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Technical Notes

The Network Analysis Profiler (NAP v2.0): a web tool for visual topological comparison between multiple networks

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Abstract

In this article we present the Network Analysis Profiler (NAP v2.0), a web tool to directly compare the topological features of multiple networks simultaneously. NAP is written in R and Shiny and currently offers both 2D and 3D network visualisation, as well as simultaneous visual comparisons of node- and edge-based topological features as bar charts or scatterplot matrix. NAP is fully interactive, and users can easily export and visualise the intersection between any pair of networks using Venn diagrams or a 2D and a 3D multi-layer graph-based visualisation. NAP supports weighted, unweighted, directed, undirected and bipartite graphs.

Introduction

Networks are key representations that can capture the associations and interactions between any kind of bioentity such as genes, proteins, diseases, drugs, small molecules and others (Pavlopoulos *et al.*, 2011, 2015; Pavlopoulos, Wegener, *et al.*, 2008; Pavlopoulos *et al.*, 2013; Kontou *et al.*, 2016; Koutrouli *et al.*, 2020). Gene co-expression networks, gene regulatory networks, protein-protein interaction networks (PPIs), signal transduction networks, metabolic networks, gene-disease networks, sequence similarity networks, phylogenetic networks, ecological networks, epidemiological networks, drug-disease networks, disease-symptom networks, literature co-occurrence networks, food webs, semantic and knowledge networks are the most widely known in the biomedical and biomedical-related fields (Koutrouli *et al.*, 2020). However, not all networks are the same in terms of structure and come with certain topological features. For example, Erdos–Rényi networks are random graphs with no specific structure (Bollobás, 2001), Watts-Strogatz networks are random graphs with small communities (Watts and Strogatz, 1998), and Barabási–Albert networks are random scale-free networks whose degree distribution follows a power law (Barabási and Albert, 1999). While basic topological network analysis is offered by widely used network visualisation applications (Pavlopoulos, Wegener, *et al.*, 2008) such as the Cytoscape (Shannon *et al.*, 2003) and Gephi (Bastian *et al.*, 2009), in this article we present the Network Analysis Profiler (NAP v2.0), a complementary web-based tool designed to fill certain gaps and aid non-experts in not only analysing the topological features of a network, but also to visually perform direct comparisons across multiple network in an easy and user-friendly way.

The application

In its current version, NAP (Theodosiou *et al.*, 2017) supports weighted, unweighted, directed, undirected, simple and bipartite networks. It is implemented in R and Shiny and most of its backend calculations are based on the igraph library (Csardi and Nepusz, 2006). It accepts as input a tab-delimited file in which the first two columns indicate the connections between the nodes and the third column the weight between these edges. Users have the option to upload as many networks as they like, name them accordingly, and process them simultaneously. NAP v2.0 has four main functions: i) Basic Visualisation, ii) Topological analysis, iii) Node/Edge ranking and iv) Intersection network hosting the common vertices and edges between two selected networks.

Basic 2D/3D visualisation

Once a network has been uploaded and named, it is visualised with the use of visNetwork library. VisNetwork

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offers a fully interactive visualisation as it allows network zooming, dragging, and panning. Nodes can be selected and placed anywhere on the plane, whereas the first neighbors of any node can be highlighted upon selection. This network view can show one network at a time and is automatically updated when a different network is selected. In this view, NAP supports the following igraph layouts (Pavlopoulos *et al.*, 2017):

- Fruchterman-Reingold (Fruchterman and Reingold, 1991): it places nodes on the plane using a force-directed layout.
- Random: it places the vertices on a 2D plane uniformly using random coordinates.
- Circle: it places vertices on a circle, ordered by name.
- Kamada-Kawai (Kamada and Kawai, 1989): it places the vertices on a 2D plane by simulating a physical model of springs.
- Reingold-Tilford (Reingold and Tilford, 1981): this is a tree-like layout and is suitable for trees, ontologies and hierarchies.
- LGL (Adai *et al.*, 2004): a force-directed layout suitable for larger graphs.
- Grid: this layout places vertices on a rectangular 2D grid.
- Sphere: this layout places vertices on a rectangular 3D-like sphere.

In addition to the 2D visualisation, NAP offers a fully interactive 3D network visualisation using a force-directed layout. Users can zoom-in and out and interactively drag and drop a node or the whole network and place it anywhere in space. This visualisation is based on the D3.js library and is sufficient for larger graphs, especially when the 2D view becomes overcrowded. An example of a Yeast PPI (Gavin *et al.*, 2002) is shown in Figure 1.

The topological features

In its current version, NAP supports the following igraph-based topological features:

- Number of nodes: the number of vertices in the network.
- Diameter: the length of the longest geodesic. The diameter is calculated by using a breadth-first search like method. The graph-theoretic or geodesic distance between two points is defined as the length of the shortest path between them.
- Radius: the eccentricity of a vertex is its shortest path distance from the farthest other node in the graph. The smallest eccentricity in a graph is called its radius.
- Density: the density of a graph is the ratio of the number of edges divided by the number of possible edges.
- Average path length: the average number of steps needed to go from a node to any other.
- Clustering Coefficient: a metric to show if the network has the tendency to form clusters.
- Modularity: this function calculates how modular is a given division of a graph into subgraphs.
- Number of self-loops: the number of nodes connected to themselves.
- Average Eccentricity: the eccentricity of a vertex is its shortest path distance from the farthest other node in the graph.
- Average Eigenvector Centrality: the influence of a node in a network.

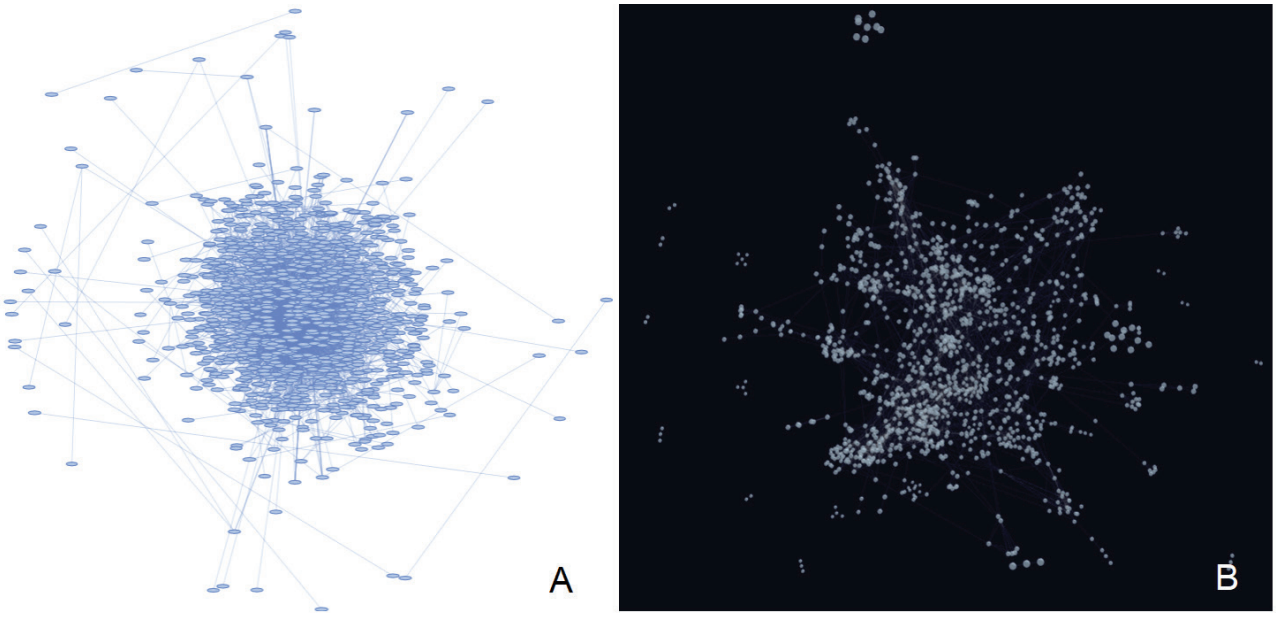

Figure 1. NAP's basic visualisation.
A) 2D visualisation of a Yeast PPI (Gavin *et al.*, 2002) using the Kamada-Kawai layout. **B)** The same network visualised in 3D.

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- Assortativity degree: the assortativity coefficient is positive if similar vertices (based on some external property) tend to connect or negative otherwise.
- Directed acyclic graph: it shows if a graph has cycles or not.
- Average number of Neighbors: the number of neighbors each node of the network has on average.
- Centralization betweenness: an indicator of a node's centrality in a network. It is equal to the number of shortest paths from all vertices to all others that pass through that node. Betweenness centrality quantifies the number of times a node acts as a bridge along the shortest path between two other nodes.
- Centralization closeness: measures the speed with which randomly walking messages reach a vertex from elsewhere in the graph.
- Centralization degree: defined as the number of links incident upon a node.
- Graph mincut: calculates the minimum st-cut between two vertices in a graph. The minimum st-cut between source and target is the minimum total weight of edges needed to remove to eliminate all paths from source to target.
- Motifs-3: searches a graph for motifs of size 3 (Koutrouli *et al.*, 2020).
- Motifs-4: searches a graph for motifs of size 4 (Koutrouli *et al.*, 2020).

While users can select and visualise each topological measure in a numeric form, one can select several of the uploaded networks and directly compare their topological features in different bar charts. Figure 2 shows an example of a direct comparison between two Yeast PPI networks (Gavin *et al.*, 2002, 2006) (generated in 2002 and 2006 respectively) and a random scale-free Albert-Barabasi network consisting of 1000 nodes (generated by NAP's automatic network generators). Bar charts are fully interactive and are produced with the use of the plotly library.

Topological feature pairwise comparison and node/edge ranking

As explained in NAP's v1.0 article (Theodosiou *et al.*, 2017), nodes can be ranked by centralisation degree, centralisation betweenness, clustering coefficient, page rank, eccentricity, eigenvector and subgraph centrality, whereas edges can be ranked by betweenness centrality only. An all-versus-all scatterplot matrix can be generated to show the pairwise correlations between any of the selected topological features (Figure 3). The upper

Figure 2. Direct comparison of fourteen topological features across three different networks.

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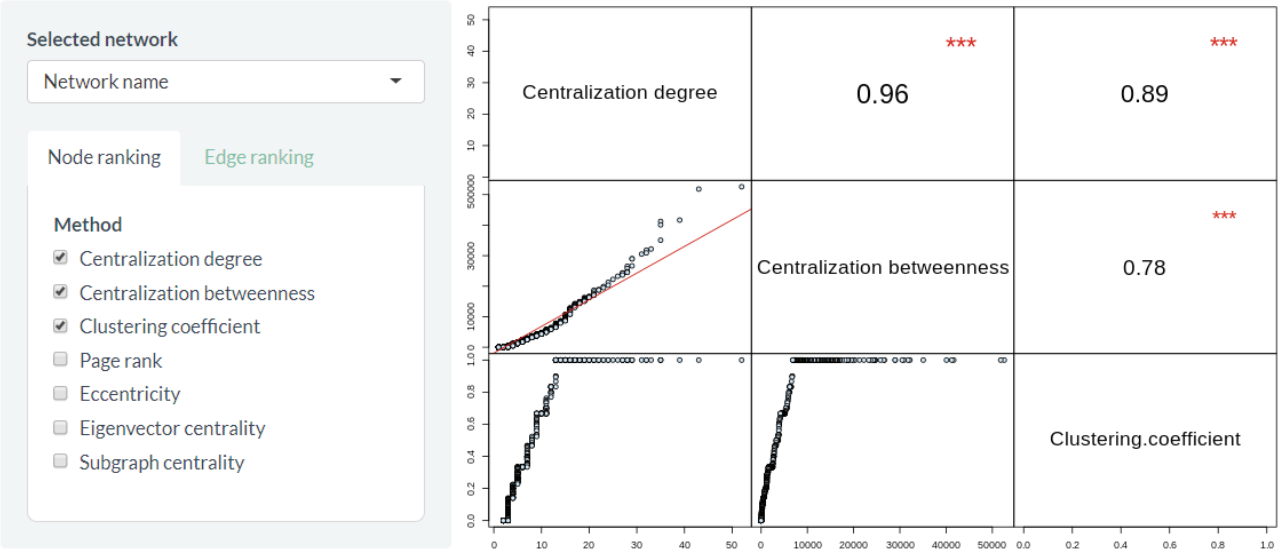

Figure 3. Intra-network pairwise topological feature comparison.

part of the matrix shows the correlation between any pair of features in a numerical form, whereas its lower part shows these correlations in a scatterplot. If only one option has been selected, the viewer will generate a chart showing the values of the selected topological feature in a histogram.

Network intersection

With NAP, users can automatically extract, export, and visualise the common edges and nodes between any selected pair of networks. Common node and edge names will be initially reported in interactive tables as text. In contrast, Venn diagrams are used to show the node/edge union and intersection between the two networks. Venn

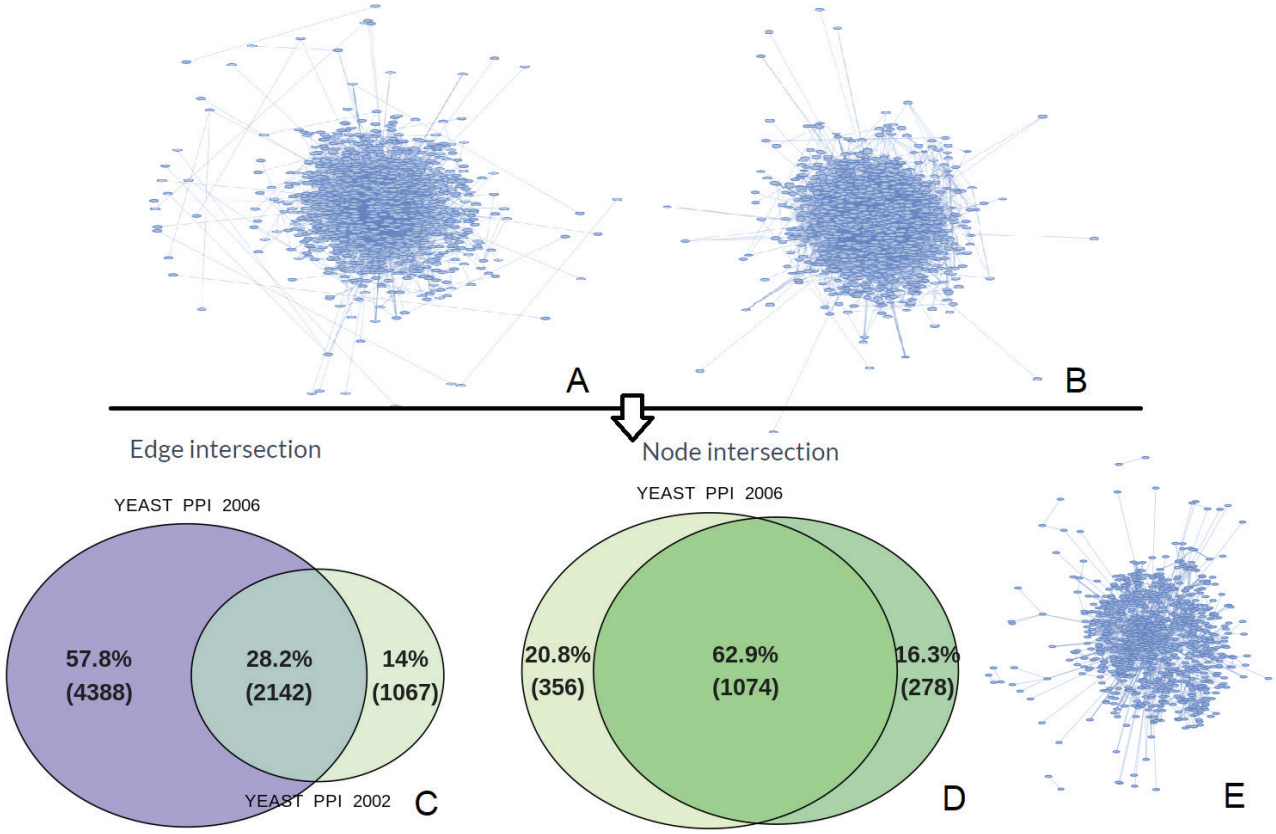

Figure 4. Automatic generation of common edges and nodes between two selected networks. **A)** A Yeast PPI network generated in 2002 (Gavin *et al.*, 2002). **B)** A Yeast PPI network generated in 2006 (Gavin *et al.*, 2006). **C)** 2142 common edges shown in a Venn diagram. **D)** 1074 common nodes shown in a Venn diagram. **E)** The generated network consisting of the common edges between the 2002 and 2006 yeast PPI networks.

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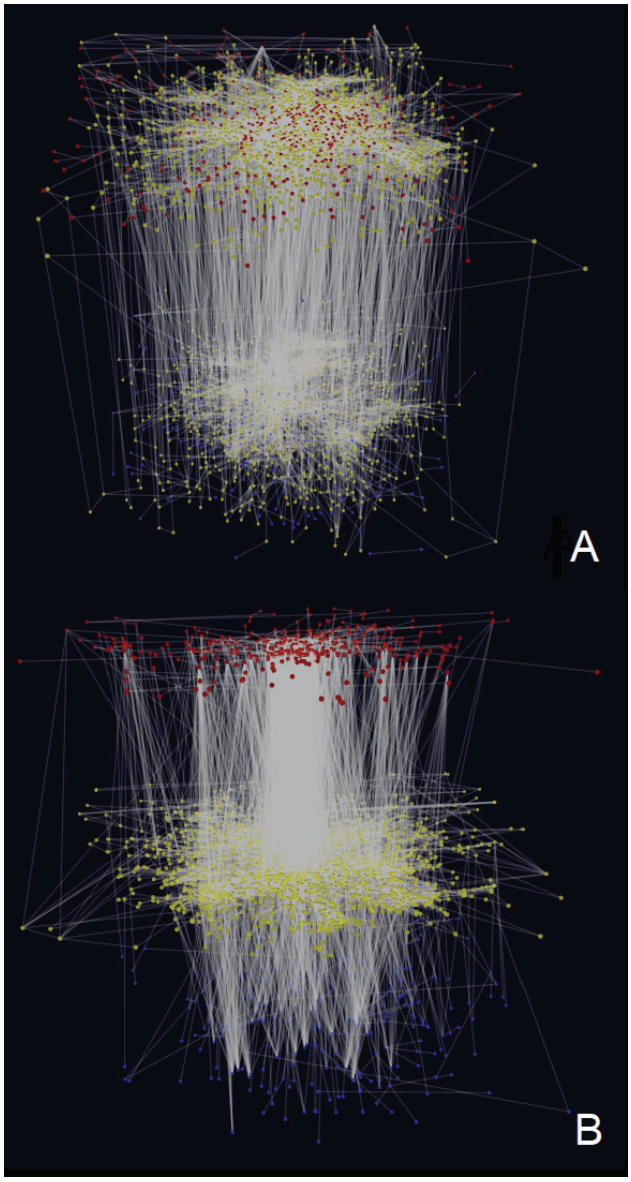

Figure 5. Visualisation of common nodes between two networks using a 3D multi-layer graph. A) Two Yeast PPI networks (2002 and 2006 accordingly) are placed in two different layers and their common nodes are marked yellow. B) Alternatively, common nodes are separated and placed on a third middle layer.

diagrams are generated with the use of Venndiagrams library whereas VisNetwork library is used to visualise the network's intersection in an interactive 2D view. In Figure 4, a comparison between two Yeast PPI networks (Gavin *et al.*, 2002, 2006), generated in 2002 and 2006 respectively is shown.

In addition to the 2D view, NAP gives the option to visualise the common parts between two selected networks using a 3D multi-layer graph implemented in D3.js. Nodes of the first network are placed on a layer and are colored in blue, whereas nodes from the second network are placed on a different layer and are colored in red. Nodes that belong to the two different networks but have the same name are considered as common and are colored in yellow, whereas edges are drawn to connect these nodes across the two layers. Notably, users can use a 3-layer representation to place the common nodes on a third middle layer for a more comprehensive view (not always better).

To minimize the crossovers between the lines across layers, a layout can be initially applied on the whole network and nodes can be separated on their two distinct layers upon completion by adjusting their height coordinate. The layouts that are currently supported by NAP for this view are the random, circular, fruchterman-reingold, fruchterman-reingold grid, kamada-kawai, spring, and LGL force-directed algorithms.

The multi-layer 3D graph is fully interactive, and users can zoom in/out and drag and rotate each node or the whole network in 3D space for easier exploration. In addition, users can export the network in a text file in order to be processed by more advanced third-party 3D visualisers like, for example, Arena3D (Pavlopoulos *et al.*, 2008; Secrier *et al.*, 2012). The whole concept is schematically shown in Figure 5.

Availability

NAP is available at http://bib.fleming.gr:3838/NAP/ and its code can be found at https://github.com/PavlopoulosLab/NAP/

Key Points

- Exploration of network topological features.
- Node/edge ranking by topological properties.
- Simultaneous comparison of topological features between several networks.
- Distribution plotting of any topological feature.
- Usage of various layouts to visualise a network in using interactive 2D/3D views.

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Reviews

COVID-19 features in children and adolescents: a systematic review and pooled analysis

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Abstract

The purpose of the present study was to evaluate special features and probable correlations between symptoms, laboratory findings, treatment, and outcomes of COVID-19 in children and adolescents, through a systematic review and pooled analysis. Following database (Pubmed, Google Scholar, Scopus and Embase) search, forty articles were considered eligible identifying a total of 2,971 confirmed pediatric COVID-19 patients. Fever was reported in 55.1% of the cases, while 28.4% were asymptomatic. Radiological signs of pneumonia were observed in more than half of the cases and in 40.7% of asymptomatic patients. Fever showed the highest sensitivity (sensitivity: 60.3%, specificity: 48.8%), followed by cough (sensitivity: 47.4%, specificity: 76.7%), rhinorrhea (sensitivity: 21.1%, specificity: 88.4%) and diarrhea (sensitivity: 10.3%, specificity: 88.4%), in differentiating cases with positive radiological signs for pneumonia. Compared to school age children, preschoolers (adjusted OR=6.01, 95%CI: 1.73-20.91) were more prone to pneumonia findings. Various combinations of treatments were used across studies, without following any strict guidelines. Most children (>90%) had full recovery and rarely presented complications. Fever seems to be the most frequent symptom in pediatric COVID-19, but pediatricians should additionally evaluate cough, rhinorrhea, and diarrhea as indicators of SARS-CoV-2 infection. Asymptomatic cases were common, but not the majority, and a significant percentage had developed radiologic findings of pneumonia. Thorough reassessment of treatment and management guidelines should be helpful.

Introduction

Since December 2019, when there was the initial outbreak of the novel Coronavirus disease (COVID-19) (Zhu *et al.*, 2020) and after its classification by the World Health Organization (WHO) as a pandemic, on 11 March, 2020, the world is struggling to solve the issues arising by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). The accumulating knowledge and experience, resulting from the numerous cases around the globe, overwhelms the medical community with information that needs to be critically synthesized and presented in a reliable way, so it can be helpful for physicians. By May 1, 2020, there have been more than 3 million confirmed cases and around 233,000 deaths due to COVID-19 (WHO, 2020). According to the literature, 0.9% of the recorded cases were less than 9 years old, and 1.2% were aged between 10 and 19 years (WHO, 2020).

Although there is a number of studies (Hu *et al.*, 2020) reviewing characteristics and symptoms of COVID-19, they are principally referring to adult population. Most review studies are management recommendations (Chen *et al.*, 2020; Kanne, 2020; Shen *et al.*, 2020), based on previously acquired knowledge on SARS caused by other known coronaviruses. There are only few studies or case reports referring exclusively to children and adolescents, that describe with detail COVID-19 characteristics (Ludvigsson, 2020). This might be due to the fact that children and adolescents are more resilient to the disease (Ludvigsson, 2020), presenting with milder symptoms and have a very low mortality rate. Nevertheless, infants (0-1 years) seem to

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be more prone to every kind of infection. The majority of deaths have been described in the age group between 10-19 years (Castagnoli *et al.*, 2020). Thus, there is a need for a full description of the virus characteristics in children and adolescents, to guide early diagnosis and successful management.

Until now, there have been a few systematic reviews considering COVID-19 in children (Castagnoli *et al.*, 2020; Chang *et al.*, 2020; Ludvigsson, 2020). All of them have been based on a small number of reports, the majority of which are derived from China and often suffer from missing data. Castagnoli *et al.* (2020) have highlighted the need for further studies and evaluation in a greater sample. The purpose of the present study is to perform a systematic review and pooled analysis in order to evaluate correlations between symptoms, laboratory findings, treatment and outcome of COVID-19 in children and adolescents. Specifically, this study aims to evaluate sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of symptoms predicting pneumonia in radiological exams, as well as the association of pneumonia radiological findings with sex and age of children and adolescents.

Materials, Methodologies and Techniques

Study Design

The present systematic review and pooled analysis was performed according to the PRISMA guidelines (Liberati *et al.*, 2009). For this review, the Pubmed, Google Scholar, Scopus and Embase databases were searched for eligible studies for the period up to 15 April 2020. The search was limited to this year's publications, as SARS-CoV-2 was first identified in December 2019. The following search algorithm was used: (Covid-19 OR SARS-CoV-19 OR SARS-CoV-2 OR "2019-nCoV" OR "novel coronavirus") AND (child OR children OR pediatric OR pediatrics OR kid OR kids OR youngster OR youngsters OR adolescent OR adolescents OR teen OR teens OR teenager OR teenagers). The references of all the articles that were considered eligible were also thoroughly checked.

Inclusion criteria

Only original research articles (cohort studies, cross-sectional studies, clinical studies, and case series) and case reports written in English were included. The eligible studies should refer to the symptoms, laboratory findings, treatment and infection outcome in children and adolescents exposed to SARS-CoV-2. In order to avoid misleading data, studies with several data missing, or the infection was categorized into "types" without clearly mentioning the symptoms or several data were missing, were excluded. The reported patients should be under 18 years old with confirmed positive COVID-19 infection. No limitations concerning race, sex or journal were imposed. Overlapping populations and any type of unpublished material were excluded.

Eligibility assessment and risk of bias assessment

Two independent reviewers (E.P. and A.T.) performed the screening for eligibility of the retrieved studies. Concerning the risk of bias, the Newcastle-Ottawa Quality Scale (Stang, 2010) was used to evaluate the quality of the included studies. Studies that did not meet the eligibility criteria, studies containing incomplete or irrelevant data, or studies with risk of bias were excluded.

Data extraction

The two reviewers screened the studies that were considered eligible and extracted all relevant data. For each study, the following parameters were collected: Author and year of publication, country where the study was conducted, study design, study period, number of specimens, mean age and age range, gender, health condition of patients before infection, symptoms caused by COVID-19, laboratory findings and outcome of the disease. After the evaluation of data, results were tabulated. Case reports and case studies were categorized separately. All kinds of symptoms mentioned in every eligible study were recorded and infection severity was classified accordingly. Concerning laboratory findings, data were extracted about the total number of white blood cells (WBC), lymphocyte count, neutrophil count, C-reactive protein (CRP), procalcitonin (PCT), d-dimer and imaging findings, computed tomography (CT) scan and where not available, X-rays.

Statistical analysis

All data were recorded in the form of tables and were subjected to statistical analysis (pooled analysis). For categorical variables, frequency and percentage were calculated, while the mean, range and standard deviation (SD) were calculated for continuous variables. Pearson's chi-squared test was used to evaluate associations between nominal variables. Univariate and multivariate logistic regression analysis was performed to evaluate gender and age as potential risk factors of pneumonia radiological findings; odds ratios (ORs) and 95% confidence intervals (CIs) are reported. Kaplan-Meier curves were estimated for time to negativity in nasal/throat swab and fecal tests by age groups and log-rank tests were employed to examine any difference (Šimundić, 2009). Statistical analysis was performed with STATA/SE version 13 statistical software (Stata Corp., College Station, TX, USA).

Results

The database search produced 1,320 studies. After the removal of duplicates and the assessment of 401 items, a total of 40 articles (Zhang, 2020; Cai *et al.*, 2020; Canarutto *et al.*, 2020; Chan *et al.*, 2020; CDC, 2020; Cui *et al.*, 2020; Han *et al.*, 2020; Z. Hu *et al.*, 2020; Huang *et al.*, 2020; Ji *et al.*, 2020; Kam *et al.*, 2020; Le *et al.*, 2020; B. Li *et al.*, 2020; W. Li *et al.*, 2020; Li and Guo, 2020;

Lin *et al.*, 2020; H. Liu *et al.*, 2020; M. Liu *et al.*, 2020; Liu and Zhang, 2020; Y. Liu *et al.*, 2020; Lou *et al.*, 2020; Lu *et al.*, 2020; Ma *et al.*, 2020; Pan *et al.*, 2020; Park and Han, 2020; Qian *et al.*, 2020; Qiu *et al.*, 2020; Robbins *et al.*, 2020; Q. Shen *et al.*, 2020; Sun *et al.*, 2020; Tang *et al.*, 2020; Wang *et al.*, 2020; Wei *et al.*, 2020; Xia and Shao, 2020; Xing *et al.*, 2020; R. Xu *et al.*, 2020; Y. Xu *et al.*, 2020; Zhang *et al.*, 2020; Zheng *et al.*, 2020;Zhu *et al.*, 2020) were considered eligible. The steps regarding the selection of eligible studies are presented in Figure 1.

Among them, 33 were case reports and case studies (118 patients), which presented detailed characteristics of the patients involved, and seven were retrospective cohort studies (2,853 patients), in total 2,971 patients. Low risk of bias was observed for cohort studies; however, the short follow-up periods could represent a compromising factor for the quality of studies.

Case reports and case series

Demographics

Data of case reports and case series (33 in total) are presented in Tables 1 and 2 in Supplementary Data[1]. Most studies derived from China, but there were also cases from Italy, Vietnam, USA and Singapore; a total of 118 children positive for SARS-CoV-2 were recorded [61 (51.7%) males and 57 (48.3%) females]. Their age ranged between 2 days and 18 years (mean age ± SD 6.0 ± 4.8 years). Only 13.5% of the sample were adolescents (>12 years). In most patients (97.4%) the presence of SARS-CoV-2 RNA was detected by real-time fluorescence reverse-transcriptase polymerase-chain reaction (RT-PCR) either in nasopharyngeal and throat swabs or feces. Health status and comorbidity were not clearly mentioned in most studies. Nevertheless, the majority did not seem to have other health problems. Only one case of a 2-month-old male with respiratory syncytial virus (RSV), one case of a 7-year-old female with influenza, one case of an 8-year-old male with acute lymphoblastic leukemia, one case of a 10-month-old female with lacrimal sac dredge, and one case of a 9-year-old male with tonsillitis were reported (Table 1 in Supplementary Data[1]).

Clinical Symptoms

The most frequently reported clinical finding of COVID-19 in children was fever (55.1% of the cases, 64/116), combined or not with other symptoms, while 28.4% (33/116) of the cases were asymptomatic. Fever was the only symptom in 19.8% of the cases (23/116). In a small percentage (16.4%, 19/116), fever was absent. The most commonly recorded symptoms and signs in these cases were cough, sore throat, diarrhea, vomiting, rhinorrhea, tachypnea and crackles, especially in infants. In two studies the clinical symptoms were not recorded (1.7%). It should be mentioned that all cases with

[1]http://journal.embnet.org/index.php/embnetjournal/article/downloadSuppFile/946/946_supp_1

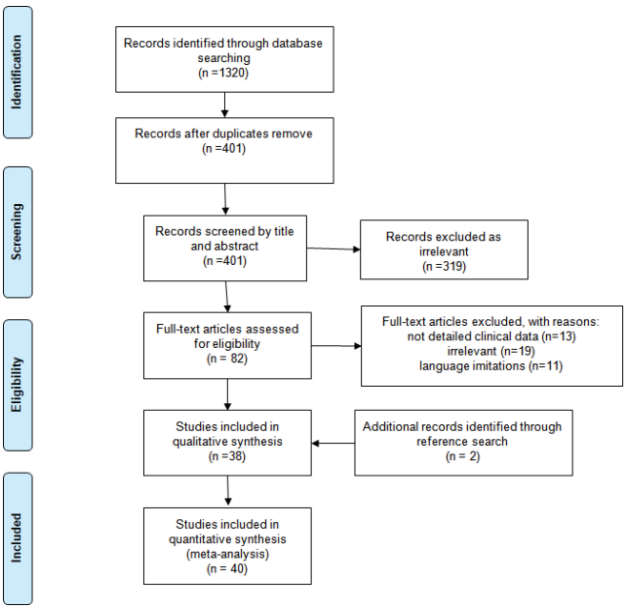

Figure 1. Prisma flow diagram.

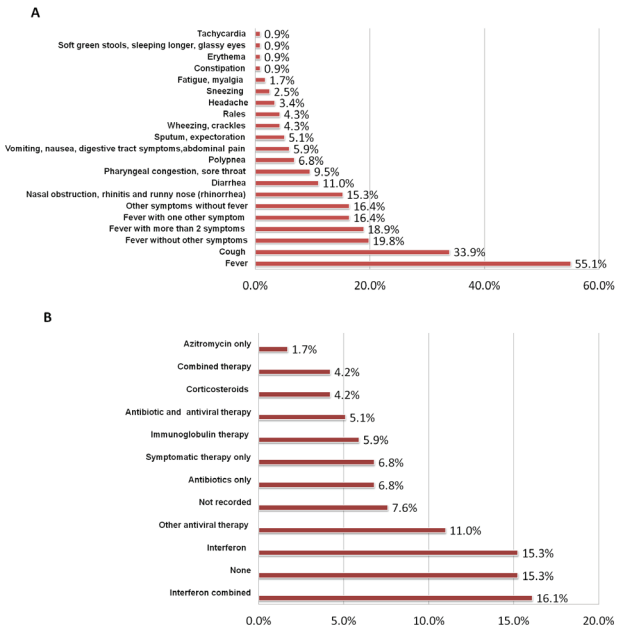

Figure 2. Diagrams - A. Symptoms in children positive with Covid-19. B. Distribution of administered drugs and treatments. Combined therapy: Antibiotic treatment and antiviral treatment and interferon (spray inhalation or nebulization) and glucocorticoids and intravenous immunoglobulin and symptomatic treatment. **Corticosteroids:** alone or combined with other therapies. **Immunoglobulin therapy:** alone or with antivirals and antibiotics or interferon (spray inhalation or nebulization). Other antiviral therapy such as lopinavir, ritonavir, ribavirin, oseltamivir, virazole. **Interferon:** spray inhalation or nebulization. **Interferon combined:** spray inhalation or nebulization, together with antibiotic, other antiviral or symptomatic therapy.

tachypnea were admitted to intensive care unit (ICU) (Sun *et al.*, 2020). There may be a potential association between asymptomatic status and male gender (63.6% cases, Pearson's chi-squared=3.01, p=0.08). Clinical findings in children are represented in Figure 2A.

Laboratory and radiological findings

A detailed analysis of laboratory and radiological findings for each case is presented in Table 2 in Supplementary Data[1]. Some of the included studies did not provide laboratory or radiological findings (14.4%, 17/118). Less than 4% of cases presented deviations from the normal values of WBC, lymphocytes, neutrophils, CRP, PCT or d-dimer (Table 2 in Supplementary Data[1]). More than half of children (57.4 %, 58/101) had positive imaging findings (CT scans or X-rays) suggestive of unilateral or bilateral pneumonia. Interestingly, eleven of them were asymptomatic. The rest of the cases had normal CT scans or X-rays (42.6%, 43/101); 64.3% of them (27/43) presented various clinical symptoms and the rest were asymptomatic. It is worth mentioning that in 4 cases, elevated levels of aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were recorded and that in 22 cases prolonged viral shedding was observed in the feces of patients (Table 2 in Supplementary Data[1]).

Time to negativity in nasal/throat swab RT-PCR test (Table 1 in Supplementary Data[1]), by age groups, is shown in the Kaplan-Meier curve of Figure 3; no significant difference was observed regarding age groups (p=0.43, log-rank test) or gender (p=0.71, log-rank test). Similarly, no difference was noted in time to negativity of fecal tests by age (p=0.55) or gender (p=0.27).

Gender and age as risk factors of pneumonia

As noted above, 57.4% of the patients eventually developed radiological findings suggestive of pneumonia. Table 3 in Supplementary Data[1] presents the results of univariate and multivariate logistic regression analysis examining risk factors for such radiological signs. Compared to children aged 5-11 years, those aged 1 to 4 years presented with 6-fold increased odds of pneumonia findings in CT or X-ray (adjusted OR=6.01, 95%CI: 1.73-20.91); adolescents also showed more frequently radiological images compatible with pneumonia (adjusted OR=2.52, 95%CI:0.79-8.03). Gender was not associated with pneumonia radiological findings (adjusted OR=0.75, 95%CI: 0.32-1.73).

Sensitivity and specificity of symptoms to predict pneumonia

The presence of symptoms predicted radiological pneumonia with a pooled sensitivity of 81.0% (47 out of 58 pneumonias, 95%CI: 68.6-90.1%) and a pooled specificity of 37.2% (16 out of 43 pneumonia-free cases, 95%CI: 23.0-53.3%). The pooled positive predictive value

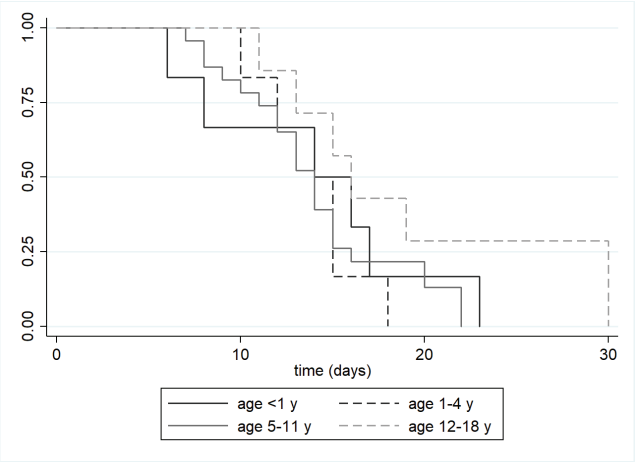

Figure 3. Kaplan Meier curve - Kaplan Meier estimates for negativity in nasal/throat swab RT-PCR test.

was 63.5% (95%CI: 51.5-74.4%), whereas the pooled negative predictive value was 59.3% (95%CI: 38.8-77.6%).

Among individual symptoms, fever (sensitivity: 60.3%, specificity: 48.8%) was most common, followed by cough (sensitivity 47.4%, specificity: 76.7%), rhinorrhea (sensitivity: 21.1%, specificity: 88.4%) and diarrhea (sensitivity: 10.3%, specificity: 88.4%). On the other hand, rhinorrhea and diarrhea showed the highest specificity in differentiating cases with positive radiological signs for pneumonia from negative ones.

Therapeutic management

Multiple combinations of treatments were used in each study (Figure 2B). In a small percentage (7.6%, 9/118) the treatment was not clearly recorded. Many cases, 83.5% (91/109), received therapy 24.2% (22/91) of which were asymptomatic. The remaining 16.5% (18/109) received no therapy at all. Most common treatments were symptomatic (antipyretics, oxygen therapy, vitamin C and Montelukast sodium chewable tablets). Alternative therapies were also applied, such as traditional Chinese medicine and oral probiotics. Antiviral therapy, such as lopinavir (9/109), ritonavir (9/109), ribavirin (14/109), oseltamivir (16/109), virazole (8/109), was mainly administered orally, while interferon was applied as a spray for inhalation or nebulization. Azithromycin was the most frequently used antibiotic (6/109), others being ceftriaxone (2/109), moxifloxacin (1/109), and penicillin G (1/109). Patients in ICU received combined therapies together with hemopurification, enterostomy, transfusions of red blood cells, plasma and thrombocytes (1 case) and plasmapheresis (1 case). It should be noted that most studies referred to therapies generally as "antiviral" or "antibiotics", without providing further details.

Outcome

Missing data concerning the outcome of pediatric COVID-19 were acknowledged in 6 cases (5.1%).

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Most children had full recovery and presented no complications (105/112, 93.7%). Among them, 68.7% (77/112) were hospitalized, of which 24.6% (19/77) were asymptomatic. Only nine children (age range 2m to 15 years, mean ± SD 7.3 ± 5.8 years) were admitted to ICU (8.0%), among them the patient with acute leukemia whose infection was surprisingly uncomplicated. No significant differences were observed between males and females concerning hospitalization (Pearson's chi-squared=1.06, p=0.30) and admission to ICU (Pearson's chi-squared=0.77, p=0.38). Radiological findings of pneumonia were strongly associated with admission to ICU (9/54 children with pneumonia were admitted to ICU vs. 0/41 without pneumonia, p=0.009, Fisher's exact test). Complications were recorded in 3.6% (4/112, 3 males and 1 female) of cases, leading to ICU admission. No deaths were reported.

Retrospective cohort studies

Demographic data about retrospective cohort studies (7 in total) are presented in Table 1 in Supplementary Data[1]. Studies that did not provide clear data about COVID-19 characteristics in children and adolescents were excluded. Regardless of the small sample, the study by Han *et al.* was included in this category as it did not provide personalized details about the patients and could not be considered as a case report. Most studies derived from China, with one study from the USA. The percentage of males ranged between 54.5% and 63.9% , while mean age ranged from 2 to 11 years. Comorbidities were observed more commonly in these studies, although in small percentages, except for the series of Xia *et al.* (35% observed comorbidities) (Xia *et al.*, 2020). Symptoms, laboratory findings, treatments, and outcomes are summarized in Table 2 in Supplementary Data[1]. Fever was reported in the greater part of cases (ranging from 6.3% to 71.4%), while radiological findings of pneumonia were also observed in most of them (rate ranging from 52.8% to 72.7%). Other laboratory findings were relatively normal, expect for the series of Xia *et al.*, where CRP was elevated in 35% of the cases and procalcitonin in 80%; in this study, other pathogens such as Mycoplasma pneumoniae (12%), influenza virus type B (8%), and Enterobacter aerogenes (8%) were also identified (Xia *et al.*, 2020). Diarrhea was also a common symptom with rates up to 57.1% while Han *et al.* reported that digestive tract symptoms were more common in children than adults (p=0.012) (Han *et al.*, 2020). Additionally, elevated AST and ALT levels were also recorded as in case series (Table 2 in Supplementary Data[1]). There were a few data about treatment (3 out of 7 studies), with antiviral therapy and interferon being the most common, with rates up to 100% of the pediatric patients. No complications were observed in the cohort studies but one case of death was reported, in a 10-month-old child with intussusception who presented multi-organ failure and died 4 weeks after admission (Lu *et al.*, 2020); the gender or other details of the deceased child were not reported. Three more deaths are recorded in the case series from the USA, but COVID-19 was not confirmed as the likely cause of death, without providing further information about the latter. Admission to ICU also showed a low rate (0.6-1.8%), while almost all patients presented full recovery.

Discussion

COVID-19 targets mostly adults, with the majority of cases being in the age group between 30 and 79 years old (Chang *et al.*, 2020). Children and adolescents under 18 years old represent less than 5% of cases, a lot of them being asymptomatic (Ludvigsson, 2020). The pandemic led to a great number of reports, mostly referring to adults and presenting insufficient data about children. The descriptive and detailed analysis of pediatric COVID-19 is essential to address special treatment needs and avoid complications in children and adolescents.

A total of 33 case reports and small case series were retrieved in this systematic review. These studies provided sufficient patient data and were subjected to pooled analysis. Additionally, a total of 7 cohort studies were identified, which did not present data at an individual level, but their findings confirmed the results of case reports. Considering the 33 studies, the pooled sample presented a wide age range (between 2 days and 18 years); on the other hand in cohort studies mean age ranged from 2 to 11 years, while male gender slightly predominated (54.5-63.9%).

According to our systematic review and pooled analysis of 33 studies, fever was the most frequent symptom in pediatric patients with an incidence of 54.2% Asymptomatic patients, while not rare, were not the majority of reported cases (28.4%, 33/116), as described in previous studies (Castagnoli *et al.*, 2020; Chang *et al.*, 2020; Ludvigsson, 2020). There was a trend (p=0.08) towards male sex among asymptomatic cases, which was an interesting finding as male sex in adults is considered a risk factor. Diarrhea was the most frequent symptom (11%) after upper respiratory tract symptoms, a pattern that confirms previous reports (Castagnoli *et al.*, 2020; Chang *et al.*, 2020; Ludvigsson, 2020); accordingly, Han *et al.* reported a greater prevalence of digestive tract symptoms in children, compared to adults.

A high prevalence of radiological findings suggestive of pneumonia was noted in cohort studies, ranging between 52.8% and 72.7% (Table 2 in Supplementary Data[1]). Such findings were also observed in more than half of case reports while the pooled analysis revealed that 40.7% of asymptomatic cases might have pneumonia on radiologic exams (pooled NPV=59.3% (95%CI: 38.8-77.6%). This is an important observation that raises the question whether all positive pediatric patients need radiologic examination, a strategy that has been proposed by other authors as well (Ludvigsson, 2020; Shen and Yang, 2020), but not widely adopted as COVID-19 associated pneumonia seems to be mild in children.

The presence of radiologic pneumonia was related to age, as preschoolers were found to develop pneumonia findings more frequently, with a 6-fold increase in odds of positive radiological signs of pneumonia. Fever (sensitivity: 60.3%, specificity: 48.8%) showed the highest sensitivity, followed by (sensitivity 47.4%, specificity: 76.7%), rhinorrhea (sensitivity: 21.1%, specificity: 88.4%) and diarrhea (sensitivity: 10.3%, specificity: 88.4%) in the diagnosis of radiologic pneumonia. Additionally, radiological findings of pneumonia were strongly associated with admission to ICU. This may suggest that presence of radiological/CT lesions in the lungs could be used as an indicator to monitor pediatric patients more closely.

Other laboratory findings did not seem to be affected in the vast majority of case reports and case series. The findings in cohort studies were similar, except for the series of Xia *et al.*, which presented high levels of co-infection with other pathogens. Elevated AST and ALT levels were also recorded in both sets of studies, a fact that should be taken into consideration.

An interesting remark pertains to the fact that administered treatments did not seem to follow any published recommendations (Shen and Yang, 2020); different drugs were administered, regardless of the presence or absence of pneumonia radiological signs. Interferon in the form of nebulization was widely administered in both types of studies; nevertheless, none of the retrieved studies clarified whether the treatment had any effect upon the infection outcome. No complication or delay in the recovery was recorded in cases where no treatment was given. Additionally, no clear guidelines for hospitalization existed, as even asymptomatic children were hospitalized (24.6% of case series). About 90% of the cases had complete recovery, regardless of hospitalization or treatment administration. Thus, there is a need of further longitudinal studies, considering therapy management and guidelines.

Even if pediatric patients seem to have better outcomes, a small percentage was admitted in ICU (8% in case reports/case series and 0.6%-1.8% in cohort studies). Most recently, eight children's cases were described in the UK that were transferred to ICU presenting a Toxic Shock Syndrome (TSS)- Kawasaki-like inflammatory syndrome; four of them had confirmed family exposure to the novel coronavirus but only two of them were tested positive for SARS-CoV-2 (one of them post-mortem) (Riphagen *et al.*, 2020). Additionally, an increase was observed in inflammatory syndromes and TSS in many countries, not directly linked to COVID-19, but raising awareness (ECDPC, 2020). Two of the ICU patients in our systematic review (Sun *et al.*, 2020) were reported with septic shock syndrome. No complications were observed in the cohort studies and full recovery was mentioned in both case series and cohort studies. It should be noted that all patients who required ICU admission in the case series presented tachypnea, which should be considered as a manifestation of more severe disease. Therefore, pediatricians should keep in mind that severe complications of COVID-19, while rare, may eventually develop.

None of the included case reports and case studies has recorded any deaths. Only one case of death was retrieved from the cohort studies, referring to a 10-month-old child with intussusception (Lu *et al.*, 2020). Three deaths were reported in the series from USA (CDC, 2020) but COVID-19 was not confirmed as the likely cause of death. Infection fatality ratio of COVID-19 under 9 years old is estimated to be 0.00016%, and 0.00695% in age groups between 10 and 19 years old (Verity *et al.*, 2020).

Most studies from China followed a classification severity system with five classes and a modified one with four classes, according to officially published guidelines in China. Han *et al.* additionally classified pneumonia into mild (mild pneumonia, asymptomatic infection) and severe. No other specific severity stratification systems for children and adolescents with COVID-19 were recorded in the remaining studies.

Commenting on the limitations of the study, due to the emergency of the subject, the research period was brief, a problem also encountered in previous studies (Castagnoli *et al.*, 2020). Most reports did not provide detailed data, leading to exclusion and reduction of the sample size. Numerous case series and studies were published at the outset of the pandemic and the presence of overlapping individuals in the populations under study cannot be totally ruled out. Language restrictions may also have limited the pool of eligible reports. Another inherent limitation of the pooled analysis pertains to the fact that published case reports/case series are subject to considerable selection bias, as they may represent a subset of more severe cases, seeking treatment in health services.

On the other hand, strengths of this systematic review and pooled analysis include the larger study sample, the separation of case reports and small case series from larger cohort studies, and the inclusion of a substantial proportion of cases from Europe and the USA, while previous reviews contained almost exclusively reports from China.

In conclusion, this systematic review and pooled analysis, highlighted fever as the most frequently reported clinical finding in pediatric COVID-19, followed by cough, rhinorrhea, and diarrhea. Asymptomatic cases, although not rare, were not the majority, whereas male gender might be weakly associated with asymptomatic status. Positive radiological findings of pneumonia were recorded in more than half of the patients, with higher prevalence in preschoolers. Interestingly, radiological lesions were prevalent in patients requiring ICU treatment and 40.7% of asymptomatic cases had pneumonia on radiologic examination. This may suggest that even if many pediatric patients are asymptomatic, they still need close monitoring. Another interesting observation was that rhinorrhea and diarrhea present high specificity in cases with positive radiological findings, while tachypnea may be considered as a predictor of severity. Concerning

the outcome, our study confirms accepted wisdom that pediatric patients tend to have full recovery and rarely present complications, while there is need for a thorough reassessment of treatment and management guidelines.

Key Points

- Fever seems to be the most common symptom in pediatric patients with COVID-19.
- Pneumonia radiologic signs were observed even in asymptomatic pediatric patients.
- Preschoolers seem to be more prone to COVID-19 pneumonia findings.
- Most pediatric patients had full recovery.

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Reviews

The impact of COVID-19 during pregnancy on maternal and neonatal outcomes: a systematic review

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Abstract

Several months after the onset of the epidemic, COVID-19 remains a global health issue. Scientific data on pregnancy, perinatal outcomes and vertical transmission of SARS-CoV-2 are constantly emerging but are still limited and unclear. The purpose of this systematic review was to summarize current evidence on vertical transmission rates, maternal, perinatal and neonatal outcomes and mode of delivery in pregnancies affected by COVID-19. An extensive search was conducted in PubMed, Google Scholar, Embase, and Scopus databases up to June 20, 2020. A total of 133 articles (51 case reports, 31 case series, 40 cohort studies and 2 case-control studies) reporting data from 8,092 subjects (6,046 pregnant women and 2,046 neonates) were considered eligible for inclusion in the systematic review. A substantial proportion of pregnant women with COVID-19 underwent caesarean section (case reports 82.2%, case series 74.2% and cohort studies 66.0%). Regarding vertical transmission, most neonates were tested negative (case reports 92.7%, case series studies 84.2%, cohort studies 97.1% and case control studies 100%). Maternal mortality rates ranged from 1% in cohort studies to 5.7% in case reports; neonatal mortality ranged from 2% in case reports to 3.3% in case series. Vertical transmission of SARS-CoV-2 from mother to child is rare. Careful screening of pregnant women seems important and specific guidelines with evidence-based decision algorithms for the mode of delivery in the context of a pregnancy affected by COVID-19 should be established.

Introduction

Coronavirus disease (COVID-19) is caused by SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) and was first described in Wuhan, China in December of 2019 (Jin *et al.*, 2020). COVID-19 was declared by the World Health Organization as pandemic on March 11, 2020 (Ng *et al.*, 2020) and can result in severe pneumonia, multi-organ failure and death (Hui *et al.*, 2020). Over the last twenty years, two large epidemics of coronaviruses have been recorded, the SARS (Severe Acute Respiratory Syndrome) epidemic with a case fatality rate about 10.5% (WHO) and the MERS (Middle East Respiratory Syndrome) epidemic with a case fatality rate of 34.3% (WHO). According to the literature, the infections caused from SARS and MERS coronaviruses have been associated with serious maternal and neonatal morbidity and mortality, stillbirth and high percentage of spontaneous abortion (Schwartz and Graham, 2020; Wong *et al.*, 2004). The epidemiological data from China

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about COVID-19 have shown that most cases had mild symptoms with a case fatality rate about 2.3%. SARS-CoV-2 seems to be more contagious on close contacts (Wu and McGoogan, 2019), albeit less aggressive than the aforementioned two coronaviruses.

Pregnancy is considered a state of relative immunological suppression, with a reduction in cellular immunity and potential susceptibility to infections (Birkeland and Kristoffersen, 1980; Goodnight and Soper, 2005); changes in hormonal levels, such as beta human chorionic gonadotropin (β-hCG), progesterone and cortisol may mediate pregnancy-related cellular immunity immunosuppression. Additionally, the increase in uterine size causes the diaphragm to rise by 4 cm, enlarging the transverse diameter of the chest by 2 cm and affecting pulmonary volume. On the other hand, the immaturity of the immune system of fetuses and neonates makes them more vulnerable to infections (van Well *et al.*, 2017). Therefore, pregnant women and neonates could be considered a high-risk group for infection during the present pandemic.

Scientific data on pregnancy, perinatal outcomes and vertical transmission of SARS-CoV-2 are rather limited but rapidly accumulating. Over the past months, case reports and cohort studies have reported variable results on the mode of delivery, perinatal outcomes, vertical transmission from mother to infant or intrauterine transmission, and treatment modalities (Lang and Zhao, 2020; Martinelli *et al.*, 2020; Ahmed *et al.*, 2020; Liu W *et al.*, 2020). The purpose of this systematic review was to summarize current evidence on vertical transmission rates, maternal, perinatal and neonatal outcomes and mode of delivery in pregnancies affected by COVID-19.

Materials, Methodologies and Techniques

Study design

The present systematic review was performed according to the PRISMA guidelines (Liberati *et al.*, 2009). A search was performed in PubMed, Google Scholar, Embase, and Scopus databases up to June 20, 2020. The following search terms were used: (Covid-19 OR COVID-19 OR SARS-CoV-2 OR "2019-nCoV" OR "novel coronavirus") AND (gestation OR pregnancy OR pregnant OR gestational OR neonate OR neonatal). Additionally, references of all articles were checked thoroughly.

Inclusion criteria

Only original research articles (cohort studies, cross-sectional studies, case-control studies, case series and case reports) published in the English language were included. Studies referring to pregnancies and/or deliveries of all ages with maternal confirmed COVID-19, with reverse transcription polymerase chain reaction (RT-PCR) and/or positive computed tomography (CT) findings, were deemed eligible. No limitations, such as ethnicity or journal, were considered. Studies with overlapping populations were excluded.

Eligibility assessment and risk of bias assessment

The retrieved studies were screened by three reviewers independently (D.M., A.S. and E.P.). The Newcastle-Ottawa Quality Scale (Ottawa Hospital Research Institute) was used to evaluate the quality of the studies. If there was a disagreement, team consensus followed.

Data extraction

Three authors (D.M, A.S. and E.P.) extracted all relevant data. General information, such as first author's name, location or country, study design, study period, number of participants (pregnancies or neonates), maternal age, gestational age, mode of delivery, treatment, co-morbidity of the mother, maternal and neonatal outcomes and test for COVID-19 were recorded. Data were tabulated; frequencies and percentages for categorical variables were estimated.

Results

Selection of studies

After search in the databases, a total of 666 articles were retrieved. The flow chart describing the selection of studies is presented in Figure 1.

