernandez CA**, Choi KW, Marshall BDL, Vicente B, Saldivia S, Kohn R, Koenen KC, Arheart KL, Buka SL. Assessing the relationship between psychosocial stressors and psychiatric resilience among Chilean disaster survivors. *Br J Psychiatry* 2020; **217**: 630-637 [PMID: 32522300 DOI: 10.1192/bjp.2020.88]

18 **Khan F**, Eskander N, Limbana T, Salman Z, Siddiqui PA, Hussaini S. Refugee and Migrant Children's Mental Healthcare: Serving the Voiceless, Invisible, and the Vulnerable Global Citizens. *Cureus* 2020; **12**: e9944 [PMID: 32968603 DOI: 10.7759/cureus.9944]

19 **Bremner JD**, Wittbrodt MT. Stress, the brain, and trauma spectrum disorders. *Int Rev Neurobiol* 2020; **152**: 1-22 [PMID: 32450992 DOI: 10.1016/bs.irn.2020.01.004]

20 **Bustamante LHU**, Cerqueira RO, Leclerc E, Brietzke E. Stress, trauma, and posttraumatic stress disorder in migrants: a comprehensive review. *Braz J Psychiatry* 2018; **40**: 220-225 [PMID: 29069252 DOI: 10.1590/1516-4446-2017-2290]

21 **Arial M**, Gonik V, Wild P, Danuser B. Association of work related chronic stressors and psychiatric symptoms in a Swiss sample of police officers; a cross sectional questionnaire study. *Int Arch Occup Environ Health* 2010; **83**: 323-331 [PMID: 20039177 DOI: 10.1007/s00420-009-0500-z]

22 **Costa E Silva JA**, Steffen RE. Urban environment and psychiatric disorders: a review of the neuroscience and biology. *Metabolism* 2019; **100S**: 153940 [PMID: 31610855 DOI: 10.1016/j.metabol.2019.07.004]

23 **Szabo CP**. Urbanization and mental health: a developing world perspective. *Curr Opin Psychiatry* 2018; **31**: 256-257 [PMID: 29528903 DOI: 10.1097/YCO.0000000000000414]

24 **Goldstein Ferber S**, Shoval G, Zalsman G, Weller A. Does COVID-19 related symptomatology indicate a transdiagnostic neuropsychiatric disorder? - Multidisciplinary implications. *World J Psychiatry* 2022; **12**: 1004-1015 [PMID: 36158308 DOI: 10.5498/wjp.v12.i8.1004]

25 **Goldstein Ferber S**, Shoval G, Rossi R, Trezza V, Di Lorenzo G, Zalsman G, Weller A, Mann JJ. Transdiagnostic considerations of mental health for the post-COVID era: Lessons from the first surge of the pandemic. *World J Clin Cases* 2023; **11**: 809-820 [PMID: 36818632 DOI: 10.12998/wjcc.v11.i4.809]

26 **Lazarus RS**, Folkman S. Stress, Appraisal, and Coping. New York: Springer, 1984

27 **Ferber SG**, Weller A, Maor R, Feldman Y, Harel-Fisch Y, Mikulincer M. Perceived social support in the social distancing era: the association between circles of potential support and COVID-19 reactive psychopathology. *Anxiety Stress Coping* 2022; **35**: 58-71 [PMID: 34652983 DOI: 10.1080/10615806.2021.1987418]

28 **Liu X**, Zhu M, Zhang R, Zhang J, Zhang C, Liu P, Feng Z, Chen Z. Public mental health problems during COVID-19 pandemic: a large-scale meta-analysis of the evidence. *Transl Psychiatry* 2021; **11**: 384 [PMID: 34244469 DOI: 10.1038/s41398-021-01501-9]

29 **van Hees ML**, Rotter T, Ellermann T, Evers SM. The effectiveness of individual interpersonal psychotherapy as a treatment for major depressive disorder in adult outpatients: a systematic review. *BMC Psychiatry* 2013; **13**: 22 [PMID: 23312024 DOI: 10.1186/1471-244X-13-22]

30 **Fairburn CG**, Bailey-Straebler S, Basden S, Doll HA, Jones R, Murphy R, O'Connor ME, Cooper Z. A transdiagnostic comparison of enhanced cognitive behaviour therapy (CBT-E) and interpersonal psychotherapy in the treatment of eating disorders. *Behav Res Ther* 2015; **70**: 64-71 [PMID: 26000757 DOI: 10.1016/j.brat.2015.04.010]

31 **Luty SE**, Carter JD, McKenzie JM, Rae AM, Frampton CM, Mulder RT, Joyce PR. Randomised controlled trial of interpersonal psychotherapy and cognitive-behavioural therapy for depression. *Br J Psychiatry* 2007; **190**: 496-502 [PMID: 17541109 DOI: 10.1192/bjp.bp.106.024729]

