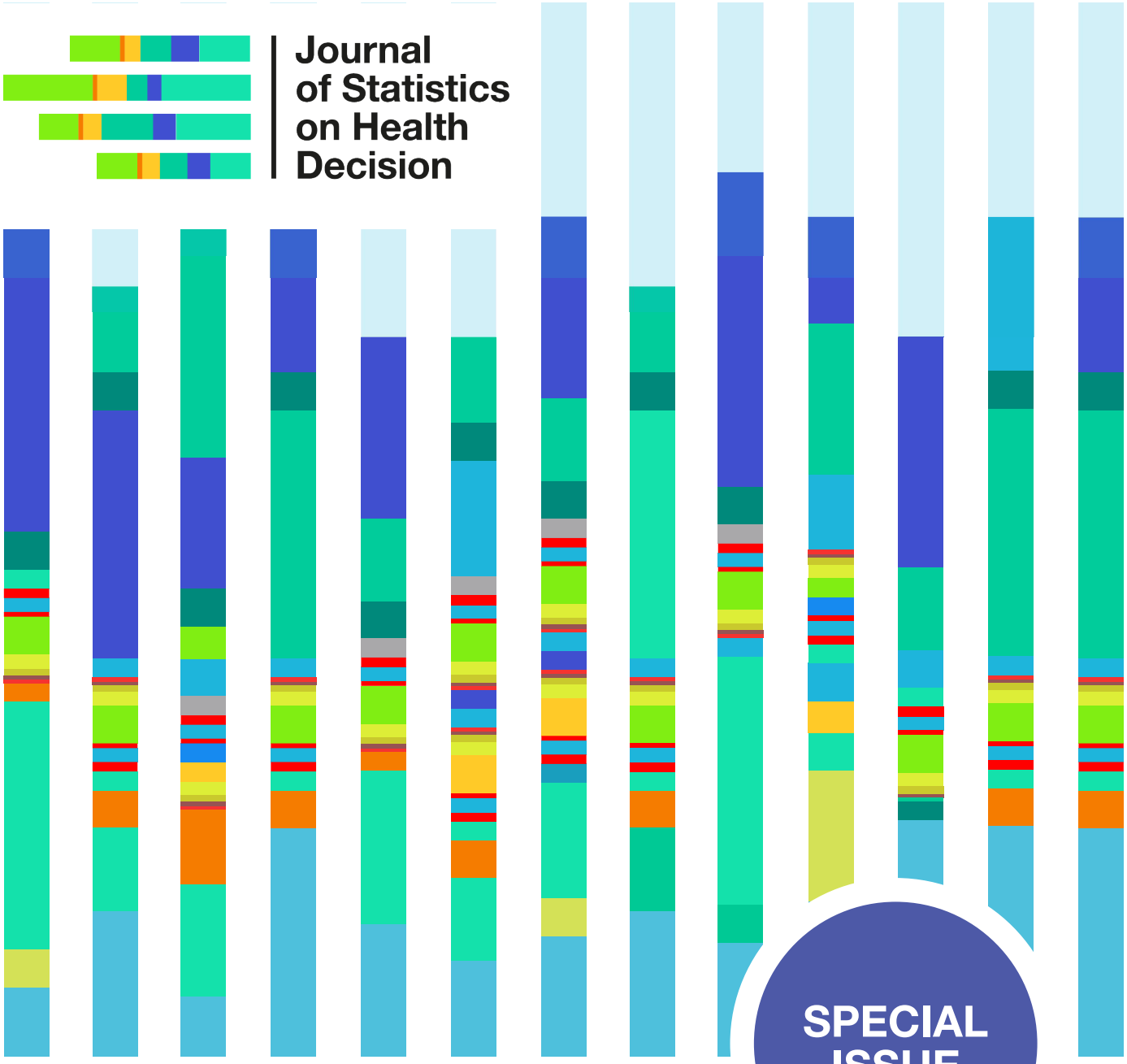
Journal of Statistics on Health Decision



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EXTENDED ABSTRACT

Analysis of the pattern of Oral and Maxillofacial Trauma in the world: A Systematic Review and Meta-Analysis

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Introduction

Trauma is defined as an unexpected event beyond the victim's control, constituting one of the greatest health concerns worldwide [1-22]. In the event of a traumatic situation, this can culminate in the full recovery, in the presence of a temporary injury or a sequelae [23, 24].