After removal of duplicates, 354 items were selected for extensive review. Out of them, 162 articles were excluded as irrelevant to the topic and 42 articles as reviews (15 systematic reviews and 27 reviews). The remaining 150 full-text articles were subjected to further consideration; of them, 17 articles were excluded because of language (eleven in Chinese, four in French, and two in Spanish). Finally, 133 articles were included in the systematic review (Wang S *et al.*, 2020; Dong L *et al.*, 2020; Wen *et al.*, 2020; Lee *et al.*, 2020; Kalafat *et al.*, 2020; Chen R, Chen *et al.*, 2020; Peng *et al.*, 2020; Lowe and Bopp, 2020; Xiong *et al.*, 2020; Wang *et al.*, 2020; Li *et al.*, 2020; Lang and Zhao, 2020; Schnettler *et al.*, 2020; Iqbal *et al.*, 2020; Piersigilli *et al.*, 2020; Taghizadieh *et al.*, 2020; Xia *et al.*, 2020; Lu *et al.*, 2020; Hong *et al.*, 2020; Blauvelt *et al.*, 2020; Lyra *et al.*, 2020; Kelly *et al.*, 2020; Martinelli *et al.*, 2020; Du *et al.*, 2020; Bani *et al.*, 2020; Rabice *et al.*, 2020; AlZaghal *et al.*, 2020; Nesr *et al.*, 2020; Carosso *et al.*, 2020; Yu *et al.*, 2020; Oh *et al.*, 2020; Kuhrt *et al.*, 2020; Ahmed *et al.*, 2020; Kirtsman *et al.*, 2020; Mehta *et al.*, 2020; Anderson *et al.*, 2020; Dong Y *et al.*, 2020; De Socio *et al.*, 2020; Yilmaz *et al.*, 2020; Baud *et al.*, 2020; Fontanella *et al.*, 2020; Gidlöf *et al.*, 2020; Alonso Díaz *et al.*, 2020; Liao X *et al.*, 2020; Mohammadi *et al.*, 2020; Sinkey *et al.*, 2020; Panichaya *et al.*, 2020; Zamaniyan *et al.*, 2020; Zambrano *et al.*, 2020; Liao *et al.*, 2020; Liu *et al.*, 2020; Yu *et al.*, 2020; Chen *et al.*, 2020; Zhu *et al.*, 2020; Fan *et al.*, 2020; Zeng *et al.*, 2020; Yang *et al.*, 2020; Chen *et al.*, 2020; Vlachodimitropoulou *et al.*, 2020; Khan *et al.*, 2020; Buonsenso *et al.*, 2020; Wu C *et al.*, 2020; Hu *et al.*, 2020; Hantoushzadeh *et al.*, 2020; Baergen and Heller, 2020; Buonsenso *et al.*, 2020;

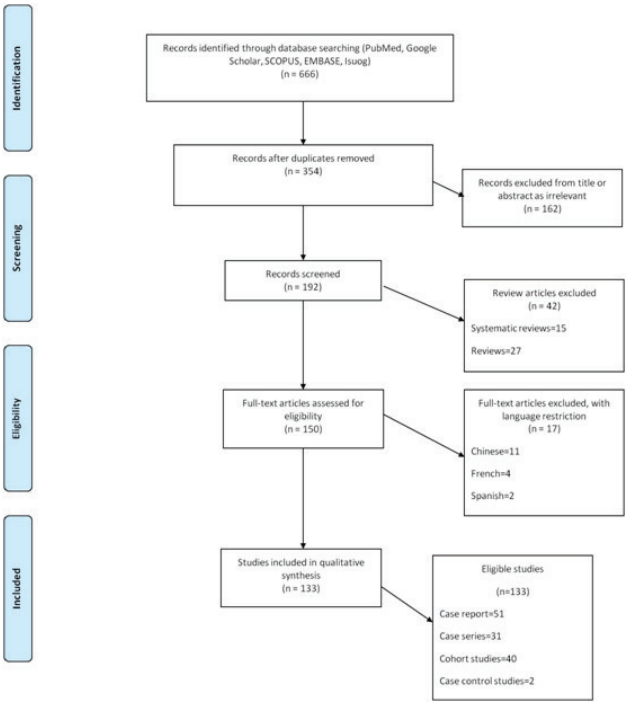

Figure 1. PRISMA flow chart of included studies.

Yu *et al.*, 2020; Juusela *et al.*, 2020; Silverstein *et al.*, 2020; Yassa *et al.*, 2020a; Lucarelli *et al.*, 2020; Govind *et al.*, 2020; Cooke *et al.*, 2020; Dória *et al.*, 2020; Xu *et al.*, 2020; Cao *et al.*, 2020; Andrikopoulou *et al.*, 2020; Huang *et al.*, 2020; McLaren *et al.*, 2020; Breslin *et al.*, 2020; Chen R, Zhang, *et al.*, 2020; Liu H *et al.*, 2020; Liu *et al.*, 2020; Yan *et al.*, 2020; Wu Y *et al.*, 2020; Shanes *et al.*, 2020; Ferrazzi *et al.*, 2020; Penfield *et al.*, 2020; Collin *et al.*, 2020; Qadri and Mariona, 2020; Qiancheng *et al.*, 2020; Wu Xiaoqing *et al.*, 2020; Pierce-Williams *et al.*, 2020; Yang H *et al.*, 2020; Kayem *et al.*, 2020; Knight *et al.*, 2020; Khalil *et al.*, 2020; Chen L, Li, *et al.*, 2020; Lokken *et al.*, 2020; Liao J *et al.*, 2020; London *et al.*, 2020; Patanè *et al.*, 2020; Savasi *et al.*, 2020; Pereira *et al.*, 2020; Khoury *et al.*, 2020; Zeng Y *et al.*, 2020; Sentilhes *et al.*, 2020; Zeng Q-L *et al.*, 2020; Mendoza *et al.*, 2020; Wang Z *et al.*, 2020; Martínez-Perez *et al.*, 2020; Miller *et al.*, 2020; Blitz *et al.*, 2020; Fox and Melka, 2020; Campbell *et al.*, 2020; Emeruwa *et al.*, 2020; Gagliardi *et al.*, 2020; Goldfarb *et al.*, 2020; Li N *et al.*, 2020; Tekbali *et al.*, 2020; Sutton *et al.*, 2020; Fassett *et al.*, 2020; RCOG; Ashokka *et al.*, 2020; Zaigham and Andersson, 2020; Juan *et al.*, 2020; Kotabagi *et al.*, 2020; Ifdil *et al.*, 2020; Zeng L-N *et al.*, 2020; Masjoudi *et al.*, 2020; Wu Yanting *et al.*, 2020; Lee T-Y *et al.*, 2020; Suzuki 2020; Huang J-W *et al.*, 2020; Berthelot *et al.*, 2020; Durankuş and Aksu, 2020). Among them 51 were case reports (100 patients, 52 pregnant women and 48 neonates), 31 case series (390 patients, 211 pregnant women and 179 neonates), 40 cohort studies (4,474 patients, 2,685 pregnant women and 1,789 neonates) and 2 case-control studies (3,128 patients, 3,098 pregnant women and 30 neonates). A total of 8,092 patients, 6,046 pregnant women and 2,046 neonates were included in the systematic review.

Case reports

Demographics in case reports: The 51 case reports (Wang S *et al.*, 2020; Dong L *et al.*, 2020; Alzamora *et al.*, 2020; Wen *et al.*, 2020; Lee DH *et al.*, 2020; Kalafat *et al.*, 2020; Chen R., Chen, *et al.*, 2020; Li Y *et al.*, 2020; Peng *et al.*, 2020; Lowe and Bopp, 2020; Xiong *et al.*, 2020; Wang X *et al.*, 2020; Li J *et al.*, 2020; Lang and Zhao, 2020; Schnettler *et al.*, 2020; Iqbal *et al.*, 2020; Piersigilli *et al.*, 2020; Taghizadieh *et al.*, 2020; Xia *et al.*, 2020; Lu *et al.*, 2020; Hong *et al.*, 2020; Blauvelt *et al.*, 2020; Lyra *et al.*, 2020; Kelly *et al.*, 2020; Martinelli *et al.*, 2020; Du *et al.*, 2020; Bani Hani *et al.*, 2020; Rabice *et al.*, 2020; AlZaghal *et al.*, 2020; Nesr *et al.*, 2020; Carosso *et al.*, 2020; Yu Y *et al.*, 2020; Oh *et al.*, 2020; Kuhrt *et al.*, 2020; Ahmed *et al.*, 2020; Kirtsman *et al.*, 2020; Mehta *et al.*, 2020; Anderson *et al.*, 2020; DongY. *et al.*, 2020; De Socio *et al.*, 2020; Yilmaz *et al.*, 2020; Baud *et al.*, 2020; Fontanella *et al.*, 2020; Gidlöf *et al.*, 2020; Alonso Díaz *et al.*, 2020; Liao X *et al.*, 2020; Mohammadi *et al.*, 2020; Sinkey *et al.*, 2020; Panichaya *et al.*, 2020; Zamaniyan *et al.*, 2020; Zambrano *et al.*, 2020) identified 52 pregnant women (mean ± SD; age 29.7 ± 9.1 years; gestational age 33.1 ± 6.3 weeks) from January 2020 to May 2020. The characteristics of case reports are summarized in Table 1 in Supplementary Data[1]. The cases derived mostly from China (n=15), with US being the second most frequent location (n=11), followed by Italy, UK, Iran, Jordan, and Turkey (n=3), while Korea, Honduras, Sweden, Peru, Australia, Thailand, Spain, Switzerland, Portugal, Belgium, contributed one case each. All women presented to the emergency room for respiratory complications. Among them, 29 women had co-morbid health conditions, *i.e.* gestational diabetes (n=9), obesity (n=9), hypothyroidism (n=5), hypertension (n=3), asthma (n=2), thalassemia (n=1), myotonic dystrophy (n=1), pneumonia (n=1), respiratory failure (n=1), HELLP (hemolysis, elevated liver enzymes, and low platelet count) syndrome (n=1), hepatitis B (n=1), thyroidectomy (n=1), immune thrombocytopenia (ITP) (n=1) and cholecystitis (n=1). All 52 pregnant women had COVID-19, confirmed either through RT-PCR or RT-PCR and CT scans.

Data about delivery in case reports: From the 52 pregnant women, 45 delivered (86%, 45/52) with caesarean section (C-section) (82.2%, 37/45); 7 delivered (15.6%, 7/45) by vaginal route. In one case the mode of delivery was not reported (2.2%, 1/45). From the remaining cases, one had a miscarriage (2%, 1/52), one pregnancy was terminated due to fetal Down syndrome (2%, 1/52) and in 5 cases pregnancy was still on-going or delivery was not reported (10%, 5/52). Fetal distress (19.5%, 7/37), respiratory distress/dyspnea of the mother and pneumonia due to COVID-19 (16.7%, 6/37) and preeclampsia (5.6%, 2/37) were the most common indications for C-section delivery (Table 1

[1]http://journal.embnet.org/index.php/embnetjournal/article/downloadSuppFile/969/969_supp_1

in Supplementary Data[1]). In 12 cases the reason for C-section was not reported (12/37, 37.5%).

Therapeutic management in case reports: Thirty-seven (71.1%, 37/52) women received medication, including hydroxychloroquine (27%, 10/37), azithromycin (27%, 10/37), oseltamivir (16.2%, 6/37), ceftriaxone (13.5%, 5/37), O2 support (13.5%, 5/37), lopinavir (8.1%, 3/37), corticosteroids (without information about the specific agent administered) (13.5%, 5/37), methylprednisolone (8.1%, 3/37), dexamethasone (5.4%, 2/37), remdesivir (5.4%, 2/37), interferon (5.4%, 2/37), oxytocin (2.7%, 1/37) and plasma (2.7%, 1/37). Administration of antivirals (18.9%, 7/37) and antibiotics (21.6%, 8/37) without any other specification were also reported. Due to COVID-19 complications 13 pregnant women were admitted to intensive care unit (ICU) (25% admission rate, 13/52) (Table 1 in Supplementary Data[1]).

Neonatal and maternal outcomes in case reports: A total of 48 neonates were born from the 45 deliveries, including 3 pairs of twins (12.5%, 6/48). The majority of neonates were tested negative for SARS-CoV-2 (84.3%, 32/38), 6 (15.7%, 6/38) were positive for the virus, while for 10 neonates it was not mentioned whether they were tested or not (20.9%, 10/48). Thirty-two neonates were considered healthy (66.6%, 32/48), while 10 were admitted to neonatal intensive care unit (NICU) (20.8%, 10/48) due to prematurity (20%, 2/10), feeding difficulties (10%, 1/10) and precautionary measures for COVID-19 (70%, 7/10). One death was reported 2 hours after birth (2%, 1/48) probably due to maternal COVID-19 and rapid deterioration of her health.

Concerning mother's health, 10 pregnant women (19.2%, 10/52) were in good condition after hospitalization, 13 were discharged (25%, 13/52), 3 were still hospitalized (5.7%, 3/52) and 3 (5.7%, 3/52) succumbed to COVID-19 complications (Table 1 in Supplementary Data[1]).

Case series

Demographics in case series: From the 31 case series, 16 derived from China, 5 from New York City, 2 from Italy, 2 from the UK, 2 from New Jersey, and 1 from Canada, Iran, Portugal and Turkey, respectively, as presented in Table 2 in Supplementary Data[1] (Chen S , *et al.*, 2020; Liu Y *et al.*, 2020; Yu N *et al.*, 2020; Chen H *et al.*, 2020; Zhu *et al.*, 2020; Fan *et al.*, 2020; Zeng L *et al.*, 2020; Yang P *et al.*, 2020; Chen Y., Peng, *et al.*, 2020; Vlachodimitropoulou Koumoutsea *et al.*, 2020; Khan *et al.*, 2020; Buonsenso *et al.*, 2020; Wu C *et al.*, 2020; Hu *et al.*, 2020; Hantoushzadeh *et al.*, 2020; Baergen and Heller, 2020; Buonsenso D *et al.*, 2020; Yu N, Li, Kang, Zeng, *et al.*, 2020; Juusela *et al.*, 2020; Silverstein *et al.*, 2020; Yassa *et al.*, 2020a; Lucarelli *et al.*, 2020; Govind *et al.*, 2020; Cooke *et al.*, 2020; Dória *et al.*, 2020; Xu *et al.*, 2020; Cao *et al.*, 2020; Andrikopoulou *et al.*, 2020; Huang W *et al.*, 2020; Breslin *et al.*, 2020). The 31 case series identified 211 pregnant women (mean ± SD; age 31.4 ± 5.5 years; gestational age 35.7 ± 3.8 weeks). Concerning women's medical history, diabetes (n=18), hypertension (n=15), asthma (n=6), anemia (n=4), hypoxia (n=3), hypothyroidism (n=2), influenza (n=1), polycystic ovary syndrome (n=1), gestational cholecystitis (n=1), placenta previa (n=1), septic shock (n=1), hepatitis B (n=1), anorexia (n=1), vaginal bleeding (n=1), psoriasis (n=1), scoliosis (n=1), severe myopia (n=1) and liver dysfunction (n=1) were recorded (Table 2 in Supplementary Data[1]). All 211 women were confirmed COVID-19 cases through RT-PCR or presented positive findings in CT.

Data about delivery in case series: From 211 pregnant women, 83% (175/211) gave birth, while the remaining were still pregnant during the study period. Concerning the mode of delivery, 130 women (74.2%, 130/175) were subjected to C-section and 45 women (25.8%, 45/175) delivered through vaginal route. The most common indication for C-section was COVID-19 pneumonia (25.4%, 33/130), followed by fetal distress (10%, 13/130) and pre-eclampsia (6.9%, 9/130), while indications were not reported in 43.1% of cases (Table 2 in Supplementary Data[1]).

Therapeutic management in case series: During hospitalization, information about treatment was provided for 70 out of 211 cases (33.2%); in the other 66.8% of cases, treatment-related information was not reported. Hydroxychloroquine (28.5%, 20/70), azithromycin (25.7%, 18/70), lopinavir/ritonavir (21.4%, 15/70), oseltamivir (14.2%, 10/70), ceftriaxone (12.8%, 9/70), and methylprednisolone (7.1%, 5/70) were administered more often. Most women were treated with antivirals and antibiotics and 29 of them (41.4%, 29/70) needed O2 support; 24 women were transferred to ICU (11.4%, 24/211) due to respiratory deterioration and COVID-19 complications (Table 2 in Supplementary Data[1]).

Neonatal and maternal outcomes in case series: A total of 179 neonates were born, including 4 pairs of twins (4.5%, 8/179); 173 were born alive and 6 died (3.3% 6/179). Causes of deaths included refractory shock, multiple organ failure, intrauterine fetal death (n=2) and pre-eclampsia (n=2) of the mother. In many cases neonates were tested for SARS-CoV-2 shortly after birth; 101 were negative (92.7%, 101/109) and 8 were positive (7.3%, 8/109). 70 neonates were not tested or no test was reported (43.6%, 70/179). Most of the neonates were healthy, with some exceptions including fetal growth restriction (n=7), premature rupture of membranes (PROM) (n=3), respiratory distress syndrome (RDS) (n=2), mild pneumonia (n=2), fever (n=1), tachypnea (n=1), asphyxia (n=1), fetal growth discordance (n=1), spontaneous bowel perforation (n=1), talipes (n=1), pyrexia (n=1), cyanosis (n=1) and admission to NICU (n=11) due to precautionary measures for COVID-19 and prematurity (Table 2 in Supplementary Data[1]).

Nine pregnant women presented pneumonia, with respiratory symptoms in most cases (4.3%, 9/211). Twenty-six women were in good health (26.5%, 56/211), twenty-eight were discharged from hospital (13.3%, 28/211), while no data were reported regarding the health of 105 women (49.7%, 105/211). Some women

needed more care, including ventilator support (n=1), support by extracorporeal membrane oxygenation (ECMO) (n=1), ICU (n=1) and re-admission (n=3) in hospital. Seven deaths were reported in mothers (3.3%, 7/211) due to COVID-19 complications (Table 2 in Supplementary Data[1]).

Cohort Studies

Demographics in cohort studies: The 40 cohort studies identified 5,242 pregnant women, from which 2,685 (51% 2,685/5,242) were confirmed cases of COVID-19 through RT-PCR or CT scan (Table 3 in Supplementary Data[1]) and were included in the present study (Chen *et al.*, 2020; Liu *et al.*, 2020; Liu *et al.*, 2020; Liu *et al.*, 2020; Yan *et al.*, 2020; Wu *et al.*, 2020; Shanes *et al.*, 2020; Ferrazzi *et al.*, 2020; Penfield *et al.*, 2020; Collin *et al.*, 2020; Qadri and Mariona, 2020; Qiancheng *et al.*, 2020; Wu *et al.*, 2020; Pierce-Williams *et al.*, 2020; Yang *et al.*, 2020; Kayem *et al.*, 2020; Knight *et al.*, 2020; Khalil *et al.*, 2020; Chen *et al.*, 2020; Lokken *et al.*, 2020; Liao *et al.*, 2020; London *et al.*, 2020; Patanè *et al.*, 2020; Savasi *et al.*, 2020; Pereira *et al.*, 2020; Khoury *et al.*, 2020; Zeng Y *et al.*, 2020; Sentilhes *et al.*, 2020; Zeng Q-L *et al.*, 2020; Mendoza *et al.*, 2020; Wang *et al.*, 2020; Martínez-Perez *et al.*, 2020; Miller *et al.*, 2020; Blitz *et al.*, 2020; Fox and Melka, 2020; Campbell *et al.*, 2020; Emeruwa *et al.*, 2020; Gagliardi *et al.*, 2020; Goldfarb *et al.*, 2020). The age range of women was 18-41 years and the gestational age ranged from 5 to 40 weeks. The majority of studies derived mainly from China (35%, 14/40) and US (35%, 14/40), 4 from Italy (10%, 4/40), 3 from Spain (7.5%, 3/40), 2 from UK (5%, 2/40), 2 from France (5%, 2/40) and 1 from Sweden (2.5%, 1/40), as shown in Table 3 in Supplementary Data[1]. Co-morbidities were reported in 249 pregnant women and included gestational diabetes (22.8%, 57/249), obesity (21.6%, 54/249), hypertension (20.8%, 52/249), hypothyroidism (14.4 %, 36/249), asthma (8.0%, 20/249), and hepatitis B (2%, 5/249).

Data about delivery in cohort studies: In cohort studies, 1,789 neonates were born, including 3 pairs of twins (0.3%, 6/1789) from 1,786 pregnancies. In 378 cases the delivery mode was not mentioned; in the remaining 1,408 pregnancies 929 C-sections (66.0%, 929/1,408) and 479 vaginal deliveries were reported (34.0%, 479/1408). Indicators for C-section were mainly related to COVID-19 symptoms (8.1%, 75/929), fetal distress (3.6%, 34/929) and fetal heart complications (2.4%, 23/929) (Table 3 in Supplementary Data[1]).

Therapeutic management in cohort studies: Treatment details were recorded in 1,267 cases; 25.8% (327/1,267) of pregnant women received antiviral therapy, 18.2% (231/1,267) O2 support, 19.7% (250/1,267) antibiotics, 16.2 % (206/1,267) corticosteroids, 6.4% (82/1,267) hydroxychloroquine, 2.2% (29/1,267) remdesivir, 1.6% (21/1,267) azithromycin, 1%, (13/1,267) interleukin-6 inhibitors, 1%, (13/1,267) convalescent plasma, 0.6% (8/1,267) oseltamivir, 0.3% (4/1,267) lopinavir/ritonavir, and 46 were admitted to ICU (3.6%, 46/1,267) (Table 3 in Supplementary Data[1]).

Neonatal and maternal outcomes in cohort studies: The health status was reported in 316 neonates from a total of 1,789 cases, with 62.2% being admitted to neonatal intensive care unit (NICU) (197/316), 18.6% being completely healthy (59/316), 15.8% being discharged from hospital shortly after birth (50/316), 0.3% presenting with pneumonia (1/316) and 0.3% remaining in hospital (1/316). Neonatal deaths were reported in 2.5% of cases (8/316); five due to COVID-19 (5/316, 1.6%), one to neonatal asphyxia, one to prematurity and one to intrauterine fetal death (IUFD). The majority of neonates (97.1%, 698/719) were tested negative for SARS-CoV-2; 21 were tested positive (2.9%, 21/719); the remaining 1,070 were either not tested or relevant data were not reported (59.8%, 1,070/1,789) (Table 3 in Supplementary Data[1]).

Maternal health outcome was reported in 779 cases. Forty-four pregnant women remained hospitalized (5.6%, 44/779) during the study period, 80.6% were discharged (629/779) and 12.3% were in good health (96/779). One woman needed ventilation and one plasmapheresis. Eight women died (1%, 8/779), due to COVID-19 complications, multiple organ failure and severe respiratory distress (Table 3 in Supplementary Data[1]).

Case-control studies

Two case-control studies were identified (Li N *et al.*, 2020; Tekbali *et al.*, 2020). One study in New York City, in March 2020, compared 3,064 pregnant with 18,916 non-pregnant control women concerning COVID-19-related admission to hospitals. The rates of admission of pregnant/postpartum and control women increased from week 1 to week 4 of the COVID-19 outbreak from 0.14% to 5.65% and from 1.21% to 56.79%, respectively (Table 4 in Supplementary Data[1]).

Another study, conducted in Wuhan, in January to February 2020, compared 34 pregnant women with COVID-19 (n=16) or suspected COVID-19 (n=18) with 121 pregnant women without COVID-19 and 121 pregnant women who had been admitted for other reasons in the past (2019). The COVID-19 group gave birth to 30 neonates (all via C-section) and the control group to 101 neonates (all via C-section). Concerning the health of the pregnant women, three presented with gestational diabetes (8.8%, 3/34), three with gestational hypertension (8.8%, 3/34), one with hypothyroidism (2.9%, 1/34), one with sinus tachycardia (2.9%, 1/34) and one with pre-eclampsia (2.9%, 1/34), and were all discharged home. The main therapeutic treatment administered was antibiotics (100%, 34/34) and antivirals (11.7%, 4/34). No complications in neonatal health were mentioned and all neonates were negative for SARS-CoV-2 (n=30) (Table 4 in Supplementary Data[1]).

Risk of bias: According to Newcastle-Ottawa scale ratings the majority of the 40 cohort studies were

identified as good or fair quality studies (11/40 and 17/40, respectively). Eleven studies were scored as poor quality (Breslin *et al.*, 2020; McLaren *et al.*, 2020; Liu H *et al.*, 2020; Liu W *et al.*, 2020; Ferrazzi *et al.*, 2020; Khalil *et al.*, 2020; Chen L *et al.*, 2020; Lokken *et al.*, 2020; Martínez-Perez *et al.*, 2020; Miller *et al.*, 2020) . Short follow-up period was the most prominent factor compromising the quality of studies. Most studies presented clear inclusion criteria, with detailed description of the sample (pregnant women exposed to SARS-CoV-2, randomly selected) while data were derived from reliable, hospital records. Unadjusted (univariate) estimates were provided as a rule; almost half of the studies included a non-exposed group that matched with the exposed group in factors, such as age, gestational age, delivery mode and comorbidities. In the studies of poor quality, there was no description of the non-exposed group or any comparison with the exposed one.

Discussion

COVID-19 is a global health issue, several months after the onset of the outbreak. Pregnant women are considered a high risk group, not only physically, but psychologically as well (Birkeland and Kristoffersen, 1980; Goodnight and Soper, 2005; Kotabagi *et al.*, 2020; Ifdil *et al.*, 2020; Zeng L-N *et al.*, 2020; Masjoudi *et al.*, 2020; Wu, Zhang *et al.*, 2020; Lee T-Y *et al.*, 2020; Suzuki, 2020; Huang J-W *et al.*, 2020; Berthelot *et al.*, 2020; Durankuş and Aksu, 2020; Yassa *et al.*, 2020b; Corbett *et al.*, 2020). As new data concerning the virus and its transmission are constantly emerging, the present systematic review comprises various types of studies and a considerably larger sample (8,092 patients, 6,046 pregnant women and 2,046 neonates) compared to previous efforts.

There has been a great controversy conserning the vertical transmission of SARS-CoV-2 between positive mothers and embryos. In the present systematic review, the majority of neonates were tested negative (case reports 92.7%, case series studies 84.2%, cohort studies 97.1% and case control studies 100%), while all mothers were tested positive. Our findings are in line with the literature (Dong L *et al.*, 2020; Carosso *et al.*, 2020; Kirtsman *et al.*, 2020; Zeng L *et al.*, 2020; Ferrazzi *et al.*, 2020; Kayem *et al.*, 2020) supporting that vertical transmission does not occur in the majority of neonates (Wang S *et al.*, 2020; Dong L *et al.*, 2020; Wen *et al.*, 2020; Wang X *et al.*, 2020; Bani Hani *et al.*, 2020; Rabice *et al.*, 2020), as there are only a few reports of potential transplacental transmission of the virus (Vivanti *et al.*, 2020). Most studies have shown that there were no clinical findings of COVID-19 in neonates born to affected mothers and all samples concerning amniotic fluid, cord blood, placentas and breast milk, were negative (Chen S., Liao, *et al.*, 2020; Liu Y *et al.*, 2020; Zhu *et al.*, 2020; Breslin *et al.*, 2020; Chen, Zhang *et al.*, 2020). In cases where the neonates were tested positive, the virus might have been transmitted in other ways, such as with touch, droplets or breast milk (Buonsenso *et al.*, 2020); therefore, the value of universal screening of women admitted for delivery has been supported, especially because many positive women are asymptomatic. Thus, it is of paramount importance to screen pregnant women before labor (Sutton *et al.*, 2020; Fassett *et al.*, 2020).

Caesarean section has been the most common mode of delivery since the start of the COVID-19 epidemic and especially in China, with a rate over 90% (Yang H *et al.*, 2020). A previous systematic review reported that about 75% of the infected women delivered by C-section (Corbett *et al.*, 2020). According to the present systematic review, a substantial proportion of pregnant women with COVID-19 underwent C-section (case reports 82.2%, case series 74.2% and cohort studies 66.0%). Recent guidelines suggest C-section to be considered in cases of severe and critical infections while taking into account possible risks (Royal College of Obstetricians and Gynecologists, 2020). On the other hand, a study from Spain reported that deliveries by C-section were significantly associated with clinical deterioration of positive mothers (Martínez-Perez *et al.*, 2020). Additionally, there is no evidence that the rate of neonatal COVID-19 is lower when the baby is born by C-section (Walker *et al.*, 2020), hence, C-section could be applied in cases where other indications also exist (Ashokka *et al.*, 2020).

In many studies the reason for C-section was not mentioned. It is possible that, because COVID-19 complications are not well-known, especially in the vulnerable group of pregnant women and neonates, increased anxiety of both mothers and doctors might have led to rash decisions. Actually, as already mentioned, C-section was the rule in China and other countries during the first months of the pandemic (Martínez-Perez *et al.*, 2020).

According to Zaigham and Andersson (Zaigham and Andersson, 2020), COVID-19 is a risk factor for increased maternal and perinatal morbidity, probably due to higher rates of preterm birth in mothers with COVID-19 (Allotey *et al.*, 2020). Two maternal deaths and only one neonatal death were reported in a recent systematic review, including 324 pregnant women (Juan *et al.*, 2020). Our study comprised a larger sample with mortality rates ranging from 1% in cohort studies to 5.7% in case reports in mothers, and from 2% in case reports to 3.3 % in case series in neonates. Further studies are needed to estimate standardized mortality ratios in COVID-19 pregnant women and their neonates versus pregnant control women, addressing the confounding effects of comorbidities, as pre-existing comorbidities of the mother such as advanced maternal age and high body mass index are potential risk factors for severe COVID-19 during pregnancy (Allotey *et al.*, 2020).

The main limitation of the present systematic review is that most of the currently available studies did

not provide detailed data for participants, probably due to the emergency nature of the subject. Additionally, a substantial amount of evidence was derived from case reports and case series. Moreover, the inadequacy of follow-up periods reduced the validity of cohort studies. Finally, the lack of important data in many studies, such as the positivity of neonates in SARS-CoV-2 testing, mode of delivery and indication for C-section, did not allow extensive analyses.

On the other hand, this systematic review has several strengths as it includes a large sample with detailed data about the mode of labour, morbidity, and vertical transmission. Case reports and case series highlighted important aspects of the disease. Moreover, studies from all continents, except Africa, were included, whereas existing systematic reviews refer mostly to studies derived from China.

In conclusion, according to the present systematic review, vertical transmission of COVID-19 from mother to child is rare. Nevertheless, careful screening of pregnant women seems important in view of adverse health outcomes for the mother and the neonate. Specific guidelines with evidence-based decision algorithms for the mode of delivery in the context of a pregnancy affected by COVID-19 are needed.

Key Points

- Vertical transmission of SARS-CoV-2 from mother to child seems to be rare.
- A substantial proportion of pregnant women with COVID-19 underwent caesarean section.
- Maternal mortality rates ranged from 1% to 5.7% and neonatal mortality from 2% to 3.3%.
- Specific guidelines in the context of a pregnancy affected by COVID-19 are needed.

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Reviews

Stress among pediatric oncology staff. A systematic review

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Abstract

Cancer is considered one of the dominant life-threatening diseases in children. Working in the field of pediatric oncology, although rewarding, can be a source of stress and emotional burden for health care providers. The aim of this systematic review was to summarise the evidence regarding the occupational stress of health care providers working with pediatric cancer patients. Extensive search of the Pubmed and Scopus databases was performed to identify studies relevant to the topic. Initial search retrieved 657 studies. The reviewing investigators, after applying the inclusion/exclusion criteria, extracted data to critically appraise the quality of evidence. The final step of search concluded in 23 studies of heterogeneous design. Results revealed two main domains of which occupational stress derived from i) the interaction of the health care provider with the patient and the family, and ii) several organisational factors, such as hierarchical structures, experience, workload, and low organisational support. Literature on the stress of pediatric oncology staff is limited. The rather small sample sizes of the studies, the heterogeneity of methodological design, the lack of assessment from a sociological point of view, as well as the limited psychometric instruments adapted to pediatric oncology staff, make the validity of the results questionable. Further research is warranted to obtain a more accurate view of the field, to identify a cause-effect relation between work-related stress and pediatric oncology staff, and, more importantly, to guide future recommendations on support systems and stress management training within pediatric oncology settings.

Introduction

Cancer is considered one of the dominant life-threatening diseases in children. According to the World Health Organization, 300,000 new cases are recorded annually up to the age of 19 years (WHO,2020). Working in the field of pediatric oncology and providing psychological and medical assistance in a hospitalsetting can be a rewarding experience. Nevertheless, it can simultaneously be a source of stress and emotional burden for health care practitioners. An intimate interaction between children, parents and pediatric oncology staff is usually developed as part of the hospitalization process. Health care professionals are obliged to deal with the pain of both children and parents (Dilek *et al.*, 2019) due to the frustration deriving from ineffective treatments (Himelstein *et al.*, 2004). Most studies on the occupational stress of oncology practitioners have focused on nurses, mainly because they are those who appear to have the most frequent and intense relationship with children compared to other staff members. Even though a child's condition may not be lethal, solely the fear of death experienced by the family and the child, is an additive stressful factor that nurses are expected to manage. A nurse becomes a personal brace, a care provider, and a family supporter onadaily basis. The multiple roles increase the risk of distress, fatigue, grief and burnout. Emotional distress for pediatric oncology nurses can be provoked by the additional requirements they need to meet, which are often off the job description, the different parental perspectives regarding the illness, and the lack or insufficiency of coping mechanisms. Research has

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shown that two-thirds of nurses do not feel comfortable providing psychological support to families of dying children (Plante and Cyr, 2011), while in another study nurses found communication with the patient's familyas one of the hardest skills to master (Pearson, 2013). Moreover, health care professionals in oncology settings have reported feelings of despair and disturbance as they felt unable to treat the pain of the young patients (Ergün *et al.*, 2005). Under these circumstances, stress is inevitable and may interfere with the professionals' work performance. According to Lazarus and Folkman, work-related stress is considered as a physical and emotional reaction to conditions in which the employee's abilities, resources, or needs are inadequate to meet the work demands (Lazarus and Folkman,1984).

Taking these findings into consideration, the aim of this review was to summarise the literature regarding the most common, high-risk factors that might have caused stress in pediatric oncology health care providers.

Materials, Methodologies and Techniques

Study selection

A comprehensive search of the Pubmed and Scopus databases was conducted to identify research papers relevant to the examined topic. The following search terms were used in each database: "pediatric oncology" OR "paediatric oncology" AND "job stress" OR "work related stress" OR "occupational stress". All search terms were investigated in titles, abstracts and keywords.

Inclusion and exclusion criteria

Studies were eligible for inclusion if published in peer reviewed journals, only in the English language. Studies had to focus on the occupational stress of health care providers solely of pediatric cancer patients, regardless of their profession (*e.g.*, medical or non-medical staff). Other relevant reviews or meta-analyses were not included. Research protocols that did not provide sufficient data were also excluded. Studies focusing on burnout syndrome and not on occupational stress were also excluded from the study.

Results

Basic characteristics of included studies

Initial search yielded 657 studies. After applying the inclusion/exclusion criteria 23 studies were identified and included in this review. The full screening process is illustrated in Figure 1. Data extracted from each study included the first author and year of publication, sample's characteristics, and main results on work-related stress. The characteristics of the included studies are outlined in Table 1 in Supplementary Data[1].

[1]http://journal.embnet.org/index.php/embnetjournal/article/downloadSuppFile/981/981_supp_1

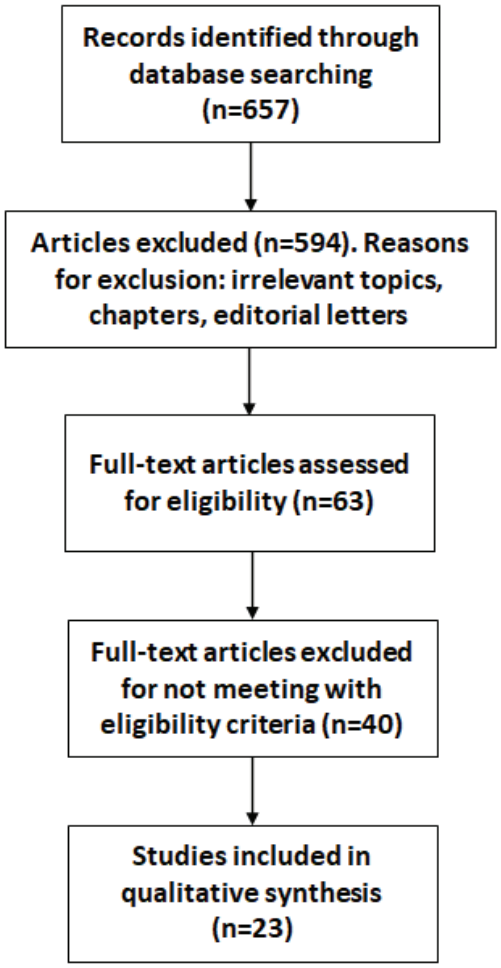

Figure 1. Flow chart of the studies included in the review.

Main Findings

In the study of Kpassagou and Soedje, health practitioners demonstrated high levels of emotional distress which derived from the lack of qualitative medical equipment (Kpassagou and Soedje, 2017). In addition, McCloskey and Taggart highlighted the lack of services, funding and high administration responsibilities, as work-related stress factors (McCloskey and Taggart, 2010). Less experienced nurses have mentioned the lack of consideration by physicians, unit management, and parents as additional stressful factors (Morrison and Morris, 2017), while staff support interventions have appeared available but mostly for doctors compared to nurses (Beresford*et al.*, 2018). Team conflict, bad functioning, and feeling of not being valued by the organization were identified as main stressors (McCloskey and Taggart, 2010; Taylor and Aldridge, 2017; Ostadhashemi *et al.*, 2019; Beresford *et al.*, 2018). In addition, Gallagher and Gormley noted that bone marrow transplant (BMT) nurses experienced lower levels of stress related to the patients'critical condition as years of professional experience increased (Gallagher and Gormley, 2009). Pediatric BMT nurses have also reportedrotating shiftsand short staffing as sources of stress with long working hours as the least

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stressful factor (McCloskey and Taggart, 2010; Gallagher and Gormley, 2009; Hinds, 2000). Stenmarker *et al.* identified as oncologists' stressful factors tasks affecting their leisure time (31.1%), economic discussions (15.5%) and organizational aspects at the place of work (36.6%) (Stenmarker *et al.*, 2009). In another study, oncologists reported both workload and lack of time as their main work burden. However, pediatric oncologists in this study demonstrated low levels of emotional distress (Stenmarker *et al.*,2009). Taylor *et al.* identified as a key stressor the unfamiliarity with a specific treatment for children (Taylor and Aldridge, 2017). Furthermore, social workers' experiences in another study, indicated that a combination of lack of professional competence, low organizational support and professional inferiority caused stress and personal exhaustion (Pergert *et al.*, 2019).

According to Chang *et al.*, nurses noted that 'making mistakes' had the highest mean score in the stressor scale for pediatric oncology nurses (SSPON) despite the availability of clinical support nurses (CSNs). Also, nurses without CSNs pointed higher levels of work-related stress (Chang*et al.*, 2007). This finding was supported by another study where no stress management training was provided (Kpassagou and Soedje, 2017). Another research demonstrated that higher levels of organizational commitment were associated with higher perception of role-related stressors. Also, the level of expertise and different levels of education in nursing were identified as factors affecting stress levels (Hinds *et al.*, 2003). Stress levels seem to be further elevated by increased levels of uncertainty (Af Sandeberg *et al.*, 2020). Mukherjee *et al.*, in a validation study of two psychometric tools, the Work Stressors Scale – Paediatric Oncology (WSS-PO) and the Work Rewards Scale – Paediatric Oncology (WRS-PO) have shown that the sources of work-related stress were multi-dimensional and included general team-centered/organizational stressors (*e.g.* workload, team conflict) (Mukherjee *et al.*, 2014).

Kpassagou and Soedje found that health practitioners experienced high levels of emotional distress which derived from unpredicted treatment failure. Additional sources of emotional distress comprise delivery of bad news to the patients' family (Kpassagou and Soedje, 2017; Bowden *et al.*, 2015; Cline *et al.*, 2020), as well as informing adolescents about their disease (Stenmarker *et al.*,2009). In cases where recovery is not possible, nurses may be asked by the parents to withhold the truth from their child, which is reported to be a cause of great distress (Hopia and Heino-Tolonen, 2019). Another study reported multiple sources of nurses' stress *i.e.*, multiple caregiver roles (*e.g.*, medical, emotional and spiritual care, therapeutic relationships, setting boundaries) (Morrison and Morris, 2017; McCloskey and Taggart, 2010; Taylor and Aldridge, 2017). According to Klassen *et al.* some health care providers described communication problems/conflicts with the patients' parents (*e.g.*, family refuses to stop treatment) as additional stressors (Klassen *et al.*, 2012). On the other hand, pediatric nurses experienced distress derived from the lack of time to build a close relationship with the family (McCloskey and Taggart, 2010). Papadatou *et al.*, identified additional sources of stress with the use of a scale with the most and least stressful conditions as perceived by oncologists and nurses. The participants organised, in hierarchical order, the conditions of distress (Papadatou *et al.*, 2002). Caring for a dying child and witnessing pain were considered the most stressful conditions (McCloskey and Taggart 2010; Chang, 2007; Papadatou *et al.*, 2002; Hinds, 2000). For both the doctors and nurses, the unexpected death of a patient was considered as a highly stressful event. Half of the nurses were more distressed than the physicians because of their longstanding relationship with the children (Papadatou *et al.*, 2002). The intimate relationship built with children and families was addressed asboth stressful and rewarding (Taylor and Aldridge, 2017; Bowden *et al.*, 2015), while being the bearer of "bad news" was found to be very stressful amongst translators for families of different nationalities (Cline *et al.*, 2020). Furthermore, nurses rated as less stressful losing the patient at home rather than in the hospital (De Carvalho *et al.*, 2005). In another study, pediatric BMT nurses ranked the three top work-related stressors in order of importance and the most stressful factor was critical illness of the patients (Gallagher and Gormley, 2009). Furthermore, nurses reported demanding families and dying patients as sources of stress (Gallagher and Gormley, 2009; Bowden *et al.*, 2015).

Provision of palliative care seemed to be a burden for physical and mental health, causing repetitive distressing dreams (Fanos, 2007) and high levels of somatization (Stenmarker *et al.*, 2009). According to some studies, job satisfaction, life satisfaction, high sense of coherence, social support and perceived effectiveness seemed to mediate stress responses (Stenmarker *et al.*, 2009; Rheingans, 2008; Hinds *et al.*, 2003).

The importance of a parents' capability and resources to support the upbringing and development of their children during hospitalization has been addressed by Hopia and Heino-Tolonen. According to their study, the lack of resources prevented some parents from spending enough time with their children and resulted in feelings of loneliness for the child. These situations generated stress and feelings of sadness in the nursing staff as well (Hopia and Heino-Tolonen, 2019).

Discussion

In this review two domains of work-related stress among pediatric oncology staff were identified. The first domain included organizational issues such as workload and time pressure, and communication with colleagues. Specifically, health care providers were affected by the lack of colleagues' consideration, medical supplies, medical staff, and the fear of making mistakes. The second domain included interactions of the health care provider with the patient and the family *i.e.*, provision of

palliative care, conflicting points of view about necessary patient care, communication with patients' families, multiple responsibilities, witnessing pain and patient loss. Although most health care providers experienced high levels of stress, no support systems were provided by the hospitals' administration systems. Health care practitioners in the study of Kpassagou and Soedje reported increased emotional distress due to the lack of training in coping with loss of a life and prolonged patient suffering (Kpassagou and Soedje, 2017). Even in cases where support was provided, only one study concluded that health care providers benefited from it with respect to their stress levels (Chang *et al.*, 2007).

Literature on stress of pediatric oncology staff up to date is limited. The relatively small sample sizes, as well as the limited psychometric instruments adapted to pediatric oncology staff, make the results' validity questionable. Furthermore, most quantitative studies did not apply the same measurements. In addition, the heterogeneous methodological approaches with respect to study design cannot conclude in results with certainty. Worth mentioning is the fact that the cross-sectional design of some of the studies cannot investigate cause-effect relationship, and mediating factors may have affected the results.

Further research is needed to establish the cause-effect relation between work-related stress and pediatric oncology staff. Future recommendations should include support systems and stress management training within hospitals especially to pediatric oncology staff exposed to highly stressful circumstances. Policy makers should develop and implement interventional programs on the management of pediatric oncology workers' stress. Common interventions implemented to increase nurse's resilience include workshops, focus groups, mindfulness techniques and educational seminars regarding the effects of stress and possible ways of its management (Boyle and Bush, 2018). Concerns have been raised regarding the psychological support that doctors and nurses need (Beresford *et al.*, 2018). This is on some degree questionable, since research demonstrated that nurses and not doctors are those who are mostly exposed to work-related stress. Finally, a factor that should be considered while developing prevention programs in pediatric oncology settings, is that of accessible clinical support by all professionals. This is of high importance due to cultural differences among doctors and nurses, with the former appearing in less need for support as they appear more "resilient" and distant (Hopia and Heino-Tolonen, 2019). Careful development of effective intervention programs for stress management of pediatric oncology staff could lead to a more sufficient clinical practice and consequently contribute to the amelioration of life quality of hospitalized children suffering from cancer.

Key Points

- Working in pediatric oncology settings can be a source of stress for health professionals.
- Organisational issues, interaction with families and coping with illness and death are among the most stressful factors.
- Nurses experience higher stress levels compared to other health professions dealing with pediatric cancer.
- Stress management intervention programs for health care providers should be embedded in pediatric oncology settings.

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Research Papers

Study of the Langat virus RNA-dependent RNA polymerase through homology modeling

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Abstract

Langat virus is a member of the *Flaviviridae* family and a close relative of a group of important tick-borne viruses that cause human encephalitis. RNA-dependent RNA polymerase is a significant component of the replication mechanism of the *Flaviviridae* viral family. In the present work, a three-dimensional model of the Langat virus RNA-dependent RNA polymerase was designed through homology modeling. The experimentally determined structure of the RNA-dependent RNA polymerase of Dengue virus type II, another member of the same viral family, was employed as template for the homology modeling process. The resulting model underwent a series of optimisations and its quality was verified using the Verify3D algorithm. Important functional characteristics of the family of viral RNA-dependent RNA polymerases were identified in the generated model, thus affirming the potential for its use in the possible design of anti-viral agents for Langat virus.

Introduction

The genome of the *Flaviviridae* viral family is a single-stranded, non-segmented RNA, usually 9.5-12.3 kilobases long. It contains a large open reading frame (ORF), with untranslated regions (UTRs) at the 5' and 3' ends. The 3' end of the RNA molecule is non-polyadenylated, while the 5' region presents variability among the various genera (Dimmock *et al.*, 2016). The open reading frame codes for a polyprotein, which is subsequently cleaved by viral and cellular proteases in specific positions, resulting in roughly ten to twelve structural and non-structural proteins. The structural proteins are located in the N-terminal part of the polyprotein, while the non-structural (NS) proteins are located in the C-terminal part (Vlachakis *et al.*, 2012). Structural proteins play a key role in the formation of the viral capsid and envelope, while the non-structural proteins participate in the replication of the viral genome in the cytoplasm (Choi and Rossmann, 2009).

One of the non-structural proteins produced by the cleavage of the polyprotein is NS5, which contains two domains, the N-terminal methyltransferase domain, and the C-terminal RNA-dependent RNA polymerase (RdRp) domain (Murray *et al.*, 2008). RdRp is a critical component of the replication complex, along with helicase and other viral and cellular proteins (Vlachakis and Kossida, 2013; Vlachakis *et al.*, 2013a). During viral replication, the complex first synthesises the complementary strand of the positive-sense RNA strand, creating a double-stranded RNA intermediate. The negative-sense strand of this double-stranded RNA then serves as the template for the synthesis of a new positive-sense RNA strand, which in turn can function as an mRNA molecule for the production of viral proteins, and as genetic material to be packaged into newly-formed virions (Dimmock *et al.*, 2016).

The conformation of viral RdRps resembles a right hand, with subdomains of "fingers", "palm" and "thumb" that internally form a channel for binding of the template molecule (Wu *et al.*, 2015; Papageorgiou *et al.*, 2016). The RdRp of the flavivirus genus follows the same architecture, with the three mentioned subdomains and a

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priming loop in the thumb subdomain that is speculated to play a role in making certain that de novo initiation is correct (Duan *et al.*, 2019). The subdomains include seven structural motifs, motifs A to G, that assume key roles in the enzyme's function, including binding of nucleoside triphosphates (NTPs) and catalysis (Choi and Rossmann 2009; Venkataraman *et al.*, 2018).

Langat virus is a flavivirus and a member of the Tick-borne Encephalitis Virus serocomplex (TBEV serocomplex), along with several other important pathogens that cause human disease, such as Tick-borne Encephalitis virus, Powassan virus and Omsk hemorrhagic fever virus (Gritsun *et al.*, 2003). There have been no recorded cases of human disease caused by Langat virus, a fact that has previously led to the experimental usage of the virus in attenuated vaccines against the more virulent members of the aforementioned serocomplex. However, studies involving the inoculation of lab mice with Langat strains as well as preliminary studies in primates and human volunteers, showed a considerable rate of neurological disease post vaccination (1:10.000 vaccinations) (Seamer and Randles, 1967; Gritsun *et al.*, 2003; Rumyantsev *et al.*, 2006; Maffioli *et al.*, 2014). These findings possibly indicate a potential risk for Langat virus to acquire pathogenic status concerning humans. In this mindset, insights into the molecular mechanisms of the virus' replication can prove useful towards the understanding of the virus' life cycle, as well as towards the possible future development of anti-viral agents (Vlachakis, 2009; Vlachakis *et al.*, 2013b). So far, the crystal structure of the RNA-dependent RNA polymerase of Langat virus has not been determined. Hence, in the present work, the three-dimensional (3D) model of the Langat virus RNA-dependent RNA polymerase was designed using a homology modeling approach, by employing the experimentally determined crystal structure of the RNA-dependent RNA polymerase of a virus of the same family, Dengue virus type II (DENV2), as template. The construction of such model can offer a reliable basis for the potential design of anti-viral agents, such as inhibitors (Papageorgiou *et al.*, 2014), in the hypothetical scenario that the virus exhibits capabilities of infecting humans.

Methods

Sequence analysis

The amino acid sequence of Langat virus NS5 was retrieved from GenBank database (accession no.: NP_740302.1, entry name: nonstructural protein NS5 [Langat virus]). Protein-protein BLAST algorithm (Altschul *et al.*, 1997) was used through NCBI (Benson *et al.*, 2017) to search for similar protein sequences, using RCSB as the search set. Dengue virus type II NS5 was highlighted as the most suitable to be used as a template. More detailed sequence alignment between the two proteins was carried out using CLUSTALW (Thompson *et al.*, 1994), while the visualisation of conserved residues and RdRp motifs present in the two amino acid sequences was performed with GeneDoc (Nicholas and Nicholas 1997). Secondary structure prediction was carried out using the NPS server (Combet *et al.*, 2000), to ascertain that the alignment would allow the continuation of the process to the next step of homology modeling.

Homology modeling

The 3D modeling of the Langat virus RdRp was carried out using MOE (Molecular Operating Environment, version: 2016.0801) and the incorporated structure-based homology modeling module (Santiago *et al.*, 2008). The crystal structure of DENV 2 NS5, chain A (PDB entry: 4V0R), was used as the template for the homology modeling process (Zhao *et al.*,2015). Homology modeling in MOE adheres to the following general outline. Regions of the template are copied to assign an initial partial geometry for the sequence. Subsequently, residues with unassigned backbone coordinates are modeled. Lastly, loops are chosen, and side chains are modeled, producing a set of independent models, out of which the best scoring one is selected as the final model. Evaluation of the generated model's stereochemistry is carried out by the incorporated "Protein Geometry" function.

Model optimisation

The produced model was further refined with the energy minimisation tool in MOE, using CHARMM27 force field and a dielectric constant of 4 until the conjugate gradient was less than 10-5 kJ/(mol Å), to remove geometrical strain. Additional evaluation of the model's quality was carried out using Verify3D. This method investigates the similarity of a 3D model with its own amino acid sequence. Considering the environment of every residue, an assortment of known, reliable structures is used to assign a score to each of the twenty amino acids, resulting in a 1D-3D profile (Eisenberg *et al.*, 1997). Finally, the produced model of the Langat virus RdRp was superimposed on the 3D structure of the DENV2 RdRp template to explore similarities and differences between them in terms of secondary and tertiary structure elements, as well as in terms of the respective residues in the amino acid sequences.

Results

The amino acid sequences of Langat virus NS5 and DENV2 NS5 were first aligned using the protein-protein BLAST algorithm, resulting in a query cover value of 98% and a percent identity value of 58.8%. Subsequently, CLUSTALW was used for a more detailed alignment of the two sequences and all known RdRp motifs were found to be conserved in the amino acid sequence of Langat virus NS5 (Figure 1).

Since sequence alignments are unable to take secondary structure elements into account, it was important to evaluate the quality of our alignment and the gaps that the alignment program may have inserted

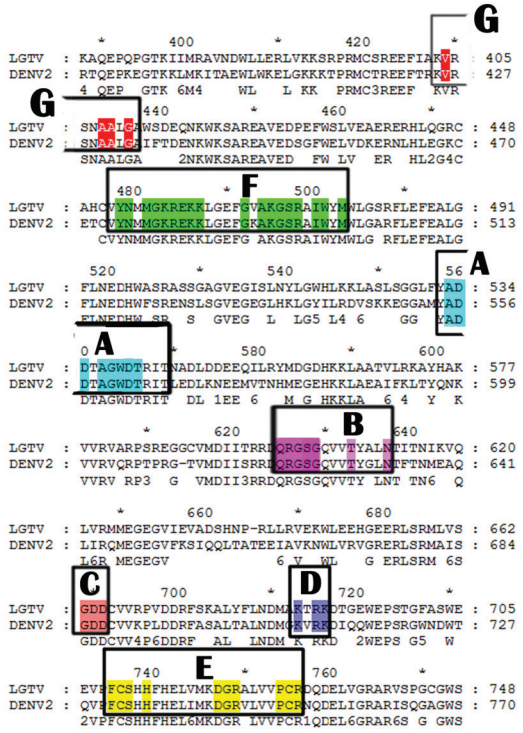

Figure 1. Sequence alignment of the Langat virus (LGTV) RdRp and Dengue virus type II (DENV2) RdRp (entirety of alignment not depicted). The seven major motifs (A-G) of *Flaviviridae* RdRps are highlighted.

during the alignment. Towards that goal, the NPS server was used to generate a prediction of the secondary structure elements of the Langat virus NS5. As shown in Figure 2, areas of the target sequence with insertion of gaps during the alignment did not correspond to areas where secondary elements such as an alpha-helix or a beta-sheet had been predicted. Hence, these secondary elements appeared intact, ensuring the alignment was correct and allowing a homology modeling approach.

The DENV2 RdRp has been experimentally determined by X-ray crystallography at 2.3Å. Secondary structure prediction performed on the Langat virus RdRp revealed significant similarity to the corresponding structural elements of the DENV2 RdRp. Following the completion of the homology modeling process, the produced model was superimposed to the template, exhibiting an RMSD value of 0.86Å, and was subsequently evaluated within MOE and the incorporated "Protein Geometry" module. The Verify3D algorithm was subsequently used on the model, resulting in scores that ranged from +0.2 to +0.7, confirming the model's quality, given the fact that low-quality models present scoring below +0.1 (Dym *et al.*, 2001).

The generated model of Langat virus RdRp possessed the characteristic structural features of viral RdRps, including the described subdomains of "palm", "fingers" and "thumb", as shown by the superposition of the model and the template (Figure 3). Furthermore, motifs of critical importance to the function of viral RdRps, as explained above, were observed to be conserved on a structural level in the produced model.