32 **Lemmens LHJM**, Galindo-Garre F, Arntz A, Peeters F, Hollon SD, DeRubeis RJ, Huibers MJH. Exploring mechanisms of change in cognitive therapy and interpersonal psychotherapy for adult depression. *Behav Res Ther* 2017; **94**: 81-92 [PMID: 28544896 DOI: 10.1016/j.brat.2017.05.005]

33 **Southward MW**, Terrill DR, Sauer-Zavala S. The effects of the Unified Protocol and Unified Protocol skills on loneliness in the COVID-19 pandemic. *Depress Anxiety* 2022; **39**: 913-921 [PMID: 36372958 DOI: 10.1002/da.23297]

34 **Yan K**, Yusufi MH, Nazari N. Application of unified protocol as a transdiagnostic treatment for emotional disorders during COVID-19: An internet-delivered randomized controlled trial. *World J Clin Cases* 2022; **10**: 8599-8614 [PMID: 36157826 DOI: 10.12998/wjcc.v10.i24.8599]

35 **Halliday ER**, Cepeda SL, Grassie HL, Jensen-Doss A, Ehrenreich-May J. Initial Effects of a Brief Transdiagnostic Intervention on Parent Emotion Management During COVID-19. *Child Psychiatry Hum Dev* 2022: 1-12 [PMID: 35976544 DOI: 10.1007/s10578-022-01409-5]

36 **Ehrenreich-May J**, Halliday ER, Karlovich AR, Gruen RL, Pino AC, Tonarely NA. Brief Transdiagnostic Intervention for Parents With Emotional Disorder Symptoms During the COVID-19 Pandemic: A Case Example. *Cogn Behav Pract* 2021; **28**: 690-700 [PMID: 34629841 DOI: 10.1016/j.cbpra.2021.01.002]

37 **Goldstein Ferber S**, Shoval G, Zalsman G, Mikulincer M, Weller A. Between Action and Emotional Survival During the COVID-19 era: Sensorimotor Pathways as Control Systems of Transdiagnostic Anxiety-Related Intolerance to Uncertainty. *Front Psychiatry* 2021; **12**: 680403 [PMID: 34393847 DOI: 10.3389/fpsyt.2021.680403]

38 **Xiong J**, Lipsitz O, Nasri F, Lui LMW, Gill H, Phan L, Chen-Li D, Iacobucci M, Ho R, Majeed A, McIntyre RS. Impact of COVID-19 pandemic on mental health in the general population: A systematic review. *J Affect Disord* 2020; **277**: 55-64 [PMID: 32799105 DOI: 10.1016/j.jad.2020.08.001]

39 **World Health Organization**. Mental health in emergencies. [cited 10 January 2023]. Available from: https://www.who.int/news-room/fact-sheets/detail/mental-health-in-emergencies

40 **Marciano L**, Ostroumova M, Schulz PJ, Camerini AL. Digital Media Use and Adolescents' Mental Health During the Covid-19 Pandemic: A Systematic Review and Meta-Analysis. *Front Public Health* 2021; **9**: 793868 [PMID: 35186872 DOI: 10.3389/fpubh.2021.793868]

41 **Cauberghe V**, Van Wesenbeeck I, De Jans S, Hudders L, Ponnet K. How Adolescents Use Social Media to Cope with Feelings of Loneliness and Anxiety During COVID-19 Lockdown. *Cyberpsychol Behav Soc Netw* 2021; **24**: 250-257 [PMID: 33185488 DOI: 10.1089/cyber.2020.0478]

42 **Kellerman JK**, Hamilton JL, Selby EA, Kleiman EM. The Mental Health Impact of Daily News Exposure During the COVID-19 Pandemic: Ecological Momentary Assessment Study. *JMIR Ment Health* 2022; **9**: e36966 [PMID: 35377320 DOI: 10.2196/36966]

43 **Pierce M**, Hope H, Ford T, Hatch S, Hotopf M, John A, Kontopantelis E, Webb R, Wessely S, McManus S, Abel KM. Mental health before and during the COVID-19 pandemic: a longitudinal probability sample survey of the UK population. *Lancet Psychiatry* 2020; **7**: 883-892 [PMID: 32707037 DOI: 10.1016/S2215-0366(20)30308-4]

44 **Witteveen AB**, Young SY, Cuijpers P, Ayuso-Mateos JL, Barbui C, Bertolini F, Cabello M, Cadorin C, Downes N, Franzoi D, Gasior M, Gray B, Melchior M, van Ommeren M, Palantza C, Purgato M, van der Waerden J, Wang S, Sijbrandij M. COVID-19 and common mental health symptoms in the early phase of the pandemic: An umbrella review of the evidence. *PLoS Med* 2023; **20**: e1004206 [PMID: 37098048 DOI: 10.1371/journal.pmed.1004206]