These lesions can occur in any part of the body, and in this case, their focus will be at the oral maxillofacial level, following the classification of Andreasen for the teeth [25, 26].

Oral maxillofacial trauma represents between 7.4 to 8.7% of medical emergencies, both in developed and developing countries [27-29]. Their causes differ from country to country, depending on culture, socioeconomic level, and environmental factors [3-5, 12, 30-53], the main causes being road accidents, falls and aggression.

Understanding the epidemiology of oral and maxillofacial trauma is essential to shape public health policy and adequate better tables for disabilities evaluation. Therefore, the aim of this study was to investigate the epidemiological characteristics of oral maxillofacial trauma, namely to analyze the following features:

- Probabilities of attaining each type of oral and maxillofacial trauma by etiology.
- Descriptive statistics on age and sex distribution within the different types of oral and maxillofacial traumas.
- Association between oral and maxillofacial trauma type, sequelae's, etiology, age and gender.

Methods

Protocol and registration

In carrying out this systematic review, the guidelines of the PRISMA recommendations (Preferred Reporting Items for Systematic Reviews and Meta-analyses) were followed. The protocol was registered in the PROSPERO database (International Prospective Register of Systematic Review).

Information sources and search strategy

In this study, the following databases were searched: PubMed/MEDLINE and SCOPUS between the years 2010 and 2020 with Mandarin language restriction. This study included individuals aged 21 years or older who had trauma in the oral maxillofacial region. Moreover, no restriction regarding the type of study (retrospective or prospective) were considered. Letters to the editor and studies on subjects that have injuries caused by military service were excluded.

The Medical Subject Headings (MeSH) terms selected for the purposes of this search included 'oral maxillofacial', 'trauma', 'accident' and 'injuries', and include all possible combinations.

Subsequently, we used the PICO framework, Population (adults with oral maxillofacial injuries), Exposure (etiology of oral maxillofacial trauma), Comparison (different countries on different emergency services) and Outcome (association between etiology, age, sex and type of trauma).

Quality of the studies

The Joanna Briggs Institute Checklist for Prevalence Studies was used to assess the risk of bias in all identified and collected full text articles included in this study. Moreover, GRADE (Grading of Recommendations, Assessment, Development, and Evaluation) method was applied to assess the quality of the

Keywords:
Accidents; Epidemiology; Injuries; Oro-maxillofacial; Trauma

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evidence. After confirming the quality of each study, 2 authors independently extracted the data to the pre-specified data extraction sheet in Microsoft Excel.

Results

The review search process yielded 404 articles. Of these, 16 were duplicated. Therefore, 388 articles were screened by titles and abstracts evaluation, 5 due to discrepancies in the results, and only 78 articles were included (Figure 1).