Discussion

Non-structural protein 5 (NS5) is the most conserved protein across the flavivirus genus, and its RNA-dependent RNA polymerase domain is of paramount importance for the successful replication of viruses in the *Flaviviridae* family (Bollati *et al.*, 2010). Whereas the RdRp structures of many members of the family, such

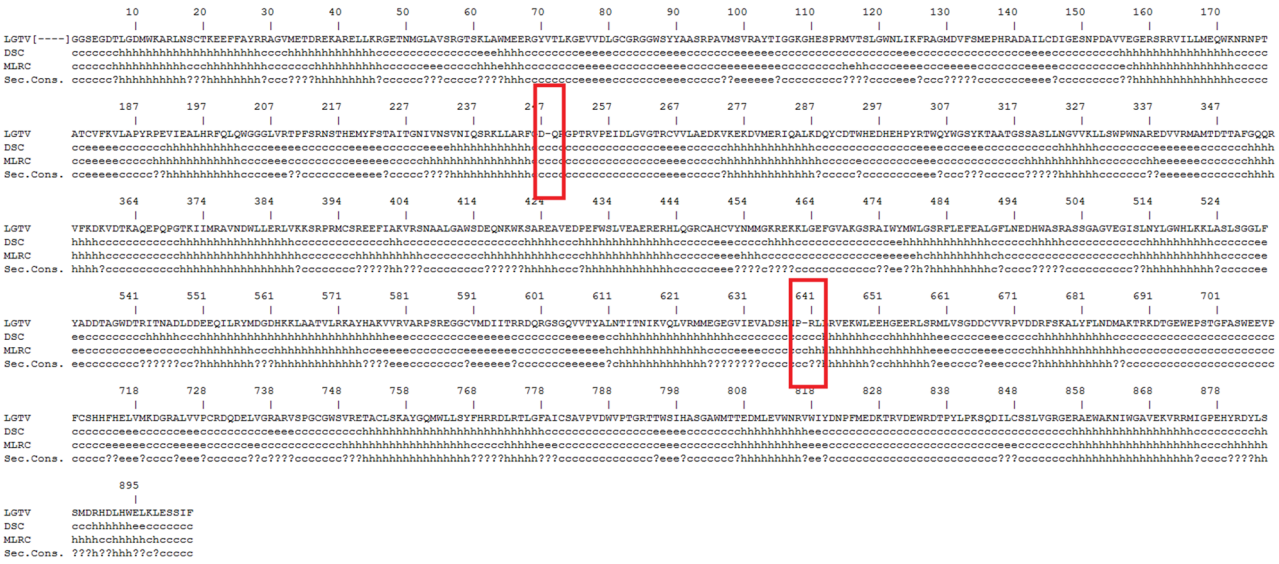

Figure 2. Collective representation of the amino acid sequence of the Langat virus RdRp, including gaps that had been inserted during alignment with DENV2 RdRp. Below them are the predicted secondary structural elements (c: coil, h: helix, e: strand, and (?): ambiguous state are depicted). The areas with inserted gaps and the respective secondary structural elements are denoted in a red box.

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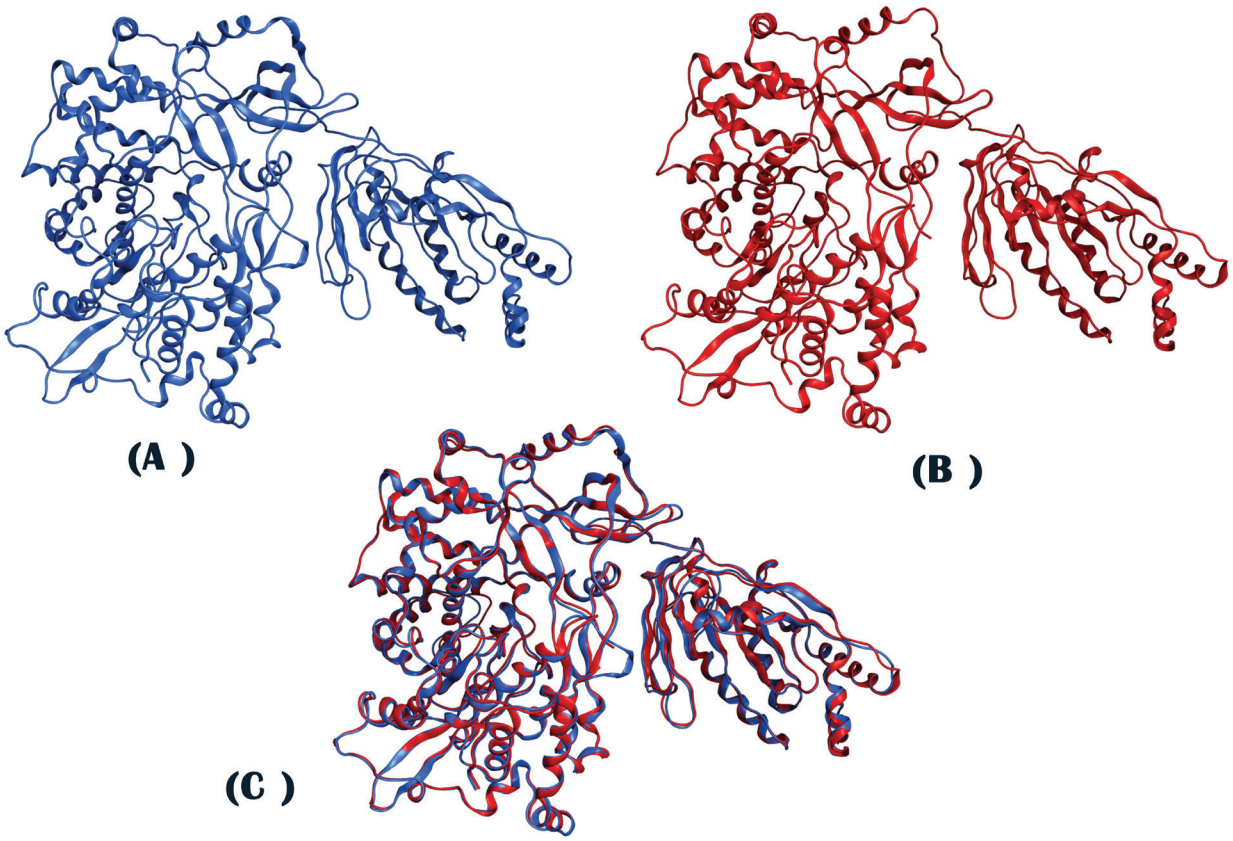

Figure 3. **(A):** Ribbon representation of the generated Langat virus RdRp model in MOE. **(B):** Ribbon representation of the experimentally determined DENV2 RdRp. **(C):** Superposition of the two 3D structures (Blue ribbon: Langat virus RdRp, Red ribbon: DENV2 RdRp).

as Zika virus or Dengue virus, have been experimentally determined, there is an absence of a structure for Langat virus. To bridge this gap, the three-dimensional model of the Langat virus RNA-dependent RNA polymerase enzyme was designed through a homology modeling approach, with the DENV2 RNA-dependent RNA-polymerase used as template. The produced model was found to meet the standards of stereochemical evaluations, ensuring that there were no aberrations in terms of stereochemical characteristics such as bond angles, hydrogen atoms etc. Upon inspection, the model of the Langat RdRp was found to exhibit the key structural characteristics of viral RNA-dependent RNA polymerase enzymes. The conservation of structural characteristics, such as the subdomains, is of great importance for the construction of a reliable enzyme model. The catalytic function of the viral RdRps relies on the correct conformation of the molecule in the three-dimensional space, with experimentally observed changes in activity in the case of alterations of secondary and tertiary structural elements (Malet *et al.*, 2008). The generated model was additionally examined on the level of the RdRp motifs, another essential component of the enzyme activity. The seven motifs that have been described for the RNA-dependent RNA-polymerases, which were conserved on the amino acid sequence of the Langat virus, were also found to be structurally conserved in the model. In summary, the homology modeling process has yielded a three-dimensional model of the Langat virus RdRp enzyme in line with the structural features described for the enzyme family, as well as the *Flaviviridae* family. The generated model remains under the limitations that come with the theoretical nature of the homology modeling process. Nevertheless, the produced three-dimensional model of the Langat virus RdRp can serve as a reliable basis for the exploration of the enzyme's functions and the virus' life cycle, until a structure becomes available through an experimental approach.

Conclusion

Viral infections with members of the *Flaviviridae* viral family as the root cause continue to pose a threat to human health on a global scale. Viruses in the Tick-borne Encephalitis virus serocomplex are responsible for a rising number of cases around the world, a fact that calls for attention from the scientific and medical community. Langat virus, a member of the serocomplex, is a pathogen which while thus far naturally attenuated when it comes to humans, cannot be excluded as a potential future threat. From that perspective, the study of Langat virus' life cycle is an essential step, in order to be proactive and prepared in case of such outcome.

Replication mechanisms are at the core of the virus' life and transmission, which is why the availability of a structure of the Langat virus RNA-dependent RNA polymerase is of great significance. In the absence of an experimentally determined structure, the 3D model of the enzyme designed through homology modeling can facilitate the analysis of its structure and function in a reliable manner. The extraction of this kind of information can pave the way for further research approaches. For example, the model of the Langat virus RdRp may assist in the rational design of anti-viral agents. These agents, such as potential inhibitors, can be employed in the possible event that Langat virus manifests the ability to cause disease in the human population, reinforcing the level of preparedness of the medical and scientific community.

Key Points

- Langat virus is serologically related to flaviviruses that cause severe human disease.
- Homology modeling techniques can be used to create a model of the 3D structure of the Langat virus RNA-dependent RNA polymerase, in the absence of an experimentally resolved structure.
- Motifs critical for the enzyme's functions are present in the resulting model, a significant factor in the construction of a reliable model. An accurate model can be of potential use in the design of anti-viral agents against Langat virus.

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Research Papers

Land Suitability Assessment for Olive Mill Wastewater Disposal by Integrating Multicriteria Decision Support Tools

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Abstract

Many on-site waste disposal systems fail regularly due to problems concerning suitable location and management. A potential environmental threat is inevitably propagated through on-site, off-site, downstream, soil surface and ground water pollution. Soil is a key component of land suitability for waste disposal. This paper presents a Geographic Information Systems (GIS) – based integrated multicriteria decision support system for evaluating the land suitability for olive mill wastewater (OMWW) disposal in the Mediterranean region. Two-scaled classification schemes are developed, the global scheme for Central and South Greece (scale: 1:30.000) and the local scheme for the study area in Xiromero, Aetolia-Acarnania Prefecture, Western Greece, scale 1:10.000. Constrains and factors are included into the spatial decision-making framework, where geostatistical and fuzzy set theory techniques, as well as Analytical Hierarchy Process (AHP) are appropriately integrated. Physical, chemical, and socioeconomic variables adapted to the Mediterranean soil conditions are incorporated as driving forces for the land suitability assessment and the produced maps reveal valuable results for final end-users, such as municipal authorities, agriculturalists, farmers and other national and local stakeholders.

Introduction

Most of the world's olive oil (98%) is produced in Mediterranean countries (Shabou *et al.*, 2009a; Jarboui *et al.*, 2010); Spain produces 36%, Italy 24% and Greece 17% of global production (Lopes *et al.*, 2009). Olive oil extraction generates a high amount of waste that requires appropriate management due to the negative impact in case of uncontrolled disposal. Several methods have been applied to OMWW treatment: a) disposal in soil, b) incineration and c) fermentation products (Komnitsas and Zaharaki, 2012).

No common policy practices are applied in the European Union, and therefore each European country applies its own restrictions on OMWW management. Nevertheless, some main EU directives, such as 86/278/EEC, 91/271/EEC, 91/689/EEC and 91/676/EEC, are partially used to handle the existing gap (Williams, 2005). There is an undoubted need to adopt common soil and site evaluation criteria, and also to plan for strategic management activities involving all relevant stakeholders *e.g.*, farmers, decision makers, public bodies. Therefore, any management plan should consider human participation factors along with any environmental or socio-economic variable.

Our approach uses multicriteria decision support tools to assess the soil land and site suitability for olive mill wastewater (OMWW) disposal. These tools consist of commonly used practices which are highly validated

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for a number of land evaluation applications (Joerin *et al.*, 2001; Goncalves *et al.*, 2002; Geneletti and van Duren, 2008; Chen *et al.*, 2010; Rahman *et al.*, 2012; Sahnoun *et al.*, 2012; Papadopoulou-Vrynioti *et al.*, 2013; Triantakonstantis *et al.*, 2013). Traditional land classification techniques that use the most limiting factor for each class (Davidson *et al.*, 1994; Hossain and Das, 2010) are adopted. Moreover, Analytical Hierarchy Process (AHP) combined with fuzzy set theory techniques and geostatistical methods are also used for assessing the land suitability for OMWW disposal. AHP is a widely accepted modelling framework for decision making problems (Saaty, 1980; Saaty, 1994a,b; Saaty, 1995), while fuzzy sets produce a more realistic suitability classification system by applying the uncertainty and continuously changing nature of our environment (Burrough *et al.*, 1992; Burrough *et al.*, 2015).

Our principal objective is to produce a land evaluation model framework for OMWW disposal to support current legislation within the European Union, using multi-criteria decision tools under a Geographic Information System (GIS) umbrella. The results will be useful to any decision-making authority and planning organization, enriching their capabilities when facing OMWW disposal problems.

Materials and Methods

Study Area and Data Sources

Our land evaluation model is applied in two scaled-study areas. The first refers to a global scale using about half of the Greek territory (Central and South Greece), where olive trees are cultivated, while the local-scaled area is in the Xiromero rural area (Aetolia-Acarnania prefecture). The global study area, in which most olive production occurs, includes twenty prefectures with a total area of 1.47 million ha.

For the global area, open data including the soil map of Greece (Payment and Control Agency for Guidance and Guarantee Community Aid - OPEKEPE, scale: 1:30.000) as well as rivers, water bodies and urban areas www.geodata.gov.gr were used. The area of the mapping units is 1.470.836 ha. For the local areas, the soil maps of ELGO "DEMETER" (scale: 1:10.000) was used. The Xiromero area is 2.601ha. Figure 1 presents the global and local study areas.

The driving factors for OMWW disposal

In Table 1 a literature review of synthesis of OMWW is presented (Tsagaraki *et al.*, 2007; Doula *et al.*, 2012). The most important organic properties of OMWW are phenolic compounds, sugars, and some organic acids. Concerning inorganic compounds, OMWW has high potassium content (≈4 g/L) and important levels of nitrogen, phosphorous, calcium, magnesium, and iron compared to other organic wastes (Tsagaraki *et al.*, 2007). The proper management of OMWW disposal highly depends not only on chemical characteristics, but also

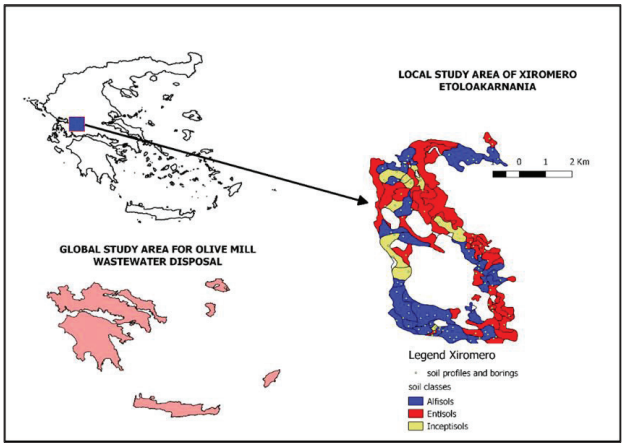

Figure 1. Global and local study areas for OMWW disposal.

on physical and socioeconomic properties, which are important for an effective waste management system. The suitability of these properties for OMWW disposal on soils is analytically presented below.

Physical Properties

Generally, soil should be deep, well-structured with high microbial activity, permeable enough to appropriately filter and adsorb nutrients and degrade pollutants such as phenols.

Sufficient soil volume, that is determined by plentiful soil depth and coarse fragments amount, may prevent waterlogging or excessive runoff. Soil permeability declares the capability of soil to store water before it is recharged by flow to groundwater. High saturated or unsaturated permeability may allow waste to directly reach the ground water lever and produce contamination in underground water, while not permeable soils may result to stagnation and surface runoff in slopping soils. More specifically:

Soil permeability – Soil structure – Soil texture: Soil permeability greatly influences the time and the 3-D fate and distribution of waste how much pollutant is reaching ground and surface water before the soil microorganisms involvement escaping an OMWW disposal site. According to the characteristics of soil texture of the area, soils having high rate of permeability are sandy soils and are considered unsuitable for being used as an OMWW disposal site, while soils with very low permeability are clay soils and are considered fairly suitable and optimal to site an OMWW disposal. (Aydi *et al.*, 2016).

Groundwater depth: The OMWW disposal site mapping should consider the ground and surface hydrology; the existence of the depth of vadose zone and the aquifers to prevent groundwater contamination. In this study, a 50-cm minimal depth to groundwater is considered unsuitable for OMWW disposal (Theocharopoulos *et al.*, 1996).

Soil Units: Vertisols are soils with high content of clay (montmorillonite) that forms deep cracks in drier

Table 1. A literature review of synthesis of OMWW.

Property	Azbar *et al.* (2004)	Niaounakis and Halvadakis (2004)	Borsani and Ferrando (1996)	Paredes *et al.* (1999)	Sierra *et al.* (2001)	Galiatsatou *et al.* (2002)	Eroglu *et al.* (2004)	Al-Malah *et al.* (2000)	Doula *et al.* (2012)
pH	3–5.9	4–6		4.8–5.5	4.5–6	4.9–6.5	4.86	4.52	5.23
Water (%)			83						
BOD (g/L)	23–100	35–110			35–100	15–120	17.88	13.2	45.5
COD (g/L)	40–220	40–220			40–195	30–150	72.20	320	86
Carbohydrates (%)			2–8	3.37–32.91		2–8			
Polyphenols (g/L)	0.002–80	0.5–24		1.32–3.99%	3–24	1.5–2.4	0.13	3.12	2.7
Fats, oils (g/L)	1–23		0.03–1%	0.55–11.37%	0.3–23	1.3			5.8
Pectins (%)			1–1.5			1–1.5			
VOC (g/L)		25–45							
TS (g/L)	1–102.5						42.24		
SS (g/L)							3.48	2.17	
N (g/L)	0.3–1.2			0.58–1.13%	5–15	0.5–2%			0.4
K (g/L)		4	0.87% K_2O	3.30–6.94%	2.7–7.2		7.81		0.95
P (g/L)			0.22% P_2O_5	0.06–0.32%	0.3–1.1				0.18
Ca (g/L)				0.32–0.53%	0.12–0.75		0.55		0.07
Na (g/L)				0.04–0.48%	0.04–0.90		0.41		0.03
Mg (g/L)				0.06–0.22%	0.10–0.40		0.28		0.09

seasons or years. They are considered a limiting factor, due to their shrink and swell properties that depend on the moisture content, making the management very difficult (Oliveira *et al.*, 2016).

Soil depth: In small soil depth, contaminants can flow into groundwater. Moreover, in a single application at high rates of waste, they may produce potential waste overloading in the soil (USDA, 1996).

The suitability of other physical characteristics should be carefully taken into consideration in land evaluation of OMWW disposal. For example, slope needs to be shallow enough to avoid surface runoff and therefore, soils with high slopes are excluded. Drainage should be appropriate, and the ground water level should not be fluctuated in a way to reach the surface applied pollutants of the waste to prevent waste movement away from the application area.

Slope: Slope is a crucial factor for OMWW disposal since higher slopes would increase runoff of pollutants from the disposal site. Therefore, the contamination will increase in the surrounding areas. Slope values over 10 % are considered a limiting factor for hazardous waste landfill siting (Sharifi *et al.*, 2009).

Drainage: In poorly drained soils, the application and incorporation of waste should be made during periods when flooding is unlikely, because contaminants can enter surface water (Rowe *et al.*, 1981).

Chemical Properties

Electrical Conductivity: In severe soil salinity (EC > 8 mS cm^{-1}) the application of high C:N and low salt wastes may improve soil infiltration, permeability, and structure and reduce plant toxicity. Moreover, the application of saline wastes may increase soil salinity if applied at continuous high rates (USDA, 1996). Generally, values of EC greater than 4 mS cm^{-1} are considered excessive and therefore, any OMWW disposal should not increase the EC more than this threshold (MAFF, 1988; Ilaco, 1985).

pH: High soil pH values and high content of calcium carbonate neutralize the strong acidity of the waste, both in the areas of disposal containers, and in places where there is land surface disposal. Normal range of soil pH is 6 – 8 (CCME, 2007) and should be kept at this range after the OMWW disposal considering the soil resilience.

Organic Matter: Organic matter improves soil aggregation, water-holding capacity, hydraulic conductivity, bulk density, fertility and resistance to water and wind erosion. Moreover, soil organic matter is a crucial source of nutrients for the microflora, microfauna and plants. Therefore, the organic matter of soil is not a limiting factor for OMWW disposal. Values greater than 3.4 % on soils are considered normal (Loveland and Webb, 2003).

Calcium (Ca), Magnesium (Mg) and Potassium (K): OMWW contains high concentrations of calcium, magnesium and particularly potassium (Arienzo and Capanso, 2000). Calcium has a positive effect on soil

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properties. It improves soil structure, increases water penetration, and contributes to the growth of plant roots and soil microorganisms. Magnesium is essential to produce chlorophyll. As soil pH increases, the supply of available calcium and magnesium to soils increases. If potassium is more than adequate to meet a crop's needs, it will be adsorbed by the soil colloids absorbed by plants and will lead to high concentrations of K in plants, which is called "luxury consumption", with no negative impact on plant growth (Kaiser *et al.*, 2016). Low values of these cations are more suitable for OMWW disposal, because OMWW increases their concentrations, and risk of toxicity is much higher in case of high values of cations. Carrow *et al.* gave the normal / average range of the concentrations of these elements on soils: 2.5-3.8 cmol kg^{-1} for Ca, 1.2-2.2 cmol kg^{-1} for Mg and 0.26-0.60 cmol kg^{-1} for K.

Phosphorus (P): Phosphorus (P) is an essential element in food production, but its availability is limited in global scale. Therefore, the supply of this non-renewable resource is more than urgent. OMWW disposal can enhance the long-term supply of this important plant nutrient and areas with low values of P are more suitable for OMWW disposal. Large values may produce toxicity in plants. Normal values of P on soils range between 12-28 mg kg^{-1} (Carrow *et al.*, 2001), while values of 40-50 mg kg^{-1} are considered high (MAFF, 1988; Ilaco, 1985).

Cation Exchange Capacity: Cation exchange capacity (CEC) is the ability of the soil to hold positively charged ions. It influences soil structure stability, nutrient availability, pH and the soil's reaction to fertilizers and other soil additives (Hazelton and Murphy, 2007). High CEC is more suitable for OMWW disposal because cations of waste can be easier retained and given back to plants and enhance ion exchange with the cations of the waste.

Degree of base saturation: The degree of base saturation is the percentage of exchangeable cations Ca^{2+}, Mg^{2+}, K^{+}, Na^{+} in Cation Exchange Capacity. The degree of base saturation is an important soil property which reflects the extent of weathering of the soil. The easiness of cation absorption by plants is related to the degree of base saturation. The availability of plant nutrients increases with the degree of base saturation. High degree of base saturation is more suitable for OMWW disposal because cations of waste can be easier retained and given back to plants (Cabrera *et al.*, 1996).

Socioeconomic properties

These are some other site properties which have a socioeconomic effect on OMWW disposal. For example, keeping a buffer distance from residential areas, water bodies and drainage channels is highly recommended. Additional details of these characteristics are given in the following paragraphs:

Distance from Residential Areas: Sitting an OMWW disposal site close to residential areas may possibly cause negative health impacts and smells on the population and create negative effects on waste recycling. Therefore, distance should be kept to protect the general public health from possible environmental hazards released from OMWW disposal site (Aydi, 2016). While some studies suggest different range of distance to residential areas for OMWW disposal (*e.g.* Abessi and Saeedi 2010), in our study, distance smaller than 200 m is considered unsuitable, while distances greater than 500 m are acceptable for allocating OMWW disposal site.

Distance from Rivers: According to the EU directives, a landfill should not be close to any source of water. It is suggested that a distance up to 500 m away from water bodies could be acceptable (Kontos *et al.*, 2003). In our study, a buffer distance of 200 m for water bodies is considered unsuitable for allocating OMWW disposal sites (Shabou *et al.*, 2009b), always depending on the pattern of channels and the general hydrology of the first order catchment.

Land Evaluation Assessment Methods

Land Suitability Classification by FAO

According to the United Nations Food and Agriculture Organization—FAO (1976):

- Land evaluation is the process of estimating the potential of land for alternative kinds of land use, so that the consequences of change can be predicted.
- Land suitability is the fitness of a given area for a land utilization type (or land use), or the degree to which it satisfies the land user. It is generally presented as a class or rating.

If a landscape characteristic does not meet the selected criteria for a particular land use, a potential limitation or "constraint" is appeared. The suitability classes outlined by FAO are internationally acceptable and can be adapted and applied to any scale. FAO (1976) suitability classes are: S1 (highly suitable), S2 (moderately suitable), S3 (marginally suitable), N1 (not suitable) and N2 (not suitable). These classes have been adopted to the Mediterranean soils of Greece by Davidson et al. and Theocharopoulos et al. for sewage sludge application.

Analytical Hierarchy Process (AHP)

The AHP multicriteria method was employed to define the OMWW disposal in local study areas of Xiromero Aetolia-Acarnania and Eleonas Phocis study areas. Analytical hierarchy process (AHP) is a mathematical method, where complex decisions can be made by multiple criteria selection. It measures the relative importance of the factors and has been widely applied to tackle environmental problems (Schmoldt *et al.*, 2001).

The AHP method (Saaty 1977) is a common technique for tackling spatial decision-making problems. It is a multi-attribute method based on the weights assigned to each factor. The importance of each factor is then determined. A total score is calculated by multiplying each weight by the scaled value of each factor. The AHP methodology presented in Saaty (1977) calculates the final factor weight.

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First, AHP makes pairwise comparisons of all factors. It is expressed on a nine-point scale. Pairwise weights of 1, 3, 5, 7 and 9 indicate equal preference, weak preference, strong preference, very strong preference, and extreme preference respectively of one variable over the other. The values of 2, 4, 6 and 8 are intermediate values (Saaty, 1977). Because pairwise comparison based on human decisions usually have inconsistencies, AHP calculates the degree of inconsistency of the comparison matrix (consistency index, CI, and consistency ratio, CR). A CR of 0.1 or less is usually considered acceptable. If the CR is greater than 0.1 then the pairwise comparison should be reconsidered (Saaty, 1994a, b).

Geostatistics - Kriging interpolation

In-depth discussions about interpolation techniques are given by Journel and Huijbregts (1978), Isaaks and Srivastava (1989) and Burrough *et al.* (2015). The values of each soil property were used for the prediction of values at unknown points using the interpolation methods or Ordinary Kriging.

The spatial prediction of the values of a soil variable Z at an unsampled point x_0 is given by Eq (1):

$$Z'(x_0) = \sum_{i=1}^{n} \lambda_i z(x_i) \quad (1)$$

where x denotes the set of spatial coordinates $\{x_1, x_2\}$ and λ_i are the weights of the sampling points x_i.
In Kriging, the weights are chosen so that the value of Eq (1) for $z(x_0)$ is unbiased, and the prediction variance $\sigma^2(x_0)$ is minimized. That is:

$$E[Z'(x_0) - Z(x_0)] = 0 \text{ and } \sigma^2(x_0) = var[Z'(x_0) - Z(x_0)] = \text{minimum} \quad (2)$$

To ensure that the prediction is unbiased, the weights placed on each neighbouring point must satisfy Eq (3):

$$\sum_{i=1}^{n} \lambda_i = 1 \quad (3)$$

The spatial variation of the soil properties was quantified by semivariogram. The semivariogram is a function that connects the semivariance (γ) with h, where:

$$\gamma(h) = (1 / 2m(h)).\Sigma\{Z(x) - Z(x + h)\}^2 \quad (4)$$

where $m(h)$ is the number of pairs within a distance h.
A variable of the semivariogram satisfies the following conditions, Eqs (5-8):

$$E\{Z(x)\} = m \quad (5)$$

$$C(h) = E[\{Z(x) - m\}\{Z(x + h) - m\}] = E[Z(x) - Z(x + h)] - m^2 \quad (6)$$

$$C(0) = E[Z'(x)] - m^2 = \sigma^2 \quad (7)$$

$$c(h) = C(0) - C(h) \quad (8)$$

The type of the theoretical model, which fitted best to the experimental variogram of each variable, was the spherical model, which is given from the following Eqs (9-11):

$$\gamma(h) = C_0 + C\{3h/2\alpha - 1/2(h/\alpha)^3\}, \text{ for } 0 < h <= \alpha \quad (9)$$

$$\gamma(h) = C_0 + C, \text{ for } h > \alpha \quad (10)$$

$$\gamma(0) = 0 \quad (11)$$

Fuzzy Sets

Considering a set $X = \{x\}$, where x may be entities, properties, a fuzzy subset A of X, is defined by a function μA as the set of pairs $A = \{x, \mu A(x)\}$ for each x of X. The value $\mu A(x)$ represents the membership grade of x in A. The membership grade of an object takes values in [0,1]. A value of 1 indicates full participation in the fuzzy set and as the degree of involvement approaches zero the participation in the fuzzy set becomes weaker (Zadeh, 1965; 1978, Comber *et al.*, 2016). The membership grade of an object in a fuzzy set is usually calculated by a membership function. In the literature, there is a large number of membership functions that describe soil data (Kandel, 1986; Burrough, 1989).

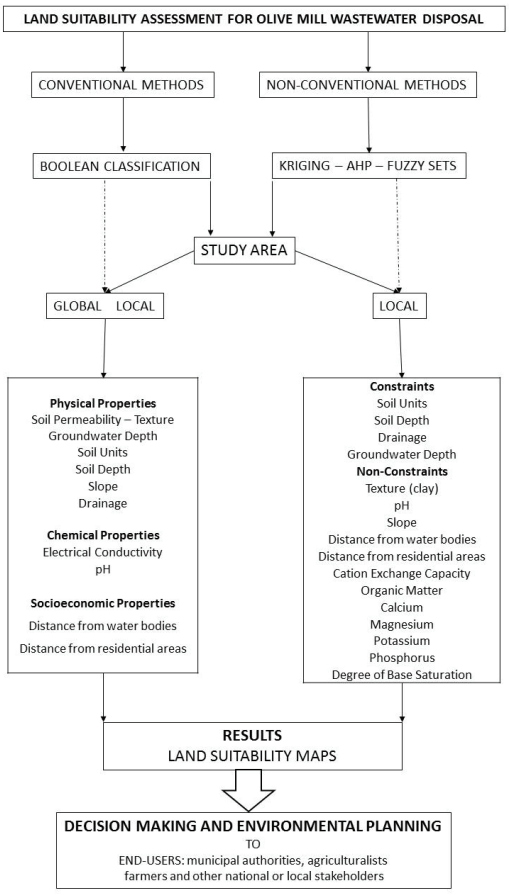

Figure 2. Flowchart of land suitability assessment for OMWW disposal.

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Table 2. Soil and site characteristics for land suitability for OMWW disposal of global study area.

Physical Properties	**S1**	**S2**	**S3**	**N1**	**N2**
Soil Permeability Texture	medium clay, clay	Medium textured	Sandy	High sandy	High sandy
Groundwater Depth	All except				
S3, N1, N2	All except				
S3, N1, N2	50-150 cm	>50 cm	>50 cm		
Soil Units	All except Vertisols	All except Vertisols	All except Vertisols	Vertisols	Vertisols
Soil Depth (cm)	>120	80-120	50-80	30-50	<30
Slope %	<3	3-8	8-12	12-18	>18
Drainage	Very well-drained	Well-drained	Moderate drained	Poorly drained	Very Poorly drained
Chemical Properties	**S1**	**S2**	**S3**	**N1**	**N2**
Electrical Conductivity (mS/cm)	<2	2-4	4-6	6-8	>8
pH	>7,3	6,6 – 7,3	5,6 – 6,5	<5,6	<5,6
Socioeconomic Properties	**S1**	**S2**	**S3**	**N1**	**N2**
Distance from water bodies (m)	>500	300-500	200-300	<200	<200
Distance from residential areas (m)	>500	300-500	200-300	<200	<200

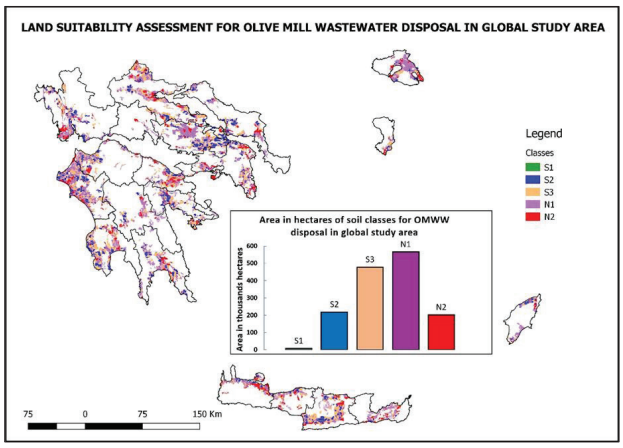

Figure 3. Land suitability for OMWW disposal in global study area.

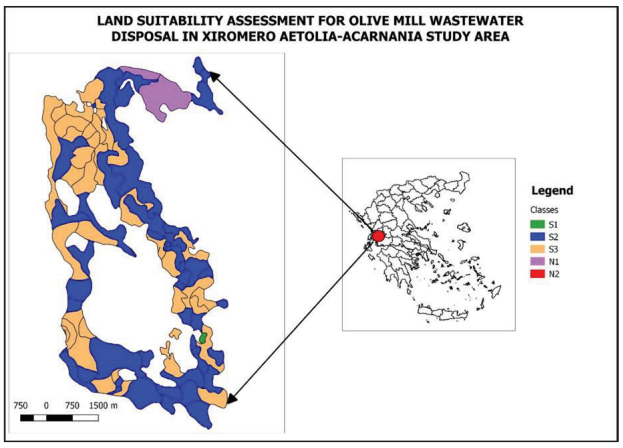

Figure 4. Land suitability for OMWW disposal in Xiromero Aetolia-Acarnania study area.

The research methodology adopted in this study is graphically presented in Figure 2. This flowchart describes the steps needed to reach our overarching goal.

Results and Discussion

Land Evaluation (FAO Classification) of Global and Local Study Areas

The Land Suitability Classification (FAO, 1976; Theocharopoulos *et al.*, 1996; Doula *et al.*, 2013) using the selected criteria (physical, chemical, and socioeconomic properties of Table 2) produce the results of Figures 3 and 4. In the global study area, most of area (70,9%) belongs to S3 and N1 classes, while only 15,3% is classified to S1 and S2. In Xiromero study area, most of area belongs to S2 and S3 classes.

Land Evaluation (AHP – Kriging - Fuzzy)

The land evaluation using the AHP, Kriging and Fuzzy Sets methods was applied in Xiromero Aetolia-Acarnania study area. Four OMWW disposal constraints were chosen according to the Greek legislation (Part B, 3924/07.12.2016 FEK - Government Gazette Issue). The

Table 3. The resulting weights for the criteria based on pairwise comparisons.

Category		Priority
1	clay	8.9%
2	pH	7.3%
3	slope	15.5%
4	Distance from water bodies	16.3%
5	Distance from residential areas	17.0%
6	CEC	6.2%
7	organic matter	7.3%
8	Ca	4.0%
9	Mg	4.0%
10	K	4.0%
11	P	4.0%
12	Degree of base saturation	5.5%

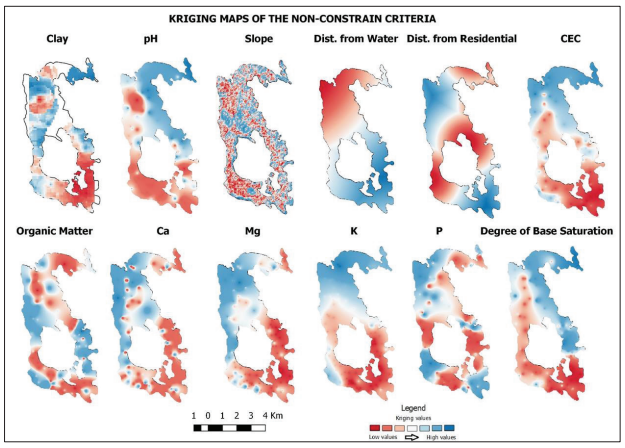

Figure 5. The Grids of Non-Constraint Criteria after Kriging interpolation.

constraints criteria include soil units, soil depth, drainage, and groundwater depth. Twelve factors including texture (clay), pH, slope, distance from rivers, distance from residential areas, cation exchange capacity, organic matter, calcium, magnesium, potassium, phosphorus and degree of base saturation were calculated using the geostatistical method of Kriging on a point coverage. This point coverage contains the values of the variables after chemical analysis of the respective borings. The grids after Kriging interpolation are given in Figure 5. These maps were standardized using fuzzy membership functions, which were set after experience and statistical analysis of the data. The fuzzy functions for each of these factors are presented in Figure 6.

The pairwise comparison method was used to assign weights and establish importance of the non-constraint criteria (Table 3) using experience and characteristics of the study area. The highest weights were assigned to

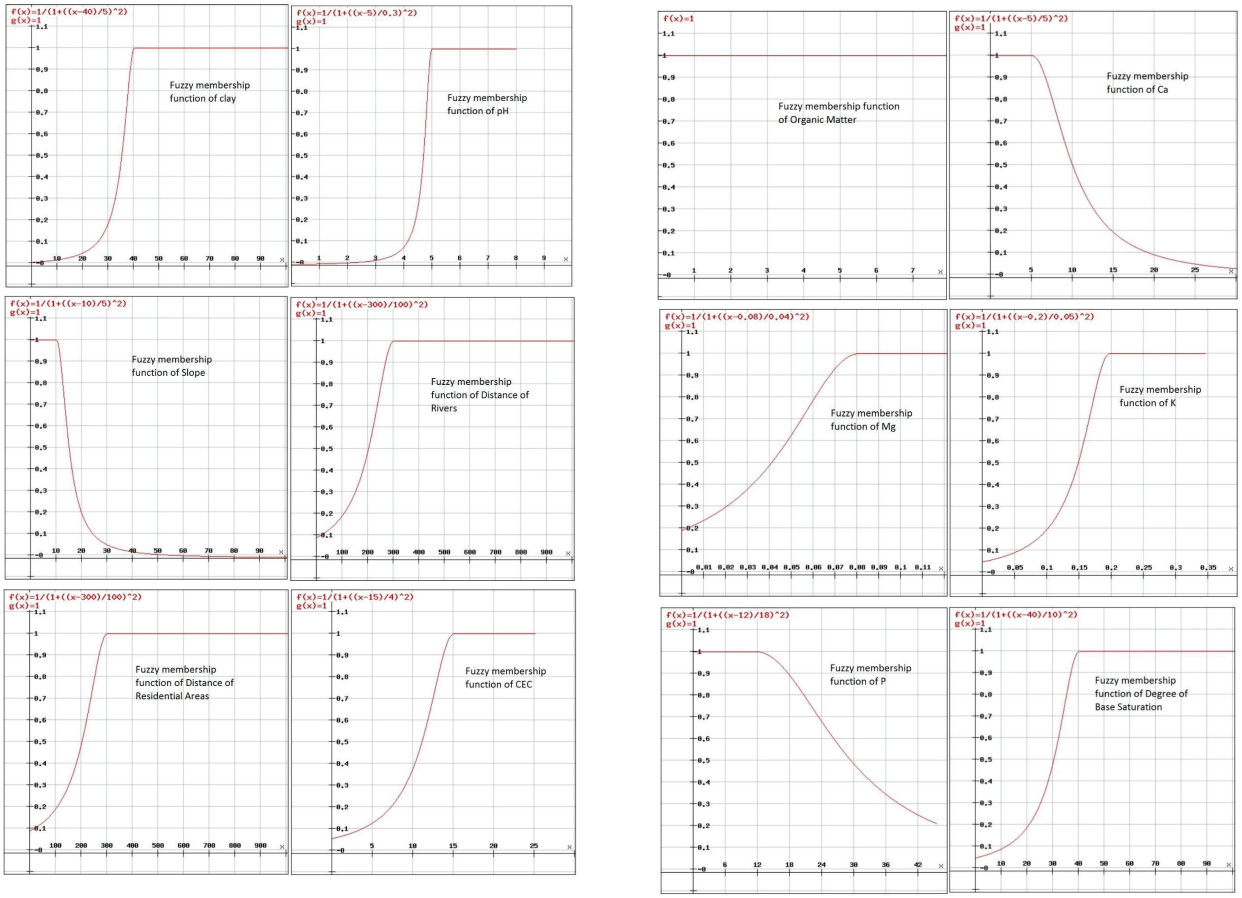

Figure 6. Fuzzy membership functions for the non-constrain criteria.

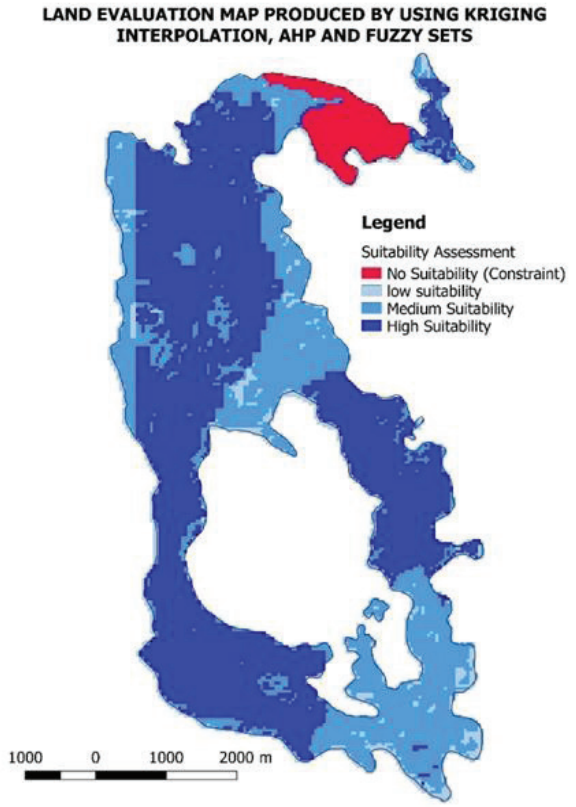

Figure 7. Final Land Evaluation Map of Xiromero Aetolia-Acarnania study area.

the distances from rivers and residential areas, as well as slope, as the most important for OMWW disposal. Nutrients, *i.e.* Ca, Mg, K, P, were considered to have equal importance and therefore, they were assigned equal weights. The Consistency Ratio (CR) is 0.027 which is considered acceptable (less than 0.1).

Intermediate suitability maps were created for these criteria respectively. Final aggregation was implemented to demonstrate the importance of the weights and therefore, the final OMWW disposal site suitability map was produced considering the constraint and non-constraint criteria (Figure 7). The higher values on the final map indicate more suitable areas for OMWW disposal.

Conclusions

OMWW disposal on soils is undoubtedly an existing need. To this challenge, spatial analysis combined with conventional and non-conventional methods is a promising field where valuable decision support tools can be developed. Conventional methods include land suitability, where Boolean logic is used for determining soil suitability classes. Non-conventional methods used in this study are geostatistical interpolation techniques, analytical hierarchy process and fuzzy set theory. Conventional methods were applied in both global and local scales, while non-conventional methods were applied only for local scale where analytical soil data were available in point coverage (soil borings).

The proposed methodology would aid the decision-making procedure taking into consideration constraints and factors. Depending on the defined goal, decision makers and environmental planners could design their strategies for waste management more efficiently, and therefore treat waste with environmentally friendly zero-waste practices. Our approach illustrates the flexibility of the methods applied and provides a valuable tool for multi-criteria decision support processes.

While the proposed methodology is not exhaustive, our future endeavors will rely on deeper analysis of multicriteria methods by incorporating the feedback of our approach with real data and applications. Therefore, the end-users of our methodology, such as municipal authorities, agriculturalists, farmers and any other national or local stakeholders, can evaluate and further enhance this approach with their contribution.

Key Points

- An integrated GIS multicriteria decision support system for evaluating the land suitability for olive mill wastewater disposal.
- Physical, chemical, and socioeconomic variables adapted to the Mediterranean soil conditions are used as driving forces to the land suitability assessment.
- Geostatistical, fuzzy set theory techniques, as well as Analytical Hierarchy Process (AHP) are appropriately integrated.
- A valuable tool for municipal authorities, agriculturalists, farmers, and other national and local stakeholders.

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Research Papers

Environmental impacts of war's social consequences. Case Study: Aleppo Governorate Syria

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Abstract

War is an anthropogenic phenomenon with devastating effects, which cause loss of human life, alongside the disastrous effects on the natural environment. The environmental impacts of armed conflicts can be either direct, arising from the act of war itself, or indirect due to the massive population displacement, infrastructure breakdown, and militarised zones. Impacts may be irreversible, affecting areas even far away from the territory of the conflict where they manifest. The environmental impacts of war create social and economic consequences that lead to greater environmental degradation by showing the interdependent relationship between the environment, society, and economy. It is imperative to address the subject in a multidisciplinary approach and implement stricter international legislation on environmental disasters during wars. This study aims to identify environmental impacts by using satellite-derived images at Aleppo Governorate, analyse them via statistics supplemented with the available information for the research region, and demonstrate the subsequent social and economic consequences by creating indices, such as the Normalised Difference Vegetation Index (NDVI), digital image composites and classified images, which record the extent of reduction of healthy vegetation and the extent of destruction at the city of Aleppo. Data from international organisations corroborated the findings, and hereinafter societal and economic effects were analysed. Using remote sensing alongside with geographic information systems can be a useful tool as it offers access to war zones where physical observations are usually impossible.

Introduction

Armed conflicts are one of the most devastating human activities, creating enormous humanitarian crises in addition to destroying the natural environment. The effects of armed conflict do not only occur during its duration but may continue to manifest for many years after its end. In most cases, the impacts of war are particularly serious, long-lasting, and irreversible. To better understand these impacts, a classification of wars into three stages: preparation, armed conflict, and post-war period, introducing the term "warfare ecology", was reported (Machlis and Hanson, 2008).

In 2017, 90,000 deaths were recorded worldwide, due to armed conflicts. Moreover, 49 active fronts were recorded in the same year (Pettersson and Eck, 2018), while most of them were in Syria. According to the Uppsala Conflict Data Program, 313,418 deaths in armed conflicts have occurred in Syria since the start of the war in 2012 (UCDP, 2018).

The ongoing war in Syria has forced 5.63 million people to immigrate from their country, according to

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the United Nations High Commissioner for Refugees (OCHA, 2018; UNRA, 2018), while the number of internally displaced people was as high as 5.7 million until January 2017 (The World Bank, 2017b). With almost half of its population displaced, Syria is experiencing the largest forced population movement in modern history since World War II. The destruction of urban and semi-urban centres and the abandonment of cultivated lands and areas which had intense human activity in the past, have disturbed the balance of the ecosystem. These disturbances have a good impact on wildlife but cannot be considered positive due to the huge disaster caused (Gaynor *et al.*, 2016).

The importance of the environment has emerged in recent years as a major issue. The environmental impact of war has not received proper attention, even though it contributes to ecological degradation (Clark and Jorgenson, 2012). Limited publications are referring to the environmental impacts of war which mainly address specific areas (Sudan, Iraq, Vietnam, Congo), neglecting many areas that have experienced successive military conflicts, such as the Philippines or Myanmar. A particularly large number of publications are addressing the Gulf War (1991) considering the soil contamination due to the destruction of oil wells and air pollution caused by their combustion (Al Ajmi and Ud din, 2009; Khordagui and Al-Ajmi, 1993; Misak *et al.*, 2009; Omar *et al.*, 2009).

One of the restrictions that recognise and document the effects of war, is that the collection of on-site data in war zones involves practically impossible space-time constraints. Therefore, satellite technologies represent a useful tool for observing and recording the impact of environmental indicators in war-torn areas. With the use of Geographic Information Systems (G.I.S.), an effort is made to identify and record the environmental impacts in the Aleppo region, which has been in constant war since 2011. Moreover, this study reports the resulting socio-economic consequences which emerge from the environmental issues created by war. The aim is to create correlations between the war in Syria, and in particular in the area of the Aleppo Governorate, and its consequences on the three main pillars of sustainability (environment-society-economy) with particular emphasis on environmental impacts. Finally, this research highlights the devastating impacts of war in the study area, thus, showing the need to create a database for the immediate and targeted restoration of the impacts at the end of the conflict.

The ongoing war in Syria has created debris on urban and rural areas, degrading the already burdened status of the environment and its natural resources due to the debris dust. Especially, the disaster in the big urban centres is excessive, with the city of Aleppo and its region counting the largest percentage of disasters.

One of the most obvious effects of the conflict is the volume of debris created by the damage of urban centres, which poses a great risk to public health and the environment, as they contain dust and can contaminate soil and aquifers. In the city of Aleppo alone, it is estimated that there are (as of February 2017) 14.9 million tonnes of debris, and it is estimated that they require 6 years of continuous work and 26 million kilometres of transport to be completely removed (The World Bank, 2017b). In an effort to determine the economic dimension to a precise scale of urban disasters, the World Bank, in a report of the assessment of disasters in three urban areas of Syria (The World Bank, 2017a), estimates that the housing/building damages in the Aleppo region range from $6.2 to $7.5 million.

The loss in Gross Domestic Product (G.D.P.) since the first year of the crisis amounted to 24,098 million dollars, as the tourism sector and the manufacturing (public and private) sector showed a decrease in revenue of 90% and 76%, respectively (Nasser *et al.*, 2013). The country's public debt increased from 30% of Gross Domestic Product in 2010 to 150% in 2015 (The World Bank, 2017b). There has been a sharp rise in domestic consumer prices with a direct impact on poor and high-risk social groups, leading three million people to poverty in the first year of the war, and by the end of 2015, six in ten people to live in extreme poverty (Nasser *et al.*, 2013; The World Bank, 2017b).

Rural areas accounted for 75% of Syria's total area (CBS, 2004) and, before the crisis, contributed 18% to gross domestic product and 23% to exports (FAO, 2016). Given that annual precipitation in Syria counts up to 68.5% of the main source of water available for irrigation, as well as the drought that hit the region during the first decade of the new millennium (Erian, 2011), it is clear that rural areas were already facing serious problems even before the start of the war. The war has led to a reshuffle of water use, drastically reducing access to irrigation due to ongoing conflicts, population movements, damage of water transport infrastructure, and a lack of energy and agricultural inflows (Saadé-Sbeih, *et al.*, 2016).

Additionally, the ongoing crisis in Syria has drastically changed the population distribution, due to mass and recurring immigration movements. The birth rate in the remaining population has decreased by 27%, while the male life expectancy, aged 15 to 24 years, has decreased by 31%, from 69.7 years in 2010 to 48.2 in 2014 (SCPR, 2016). Specifically, the percentage of young people aged 15 to 39 has dropped dramatically between the remaining population and the population moving within the country. Within Syrian governments, the degree of change in population distribution also varies. There is a significant decrease in population in governments such as Aleppo, the rural area of Damascus, Homs, but an increase in populations in Latakia and Hamah (SCPR, 2016). Statistics reflect a structural distortion of the population in terms of age.

An age group that faces many problems is children. Most of them do not go to school, and many of them are forced to work in harsh conditions to help their family survive. In the future, as the country's population grows, the number of people with low education will increase. In addition, the number of vaccinated children decreased

from 98.9% before the crisis to 32.6% after the crisis, and especially in the government of Aleppo, the decrease reached 32.6% (SCPR, 2016). As a result, diseases such as poliomyelitis, leishmaniasis and measles are widely spread (WHO, 2017).

Materials and Methods

Study area

Syria was considered one of the most peaceful countries in the region until the spring of 2011, when the first conflicts broke out in southern Syria in the province of Daraa, as a continuation of the so-called Arab Spring. The majority of Syria's population is Arab, except for a 9.7% of the population which is Kurds, Armenians, and other minorities, while before the conflicts, there were almost 1.8 million refugees mainly from Iraq (Zwijnenburg and Pas, 2015). According to the Statistical Service of Syria (2010), Aleppo Governorate is the most populous governorate in Syria, with 24% of the total country's population. It is located in the northern part of the country within an area of 18,482 km2. According to the last census of the Statistical Service of Syria in 2004, the total population of the governorate was 4,045,166, while according to the 2014 population survey it was estimated that the population was 4,275,000. 70% of the population is Sunni, however, in Aleppo, there are minorities of Christians, Armenians, Kurds, and Turkmens (SNAP, 2013).

The capital of the governorate is Aleppo city, which was the economic capital of Syria, as well as its industrial, agricultural, and commercial centre. Nevertheless, the Aleppo governorate is the poorest, especially in its rural areas where the poverty rate is twice the national average and three times the average urban population (SNAP, 2013). The governorate has a total of 22 cities, 1,476 villages and 1,312 farms. The wider area is a base for textile, chemical, mechanical and food industries. In the governorate of Aleppo, 20% of the country's total wheat production was produced. The total arable land of Aleppo was estimated at 1.11 million hectares in 2011 (CBS, 2003~2017), equal to about 25% of the total cultivated land in the country.

Methods and Techniques

The process of assessing the environmental impacts of armed conflict requires a multi-level view and relevant correlations. Any attempt to assess these impacts is de facto accompanied by the uncertainty of the results, due to lack of data from international and domestic organisations, which estimate that the magnitude of disaster is very difficult to be accurately captured, especially for the region of Syria.

Three stages of data collection were adopted in this study, as following:

1. Elaboration of existing international literature referring to the effects of armed conflicts, both in terms of environmental impact and socio-economic impact.
2. Collection of statistical data of the area by the Statistical Service of Syria and international organisations, such as the World Bank and United Nations.
3. Collection and Use of Landsat8 satellite images by the United States Geological Survey (USGS). Also, the employment of higher resolution satellite imagery via Google Earth Pro.

The main source of data collection in this study is the Central Bureau of Statistics in Syria. However, due to the ongoing war situation in the region, the data collected is accurate until 2010, while for the years 2011-2017 the available data are either based on estimates or are non-existent for some areas. Indicatively, it is reported that population data for the governorate of Aleppo do not exist for the above-mentioned period.

Part of the collected data relates to population changes, and especially deaths and immigration characteristics. In particular, the data for deaths and population movements were derived from the Uppsala Conflict Data Program of the University of Uppsala's Department of Peace and Conflict Research. Data collected for cultivated areas in the region were extracted from the World Bank, the United Nations (UN) and the Food and Agriculture Organization (FAO). To determine the magnitude of the disaster in the city of Aleppo, UNOSAT data were used, which is a program to provide humanitarian data through the processing of high-resolution satellite images, intending to use them for humanitarian aid and security, as well as for strategic, territorial and development planning in the affected areas. The images used by UNOSAT came from the satellites WorldView-1, WorldView-2, Pleiades, GeoEye-1, and QuickBird-2 and concern the period 2011-2015.

The source used to collect the satellite images was the United States Geological Survey (USGS). The Landsat8 satellite, which has two sensors, the Operational Land Imager (OLI) and Thermal Infrared Sensor (TIRS), was selected. The satellite images have undergone level one processing, which includes corrections via the Level Product Generation System (LPGS) algorithm for radiometric image correction to achieve greater absolute and relative geometric accuracy (USGS, 2016).

For the government of Aleppo, images were selected in two time periods, October 2013, and the corresponding month of 2017. The choice of month of the satellite images was not unintentional. The largest percentage of the area is covered by agricultural lands and therefore, to avoid taking images during the cultivation periods in winter and spring that could lead to false results, October was selected. Moreover, at this period the research area has low rainfall, in contrast to the above-mentioned periods where the soil is covered with crops and weeds.

The government of Aleppo is shown in two images with path 173 and 174 and row 35. The four images

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Table 1. Details of the satellite images for 2013 and 2017.

Image ID	PATH	ROW	DATE	QUALITY	CLOUD COVER	CLOUD COVER
LC81730352013274LGN01	173	35	2013-10-01	9	0.04	0.04
LC81740352013281LGN01	174	35	2013-10-08	9	0.13	0.23
LC81730352017285LGN01	173	35	2017-10-12	9	0.35	0.35
LC81740352017292LGN00	174	35	2017-10-19	9	0.16	0.19

(two for each year) selected have quality 9 and no cloud coverage in the area of interest. Their details are given in Table 1. The projected coordinate system used is the transverse Mercator UTM projection in zone 37 and WGS84 as ellipsoidal.