45 **Hjorthøj C**, Madsen T. Mental health and the covid-19 pandemic. *BMJ* 2023; **380**: 435 [PMID: 36889801 DOI: 10.1136/bmj.p435]

46 **Goodwin GM**. The overlap between anxiety, depression, and obsessive-compulsive disorder. *Dialogues Clin Neurosci* 2015; **17**: 249-260 [PMID: 26487806 DOI: 10.31887/DCNS.2015.17.3/ggoodwin]

47 **Simon GE**, VonKorff M, Piccinelli M, Fullerton C, Ormel J. An international study of the relation between somatic symptoms and depression. *N Engl J Med* 1999; **341**: 1329-1335 [PMID: 10536124 DOI: 10.1056/NEJM199910283411801]

48 **Selvakumar J**, Havdal LB, Drevvatne M, Brodwall EM, Lund Berven L, Stiansen-Sonerud T, Einvik G, Leegaard TM, Tjade T, Michelsen AE, Mollnes TE, Lund-Johansen F, Holmøy T, Zetterberg H, Blennow K, Sandler CX, Cvejic E, Lloyd AR, Wyller VBB. Prevalence and Characteristics Associated With Post-COVID-19 Condition Among Nonhospitalized Adolescents and Young Adults. *JAMA Netw Open* 2023; **6**: e235763 [PMID: 36995712 DOI: 10.1001/jamanetworkopen.2023.5763]

49 **Di Nicola V**, Stoyanov D. Psychiatric Nosology Revisited: At the Crossroads of Psychology and Medicine. *Psychiatry Cris* 2021: 31-41 [DOI: 10.1007/978-3-030-55140-7\_3]

50 **Curtiss J**, Klemanski DH. Taxonicity and network structure of generalized anxiety disorder and major depressive disorder: An admixture analysis and complex network analysis. *J Affect Disord* 2016; **199**: 99-105 [PMID: 27100054 DOI: 10.1016/j.jad.2016.04.007]

51 **Cloitre M**, Brewin CR, Bisson JI, Hyland P, Karatzias T, Lueger-Schuster B, Maercker A, Roberts NP, Shevlin M. Evidence for the coherence and integrity of the complex PTSD (CPTSD) diagnosis: response to Achterhof et al., (2019) and Ford (2020). *Eur J Psychotraumatol* 2020; **11**: 1739873 [PMID: 32341764 DOI: 10.1080/20008198.2020.1739873]

52 **Goldstein Ferber S**, Weller A, Soreq H. Control System Theory revisited: New insights on the brain clocks of time-to-action reactions. *Front Neurosci* 2023; 17 [DOI: 10.3389/fnins.2023.1171765]

53 **Sirois S**, Spratling M, Thomas MS, Westermann G, Mareschal D, Johnson MH. Précis of neuroconstructivism: how the brain constructs cognition. *Behav Brain Sci* 2008; **31**: 321-31; discussion 331-56 [PMID: 18578929 DOI: 10.1017/S0140525X0800407X]

54 **Ferber SG**. The concept of coregulation between neurobehavioral subsystems: the logic interplay between excitatory and inhibitory ends. *Behavior Brain Sci* 2008; **31**: 337-338 [DOI: 10.1017/S0140525X08004123]

55 **Broadbent H**, Mareschal D. Neuroconstructivism. In: The Encyclopedia of Child and Adolescent Development. United States: John Wiley & Sons, 2020

56 **Smith RC**. Making the biopsychosocial model more scientific-its general and specific models. *Soc Sci Med* 2021; **272**: 113568 [PMID: 33423810 DOI: 10.1016/j.socscimed.2020.113568]

57 **Mezzich JE**, Salloum IM, Cloninger CR, Salvador-Carulla L, Kirmayer LJ, Banzato CE, Wallcraft J, Botbol M. Person-centred integrative diagnosis: conceptual bases and structural model. *Can J Psychiatry* 2010; **55**: 701-708 [PMID: 21070697 DOI: 10.1177/070674371005501103]

58 **Di Nicola V**, Stoyanov D. Psychiatry in crisis: At the crossroads of social sciences, the humanities, and neuroscience. *Psychiatry Cris* 2020; 1-174 [DOI: 10.1007/978-3-030-55140-7]

**Footnotes**

**Conflict-of-interest statement:** All the authors report no relevant conflicts of interest for this article.

**Open-Access:** This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: https://creativecommons.org/Licenses/by-nc/4.0/