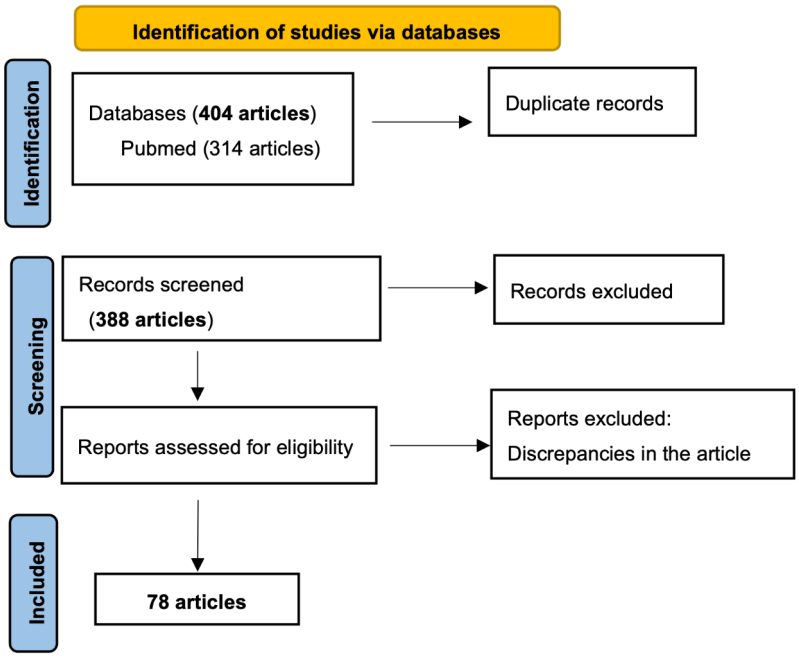

Figure 1 - Prisma flow diagram (studies included).

Dental injuries were reported in 26 studies, fractures were described in 67 and only 31 articles present information on soft tissue injury.

Through the random effects model, it was concluded that the main cause of trauma was road traffic accidents with a prevalence of 55.37%, followed by assault with 17.56% and falls with 10.21% (Fig. 2).

By performing a meta-regression, it was possible to establish an association between assaults and males at Africa (p-value <0.001). Falls increase with age and usually occur in women and in the European and Muslin countries (p-value <0.001). The frequency of road traffic accidents is higher in Asia (p-value between 0.01 and 0.05) and lower in Europe.

The most frequent type of injuries is fractures with a prevalence of 84.30% (Fig. 3), followed by soft tissues injuries, 52.11%. Dental injuries represent 25.41% and a statistical association has been made between these injuries, young ages and Europe and Asia (p-value <0.001).

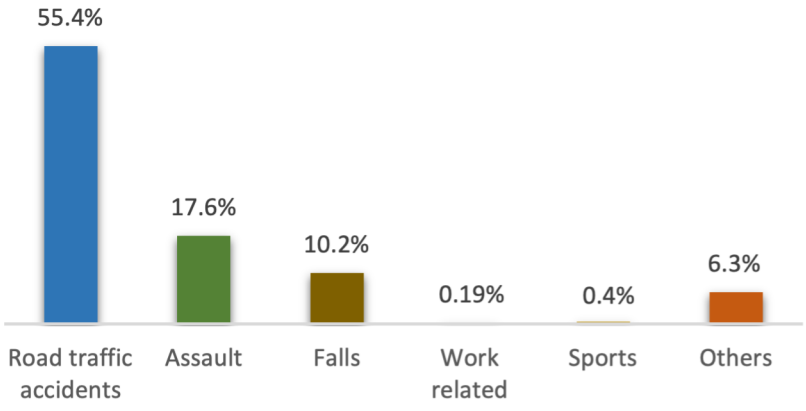

Figure 2 - Etiology of trauma

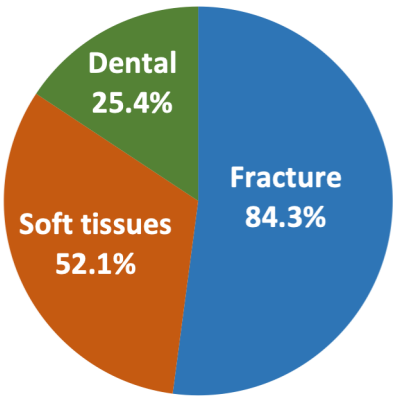

Figure 3 - Types of trauma

Discussion:

The main etiology differs from country to country, being influenced by culture, social environment and laws. The results regarding the road traffic accidents being the most frequent cause of trauma corroborate the literature [15, 54-59]. This findings can be explained by the lack of safety measures or negligence in complying with them, the poor quality of the roads and aggressive driving [15, 54, 56-59].