Indices were created in the study area, for the dates 2013 and 2017 in order to analyse the spatial-temporal results. One of the most well-known and widespread indicators is the Normalised Difference Vegetation Index (NDVI). The index is derived from the ratio:

$$NDVI = (NIR - red) / (NIR + red)$$

and counts values from -1 to 1, with healthy vegetation ranging from 0.20 to 0.80. Due to the fact that the reflected radiation in the near-infrared is much higher than in visible, and given the intense reflection due to the cellular structure of the leaves, the vegetation will be more photosynthetically active in places where the local maximum occurs. The change in the use of cultivated lands is one of the effects of war which is often investigated with the selection of NVDI index (Brown, 2010; Witmer and O'Loughlin, 2011; Muller *et al.*, 2016).

In addition, the Normalised Burn Ratio (NBR) was used as an indicator. The NBR index follows the NDVI philosophy and is mainly used to highlight burned areas. It is based on the rationale that an area with healthy vegetation has high reflectivity in the near-infrared (NIR-band5) and low in the small infrared (SWIR2-Band7), while on the contrary, a burned area has low reflection in near infrared and large in small infrared. A high NBR value indicates an area with healthy vegetation, while a small value indicates a newly burned area or bare ground. The index is derived from the ratio:

$$NBR = (NIR - SWIR2) / (NIR + SWIR2)$$

The difference between the NBR indicators ΔNBR=NBR2013-NBR2017 is also used, and the result can be employed as an indication of the areas that have been most damaged, to identify them and take the necessary measures. High values of ΔNBR's indicate areas with high damage, while negative values may indicate areas with possibly increased vegetation followed by a fire. Sampling areas with high NBR have been detected and verified using higher resolution images via Google Earth Pro.

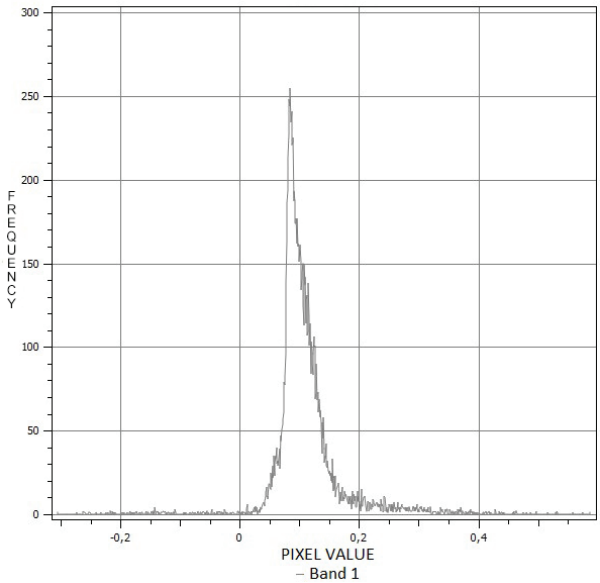

Figure 1. Histogram NDVI for 2013.

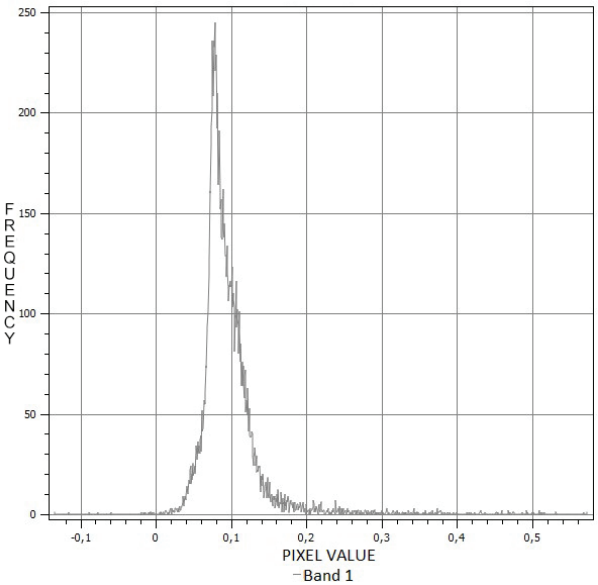

Figure 2. Histogram NDVI for 2017.

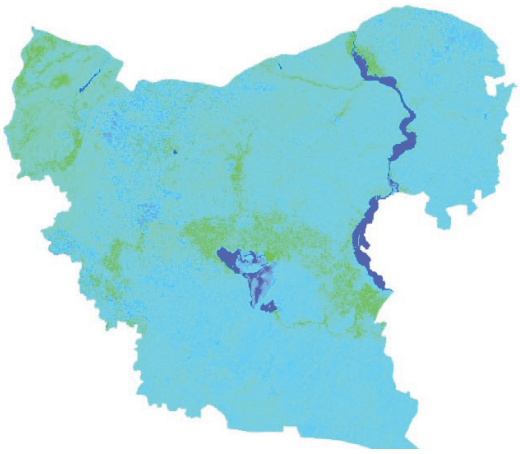

Figure 3. NDVI October 2013.

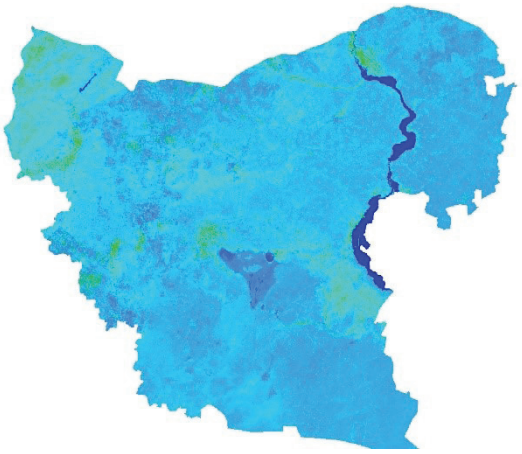

Figure 4. NDVI October 2017.

Results

Satellite Sensing - Processing of satellite data and indicators.

a) Normalised Difference Vegetation Index, NDVI.

The histograms of the produced NDVI image for the year 2013 and year 2017 are shown in Figure 1 and Figure 2, respectively. The NDVI indices created for the year 2013 and 2017, are shown in Figure 3 and Figure 4, respectively. The reference month for both years is October. The bright green areas are the most photosynthetically active. We note that for the year 2013, these areas are located in the north-western part of the government, on the east bank of Euphrates river, in the north-eastern part of the region and in a small part in the west. But most of it is in the area between Al-Assad and Jabbul lakes. According to the histogram of the produced NDVI image for the year 2013 (Figure 1), the minimum and maximum values define the interval from -0.36 to 0.61, with an average value of 0.10 and a standard deviation of 0.05. This means that the majority of pixel values range from 0.05 to 0.15.

In October 2017 (Figure 4), it was found that areas with healthy vegetation were drastically reduced. They were located in the same areas as in October 2013 but occupy smaller areas. Particularly, in the area between Al-Assad and Jabbul lakes, there is no longer any area with healthy vegetation, except for a small section northeast of lake Jabbul. From the NVDI histogram for the year 2017 (Figure 2), it appears that the values of the pixels range from -0.23 to 0.61, with an average value of 0.09 and a standard deviation of 0.04. That is, most pixels take values from 0.05 to 0.12.

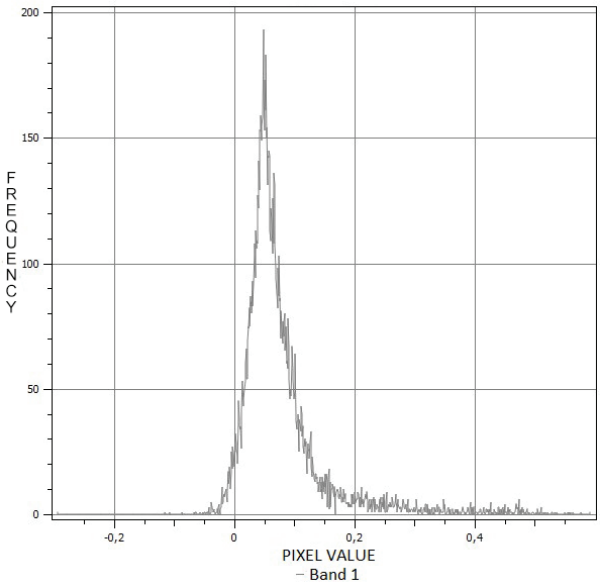

Figure 5. Histogram NBR for October 2013.

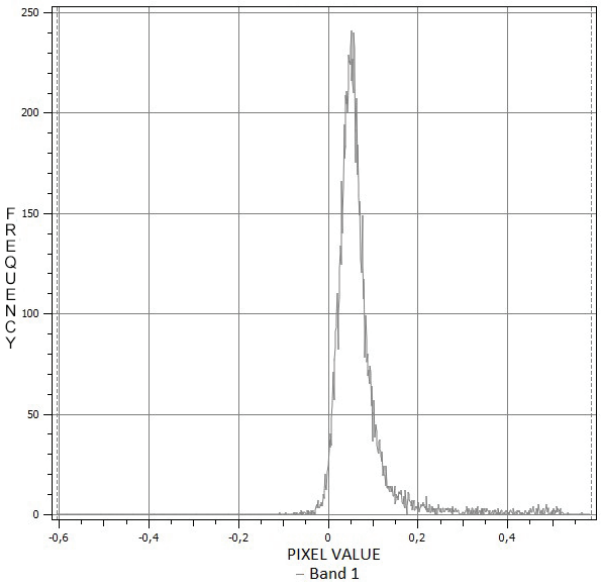

Figure 6. Histogram NBR for October 2017.

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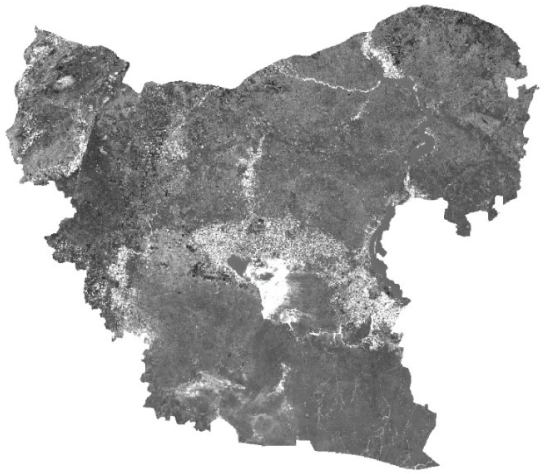

Figure 7. NBR October 2013.

Figure 8. NBR October 2017.

b) Normalised Burn Ratio, NBR.

From the calculation of the normalised burn ratio NBR, for October 2013 (Figure 5), it appeared that the values of the pixels range from -0.74 (minimum) to 0.62 (maximum), with an average of 0.07 and standard deviation 0.06. Thus, areas with healthy vegetation show high values and are depicted in white, while areas with burnt soil are represented by very low values and intense dark colour (Figure 7).

In October 2017 (Figure 6), the corresponding index shows a decrease in the maximum value of pixels, from 0.62 to 0.59, while the minimum value remains almost constant, with a value of -0.73. The average value is 0.06 and the standard deviation is 0.06. Comparing the two images, it seems that in October 2017 healthy soils, mainly in the section between the two main lakes (Al Assad and Jabbul), are significantly reduced (Figure 8).

Additionally, the difference ΔNBR = NBR2013 – NBR2017 was calculated and used as a benchmark between two time periods (Figure 9). With values ranging from -0.78 (minimum) to 0.89 (maximum), the average value was estimated at 0.009 with standard deviation 0.06 (Figure 10). The lighter the colour of the pixels that represent higher values, the greater the probability of the destruction in the area. From the range of most values, as shown by the standard deviation, most of the government area falls into the value range -0.1 to +0.1. In other words, these are unburned areas.

c) Colour Infrared digital image composites.

Two digital image-composites were produced with their respective histograms for October 2013 and 2017 (Figures 11-14). For the image-composite obtained from the combination of the spectral classes 5,4,3 for October 2013, it is noted that the areas with the healthiest vegetation are located initially in the north-west, and specifically in the area of Afrin, along the homonymous river and almost for the most part of its area, and, along

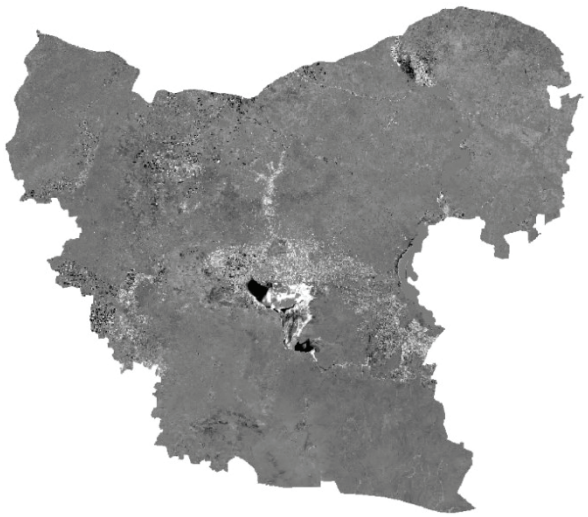

Figure 9. ΔNBR.

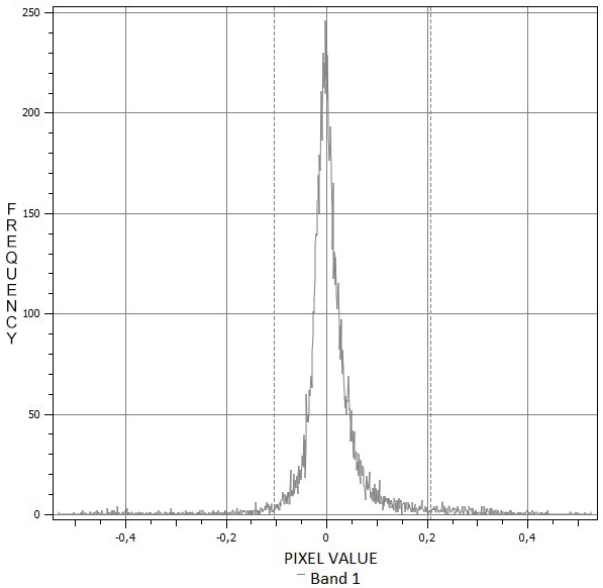

Figure 10. Histogram ΔNBR.

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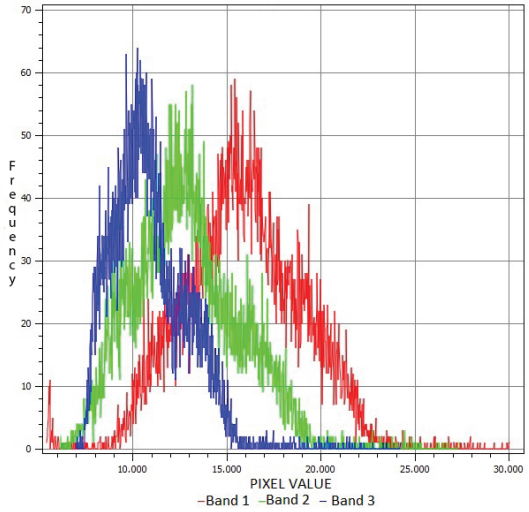

Figure 11. Histogram image-composite 2013.

Figure 12. Image-composite 2013.

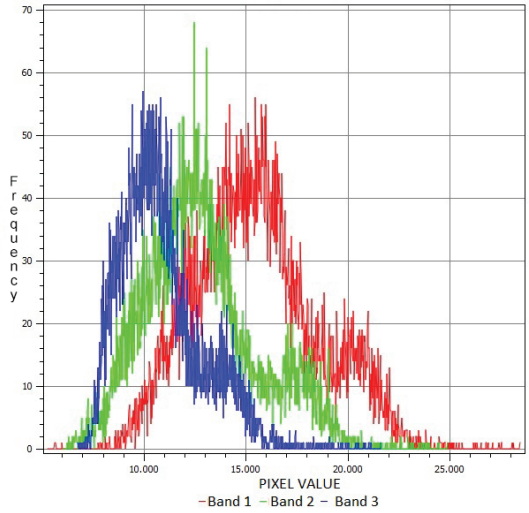

Figure 13. Histogram image composite 2017.

Figure 14. Image composite 2017.

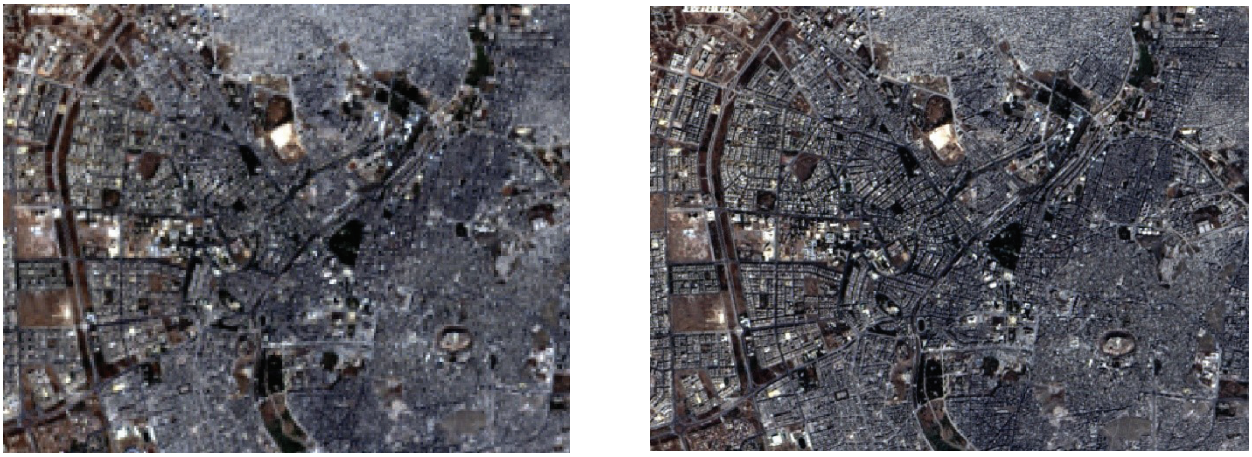

Figure 15. Part of the image pseudo-coloured composite before and after the application of the Brovey's algorithm for October 2013.

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Figure 16. Part of the image pseudo-coloured composite before and after the application of the Brovey's algorithm for October 2017.

the banks of the Euphrates river in the Jarablus and Ain Al Arab areas, in the western part of the Jebel Saman area. The most extensive area of healthy vegetation is divided spatially between the administrative divisions of As-Safira, Al Bab and Menbij and is located in the eastern part of the government from the natural border of the Euphrates up to lake Jabbul.

In the Aleppo governorates' image-composite for October 2017, the areas of healthy vegetation appear to be significantly reduced in the eastern part of the government. Especially in the areas of Al Bab and Menbij, the reduction of healthy vegetation is extended. In the Afrin region, on the other hand, healthy vegetation is almost constant at both times.

d) Pseudo-coloured image-composites.

The image pseudo-coloured composite was produced using Landsat8's 4,3,2 spectral bands and was cut to the administrative boundaries of the city of Aleppo. The pan-sharpening process was then selected.

In the 2017 pseudo-coloured composite image, after the application of Brovey's algorithm, the areas that stand out with intense grey are the ones with the least damages (Figure 16). On the contrary, areas of light colour tonality are the ones that have suffered extensive damage from the attacks. Such sharp differences were not detected in the city's pseudo-coloured image for October 2013 (Figure 15).

Analysing the data concerning the destroyed buildings in the neighbourhoods of Aleppo city, collected by UNOSAT for July 2015, it emerged that in all 115 areas where damage was recorded, 53.91% of them suffered damages of their building structures up to 20%, while 28.70% reached 20%~40% damage of their building structures. At a rate of 17.39%, more than 40% of their building structures were destroyed. The Al Aqabeh, Tal Az-Zarazi (Al-Ameria) and Handarat regions recorded the largest disasters with 65.61%, 61.42% and 61.20%, respectively.

e) Classification of digital image composites.

The two image-composites of spectral bands 6,5,2 (short infrared, near-infrared and blue), for October 2013 (Figure 17) and 2017 (Figure 18), were classified into six classes, due to the ability to separate active crops that appear with bright green colour. The rest of the classes

Figure 17. Image composite 6,5,2 (2013).

Figure 18. Image composite 6,5,2 (2017).

Table 2. Reference points to evaluate accuracy of classification.

	2013	2017
Bare soil	107	124
Water bodies	11	11
Urban areas	13	13
Active cropland	37	14
Inactive cropland	76	83
Small trees	6	5

created are also adequately separated since water bodies appear in blue, urban areas in grey, and bare soil in light shades of brown.

From the classified images for 2013 (Figure 17) and 2017 (Figure 18), it is demonstrated that there has been a reduction in active crops in 2017, as well as an increase in areas classified as bare soil. The small trees class, in the north-eastern part of the governorate is declining in 2017. Easily distinguishable are the area's dominant water bodies, the Euphrates river, lake Al Assad and Jabbul, as well as the lake Maydanki. However, there have been alterations noticed in the size of lake Jabbul in 2017. The urban network of Aleppo is quite visible in both classified images.

Both images were examined for the accuracy of their classification. 250 reference points were used, randomly selected, and placed in one of the six classes based on observations via digital images of high spatial resolution available in Google Earth Pro. These points due to their random selection are not evenly distributed in each class (Table 2). Most of the points belong to the classes of bare soil and inactive crops, while the minority belongs to the class of small trees. There is also a decrease in the reference points of the class of active crops in 2017 compared to 2013.

The results of the evaluation of the accuracy of the two classified images (Figure 19 and 20) are presented in Table 3 for October 2013 and Table 4 for October 2017.

There is an increase in bare soil areas and areas with inactive cropland. The area covered by urban areas remains the same at both times. Reduction of the area is presented in the classes of active crops, waterbodies, and small trees. Particularly in active crops, the reduction in area is 61.64%, as shown by the values of the area of the category from the classification accuracy classification tables. The confidence interval column shows the degree of uncertainty of the sample, i.e., for each class, and shows the extent to which it is considered to have been classified in the wrong class. Particularly high uncertainty is found in the classification of tree cover in both classified images.

Discussion

Most of the conflicts, especially in the case of Syria, have resulted in large population immigration phenomena, changing existing land use, and creating new dynamics in natural ecosystems. The environmental consequences of war are not limited to terrestrial ecosystems, but also to aquatic ecosystems as they are as intense as the contamination of both surface and groundwaters (Biswas, 2001). In addition, the effects on the atmosphere and their possible dispersion depend on the atmospheric and weather conditions of each region.

The use of satellite sensing techniques with the help of G.I.S. is a useful tool while trying to record the environmental impacts of war. By processing and analysing them, researchers are able to collect useful data for war zones that would be otherwise difficult and/or impossible to access. This makes it possible to assess and evaluate the situation and establish an immediate intervention. The analysis of satellite images gives the advantage of the spatial-temporal study of the war zones with the use of indicators, such as the NDVI index, which provides information on vegetation status. The use of the NDVI index has been shown in many cases to be related to armed conflicts with changes in vegetation, whether it was due to direct use, the use of weapons, or indirectly from the abandonment of rural areas and/or the use of forest areas for timber. (Witmer, 2008; Brown, 2010; Witmer and O'Loughlin, 2011; Mitri *et al.*, 2014; Muller *et al.*, 2016).

In the present study, the use of the normalised vegetation index (NDVI) showed that there is a decrease

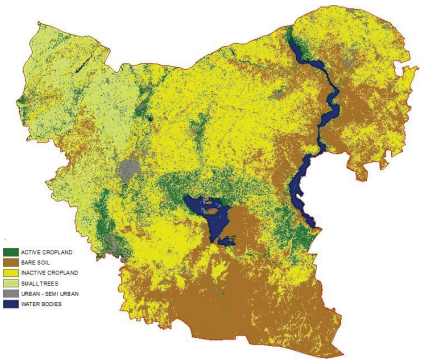

Figure 19. Classified image October 2013.

Table 3. Integrated classification accuracy scoreboard –2013.

Classes	Area (ha)	± 95% CI	Observer accuracy (%)	Analyst accuracy (%)	Total accuracy (%)
Bare soil	838,726.80	104,424.86	81.2	61.7	56.9
Water bodies	53,575.17	9,546.12	91.7	100	
Urban areas	100,296.75	49,821.78	46.2	41.9	
Active cropland	303,022.65	84,196.22	47.8	26.7	
Inactive cropland	645,680.95	108,994.40	52.1	67.9	
Small trees	46,892.90	37,155.03	0	0	

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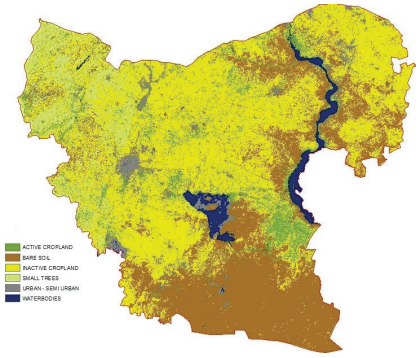

Figure 20. Classified image October 2017.

Table 4. Integrated classification accuracy scoreboard –2017.

Classes	Area (ha)	± 95% CI	Observer accuracy (%)	Analyst accuracy (%)	Total accuracy (%)
Bare soil	954,329.71	107,468.43	85.5	51.3	54.8
Water bodies	60,229.16	24,581.03	81.8	75.2	
Urban areas	100,894.70	52,607.54	27.8	34.6	
Active cropland	116,233.69	55,853.37	27.8	34.1	
Inactive cropland	717,530.37	111,922.42	49.5	66.9	
Small trees	38,977.58	34,054.30	0	0	

in healthy vegetation between 2013 and 2017, mainly in the riverine areas of the Euphrates, in the north-western area of the government, and especially in the rural area southeast of Aleppo, in Al-Assad and Jabbul lakes. The vegetation for October 2017 remains healthy in the northeast of lake Jabbul. The same conclusion emerges from the interpretation of the colour-infrared image-composites created. The NBR's burn rate index, as well as the ΔNBR difference between the two indices for October 2013 and 2017, identified some burned areas but had to be confirmed by high-resolution images, and/or observers in the area. Even if it may not be highly suitable for areas with sparse vegetation, such as the governorate of Aleppo, it is particularly useful in areas with intense vegetation. Still, its use is recommended as long as there is a way to strongly identify the results.

The pseudo-coloured image-composites for the city of Aleppo were also the first indication of the areas damaged. With the analysis of statistical data and their representation, along with the help of geographic information systems, the indications of the image-composites were confirmed. Correspondingly, the classified digital images also showed a significant decrease in cultivated areas with an increase in abandoned agricultural areas and areas of intense soil erosion. Although the overall accuracy of the classified images was relatively low, statistics on the Aleppo government confirm these changes.

In conclusion, the consequences of a war on the environment are multidimensional, either direct or indirect, affecting natural ecosystems in ways that are often irreversible. The environmental impact of war creates social and economic consequences, which further degrade the environment by showing the need to consider the effects in a more comprehensive approach, while the synergy of the already degraded environment in the scale of the humanitarian crisis must not be underestimated.

Key Points

- War has great environmental impacts that create social and economic consequences.
- Environmental impacts are identified using satellite-derived images.
- Geographic information systems can be a useful to remotely analyse war zones where physical observations are impossible.

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Stress management intervention to enhance adolescent resilience: a randomized controlled trial

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Abstract

The purpose of this study was to examine the effects of an 8-week stress management intervention to enhance resilience and coping techniques and decrease stress in adolescent students. Teenagers, 11 to 17 years old, recruited from two tertiary Adolescent Medicine Centers of the National and Kapodistrian University of Athens, Greece, were randomly assigned into two groups: the stress management group (n=24) and the control group (n=25). Resilience, stress, anxiety, everyday use of social media, school performance and cognitive skills were measured in adolescents of both groups, pre- and post-intervention. Post-intervention, the stress management group had significantly higher resilience scores and school performance self-evaluation scores, lower scores of stress, anxiety and everyday use of social media and better cognitive skills than the control group. Regarding cognitive skills, the stress management group significantly improved the speed of information processing and memory. Adolescents following stress management experienced significantly reduced stress from interacting with teachers/parents, from peer pressure, from school/leisure conflict as well as compulsive behaviours. With respect to resilience, the intervention improved adolescents' individual skills and resources, relationships with primary caregivers, and environmental factors that facilitated the sense of belonging. Future studies of large adolescent samples are required to evaluate the long-term benefits of stress management techniques on adolescents' health and resilience, as well as the need of continued support to preserve these benefits throughout transition to adulthood.

Introduction

Adolescence is a crucial transition period from childhood to adulthood, during which teenagers experience many challenges that can ultimately affect their health. These challenges can also be referred to as stressors, and can be intrapersonal (*e.g.*, changes in sleeping and eating habits), academic (*e.g.*, increased class workload), interpersonal (*e.g.*, change in social activities) and environmental (*e.g.*, increased screen time) (Ross *et al.*, 1999). Stress is a multidimensional term. In 1970, psychologists Richard Lazarus and Susan Folkman introduced the concept of perceived stress and defined stress as a transaction between the person and the environment. They argued that when a person feels unable to cope with the demands of the environment, based on personal abilities and skills, then he or she experiences stress (Lazarus and Folkman, 1984). Later, the pediatrician-endocrinologist George Chrousos defined stress as the situation of real or perceived threat to homeostasis and described the complex network of behavioural and physiological adaptation responses (Chrousos and Gold,

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1992). Resilience refers to successful adaptation to stress; Flora Bacopoulou and George Chrousos have defined resilience as the ability of the individual to maintain, regain or improve homeostasis - eustasis or hyperstasis - despite adverse life experiences (Bacopoulou and Chrousos, 2013). There are several literature reports of everyday hassles and major stressful life events (natural disasters, poverty, parental divorce, and parental psychopathology) as risk factors for depression, reduced skills and low resilience (Luthar and Zigler, 1991). Resilience is a dynamic process of positive adjustment in the context of significant adversity (Luthar *et al.*, 2000). Resilience can be perceived as the positive response and recovery capacity after major setbacks, excessive demands, and intensely stressful situations. The main feature of resilience is the ability of the individual to return to his / her original level of function after any stressful event (Carver, 1998; O'Leary and Ickovics, 1995; Block and Block, 1980; Block and Kremen, 1996; Lazarus, 1993). Psychologists have studied resilience for years, but nowadays the goal is to enhance resilience before the exposure to a stressful or traumatic event (Everly *et al.*, 2008). Resilience is positively correlated with self-efficacy (Bandura, 1997; 2003), hardiness (Kobasa *et al.*, 1982), internal locus of control (Luthar, 1991; Sandler *et al.*, 2000; Grobet *et al.*, 1995; Wyman, 2003), social skills and social support, adolescent coping skills (WHO, 2004; Jensenet *et al.*, 2006; Everly and Lating, 2002; Steinhardt and Dolbier, 2008) and moderate use of social media. High intelligence, on the other hand, may have a negative impact on resilience according to some investigators. Stress management techniques seem to minimize its negative impact on health and, thus, on resilience and quality of life (Steinhardt and Dolbier, 2008). People with high resilience usually have better ways to manage their stress (coping process) (Frederickson, 2000).

Increasing numbers of researchers have evaluated the effects of stress management programs for students. Such interventions aim at reducing stress and improving health by focusing on relaxation techniques (*e.g.*, diaphragmatic breathing, muscle relaxation, imagery, meditation biofeedback) and cognitive-behavioural strategies which help to identify and change maladaptive thinking (*e.g.*, all- or- none, perfectionism, self-punishing) and behaviour (*e.g.*, alcohol and drug use, smoking, internet addiction). Social support is thought to be a buffer against negative effects of stress and increases resilience. Social support provides a safe environment where individuals are encouraged to share their experiences, thoughts, and feelings.

The purpose of this study was to assess the effects of a stress management technique designed to enhance adolescents' resilience, adaptive coping strategies, and protective factors, as well as decrease maladaptive coping strategies, thinking and behaviours. We hypothesized that adolescent students who attended an 8-week stress management intervention would demonstrate enhanced resilience, coping skills and protective factors, better school performance, as well as decreased maladaptive thinking and behaviours such as time spent on social media, compared to students in the control group.

Materials, Methodologies and Techniques

Study Sample

The minimum sample size calculated for each group was 20 (N = 40). The sample was recruited from two tertiary Adolescent Medicine Centers of the National and Kapodistrian University of Athens, the Center for Adolescent Medicine and UNESCO Chair on Adolescent Health Care at the "Aghia Sophia" Children's Hospital and the Adolescent Health Unit at the "P. & A. Kyriakou" Children's Hospital. The study protocol was approved by the Scientific and Ethics Committee of the "Aghia Sophia" Children's Hospital.

Inclusion and exclusion criteria

Healthy teenagers, 11-17 years old, students able to read and write in Greek, were eligible to participate in the study. Adolescents with diagnosed psychiatric disorders or other diseases, adolescents under psychological or psychiatric treatment, and substance users were excluded.

Study Design

Adolescents were randomized into two groups, the stress management (SM) group and the control group, based on random numbers derived from a random number generator (random.org). Participants in both groups and their parents or guardians were informed about the program's purposes and signed consent forms prior to study entry.

The intervention comprised health promotion and stress management techniques such as diaphragmatic breathing, progressive muscle relaxation and guided imagery (Steinhardt and Dolbier, 2008). The SM group followed an 8-week stress management program based on the following timetable. Appointments were scheduled with the adolescents.

Stress Management Intervention according to Weeks:

1. Completion of pre-intervention questionnaires. Power point presentation and discussion about stress, healthy lifestyle, and everyday routine. Tips for exercise, systematic walking, disposal of individual pedometers and practical guide on stress management and healthy behaviours in print. Emphasis placed on the implementation of systematic exercise.
2. Power point presentation on application of "Diaphragmatic Breathing" technique, individually or in groups. Learning of diaphragmatic breathing was facilitated by the use of Biofeedback. Recommendation to apply relaxation techniques twice a day (morning and evening). Quality data recorded.
3. Power point presentation on implementation of "Progressive Muscle Relaxation", individually or in

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groups. Learning of progressive muscle relaxation facilitated through a CD. Recommendation to apply the relaxation technique twice a day (morning and evening). Provision of a CD and a booklet of relaxation techniques. Quality data recorded.

4. Power point presentation on "Cognitive Behavioural Therapy". Discussion of the so far implemented techniques and empowerment to continue the program. Quality data recorded.
5. Power point presentation on "Healthy Diet". Empowerment to continue the program. Quality data recorded.
6. Learning and application of the relaxation technique of "Guided imagery", with the use of a CD. Recommendation to apply the technique twice a day (morning and evening). Quality data recorded.
7. Re-check with each participant separately relaxation techniques and encourage healthy behaviours. Quality data recorded.
8. Completion of post-intervention questionnaires. Quality data recorded. Relevant questions and queries were solved, clarifications were given.

Each participant was advised to practice the stress management intervention twice a day; to begin with diaphragmatic breaths and progressive muscle relaxation, and then, after learning the technique of guided imagery, to replace one of the former two techniques, depending on what was best suited for the adolescent. At each session, a qualitative assessment of the changes (benefits) was made, as the individual recorded the results of the intervention. To monitor compliance and solve potential adolescents' problems, a once-a-week appointment was scheduled with participants, who were encouraged to communicate with the researchers through telephone or via e-mail if any problem occurred.

Measures

Adolescents of both groups, before and after the 8-week intervention, were assessed for their levels of stress, anxiety, resilience and school performance, the frequency of use of social media, as well as their cognitive skills, as follows:

Assessment of Stress levels: Stress levels were assessed with the Adolescent Stress Questionnaire (ASQ) (Darviri *et al.*, 2004; Byrne *et al.*, 2007; Moksnes and Espnes, 2011; De Vriendt *et al.*, 2011). The questionnaire consists of 58 questions about the stress experienced by the teenager in the last year, circling a number from 1 to 5, based on a 5-level Likert type scale [1 = No stress (or not applicable to me), 2 = Some Stress, 3 = Moderate Stress, 4 = Enough Stress, 5 = A Lot of Stress].

Assessment of Anxiety levels: Anxiety levels were assessed with the Spence Children's Anxiety Scale (SCAS). The questionnaire consists of 46 questions about the anxiety felt by the teenager. The person is asked to answer the questions based on a 4-stage Likert type scale (1 = Never, 2 = Sometimes, 3 = Often, 4 = Always), by circling the appropriate word. The highest score that anyone can get is 114 (Mellon and Moutavelis, 2007).

Assessment of Resilience levels:The Child and Youth Resilience Measure (CYRM) –The Youth version was used to measure adolescents' resilience. The questionnaire consists of 28 questions about the person's personal, social, and interpersonal abilities and his / her level of resilience. The person is asked to answer the questions based on a 3-stage Likert type scale (No, Sometimes, Yes) by circling the appropriate word. Good psychometric properties have been reported with great internal credibility of this tool in other countries (Liebenberg *et al.*, 2012).

Assessment of School Performance: A self-report question about school performance. The question will be answered by the teenager. The question was: "How good do you think you are as a student when you take into account your overall presence in the classroom (homework preparation, classroom participation, performance in tests)?" Respondents will place their answer on a number line from 0 to 10, with 0 meaning "no good at all" and 10 "excellent".

Assessment of the frequency of use of Social Media: The frequency of social media use was assessed with the self-report question "How many hours do you spend on social networking pages per day on a mobile / tablet / computer?"

Assessment of Cognitive Skills: Cognitive tests assess cognitive skills such as memory, concentration, speed of recall and information processing (Langdon *et al.*, 2012; Sheridan *et al.*, 2006; Stegen *et al.*, 2010; Benedict, 1997). The following cognitive assessment tests were used:

- Normative Symbol Digit Modalities Test (SDMT): The SDMT is a screening instrument. Performance on the SDMT is underpinned by attention, perceptual speed, motor speed and visual scanning. The SDMT consists of a key with two rows, with nine stimulus symbols in the upper row and matched numbers (1–9) in the row below it. The task sequence consists of a series of symbols, each with a blank space underneath that the subject is asked to consecutively fill with the corresponding numbers as fast as possible in 90 seconds after completing a 10-item practice trial. The score of the test is the number of correct substitutions completed within the time limit, with the maximum score of 110.California Verbal Learning Test-II (CVLT-II): The CVLT-II measures both recall and recognition of two lists of words over several immediate- and delayed-memory trials. List A is composed of 16 words, four words each of four semantic categories. An interference list (List B) of 16 words is then presented for one trial. The interference trial is followed by short-delay free-recall and short-delay cued-recall trials for List A. The CVLT-II ends with a new, optional forced-choice recognition trial that is administered approximately 10 minutes following the yes/no recognition trial.

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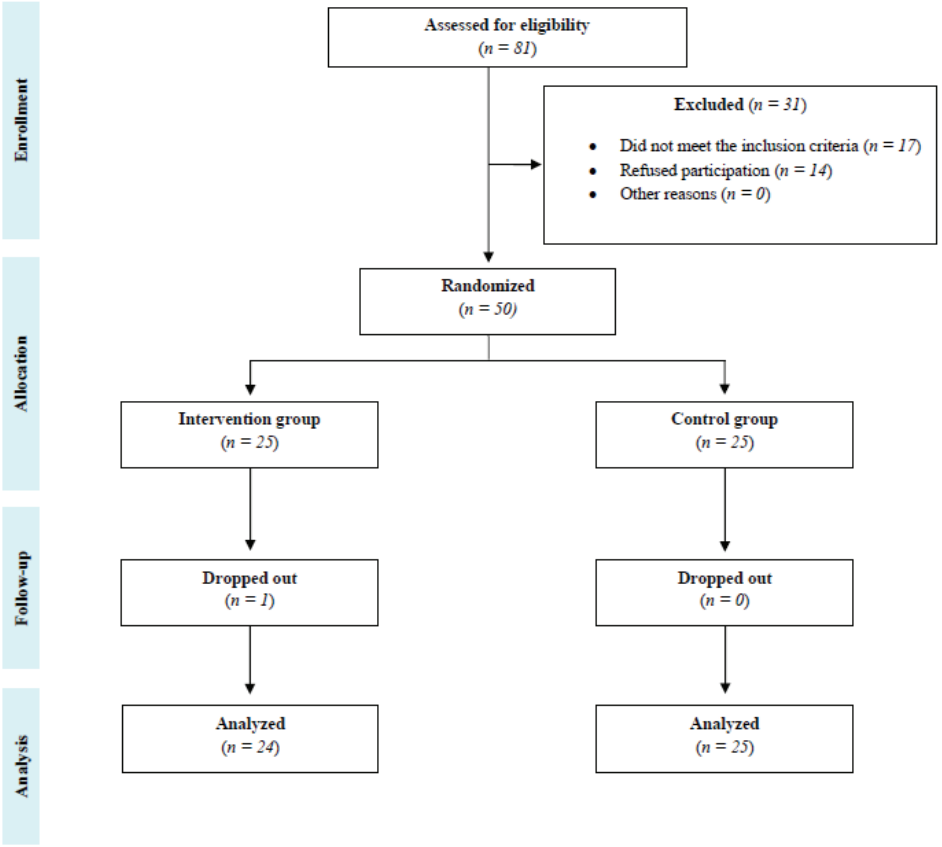

Figure 1. Study flowchart.

- Brief Visuospatial Memory Test-Revised (BVMT-R) (Langdon *et al.*, 2012; Sheridan *et al.*, 2006; Stegen *et al.*, 2010; Benedict, 1997): The BVMT-R was designed as an equivalent multiple test for assessment of visual memory. The BVMT-R comprises six alternate, equivalent forms (Forms 1 through 6). Each form consists of a) 6 geometric figures printed on a 2x3 array on a separate page of the Recall Stimulus Booklet, and b) 12 recognition items, each printed on a separate page in the Recognition Stimulus Booklet. A manual is required for precise scoring and interpretation, but it is not necessary to have the manual present during the administration of the test.

Statistical analysis

Longitudinal changes in outcome measures from baseline to 8 weeks (or rate of outcome change) were analysed using linear mixed-effects models with interaction terms for study group and time points. Random intercepts were used for the random effect of each participant in the model using variance components structure (Supplementary models' formula). Means of observed and the adjusted (estimated marginal means for group x time) outcome changes and their SEs are presented (Table 2). The level of significance was set at 0.05. Analyses were performed using SPSS version 22.0 (Chicago IL).

Results

Overall, 81 teens were approached. Of these, 31 were excluded (17 did not meet the inclusion criteria, 14 refused to participate). Fifty adolescents were randomized to the SM intervention group and the control group. One adolescent from the SM group discontinued the follow-up without a known reason. Finally, 24 adolescents were included in the SM group and 25 in the control group. The study flowchart is presented in Figure 1.

Girls were represented in approximately 70% in both groups. The median ages in the SM group and the control group were 16.1 and 14.6 years, respectively (Table 1).

Data were compared before and after the intervention, but also between groups, and statistical criteria were used depending on the size and type of the variable (within and between analysis).

Table 1. Demographics of the study sample.

Characteristic	SM Group (N=24)	Control group (N=25)	p value
Girls N, (%)	17 (70.8)	18 (72.0)	0.01*
Median Age (Min,Max), years	16.08 (11,17)	14.60 (11,17)	<0.001*

SM: stress management

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Table 2. Results of the Linear Mixed-Effects Models with Random Intercepts for the Rates of Outcome Change.

Characteristic	b for group × time interaction (SM group vs. Control group)±SE	p value
School performance, self-evaluation	0.54 ± 0.17	0.003*
Hours spent daily on social media	-1.05 ± 0.33	0.003*
Cognitive test- Mathematical test (countdown- right answers)	1.98 ± 0.48	0.000*
Cognitive test- Mathematical test (countdown)- minutes needed to complete	-6.15 ± 7.08	0.390
Cognitive test- the three keywords	0.00 ± 0.10	1.000
Physical exhaustion	-0.38 ± 0.46	0.410
Mental exhaustion	-1.03 ± 0.63	0.107
Psychological exhaustion	-1.31 ± 0.74	0.085
Cognitive test- Normative Symbol Digit Modalities Test	18.87 ± 2.80	0.000*
Cognitive test- California Verbal Learning Test–II (CVLT-II)	7.16 ± 2.20	0.002*
Cognitive test- Brief Visuospatial Memory Test Revised (BVMT-R)	1.02 ± 1.55	0.515
Stress of teacher/adult interaction (ASQ)	-4.31 ± 0.99	0.000*
Stress of peer pressure (ASQ)	-2.54 ± 0.81	0.003*
Stress of home life (ASQ)	-3.36 ± 1.97	0.095
Stress of adult responsibility (ASQ)	-0.92 ± 0.49	0.065
Stress of romantic relationship (ASQ)	0.42 ± 0.83	0.619
Stress of school attendance (ASQ)	-1.22 ± 0.74	0.108
Stress of school/leisure conflict (ASQ)	-3.05 ± 1.08	0.007*
Stress of school performance (ASQ)	-1.37 ± 0.76	0.077
Stress of financial pressure (ASQ)	-0.38 ± 0.69	0.585
Panic disorder and agoraphobia (SCAS)	-0.86 ± 0.81	0.292
Generalized anxiety disorder (SCAS)	-0.58 ± 0.78	0.462
Separation anxiety disorder (SCAS)	-0.76 ± 0.54	0.166
Physical injury fears (SCAS)	-0.46 ± 0.65	0.483
Social phobia (SCAS)	-0.46 ± 0.66	0.486
Compulsive behaviour (SCAS)	-1.14 ± 0.36	0.002*
Individual capacities/resources (CYRM)	1.74 ± 0.56	0.003*
Relationship with primary caregiver (CYRM)	1.16 ± 0.43	0.010*
Contextual factors that facilitate the sense of belonging (CYRM)	1.20 ± 0.45	0.011*

SM: stress management, SE: standard error, ASQ: Adolescent Stress Questionnaire, SCAS: Spence Children's Anxiety Scale, CYRM: Child and Youth Resilience Measure

Table 2 presents the results of mixed effects models concerning changes over time.

Patients in the SM intervention group demonstrated statistically significant reductions in the hours spent daily on social media, in stress (ASQ) and in anxiety (SCAS), and significant increases in resilience (CYRM) and in self-evaluation of school performance. More specifically, in terms of the adolescents' stress, statistically significant lower scores were recorded in stress derived from teacher/adult interaction, from peer pressure and in stress derived from school/leisure conflict. Statistically significant lower scores were also recorded in the compulsive behaviour, assessed by SCAS. Finally, resilience assessed by CYRM showed higher scores in the individual abilities/resources, in the relationship with the primary caregiver and in the factors facilitating the sense of belonging. In terms of cognitive functions, statistically significant differences were noted in the mathematical test (countdown), in the Normative Symbol Digit Modalities Test and in the California Verbal Learning Test–II (CVLT-II).

As shown in Table 3, 8.3-16.7% of the adolescents exhibited significant score changes according to the Reliable Change Index (RCI) used for the questionnaires. Based on the Number Needed to Treat (NNT) values the strongest effect was noted for processing speed as assessed by the Normative Symbol Digit Modalities Test.

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Table 3. Number of individuals with beneficial significant score changes according to the Reliable Change Index and the corresponding Number Needed to Treat (NNT) values.

Characteristic (Cronbachs' alpha before, after)	SM group N (%)	Control group N (%)	NNT
School performance- self-evaluation	0 (0)	0 (0)	-
Hours spent daily on social media	1 (4.2)	0 (0)	24
Cognitive test- Mathematical test (countdown- right answers)	1 (4.2)	0 (0)	24
Cognitive test- Normative Symbol Digit Modalities Test	4 (16.7)	0 (0)	6
Cognitive test- California Verbal Learning Test–II (CVLT-II)	0 (0)	0 (0)	-
Stress of teacher/ adult interaction	1 (4.2)	0 (0)	24
Stress of peer pressure	0 (0)	0 (0)	-
Stress of school/leisure conflict	0 (0)	0 (0)	-
Compulsive behaviour	0 (0)	0 (0)	-
Individual capacities/ resources	2 (8.3)	0 (0)	12
Relationship with primary caregiver	1 (4.2)	0 (0)	24
Contextual factors that facilitate the sense of belonging	0 (0)	0 (0)	-

SM: stress management, NNT: number needed to treat

Discussion

The aim of this research was to examine whether adolescents following stress management techniques for 8 weeks could improve their resilience, their ability to cope and recover after adversities. This would help them manage more effectively their stress of school and perform better, adopt a healthier lifestyle *i.e.* reduce hours in social media, and build stronger relationships. The study results demonstrated statistically significant differences between the SM intervention group and the control group in several areas. More specifically, the SM group (vs. the control group) experienced improvement in school performance (by self-evaluation) and reduced the hours spent on social media. Regarding cognitive skills, the SM group significantly improved the speed of information processing and memory. Stress management techniques seem to have helped in reducing adolescents' stress from interacting with teachers/parents, from peer pressure, from school/leisure conflict as well as compulsive behaviours. Adolescents in the SM group improved their resilience, their individual skills and resources, their relationship with primary caregivers, and the environmental factors that facilitated the sense of belonging.

The teenagers who participated in the SM group significantly reduced the stress they experienced in relation to their social environment. This concept is inextricably linked to the concept of resilience. Self-efficacy and support from the social environment (as well as the teen's ability to ask for this support without being ashamed or afraid) are important to enhance resilience (Werner and Smith, 1982; Fergus and Zimmerman, 2005; Zolkoski and Bullock, 2012). On the other hand, academic success/performance is also a very important factor which enhances adolescents' resilience, according to the protective factor model of resilience (Fergus and Zimmerman, 2005; Zolkoski and Bullock, 2012). Daily adversities in adolescent life can be offset by other buffers such as academic performance and supportive social environment. Similarly, protective or reinforcing factors for young people can also be considered the improvement of cognitive abilities, such as the speed of processing information and memory but also the improvement of individual capacities and resources, the relationship with primary caregivers and other environmental factors that facilitate the sense of belonging. All the aforementioned variables were significantly improved in the intervention group, as already mentioned. Furthermore, personal self-control (Fergus and Zimmerman, 2005; Zolkoski and Bullock, 2012) has an impact on everyday routine (mainly in eating and sleeping) and is very important in enhancing resilience. The reduction of stress in many aspects of the teen's daily routine, is very important and is being pursued by many programs trying to enhance adolescents' resistance and resilience against adversities (Daining and DePanfilis, 2007; Steinhardt and Dolbier, 2008; Abolghasemi and Varaniyaba, 2010).

The adolescents who participated in the SM intervention group experienced statistically significant improvement in their routine, since they improved the self-evaluation of their school performance and they reduced the hours spent daily on social media. Cognitive skills also recorded significantly higher scores. The relationship between stress and cognitive functions has been highlighted and fully elucidated by a very large volume of literature (McEwen and Sapolsky, 1995; Pechtel and Pizzagalli, 2011; Yuen *et al.*, 2012). Lupien *et al.* (Lupien *et al.*, 2009) showed that chronic exposure to stress hormones during the prenatal period, infancy, childhood, adolescence, adulthood, or old age, has an

impact on brain structures involved in cognition and mental health. In this study, it appeared, also, that stress management in adolescents helped them improve some of their cognitive functions.

There are some limitations that must be considered before interpreting the results of this study. The sample was small (a total of 49 adolescents, mainly girls), therefore, the results cannot be generalized to the broader adolescent population. The study included self-reported questionnaires and thus, a subjective view of the sample responses. Furthermore, there was no objective measurement of compliance to the stress management techniques during the program despite the frequent feedback from the adolescents. Finally, it is not known whether the benefits were maintained after the completion of the program, as there was no follow-up. However, despite the short duration of the program, several beneficial outcomes were reported.

Future studies of large adolescent samples are required to evaluate the long-term benefits of stress management techniques on adolescents' health and resilience, as well as the need of continued support to preserve these benefits throughout transition to adulthood.

Key Points

- An 8-week stress management intervention enhanced resilience in adolescents.
- Stress, compulsive behaviours and social media time were reduced post-intervention.
- Adolescents experienced improvement in school performance and cognitive skills.

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Pythagorean Self Awareness Intervention in Caregivers of Patients with Motor Disabilities

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Abstract

Caregiving for disabled people is a strenuous task often provided by family members, with adverse repercussions on the caregivers' health. The aim of this study was to evaluate, for the first time, the effects of a novel cognitive-based stress management technique, the Pythagorean Self-Awareness Intervention (PSAI) on the stress levels and other cognitive and psychological characteristics of non-paid caregivers of patients with motor disability. In this quasi-experimental study, 59 caregivers of first-degree relatives with motor disabilities due to chronic neurological diseases, inpatients at a Rehabilitation Center, in Athens, Greece, were assigned to an intervention (PSAI, n=28) and a control group (received unstructured consultation, n=31). Psychological, cognitive, and sleep-related measurements (Zarit Burden Interview tool, Pittsburgh Sleep Quality Index, Self-Efficacy Scale, Depression, Anxiety and Stress Scale, Symbol Digit Modalities Test, California Verbal Learning Test-II, Brief Visuospatial Memory Test-Revised) were held at baseline and after 8 weeks (at completion of PSAI) in both groups. PSAI was found to decrease caregivers' stress, depressive symptoms and anxiety and improve their sleep quality, visual memory, self-efficacy, and cognitive speed processing. Future randomized controlled studies are needed to investigate the effects of this novel intervention in larger samples of caregivers.

Introduction

Disability can be defined as the reduced functional capacity due to mobility-related or other problems deriving from chronic illness or advanced age. Caregiving for disabled people is a strenuous and complex task which is often provided by family members, and has several repercussions (Roth *et al.*, 2015). Caregivers may experience high levels of distress in the four aspects of their life; physical (Portenoy *et al.*, 1994), spiritual, social and psychological (Carlson *et al.*, 2004; Carlson and Bultz, 2003). Caregivers' stress might be as high as it is for the patients themselves (Nijboer *et al.*, 1998). More specifically, increased and/or long-term stress caused by caregiving has been linked to impaired social life, work-related problems, depression, chronic anxiety, cognitive problems, sleep disturbances, cardiac and metabolic diseases and even increased mortality (Lwi *et al.*, 2017; Roth *et al.*, 2015). These consequences are caused either directly by the hyperactivity of the stress system, or indirectly by the unhealthy lifestyle and social behaviours ascribed to the stress of caregiving (Allen *et al.*, 2017). Stress-management seems to alleviate the adverse outcomes related to caregiving, as shown by two meta-analyses (Dharmawardene *et al.*, 2016; Gilhooly *et al.*, 2016).

The Pythagorean Self-Awareness intervention (PSAI) is a novel cognitive intervention based on 71 moral values (Golden Verses) described by the ancient philosopher Pythagoras (Guthrie, 1962). The PSAI

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incorporates these Pythagorean values to promote individuals' self-awareness by changing the way they view others and themselves. The technique consists of three basic stages. On the first stage, individuals are called to sequentially recall daily events; on the second stage, to contemplate on thoughts and emotions derived from the recalled events; on the third and last stage, to critically appraise their attitude as internal observers. The difference of the PSAI from other relaxation techniques is the lack of focusing on objects, breathing or senses. For example, the Pythagorean Self-Awareness technique requires critical self-evaluation compared to the non-judgmental approach of mindfulness (Creswell, 2017). This difference encourages individuals practicing the technique to evaluate and modify their lifestyle, the way they connect with others and their behaviour. Via Pythagorean Self-Awareness, thought process and feelings interact and coordinate. To activate the internal observer, the individual must focus on inner self, concentrate, and mobilize the memory. On a neurobiological level, the key point of the technique is the Default Mode Network (DMN), a neural brain connection system related to the processes of cognition (Buckner *et al.*, 2008). The role of DMN is significant in meta-cognitive processes and in adjusting individual behaviour via impulse's inhibition (Shapira-Lichter *et al.*, 2013). Through the three stages of the Pythagorean Self-Awareness technique individuals identify wrong choices and unhealthy behaviours and are motivated to change. This internal dialogue promotes a healthier lifestyle and may reduce stress and anxiety. The PSAI has been implemented in different populations, with positive results so far. The technique has been applied to obese, breast cancer and multiple sclerosis patients, as well as females with acne vulgaris (Anagnostouli *et al.*, 2018; Charalampopoulou *et al.*, 2020; Chatzikonstantinou *et al.*, 2019; Simos *et al.*, 2019). All studies demonstrated significant improvements of participants' subjective stress levels, quality of life, cognitive tests, and other psychosocial characteristics.