**Provenance and peer review:** Invited article; Externally peer reviewed.

**Peer-review model:** Single blind

**Peer-review started:** April 27, 2023

**First decision:** May 25, 2023

**Article in press:** June 19, 2023

**Specialty type:** Psychiatry

**Country/Territory of origin:** United States

**Peer-review report’s scientific quality classification**

Grade A (Excellent): 0

Grade B (Very good): B

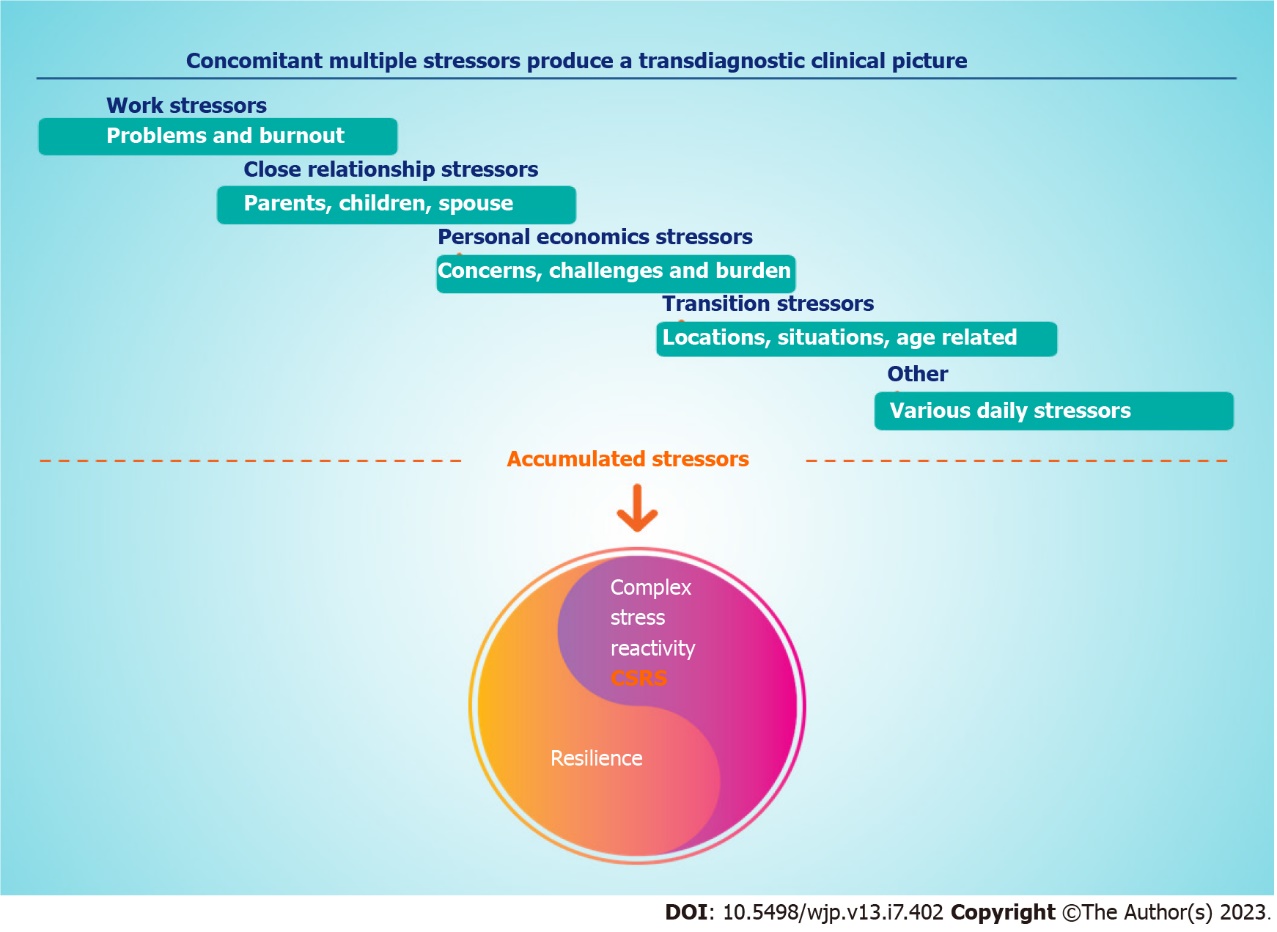
Grade C (Good): C

Grade D (Fair): 0

Grade E (Poor): 0

**P-Reviewer:** Chakrabarti S, India; Stoyanov D, Bulgaria **S-Editor:** Wang JJ **L-Editor:** A **P-Editor:** Wang JJ

**Figure Legends**



**Figure 1 Accumulated stressors in daily life are associated with a mixed clinical picture in the general population.** CSRS: Complex Stress Reaction Syndrome.



Published by **Baishideng Publishing Group Inc**

7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA

**Telephone:** +19253991568

**Email:** bpgoffice@wjgnet.com

**Help Desk:** https://www.f6publishing.com/helpdesk

https://www.wjgnet.com



**© 2023 Baishideng Publishing Group Inc. All rights reserved.**