Assault is more usual [56, 59] in the European and Latin America countries, while the falls are more frequent in Europe [57, 59].

The systematic reviews of Al Qahtani et al. [56, 57] and Boffano et al. [15] show that falls are more frequent in elderly people and Chrcanovic [59] reveal that females are more likely to fall. These studies are in agreement with the obtained results.

Despite the fact of the male/female ratio between the studies being quite discrepant, we can observe a higher number of males, which is corroborated by several authors [55-59].

As for the type of injury, the prevalence of fractures is significant [56-59], although few systematic reviews address the different types of injuries.

Our study has some limitations, one of them is the high heterogeneity, which can be explained by the different sample sizes and the fact that the majority of the studies are observational.

Conclusion:

Based on the results of our review, it was concluded that road traffic accidents are the main etiology of oral maxillofacial trauma and special attention should be given to Asia, which presented the highest prevalence. Assault is also a main cause of trauma, being more frequent in males, while falls were more evident in European countries, females and with aging.

Regarding the type of trauma, fractures were the main type and dental injuries are frequent seen in young people and Europa/Asia.

Ethics committee and informed consent:

Study performed was approved and realized in accordance with the ethical standards specified by the Health Ethics Committee of the Faculty of Dental Medicine, University of Lisbon, Lisbon, Portugal

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EXTENDED ABSTRACT

Epidemiological pattern and etiology of Oral and Maxillofacial Trauma: A Retrospective Study among Patients from a Portuguese Central Hospital

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Introduction

The human being as a whole encompasses four fundamental aspects: function, organism, psychological facet, and social interaction. Whenever one of these aspects is affected, bodily harm occurs. There are several types of trauma, where the most common are those caused by physical injuries, constituting one of the major health concerns worldwide[1-22]. Their causes differ from country to country [3,4,6,12,23-46], with the main causes being traffic accidents, falls and assault.

Therefore, the present study aims to evaluate in the form of an observational retrospective clinical study, the etiology and types of oral and maxillofacial injuries in Portugal.

Methods

An observational retrospective study was conducted in the Stomatology Service at the "Centro Hospitalar Lisboa Norte" (CHLN), covering the period from 2018 to 2020. The target population were patients aged 21 years or over, who presented oral and maxillofacial injuries. The charts of all patients were reviewed, and the data was compiled using Excel. Subsequently, data were transferred and analyzed using the Statistical Package for the Social Sciences (SPSS), version 27.

Results

384 patients were included in this study, 49.48% females and 50.52% males. The year 2018 had 188 patients with trauma, 2019 with 175 and 2020 with 81 (Table 1). The most frequent cause of maxillofacial injuries was falls, which accounted for 44.3% (170 patients), followed by assault (24.7%, 95 patients) (Figure 1). Falls are more frequent in women (60.4%), whereas men suffered more from assault (33.5%). There is also an association between the etiology and age (p-value < 0.001; contingency coefficient = 0.526), the younger individuals present more assaults, while with increasing age there are more falls.

Of the 384 patients, 314 have soft tissues injuries, 57 present bone fractures, 192 have periodontal injuries, 176 with dental injuries and only 5 have neurological ones. The bone fractures are frequent in the mandibular region (20 patients) and Figure 2 shows the bone fracture distribution. Uncomplicated crown fractures were the main type of dental injuries in the upper incisors.

Regarding the type of treatment performed was surgical in 218 patients, dental in 79, conservative in 210 and pharmacological in 278 patients. The most frequent pharmacological treatment was prescription of painkillers.

Table 2 – Sex distribution according to decades of age and year

Year/Age	21-29	30-39	40-49	50-59	60-69	70-79	80-89	90-93	Total
2018	35	26	19	13	20	8	6	1	128
2019	37	43	42	11	21	13	8	0	175
2020	27	16	17	6	9	4	2	0	81
Total	99	85	78	30	50	25	16	1	384

Keywords:
Oral and maxillofacial trauma;
Oral and maxillofacial injuries;
Retrospective Study.