The aim of this study was to evaluate, for the first time, the effect of PSAI on the stress levels and other cognitive and psychological characteristics of caregivers of inpatients with motor disability due to chronic neurological diseases. The initial hypothesis was that a holistic program of cognitive-based stress management such as the PSAI would improve the psychological dimensions, sleep quality and cognitive aspects of caregivers.

Materials, Methodologies and Techniques

Study design and participants

This non-randomized two-armed study was conducted at the Filoktitis Rehabilitation Center, in Athens, Greece. Study participants were recruited over a period of 6 months and were eligible for inclusion if they were i) 18 years or older, ii) caregivers of first-degree relatives of patients with motor disability due to chronic neurological diseases, iii) not receiving remuneration for caregiving, iv) providing care for at least 1 hour per day over at least one year, and v) able to read and write in Greek. Caregivers with a history of major psychiatric disease (*i.e.* depression, drug abuse etc.), under any type of psychotherapy, practicing any type of relaxation techniques, or having experienced a major life event within the previous 6 months, were excluded. Participants were allocated to either the PSAI group or the control group that received unstructured consultation. Assignment was made in a non-randomized fashion due to the time required to take part in the PSAI; considering the burden of responsibility a caregiver carries and the shortage of free time, the researchers decided to ask which caregivers were able to participate in the PSAI group, and thereby, the non-randomized fashion can be justified.

Ethical considerations

The study protocol was approved by the Center's Ethics Committee and was consistent with the Declaration of Helsinki. All participants were informed about the purpose of the study and provided written, signed consent prior to study entry. Participants were reassured that they could withdraw from the study at any stage without any consequences.

Measures

Sociodemographic characteristics: Participants had to complete a form regarding their sex, age, educational level, and family status.

The following psychological, cognitive, and sleep-related measurements were held at baseline and after 8 weeks (at completion of PSAI).

Zarit Burden Interview tool: This is a 29-item caregiver self-report measure of burden. Each item on the interview is a statement which the caregiver is asked to endorse using a 5-point scale. Response options range from 0 (never) to 4 (nearly always) (Zarit *et al.*, 1980).

Pittsburgh Sleep Quality Index (PSQI): This is a 19-item self-report questionnaire that assesses the quality of sleep over a 1-month time interval. PSQI measures several aspects of sleep, with seven component scores and one composite score. The component scores consist of subjective sleep quality, sleep latency (*i.e.*, how long it takes to fall asleep), sleep duration, habitual sleep efficiency (*i.e.*, the percentage of time in bed that one is asleep), sleep disturbances, use of sleeping medication, and daytime dysfunction. Each item is weighted on a 0–3 interval scale. The global PSQI score is then calculated by totaling the seven component scores, providing an overall score ranging from 0 to 21, where lower scores denote a healthier sleep quality (Buysse *et al.*, 1989).

Self-Efficacy Scale: It consists of 17 items that assess a "general set of expectations that the individual carries into new situations, rated on a five-point scale ranging from "agree strongly" to "disagree strongly".

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Higher scores represent higher general self-efficacy (Sherer and Maddux, 1982).

Depression, Anxiety and Stress Scale (DASS-21): This is a set of three self-report scales designed to measure the emotional states of depression, anxiety, and stress. Each of the three DASS-21 scales contains 7items, divided into subscales with similar content. Scores on the DASS-21 are added and multiplied by 2 to calculate the final score (Henry, 1995).

Symbol Digit Modalities Test (SDMT): This is a screening instrument commonly used in clinical and research settings to assess neurological dysfunction. Performance on the SDMT is underpinned by attention, perceptual speed, motor speed, and visual scanning (Smith, 1973).

California Verbal Learning Test-II (CVLT-II): This is an updated version of the original CVLT, which has been standardised and provides normative data. It is one of the most widely used neuropsychological tests. It was designed to not only measure how much a subject learned, but also reveal the strategies employed and the types of errors made. The CVLT indexes free and cued recall, serial position effects (including primacy and recency), semantic clustering, intrusions, interference and recognition (Delis *et al.*, 1987).

Brief Visuospatial Memory Test-Revised (BVMT-R): This is used to evaluate visuospatial memory. The individual is presented with a matrix of six items for ten seconds and asked to replicate the matrix using pencil and paper while taking as much time as needed. The process is repeated three times. Each drawing is evaluated for both its placement (1 point) and its accuracy (1 point). The maximum score yielded by the three trials is 36 (Benedict, 1997).

Pythagorean Self Awareness Intervention: The PSAI technique was delivered by health professionals (FV and CD) with expertise in stress management, who provided weekly guidance to the enrolled caregivers, during group sessions (the PSAI technique was taught during the first session, whereas problems and barriers of PSAI practice were resolved in the ensuing sessions). The PSAI sessions took place once a week and lasted for 8 weeks. Health professionals also administered diaries to the participants to record their PSAI practice at home. The five steps were followed in a precise order twice a day, as briefly outlined in Table 1. To begin, right before bedtime participants need to sit in a quiet and relaxing place and practice diaphragmatic breathing for 5 minutes, to concentrate. Participants are then expected to recall every event that occurred during the day, all their actions, and reactions to feelings they experienced. In the third step, participants need to examine whether they followed a healthy lifestyle during the day or not. In the fourth step, they critically appraise their actions and decide what was done as it should have been done, and what could have been done in a better manner.

Table 1. Pythagorean Self Awareness Intervention steps.

Step 1	Sit at bedside and read the Pythagorean verses
Step 2	Recall every event of the day in the sequence they occurred
Step 3	Visualise yourself as an observer and contemplate on day's physical activity, diet, sleep and interpersonal interactions
Step 4	Critically appraise each event by asking yourself "In what have I done wrong ?What have I done right ? What have I omitted that I ought to have done?"
Step 5	After wake-time, summarize the conclusions from the previous night and set goals for the day

During the fifth and final step in the following morning, participants summarize their conclusions from the night before and set the goals for the day.

Statistical analysis

Statistical analysis included simple univariate tests (Pearson's chi-square test for categorical variables and Student's t tests for numerical variables). The Cohen's d effect size was calculated. A per-protocol analysis was conducted, although no dropouts were noted. The level of significance was set at 0.05. The SPSS 21.0 (Chicago IL) software was used for the analyses.

Results

A total of 59 non-paid caregivers participated in this quasi-experimental study and were assigned to either the PSAI group (n=28) or the control group (n=31). Caregivers of the PSAI group demonstrated full compliance with the intervention. No side-effect was reported by any of the participants. Sociodemographic characteristics of study's groups are presented in Table 2. No dropouts occurred during the follow-up in either of the groups.

No significant differences were noted between study groups at baseline. Table 3 presents the outcome measures' differences before and after the intervention for both groups. Significant improvements were found for all outcomes based on the effect size (*i.e.*, Cohen's d).

Table 2. Sociodemographic characteristics of participants.

Characteristic	PSAI group (n=28)	Control group (n=31)
Age (mean ± SD)	52.2 ± 12.9 %	53 ± 13.8 %
Females	78.6	87.1
Tertiary education	75	74.2
Married	50	48.4
Employed	75	77.4

PSAI: Pythagorean Self Awareness Intervention, SD: Standard deviation

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Table 3. Comparisons of outcome change differences between study groups.

Measure	PSAI (N=28)	Controls (N=31)	p value[1]
Stress	-12.5 ± 4.5	-1.0 ± 2.3	<0.0001*
Anxiety	-2.4 ± 2.6	-0.3 ± 1.6	<0.0001*
Depression	-2.9 ± 3.2	0.7 ± 2.0	0.003*
Sleep Quality	-2.4 ± 2.0	0.1 ± 0.6	<0.0001*
Self-efficacy	2.5 ± 2.5	-0.4 ± 1.0	<0.0001*
Cognitive Speed Processing	2.43 ± 3.70	0.90 ± 1.58	0.04*
Verbal Memory	2.32 ± 6.85	0.74 ± 1.98	0.224
Visual Memory	4.3 ± 2.8	0.7 ± 1.5	<0.0001*

*Values represent means ± standard deviations. Outcome measures' differences calculated as baseline minus follow up. 1Student's t-test, *Significant difference at p ≤0.05*
PSAI: Pythagorean Self Awareness Intervention

Discussion

The aim of the present study was to assess the effects of the novel Pythagorean Self-Awareness Intervention on the stress levels and specific psychological and cognitive functions of caregivers of inpatients with motor disabilities due to chronic neurological diseases. The initial hypothesis that the PSAI would improve caregivers' psychological dimensions, sleep quality, and cognitive aspects was verified. Although there were significant improvements in all measured characteristics, the strongest effect sizes were observed in stress, anxiety, sleep quality, self-efficacy, and visual memory. In 1990, Pearlin proposed a stress model for caregivers, which divided stressors in primary and secondary, *i.e.* daily activities, role factors (intra-family relationships), behavioural disturbances, social isolation, lack of knowledge about the patient's disease and economic concerns were included (Pearlin *et al.*, 1990). Positive effects of the PSAI on the stress level could result in improved quality of life. Improvement of anxiety levels is of high importance for the caregivers of patients (Moss *et al.*, 2019); caregivers carry a variety of responsibilities thatrange from managing the patient's anxiety to performing practical tasks (such as bathing, feeding and dressing of the patient). It is estimated that almost three quarters of a caregiver's life is dedicated in caregiving (Aguglia *et al.*, 2004), while the reported prevalence of anxiety in caregivers is high, up to 43% (Sallim *et al.*, 2015). Thereby, the strong effect size of the PSAI program on anxiety levels could be extremely beneficial and smoothening for them.

The findings of this study are in line with the results of other studies reporting the positive effects of the PSAI. Charalampopoulou *et al.*, investigated the effects of the PSAI on the psychological symptoms of breast cancer patients on cancer treatment, and found a reduction in perceived stress and anxiety symptoms of the patients. Secondary outcomes *i.e.*, sleep quality and self-efficacy were also improved after PSAI (Charalampopoulou *et al.*, 2020). Encouraging results have been also reported by Simos *et al.* who implemented the PSAI on obese/overweight individuals and found significant effect sizes with respect to perceived stress levels, lifestyle and eating behaviours (Simos *et al.*, 2019).

Many studies have investigated the effects of different stress management methods on caregivers. A meta-analysis of the effects of internet-based interventions for stress reduction of caregivers of dementia patients showed not only positive but also negative effects (Zhao *et al.*, 2019). On the contrary, a systematic review on the effects of cognitive behaviouural therapy for depression, anxiety and stress in caregivers of dementia patients, revealed positive effects on depression and stress, but no significant difference in anxiety (Hopkinson *et al.*, 2019). Another meta-analysis that studied the distress of caregivers of mentally ill patients as a secondary outcome, included studies implementing various techniques, such as psychoeducation, group support and self-management techniques. Overall, all methods showed positive results, but for some of them these results were not maintained in follow-up measurements (Yesufu-Udechuku *et al.*, 2015).

The present study examined the effects of the novel and introspective PSAI. PSAI shares similarities with other cognitive based interventions (CBIs), as it aims to cognitively reconstruct problematic behavioural characteristics and rectify harmful aspects of individuals' lifestyle. Yet, there are specific elements of the PSAI which could render it more effective and a better choice than other CBIs. Cognitive based interventions usually demand at least few months of over 24 sessions to start bringing about behavioural alterations, as well as the constant presence and guidance of a trained therapist. Therefore, these types of interventions or treatments carry a great financial cost, making them accessible only to a portion of people. The PSAI overcomes these obstacles; individuals need only a short period of training by professionals, who will teach them the theory behind it and can subsequently implement the steps of the intervention on their own, whenever and wherever they wish.

Study limitations include the small sample size that impedes generalization of the results, the lack of randomization and the use of subjective self-report measures that might compromise the validity of results, and the short follow-up period. However, large effect sizes were attested for crucial endpoints concerning caregiving, thus further research is warranted.

The psychosocial burden of caregivers, especially when family-related to patients, may lead to detrimental results such as anxiety, depression, and distress. Various techniques have been used to manage the negative impact on the individuals with caregiving responsibilities. In the small sample studied, the PSAI was promising in reducing stress, anxiety, and depressive symptoms as well as improving sleep quality, self-efficacy, and

cognitive processes in caregivers of inpatients with motor disabilities. Future randomized controlled studies are needed to investigate the effects of this novel intervention in larger samples of caregivers.

Key Points

- Pythagorean Self-Awareness Intervention (PSAI) is a novel stress management technique.
- Caregivers of inpatients with motor disabilities practiced the PSAI for 8 weeks.
- PSAI reduced caregivers' stress, anxiety, and depressive symptoms.
- PSAI improved caregivers' sleep quality, self-efficacy, and cognitive processes.

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Validation of the Cosmetic Procedure Screening (COPS) Questionnaire in the Greek language

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Abstract

Practitioners in cosmetic and aesthetic treatment practices are likely to unknowingly work with patients with Body Dysmorphic Disorder (BDD). Screening questionnaires to identify the disorder in Greece are lacking. The purpose of this study was to validate a Greek version of the Cosmetic Procedure Screening (COPS) questionnaire, a self-report measure of how the respondents feel about their appearance, before an aesthetic intervention. The COPS was translated into Greek and was completed by 216 adult females from several areas of Attica (four private beauty centers, three dermatology clinics, five plastic surgery clinics, and Thriasio General Hospital of Elefsina) who pursued a cosmetic procedure. Participants also completed the Perceived Stress Scale (PSS-14). The Greek version of the COPS questionnaire demonstrated high internal consistency (Cronbach's α of 0.856) with corrected item's total range 0.468 to 0.687. Two of the factors explained 58.98% of total variance. Twenty (9.26%) women had a possible diagnosis of BDD (80% were unmarried, 95% had no children, 80% had university education). An increase in perceived stress levels was associated with an increase in the likelihood of being diagnosed with BDD (Pearson's r=0.726). The Greek version of the COPS questionnaire is a valid instrument that can be used by professionals to screen adult women for BDD.

Introduction

Body Dysmorphic Disorder (BDD) is a psychiatric condition which is not well-known, nor has been investigated for long as other established psychiatric disorders. However, before the disorder's first inclusion in the 3rd edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-III), case reports of individuals with characteristics of the disorder did appear in the cosmetic surgery literature (APA, 1980). Edgerton *et al.* described patients who were preoccupied with "minor deformities" as well as others who could not be satisfied with the cosmetic surgery result and returned for additional procedures (Edgerton *et al.*, 1960; Knorr *et al.*, 1967). Similar findings were reported in the field of dermatology research (Cotterill *et al.*, 1981). Thus, it appears that clinicians involved with cosmetic surgical treatments were familiar with some of the characteristics of the condition before its formal recognition as a diagnostic entity in the psychiatry literature.

The incidence of BDD increases among patients who seek aesthetic medical treatments. Studies that have examined BDD regardless of the type of treatment, consistently suggest that 5% to 15% of patients have some form of the disorder (Sarwer *et al.*, 1998; Aouizerate *et al.*, 2003; Vulink *et al.*, 2006), while other authors that conducted clinical interviews of patients, report higher rates, up to approximately 20% of patients (Altamura *et al.*, 2001; Vargel *et al.*, 2001; Bellino *et al.*, 2006). Others have investigated the presence of BDD in people who sought dermatological treatment. Among these studies, the rates of BDD were quite similar to those in patients

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interested in purely aesthetic treatments, ranging from 8.5% to 15% (Uzun *et al.*, 2003; Bowe *et al.*, 2007).

According to the systematic review of Veale *et al.* who aimed to determine the prevalence of BDD in different settings and the differences between the sexes, the total prevalence in the category of aesthetic dermatology was 9.2% with women (14.7%) outnumbering men (7.1%), total prevalence in the category of general cosmetic surgery was 13.2% with men (15.3%) outnumbering women (10.9%), and total prevalence in the category of acne treatment clinics was 11.1% without differences between the two sexes (Veale *et al.*, 2016). A meta-analysis conducted one year later by Ribeiro on the prevalence of BDD among plastic surgery and dermatology patients, came to add to the existing literature that 15.04% of plastic surgery patients with a mean age (± SD) of 34.54 (± 12.41) years had a BDD, while among the dermatological patients, 12.65% had the disorder with an average age (± SD) of 27.79 (± 9.03) years. The majority of BDD cases in both categories were women (Ribeiro, 2017). In a more recent review by Sarwer, it was typically reported that many individuals underwent cosmetic interventions experiencing strong dissatisfaction with their image, a clinical picture similar to that of BDD and it is speculated that 5-15% of people seeking cosmetic treatment suffer from BDD (Sarwer, 2019). According to the literature so far, there have been increased rates of BDD worldwide among the facilities that deal with aesthetics (Veale *et al.*, 2016).

Body dysmorphic disorder is considered a "silent" psychiatric disorder. Patients are reluctant to discuss their concerns with medical professionals, fearing that their stress originating from their appearance will be disregarded. Therefore, they seek comfort without ever being properly diagnosed (Lai *et al.*, 2010). Their unrealistic expectations maintain their dissatisfaction even after a successful operation, and thus intensify the feeling of discomfort and stress that accompanies them (Castle *et al.*, 2002). A meta-analysis that compared the quality of life of individuals without BDD who underwent cosmetic surgery, pre- and post-operatively, showed that their quality of life at a psychological and practical level had greatly improved post-operatively (Dreher *et al.*, 2016; Wang *et al.*, 2016). However, this does not seem to be the case with BDD patients. Most of them do not see real improvement after a successful aesthetic intervention, which leaves them unhappy and may aggravate the symptoms of the disorder. Therefore, BDD is considered a contraindication for cosmetic medicine treatments (Phillips, 2009; Wang *et al.*, 2016; Higgins *et al.*, 2017; Sarwer, 2019).

An early diagnosis of BDD, facilitated by appropriate diagnostic tools, could play a decisive role in the professional-patient relationship, and would allow the health scientist (dermatologist, plastic surgeon) to adequately predict the needs of the particular patient (Jakubietz *et al.*, 2007; Kyle, 2012).

Data are scarce regarding the prevalence of BDD in such patients in Greece and there is also lack of validated screening instruments. The Cosmetic Procedure Screening (COPS) questionnaire is a self-report measure based on the DSM-IV criteria (APA, 1994) for BDD, that aims to gather information about how the respondent feels about his/her appearance, before an aesthetic intervention. The aim of the present study was to translate and validate the COPS questionnaire in the Greek language.

Materials, Methodologies and Techniques

Translation procedure

The research team was authorized by Dr. David Veale to validate the Greek version of the COPS questionnaire.
A bilingual translation was performed in two directions (forward translation, backward translation). At first the COPS questionnaire was translated from the English into the Greek language by two different Greek native speakers with very good knowledge of English (forward translation). Comparison of the two translations resulted in the 1st version of the questionnaire in Greek, which was re-translated into English by a professional Greek translator (backward translation). The result of this translation was compared with the original questionnaire to record any differences and comments, which were then incorporated into the already existing Greek translation (1st version). As a result of this comparison and the corrections that were needed, a 2nd version of the Greek questionnaire emerged which was applied to a small sample of volunteers to check the understanding and the proper wording of the questions to correct any possible mistakes or omissions. Observations and comments from this test sample were recorded and then incorporated in the 2nd version of the Greek questionnaire. With the completion of the above procedure, the final Greek version of the COPS questionnaire emerged, which was then subjected to a final reliability and validity test.

Participants

The study sample was recruited from several areas of Attica, 4 private beauty centers, 3 dermatology clinics, 5 plastic surgery clinics and the Thriasio General Hospital of Elefsina. Females seeking a cosmetic procedure were included in the study if they were 18 years of age or older and were able to read and write in the Greek language. The study was performed in accordance with the ethical standards of the 1964 Declaration of Helsinki and its later amendments. The study protocol was approved by the Ethics committee of the Thriasio General Hospital (protocol no 405/03-12-2019). Women were informed about the purpose of the study and signed a consent form prior to study entry. All participants completed the Greek version of the COPS questionnaire, the Perceived Stress Scale, as well as a structured questionnaire for socio-demographic characteristics.

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Measures

Socio-demographic data: A properly structured questionnaire was used to gather information about the demographic characteristics of the respondents. These included age, location of residence, educational level, employment, marital status, and whether they had children or not.

Cosmetic Procedure Screening (COPS) questionnaire: The COPS questionnaire comprises 10 items. Only items 2 to 10 are scored on a 9-point scale from 0 (least impaired) to 8 (most impaired). The first item defines the features that the person finds unattractive in his/her appearance and is not part of the total score. The remaining 9 items of the COPS questionnaire investigate the extent to which the features reported in question 1 concern the individual and how much stress is caused (distress) by them or make him/her dysfunctional in important areas of life, according to the diagnostic criteria of the BDD.

The questionnaire examines the following: A. the individual's excessive concern for a perceived or existing defect in his/her appearance (questions Q 2,3,4,6), and B. the clinically significant discomfort or dysfunction in social, professional or other important areas of life caused by this concern (questions Q 5,7,8,9,10). The score is achieved by summing Q 2-10. Items 2, 3 and 5 are reversed. The total score ranges from 0 to 72 with a higher score reflecting greater impairment and symptoms of BDD. Individuals who score 40 or more are likely to have a diagnosis of BDD (Veale *et al.*, 2012).

Perceived Stress Scale (PSS-14): The Greek version of the PSS-14 was used (Andreou *et al.*, 2011). This is a 14-item self-report instrument that measures the degree to which situations in a person's life are reported as stressful or not. The frequency of emotions and thoughts during the previous month is rated on a 5-point Likert scale (from 0 = never to 4 = very often). There are seven positive and seven negative elements, and the total score is calculated by summing the score of each element, after all the positive elements have been reversed (minimum total score = 0, maximum total score = 56). Higher scores indicate a higher level of perceived stress of the person during the last month. PSS-14 was found to have satisfactory internal consistency (Cronbach's alpha=0.85) (Cohen *et al.*, 1983).

Statistical analysis

Descriptive analyses were used to calculate frequencies (%), means (min-max) and standard deviations (SD). The Kaiser-Meyer-Olkin (KMO) statistic and Barlett's Sphericity Test were used to examine sample's adequacy. Exploratory Factor Analysis was performed to identify items' factors. Cronbach's alpha values were calculated to assess internal consistency of the questionnaire. Total scores of the instrument were calculated and the association with demographic characteristics of the sample was explored with One-way ANOVA test.

Table 1. Descriptive characteristics of the study sample.

		Participants N=216	COPS >=40	% BDD cases in category	% BDD cases out of total BDD cases	% BDD cases out of total cases
Age (years)	18-30	67	8	12%	40%	4%
	31-45	107	8	7%	40%	4%
	46+	42	4	10%	20%	2%
Educational level	Primary Education	3	0	0%	0%	0%
	Secondary Education	28	2	7%	10%	1%
	Higher Education	131	16	12%	80%	7%
	Postgraduate Education	54	2	4%	10%	1%
Employment status	Freelancer	45	1	2%	5%	0%
	State Employee	35	5	14%	25%	2%
	Private Employee	99	12	12%	60%	6%
	University Student	21	2	10%	10%	1%
	Retired	3	0	0%	0%	0%
	Unemployed	13	0	0%	0%	0%
Marital status	Married	82	3	4%	15%	1%
	In Relationship	52	10	19%	50%	5%
	Single	60	6	10%	30%	3%
	Separated/ Divorced	22	1	5%	5%	0%
Children	Yes	58	1	2%	5%	0%
	No	158	19	12%	95%	9%

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Table 2. Rotated factor loadings of PCA for the 9 items of COPS questionnaire (N=216).

Items	Initial	Extraction
Q02	1.000	.353
Q03	1.000	.713
Q04	1.000	.680
Q05	1.000	.484
Q06	1.000	.726
Q07	1.000	.601
Q08	1.000	.605
Q09	1.000	.645
Q10	1.000	.501
% of Variance		58.98
Cronbach's α		0.88

PCA: Principal Component Analysis, COPS: Cosmetic Procedure Screening, Q: question

Table 3. Descriptive statistics for the COPS questionnaire.

Item Statistics	Mean	Std. Deviation	Cronbach's α if item deleted
Q02	2.37	1.485	.850
Q03	3.10	1.947	.845
Q04	2.68	2.017	.829
Q05	1.06	1.707	.846
Q06	3.23	1.937	.833
Q07	1.93	2.140	.830
Q08	.51	1.181	.845
Q09	1.60	1.977	.837
Q10	2.56	2.059	.845

COPS: Cosmetic Procedure Screening, Q: question

Statistical analyses were performed using IBM SPSS version 24.0.

Results

The questionnaire was completed by 216 adult women who pursued a cosmetic procedure. According to the scale of the COPS questionnaire, 9.26% (N = 20) of participating women had a possible diagnosis of BDD. The socio-demographic characteristics of the study sample are presented in Table 1.

The KMO coefficient and Barlett's Sphericity test ($\chi 2$) were first calculated, to examine the adequacy and suitability of the data collected. KMO fit coefficient was 0.88, which verified the sample's adequacy for analysis and $\chi 2$ was 689.586, P<.001, which indicated that correlations between items were sufficiently large enough to perform Exploratory Factor Analysis (EFA). EFA was performed with Principal Component Analysis (PCA). With regards to the internal consistency of the questionnaire Cronbach's α was 0.856, with corrected item total range 0.468 to 0.687 which indicates a high internal consistency. Table 2 presents the results of the PCA. Two of the factors had an eigenvalue greater than Kaiser's criterion of 1 and explained 58.98% of the total variance.

Reliability of the COPS questionnaire was explored by internal consistency (Cronbach's α). The average coefficient alpha value was 0.88, quite similar to that observed in the original study. Table 3 presents the means, standard deviations, and Cronbach's α values if items of the scale were deleted.

Associations between COPS scores and the socio-demographic characteristics of the sample were explored and presented in Table 4. Statistically significant correlations (P <.05) of BDD were observed with the educational level, the presence or absence of children and the marital status of the participants, while non-significant correlations (P>.05) were found between the BDD scores and type of employment and age.

A regression analysis was applied to examine the causal relationship between the study quantitative variables (COPS and PSS-14), as shown in Table 5.

According to the regression data there is a statistically significant correlation (P<.05) between COPS and PSS-14. More specifically, an increase in perceived stress levels was associated with an increase in the likelihood of being diagnosed with BDD (Pearson's r = 0.726).

Discussion

The aim of this study was to validate the COPS questionnaire in the Greek language. Body dysmorphic disorder is characterized by preoccupation with thoughts and behaviours regarding appearance concerns. It is a disabling mental health condition where a perceived physical defect impairs everyday life functioning (Bowyer *et al.*, 2016; Singh and Veale, 2019). BDD is commonly under-diagnosed or mis-diagnosed by physicians and practitioners in cosmetic procedures (Bowyer *et al.*, 2016). Moreover, a large proportion of BDD patients presenting to non-psychiatry-related specialists may not identify themselves as suffering from a mental disorder (Singh and Veale, 2019). Many BDD patients seek dermatological, surgical, or cosmetic interventions trying to correct their perceived defect, and instead of the psychiatric help that they actually need, they receive treatments which often lead to lack of satisfaction with the performed procedure (Bowyer *et al.*, 2016). Among other questionnaires assessing BDD symptoms, the COPS questionnaire is the only one created for patients undergoing cosmetic procedures (Phillips *et al.*, 1997; Phillips, 2005; Phillips, 2009; Phillips, 2017). Compared to the original version, the translated Greek version of the COPS questionnaire

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Table 4. One-way ANOVA test with the results of the F-test.

		Sum of Squares	Df	Mean Square	F	Sig.
Age	Between Groups	324.024	2	162.012	1.260	.286
	Within Groups	27381.809	213	128.553		
	Total	27705.833	215			
Source	Between Groups	1028.404	3	342.801	2.724	.045
	Within Groups	26677.429	212	125.837		
	Total	27705.833	215			
Educational Level	Between Groups	1198.979	2	599.490	4.817	.009
	Within Groups	26506.854	213	124.445		
	Total	27705.833	215			
Marital Status	Between Groups	1425.275	3	475.092	3.832	.011
	Within Groups	26280.558	212	123.965		
	Total	27705.833	215			
Kids	Between Groups	820.812	1	820.812	6.534	.011
	Within Groups	26885.021	214	125.631		
	Total	27705.833	215			
Employment Status	Between Groups	375.662	4	93.916	0.725	.576
	Within Groups	27330.171	211	129.527		
	Total	27705.833	215			

showed a lower, however sufficient, value of Cronbach α coefficient (0.91 vs. 0.88, respectively). Nonetheless, the results of convergent validity revealed remarkably similar results to those obtained in the original paper, showing a significant relationship with perceived psychological distress. The Greek validation showed that among the 216 participants, 20 cases had a possible diagnosis of BDD, which corresponds to a percentage of 9.26% that coincides with the existing literature (Veale *et al.*, 2016). The results of this study are also in line with previous literature with regards to the importance of age and marital status. The majority of BDD cases were not in a committed relationship (80% were unmarried and 95% had no children) (Hartmann and Buhlmann, 2017). Interestingly, age did not seem to affect the likelihood of diagnosis as there was no correlation between possible diagnosis of BDD and age of the respondents (Phillips, 2020). The educational level was found to have a statistically significant correlation with the disorder with 80% of BDD possible cases reporting to have university education.

Table 5. Linear Regression.

	B	Std. Error	t	Sig.
Constant	-5.0276	1.6447	-3.0569	.003
PSS-14	0.9418	0.0609	15.4577	.000
Pearson's r = 0.726				

PSS-14: Perceived Stress Scale

Screening for BDD is essential in cosmetic surgery practice. To our knowledge, the Greek version of the COPS questionnaire is the first instrument for BDD screening in the Greek language. It is a valid instrument that can be used in cosmetic procedure settings to screen adult women for BDD. It can also be used as an outcome measure after treatment to determine if there is any improvement or persistence in the symptoms of BDD following a cosmetic procedure.

Key Points

- Screening questionnaires for Body Dysmorphic Disorder (BDD) in Greece are lacking.
- The incidence of BDD increases in patients seeking aesthetic/ cosmetic treatments .
- The Cosmetic Procedure Screening (COPS) questionnaire is a screening tool for BBD.
- The Greek version of the COPS questionnaire demonstrated high internal consistency.
- The Greek version of COPS can be used for screening adult women for BDD in Greece.

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Studying Depression, Anxiety, Distress and Somatisation in a Community Sample of 2,425 Adults in Greece

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Abstract

A growing part of the literature has focused on depression, anxiety, distress and somatisation. Identifying their prevalence and populations at risk is essential to form relevant interventions. The aim of this study was to examine the prevalence and associated factors of distress, depression, anxiety, and somatisation in a community adult sample in Greece. Participants were recruited from two Greek cities; Giannitsa in the northern area and Athens in the southern area of the country, and completed sociodemographic assessments, as well as the 4-Dimensional Symptom Questionnaire (4-DSQ), a self-reported instrument assessing depression, anxiety, distress, and somatisation.

A total of 2,425 adults, females (60.1%) and males (39.9%), 18 to 84 years of age (mean age±SD, 46.98±9.57 years) participated in the study. Mental health symptoms were reported by 10.8% for depression, 12% for anxiety, 13% for distress and 5.3% for somatisation. Females scored higher than males in anxiety, distress, and somatisation (p=0.000 in all cases), while there were no significant sex differences in depression (p=0.593). Statistically significant associations were found between age and depression, anxiety and distress (p=0.000 in all cases), since those between 18-34 years of age had higher scores than the older age groups in all variables. Higher scores of depression, anxiety and distress were reported by students and unemployed participants (p=0.000 in all cases) than participants with other occupations.

This study mapped several sociodemographic groups with worse mental health. Studies in representative population samples are needed to guide public health interventions to improve the well-being of high-risk populations.

Introduction

According to the Global Burden of Disease Study, the prevalence of mental health disorders, such as depressive and anxiety disorders, has increased during the previous decades (Global Burden of Disease Study 2013 Collaborators, 2015). A wide range of changes in the way of living, which were intensified after the middle of the 20th century, such as urbanization, consumerism and secularization, are held responsible for the increased prevalence of these disorders (Hidaka, 2012).

Apart from clinically significant disorders, a major part of the research has focused on the impact of stress, which is causally related to the onset of several psychiatric disorders (Hammen, 2005; Pittenger and Duman, 2008). In addition, stress is related to various somatic disorders, such as coronary heart disease, breast cancer, multiple sclerosis, and diabetes type II (Antonova *et al.*, 2011; Kelly and Ismail, 2015; Lin *et al.*, 2013; Lloyd *et al.*, 2005; McKay *et al.*, 2017; Wirtz and von Känel, 2017). Hence,

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stress should be considered as a major threat for public health.

Due to the aforementioned aggravating effects, it is of most importance to form a mechanism explaining the pathway from stress to chronic morbidity. As supported by several prominent professors in stress research, this effect can be explained by the negative impact of stress on the cardiovascular, gastrointestinal, muscular, immune and pulmonary function (Chrousos and Gold, 1992; McEwen, 1998). Somatisation refers to the process in which stress is experienced at a somatic level, affecting the homeostasis of such systems (Dantzer, 1995). As supported by Ford (1997), impaired capacity to communicate psychological experiences related to stress leads to somatisation.

Despite the fact that stress is experienced by literally everyone, some people are predisposed for increased stress levels, based on their sociodemographic profile. For example, the unemployed are a group experiencing high stress levels (Frasquilho *et al.*, 2016). Yet, the impact of such factors is influenced by cultural parameters, highlighting the need to investigate such effects on different contexts (Marsh and Alvaro, 1990). Indeed, the heterogeneity of cultural norms indicates the necessity to study the mental health phenomena in divergent cultural contexts, to investigate if the recorded effects are common across the different contexts or not (Robson, 2002).

Based on the aforementioned evidence, it is of most importance to map high-risk populations for stress, anxiety, depression and somatisation, to provide a target for public health policies. The aim of this study was to examine the prevalence and associated factors of distress, depression, anxiety and somatisation in a community adult sample in Greece.

Materials, Methodologies and Techniques

Study design

The design of the study was cross-sectional. Recruitment to the study was carried out in two different cities, in Athens, the capital city of Greece (664,046 inhabitants) and in Giannitsa, a city in northern Greece (29,789 inhabitants). The recruitment process began on 6 December 2018 and ended on 16 May 2019.

Participants

Study participants were adults, able to communicate verbally and in writing in Greek.

Measurements

Sociodemographic data: Participants' sociodemographic data included age (years), sex (male / female), family status (unmarried living alone/ unmarried living with a partner/ married/ widowed/ divorced), number of children, educational level (Primary / Gymnasium / Lyceum / Tertiary / MSc / PhD), smoking status (current smoker / occasional smoker / non-smoker), and occupational status (unemployed / student / private sector worker / public sector worker / freelancer or businessman-woman / pensioner / house worker).

The 4-Dimensional Symptom Questionnaire: The 4-Dimensional Symptom Questionnaire (4-DSQ) is a self-reported instrument, including 50 items scored on a five Likert-type scale (zero=no to four=very much or always). This instrument includes four different subscales, measuring distress, depression, anxiety and somatisation (Terluin *et al.*, 2006). The 4-DSQ has been validated in Greek (Tsourela *et al.*, 2013). The range of α level was 0.90 for depression, 0.89 for anxiety, 0.92 for distress and 0.87 for somatisation.

Procedures

Prior to the beginning of the study, approval was obtained by the ethics committee of the Medical School of the National and Kapodistrian University of Athens. The study was in line with the Declaration of Helsinki. The recruitment process was carried out by a health visitor (ML) in Universities, public services, private companies and public spaces. A total of 3,000 participants were invited to participate and were informed about the purpose of the study, in face-to-face meetings. Those agreeing to participate provided informed consent and completed the assessments instantly or returned them on another day, based on relevant communication. The data collection was anonymous and confidential. The assessments were returned by 2,555 participants (response rate 85.17%) and 2,425 completed questionnaires were further analysed. The average response time was approximately ten minutes.

Statistical analysis

The statistical analysis was carried out with the SPSS vol. 25 statistical software for Windows (Chicago Inc.). At first, descriptive statistics were applied to calculate the sociodemographic characteristics of the study sample. Descriptive statistics were also used to calculate the prevalence of elevated depression, anxiety, distress and somatisation levels, based on the cut-offs suggested by the developers of the 4-DSQ instrument (Terluin *et al.*, 2006). Subsequently, inductive statistics were applied to search for relationships between the sociodemographic data of the study and the participants' score on the 4-DSQ. The independent samples T-Test was used when the sociodemographic variables were binary, and ANOVA when the sociodemographic variables had more than two values. Bonferroni post-hoc test and Mean Difference (M.D.) calculation followed the ANOVA analysis, in case of statistical significance. The level of significance was set at 0.05 for all the analyses.

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Table 1. Sociodemographic characteristics of the study participants.

Characteristic	Absolute value (%)
Sex	
Female	1.458 (60.1%)
Male	967 (39.9%)
Age	
18-34	1.268 (52.3%)
35-49	754 (31.3%)
50-64	369 (15.2%)
65 or more	34 (1.4%)
Area of Residence	
Athens	1.791 (73.9%)
Giannitsa	634 (26.1%)
Family status	
Married	834 (34.4%)
Unmarried, living alone	1.022 (42.1%)
Unmarried, living with a partner	417 (17.2%)
Widowed or divorced	151 (6.2%)
Number of children	
None	1.584 (65.3%)
One	385 (15.9%)
Two	374 (15.4%)
Three or more	82 (3.4%)
Educational status	
Primary	11 (0.5%)
Gymnasium	18 (1.6%)
Lyceum	661 (27.3%)
Vocational training	300 (12.4%)
Tertiary	1.033 (42.6%)
MSc	343 (14.1%)
PhD	39 (1.6%)
Occupational status	
Private sector worker	801 (33%)
Freelancer/businessman	560 (23.1%)
Public sector worker	474 (19.5%)
Student	396 (16.3%)
Unemployed	138 (5.7%)
Pensioner	38 (1.6%)
Houseworker	18 (0.7%)
Smoking status	
Non-smoker	1.387 (57.2%)
Current smoker	741 (30.6%)
Occasional smoker	297 (12.2%)

Results

The descriptive data of the study sample are presented in Table 1.

Most participants were females (60.1%), between 18-34 years of age (52.3%), living in Athens (73.9%), not having children (65.3%). Concerning family status, the majority were unmarried, living alone (42.1%), many were married (34.4%), fewer were unmarried living with a partner (17.2%), while the minority were widowed or divorced (6.2%). As for the educational status, 42.6% were of tertiary education, while 27.3% were lyceum graduates. Regarding their occupational status, 33% were private sector workers, 23.1% freelancers, 19.5% public sector workers and 16.3% were students. Finally, 57.2% were non-smokers, 30.6% were smokers and 12.2% were occasional smokers.

Table 2. Prevalence of levels depression, anxiety, distress and somatisation, according to the 4-DSQ.

	Number of Participants (%)		
	Normal or mild	Moderate	Severe
Depression	1,803 (74.4%)	358 (14.8%)	262 (10.8%)
Anxiety	1,582 (65.3%)	549 (22.7%)	290 (12.0%)
Distress	1,381 (57.1%)	725 (30.0%)	314 (13.0%)
Somatisation	1,713 (70.8%)	577 (23.9%)	128 (5.3%)

Table 3. Prevalence of levels depression, anxiety, distress and somatisation, by sex.

	Number of Participants (%)			
	Males		Females	
	Normal, mild or moderate	Severe	Normal, mild or moderate	Severe
Depression	883 (91.4%)	83 (8.6%)	1,324 (90.9%)	133 (9.1%)
Anxiety	904 (93.8%)	60 (6.2%)	1,322 (90.7%)	135 (9.3%)
Distress	877 (91.1%)	86 (8.9%)	1,229 (84.4%)	228 (15.6%)
Somatisation	946 (98.0%)	19 (2.0%)	1,368 (94.2%)	85 (5.8%)
Total	967 (100%)		1.458 (100%)	

The prevalence of depression, anxiety, distress and somatisation in the study sample is presented at Table 2. Most participants had normal or mild levels of depression (74.4%), anxiety (65.3%), distress (57.1%) and somatisation (70.8%).

The prevalence of severely elevated levels of depression, anxiety, distress and somatisation by participants' sex is presented in Table 3. Females had higher scores than males in all sub-scales of 4-DSQ.

As indicated in Table 4, statistically significant associations were found between family status, educational status and occupational status in all sub-scales of the 4-DSQ. Concerning the age and number of the children, statistically significant associations were found in all sub-scales except for the somatisation subscale. Concerning participants' sex and smoking status, statistically significant associations were found in all sub-scales except the depression subscale. More specifically, males had lower scores than females (p=0.000). As for the area of residence, no association was found with the depression, anxiety, distress or somatisation levels.

Table 4. Associations of participants' sociodemographic variables and the 4-DSQ sub-scales.

	Distress sub-scale		Anxiety sub-scale		Depression sub-scale		Somatisation sub-scale	
	Mean value (S.D)	**P**	**Mean value (S.D)**	**P**	**Mean value (S.D)**	**P**	**Mean value (S.D)**	**P**
Sex		**0.000**		**0.000**		**0.593**		**0.000**
Male	8.52 (7.22)		2.34 (3.84)		1.34 (2.64)		5.56 (5.22)	
Female	10.79 (7.99)		3.23 (4.31)		1.40 (2.67)		8.65 (6.28)	
Age		**0.000**		**0.000**		**0.009**		**0.325**
18-34	10.92 (7.89)		3.42 (4.36)		1.55 (2.78)		7.65 (6.04)	
35-49	9.05 (7.52)		2.38 (3.86)		1.18 (2.48)		7.24 (5.99)	
50-64	8.20 (7.40)		2.02 (3.72)		1.18 (2.54)		7.17 (6.35)	
65 or more	8.14 (7.07)		2.94 (4.53)		1.12 (3.05)		6.69 (0.12)	
Area of residence		**0.178**		**0.604**		**0.602**		**0.336**
Athens	10.01 (7.82)		2.85 (4.18)		1.39 (2.72)		7.36 (5.94)	
Giannitsa	9.53 (7.63)		2.95 (4.10)		1.33 (2.48)		7.63 (6.40)	
Family status		**0.000**		**0.000**		**0.000**		**0.005**
Married	8.34 (7.33)		2.12 (3.57)		1.05 (2.35)		7.15 (6.04)	
Unmarried, living with a partner	10.84 (8.27)		3.13 (4.16)		1.54 (2.84)		8.22 (6.09)	
Unmarried, living alone	10.72 (7.76		3.37 (4.44)		1.57 (2.79)		7.22 (5.95)	
Widowed or divorced	10.12 (7.52)		3.01 (4.53)		1.45 (2.77)		8.28 (6.71)	
Number of children		**0.000**		**0.000**		**0.001**		**0.955**
None	10.59 (7.86)		3.20 (4.30)		1.51 (2.75)		7.43 (5.94)	
One	8.66 (7.23)		2.39 (3.90)		1.01 (2.29)		7.57 (6.26)	
Two	8.16 (7.19)		2.05 (3.44)		1.10 (2.51)		7.33 (6.26)	
Three or more	9.90 (9.08)		2.74 (4.64)		1.80 (3.09)		7.32 (6.74)	
Educational status		**0.010**		**0.000**		**0.000**		**0.000**
Primary	7.63 (11.02)		3.18 (6.63)		1.54 (3.38)		8.90 (10.24)	
Gymnasium	11.26 (8.11)		4.10 (5.42)		2.44 (3.64)		8.28 (6.78)	
Lyceum	10.59 (8.13)		3.38 (4.54)		1.75 (3.02)		7.57 (6.44)	
Vocational training	9.52 (7.66)		2.96 (4.18)		1.12 (2.22)		8.35 (6.19)	
Tertiary	9.81 (7.65)		2.72 (3.93)		1.26 (2.54)		7.40 (5.88)	
MSc	9.34 (7.39)		2.29 (3.78)		1.17 (2.52)		6.72 (5.52)	
PhD	6.63 (6.66)		1.58 (2.63)		0.53 (1.46)		4.02 (4.18)	
Occupational status		**0.000**		**0.000**		**0.000**		**0.000**
Unemployed	12.12 (8.51)		4.25 (5.06)		2.22 (3.54)		8.10 (6.44)	
Student	11.98 (7.97)		4.17 (4.77)		1.82 (3.03)		7.82 (6.14)	
Public sector worker	8.63 (7.43)		2.26 (3.63)		1.04 (2.32)		6.85 (6.04)	
Private sector worker	9.78 (7.85)		2.85 (4.16)		1.34 (2.59)		8.10 (6.35)	
Freelancer/businessman	9.30 (7.22)		2.23 (3.56)		1.20 (2.42)		6.58 (5.34)	
Pensioner	7.34 (6.09)		1.89 (2.20)		0.94 (2.25)		6.64 (4.96)	
Houseworker	8.05 (9.82)		3.22 (6.19)		1.72 (3.30)		8.00 (6.07)	
Smoking status		**0.001**		**0.031**		**0.080**		**0.000**
Current smoker	10.51 (8.20)		3.07 (4.34)		1.55 (2.84)		8.25 (6.51)	
Non-smoker	9.37 (7.50)		2.69 (4.04)		1.28 (2.58)		6.97 (5.82)	
Occasional smoker	10.71 (7.73)		3.25 (4.19)		1.38 (2.58)		7.54 (5.86)	

Post-hoc analysis demonstrated several differences between groups. Specifically, participants aged 18-34 years showed higher levels of distress (M.D. 1.86, p=0.000), anxiety (M.D. 1.04, p=0.000) and depression (M.D. 0.37, p=0.028) than the 35-49 age group. Also, participants aged 18-34 years reported higher levels of distress (M.D. 2.72, p=0.000) and anxiety (M.D. 1.40, p=0.000) than the 50-64 age group.

With regards to family status, statistically significant differences were found between married and unmarried living with a partner participants; the latter group reported higher levels of distress (M.D. -2.50, p=0.000), anxiety (M.D. -1.00, p=0.001), depression (M.D. -0.488,

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p=0.025), and somatisation (M.D. 1.072, p=0.019). Nevertheless, married participants demonstrated lower levels of distress (M.D. -2.37, p=0.000), anxiety (M.D. 1.25, p=0.000), depression (M.D. -0.517, p=0.001), and somatisation (M.D. 1.003, p=0.027) than those living alone.

With respect to children, participants who did not have children reported higher scores in distress (M.D. 1.92, p=0.000), anxiety (M.D. 0.80, p=0.008), and depression (M.D. 0.498, p=0.013) than those with one child, as well as higher levels of distress (M.D. 2.43, p=0.000), and anxiety (M.D. 1.15, p=0.000) than those with two children.

With reference to occupational status, the unemployed participants reported higher levels of distress (M.D. 3.55, p=0.001), anxiety (M.D. 1.99, p=0.000), and depression (M.D. 1.17, p=0.002) than the public sector workers, as well as higher levels of distress (M.D. 2.88, p=0.002), anxiety (M.D. 2.01, p=0.000), and depression (M.D. 1.02, p=0.012) than the freelancers. Furthermore, the unemployed participants reported higher levels of distress (M.D. 2.40, p=0.015), anxiety (M.D. 1.39, p=0.034), and depression (M.D. 0.877, p=0.045) than the private sector workers. Also, students reported higher levels of distress (M.D. 3.35, p=0.000), and depression (M.D. 0.776, p=0.005) than public sector workers, higher levels of distress (M.D. 2.19, p=0.001) than private sector workers, and higher levels of distress (M.D. 2.68, p=0.000), anxiety (M.D. 1.94, p=0.000), and depression (M.D. 0.621, p=0.048) than the freelancers. Moreover, private sector workers reported higher levels of somatisation than public sector workers (M.D. 1.24, p=0.049) and freelancers (M.D. 1.51, p=0.002).

Likewise, statistically significant differences were found between smokers and non-smokers with the latter group reporting lower scores in distress (M.D. 1.13, p=0.006) and somatisation (M.D. 1.28, p=0.000), as well as between occasional smokers and non-smokers, with the latter group reporting lower scores in distress (M.D. 1.33, p=0.027).

With regards to the educational status, PhD students reported lower levels of distress (M.D.-3.966, p=0.046) than the Lyceum graduates. As for anxiety, statistically significant differences were noted between Lyceum and MSc participants, (M.D. 1.094, p=0.002), as well as between Lyceum and tertiary education participants (M.D. 0.663, p=0.028). As for depression, statistically significant differences were found between Lyceum and tertiary educational level (M.D. 0.490, p=0.033) participants, Lyceum and MSc participants (M.D. 0.584, p=0.020), Lyceum and vocational training (M.D. 0.632, p=0.014) participants. Differences were also noted between PhD participants and other educational groups; more specifically PhD participants, demonstrated lower distress levels (M.D. -1.908, p=0.034) than Gymnasium participants, as well as lower levels of somatisation than tertiary education participants (M.D. -3.375, p=0.013), Lyceum graduates (M.D. -3.547, p=0.008), vocational training graduates (M.D. -4.331, p=0.001) and Gymnasium graduates (M.D. -4.263, p=0.042).

Discussion

This study investigated the prevalence of depression, anxiety, distress and somatisation in an adult community sample in Greece, as well as associated factors. In the sample studied, 10.8% of the participants had severe depressive symptoms, while anxiety, distress and somatisation were reported by 12%, 13% and 5.3% of the participants, respectively. Higher prevalence was noted for moderate distress (43%) compared to the other studied parameters (24.8% -34.7%). As for the associated factors, there were significant sex differences in anxiety, distress, and somatisation, since females had higher scores, while there were no significant differences for depression. Concerning age, higher scores of depression, anxiety, distress and somatisation were found for younger participants, especially for those aged 18-34 years old. Higher scores of depression, anxiety and distress were found for students and the unemployed, whereas private sector workers had higher scores of somatisation compared to public sector workers and freelancers. Also, participants who were married and those with children had lower scores of distress, anxiety, depression and somatisation, while the unmarried living with a partner or not and those with no children had higher scores in all subscales. Smokers experienced worse mental health and somatisation compared to the others. Finally, participants with a PhD had lower scores in all subscales. At last, there are no statistically significant differences in the parameters studied between participants residing in the two cities in the northern and southern areas of the country.

The prevalence of severe depressive symptoms (10.8%) in this study is similar to that reported in other countries. For example, Johansson *et al.* (2013) found that 10.8% of the Swedish general population had clinically significant depressive symptoms, while Doğan *et al.* (2011) found that 12.8% of the general population in Turkey had such symptoms. In addition, Johansson *et al.* (2013) found that 14.7% of the responders had severe anxiety, which is slightly higher compared to the 12% found in the present study. As for somatisation, the reported 5.3% of severe symptoms in the present study is quite similar to the 5% found by Lee *et al.* (2015), who investigated somatisation in the general population in Hong Kong and to the 6.3% of somatoform disorders found by Wittchen *et al.* (2011) across the EU countries. Thus, it seems that the prevalence of depression, anxiety and somatisation is quite similar across different countries and is not strongly affected by cultural norms.

Most of the study findings concerning the associated factors are in line with previous research. For example, the findings of the present study support that those living in a family and having children have better mental health and lower somatisation compared to the others. This finding confirms the already known theories about the

protective effect of social ties on human health (Moore and Kawachi, 2017). However, a finding that is not in line with other studies is the absence of statistically significant differences between males and females in depression, since according to the World Health Organization (2017) males experience lower depression levels.

Another finding that is in line with the previous literature concerns the association of smoking status with mental health and somatisation. As supported by West (2017), this association is quite common in the literature, although there is no commonly accepted mechanism of why smokers experience worse mental health. According to his point of view, this effect could be explained by the higher levels of life satisfaction of the non-smokers. An alternative explanation could be that smokers are aware of the potentially harmful effect of smoking, as well as that they feel guilt for placing their health under threat. These findings are in line with research in patients affected by smoking-related diseases, especially lung cancer (Weiss *et al.*, 2017). In addition, it could be supported that smokers have higher trait anxiety levels, since smoking is considered as a maladaptive way to set anxiety under control (Wiggert *et al.*, 2016).

As for the effect of educational status on the components of mental and physical well-being, the findings of the present study contradict previous research supporting that high education in general leads to better mental and physical health outcomes (Berkman *et al.*, 2014), since only those with extremely high educational level were found to be protected. It could be supported that in the Greek market there is no strong association between education and work positions, since many people do not work on their field of expertise, a problematic condition present in Greece even before the economic crisis period (Liagouras *et al.*, 2003; Livanos, 2010). Hence, the protective effect might exist only for those with extremely high education, which might work on their field of expertise and have better career prospects.

In general, the results of the present study have to be examined in parallel with the effects of the recent economic crisis on Greece. The unemployment and insecurity for younger people (Frangos *et al.*, 2012) could be responsible for their worse mental health compared to older participants. Similarly, the worse mental health of students could be explained by such an effect. Yet, this might not account only for Greece, since a wide range of studies across different populations confirms that students have high rates of mental health problems (Al-Daghri *et al.*, 2014; Auerbach *et al.*, 2016; Bayram and Bigel, 2008).

Finally, the higher levels of somatisation of the private sector workers compared to public sector workers and freelancers, is a quite interesting finding with no obvious explanation. It could be supported that public sector workers experience higher levels of security in their employment status (since according to Greek laws they can't be fired), while freelancers experience a higher degree of freedom and opportunities for further financial growth. However, private sector workers do not experience any of those benefits. As supported by Ford (1997), somatisation is experienced because of inability to express the psychological burden, a justified and forced "inability" in a workplace environment. Thus, it might be easier for private sector workers to somatise their emotional burden.

A few limitations have to be reported concerning this study. Firstly, some sociodemographic data such as participants' body mass index (BMI), the presence of chronic disease and the income status were not assessed. The study followed a convenient sampling approach, nevertheless the sample size was quite large and was recruited from two different areas of the country (urban and rural). Although mental health was assessed with self-reported instruments with high psychometric properties, the use of interviews is considered as a more reliable way to study depression (Robson, 2002).

Based on the findings and the limitations of the present study, some suggestions could be made for future research. As quantitative studies are not extremely reliable to shed light on the mechanism of the studied phenomena (Robson, 2002), the use of qualitative methods (*e.g.* interviews) could be more reasonable to investigate the potential mechanism for these effects (*e.g.* the worse mental health of smokers and young people), to provide in-depth explorations, and to form relevant theories (Babbie, 2013).

As for practical implications, the high percentage of participants experiencing moderate or severe distress (42.9%) indicates the need to develop stress-management interventions in the community. Finally, this study highlighted specific populations, such as students and those aged 18-34 years, who experience poor mental health and high somatisation. For that reason, public health policy makers should focus on the development of interventions aiming at the improvement of mental and physical well-being especially for those age groups.

Key Points

- Approximately one third of an adult community sample in Greece suffered from moderate to severe mental health symptoms.
- Marriage, having children, non-smoking and higher educational status had protective effect on mental health.
- Students, unemployed and private sector workers had higher levels of depressive, anxiety, distress and somatisation symptoms.
- Youth's mental health was worse than the elder's.
- Sex differences were noted in all aspects of mental health symptoms except for depression.

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Research Papers

Validation of the Instagram Addiction Scale in Greek Youth

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Abstract

Instagram is one of the fastest growing social networking platforms. A body of evidence suggests that Instagram problematic use and addiction have negative effects on the psychological well-being of young people. The Instagram Addiction Scale, a self-report tool assessing Instagram problematic use and addiction, has been developed recently. The aim of the present study was to validate the Instagram Addiction Scale in the Greek language and to assess its psychometric properties. An online and on-print self-report survey was conducted among Greek youth, aged between 18 and 24 years. The survey included the Instagram Addiction Scale, the Rosenberg Self-esteem Scale, the Perceived Stress Scale, and the Big Five Inventory. A total of 967 respondents participated in the study. The analysis suggested that the Greek version of the Instagram Addiction Scale has good psychometric properties. The principal component factor analysis for construct validity generated two subscales as the original instrument: social effect and impulsion. Internal consistency for the two subscales and the scale's total score was satisfactory, with Cronbach's α at 0.76, 0.85 and 0.88, respectively. Correlation analyses revealed positive associations between the perceived stress scale and social effect, and the Instagram Addiction Scale's total score ($p<0.0001$ and $p=0.002$ respectively). This is the first study validating the Instagram Addiction Scale in Greek youth, which can be used by researchers and practitioners for the evaluation of youth problematic use of Instagram.

Introduction

Over the last two decades, the use of Social Networking Sites, such as Facebook, Twitter and Instagram, has evoked rapidly. Research has shown that social media use may improve human interaction, psychological well-being and the learning process (Baumer, 2013; Garrett and Cutting, 2012; Baumöl *et al.*, 2016; Schultz, 2016; Hutter *et al.*, 2013). Nevertheless, a growing body of evidence has shown that a negative side of social media also exists (Mäntymäki, and Islam, 2016). The adverse effects of social media pertain to several domains *i.e.*, satisfaction with life (Satici, 2019; Satici and Uysal, 2015), loneliness (Błachnio *et al.*, 2016; Ryan and Xenos, 2011), academic performance (Al-Yafi *et al.*, 2018; Junco and Cotten, 2012), and low self-esteem (Hawi and Samaha, 2017).

Specifically, Instagram, with more than a billion active users worldwide and more than 500 million daily users, represents one of the fastest growing social networking platforms and the most popular among young people with more that 59% of its users being between 18 and 29 years old (Alhabash and Ma, 2017). Casaló *et al.* attributed the success and popularity of Instagram among young adults to the fact that the platform enables users to gain instant popularity and co-create value with opinion leaders (Casaló *et al.*, 2018).

According to research conducted by the Royal Society for Public Health and the UK's Youth Health

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Movement, Instagram is considered the most negatively affecting social media platform in terms of its impact on young people's mental health. Specifically, both positive and negative effects of all social media on the health of young people were investigated. The study involved 1,479 young people aged 14 to 24 years. Participants rated popular applications on topics related to stress, depression, loneliness, bullying and body image. According to the results of the research, the YouTube platform emerged as the most positive, whereas Instagram and Snapchat were considered particularly harmful to the mental health and well-being of young people. However, a good aspect of these two applications has been reported by Cramer; Instagram was found to have a positive effect on self-expression and self-identity. Based on the findings of the Royal Society for Public Health and the UK Youth Health Movement, public health experts called social media to introduce a series of tests and measures, such as pop-up windows, to warn users when using social media for a long time and to protect mental health (supported by 70% of young people surveyed) (Cramer, 2017). Another suggestion addressed to the social media platforms was to develop user tracking tools for mental health issues, and thus urge users to seek help from mental health professionals. Similarly, other studies (Zalsman *et al.*, 2016; Whitaker *et al.*, 2017) concluded that the use of social media can help in the early diagnosis of depression. De Choudhury *et al.*, analysed the profile of 476 people on Twitter and created a protocol that could predict depression before serious symptoms appeared in 7 out of 10 cases (De Choudhury *et al.*, 2013).

Contrary to this preventive to mental health use of Instagram, a growing body of evidence indicates some concerning effects from the excessive use of this platform. Although social media platform use is a rising phenomenon during the last decade, a psychiatric diagnosis for "internet addiction" or "social media addiction" does not yet exist. Nonetheless, even informally, the term "addiction" is used and investigated thoroughly in terms of social media use among teenagers and young adults.

One of the reasons why "internet addiction" has not yet come to light as a formal term is because it is not a substance. However, in terms of behavioural addiction the outcomes are similar to the ones caused by a substance (Griffiths, 2005). In excessive "doses", negative effects may arise and become addictive, especially in adolescents and young adults (Griffiths *et al.*, 2016; World Health Organization, 2011). Most frequently observed symptoms which resemble those of substance abuse include compulsive behavioural involvement, lack of motivation to engage in other activities, and mental and physical symptoms when "deprivation" from the platforms is attempted (D'Arienzo *et al.*, 2019). These symptoms are common among undergraduate students who are shy and prefer the online to the offline world (Orr *et al.*, 2009). This "virtual reality" is also very tempting for individuals with social anxiety (Buote *et al.*, 2009) or depression (Andreassen *et al.*, 2016).

Despite Instagram's addictive aspects and negative effects on the physical and mental well-being, only recently a self-report questionnaire aiming to assess Instagram problematic use and addiction was developed. Kircaburun and Griffiths developed the Instagram Addiction Scale (IAS) by using a modified version of the Internet Addiction Test (Young *et al.*, 1999) and found that IAS had a satisfying internal consistency when evaluated in a sample of 752 university students. Furthermore, Instagram addiction was negatively associated with agreeableness, conscientiousness, and self-liking, whereas daily Internet use was positively associated with Instagram addiction (Kircaburun and Griffiths, 2018).

Materials, Methodologies and Techniques

Translation procedure

The first step of the validation process was to receive authorization by Kircaburun K. and Griffiths M.D. The translation procedure was then performed according to the World Health Organization's guidelines (WHO, 2020) by an expert panel. When all the forward-backwards steps were completed by the panel, a test-pretest of the questionnaire was conducted to identify unclear expressions. Participants in this test (20 males, 20 females) were representative of the study's population, with regards to age and native language. The Greek version of the instrument was then finalised.

Participants and procedures

This study was performed in the province of Attica, Greece in November of 2020. Participant inclusion criteria were age between 18 and 24 years, and ability to read and write in the Greek language. The questionnaire was distributed mainly online on Google Forms. Online distribution was held through various social media platforms, mostly via Facebook, whereas a printed form of the questionnaire was distributed to various universities.

Ethical considerations

The study's protocol was approved by the ethics committee of the Medical School of the National and Kapodistrian University of Athens and was in accordance with the 1975 Helsinki Declaration. For the online version, a brief text of the study's protocol informed the respondents about the study's aim and submission of their response was considered as an online consent. For the printed version, respondents were informed and signed a consent form prior to participation.

Measures

Sociodemographic characteristics: Participants were asked about their sex, age, family and income status as well as their educational level.

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Instagram Addiction Scale (IAS): IAS consists of 15 items and provides a distinguishing cut off point for Instagram addictive and non-addictive users. Answers are given on a 6-point Likert scale ranging from "never" to "always" and score can range from 15 to 90. The cut-off points were determined as following: scores between 15-37 classify participants as non-addicts, scores ranging from 38 to 58 as mildly addicted, moderately addicted are those who score from 59 to 73, and scores above 73 indicate severe addiction (Kircaburun and Griffiths, 2018).

Perceived Stress Scale-14 (PSS): This is a 14-item questionnaire that measures the self-reported level of stress. Answers are given on a 5-point Likert scale, ranging from 0=never to 4=very often. Seven items are considered positive and the other seven negative. Total scores are calculated after reversing the scores for the positive items and then summing all answers' scores. Higher scores indicate higher levels of stress. The PSS has been translated and validated in the Greek language with good psychometric properties and a satisfying Cronbach's α coefficient (0.82) (Andreou *et al.*, 2011).

Big Five Personality Inventory (BFI): This is a 5-point Likert scale that includes 44 items, allowing the assessment of the five personality dimensions. Participants rate each BFI item on a 5-point scale ranging from 1 (disagree strongly) to 5 (agree strongly); scale scores are computed as the participant's mean item response. The model of 44 questions measuring the personality traits, has been translated in the Greek language and used in the present study (Panayiotou *et al.*, 2004).

Rosenberg Self-Esteem Scale: This is a 4-Likert scale including 10 items. The scale measures self-worth by examining both positive and negative feelings about the respondent's self. Scores between 15 and 25 are considered average. The Greek version of the Rosenberg Self-Esteem Scale was used in this research (Galanou *et al.*, 2014).

Data analysis

Data is presented as N (%) for qualitative variables, and as mean (SD) for quantitative variables. Principal component analysis (PCA) was conducted to extract the factors of the IAS scale. Sample's adequacy and the correlation among the items were tested with the Kaiser-Meyer-Olkin measure and Bartlett's test of sphericity, respectively. The varimax rotation method was used and when questions' loadings were greater than 0.3, the items were assigned into specific factors. Cronbach's alpha was calculated to examine internal consistency. Independent samples t-test and ANOVA test were conducted to evaluate differences between groups. Correlations between IAS subscales, as well as between IAS subscales and other measurements of the study were calculated. Pearson's rho coefficient was used to assess correlations between quantitative variables. SPSS v.24 for Windows was used to perform statistical analyses and the level of significance for all analyses was 0.05.

Results

A total of 967 valid responses were collected. Participants' sociodemographic characteristics and descriptive

Table 1. Participants' sociodemographic characteristics and descriptive statistics for Big-Five Personality Inventory, Rosenberg's Self-Esteem Scale and Perceived Stress Scale (PSS) scores.

Sex	**N (%)**	**Big-Five Personality Inventory Score**	**Mean (SD)**
Females	842 (87.1)		
Males	125 (12.9)		
Age Groups		Extroversion	3.13 (0.63)
18-20 years	156 (16.1)	Pleasantness	3.78 (0.51)
20-22 years	297 (30.7)	Conscientiousness	3.56 (0.60)
22-24 years	514 (53.2)	Neuroticism	3.38 (0.68)
		Openness	3.20 (0.54)
Marital status		**Rosenberg's Self-Esteem Scale Score**	27.00 (7.00)
Unmarried	949 (98.1)		
Married	15 (1.6)	PSS Score	31.00 (8.90)
Divorced	3(0.3)		
Education level			
High School	4 (0.4)		
Lyceum	97 (10.0)		
IVET/IPS	143 (14.8)		
BSc	620 (64.1)		
MSc	103 (10.7)		
Cohabitation			
Yes	652 (67.4)		
No	315 (32.6)		

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statistics for the Big-Five Personality Inventory, Rosenberg's Self-Esteem Scale and Perceived Stress Scale scores are presented in Table 1. In total, 156 participants were between 18 and 20 years old, 297 participants were between 20 and 22 years old and 514 participants were between 22 and 24 years old. The majority of participants were females (87.1%), unmarried (98.1%), had a Bachelor's degree (64.1%) and cohabitated (67.4%).

The results of the Principal Component Analysis (PCA) of the 14 items with orthogonal rotation (varimax) are presented in Table 2. It was observed that the 14 items were able to explain 48.45% of the total variance and the scale was composed by two factors with eigenvalue greater than Kaiser's criterion of 1. The two factors were named as social effect and compulsion consisting of seven (minus one question comparing to the original subscale) and seven items, respectively. The sampling adequacy for the analysis was verified with the Kaiser-Meyer-Olkin measure (KMO = 0.914). Furthermore, Bartlett's test of sphericity, $x^2(105) = 5382{,}20$, $p<0.0001$, showed that correlations between items were sufficiently large to perform PCA. The item "How often do you form new relationships with fellow Instagram users?" did not load adequately to any of the factors and it was excluded from the final list of items. Cronbach' α coefficients for social effect, compulsion and total scale were 0.76 and 0.85, respectively, indicating satisfactory internal consistency.

Table 3 presents descriptive statistics for the two IAS subscales and the total IAS score. Correlations between the social effect and compulsion subscale and total IAS scores are presented in Table 4. Overall, a strong positive correlation between social effect and compulsion was found, indicating that negative effects from the Instagram addictive use on individuals' real-life relationships are associated to their increasing need to use the platform. The Spearman's correlation coefficient between social effect and compulsion, social effect and total scale, and compulsion and total scale were 0.66, 0.88 and 0.94, respectively.

Table 5 presents associations between social effect, compulsion, IAS total score and the study variables. Overall, there were statistically significant differences between males and females, with females scoring higher in all scales. Age groups and educational level subscales did not seem to present any significant differences. Statistically significant correlations were found between perceived stress and social effect ($p<0.0001$) and total IAS score ($p=0.002$). From the BFI scale, pleasantness score was negatively associated to social effect and total IAS score ($p<0.0001$ and 0.030 respectively), and conscientiousness score was also negatively associated to social effect, impulsion, and total IAS scores ($p<0.0001$ for all). Finally, neuroticism score was positively associated to social effect, impulsion, and total IAS scores ($p<0.0001$, $p=0.011$ and $p<0.0001$ respectively).

Discussion

The development of the IAS addressed the need of measuring individuals' addiction to Instagram, one of the most widely used social networking sites, in view of emerging evidence supporting that problematic Instagram use can lead to addiction. The aim of the current study was to validate the Instagram Addiction Scale in a Greek youth population sample, aged between 18 and 24 years, and evaluate its psychometric properties.

In line with the findings of Kircaburum and Griffiths (2018), the PCA resulted in two factors: 1. Social effect, consisting of eight items, and 2. Compulsion, consisting of seven items. The social effect sub-factor reflected negative effects from the Instagram use on individuals' real life social relations and on networking (*i.e.*, "How often do you prefer the excitement of Instagram instead of being with your close friends?"). The compulsion sub-factor reflected the increased need for Instagram use, the frequency of forgetting about time while logged on to Instagram, and the avoidance of real-life concerns using Instagram (*i.e.*, "How often do you try to cut down the amount of time you spend on Instagram and fail?"). Both factors showed satisfactory internal consistency. Strong correlation was found between social effect and compulsion indicating that they collectively and cooperatively represented individuals' problematic use and addiction to Instagram. Correlation analyses between IAS subscales and IAS total score, and participants' sociodemographic characteristics revealed differences between males and females, with greater scores in females in both subscales as well as in the IAS total score.

Positive strong correlations were found between perceived stress and the IAS subscale regarding negative effect, as well as between perceived stress and total IAS score. This finding supports previous research showing that social networking sites constitute a source of stress (Maier *et al.*, 2012). With respect to Instagram, it has been recently shown that time spent on Instagram is a significant predictor of stress (Lowe-Calverley *et al.*, 2019). Similarly, Sanz-Blas *et al.*, (Sanz-Blas *et al.*, 2019) in a study of 342 active Instagram users examined the negative impact of excessive use of Instagram on individuals' psychological well-being and found that Instagram overuse resulted in elevated levels of stress and emotional fatigue. A question, therefore, emerges regarding the mechanisms that underlie the association between stress and use of Instagram. As new technologies and incoming information increase, individuals feel unable to absorb all the amount of information and thus experience more stress (Wurman, 1989). The loss of information that derives from the gap between the available information and the users' cognitive capacity may lead to discomfort, negative feelings, and increased activation (Ragu-Nathan *et al.*, 2008). With regards to Instagram, as new information is constantly updated on the platform, heavy Instagram users may experience incompetence and thus overuse the platform to access

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Table 2. Rotated factor loadings of the principal components analysis (PCA) for 14 Instagram Addiction Scale items (N=967).

	Social Effect Subscale	Compulsion Subscale
1. How often do you prefer the excitement of Instagram instead of being with your close friends?	0.703	
2. How often do you form new relationships with fellow Instagram users?	-	-
3. How often do you become defensive or secretive when anyone asks you what you do on Instagram?	0.409	
4. How often do your grades or schoolwork suffer because of the amount of time you spend on Instagram?	0.415	
5. How often do you snap, yell, or act annoyed if someone bothers you while you are on Instagram?	0.668	
6. How often do you try to hide how long you have been on Instagram?	0.606	
7. How often do you choose to spend more time on Instagram over going out with others?	0.759	
8. How often do you feel depressed, moody or nervous when you are not on Instagram, which goes away once you are back on Instagram?	0.574	
9. How often do you try to cut down the amount of time you spend on Instagram and fail?		0.637
10. How often do you check your Instagram before something else that you need to do?		0.778
11. How often do you block out disturbing thoughts about your life with soothing thoughts of the Instagram?		0.516
12. How often do you find yourself anticipating when you will go on Instagram again?		0.633
13. How often do you fear that life without the Instagram would be boring, empty, and joyless?		0.528
14. How often do you lose sleep due to late night log-ins to Instagram?		0.782
15. How often do you find yourself saying "just a few more minutes" when on Instagram?		0.786
Eigenvalues	5.952	1.316
% of Variance	39.679	8.775
Croncbach's α	0.761	0.853

Table 3. Descriptive characteristics of the two subscales of IAS and total IAS score.

Subscale	Items	Range	Mean	SD	Minimum	Maximum
Social Effect score	7	6-42	12.25	5.17	7	39
Compulsion score	7	6-42	15.43	6.97	7	40
Total IAS score	14	6-84	27.68	11.08	14	78

IAS: Instagram Addiction Scale

Table 4. Correlations (Spearman's rho) between IAS subscales and total IAS score.

	Social Effects core	Compulsions core	Total IAS score
Social Effects core	1		
Compulsion score	0.660**	1	
Total IAS score	0.882**	0.937**	1

IAS: Instagram Addiction Scale

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Table 5. Associations between IAS subscales and total score and other study variables.

Study measurements	Categories	Social Effect score	Compulsion score	Total IAS score
Sex	Males	11.74 (4.99)	13.51 (6.00)	25.25 (9.94)
	Females	12.33 (5.19)	15.71 (7.06)	28.04 (11.20)
	p-value	0.232	<0.0001	0.004
Age groups	18-20 years	13.22 (5.30)*	16.71 (7.45)*	29.94 (11.59)*
	20-22 years	12.54(5.33)	15.53(6.78)	28.07(11.11)
	22-24 years	11.79 (4.99)*	14.98 (6.88)*	26.77 (10.81)*
	p-value	0.005	0.023	0.006
Educational level	High School	12.25 (2.50)	12.25 (4.65)	24.50 (7.00)
	Lyceum	12.06 (4.84)	14.52 (7.10)	26.58(11.18)
	IVET/IPS	11.47 (4.82)	14.34 (6.53)	25.80 (10.23)
	BSc	12.39 (5.10)	15.79 (6.95)	28.18 (10.92)
	MSc	12.70 (6.31)	15.76 (7.40)	28.46 (12.87)
	p-value	0.254	0.095	0.129
Marital status	Unmarried	12.24 (5.19)	15.44 (6.98)	27.69 (11.14)
	Married	12.07 (3.77)	15.20 (6.06)	27.27 (7.25)
	Divorced	15.67 (3.21)	11.67 (6.43)	27.33 (9.07)
	p-value	0.515	0.640	0.988
PSS Total	Spearman rho	0.138	0.057	0.100
	p-value	<0.0001	0.076	0.002
Self-Esteem Total	Spearman rho	-0.51	-0.001	-0.24
	p-value	0.113	0.981	0.451
Extroversion Score				
	Spearman rho	-0.44	0.031	-0.01
	p-value	0.169	0.332	0.975
Pleasantness Score	Spearman rho	-0.129	-0.015	-0.70
	p-value	<0.0001	0.636	0.030
Conscientiousness Score	Spearman rho	-0.171	-0.117	-0.153
	p-value	<0.0001	<0.0001	<0.0001
Neuroticism Score	Spearman rho	0.134	0.081	0.114
	p-value	<0.0001	0.011	<0.0001
Openness Score	Spearman rho	-0.041	0.013	-0.011
	p-value	0.201	0.675	0.739

IAS: Instagram Addiction Scale; PSS: Perceived Stress Scale-14

more information (Hong *et al.*, 2014). Furthermore, for individuals with high perceived stress who tend to perceive life events as stressful, Instagram with its colorful photos and videos from all over the world portrays a safe escape from real life.

Neuroticism, the individual temperamental tendency towards anxiety, self-doubt, and depression, is closely related to the psychological construct of stress. The present study revealed significant associations between participants' perceived stress and level of neuroticism, and addiction to Instagram. According to Ershad and Aghajani (Ershad and Aghajani, 2017), elevated levels of individuals' neuroticism increase the probability of Instagram social networking. These findings are in line with the results of Wang *et al.* (Wang *et al.*, 2015), who found that higher neuroticism is associated with internet addiction in general. It was hypothesized that since neurotic individuals are interested in what other people think or say about them, they tend to spend too much time on Instagram by stalking others' profiles or reading comments, which may result in addiction (Choi *et al.*, 2017).

Furthermore, non-significant results were found regarding the extraversion subscale of the Big Five Inventory Scale and Instagram Addiction Scale. This finding verified the study of Wang *et al.* (Wang *et al.*, 2015) who found an opposite-direction relationship between extraversion and addictive use of social media.

Yang (Yang, 2016) found that higher loneliness, which is related to lower extraversion (Cheng and Furnham, 2002), was associated to increased photograph and video sharing on Instagram. In the study of Kircaburum and Griffiths (2018), participants' extraversion was not related to IAS scores. With regards to this finding, it is hypothesized that extraverted individuals could reveal a tendency towards Instagram addiction, as they could become dependent on the popularity and excessive chances for interaction that a platform like Instagram can offer.

Finally, regarding the dimension of self-esteem, no strong correlations with the IAS subscales were found. This outcome was surprising, because it is common for people with low self-esteem to spend an increased amount of time on social media. A possible explanation is that self-image and self-esteem may improve through posting (Błachnio *et al.*, 2016).

This study has some limitations. Confirmatory Factor Analysis was not performed, which could have validated the study's findings further. Also, a test-retest design was not included to assess variability between measurements. Although a large sample was employed, generalization of the results cannot be easily verified because the sample was recruited mainly from the capital of Athens and was not representative of the entire youth population of Greece.

In conclusion, IAS is a newly introduced instrument aiming to evaluate problematic use and addiction to Instagram that is considered to adversely affect young people's mental health. This is the first study validating the Instagram Addiction Scale in Greek youth, which can be used by researchers and practitioners for the evaluation of youth problematic use of Instagram. Future research studies are needed to compare IAS to other standardised tests measuring youth addictive behaviours and personality traits, and include youth samples deriving from different socioeconomic and cultural backgrounds.

Key Points

- Instagram is one of the fastest growing social networking platforms.
- Instagram Addiction Scale (IAS) is a self-report tool assessing Instagram problematic use and addiction.
- The Greek version of the IAS demonstrated satisfying internal consistency.
- The Greek version of IAS can be used for the evaluation of youth problematic use of Instagram.

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Research Papers

Reliability and validity of the Peer Relation Questionnaire in a sample of Greek school children and adolescents

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Abstract

Bullying among children and adolescents can have detrimental effects on their physical and mental health. The first step in the identification of bullying is the detection of relevant signs and behaviours, with the use of appropriate instruments. The widely used Peer Relation Questionnaire (PRQ)has been developed to measure bullying behaviour in children and adolescents. The aim of this study was to translate and validate this instrument in the Greek language in a school sample of children and adolescents. A sample of 193 students (mean age ± SD 11.44 ± 1.26 years, girls 49.7%), was recruited from elementary and junior high schools of the public and private sector, in the capital of Athens, Greece. Along with the Peer Relation Questionnaire, the Stress in Children questionnaire and a structured inquiry regarding satisfaction from various aspects of life were used to assess the criterion validity of the Peer Relation Questionnaire. Results revealed good psychometric properties of the questionnaire in the Greek language. The principal component analysis resulted in two subscales that demonstrated an adequate internal consistency and a significant correlation with stress and satisfaction parameters, suggesting satisfying criterion validity. Meaningful associations between demographic characteristics and the subscales were also found. The Greek version of the Peer Relation Questionnaire-short form can be used as a valid tool to measure bullying behaviour in children and adolescents.

Introduction

Bullying is a major social phenomenon affecting not only children and adolescents, but adults as well (Rettew and Pawlowski, 2016). Although no scientific or legal definition exists, it is considered as an ongoing and deliberate misuse of power through repeated verbal, physical and/or social behaviour, that intends to cause physical, social and/or psychological harm (Olweus *et al.*, 1994). Victimization, aggressive behaviour and violence constitute the core elements of bullying (Smith *et al.*, 2016).

Bullying can be perceived as a chronic stressor; data from a study conducted in Sweden in 2010, in a sample of 392 students of the 8th and 9th grades showed that 'being bullied' was associated with higher perceived stress levels in both males and females (Van Ryzin and Roseth, 2018). Verbal bullying, one of the most common forms of bullying, is a high-risk factor for stress, as it represents a latent manipulation aiming to exclude victims from their social networks (Osika *et al.*, 2007). Bullying can affect children's mental and physical health (Paris *et al.*, 2017; Sulkoski *et al.*, 2018; Wandera *et al.*, 2017). From the mental health point of view, bullying has been linked to various disorders such as anxiety, psychosis, suicidality, and self-harm, which can appear during childhood and adolescence or emerge later in adulthood (Arseneault *et*

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al., 2010; 2006; Wolke *et al.*, 2013; Dieter *et al.*, 2013). The level of psychological trauma caused by bullying has been compared to that caused by abandonment or other severe types of maltreatment. Via peer bullying and victimisation, children may become less able or less inclined to relate to school and classmates (Kitagara *et al.*, 2014).

The first step in the identification of bullying is the detection of relevant signs and behaviours, which can be achieved with the use of appropriate instruments. One of these instruments is the Peer Relation Questionnaire (PRQ) that has been developed by Rigby and Slee (Rigby and Slee, 1993) with an aim to detect bullying behaviour in children and adolescents. The purpose of this study was to validate the PRQ in Greek school children and adolescents. The main hypothesis was that PRQ will correlate with the Stress in Children (SiC) questionnaire and a structured inquiry regarding several aspects of life satisfaction.

Materials, Methodologies and Techniques

Translation procedure

After receiving the authors' permission, the PRQ instrument was translated backward-forward, according to the World Health Organization's guidelines for the adaptation of instruments. A pre-test of the translated questionnaire was then held to identify the presence of unclear expressions. The seven participants of the pre-test were representative of the target population regarding age.

Participants and Procedure

The study was conducted in the capital of Athens in Greece, between February and July 2019. The questionnaire was distributed to various elementary and junior high schools of the private and public sector. Eligible students were children and adolescents aged 8 to 14 years, able to write and read in the Greek language, who provided a written, signed consent form by a parent or legal guardian. Participation was voluntarily, anonymous and no remuneration was provided.

Measures

Demographic data: Participants were asked about their basic demographic characteristics which included sex, age and presence of siblings.

Peer Relation Questionnaire for children (PRQ): The Peer Relation Questionnaire (short form) is a self-report measure of bullying. It consists of 12 items and three subscales (tendency to bully others, tendency to be victimized by others and tendency to act in a pro-social or cooperative manner). Respondents report the frequency in which they experience each statement. Answers are scored in a 4-point Likert scale. Higher scores indicate greater frequency of each behaviour measured (Rigby and Slee, 1993).

Stress in Children Questionnaire (SiC): The Stress in Children questionnaire consists of 21 items examining the stress encountered by children in various aspects of their life. It was designed by Osika (Osika *et al.*, 2007) and has been used in children aged between 9 and12 years. Questions are rated on a Likert scale with four possible answers. Higher scores indicate higher levels of stress.

Satisfaction: A structured inquiry was developed by the research team to assess the students' level of school and self-satisfaction. Children reported the frequency they felt satisfied by answering on a 4-point Likert scale, from 1 = never to 4 = very often.

Statistical analysis

Descriptive analyses were performed to calculate means, frequencies, and standard deviations (SD). The Kaiser-Meyer-Olkin (KMO) statistic and Barlett's Sphericity Test were used to examine sample's adequacy. Principal component analysis (PCA) was performed to identify items' factors. The appropriate number of factors was identified using the Scree-plot, since the study sample was not large enough to support the Kaiser criterion. The orthogonal varimax rotation was used for loadings of each item on derived factors to be maximized. Criterion-related validity was assessed by Pearson's rho correlations with SiC and satisfaction measure. Cronbach's alpha values were calculated to assess internal consistency of the identified factors. The PRQ's subscales scores were assessed for meaningful associations with the other measurements of the study. The level of significance p value was 0.05. The SPSS statistical software version 22.0 for Windows was used for all statistical analyses (SPSS Inc., Chicago, IL).

Results

The main characteristics of the study's sample are presented in Table 1.

Most participants were male (50.3%), with a mean age of 11.44 years, and had at least one sibling. The Kaiser-Meyer-Olkin measure verified the sampling adequacy for the analysis (KMO = 0.835) and all KMO measures for individual items were > 0.603, which is above the acceptable limit of 0.5. Bartlett's test of sphericity $x2 = 770{,}00$, $p < 0.001$, indicated that correlations between items were large enough to perform Principal Component Analysis (PCA). The results of the PCA of the 12 items with orthogonal rotation (varimax) are presented in Table 2.

Table 1. Sociodemographic and other characteristics of the study sample (N = 193).

Boys N (%)	97 (50.3)
Girls N (%)	96 (49.7)
Age in years, mean (SD)	11.44 (1.26)
Siblings, N (%)	118 (61.1)
Stress score, mean (SD)	2.05 (0.39)
Satisfaction score, mean (SD)	32.50 (5.14)

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Table 2. Rotated factor loadings of the principal components analysis (PCA) for 12 items of PRQ (N =193).

Item	"Bully/Victim Subscale"	"Social Subscale"
I get called names by others	0.518	
I get picked on by others	0.561	
I am part of a group that goes round teasing others	0.790	
I like to make others scared of me	0.830	
I enjoy upsetting wimps	0.412	
I like to get into a fight with someone I can easily beat	0.826	
Others make fun of me	0.659	
I get hit and pushed around by others	0.701	
I like to make friends		0.538
I like to help people are being harassed		0.801
I share things with others		0.778
I enjoy helping others		0.743
Eigenvalues	4.39	1.75
% of Variance	36.55	14.57
Cronbach's alpha	0.740	0.727

PRQ: Peer Relation Questionnaire

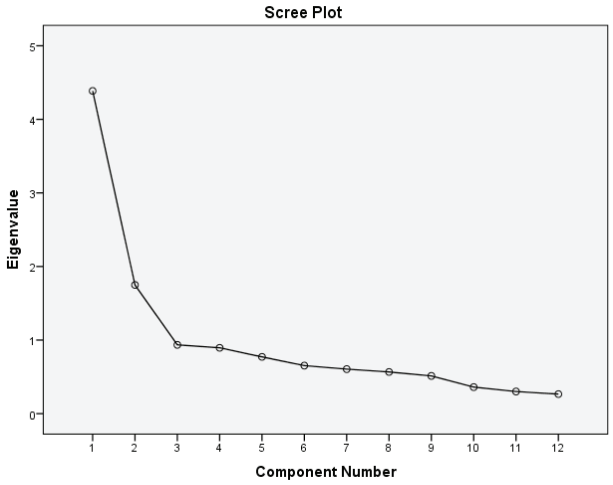

Figure 1. Scree-plot of factors' Eigenvalues regarding the PRQ.

Two components had eigenvalues greater than Kaiser's criterion of 1. The average of communalities was 0.51, which is below the Kaiser's criterion of 0.6 to be accurate. The Scree-plot (Figure 1) supported the choice for the selection of two components according to the inspection of inflexion points, which explained 51.12% of the variance.

The clusters of items, according to factor loadings (>0.3), within the two components were interpreted as following: "Bully/Victim Subscale" (BVS), "Social Subscale" (SS). Table 3 presents the mean scores of each subscale along with the theoretical and observed values of the range.

Table 3. Descriptive characteristics of the two subscales of the PRQ.

	Items	Range	Mean	SD	Mini-mum	Maxi-mum
Bully/Victim Subscale	8	16.00	11.82	2,91	8.00	24.00
Social Subscale	4	8.00	13.26	2.06	8.00	16.00

PRQ: Peer Relation Questionnaire

Table 4. Correlations (Pearson's rho) between PRQ subscales.

	"Bully/victim subscale"	"Social Subscale"
"Bully/victim subscale"	1	
"Social subscale"	-0.34*	1

PRQ: Peer Relation Questionnaire
**Correlation is significant at the 0.05 level (2-tailed)*

Table 4 presents the correlations between the two subscales.

The two subscales are negatively correlated to each other, indicating that children who tend to receive bullying or bully others, are more likely to have less social behaviour. Table 5 presents meaningful associations between the PRQ subscales and study variables.

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Table 5. Association between PRQ subscales and other study measurements.

Characteristics	"Bully/victim subscale" Mean (SD)	"Social subscale" Mean (SD)	Characteristics	"Bully/victim subscale"	"Social subscale"
Sex			Age		
Boys	14.64 (5.41)	12.47 (2.68)	Pearson's rho	0.21*	-0.18*
Girls	14.94 (5.90)	12.01 (2.52)	p-value	< 0.01	< 0.01
Statistics	t = - 0.36	t = 1.23			
p-value	0.71	0.22	Stress score		
Siblings			Pearson's rho	0.28**	-0.21**
No	15.50 (6.13)	11.77 (2.59)	p-value	<0.01	<0.01
Yes	14.34 (5.30)	12.54 (2.58)			
Statistics	t = 1.34	t = -2.00	Satisfaction		
p-value	0.18	0.04*	Pearson's rho	-0.20**	0.16*
			p-value	0.01	0.05

PRQ: Peer Relation Questionnaire
**Correlation is significant at the 0.05 level (2-tailed)*
***Correlation is significant at the 0.01 level (2-tailed)*

Significant associations with the subscales can be summarized as follows: i) children and adolescents with siblings demonstrated higher score in the social subscale of the PRQ, ii) age was positively correlated to the bully/victim subscale and negatively correlated to the social subscale of the PRQ, iii) higher stress of children and adolescents was significantly correlated to bully/victim behaviour and negatively correlated to social behaviour, and iv) higher satisfaction was negatively correlated to bully/victim behaviour.

Discussion

The current study was the first attempt to validate the PRQ in a sample of Greek school children and adolescents. The scale has been widely used as a measure of bullying behaviour mainly in cross-sectional studies. However, the fact that the PRQ has not been translated and validated in other languages apart from the original (English), restricts comparisons with other countries.
In this study, the PCA resulted in two subscales (bully/victim subscale, social subscale) unifying two of the three subscales described in the original study of the instrument. A plausible explanation could be the fact that children and adolescents who tend to bully others seem to be subjected to bullying themselves, making it difficult to differentiate bullies and victims of bullying (Cho, 2017).

As the study's results have shown, children and adolescents with siblings demonstrated higher scores in the social subscale of the PRQ, thus, having siblings was a protective factor with respect to being victimized. Furthermore, age was positively correlated to the bully/victim subscale, while the opposite correlation was found regarding the social subscale of the PRQ. Particularly, younger respondents (7-8 years of age) experienced more general aggression and mobbing than older participants. This could be explained by the fact that as age progresses, children and adolescents engage in other forms of communication and are introduced in cyber-bullying (Vlachou *et al.*, 2011; Monks *et al.*, 2006). The initial hypothesis of the study that stress would be correlated with bully/victim behaviour was verified. This could be attributed to the fact that being either a bully or a victim constitutes a stressful condition. The negative correlation of stress with the social behaviour subscale may be explained by the fact that having a strong social network and bonds help individuals build better coping strategies (Münzer *et al.*, 2017). In addition, a large cross-sectional study of 43,667 children and adolescents aged 11 to 15 years, from 9 European countries, found that any form of social support was related to less violent behaviour among school students (Mischel *et al.*, 2020; Holt *et al.*, 2007; Mishna *et al.*, 2016). Numerous studies have revealed a significant interaction between bully/victim groups and peer social support (Alcantara *et al.*, 2017); adolescents with access to social support systems are less victimized and have higher levels of self-perception (Aldridge *et al.*, 2019). Perception of low social support from peers, school and family can increase the risk for relational, verbal and physical victimization (Lin *et al.*, 2020; Chen *et al.*, 2018; Estevez *et al.*, 2019).

This study has some limitations. The generalization of the results cannot be verified, as the sample was not representative of other districts of Greece with different sociocultural backgrounds. Given the young age of participants, a test-retest procedure was not feasible, which might have affected reliability. Despite these restrictions, the adequacy of the sample size and the good criterion validity allow the use of the questionnaire in future studies in Greek elementary and high school populations. Future research should focus on other age groups as well.

In conclusion, the Greek version of the PRQ-short form demonstrated good psychometric properties and it can be safely used as a bullying measure in future studies of children and adolescents.

Key Points

- Bullying is a major social phenomenon in schools.
- Bullying can cause physical and psychological harm in children and adolescents.
- The Peer Relation Questionnaire (PRQ) is a widely used self-report measure of bullying.
- Validation of the PRQ was performed in a Greek sample of school children and adolescents.
- The Greek version of the PRQ-short form demonstrated good psychometric properties and satisfying internal consistency.

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Validation of the Greek version of the Bergen Social Media Addiction Scale in Undergraduate Students

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Abstract

Social Networking Sites (SNSs) number at least 3.81 billion users worldwide, while in Greece, 74.7% of internet users resort to SNSs. However, there is no instrument adapted to the Greek language that assesses addiction to SNSs. The Bergen Social Media Addiction Scale is a short 6-item questionnaire that assesses social media addiction. This study aimed to evaluate the psychometric properties of the Greek version of the Bergen Social Media Addiction Scale. The sample consisted of 325 University students (mean age 21.6 years, SD=5.26). Confirmatory factor analysis was performed that supported the one-factor model. The reliability of the tool was tested with various indicators and was found to be satisfactory. The regression analysis identified gender, time of SNSs use, number of SNSs held by an individual and stress as statistically significant predictors of SNSs addiction. Positive correlations were found between SNSs addiction and stress, depression, anxiety and loneliness, while negative correlations were observed between SNSs addiction, self-esteem and age. Stress fully mediated the relationship between depression and SNSs addiction. The findings of the present study indicate that the Greek version of the Bergen Social Media Addiction Scale is a valid and reliable instrument for assessing SNSs addiction. The relationship between SNSs addiction and the biopsychosocial model was confirmed.

Introduction

Social Networking Sites (SNSs) are defined as online services that enable individuals to build a public or semi-public profile and give them the opportunity to create a network of contacts to be linked to (Boyd and Ellison, 2007). According to recent data, 3.81 billion of the global population maintain an account in at least one SNS, while worldwide internet users spend 144 minutes per day in SNSs (Global Digital Population, 2020). In Greece, 74.9% of internet users connect to make use of SNSs.

Internet addiction is not included in the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-V) as a recognised disorder. However, one of the problematic aspects of internet, the internet gaming disorder (IGD), is described as a condition that requires further study (Petry and O'Brien, 2013; Yau *et al.*, 2012). Several researchers have suggested that excessive use of SNSs should be characterised as addictive behaviour that falls into the broader category of internet addiction (Kuss and Griffiths, 2011; Yau *et al.*, 2012). According to Kuss and Griffiths (2011), under the biopsychosocial model's scope, SNSs addiction exhibits the common symptoms found in substance abuse. In summary, these symptoms include salience (behavioral, cognitive and emotional obsession with the use of SNSs), mood modification (use of SNSs leads to a favorable change in emotion), tolerance (need for increasing use of SNSs), withdrawal symptoms (unpleasant physical and emotional symptoms when the use of SNSs is limited or

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discontinued), conflict (intrapersonal and interpersonal problems due to the use of SNSs) and relapse (return to excessive use of SNSs after a period of abstinence) (Kuss and Griffiths, 2011).

Apart from the growing body of research about SNSs addiction, various psychometric instruments have been developed to assess this behaviour, such as the Bergen Facebook Addiction Scale (BFAS) (Andreassen *et al.*, 2012) or the Facebook Intrusion Questionnaire (Elphinston and Noller, 2011). However, these tools focus only on Facebook, just one of the many SNSs (Griffiths, 2012). To resolve this issue, Andreassen *et al.* (2016) developed the Bergen Social Media Addiction Scale (BSMAS), an adaptation of the aforementioned BFAS and assessed SNSs addiction generally rather than one specific networking platform. Various studies have examined the psychometric properties of BSMAS. The scale has been validated in Italian (Monacis *et al.*, 2017), Iranian (Lin *et al.*, 2017), Hungarian (Bányai *et al.*, 2017) and Chinese (Chen *et al.*, 2020; Yam *et al.*, 2019). According to the literature, addiction to SNSs has been positively correlated with depression (Shensa *et al.*, 2017), stress (Vanman *et al.*, 2018), anxiety (Atroszko *et al.*, 2018), loneliness (Primack *et al.*, 2017) and negatively with self-esteem (Hawi and Samaha, 2017). In addition, various demographic factors such as sex and age, appear to be associated with excessive use of SNSs (Andreassen *et al.*, 2016). SNS addiction has also been linked to the duration of use (Koc and Gulyagci, 2013).

According to Hammen's stress generation hypothesis (1991), depressed individuals or individuals at risk of developing depression are influenced by their personal characteristics, beliefs and behavioural expectations in ways that will lead to stressful events in their lives. Therefore, individuals vulnerable to depression are more likely to experience more stressful events than less vulnerable individuals. The stress generation hypothesis has acquired a rather strong empirical documentation (Liu and Alloy, 2010; Starr *et al.*, 2012).

The main objective of this study was to evaluate the psychometric properties of the Greek version of the BSMAS. In addition, the relationships between SNSs addiction with mental health variables (stress, depression, anxiety), personality variables (self-esteem), biological variables (age, gender) and behavioural variables (SNSs use time and SNSs number) were investigated. Specifically, the mediating role of stress in the relationship between depression and SNSs addiction was also examined.

Materials, Methodologies and Techniques

Participants and Procedure

Undergraduate students of the University of Athens, able to read and write in Greek, were eligible for participation in the study. After being fully informed of the research objectives and giving their written consent, participants were asked to complete a series of questionnaires anonymously. The completion time was approximately 15 minutes.

Translation Procedure

The BSMAS was translated to Greek and then back-translated by independent translators. The back-translation was then compared with the original scale, and adjustments were made as necessary. The final version was administered to eight people who were debriefed after completing the inventory to check for clarity and comprehensibility of the items.

Measures

Questions on time spent and number of SNSs accounts. To evaluate the use of SNSs, questions regarding the hours spent on SNSs per day and the number of platforms in which the participants maintained an account were included. The question on time spent on SNSs was used to examine the criterion validity of the BSMAS. It has been argued that correlation coefficients of 0.30 to 0.40 are considered high (Alexopoulos, 2011).

Bergen Social Media Addiction Scale (BSMAS). The BSMAS consists of six items representing key addiction elements (salience, mood modification, tolerance, withdrawal symptoms, conflict and relapse). Each item is answered on a five-point Likert scale ranging from 1 (very rarely) to 5 (very often). Regarding the structure of BSMAS, a unifactorial model has been identified (Andreassen *et al.*, 2016; Monacis *et al.*, 2017).

Depression Anxiety Stress Scale – 21 items (DASS-21). The DASS-21 consists of three 7-item scales that assess depression, anxiety, and stress. Every item is rated on a four-point Likert scale ranging from 0 (did not apply to me at all) to 3 (applied to me very much or most of the time). The Greek version of DASS-21 can be used as a reliable and valid instrument in the Greek non-clinical population (Pezirkianidis *et al.*, 2018). The internal consistency of DASS-21 is acceptable (α= 0.85 for stress, 0.78 for anxiety and 0.87 for depression).

Rosenberg Self-esteem Scale (RSES). It consists of ten items that are answered on a four-point scale from strongly agree to strongly disagree. Five of the items have positively worded statements, and five have negatively worded ones. The scale measures self-worth by measuring both positive and negative feelings about the respondent's self. Scores between 15 and 25 are considered average. It has been translated and validated in the Greek language (Galanou *et al.*, 2013).

UCLA Loneliness Scale (UCLA). Emotions of perceived loneliness and social isolation were evaluated using UCLA, which is a 20-item instrument. Answers are rated on a four-point Likert scale (Anderson and Malikiosi-Loizos, 1992). The internal consistency of UCLA is acceptable (α = 0.89).

Statistical Analysis

To assess the construct validity of BSMAS, confirmatory factor analysis (CFA) was performed using the maximum

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likelihood (ML) method. To assess the good-fitting of the model $\chi 2$ and its degrees of freedom (df) were used. For $\chi 2$ values associated with $p>0.5$ were considered good-fitting models, although it has to be mentioned that the p-value of this test is sensitive to large sample sizes. Besides, the root mean square error of approximation (RMSEA) with its 90% confidence intervals (CI), the standardised root mean square residuals (SRMR) and the comparative fit index (CFI) were used. For RMSEA values < 0.06 is acceptable while for SRMR values < 0.08. For CFI, values > 0.90 were considered s indicators of good fit (Brown, 2006). The scale reliability was examined using Cronbach's α. Values > 0.7 were considered acceptable. Also, inter-item correlations were used to investigate the extent to which the items are evaluating the same content. An average inter-item correlation between 0.20 and 0.40 is considered ideal for the items to be homogenous enough while they contain sufficient unique variance (Piedmont, 2014). Finally, the standard error of measurement (SEM) was used to assess how the observed scores wavered from the measurement error. A value ≤ SD/2 is considered acceptable (Wuang *et al.*, 2012). Bivariate correlations were used to investigate the associations between the variables of the study. A multiple regression analysis was employed to examine the predictive associations between the various variables of the study and SNSs addiction. Finally, a mediation analysis was performed to investigate the relationship between depression (independent variable), stress (mediator) and addiction to SNSs (depended variable). The mediation effect was assessed by the bootstrapping procedure (10,000 samples), which provides accelerated confidence intervals (95% CI) (Tabachnick *et al.*, 2019). Statistical significance level was set at $p\leq 0.05$. For the statistical analyses SPSS 26 and JAMOVI 1.2.5 were used.

Results

Descriptive statistics

The sample consisted of 325 undergraduate students (mean age 21.6 years, SD=5.26) of the University of Athens, among which 266 (81.8%) women and 59 (18.2%) men. Descriptive statistics of the study sample are presented in Table 1. Regarding the time participants spent daily on SNSs, 50%, 30%, and approximately 13% of the participants spent 1-3, 3-5 and over 5 hours, respectively.

Reliability analysis

The internal consistency of BSMAS was α=0.75. The average inter-item correlation was relatively high (r = 0.33). Finally, the SEM (2.18) was equal to SD/2, which was acceptable according to SEM ≤ SD/2.

Correlation and regression analysis

BSMAS correlated statistically significant with all the study variables. The results are presented in Table 2. The results of the regression analysis are presented in Table 3. The model [F(8; 316)=16.4; p<0.001] suggests that 24% (R2=0.236) of the BSMAS variance can be explained through four statistically significant predictors. As shown

Table 1. Participants' descriptive statistics.

	BSMAS	Time	SNSs	Stress	ANX	DEP	RSES	UCLA
Mean	14.4	3.38	2.7	7.59	4.06	5.33	29.3	37.9
SD	4.37	1.77	1.08	4.61	3.79	4.59	4.8	9.36

*BSMAS: addiction to SNSs. Time: hours spent on SNSs daily. SNSs: number of SNSs that an individual maintains an account. ANX: anxiety. DEP: depression. RSES: self-esteem. UCLA: loneliness/social isolation.

Table 2. Pearson's correlations.

	BSMAS	Time	SNSs	Stress	DEP	ANX.	RSES	UCLA
BSMAS	-							
Time	0.36***	-						
SNSs	0.22***	0.19***	-					
Stress	0.29***	0.09	0.07	-				
DEP	0.26***	0.10	0.04	0.67***	-			
ANX.	0.21***	0.12*	0.06	0.69***	0.60***	-		
RSES	-0.18**	-0.05	-0.04	-0.38***	-0.50***	-0.36***	-	
UCLA	0.12**	-0.002	-0.1	0.40***	0.62***	0.32***	-0.47***	-

*BSMAS: addiction to SNSs. Time: hours spent on SNSs daily. SNSs: number of SNSs that an individual maintains an account. ANX: anxiety. DEP: depression. RSES: self-esteem. UCLA: loneliness/social isolation, * p< 0.1; ** p< 0.01; ***p< 0.001

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Table 3. Regression analysis for predicting addiction to SNSs.

Predictor	B	SE	B	t	p
Gender	1.45	0.57	0.33	2.56	0.01
Time	0.70	0.13	0.29	5.61	<0.001
SNSs	0.63	0.20	0.15	3.11	0.002
Stress	0.18	0.07	0.19	2.50	0.013
Anxiety	-0.06	0.08	-0.05	-0.78	0.44
Depression	0.12	0.07	0.13	1.87	0.06

*R2=0.24. Time: hours spent on SNSs daily. SNSs: number of SNSs that an individual maintains an account.

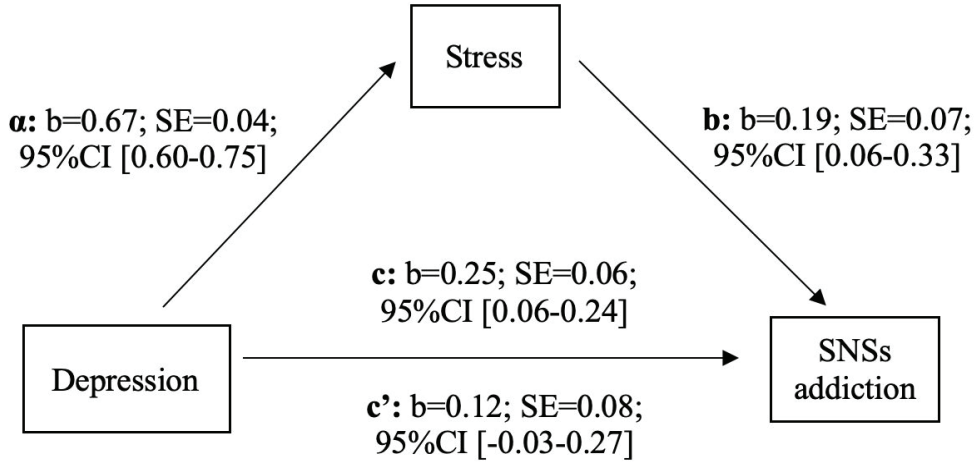

Figure 1. Mediation model with depression as a predictor, stress as mediator and SNSs addiction as the depended variable. c=total effect; c'=direct effect; b=standardized regression coefficient; SE=standard error; CI=confidence interval.

in Figure 1, stress completely mediated the relationship between depression and addiction to SNSs (total effect, c: p<0.001; direct effect, c': p=0.103). The indirect effect (a*b) was statistically significant, b=0.127; p=0.007; 95% Ci [0.0401-0.2222].

Discussion

To our knowledge, this study is the first that evaluated exclusively the SNSs addiction and how it is related to biological, social and psychological variables in a Greek sample of adult University students.

The results of this study confirmed the unifactorial solution as all the indicators of good-fit of the model were excellent and according to previous studies which examined the psychometric properties of BSMAS (Andreassen *et al.*, 2016; Chen *et al.*, 2020; Lin *et al.*, 2017; Monacis *et al.*, 2017; Yam *et al.*, 2019). Besides, to improve the RMSEA index, a covariance path between the error terms in items 1 and 2 was added to the model. This finding is consistent with the studies of Monacis *et al.* (2017) and Yam *et al.* (2019). According to Monacis *et al.* (2017), this covariance can be justified by the theory. More specifically, in item 1, which examines the criterion of salience, the demonstrated distress in the behaviour may be related to the increased time of activity required to achieve satisfaction, which is also included in the criterion of tolerance, as expressed in item 2 (Monacis *et al.*, 2017). On the other hand, Bányai *et al.* and Lin *et al.* did not report similar findings (Bányai *et al.*, 2017; Lin *et al.*, 2017). This could be explained by the fact that the samples of these studies consisted only of adolescents, while in the present study the sample concerned young adults. It has been suggested that differences in cognitive abilities between adolescents and young adults exist, which may lead to a different interpretation of the BSMAS item. At the same time, intercultural differences may also play a role (Lin *et al.*, 2017).

All correlations were found to be statistically significant regarding the relationships between SNSs addiction and demographic, social and psychological variables. More specifically, positive correlations were found between SNSs addiction and stress, depression, anxiety and loneliness, while negative correlations were observed between SNSs addiction and self-esteem and age. These results are in line with the findings of previous studies (Andreassen *et al.*, 2016; Atroszko *et*

al., 2018; Hawi and Samaha, 2017; Koc and Gulyagci, 2013; Primack *et al.*, 2017; Shensa *et al.*, 2017; Vanman *et al.*, 2018); the size of the correlation was similar to that found by others, which was between r=0.05 and 0.35 (Brailovskaia and Margraf, 2018). The present study supported the biopsychosocial model with empirical data, as it highlighted that biological (age, gender) and psychological (stress, depression, etc.) factors are associated with addiction to SNSs.

Gender, time spent on SNS and number of SNS accounts were found as predictive factors of addiction in this study. Regarding gender, it was found that women are more likely to be addicted to SNSs. This finding was consistent with the results of other validations of the scale (Andreassen *et al.*, 2016; Hawi and Rupert, 2018; Monacis *et al.*, 2017). It has been suggested that this may reflect a preference of women in activities that are characterised by social interaction and cooperation, while men show a preference for aggressive and competitive activities (Andreassen *et al.*, 2016). As previous validations of the scale, this study found that time spent on SNSs was a significant predictor of addiction (Chen *et al.*, 2020; Leong *et al.*, 2019; Lin *et al.*, 2017). In the study of Jafarkarini *et al.* (2016), time spent on SNSs was the only statistically significant predictor of addiction to SNSs. Also, the value of the correlation between the daily use of SNSs and addiction to SNSs (r=0.36; p<0.001) was considered high. It was found that the higher the number of accounts a user maintains, the more likely it is to become addicted to SNSs. This finding was consistent with the results of Pontes *et al.* (2018), who found that high-risk individuals maintained more accounts than the individuals which were at lower risk for developing SNSs addiction. In addition, this finding highlighted the importance of the transition from BFAS to BSMAS.

This study's results, which are in accordance with other studies, highlighted stress as a predictive factor of SNS addiction (Brailovskaia *et al.*, 2018). Besides, according to the mediation analysis, stress was found to fully mediate the relationship between depression and SNSs addiction, which is consistent with Hammen's (1991) stress generation hypothesis, stating that individuals vulnerable to depression experience more stressful events than non-vulnerable individuals. Subsequently, SNSs function as a stress-coping mechanism for their users. It has been found that vulnerable to depression individuals are more likely to use SNS to relieve stress than non-vulnerable to depression individuals (Brailovskaia *et al.*, 2019). This coping strategy could be helpful in the short term but could increase the risk for addiction to SNSs (Brailovskaia *et al.*, 2018). Furthermore, the increasing use of SNSs leads to various problematic behaviours (*e.g.* the user ignores intimate personal relationships), which activate a vicious cycle and negatively affect mood.

However, this study has some limitations. A test-retest examination was not held. Secondly, the sample mainly consisted of undergraduate students and primarily women, limiting the generalisation of the findings. Future studies should move in the direction of broader samples with respect to sociodemographic characteristics. Finally, the research data concerned self-report questionnaires, which are vulnerable to reporting bias.

In summary, the present study results indicated that the Greek version of the Bergen Social Media Addiction Scale is a valid and reliable instrument to assess SNSs addiction. Furthermore, it was found that biological (age, gender), psychological (stress, depression, anxiety, loneliness), and personality (self-esteem) variables are associated with addiction to SNSs. Gender, time spent on SNSs, number of accounts an individual maintains in SNSs and stress found to be predictive factors of SNSs addiction.

Key Points

- The Bergen Social Media Addiction Scale (BSMAS) is an instrument assessing Social Networking Sites (SNSs) addiction.
- The Greek version of BSMAS was validated in a sample of university students.
- The relationship between SNSs and the biopsychosocial model was confirmed.
- Gender, time of SNSs use, number of SNSs held by an individual and stress were identified as predictors of SNSs addiction.
- Stress fully mediated the relationship between depression and SNSs addiction.

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Stress Management in Elementary School Students: a Pilot Randomised Controlled Trial

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Abstract

Research has shown that stress experiences begin in early stages of life. Stress management techniques have appeared to be beneficial for the development or enhancement of stress coping skills. The aim of this pilot randomised controlled trial was to assess the effect of a 12-week intervention, comprising training in diaphragmatic breathing and progressive muscular relaxation, on elementary school students' stress levels. Outcomes on the quality of life and behavioural aspects of the students were also assessed. Standardised questionnaires were administered at baseline and after the 12-week intervention program. Fifty-two children aged 10 to 11 years were randomly assigned to intervention (n=24) and control groups (n=28). Children of the intervention group demonstrated lower levels of stress (in all three subscales of lack of well-being, distress, and lack of social support) and improved aspects of quality of life (physical, emotional, and school functioning). No significant differences were observed regarding the examined behavioural dimensions, in the intervention group. Larger randomised controlled trials with follow-up evaluations are needed to ascertain the positive outcomes of such programs on elementary school children.

Introduction

Health-related habits start to form in early life stages, even before children can realise the impact of their choices on their health and quality of life (Petosa & Oldfield, 1985). Research shows that school children experience stress frequently and the main source are daily hassles (Bridley and Jordan, 2014). Researchers have noted that multiple daily hassles interact with one another and can have cumulative effects (Stansbury and Harris, 2000). These daily stressors emerge into a non-specific risk factor for a wide range of psychosomatic and behavioural problems, such as headaches, stomach aches, sleep difficulties (Berntsson *et al.*, 2001), anxiety, depression, aggression, substance abuse, allergic or asthmatic attacks, withdrawal or outbursts, antisocial or disruptive behaviours (Van Praag and De Kloet, 2005).

Elevated stress levels can affect children's mental and physical health (Garmezy and Rutter 1983). Child development and function *i.e.* academic performance (Blashill, 2016)can be affected by stressful family issues such as divorce (Amato, 2000).These observations reinforce the notion that educational efforts regarding coping strategies to relieve stress should begin in elementary school. Early stress coping education can help children experience less stress (Petosa and Oldfield, 1985) and maintain their coping skills in adulthood.

Stress management programs have positive health outcomes, such as reduced waking and evening cortisol, fasting blood sugar and resting heart rate (Pascoe *et al.*, 2017) and beneficially effects on depression (Abbasian *et al.*, 2014), social support (Baqutayan, 2011) and academic performance (Rentala*et al.*, 2019). Several stress management programs have been implemented in healthy and non-healthy children populations;

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individual psychotherapy (March, 1998), family therapy (Bernardon, 2010), specific cognitive and behavioural strategies such as empowerment techniques (Carlier, 2020), all with positive effects on stress levels. Two of the techniques commonly taught in stress management educational programs are diaphragmatic breathing and progressive muscular relaxation (PMR). Diaphragmatic breathing is an efficient body-mind stress reduction method. It is considered to help in emotional regulation and social adaptation (Porges, 2001). Regarding PMR, it is a deep relaxation technique which is based on the simple practice of tensing one muscle group at a time followed by a relaxation phase with release of the tension (Jacobson, 1987). So far, health psychology and clinical studies have used these techniques in a complementary way (Chen *et al.*, 2017; Tsang *et al.*, 2006) and not independently from other stress management techniques.

The aim of this study was to investigate the effect of a twelve-week intervention program of diaphragmatic breathing and progressive muscle relaxation on the subjective stress levels of elementary school children. Secondary aims were to investigate the effect of the program on the children's quality of life and behavioural aspects.

Materials, Methodologies and Techniques

Study design and participant recruitment

This randomised, two-armed, pilot study was conducted in children of the 5th grade of a private elementary school in Athens, Greece over a three-month period. Eligible students should be able to write and read in Greek, not have any chronic medical condition or receive systematic medication or any type of psychological support. Study participants were randomised into two groups; the intervention group which received diaphragmatic breathing and progressive muscular relaxation training and the control group. Assignment of children to either the intervention group or the control group was based on random numbers generated by an online random number generator[1].

Ethical considerations

The study protocol was consistent with the Declaration of Helsinki and was approved by the ethics committee of the Medical School of the National and Kapodistrian University of Athens in Greece. All children and their parents or guardians were informed about the study's procedure and goals. Parental/guardian signed consent was mandatory for a child to participate in the study. All participants had the right to interrupt their participation at any step of the study, without any consequences for them.

Measurements

Stress in Children Questionnaire (SiC): This is a 21-item self-report questionnaire measuring subjective stress levels in childhood. It measures three subscales: lack of well-being, distress and lack of social support. The instrument demonstrates good psychometric properties and high internal consistence, with a Cronbach's α coefficient of 0.86 (Osika *et al.*, 2007).

Strengths and Difficulties Questionnaire (SDQ): This is a 25-item behavioural instrument, measuring 5 different dimensions; emotional symptoms, conduct problems, hyperactivity/inattention, peer relationship problems and pro-social behaviour. In community samples, the SDQ can predict the presence of a psychiatric disorder with good specificity and moderate sensitivity (Goodman, 1997;Giannakopoulos *et al.*, 2009)

Pediatric Quality of Life (PedsQL) Inventory: The 23-item Peds QL was designed to measure the core dimensions of health as delineated by the World Health Organization (physical, emotional, social, and school functioning). It measures health-related quality of life in children and adolescents either healthy or with acute and chronic health conditions (Papaevangelou *et al.*, 2007; Varni *et al.*, 1999).

Intervention: A total of 12 weekly sessions were delivered by KS (MSc in stress management) and CD (Professor of stress management and health promotion) to the intervention group. During the first session, participants of both groups completed the questionnaires and received the same information about stress and its effects on health. They were also informed about the importance of a healthy lifestyle (healthy diet, regular physical activity and sleeping routine). In the following 10 sessions participants of the intervention group were trained on and practiced diaphragmatic breathing and progressive muscular relaxation and received stress-related psycho-education. At the same time the control group, located in a different classroom, had leisure activities under their teachers' supervision. During the last session, final assessments were made for both groups by re-administering the questionnaires.

Statistical analysis

The baseline group characteristics are presented as means, standard deviations (SD), absolute and proportion values. Pearson's chi square and Fisher's exact tests were performed for frequency group comparisons; the independent two-sample Student's t-test for means differences between the groups and the paired Student's t-test for means differences within the groups. Their equivalent non-parametric tests (Mann–Whitney U test and Wilcoxon signed-rank test) were implemented in case the hypothesis of normality was violated. The normality of data was assessed with the Shapiro-Wilk test and the normal probability plots (Q-Q plots, P-P plots). All statistical tests applied were two-tailed using the <0.05 level of statistical significance. All statistical analyses were conducted using the statistical software

[1]www.random.org

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package StataSE (V. 10, Data Analysis and Statistical Software, Stata Corp LP, Texas, USA; 2009).

Results

A total of 52 students (31 females and 21 males) participated in the study. The flow diagram of the study is illustrated in Figure 1.

No dropouts occurred in either group. Given that participants of both groups were of the same school grade, their age was between 10 and 11 years. No significant difference was found between groups regarding the sex. The age and sex characteristics of each group are outlined in Table 1.

Baseline psychometric characteristics of the study groups are presented in Table 2.

As shown in Table 3, when the psychometric characteristics of the two groups after the intervention were compared, statistically significant differences were found in all three subscales of the SiC questionnaire in favor of the intervention group. There were no significant differences between the two groups after the intervention in the other quality of life and behavioural parameters.

Within group comparisons pre- and post-intervention are shown in Tables 4 and 5 for the intervention and control groups, respectively. Statistically significant increases of the PedsQL physical, emotional, and school functioning scores were found for the intervention group. Statistically significant lower scores were found for the same group in all subscales of the SiC questionnaire. Interestingly, for the control group, the score of the distress subscale of the SiC, the SDQ total score and conduct problems subscale score were significantly reduced, while the PedsQL social functioning score was significantly increased, at the end of the study.

Discussion

This pilot study examined the effects of a stress management interventional program, using the techniques of diaphragmatic breathing and PMR, to reduce stress in elementary students. Results showed a significant impact of the program on the subjective stress levels, with improvements in all three subscales *i.e.*, lack of social support, distress, and lack of well-being.

Results of this study showed that diaphragmatic breathing and PMR can result in reduction of the children's distress levels. This finding is in line with the study of Ma *et al.*, who measured saliva levels of the stress hormone cortisol, after the implementation of an 8-week diaphragmatic breathing program on healthy individuals(Ma *et al.*, 2017). Even when referring to non-healthy population, these techniques have been proven beneficial regarding stress reduction. A systematic review of the influence of PMR on patients with schizophrenia showed that the technique can reduce psychological distress and anxiety (Vancampfort *et al.*, 2013). Wilk and Turkoski (2001) reported the same positive results on cardiac patients. The researchers implemented a stress management program based on PMR in a cardiac rehabilitation facility and outcomes included lower heart rate, improved sleep quality and lower levels of anxiety, all characteristics of low stress levels (Wilk and Turkoski, 2001). Although the aforementioned studies concerned adults, positive outcomes have been reported in studies of minor subjects as well. A meta-analysis of school stress management programs that included diaphragmatic breathing and PMR, demonstrated significantly positive results in stress reduction (Kraag *et al.*, 2006).

This study examined the effect of the implemented program on the students' perception of social support and well-being, which are stress-related dimensions. Results showed that students improved their perception of social support and their sense of well-being. High social support seems to facilitate stress coping and enhances well-being (Charney and Southwick, 2007). Numerous studies have shown that long term stress and lack of social support and well-being go hand in hand with poor mental health(Mohr and Classen 2004; Michalak *et al.*, 1999; Paykel, 1994; Toussaint *et al.*, 2016).

This study confirmed the beneficial effects of diaphragmatic breathing and PMR on students' emotional functioning. According to the American Psychological Association the average stress level of the U.S. population in 2015 was 5.1 in a scale of 1 to 10 (APA, 2015). Stress

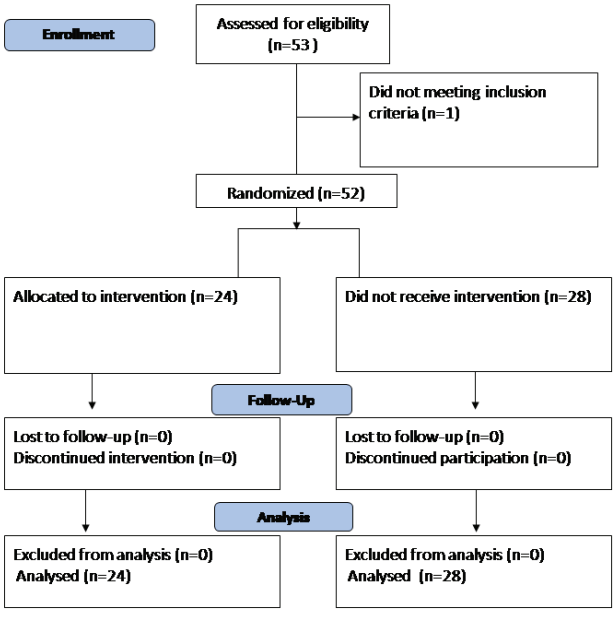

Figure 1. Participants' flow diagram.

Table 1. Study groups' characteristics.

	Intervention group	Control group	p-value
Sex	N=24 (%)	N=28 (%)	0.337
Female	16 (66.67)	15 (53.57)	
Male	8 (33.33)	13 (46.43)	

Table 2. Baseline psychometric characteristics of study groups.

	Intervention Group Mean ± SD	Control group Mean ± SD	p-value*
SDQ score			
Total	18.11 ± 7.37	18 ± 6.47	0.952
Emotional symptoms	3.26 ± 2.60	2.92 ± 2.72	0.574
Conduct problems	1.48 ± 1.80	1.40 ± 1.83	0.852
Hyperactivity score	4.25 ± 2.90	3.82 ± 3.37	0.460
Peer problem	3.30 ± 2.81	2.5 ± 2.08	0.361
Prosocial behaviour	6.37 ± 2.13	7.35 ± 2.45	0.117
PedsQL score			
Physical functioning	66.20 ± 28.10	70.75 ± 23.07	0.560
Emotional functioning	56.30 ± 30.21	56.96 ± 26.46	0.773
Social functioning	67.03 ± 33.63	67.50 ± 28.90	0.530
School functioning	66.30 ± 34.57	69.46 ± 26.60	0.852
SiC score			
Total	46.57 ± 5.86	43.85 ± 8.82	0.247
Lack of well-being	15.17 ± 4.00	14.08 ± 3.91	0.344
Distress	17.70 ± 3.36	18.20 ± 2.87	0.584
Lack of social support	14.34 ± 2.44	13.11 ± 2.98	0.123

SDQ: Strengths and Difficulties Questionnaire, PedsQL: Pediatric Quality of Life, SiC: Stress in Children

**Difference of frequencies tested with Pearson's chi square or Fisher's exact test, difference of means with Student's t-test and non-parametric Mann-Whitney U test (applied in mean weight, mean SDQ emotional symptoms, conduct problems, hyperactivity, peer problem scores, in all PedsQL scores and SiC distress sub-score).*

Table 3. Comparison of the psychometric characteristics of the two groups after the intervention.

	Intervention Group Mean ± SD	Control group Mean ± SD	p-value*
SDQ score			
Total	15.74 ± 6.00	14.35 ± 6.34	0.410
Emotional symptoms	2.51 ± 2.27	1.92 ± 1.70	0.387
Conduct problems	1.30 ± 1.61	0.82 ± 1.21	0.317
Hyperactivity score	3.30 ± 2.78	3.42 ± 3.24	0.878
Peer problem	2.96 ± 2.54	1.96 ± 1.55	0.225
Prosocial behaviour	6.14 ± 2.20	7.17 ± 2.31	0.096
PedsQL score			
Physical functioning	75.81 ± 25.40	76.00 ± 18.90	0.654
Emotional functioning	68.88 ± 25.00	65.00 ± 24.50	0.314
Social functioning	73.15 ± 28.76	77.85 ± 16.75	0.986
School functioning	77.22 ± 25.12	74.46 ± 23.50	0.401
SiC score			
Total	37.64 ± 5.29	42.26 ± 8.06	0.019
Lack of well-being	11.28 ± 3.57	13.53 ± 4.05	0.037
Distress	14.52 ± 2.51	16.11 ± 2.42	0.050
Lack of social support	11.24 ± 2.31	12.75 ± 2.68	0.034

SDQ: Strengths and Difficulties Questionnaire, PedsQL: Pediatric Quality of Life, SiC: Stress in Children

**Difference of means tested with Student's t-test and non-parametric Mann-Whitney U test (applied in mean SDQ emotional symptoms, conduct problems, hyperactivity, peer problem scores, in all PedsQL scores and in SiC distress sub-score). Statistical significance at p<0.05.*

Table 4. Comparisons of the psychometric characteristics of the intervention group pre- and post-intervention.

	Before Intervention Mean ± SD	After Intervention Mean ± SD	p-value*
SDQ score			
Total	18.11 ± 7.37	15.74 ± 6.00	0.131
Emotional symptoms	3.26 ± 2.60	2.51 ± 2.27	0.069
Conduct problems	1.48 ± 1.80	1.30 ± 1.61	0.666
Hyperactivity score	4.25 ± 2.90	3.30 ± 2.78	0.069
Peer problem	3.30 ± 2.81	2.96 ± 2.54	0.402
Prosocial behaviour	6.37 ± 2.13	6.14 ± 2.20	0.550
PedsQL score			
Physical functioning	66.20 ± 28.10	75.81 ± 25.40	0.001
Emotional functioning	56.30 ± 30.21	68.88 ± 25.00	0.003
Social functioning	67.03 ± 33.63	73.15 ± 28.76	0.226
School functioning	66.30 ± 34.57	77.22 ± 25.12	0.029
SiC score			
Total	46.57 ± 5.86	37.64 ± 5.29	< 0.001
Lack of well-being	15.17 ± 4.00	11.28 ± 3.57	0.001
Distress	17.70 ± 3.36	14.52 ± 2.51	< 0.001
Lack of social support	14.34 ± 2.44	11.24 ± 2.31	< 0.001

SDQ: Strengths and Difficulties Questionnaire, PedsQL: Pediatric Quality of Life, SiC: Stress in Children

**Difference of means tested with two dependent samples Student's t test or nonparametric Wilcoxon signed rank test (implemented in SDQ emotional symptoms, conduct problems, hyperactivity, peer problem scores, in all PedsQL scores and in SiC score). Statistical significance at p<0.05.*

Table 5. Comparison of the psychometric characteristics of the control group pre- and post- intervention.

	Before Intervention Mean ± SD	After Intervention Mean ± SD	p-value*
SDQ score			
Total	18 ± 6.47	14.35 ± 6.34	0.007
Emotional symptoms	2.92 ± 2.72	1.92 ± 1.70	0.062
Conduct problems	1.40 ± 1.83	0.82 ± 1.21	0.013
Hyperactivity score	3.82 ± 3.37	3.42 ± 3.24	0.498
Peer problem	2.5 ± 2.08	1.96 ± 1.55	0.114
Prosocial behaviour	7.35 ± 2.45	7.17 ± 2.31	0.672
PedsQL score			
Physical functioning	70.75 ± 23.07	76.00 ± 18.90	0.212
Emotional functioning	56.96 ± 26.46	65.00 ± 24.50	0.121
Social functioning	67.50 ± 28.90	77.85 ± 16.75	0.049
School functioning	69.46 ± 26.60	74.46 ± 23.50	0.166
SiC score			
Total	43.85 ± 8.82	42.26 ± 8.06	0.430
Lack of well-being	14.08 ± 3.91	13.53 ± 4.05	0.830
Distress	18.20 ± 2.87	16.11 ± 2.42	0.002
Lack of social support	13.11 ± 2.98	12.75 ± 2.68	0.500

SDQ: Strengths and Difficulties Questionnaire, PedsQL: Pediatric Quality of Life, SiC: Stress in Children

**Difference of means tested with two dependent samples Student's t test or nonparametric Wilcoxon signed rank test (implemented in SDQ emotional symptoms, conduct problems, hyperactivity, peer problem scores, in all PedsQL scores and in SiC score). Statistical significance at p<0.05.*

is related to discomforting emotional symptoms such as feelings of depression, anxiety, irritability, and low self-efficacy. The significant improvement in emotional functioning in this pediatric study is in line with previous research concerning the effects of stress management programs on the psychological symptoms of stress (Chiesa and Serretti, 2009).

The implemented program resulted in a significant improvement in the school functioning level of the students. These results contradict recent findings on the relation of cortisol to school functioning of children, where no correlation was demonstrated between cortisol levels and school behaviour (Simons *et al.*, 2017). This disagreement could be explained by the ongoing development of the cortisol circadian rhythm in childhood.

This study has some limitations. The main limitation is the lack of biological measurements for stress *i.e.*, in blood, urine or saliva (Dhama *et al.*, 2019) and the use of solely self-report questionnaires. Nevertheless, this was a low-cost intervention, easy to implement in a school setting. The lack of long-term follow-up, the small sample size and the limited age range of the participants do not allow generalization of the results. More complex, longitudinal interventions are required for children to adopt new, healthier behavioural patterns with strong stress coping skills (Baranowski *et al.*, 2003) and to attain concrete results regarding the effect of diaphragmatic breathing and PMR on children's stress levels.

Key Points

- Stress experiences begin in early stages of life.
- An elementary school program on stress coping skills was implemented for 12 weeks.
- Diaphragmatic breathing and progressive muscular relaxation reduced students' subjective stress levels.

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Validation of the Copenhagen Psychosocial Questionnaire-Long Version II (COPSOQ II) in Greek employees

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Abstract

The aim of this study was to validate the long second version of the Copenhagen Psychosocial Questionnaire (COPSOQ II) in the Greek language. The study was carried out in two phases following a mixed-method design. Six hundred and fifty-two Greek employees (response rate 93.3%) responded in the second phase of the study, either online or in writing. Both types of participation to the study were confidential for the participants and the companies as well. Most participants were females (68.1%), married (47.4%), aged 30-49 years (60.9%), with high educational level (60.4%). The majority were occupied in the health and the social care services (37.4%) and employed by the private sector (63.2%). Internal consistency of the GR-COPSOQ II was assessed with the Cronbach alpha criterion (Cronbach's a) and it was acceptable (0.8>α>0.7) for most of the scales. Mean scores were high in many scales that describe exposure to psychosocial risk factors at the workplace. Construct validity was established by exploratory factor analysis (EFA) for the entire study sample and scales. In conclusion, the Greek version of the COPSOQ-II (GR-COPSOQ II) has good psychometric properties and can be recommended as a valid tool for the assessment of psychosocial risk in Greek employees.

Introduction

All over the world dramatic changes have been observed both in the workplace design and in the "social capital" of the enterprises (Berthelsen *et al.*, 2016; Clausen *et al.*, 2019; Jensen *et al.*, 2017). The "fourth industrial revolution", mostly related to the technological revolution, automatisation and computerisation, inevitably affects workplace organisation and may also affect the health and safety of workers (Leso *et al.*, 2018). Greece, among other countries, has been under social economic reconstruction for more than ten years (Eikemo *et al.*, 2018; Zartaloudis and Kornelakis, 2017) and many changes have been noticed in plenty of parameters regarding occupational status (Karadinos, 2013; Kentikelenis *et al.*, 2011). Work design research has been based on contemporary and integrative clusters, and also on sporadically convenient work perspectives rather than substantive distinction. Work design, apart from the costs and benefits it entails, may also lead to a diverse set of outcomes (Parker *et al.*, 2017)

Thus, it is important to find valid methods to assess workplace hazards and to ensure the health and safety of the workforce worldwide. One way to achieve that goal is by making the risk assessment easier and more cost-effective. Moreover, not only is it important to ascertain the risks, but it is equally important to predict as many as possible. Self-report questionnaires are a valuable tool for measuring multiple aspects of work characteristics (Beaton *et al.*, 2000; Bland and Altman, 2002; Galanis, 2019; Guillemin *et al.*, 1993; Laake *et al.*, 2007; Maneesriwongul and Dixon, 2004). The assumption, which enables comparisons of results across different nationalities or countries, is the most valid perspective of a well standardised questionnaire among different languages (Erkut S, 2018; Prince, 2008; Weeks *et al.*, 2007). The psychosocial work environment is crucial, among other work-related parameters, for the health and wellbeing of the workers and is defined as

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all those aspects of the work environment that pertain to interpersonal and social interactions, and influence behaviour as well as workplace development (Cox and Cox, 1993; Hupke, 2018; Jacobs *et al.*, 2013; Niedhammer *et al.*, 1998; Nuebling *et al.*, 2013). Psychosocial workload can be measured either as an occupational risk factor or as a work related outcome. Moreover, it can be estimated indirectly by measuring vitality and mental health at the workplace (Burr *et al.*, 2010), job satisfaction, general health, burnout, satisfaction with life (Nuebling *et al.*, 2013), absenteeism (Clausen *et al.*, 2015, 2019; Clausen and Borg, 2010), and commitment at the work place (Clausen and Borg 2010; Clausen *et al.*, 2015).

Among other instruments, the Copenhagen Psychosocial Questionnaire (COPSOQ) is one of the most widely used self-report questionnaires for the assessment of the occupational psychosocial risk factors. COPSOQ has been developed for the needs of the studies of the Danish National Research Centre for the Working Environment, from 1995, in Denmark (Kristensen *et al.*, 2005). The COPSOQ authors, Tage Kristensen and Vilhelm Borg, kept on the development of the first version by getting feedback (*e.g.* lack of access to domains such as justice, reward, trust and discrimination). In 2010, the second version of the questionnaire (COPSOQ II) was published (Bjorner and Pejtersen, 2010; Pejtersen *et al.*, 2010). Both questionnaires are available in three versions (long, medium and short) and their usage depends on the purpose (long for surveys, middle and short in accordance with the workplace and the work environment professionals). The response options on a Likert type four or five answer scale range from 0 to 100 points. The higher scores represent high level of the concept being measured. The average scores of the included items are the overall score for the seven main domains of the instrument. Six items have to be reversed before scoring (QD4: Do you have enough time for your work task? Va 2: Do you have to do the same things over and over again? CW4: How often do you consider looking for work elsewhere? TE1: Do the employees withhold information from each other? TE2: Do the employees withhold information from the management? TM 3: Does the mangement withhold important information from the employees?). The duration for answering the questionnaire is about 20 minutes to half an hour and the total score of each scale is the average of the items scored. If less than half of the items of each scale are not answered by a respondent the subject is consided as missing for that scale.

The COPSOQ is recognized as an example of good practice by the European Occupational Safety and Health Agency (EU OSHA) and it is cited in many documents of international organisations. The COPSOQ II has already been translated in more than twenty-five languages (Alvarado *et al.*, 2012; Berthelsen *et al.*, 2016, 2017, 2018; Dicke *et al.*, 2018; Dupret *et al.*, 2012; Isha *et al.*, 2020; Moncada Lluís *et al.*, 2008; Moncada *et al.*, 2014; Nübling *et al.*, 2006; Pournik *et al.*, 2015; Ramkissoon *et al.*, 2019; Shan *et al.*, 2008. Moreover, it has been used for comparisons among countries. The COPSOQ appears in hundreds of references in indexed international scientific journals on Medline.

The third version of the COPSOQ has been structured (Burr *et al.*, 2019) and the whole procedure was coordinated by the International COPSOQ Network[1].

The aim of this study was to test the psychometric equivalence and validate the Greek translation of the long version of the Copenhagen Psychosocial Questionnaire-second version (COPSOQ II), in a sample of Greek employees.

Materials, Methodologies and Techniques

The study was conducted from September 2018 to December 2019 in Greece, following a thourough search of the international bibliography for an instrument suitable to evaluate various aspects of the work environment and not only some parameters of work-related stress risk factors and their outcomes.

The study protocol was approved by the ethics committee of the National and Kapodistrian University of Athens and the research was carried out in two phases. In the first phase, the translation and the cross-cultural adaptation of the questionnaire was performed, and in the second phase the psychometric properties of the questionnaire were evaluated in a representative number of Greek employees.

Regarding some researchers, a number between five to ten participants is considered satisfactory for the confirmation of the reliability and the validity of a questionnaire (McDermott and Palchanes, 1994; Harkness and Zentrum, 1998). Thus, a minimum number of 640 (128*5) cases/respondents or valid questionnaires would probably fit well for the purpose of this methodological study.

Process of COPSOQ II translation in the Greek language

Following the typical procedure, permission to validate the questionnaire was obtained by its creators Professors Vilhelm Borg and Tage Kristensen, in December 2017.

A mixed-method design, combining a qualitative study with probe technique characteristics (*e.g.* interviews, a committee rater judgement and CVI score) and a quantitative procedure was utilized. The instrument (COPSOQ II) for the evaluation of the psychosocial work-related risk factors among Greek employees was developed in two phases:

In the first phase, the overall item development, forward / back-translation, and cross-cultural adaptation of the questionnaire was tested by the content validity criterion (Figure 1), and in the second phase, the equivalence of other psychometric properties, such as

[1]https://www.copsoq-network.org/

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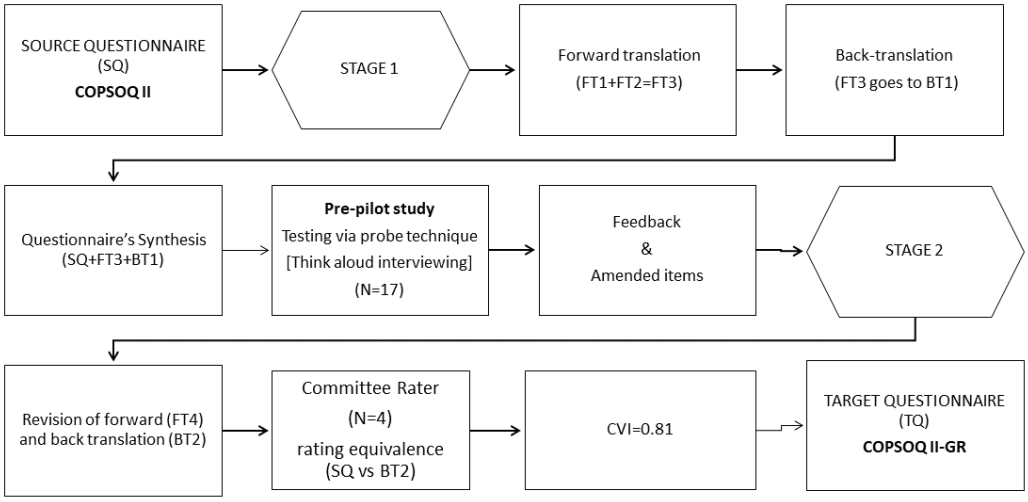

Figure 1. Linquistic adaptation process of the COPSOQ II, in the Greek lanquage.

construct validity, internal consistency and reliability were tested.

The pilot study of the questionnaire was performed in 120 workers (response rate 85%) and showed good psychometric properties, with Cronbach-alphas more than 0.70 on most scales ("Demand at Work" α=0.87, "Work Organization and Job Contents" α= 0.90, "Interpersonal Relations and Leadership" α= 0.85, "Values at Workplace" α= 0.86, Health and Well-Being" α= 0.92, "Offensive Behaviour α=0.85). The only scale with a slightly lower Cronbach alpha was the "Work Individual Interface" scale (α= 0.68).

Questions about demographic characteristics such as age, sex, marital status, occupational sector, number of employees and employment status were also included.

Greek version of the COPSOQ II

The final version of the Greek questionnaire was shared in two different ways (online and in writing). Regarding paper documentation, the questionnaire, the consent form, the cover letter explaining the purpose of the study, as well as researchers' affiliation, were enclosed in the same envelope. The file was handed over to employees who belonged to as many different occupational sectors as possible. Whenever a company or a stricter occupational sector had any doubts about the participation of their employees in the survey, the procedure was necessarily more thorough. In this case, a written approval of the scientific committee or the HR department of the company was also requested.

Regarding the online form of the questionnaire, the Research Electronic Data Capture (REDCap) application had been selected to build the electronic form of the Greek version of the COPSOQ II. REDCαp is a secure web application for building and managing online surveys and databases. While REDCap can be used to collect virtually any type of data in any environment (including compliance with 21 CFR Part 11, FISMA, HIPAA, and GDPR), it is specifically geared to support online and offline data capture for research studies and operations. REDCap is a web-based application developed by Vanderbilt University to capture data for clinical research and create databases and projects. It is Health Insurance Portability and Accountability Act (HIPAA)–compliant, highly secure, and intuitive to use (Harris *et al.*, 2009, 2019; Patridge and Bardyn, 2018).

Both types of participation to the study were confidential for the participants and the companies as well.

Psychometric properties

Reliability analysis: The internal consistency analysis of the GR-COPSOQ II was assessed with the Cronbach alpha criterion (Cronbach's a). The original Danish study (Pejtersen *et al.*, 2010) and other validation studies of the COPSOQs (Rosário *et al.*, 2017) adjust the conversional threshold of 0.70 as an acceptable value for Cronbach. Moreover, a≥0.90 is an excellent value and a≤0.50 is an unacceptable value for the internal consistency of the scale, which is accessing.

Construct validity: Construct validity was established by expolratory factor analysis (EFA) for the entire study sample (N = 652). Expolratory Factor Analysis (EFA) was used to cross-validate the derived factor structures. Values for Kaiser–Meyer–Olkin (KMO) measure of sampling adequacy and Bartlett's test of sphericity (preferably significant) were used to assess the suitability of data for factorisation. The criterion for loading and cross loading was set at 0.4. Items loading below 0.40 and cross loading over 0.40 might be necessary to be deleted.

Statistical Analysis

Statistical analysis was carried out by using SPSS version 25 (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp). For

the quantitative variables of the questionnaire (GR-COPSOQ II) data were presented as a mean and standard deviation (mean ± SD), while for the qualitative variables data were presented as frequencies (n) and percentages (%). The Cronbach -alpha criterion was used for internal consistency and values higher than 0.7 were considered as appropriate (DeVellis, 2016). The missing values were treated by listwise pairs deletion (Soley-Bori, 2019). Construct validity and more specifically factor analysis was examined by undertaking Principal-Component Exploratory Factor Analysis with a varimax rotation.

Results

The sample of the basic study consisted of 652 Greek employees (93.3% response rate) who completed the Greek version of the GR-COPSOQ II questionnaire. Descriptive statistics of the demographic and other characteristics of the sample are presented in Table 1 in Supplementary Data[2]. One third of the participants were male and 63.2% of the participants were from the private sector. The majority of the sample was married (47.4%), aged 30-39 years (31.1%), with high educational level (60.4%). Most of them declared that they were occupied at the health and the social care sectors (37.4%), in big companies with over than 500 employees (28.5%) or small with fewer than 20 employees (25.7%), and they work more than 40 working hours per week (33.8%). Also, they had 10-20 years of working experience (37.9%).

The internal consistency analysis of the GR-COPSOQ II was calculated with the Cronbach alpha criterion (Tables 2 and 3 in Supplementary Data[2]). The original Danish study (Pejtersen *et al.*, 2010) and other validation studies, *e.g.*, Portuguese (Rosário *et al.*, 2017), adjust the conversional threshold of 0.70 as an acceptable value for Cronbach (DeVellis, 2016).

For the pilot study, all Cronbach's alpha indicators for domains ranged from 0.68 to 0.92 and four scales ranged from 0.58 to 0.95 (the lower value of alpha is due to the fact that this scale consists of only two items). Twenty-six out of 33 scales with Cronbach's alpha, were found to have higher alpha in the Greek version than the original version, six of them had lower alpha and one scale had equal alpha. Compared to the Portuguese version, only three scales had lower alpha in the Greek version and one had equal value.

In the main study, domains' Cronbach's alpha indicators ranged from 0.57 to 0.91. More specifically, for "Demand at Work" Cronbach's alpha was computed as a=0.86 (scales ranged from α=0.66 to α=0.71), for "Work Organization and Job Contents" Cronbach's alpha was computed as α=0.89 (scales ranged from α=0.31 to α=0.81), for "Interpersonal Relations and Leadership" Cronbach's alpha was computed as α=0.86 (scales ranged from a=0.49 to α=0.92), for "Work Individual Interface" Cronbach's alpha was computed as α=0.57 (scales ranged from α=0.68 to α=0.87), for "Values at Workplace" Cronbach's alpha was computed as α=0.83 (scales ranged from α=0.64 to α=0.86), for "Health and Well-Being" Cronbach's alpha was computed as α=0.91 (scales ranged from α=0.76 to α=0.88), and for "Offensive Behaviour" Cronbach's alpha was computed as α=0.86.

The mean scores and standard deviations are shown in Table 3 in Supplementary Data[2], where they are compared with the original Danish study (Pejtersen *et al.*, 2010) and the Portuguese study (Rosário *et al.*, 2017)

Moreover in Table 3 in Supplementary Data[2], scales in the Greek study with negative scoring, where a high score means "bad" or "unhealthy" (*i.e.* Quantitative Demands, Cognitive Demands, Emotional Demands, Work Pace, Demands for Hiding Emotions, Role Clarity, Role Conflicts, Work-Family Conflict, Family-Work Conflict, Burnout, Stress, Sleeping Problems, Depressive Symptoms, Somatic Stress and Cognitive Stress), showed increased average values compared to the Danish and the Portuguese study. There was an exception in the scale of "Job Insecurity", whereas in the Danish study there was a lower average value in contrast to the Portuguese and the Greek study. Greek study's scales included in "Health and Well-Being" domain showed higher means scores in comparison with the original and the Portuguese study, except for those with a positive meaning such as Self-efficacy.

However, ten scales (*i.e.*, Variation of Work, Meaning of Work, Commitment to the Workplace, Predictability, Recognition-Rewards, Quality of Leadership, Social Support from Supervisors, Job Satisfaction, Mutual Trust between Employees, Trust Regarding Management, Justice and Social Inclusiveness) for which high score means "good" or "healthy", the Greek study showed lower average values. Otherwise, in "Influence at Work" and in "Social Support from Colleagues", the Greek study showed higher average values. In scales "Possibilities for Development" and "Social Community at Work", the values of the Greek studystand between the corresponding values of the Danish and Portuguese study.

Furthermore, Greek employees showed increased proportions in the domain of "Offensive Behaviour" that included meanings such as "Sexual Harassment", "Threats of Violence", "Bullying, Unpleasant Teasing", "Conflicts and Quarrels", "Gossip and Slander". Only in "Physical Violence", the Danish study showed a small difference compared to the Greek study.

An exploratory factor analysis was conducted considering the seven dimensions of the long version of the COPSOQ II, and the results are summarized in Tables 4, 5, 6, 7, 8, 9, and 10 in Supplementary Data[2].

In the Demands domain at "Work Dimension" the results support the scales (Quantitative Demands, Work Pace, Cognitive Demands, Emotional Demands and Demands for Hiding Emotions). In the scale of "Cognitive Demands", two items loaded in two factors, but still this factor can be supported sufficiently (Table 4 in Supplementary Data[2]).

[2]http://journal.embnet.org/index.php/embnetjournal/article/downloadSuppFile/977/977_supp_1

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In the "Work Organisation and Job Contents" dimension (Table 5 in Supplementary Data[2]), the results support totally the "Influence at Work", "Possibilities for Development", "Meaning of Work" scales. "Variation of Work" scale and "Commitment to the Workplace" scale are split into two factors, indicating that the construct validity of this scale is not supported. The last item of "Commitment to the Workplace" scale showed a negative loading indicating that this item should be reversed ,as should be done in the initial study.

In the "Interpersonal Relations and Leadership" dimension (Table 6 in Supplementary Data[2]), factor analysis showed six factors instead of the initial eight factors. The analysis support the "Recognition-Rewards", "Role clarity", "Quality of Leadership", "Social Support from Colleagues", "Social Support from from Supervisors" and "Social Community at Work" scales. Four scales ("Social Support from Colleagues" and "Social Community at Work") and ("Quality of Leadership" and "Social Support from Supervisors") load on the same factor. Two other scales ("Predictability" and "Role Conflicts") load on various scales.

In the "Work-individual Interface" dimension, the results fully support the initial scale structure (Table 7 in Supplementary Data[2]) as in the Danish study.

In the "Values at the Workplace" dimension, the results did not support the hypothesised scale structure for any of scales. At least one item for each scale loaded in different factor while three or more items loaded in the same factor (Table 8 in Supplementary Data[2]).

In the "Health and Well-Being" dimension, the results support the hypothesised scale structure for three scales ("Burnout", "Depressive Symptoms" and "Cognitive stress") but in this factor analysis six factor were extracted instead of the initial eight scales. The "Sleeping Problems", "Somatic Stress" and "Self-efficacy" scales had one item which loaded in a different factor. In the "Stress" scale, three of the four items loaded in two factors (Table 9 in Supplementary Data[2]).

In the "Offensive Behaviour" dimension (Table 10 in Supplementary Data[2]), factor analysis resulted into two factors; one with "Sexual Harassment", "Bullying", "Unpleasant Teasing" and "Gossip and Slander", and one with "Threats of Violence", "Physical Violence" and "Conflicts and Quarrels".

Discussion

For almost a decade, the Greek working force experiences chronic stressors due to the sustained socio-economic changes (Kentikelenis *et al.*, 2011). To detect the impact of that stressors in the workplace and improve working conditions, proper tools are necessary to monitor work-related stress. Psychosocial risk factors are work-related chronic stressors with substantial impact on the social capital and the working environment itself (Leka and Jain, 2010).

The Copenhagen Psychosocial Questionnaire is one of the most valid tools used for assessment of the psychosocial workload almost worldwide (Dicke *et al.*, 2018; Nübling *et al.*, 2014).

This study provides evidence that the Greek version of COPSOQ-II is valid and reliable. The long version of the questionnaire was tested through different techniques (probe techniques with an evaluation by four committee raters, item CVI score, S-CVI/average and content validity), at the first phase of the study, with the purpose not only to be translated into Greek but also to be cross-culturally adapted. The final adaptation (study's second phase) was conducted on a sample of 652 workers from various occupational sectors. The Greek version of COPSOQ-II revealed satisfactory psychometric properties.

The internal consistency of the seven domains was satisfactory (> 0.80) with the exception of the "Work individual interface" domain that showed low internal consistency. However, the specific subscales of this domain showed high internal consistency. This may be a matter of further investigation for testing with other criterion equivalence, *e.g.*, convergent validity.

Comparison of the Greek (GR) version Cronbach-alphas with the results of the subscales in the original survey (Danish - DN) and in another country with similar socioeconomic conditions (Portuguese - PT), showed similarities. However, internal consistency was observed in the following subscales for GR and PT vs. DN; "Predictability": GR (α=0.50), PT(α=0.49) vs. DN (α=0.74), "Mutual Trust between Employees": GR (α=0.69), PT (α=0.66) vs. DN(α=0.77), "Job Satisfaction": GR (α=0.72), PT (α=0.72) vs. DN (α=0.82). These might be explained by the fact that Denmark's labour market is established on the basis of "flexicurity" (Richard *et al.*, 2012) that leads to more predictable working conditions, while Greece and Portugal are under the control of the International Monetary Fund (IFM) (Karadinos, 2013; Kentikelenis *et al.*, 2011).

Regarding mean scores of the several subscales ("Quantitative demands", "Cognitive demands", "Emotional Demands", "Work Pace", "Demands for Hiding Emotions", "Role Clarity", "Role Conflicts", "Work-Family Conflict", "Family-Work Conflict", "Burnout", "Stress", "Sleeping Problems", "Depressive Symptoms", "Somatic Stress " and "Cognitive Stress"), Greek employees scored higher than the Portuguese and the Danish. This may be attributed to the fact that our study was conducted at a period of time where the Greek working force had been exposed to increased psychosocial workload for almost 10 years, depicting the exhaustion from the ongoing changes that had taken place in their work.

The results from the factor analysis are partially consistent with the initial version of the COPSOQ-II, as three of the subscales ("Interpersonal Relations and Leadership", "Health and Well-Being", "Offensive Behaviour") resulted in less factors. The results of the factor analysis regarding the domains of "Interpersonal Relations and Leadership" and "Offensive Behaviour" may be explained by the fact that many participants were occupied in positions free of leaderships, supervisors, or

colleagues. Health and well-being domain also resulted in less factors and possible explanations are the sample size, the inability of some participants to comprehend the items of the subscales, or the difficulty to interrelate items within this scale.

One of the strengths of the study is that it included employees from different sectors. Also, the sample size was adequate and the internal consistency of the subscales was satisfactory. However, due to the long version of the questionnaire, no test-retest reliability was performed, which is a limitation of the study.

In conclusion, the Greek version of the COPSOQ-II (GR-COPSOQ II) indicated good psychometric properties for most of the scales of the questionnaire. The GR-COPSOQ II can be recommended as a valid tool for the assessment of psychosocial risk factors in Greek employees as it meets the criteria of internal consistency and construct validity.

Key Points

- Work-related stress can manifest with a series of psychosocial, emotional, cognitive and behavioural reactions.
- Validated instruments are required to measure psychosocial risk factors in the work environment.
- The Copenhagen Psychosocial Questionnaire-II (COPSOQ-II) is a widely used tool.
- Validity and reliability of the COPSOQ-II were tested in a large sample of Greek employees.
- The Greek version of the COPSOQ-II has good psychometric properties and is recommended for psychosocial risk assessment in Greek employees.

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Research Papers

Validation of the Greek version of the Problematic Internet Use Questionnaire - Short Form (PIUQ-SF-6)

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Abstract

Internet is a necessary tool of everyday routine, however, concerns about the development of abnormal behaviours in relation to its use by adolescents are constantly growing. The need of brief screening tools for problematic internet use in teenagers in Greece is imperative. The purpose of this study was to validate the 6-item short form of the Problematic Internet Use Questionnaire (PIUQ-SF-6) in a Greek sample of adolescents. The sample consisted of 200 adolescents (55.0% males, 61.6% high school students, 38.4% junior high school students) who completed the study's questionnaires i.e., a demographic questionnaire, the PIUQ-SF-6, the Young's Diagnostic Questionnaire (YDQ) and the Adolescent Computer Addiction Test (ACAT). The internal consistency of the Greek version of PIUQ-SF-6 was sufficient and acceptable (Cronbach's alpha coefficient a = 0.80). Confirmatory Factor Analysis was significant, and goodness-of-fit was adequate. For establishing convergent validity, Pearson's and Spearman's correlation coefficients were calculated between the PIUQ-SF-6 and ACAT scales and Receiver Operating Characteristic (ROC) analysis (between PIUQ-SF-6 and YDQ) indicated an excellent accuracy. The Greek version of the PIUQ-SF-6 demonstrated satisfactory psychometric properties (reliability and validity) and is recommended as a reliable screening tool for problematic internet use in Greek adolescents.

Introduction

Over the past decade the use of the internet has increased significantly and has become an integral part of our lives. Internet overuse is a global problem causing growing concern, which has led the scientific community to introduce terms such as "Problematic Internet Use" (PIU) or "Internet Addiction Disorder" (IAD). The term of IAD was first used by the New York based psychiatrist Ivan Goldberg (Dalal and Basu, 2002). The clinical psychologist Kimberly Young, in 1998, used the term "Addictive/ Pathological Internet use", based on common features with abnormal gambling (Young, 1998).

Young *et al.* found that internet addiction covers a number of behaviours and impulse control problems and can be classified into five different types: (i) Cyber sexual addiction - compulsive use of adult websites for cybersex and cyber porn, (ii) Cyber-relationship addiction - over involvement in online relationships, (iii) Net compulsions - obsessive online gambling, shopping, or online trading, (iv) Information overload -compulsive web surfing or database search, (v) Computer addiction

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- obsessive computer game playing (Young *et al.*, 2000). Davis RA distinguished two types of pathological internet use, general pathological use of the internet that includes a general, multidimensional excessive use of the internet, and specific pathological use of the internet that includes those cases of users who are addicted to a specific function or application of internet (pornographic material and services, games, online trading, auctions, gambling, etc.) (Davis, 2001).

Various studies on internet addiction have been conducted internationally. In South Korea, internet addiction has become one of the most serious public health problems following the deaths of 10 teenagers from cardiorespiratory diseases in internet cafes (Choi, 2007). More than 210,000 children and adolescents, aged 6-19 years, are addicted, with 80% of them in need of treatment and 20%-24% in need of hospitalisation. At the same time, since 2009, more than a thousand specialists have been trained in 190 mental health structures (Ahn, 2007). In Taiwan, Tsai and Lin (2003) found that among 700 adolescents, 12.8% were addicted to the internet (Tsai and Linn, 2003). In a study conducted on a Korean sample of 1,573 adolescents, it was found that 1.6% of respondents were addicted to the internet (Kyunghee *et al.*, 2006). In Iran, among 1,968 adolescents, 3.8% were addicted (Gzassemzadeh, 2008). In Seoul, a survey of 903 adolescents showed that 10.7% were addicted and required further evaluation and intervention (Park *et al.*, 2008).

In Greece, numerous studies have been conducted on adolescents' computer addiction. One of the first studies in a random sample of 897 adolescents in the large urban center of the capital of Athens, found 12.8% of the adolescents with marginally healthy use of the internet, and only 1% with internet addiction. A key factor that determined the level of computer usage was the access points to it, as teenagers were found to spend more time online when at home or at internet cafes. In addition, users involved in social networking and video games showed a higher tendency to addiction (Tsitsika *et al.*, 2009). A study in Thessaloniki, the second largest city in Greece, showed that in a sample of 278 high school students, 91% were aware that the use of social networks can lead to addiction, while only 9% claimed that the use of social networks cannot lead to addiction. Moreover, 55% of the sample were personally aware of cases of students who had become addicted to social networks (Samaras, 2014). In the Greek province, the problem of internet addiction seemed more intense, as a survey in Thessaly in a sample of 2,200 high school students reported internet addiction in 8.2% of users, mainly in boys who played online games and visited frequented internet cafes (Siomos *et al.*, 2008). Karapetsas *et al.*, in a survey conducted in Volos in a sample of adolescents aged 13 to 15 years, found an internet addiction rate of 22%, while gender was not found to be a determining factor (Karapetsas *et al.*, 2012). A study conducted in the Greek island of Kos, in a sample of 1,270 adolescents aged 14-18 years, showed that 7.2% of boys and 5.1% of girls were addicted to the internet (Fisoun *et al.*, 2012). A survey in adolescents aged 13 to 18 years, in the areas of Attica, Halkidiki and Rhodes in Greece, showed a 12% percentage of addicted students with higher rates of addiction in boys (15%) than girls (9%). Almost all students had a computer with internet connection at home, while those who did not have a computer visited internet cafes to access the internet (Sofos *et al.*, 2011). Another study conducted in 2010 in a sample of students aged 11, 13 and 15 years, throughout Greece, found that 15.5% of the adolescents were addicted to the internet and 5.5% were addicted to electronic games. Specifically, the percentage of students who used the computer for at least 3 hours daily on weekdays, increased with age; from 14.1% at 11 years to 25.8% at 13 years and 33.7% at 15 years. In addition, more boys (26.8%) than girls (21.9%) used the computer for at least 3 hours daily on weekdays (Kokkevi *et al.*, 2010).

Therefore, the need of brief screening tools for PIU in teenagers in Greece is imperative. The purpose of this study was to validate the 6-item short form of the Problematic Internet Use Questionnaire (PIUQ-SF-6) in a Greek sample of adolescents.

Materials, Methodologies and Techniques

Participants

The study was conducted from July to September 2020. The sample was recruited from three Greek cities; Athens (the urban capital of Greece with more than 5,000,000 residents), Nafplio (middle sized rural town with 33,356 citizens) and Nemea (small rural town with 6,483 citizens). The sample was set to be able to conduct factor analysis. According to the literature, the study sample should either follow the rule of 100, (Gorsuch, 1983; Kline, 1979), or five times higher than items (this means 30 subjects in the present study) (Hatcher, 1994), or at least 150 - 300 cases (Hutcheson and Sofroniou, 1999). Prior to study entry, students and their parents/guardians were asked to provide written consent.

Materials

Participants were asked to declare few demographic characteristics such as sex, age, school class, parental educational level, and parental job status. Adolescents' habits related to internet use were assessed with four questions about i) ownership or not of a personal computer (PC) they used, ii) hours spent online, iii) main reason of internet use, and iv) social media used. Adolescents were also asked to complete three questionnaires, the Problematic Internet Use Questionnaire-short form (PIUQ-SF-6), the Young's Diagnostic Questionnaire (YDQ) and the Adolescent Computer Addiction Test (ACAT).

Problematic Internet Use Questionnaire (PIUQ) : The PIUQ comprises three versions (18-item, 9-item, and 6-item), all having reliable factor structures, and proven validity across both online and written data collection

methods in samples of different age groups (*i.e.*, adults and adolescents) (Demetrovics *et al.*, 2016). For the basic outcome of the study, the validation of a short and quick instrument to measure problematic internet use, the 6-item short form of the PIUQ (PIUQ-SF-6) was used. The original version of the PIUQ with 18 items was developed on a Hungarian sample (Demetrovics, 2008). Years later, the short 9-item version (PIUQ-9) was developed (Laconi *et al.*, 2019) with an aim to create a brief, comprehensive, non-arduous screening tool given that previous version caused fatigue and desertion. This version was evaluated in nine European samples of internet users that included 154 Greek adults. Another shorter version was developed using 6 items with an aim to assess more impulsive populations in limited time (Demetrovics *et al.*, 2016). The 3-factor structure has been retained in all versions: obsession, neglect, and control disorder. A 5-point Likert scale ("never", "rarely", "sometimes", "often", "always/almost always") was used to evaluate how much the given statements characterized the respondents. Scores range from 6 to 30, with higher scores indicating higher risk of PIU. In the original version of the PIUQ, Cronbach's alpha was 0.87 (obsession α=0.85; neglect α=0.74; control disorder α=0.76) (Demetrovics, 2008). For the shorter version PIUQ-9, internal consistency ranged from 0.81 (German subsample) to 0.90 (Turkish subsample) (Laconi *et al.*, 2019). For the 6-item version PIUQ-SF-6 Cronbach's alpha was equal to α=0.77 (Demetrovics *et al.*, 2019). The test–retest correlation of the original PIUQ was 0.90 (Demetrovics *et al.*, 2008).

Validation procedure: After obtaining permission from the developer to validate the PIUQ-SF-6 in a Greek population sample, the forward and back translation stage was carried out. Two bilingual translators, native speakers of Greek, translated the initial version of the PIUQ-SF-6 to the Greek language. They worked separately and each translator produced a written record of a translated version. Afterwards, the principal investigator unified the two translations into a single version since there were no significant differences between them. A third bilingual translator, native English speaker was recruited to translate backward the Greek version to the English language, without having ever read the original questionnaire. A three-person expert committee (including the principal investigator, a professor and a statistician experienced in cultural adaptation) supervised the translated versions and finalised the Greek version of the PIUQ-SF-6.

A pilot test in 15 participants was conducted to identify any confusing questions or meanings as well as suggestions for possible improvement. Moreover, during the pilot test the principal instigator counted the time needed for completion of the questionnaire (approximately 3 minutes). Reliability analysis, and more specifically Cronbach's alpha, was carried out in this phase to examine the internal consistency of the PIUQ-SF-6 which was found equal to a = 0.72, an acceptable value as it was higher than the threshold of 0.7 (De Vellis, 1991).

Young's Diagnostic Questionnaire (YDQ): For convergent validity and for Receiver Operating Characteristic (ROC) analysis the Young's Diagnostic Questionnaire (Young, 1996) was used, which is validated in the Greek population (Siomos *et al.*, 2008). Young developed the YDQ from the pathological gambling DSM-IV criteria, using seven of ten DSM criteria and adding an eighth item (Young, 1996; Siomos *et al.*, 2008). The YDQ consists of eight nominal questions (yes-or-no) regarding internet use. Participants who answer positively to five or more of the eight items are classified as addicted internet users, while the remaining participants are classified as normal internet users. The consistency of the Greek version of the YDQ was tested with Cronbach's alpha which was a = 0.72 (Siomos *et al.*, 2008).

Adolescent Computer Addiction Test (ACAT): A second tool used for convergent validity was the Adolescent Computer Addiction Test which was validated in Greek students in 2006 (Siomos *et al.*, 2009) The ACAT is a 20-question tool with 5-point Likert type possible answers (1, not at all; 2, rarely; 3, occasionally; 4, often; 5, always). After scoring the tool, four scales were constructed: Computer Addiction, Work Neglect, Social Life Neglect, Extreme Use. The ACAT has excellent test-retest reliability, internal consistency, and construct validity; the total scale reliability was a = 0.93, and the range for four scales was a = 0.74 to a = 0.85 (Siomos *et al.*, 2009).

Statistical analysis

Absolute and relative frequencies were used to describe categorical variables such as demographic characteristics. Mean (M), standard deviation (SD) and median (Mdn) described continuous data. The internal consistency was carried out using Cronbach's alpha; values above 0.7 were considered acceptable (Cortina, 1993). Exploratory and Confirmatory Factor Analysis (EFA and CFA, respectively) were performed to examine the validated tool. For EFA, Varimax rotation was used. For CFA, chi-square test ($\chi 2$), comparative fit index (CFI), Tucker-Lewis index (TLI), root mean square error of approximation (RMSEA) and standardized root mean residual (SRMR) were computed to evaluate the model. The model can be considered satisfactory when the CFI and TLI values are higher than or close to 0.95 and still acceptable if the values are above 0.90 (Brown, 2006; Bentler and Bonett, 1980). An RMSEA value below 0.05 indicates excellent fit, a value around 0.08 indicates adequate fit, a value above 0.10 indicates poor fit and SRMR values below 0.10 indicate good fit (Brown, 2006; Browne and Cudeck, 1993). To check the convergent validity, Pearson's and Spearman rho correlation coefficients were computed. Convergent validity was considered an adequate instrument measuring the same construct when the correlation between PIUQ-SF-6 and ACAT was >0.50 (Abma *et al.*, 2016). Also, ROC analysis

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and Area Under Curve (AUC) were established to check convergent validity as well (0.7 to 0.8 is considered acceptable, 0.8 to 0.9 is considered excellent, and more than 0.9 is considered outstanding) (Hosmer and Lemeshow, 2000).

Statistical analysis was performed using the SPSS version 25.0 (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp) and R Statistics software version 4.0.3 (R Core Team, 2020), and the ROC curve was fit and analysed using the Lavaan package (Rosseel, 2012).

Results

A total of 200 adolescents aged 12-17 years completed the questionnaires. Participants' demographic and other characteristics are presented in Table 1.

Specifically, 55.0% (n = 110) of the respondents were male, while females constituted 45.0% of the sample (n = 90). Most students were in high school (61.6%) while 38.4% were in junior high school. Almost 8 out of 10 participants had parents who were high school graduates or had a University degree. Almost 10 out of 10 fathers were employed, whereas 8 out of 10 mothers

Table 1. Demographic characteristics of the sample (N = 200).

Characteristic		Absolute frequency	Relative frequency (%)
Sex	Male	110	55.0
	Female	90	45.0
School Class	Junior high school	76	38.4
	High school	122	61.6
Paternal educational level	Junior high school	1	0.5
	High school	80	40.4
	College/Trade school	16	8.1
	University degree	96	48.5
	Master/PhD	5	2.5
Maternal educational level	Junior high school	5	2.5
	High school	68	34.3
	College/Trade school	26	13.1
	University degree	91	46.0
	Master/PhD	8	4.0
Does your father have a job?	Yes	196	99.5
	No	1	0.5
Does your mother have a job?	Yes	155	78.3
	No	43	21.7
The Personal Computer that you use:	Exclusively mine	51	25.9
	Shared with other family members	143	72.6
	I do not use at home	3	1.5
How many hours a day do you use the internet?	1-2 hours	34	17.2
	2-3 hours	75	37.9
	3-4 hours	69	34.8
	More than 4 hours	17	8.6
	I do not use at all	3	1.5
What is the main reason you use Internet?	To play videogames	66	33.8
	To find information about homework	22	11.3
	To chat with friends or other people	74	37.9
	For online shopping	3	1.5
	To download movies or songs	24	12.3
	To be informed	6	3.1
Social media that you use (multiple choice question)	Facebook	180	32.6
	Instagram	141	25.5
	Snapchat	75	13.6
	Viber/WhatsApp	129	23.4
	Twitter	12	2.2
	TikTok	15	2.7

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Table 2. Factor loadings and descriptive statistics of three factors of the PIUQ-SF-6.

	Obsession	Neglect	Control
Disorder			
1. How often do you spend time online when you would rather sleep?		0.889	
2. How often do you feel tense, irritated, or stressed if you cannot use the Internet for as long as you want to?	0.916		
3. How often does it happen to you that you wish to decrease the amount of time spent online but you do not succeed?		0.365	0.640
4. How often do you try to conceal the amount of time spent online?			0.781
5. How often do people in your life complain about spending too much time online?		0.774	0.373
6. How often does it happen to you that you feel depressed, moody, or nervous when you are not on the Internet and these feelings stop once you are back online?	0.689		0.587
Eigenvalue	1.71	1.44	1.43
Variance explained (%)	28.53	23.99	23.75
Mean	2.19	2.51	2.25
Median	2.00	2.50	2.00
Standard deviation	0.78	0.88	0.78

Values refer to loading after Varimax rotation, eigenvalue, percent of variance explained, mean, median, standard deviation.

Cronbach's alpha of the PIUQ-SF-6 was α=0.80.

PIUQ-SF-6, Problematic Internet Use Questionnaire-Short Form (6-item)

were in employment. Nine in 10 students had a personal computer at home (25.9% reported exclusive possession and 75.6% shared use with other family members). Regarding the hours they spent on the internet on a daily basis, 17.2% of the participants spent 1-2 hours, 37.9% 2-3 hours, 34.8% 3-4 hours, 8.6% more than 4 hours and the rest 1.5% did not own a computer and did not use internet at all. The main reasons for using internet were to chat with friends or other people (37.9%) and to play games (33.8%). The most popular social media were Facebook (32.6%), followed by Instagram (25.5%) and Viber/WhatsApp (23.4%).

Exploratory Factor analysis: The EFA of PIUQ-SF-6 is presented in Table 2. Factor analysis showed good adaptability in the Obsession scale and mild adaptability in the Neglect and Control Disorder scales. The total variance explained by EFA was 76.27%. The mean, median and standard deviation for Obsession were 2.19, 2.00 and 0.78, for Neglect 2.51, 2.50 and 0.88, and for Control Disorder 2.25, 2.00 and 0.78, respectively.

Regarding the internal consistency of the Greek version of the PIUQ-SF-6, Cronbach's alpha coefficient was a = 0.80 for the total scale (Table 2).

Confirmatory Factor analysis: The CFA of the PIUQ-SF-6 is presented in Table 3. Baseline model was found significant ($\chi 2 = 358.45$, $p < 0.001$). The goodness-of-fit summary was adequate; TLI = 0.88; CFI = 0.95; SRMR = 0.04. The only index that was not good enough is RMSEA which was 0.12, slightly higher than 0.10.

Convergent validity: To prove convergent validity, Pearson's and Spearman's correlation coefficients between the PIUQ-SF-6 and ACAT scales were calculated (Table 4).

Strongest correlations were found between Control Disorder and Extreme Use ($r = 0.701$, $p < 0.001$), Neglect

Table 3. Confirmatory Factor Analysis of the PIUQ-SF-6.

Latent Variables	Latent Variables	Estimate	Std. Error	z-value	p
Obsession	Q2	0.59	0.06	9.49	<0.001
	Q6	0.76	0.06	12.62	<0.001
Neglect	Q1	0.54	0.07	7.26	<0.001
	Q5	0.83	0.09	9.43	<0.001
Control Disorder	Q3	0.53	0.08	6.77	<0.001
	Q4	0.56	0.07	7.84	<0.001
Chi-square	358.45				
Df	15				
P	<0.001				
CFI	0.95				
TLI	0.88				
RMSEA [95%CI]	0.12 [0.07, 0.17]				
SRMR	0.04				
AIC	2972.26				
BIC	3021.66				
SSABIC	2974.14				

Q1 to Q6, questions of PIUQ-SF-6 as referred in Table 2.

PIUQ-SF-6, Problematic Internet Use Questionnaire-Short Form (6-item); df, degrees of freedom; CFI, Comparative Fit Index; TLI, Ticker-Lewis Index; RMSEA; Root Mean Square Error of Approximation; 95% CI, 95% Confidence Interval; SRMR, Standardized Root Mean Square Residual; AIC, Akaike Information Criteria; BIC, Bayesian Information Criteria; SSABIC, sample size adjusted Bayesian Information Criteria.

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Table 4. Correlations between PIUQ-SF-6 and ACAT scales.

	1	2	3	4	5	6	7
1.Obsession§	1	0.491***	0.574***	0.681***	0.609***	0.624***	0.570***
2. Neglect		1	0.608***	0.514***	0.510***	0.438***	0.682***
3. Control Disorder			1	0.675***	0.664***	0.617***	0.701***
4. Computer Addiction				1	0.776***	0.712***	0.713***
5. Work neglect					1	0.718***	0.641***
6. Social life neglect						1	0.564***
7. Extreme use							1

****p< 0.001; **p< 0.01; *p< 0.05 (Pearson, §Spearman rho correlation coefficients).*

PIUQ-SF-6, Problematic Internet Use Questionnaire-Short Form (6-item); ACAT, Adolescent Computer Addiction Test

Table 5. ROC analysis and AUC between PIUQ-SF-6 and YDQ.

Test Result Variables	Area	Std. Errora	Asymptotic p-valueb	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
Obsession	0.78	0.04	<0.001	0.70	0.86
Neglect	0.67	0.04	0.001	0.59	0.75
Control Disorder	0.82	0.03	<0.001	0.75	0.88
PIUQ-SF-6 Total Scale	0.81	0.03	<0.001	0.74	0.88

The test result variables: Obsession, Neglect, Control Disorder, PIUQ-SF-6.

State variable: Addicted Internet users according to YDQ.

a. Under the nonparametric assumption

b. Null hypothesis: true area = 0.5

ROC, Receiver Operating Characteristic; AUC, Area Under Curve; PIUQ-SF-6, Problematic Internet Use Questionnaire-Short Form (6-item); YDQ, Young's Diagnostic Questionnaire

and Extreme Use (r = 0.682, p < 0.001), Obsession and Computer Addiction (r = 0.381, p < 0.001).

To measure convergent validity, ROC analysis between PIUQ-SF-6 and YDQ was carried out (Table 5). For the total scale of PIUQ-SF-6, Control Disorder, and Obsession scale results indicated an excellent accuracy (AUC = 0.81, p < 0.001, 95% CI [0.74, 0.88], AUC = 0.82, p < 0.001, 95% CI [0.75, 0.88] and AUC = 0.78, p < 0.001, 95% CI [0.70, 0.86] respectively). For the Neglect scale, results indicated an acceptable accuracy (AUC = 0.67, p = 0.001, 95% CI [0.59, 0.75]).

Discussion

Internet is a means of communication, entertainment and education that is constantly evolving, exerting a significant influence on the shaping of modern reality. While internet is a necessary tool of everyday routine, the concern for development of pathological behaviours in relation to its use is constantly growing. The negative effects on young people's physical health, due to the extensive screen time and sedentary lifestyle, internet addiction, excessive involvement with online games and social networking sites are of particular concern to the scientific community. In Greece, digital literacy has not come through a coordinated learning process but through commercial engagement, resulting in high levels of internet addiction (Sfakianakis *et al.*, 2012).

The PIUQ-SF-6 is a comprehensive, brief tool that assesses three key factors in PIU; obsession (*i.e.*, obsessive thinking about the internet and mental withdrawal symptoms caused by the lack of internet use), neglect (*i.e.*, neglect of basic needs and everyday activities), and control disorder (*i.e.*, difficulties in controlling internet use).

The basic criterion for the reliability of a scale is the Cronbach's alpha coefficient with acceptable values greater than 0.7 (DeVellis, 1991). With regards to the validation of PIUQ-SF-6, the questionnaire was checked for its internal consistency and was found sufficient and acceptable. For the initial version of the PIUQ-18, the Cronbach alpha was equal to 0.87, while for the smaller version of the PIUQ-9, the internal consistency was 0.81 in the German sample and 0.90 in the Turkish sample. In our study, the CFI index was 0.95 and the SRMR index was 0.04. Furthermore, in the initial version of PIUQ-18, the questionnaire contains 6 questions per factor, while in the PIUQ-9 version the questionnaire contains 3 questions per factor, and in the smaller PIUQ-SF-6 version it contains 2 questions per factor.

The main limitation of the study was that the sample was not representative of all areas in Greece, rural and urban. In addition, the study sample was relatively

small compared to that of the original PIUQ-SF-6 questionnaire survey (n=5,005) (Demetrovics, 2016).

To conclude, the Greek version of the PIUQ-SF-6 demonstrated satisfactory psychometric properties (reliability and validity) and is recommended as a reliable screening tool for PIU in Greek adolescents. Future large surveys are needed to provide more in-depth knowledge about PIU in children and adolescents in Greece.

Key Points

- Problematic Internet Use (PIU) is prevalent among teenagers.
- The need of brief screening tools for PIU in adolescents is imperative.
- The Greek version of the PIU Questionnaire-short form (PIUQ-SF-6) has satisfactory reliability and validity.
- The PIUQ-SF-6 is a reliable screening tool for PIU in Greek adolescents.

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Validation of the Greek version of the Adolescent Sleep Hygiene Scale (ASHS)

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Abstract

Transition from childhood to adolescence is known to bring about many changes in the lifestyle and psycho-emotional state of adolescents. One of the major lifestyle factors that affect adolescents' physical and mental health is sleep. The aim of this study was to validate the Adolescent Sleep Hygiene Scale (ASHS), a tool that measures sleep hygiene, in an adolescent sample living in Greece. The study's sample consisted of 146 Greek adolescents aged 12-18 years. The Adolescent Stress Questionnaire was used for convergent validity and correlation with adolescents' stress. The pilot and the main study demonstrated sufficient internal consistency. Exploratory Factor Analysis showed an adequate adaptation of the original ASHS questionnaire to the Greek adolescents. The findings of this study support the use of ASHS as a reliable and valid tool for evaluating sleep-facilitating and sleep-inhibiting practices of Greek adolescents.

Introduction

Sleep is an important process for a person's physical and mental health, development, learning, behaviour, emotional stability, and general functioning during the day. In terms of emotional balance, research on healthy people who sleep less than they need has shown that accumulation of sleep deprivation gradually leads to worsening of a person's mood (Talbot *et al.*, 2010). The study of Yoo *et al.* in people with insufficient sleep due to an emotional stimulus, showed a 60% increase in amygdala activity compared to people who were relaxed (Yoo *et al.*, 2007). This increased activity of the amygdala affects cognitive control and executive functions (Drummond *et al.*, 1999; Muzur *et al.*, 2002). The most common sleep disorders are those related to sleep apnea, insomnia, prolonged drowsiness, narcolepsy, restless legs syndrome / recurrent sleep syndrome extreme fatigue during the day, increased arousal before bedtime and nightmares (the difference with bad dreams is that the nightmare causes a sudden cessation of sleep and waking up at night) (Nielsen *et al.*, 2000).

The transition from childhood to adolescence is known to bring about many changes in the lifestyle and psycho-emotional state of adolescents. One of the major lifestyle factors that affects adolescence is sleep. Adolescents tend to be late to sleep and want to stay up late, even on weekdays (Kirov *et al.*,2017). This seems to be due to delays in their circadian rhythm, studying, activities, many hours at the computer, as well as increased social life (Wang *et al.*, 2016). As a person gets older, sleep needs change, especially in the transition from infancy to adolescence, where there is a dramatic change during both the daytime and nighttime sleep needs. For example, an infant needs about 17 hours, a teenager 8 hours and a middle-aged man 6.5

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hours (Iglowstein *et al.*, 2003) of sleep per day. During the transition from middle childhood to adolescence, a gradual delay in the start time of sleep, as well as changes in the starting time between weekdays and weekends and longer sleep duration on weekends are observed. These changes in sleep habits have become more pronounced in recent years, with an emphasis on the transition from childhood to adolescence (Bayer *et al.*, 2007). More specifically, studies show that as the age increases from school to adolescence, the duration of sleep decreases (without it meaning that the needs decrease), usually due to delayed onset of sleep and forced waking up early in the morning (Owens *et al.*, 2008). Sleep deprivation at this age is due in large part to a delay in the onset of adolescent sleep and waking up too early for school. In Greece, there is a large percentage of adolescents who complain of unsatisfactory sleep, more girls than boys (Lazaratou *et al.*, 2008). According to the literature, most adolescents sleep later than they should due to reading, social life and use of electronic media, and get up early in the morning (Alfano *et al.*, 2010). A survey in Britain found that 30% of 15-year-old boys and 49% of 15-year-old girls report sleep problems and 36% of all 15-year-olds report not getting enough sleep to cope with school obligations (Bruce *et al.*, 2017). Lack of sleep leads to drowsiness during the day (Dewald *et al.*, 2010) that causes problems in the adolescent's cognitive skills, response to school and reading, and also in behaviour, risk-taking and emotional stability (anxiety, depression etc.) (Roberts *et al.*, 2009). Poor sleep hygiene in the form of the use of digital media (TV, mobile, computer) predicts a delay in bedtime, reduced sleep duration, increased daytime sleepiness and even nightmares (Hale and Guan, 2015; Eggermont and Van den Bulck, 2006; Higuchi *et al.*, 2005). The theory that the use of these media results in the development of sleep disorders is based on exposure to stimulating light, the content of the media (*e.g.* thrillers increase arousal), as well as the time consumed by the use of digital media (Foerster *et al.*, 2019). As for adolescents with anxiety disorder, they may rely on digital media to avoid the onset of sleep or forget their worries. However, research shows that anxious teens spend more time watching television than healthy teens because they see it as a means of coping with stress (De Wit *et al.*, 2011). The literature has reported a poor relationship between sleep hygiene and sleep problems (Mindell *et al.*, 2009; LeBourgeois *et al.*, 2005). However, there is a lack of extensive research regarding the relationship between sleep hygiene and its disorders in adolescents with anxiety disorders.

The association of sleep disorders with anxiety disorders in adolescents is a research topic of many studies in the recent years to understand if anxiety disorders cause sleep disorders and vice versa. The presence of an anxiety disorder causes a sleep problem, while the presence of a sleep disorder can subsequently cause an anxiety disorder (Sarchiapone *et al.*, 2014). Even in young people, a large percentage that shows symptoms of an anxiety disorder also has problematic sleeping habits (Telzer *et al.*, 2014). Children and adolescents with anxiety disorders tend to have a threat bias, and at the same time show an increased tendency to view dubious situations as threatening (Barrett *et al.*, 1996; Blossom *et al.*, 2013). In addition, adolescents with anxiety disorders have elevated cortisol levels at bedtime compared to groups of healthy adolescents (Forbes *et al.*, 2006). Indeed, cortisol is associated with arousal, and high levels of arousal around bedtime result in delayed onset (Hatzinger *et al.*, 2012).

The aim of this study was the cultural adaptation and validation of the Adolescent Sleep Hygiene Scale (ASHS), a tool that measures sleep hygiene, in an adolescent sample living in Greece.

Materials, Methodologies and Techniques

Participants

The study sample was recruited from the tertiary Center for Adolescent Medicine and UNESCO Chair on Adolescent Health Care of the First Department of Pediatrics at the Aghia Sophia Children's Hospital in Athens, Greece. To determine a sample size sufficient for factor analytic procedures, the following two criteria were used: (i) the sample should have 51 more cases than the number of variables to support chi-square testing in Bartlett's test of sphericity (Lawley and Maxwell, 1971; Gorsuch, 1983), (ii)the sample should include at least 100 cases and the subjects to variables (STV) ratio should be no less than 5 (Suhr, 2006; Hatcher, 1994).

Inclusion and exclusion criteria

Teenagers, 12- to 18-years of age, able to read and write in Greek, were eligible to participate in the study. Adolescents with major psychiatric disorders or other chronic diseases known to affect sleep, and substance users were excluded.

Adolescents and their parents or guardians were informed about the purpose of the study and signed consent forms prior to study entry. The study protocol was approved by the ethics committee of the Aghia Sophia Children's Hospital. The entire survey (translation, pilot, and main study) was conducted from December 2017 to December 2018.

Validation Procedure

Trying to achieve an excellent and unbiased translation for the instrument, multiple techniques were used as proposed for cross-cultural research, namely forward translation, backward translation, expert committee review and preliminary pilot testing (Tsang *et al.*, 2017; Hall*et al.*, 2018). During the forward translation procedure, two bilingual (Greek and English) translators worked independently to produce a Greek version of the ASHS. Some minor discrepancies among the two translators were resolved by an independent reviewer.

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During the backward translation procedure, the version that was produced in the previous step was back translated in English by two bilingual translators experienced in the target culture and who had never seen before the original English version of the scale. Following this, a source-language questionnaire developer highlighted each word or phrase that was discrepant. An expert committee that included a member with in-depth knowledge of adolescent health and an expert in research methodology and translation process, solved some minor discrepancies and a consensus was reached. Examining feasibility was the last stage of the cross-cultural adaptation process before producing the final version of the Greek version of ASHS. A group that included eight healthy adolescents, aged 12-18 years, was recruited to contribute to the preliminary pre-testing of the translated version and to ensure the original instructions, items and scoring materials were clearly expressed. The last step of pilot testing involved the questionnaire completion with an aim to explore how adolescents interacted and completed the instrument.
Twenty adolescents were recruited to pilot testing of the investigated tool. This step provided an opportunity to investigate the wording of the instructions, the understanding of the items, and the way of completion with the provided response scale. Moreover, in this stage, there was an opportunity of recording the time that participants needed to fill in the questionnaire.

Materials

Study participants were asked about their demographic characteristics, as well as to complete the following two tools:

Adolescent Sleep Hygiene Scale (ASHS): The Adolescent Sleep Hygiene Scale (ASHS) was initially constructed by LeBourgeois (LeBourgeois *et al.*, 2005) and was modified from the Children's Sleep Hygiene Scale (Harsh *et al.*, 2002). The ASHS is a 28-item self-report tool that assesses sleep-facilitating and sleep-inhibiting practices in 12- to 18-year-old adolescents along 9 different conceptual domains: physiological (5 items), cognitive (6 items), emotional (3 items), sleep environment (4 items), daytime sleep (1 item), substances (2 items), bedtime routine (1 item), sleep stability (4 items), and bed/bedroom sharing (2 items) (LeBourgeois *et al.*, 2005). Participants report how often behaviours related with sleep hygiene have occurred during the past months using a 6-point Likert scale (1="always," 2="frequently-if not always," 3="quite often," 4="sometimes," 5="once in a while," 6= "never").The original measure had a good reliability index and more specifically the Cronbach's Alpha reliability index for the scales that make it up ranged from 0.46 to 0.74 for the areas of sleep hygiene, and 0.80 for the whole scale (total ASHS) (LeBourgeois *et al.*, 2005).

Adolescent Stress Questionnaire (ASQ): The Adolescent Stress Questionnaire (ASQ) consists of 58 questions related to the stress of the adolescent in the last year (Byrne *et al.*, 2007). The ASQ has been translated and validated in the Greek population (Darviri *et al.*, 2017). The 58 items in the Greek validation were categorised into 10 conceptual areas: stress of home life (12 items), school performance (7 items), school attendance (3 items), romantic relationships (5 items), peer pressure (7 items), teacher interaction (7 items), future uncertainty (3 items), school/leisure conflict (5 items), financial pressure (4 items), and emerging adult responsibility (3 items). The Greek validation showed a good reliability index and, more specifically, Cronbach's alpha internal consistency for the mentioned scales ranged from 0.70 to 0.86 and was equal to 0.96 for the whole scale (total ASQ) (Darviri *et al.*, 2017). The present study showed a good internal consistency and, in particular, Cronbach's alpha for ASQ scales ranged from 0.66 to 0.90.

Statistical analysis

Data analysis was conducted using the SPSS statistical software version 25 (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.). All variables of the study were calculated with descriptive analyses including mean, standard deviation (SD), absolute and relative frequencies. Exploratory Factor Analysis (EFA) with a Varimax rotation was conducted. Internal consistency was assessed using Cronbach's alpha. Convergent validity was examined by undertaking Spearman rho correlation.

Table 1. Demographic characteristics of study participants.

Characteristics	Total sample (N=146)
	N (%)
Gender	
Male	51 (34.9)
Female	95 (65.1)
Educational Stage	
Junior High School	91 (62.3)
High School	55 (37.7)
Maternal Education level	
Up to secondary	62 (42.5)
University degree	58 (39.7)
Postgraduate studies	26 (17.8)
Paternal Education level	
Up to secondary	65 (44.5)
University degree	54 (37.0)
Postgraduate studies	27 (18.5)
	Mean ± SD
Age (years)	14.43 ± 1.90

Qualitative variables are presented as absolute and relative frequencies and quantitative variable (age) as mean ± standard deviation (SD).

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Table 2. Exploratory factor analysis of items of Adolescent Sleep Hygiene Scale (ASHS) after varimax rotation using principal components (N=146).

	Factors								
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**
Psychological									
After 6:00 pm, I have drinks with caffeine (for example: cola, pop, root beer, iced tea, coffee).	-0.051	0.188	**0.676**	0.130	0.210	0.226	0.047	0.111	0.001
During the 1 hour before bedtime, I am very active (for example: playing outside, running, wrestling).	-0.125	0.142	0.094	0.012	0.006	**0.723**	-0.193	-0.007	0.085
During the 1 hour before bedtime, I drink >4 glasses of water (or some other liquid).	0.117	-0.078	0.032	0.058	0.020	**0.787**	0.053	0.002	-0.164
I go to bed with a stomachache.	**0.446**	0.017	-0.137	-0.077	**0.582**	0.012	-0.130	0.182	-0.010
I go to bed feeling hungry.	0.076	0.155	0.207	0.002	**0.597**	-0.181	-0.066	-0.054	-0.229
Cognitive									
During the 1 hour before bedtime, I do things that make me feel very awake (for example: playing video games, watching television, talking on the telephone).	0.074	**0.728**	-0.072	0.192	0.007	0.055	0.123	0.049	0.075
I go to bed and do things in my bed that keep me awake (for example: watching television, reading).	0.085	**0.596**	0.228	**0.425**	0.140	-0.073	-0.152	0.184	0.238
I go to bed and think about things I need to do.	**0.711**	0.020	0.269	0.245	0.008	-0.053	0.036	0.039	0.072
I go to bed and replay the day's events over and over in my mind.	**0.795**	0.013	-0.053	0.117	-0.056	0.137	0.190	0.026	0.021
I use my bed for things other than sleep (for example: talking on the telephone, watching television, playing video games, doing homework).	0.103	**0.537**	0.170	**0.372**	0.059	0.196	0.164	-0.082	-0.090
I check my clock several times during the night.	0.116	**0.680**	0.107	-0.122	0.024	-0.070	0.130	-0.009	-0.060
Emotional									
During the 1 hour before bedtime, things happen that make me feel strong emotions (sadness, anger, excitement).	**0.528**	**0.536**	0.067	-0.144	0.213	0.080	0.035	-0.124	0.010
I go to bed feeling upset.	**0.480**	**0.386**	0.170	-0.190	0.214	-0.042	-0.022	-0.038	-0.129
I go to bed and worry about things happening at home or at school.	**0.703**	**0.323**	0.117	-0.187	0.106	-0.110	-0.102	0.055	-0.108
Sleep environment									
I fall asleep while listening to loud music.	0.042	0.133	0.079	**0.570**	0.052	0.027	0.103	0.005	**-0.319**
I fall asleep while watching television.	-0.009	0.066	0.024	**0.794**	0.044	0.000	0.083	-0.172	-0.085
I fall asleep in a brightly lit room (for example, the overhead light is on).	-0.245	-0.046	-0.039	**0.383**	**0.499**	0.190	0.144	-0.158	0.069
I fall asleep in a room that feels too hot or too cold.	-0.055	0.290	**0.337**	0.234	**0.432**	0.023	0.247	0.027	**-0.369**
Daytime sleep									
During the day I take a nap that lasts > 1 hour.	0.203	-0.054	**0.367**	-0.013	**0.494**	**0.303**	0.078	-0.072	0.200
Substances									
After 6:00 pm, I smoke or chew tobacco.	0.203	0.086	**0.641**	-0.146	0.055	-0.104	0.200	-0.079	**-0.359**
After 6:00 pm, I drink beer (or other drinks with alcohol).	0.143	0.061	**0.784**	0.079	0.040	-0.010	-0.011	0.027	0.053
Bedtime routine									
I use a bedtime routine (for example, bathing, brushing teeth, reading).	-0.018	0.070	0.007	-0.195	-0.017	-0.071	0.061	-0.063	**0.773**
Sleep stability									
During the school week, I stay up >1 hour past my usual bedtime.	0.002	0.288	0.195	0.174	**0.462**	0.046	**0.320**	0.054	**0.302**
During the school week, I "sleep in" >1 hour past my usual wake time.	0.080	-0.065	**0.445**	**0.424**	-0.023	0.299	0.108	0.072	0.223
On weekends, I stay up >1 hour past my usual bedtime.	0.083	0.194	0.026	0.178	0.016	-0.052	**0.714**	-0.090	0.067
On weekends, I "sleep in" >1 hour past my usual wake time.	0.009	0.048	0.105	0.011	0.024	-0.051	**0.763**	0.172	-0.038
Bed/Bedroom sharing									
I sleep alone.	0.040	-0.101	0.087	0.037	-0.043	-0.123	0.006	**0.868**	0.036
I sleep all or part of the night with someone else (for example, with your parent[s], sister, or brother).	-0.030	-0.173	0.019	**0.313**	-0.034	-0.180	-0.132	**-0.716**	0.129
Loadings	2.60	2.56	2.29	2.13	1.78	1.61	1.57	1.50	1.38
Variance explained	9.28	9.13	8.17	7.59	6.34	5.75	5.59	5.34	4.93

Five factors explaining 62.1% of the total variance; Kaiser-Meyer-Olkin (KMO) = 0.700; Bartlett's Test of Sphericity: p< 0.001. Bold values indicate factor loading of greater than 0.3. Cronbach's alpha of total scale: a=0.78.

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Table 3. Correlations between the Adolescent Sleep Hygiene Scale (ASHS) and Adolescent Stress Questionnaire (ASQ) scales.

	Stress of Home Life	Stress of School Performance	Stress of School Attendance	Stress of Romantic Relationships	Stress of Peer Pressure	Stress of Teacher Interaction	Stress of Future Uncertainty	Stress of School/ Leisure Conflict	Stress of Financial Pressure	Stress of Emerging Adult Responsibility
Psychological	0.228**	-0.024	0.167*	0.199*	0.026	0.099	0.118	0.159	0.188*	0.201*
Cognitive	0.427***	0.330***	0.338***	0.275**	0.344***	0.282**	0.453***	0.312***	0.305***	0.284**
Emotional	0.461***	0.392***	0.369***	0.331***	.407***	0.212*	0.422***	0.331***	0.333***	0.207*
Sleep environment	0.169*	0.054	0.224**	0.250**	0.158	0.232**	0.205*	0.165*	0.183*	0.154
Daytime sleep	0.194*	0.137	0.175*	0.275**	0.113	0.173*	0.176*	0.198*	0.184*	0.232**
Substances	0.273**	0.202*	0.240**	0.341***	0.188*	0.085	0.342***	0.148	0.335***	0.275**
Bedtime routine	0.045	-0.053	0.082	0.091	0.066	-0.053	-0.026	-0.020	0.018	-0.077
Sleep stability	0.224**	0.136	0.246**	0.204*	0.142	0.176*	0.244**	0.147	0.231**	0.178*
Bed/Bedroom sharing	0.000	0.013	-0.028	0.004	0.078	0.075	0.035	0.047	-0.012	0.112

****p< 0.001; **p< 0.01; *p< 0.05 (Spearman rho correlation coefficients).*

Results

Pilot study

Upon completion of the translation procedure, a pilot study was conducted among 20 adolescents. There was no difficulty by the students in completing the tool, neither in marking nor in the questions. The reliability index in the pilot study was found to be equal to Cronbach's α =0.73 and was considered satisfactory (Houser, 2008).

Main study

The sample of the main study consisted of 146 Greek adolescents. Descriptive statistics of the demographic and other characteristics of the sample are presented in Table 1.

About 2 of 3 participants were female (65.1%) and 34.9% of the participants were males. The majority of the sample was studying in junior high school (62.3%) and 37.7% in high school. The maternal education level was up to secondary level for 42.5% of the participants' mothers, 39.7% had university degrees and 17.8% had postgraduate studies. The paternal education level was up to secondary level for 44.5% of the participants' mothers, 37.0% had university degrees and 18.5% had postgraduate studies. The age of participants ranged from 12 to 18 years with a mean age of 14.43 years (SD=1.90), which also was gender-matched (p=0.650).

Factor analysis was performed, and the initial nine factors were extracted (Table 2). The total variance explained by EFA was found as 62.1%. The internal consistency of the Greek version of ASHS carried out using Cronbach's alpha coefficient was α = 0.77 for the total scale.

The Psychological scale was split into two factors indicating that the construct validity of this scale was not supported totally. The first item about drinking caffeine in the afternoon did not load better to this factor, but it was loaded in the factor with other substances. The other two items in the Substances scale (tobacco and alcohol drinks) matched perfectly into the same factor. Cognitive scales' items were divided in two factors (two out of six loaded in other factors). The Emotional scale's item perfectly loaded in the initial component. Three out of four items of the Sleep Environment scale loaded together in one factor, except for the item "I fall asleep in a room that feels too hot or too cold" which loaded higher in other factors. The Daytime scale had only one item which consisted the fifth component of the table. Three out of four items of the Sleep Stability scale loaded together in one factor, except for the item "During the school week, I "sleep in" >1 hour past my usual wake time" which loaded higher in other factors. The last scale of Bed/Bedroom Sharing was extracted in one factor with the last item showing a negative load which indicated reverse item.

Convergent validity

To prove convergent validity, Spearman's correlation coefficients were calculated between ASHS and ASQ scales. Positive but not strong correlations were found between these two tools. Strongest correlations were found between Emotional (ASHS) and Stress of Home Life (ASQ) (r_s = 0.461, p< 0.001) (Table 3).

Discussion

The aim of the present study to validate the ASHS was accomplished as confirmatory and reliability analyses were supportive of a valid tool, whileour findings were comparable with other studies that have used this measure (Galland *et al.*, 2017; de Bruin *et al.*, 2014; Alfiyah *et al.*, 2018). The main difference proposed in this

study is the item concerning caffeine to be moved to the Substance use scale.

In young people, a large percentage with symptoms of an anxiety disorder also have problematic sleep habits (Telzer *et al.*, 2014). One of the main lifestyle factors that affect adolescence is sleep, while adolescents tend to sleep late and want to stay up late, even on weekdays (Kirov *et al.*, 2017). The transition from childhood to adolescence affects a young person in many areas of life and to a great extent. Teenagers' feelings and the way they experience the changes in their life are more intense, therefore they experience the stress that these changes can bring to a greater degree. Research conducted in America has shown that adolescent sleep is also affected by the situation at home, such as stress and parental depression (Schmeer *et al.*, 2018). The same result was found in the present study where stress factors caused by living at home significantly affected sleep habits, *i.e.* it was found that as stress due to the teenager's home increases, so does poor sleep hygiene. Our results demonstrated a statistically significant correlation between stress and sleep quality in adolescents.

In conclusion, the Greek version of the ASHS constitutes a valid measure of the adolescent sleep hygiene, as the tool allows adolescents to report their own sleep-facilitating and sleep-inhibiting practices, adding to current knowledge and aiding future research in the field of adolescent health.

Key Points

- Sleep is one of the major lifestyle factors that affects adolescent physical and mental health.
- The Adolescent Sleep Hygiene Scale (ASHS) was validated in an adolescent sample living in Greece.
- ASHS is a reliable and valid tool for evaluating sleep-facilitating and sleep-inhibiting practices of Greek adolescents.

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Research Papers

A Biofeedback-Assisted Stress Management Program for Patients with Irritable Bowel Syndrome: a Randomised Controlled Trial

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Abstract

Irritable bowel syndrome (IBS) is a functional gastrointestinal disorder that affects the functionality and quality of life of the affected persons. There is a well-established detrimental reciprocal relationship between stress and IBS. In this randomised controlled trial, IBS patients were randomly assigned to an 8-week biofeedback-assisted stress management intervention group (n=24) or a control group (n=22). Psychometric measures were performed at baseline and following intervention to assess perceived stress, health locus of control and depressive symptoms. In patients of the intervention group, perceived stress and symptoms of depression were significantly decreased, while the sense of control over health was increased. The intervention program was beneficial to the health and quality of life of individuals with IBS. Future randomised controlled studies with larger samples and longer follow-up are required to establish the effectiveness of stress-management techniques in functional gastrointestinal disorders.

Introduction

Irritable Bowel Syndrome (IBS) is a chronic relapsing-remitting gastrointestinal disorder affecting 10-20% of the population worldwide (Camilleri and Choi, 1997). It is primarily characterised by abdominal pain and abdominal distension, bloating, feeling of incomplete emptying or urgency for defecation and alterations in bowel habits in the absence of structural abnormalities (Guthrie *et al.*, 2002 (Pellissier *et al.*, 2010). In general, although IBS is not a severe disease, it affects the functionality and quality of life of the affected persons (Nelessen *et al.*, 2013).

Possible risk factors for IBS are bacterial gastroenteritis, mucosal inflammation and qualitative or quantitative changes of the intestinal microflora (Tornblom *et al.*, 2007; Trabane *et al.*, 2007; Quigley *et al.*, 2013). Among the well-known triggering factors, stress constitutes a cardinal risk factor for both the IBS onset and relapse. More specifically, stressful life events tend to exacerbate IBS symptomatology in most patients, while traumatic life events (*i.e.* verbal, physical or sexual abuse) are positively correlated with high prevalence of IBS (Palsson and Whitehead, 2013). In addition, people with IBS are more likely to suffer from post-traumatic stress disorder (Drossman *et al.*, 1996) or other co-morbid psychiatric disorders, such as depression or generalised anxiety disorder (Palsson and Whitehead, 2013). People under chronic stress face severe IBS symptoms and have less chance of recovery compared to patients not exposed to stressful events (Bennett *et al.*, 1998). It is worth mentioning that both acute and chronic stress is related to poor adjustment to IBS, showing for example poor compliance to suggested medications (Zernicke *et al.*, 2012). Finally, at least

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50% of patients describe depressive symptoms and anxiety, and very often the symptoms can be the result of somatisation and expression of their negative stress (Chang *et al.*, 2011).

IBS is considered as a biopsychosocial disorder (Chang, 2011). The role of brain-gut interactions in the pathogenesis of IBS has been underlined since research has discovered the broad bidirectional communication network between them, known as brain-gut axis (Shah *et al.*, 2020). Sympathetic and parasympathetic pathways of the central nervous system (CNS) interact with enteric nervous system (ENS), regulating the gastrointestinal tract. Both hypothalamus-pituitary axis (HPA) and autonomic nervous system (ANS) over-activity have been recognised to exacerbate IBS symptoms, attesting the mediating role of stress-related neuroendocrine mechanisms on IBS pathophysiology (North *et al.*, 2004). Although few studies have been published on endocrine abnormalities in IBS patients, it has been shown by several studies that alterations in autonomic function can prompt visceral hypersensitivity and changes in gastrointestinal motility (Dobbin *et al.*, 2013; Elsenbruch and Orr, 2001). More specifically, the stress-induced activation of the sympathetic autonomic system signals an increased secretion of catecholamines (*i.e.* epinephrine and norepinephrine) which affects sympathovagal balance and gut homeostasis via neural connections of the brain-gut axis (Brzozowski *et al.*, 2016).

IBS is a benign disease which has been linked to impaired quality of life and high healthcare costs. However, it lacks trustworthy therapeutic options (Lee and Park, 2014). Given that pharmacologic approaches tend to address mainly symptom control, many patients are particularly reluctant to receive symptom alleviating drugs, preferring alternative non-pharmaceutical therapies such as cognitive behavioural therapy, psychotherapy, or even hypnotism (Drossman *et al.*, 2009). Interestingly, such interventions have been showed to be more efficient in reducing IBS than drug therapy (Zernicke *et al.*, 2012). Research has provided evidence regarding the effectiveness of stress management, mindfulness, progressive muscle relaxation, autogenic training and biofeedback training for the improvement of IBS symptoms, quality of life, body pain and overall physical and mental health among IBS patients (Kearney *et al.*, 2011; Heymann-Monnikes et al, 2000; Shinozaki *et al.*, 2010; Patcharatrakul and Gonlachanvit, 2011). Biofeedback training in particular is thought to restore sympathovagal balance leading to symptom improvement (Sowder *et al.*, 2010). Several studies have used biofeedback signals (*e.g.* EMG, HRV, thermal biofeedback etc.) as non-specific relaxation methods in order to alleviate the effects of stress in people with IBS (Blanchard and Schwarz, 1987; Dobbin *et al.*, 2013; Whitehead, 1992). The goal of biofeedback training, in general, is to help patients gain control over biological functions and reactions that are usually unaware of, so that they can self-regulate, decrease sympathetic activity and optimise their health (Chiarioni and Whitehead, 2008).

The aim of this study was to investigate the effect of a biofeedback-assisted stress management program consisting of relaxation breathing (RB) and progressive muscle relaxation (PMR) on physical symptoms and mental health, namely stress and depressive symptoms and health locus of control (HLC), of patients suffering from IBS.

Materials, Methodologies and Techniques

Study design

This was a two-armed, parallel group, non-blinded, randomised clinical trial, using balanced (1:1) groups (intervention vs. control). The study was conducted at the outpatient gastroenterology clinic of 417 Army Share Fund Hospital in Athens, over a period of 8 months. The study protocol was approved by the hospital's Scientific and Ethics Committee and was consistent with the declaration of Helsinki. Patients were informed precisely by the researcher about the study objectives and procedures and were enrolled in the study only after providing written informed consent.

Participants

The inclusion criteria were: age 18 to 65 years, diagnosis of IBS according to the diagnostic criteria of Rome III, Greek nationality, residency in Athens, and literacy of Greek language. Exclusion criteria were: psychiatric co-morbidity (*i.e.* major depression, psychosis or drug abuse), metastasis or autoimmune disease, systematic corticosteroid intake, previous participation in any study related to stress management, and inability to read or write in the Greek language.

Randomisation

All outpatients who presented at the gastroenterology clinic and met the study inclusion criteria were randomised into two groups, the control group or the intervention group, based on random numbers generated by an online random generator[1].

Intervention

All participants were given written and verbal information about stress and its effect on the onset of symptoms of IBS and quality of life. Psychometric measurements were administered to the participants before the initiation and after the end of the 8-week period. During this period, patients in the intervention group attended five sessions (one every 15 days). Similarly, patients in the control group were contacted every 15 days by the researcher via telephone and asked about their symptoms, mood state and stress. Individuals in the intervention group were administered a CD with instructions for RB and PMR and were instructed to practice them twice per day for 8 weeks. Progressive muscle relaxation is a simple

[1]www.random.org

technique, during which patients are guided to throb and progressively relax major muscle groups, starting from the toes up to the facial muscles. This technique was formulated by Jacobson in 1938 and has since proven to significantly reduce stress in healthy subjects and in patients with various diseases (Varvogli and Darviri, 2011). The same patients received biofeedback-assisted stress management training for 15 minutes in every session, focusing mainly on RB. For this purpose, the Nexus-4®a certified by the European Union medical device was used. This is a portable device used to train the patient to monitor the physical reactions (such as respiration rate, quality of a single breath, heart rate and heart rate variability with breathing) in conditions of stress and relaxation, as well as to familiarise the person with stress management techniques by observing the aforementioned physical parameters. After the completion of two months, the control group received the CD with the progressive muscle relaxation and a training session in biofeedback.

Baseline and Outcome Measures

Socio-demographic and anthropometric variables. Participants were asked about their age, gender, marital status, parenthood, educational level, smoking habits, height, and weight.

Health locus of control (HLC). The Health Locus of Control, on a theoretical level, describes the belief that one's health depends on internal factors, namely, their own behaviour (internal control center for health) versus other factors such as luck (external control center for health). It is supported by previous research that patients with a chronic disease have a less internal and more external locus of control than healthy adults (Hobbis *et al.*, 2003). The questionnaire consists of 18 formulations (Wallston *et al.* 1978). Each person is required to answer to what extent he/she agrees with each of these formulations based on a 6-point Likert-type scale (1=strongly disagree, 6=strongly agree). It consists of three subscales, "internal HLC" (HLC1), "external HLC" (HLC2), and "chance HLC" (HLC3). Internal HLC (HLC1) measures the degree to which a person believes to be responsible for his/her health. External HLC (HLC2) measures how much a person believes that other people are responsible for his/her health. And finally, chance HLC (HLC3) represents the extent to which chance determines health. Summing up the responses, for each subscale the score ranged from 6 to 36 points. Higher scores indicate higher strength of each type of faith for health. The instrument has been validated for the Greek population (Varvogli *et al.*, 2011). The internal validity for each subscale was found to be satisfactory for both the initial and final measurements (Cronbach's alpha: original, HLC1 0.687, HLC2 0.682, and HLC3 0.62, and final, HLC1 0.69, HLC2 0.69, and HLC3 0.56).

Perceived Stress Scale (PSS-14). The Greek Version of PSS was used to evaluate the extent to which people perceive certain situations in life as stressful (Cohen *et al.*, 1983). The questionnaire rates the frequency of feelings and thoughts during the previous month on a 5-point scale Likert-type (from 0 =never to 4= very often). There are seven positive and seven negative items. Scoring is from 0-56, and higher values indicate that the person felt particularly stressed in the previous month. The questionnaire was validated in the Greek language and good psychometric properties were recorded (Andreou *et al.*, 2011). Internal consistency was excellent for both the initial and final measurements (Cronbach's alpha 0.9 and 0.911, respectively).

Beck Depression Inventory (BDI). Depressive symptoms were measured using the Greek version of BDI which consists of 21 items, which describe specific symptoms (sadness, pessimism, sense of failure, loss of satisfaction, guilt, feelings of punishment, crying, irritability, social withdrawal, loss of libido etc.) and together assess the severity of depressive symptomatology (Beck *et al.*, 1961). The score ranges from 0 to 62 with higher scores indicating patients with more depressive symptoms. The questionnaire has been validated in the Greek language and good psychometric properties were recorded (Donias and Demertzis, 1983). Internal consistency was very good for both the initial and final measurements (Cronbach's alpha 0.85 and 0.834 respectively).

Self-reported Irritable Bowel Syndrome Questionnaire (SIBSQ). IBS symptoms were assessed using SIBSQ (Endo *et al.*, 2000). The questionnaire includes 14 questions related to abdominal pain, discomfort, frequency of defecation, feeling of incomplete defecation, bloating, feeling of urgent defecation, concern for bowel symptoms and the effect of stress and the meals in the symptoms of the syndrome. The rating scale is based on seven-point scale Likert (1= not at all, 7=severe symptoms present). The questionnaire has not been validated in the Greek language; however, it was translated with the permission given by the authors. Internal consistency was very good to excellent for both the initial and final measurements (Cronbach's alpha 0.847 and 0.901, respectively).

Statistical Methods

Interval variables were presented with medians and ranges (minimum and maximum) and categorical with absolute and proportional values. Between-group comparisons were performed with the use of non-parametric Mann-Whitney U-test test for two independent samples and the Pearson's exact chi-square. Then, the effect of the intervention on dependent variables such as perceived stress (PSS), health locus of control (HLC) and symptoms of the syndrome (IBS), was studied by the differences between the two groups (scores after minus scores before intervention). Effect size for each comparison was calculated according to the formula: $r = Z/N^{0,5}$ (Z is derived from the Mann-Whitney test and N is the number of patients in our sample). Cut-offs for this effect size were: 0.5, 0.3 and 0.1 for strong, medium and small effect. The level of significance was

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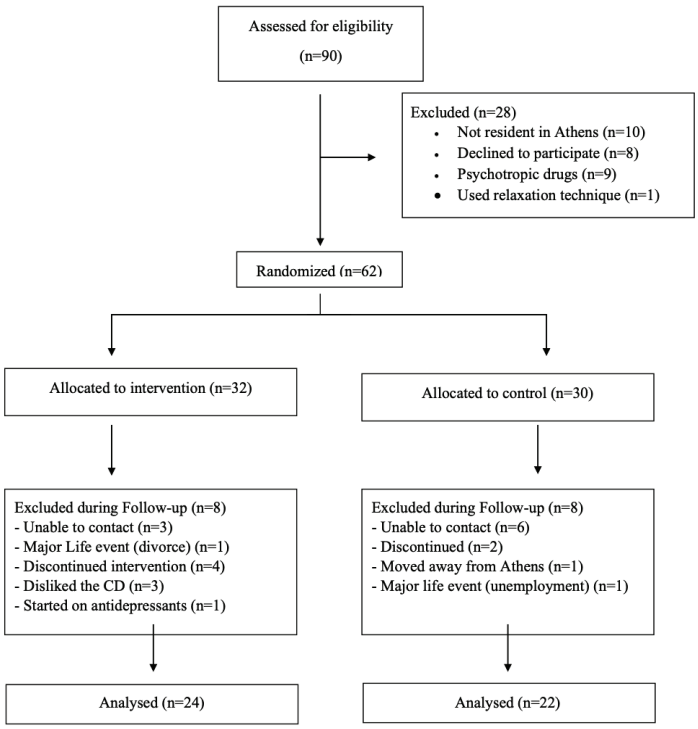

Figure 1. Flowchart of study participants.

set at p<0.05 for all analyses. Statistical calculations were performed using SPSS for Windows (version 20.0) statistical software (SPSS Inc., Chicago, IL, USA).

Results

The flow diagram of the study is illustrated in Figure 1.

Initially, 90 people were assessed for eligibility, of which 62 entered the process of randomisation, as 8 people refused to participate stating that they did not feel stressed, or did not have time for appointments, or their family did not agree to participate. The remaining 20 subjects were not included according to the exclusion criteria of the study. Specifically, 10 subjects were not residents of Athens, nine were using antidepressants and one subject applied other relaxation techniques such as dance therapy and yoga. Of the 62 people, 32 were randomised to the intervention group and 30 in the control group. During the follow up period, three individuals from the control group and 6 from the intervention group were noted as drop-outs because the researcher was unable to contact them. In addition, three people from the intervention group abandoned the technique because they were not fond of the procedure. One participant of the control group received antidepressants, while a person in the control group relocated away from Athens. Finally, a person in the intervention group got divorced and one person in the control group lost his job. Those two events are major stressful life events, so these individuals were excluded from the analysis. Finally, a total of 46 patients (22 controls and 24 subjects in the intervention group) completed the study and their results were analysed.

Baseline Analyses

The baseline characteristics of the two groups are presented in Table 1.

According to the results most participants were middle-aged women, married with children, non-smokers, with an average of 16 years of education. The median Body Mass Index (BMI) was higher than 26. There were no significant baseline differences between the two study groups (p> 0.05)

Primary Endpoint Analyses

Adjusted mean differences, standard deviations, p values, and effect sizes for the intervention group versus the control group for each primary outcome are presented in Table 2.

According to the results, in the intervention group there was a significant (p <0.001) reduction of perceived stress (mean difference ± SD: -6.16 ± 4.30) compared to the control group (mean difference ± SD: 0.50 ± 3.59). According to effect size (0.676), we conclude that the stress management program had a large effect on perceived stress of the patients. Similarly, there was a reduction of symptoms of depression. Finally, the score of symptoms of the syndrome decreased significantly after the intervention for subjects who applied the techniques (difference score = -18.08 ± 8.42), while the control's group score increased (difference score = 2.68 ± 7.03). The effect size large (0.840), therefore the effect of intervention in symptoms is significant. Additionally, significant variation was observed in the assessment of the control center for health in the control group, as individuals increased the internal control center (difference score = 2.83 ± 2.80) and reduced the external

Table 1. Baseline socio-demographic and disease-related characteristics of study participants.

Main baseline data	Intervention group (24)	Control group (22)	p - value
Median Age(range)	49 (24-76)	48.5 (24-85)	0.849
Sex			0.746
-Women	18 (75%)	15 (68.2%)	
-Men	6 (25%)	7 (31.8%)	
Maternal Status			0.72
-Married	15 (62.5%)	13 (59.1%)	
-Single	8 (33.3%)	6 (27.3)	
-Divorced	1 (4.2%)	1 (4.5%)	
Smoking Habits			0.354
-Non-smokers	13 (54.2%)	12 (54.5%)	
-Smokers	4 (16.7%)	7 (31.8%)	
-Former	7 (29.2%)	3 (13.6%)	
Children			0.763
-Yes	15 (62.5%)	15 (68.2%)	
-No	9 (37.5%)	7 (31.8%)	
Median BMI (range)	26.44 (19.53-32.87)	26.92 (20.70-33.64)	0.277
Median Education age (range)	16 (12-22)	16 (12-18)	0.063
Median PSS score (range)	29.5 (6-54)	27 (9-35)	0.311
Median HLC1 (range)	28 (18-36)	27 (15-34)	0.139
Median HLC2 (range)	25 (11-34)	25.5 (9-35)	0.935
Median HLC3 (range)	17.5 (7-34)	15.5 (7-29)	0.414
Median BDI score (range)	11.5 (0-37)	9 (0-27)	0.537
Median IBS score (range)	44.5 (19- 68)	45 (17-69)	0.952

PSS= Perceived Stress Scale, HLC= Health Locus of Control (1= internal, 2= external, 3= chance), BDI= Beck Depression Inventory, IBS.S = Irritable Bowel Syndrome Symptoms, BMI = Body Mass Index (weight/ height2). Tested by the Fisher's Exact Test chi-square and non-parametric Mann–Whitney U-test. p<0.05.

Table 2. Adjusted mean changes of primary outcomes (PSS, BDI, IBS.S) by study group before and after the intervention and effect sizes during the study.

Main baseline data (mean ± SD)	Intervention group (24)	Control group (22)	p - value	Effect size
ΔPSS_score	-6.16±4.30	0.50±3.59	<0.001	0.676
ΔBDI_score	-3.75±3.60	0.22±1.50	<0.001	0.687
ΔIBS.S_score	-18.08±8.42	2.68±7.03	<0.001	0.840
ΔHLC1	2.83±2.80	0.86±1.48	0.007	0.394
ΔHLC2	-2.12±2.77	0±2.20	<0.001	0.515
ΔHLC3	-2.45±2.39	-0.27±1.35	<0.001	0.629
ΔBMI	-0.48±0.71	0.11±0.31	<0.001	0.531

Notes: PSS= Perceived Stress Scale, BDI= Beck Depression Inventory, IBS.S = Irritable Bowel Syndrome Symptoms, HLC = Health Locus of Control (1= internal, 2= external, 3= chance), BMI= weight/ height2. Tested by the non-parametric Mann–Whitney U-test. p<0.05.

(difference score = -2.12 ± 2.77) and luck (difference score =-2.45 ± 2.39). The difference in the score after the end of the intervention between the two groups is significant, while the effect of the intervention is strong for the external control center and the center of chance, and moderate for the internal health control. Regarding body mass index this significantly decreased in the intervention group compared with the control group (p <0.001).

Discussion

It is obvious that irritable bowel syndrome is a complex disorder that negatively affects the quality of life and the functionality of patients. The exposure of individuals to chronic or acute stress constitutes a possible risk factor for the syndrome. We conducted this randomised controlled study to assess stress management treatment comprising of an 8-week program, which included training of the participants in relaxing themselves using biofeedback method, discussion of issues related to stress and application of progressive muscle relaxation at home, in a group of patients with irritable bowel syndrome. According to the results of the study, the two groups of the study did not differ on key factors such as age, sex, smoking habits, level of education and the levels of stress, depression, and symptoms of syndromes at the beginning of intervention. After 8 weeks, there was a significant reduction in perceived stress, depressive and irritable bowel syndrome symptomatology in the intervention group. Total scores of these variables differed significantly from the corresponding scores of the control group, while the degree of impact of the intervention on each parameter was strong.

Our results are consistent with previous results showing improvement of symptoms and quality of life in patients receiving a stress management program focused on coping with stress and self-improvement techniques along with drug therapy (Heymann- Monnikes *et al.*, 2000). As reported by studies using cognitive therapy, the levels of stress and depression of our intervention group were reduced, while IBS was improved (Deechakawan *et al.*, 2011; Ljotsson *et al.*, 2011). In a less complex intervention, administration of autogenic training in 21 IBS patients resulted in an additional amelioration of body pain and overall improvement of both physical and mental health (Shonozaki *et al.*, 2010). Similar results have been obtained by using different stress management techniques, such as meditation and mindfulness Relaxation Response Meditation (RRM) (Kearny *et al.*, 2011; Keefer *et al.*, 2002; Asare *et al.*, 2012). With regard to health locus of control (HLC), it has been supported that high levels of external HLC may be a partial mediator of the stress-illness relationship because of the more passive coping strategies enforced by individuals (Artemiadis *et al.*, 2012; Hutner and Locke, 1984). Our study provides further evidence on the reciprocal relationship between control attributions and development and/or exacerbation of IBS (Koloski *et*

al., 2006). Additionally, other studies have highlighted the efficacy of progressive muscular relaxation on the development of a strong internal locus of control (Pawlow and Jones, 2005).

Concerning biofeedback, our results are in line with the results of previous studies using the particular method to relieve patients for IBS symptoms (Leahy *et al.*, 1998; Dobbin et al, 2013; Tremback *et al.*, 2009). However, since no other study has used the exact same combination of relaxation techniques and assessment tools, it is quite precarious to compare these findings to other research.

The association between stress and IBS has been attested by many studies proposing diverse biological pathways (Chang *et al.*, 2011). It is clear, however, that relaxation techniques can have positive effects in the management of IBS. Based on this, we can cautiously conclude that reduction of stress can improve symptoms of the IBS, however we have not found studies to prove the physiological mechanism that explains it. Additionally, it is well known that at least 50 % of patients describe depressive symptoms and stress, IBS is therefore a disorder that is related to the psychology of the individual. In a studyconducted by North and his colleagues in 2004, 25% of women included in the study and a further 5% had somatisation that led to many gastrointestinal and other symptoms. Hence, another interpretation can be based on the effect of the benefits of relaxation techniques to the psychology of individuals (Lakhan *et al.*, 2013).

This study has some limitations. First, our primary outcome measures were based on self-administered self-reports expressing a subjective view of the IBS symptoms as opposed to objective clinical and/or laboratory assessments. Furthermore, there are no validated or clinically meaningful cut-offs for our primary outcomes. Therefore, the translation of our results to everyday clinical practice is impaired. Finally, the small sample size and short duration of the intervention program and follow-up could have influenced the results.

In conclusion, we found that the application of an 8-week stress management program with biofeedback training and other relaxation techniques improved significantly important health and quality of life indicators of individuals with IBS. Namely, it alleviated stress, depressive symptoms and IBS symptoms, and reduced externalising problems in the intervention group. Future randomised controlled studies with larger samples and longer follow-up are required to establish the effectiveness of stress-management techniques in functional gastrointestinal disorders.

Key Points

- There is a well-established reciprocal relationship between stress and irritable bowel syndrome (IBS).
- 46 IBS patients were randomly assigned to an 8-week biofeedback-assisted stress management intervention group or a control group.
- In patients of the intervention group, perceived stress and symptoms of depression were significantly alleviated, while the sense of control over health was increased.

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