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Conflict of interest:
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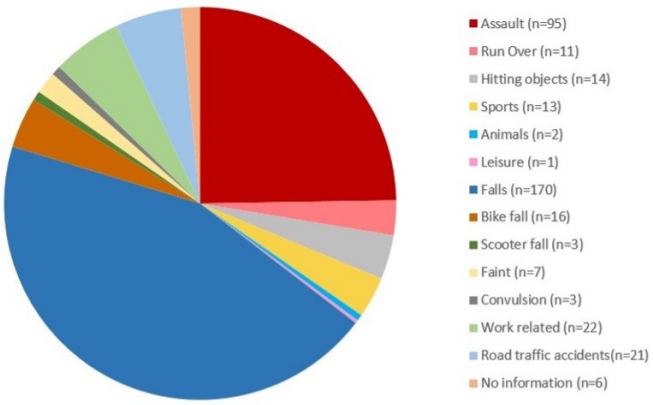

Figure 1 - Distribution of the etiology of trauma

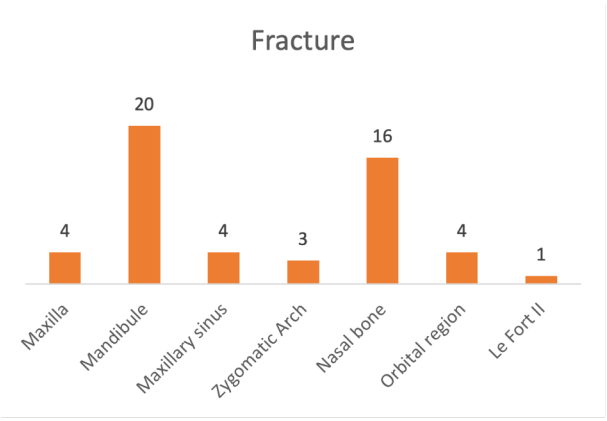

Figure 2 - Distribution of the fractures

Discussion

The year 2020 has a lower number of traumas, which is in agreement with the current pandemic situation [47,48,49] because people spend more time at home. Falls, that in the present study were considered as the most prevalent etiology are only described as such in the studies by Mahmoodi et al. [7], Brucoli et al. [50] and Toivari et al. [51]. The high probability of occurrence of these types of injury etiology in women, as well as with increasing age, is supported by some authors [50,52-54].

Most studies carried out in European countries show a trend in assault, which has become the main cause in recent years [16,23,30,48,49,55]. As mentioned in the systematic review by Barbosa et al. [56], road traffic accidents have been decreasing in Portugal since 1994, when road safety rules were implemented. Regarding the type of injuries, it is worth noting the lack of European studies that treat soft tissue and dental injuries, as most focus only on studying fractures and their treatments.

Most articles indicate the mandible as the main site of fractures [13,15,51,53,57-60], which is in agreement with our results. The difference between the occurrence of fractures in the mandible and nasal bone is minimal. The peculiar shape, location, mobility, presence of unerupted 3rd molars and lesser bone support compared to the maxilla are some of the factors that make the mandible susceptible to fracture. For the dental injuries, the upper central incisors are described as the most affected with fracture [61,62], being the uncomplicated crown fracture the most frequent [7].

As for the most performed type of treatment, pharmacological is the main, followed by surgical, conservative and finally dental. Some authors also mention that surgical treatments are more frequently performed than conservative ones [30,54]. This discrepancy may be related to cultural differences between the populations analyzed in each study, e.g. the fact that in Portugal the difference between sexes is not so pronounced. It should be noted that the sample under study does not translate statistical results extended to the Portuguese population, as it is a convenience sample, consisting of patients from the Centro Hospitalar Lisboa Norte. However, this is a Central Hospital from the capital of Portugal.

Conclusions

Falls were the most common cause of maxillofacial trauma, followed by assault.

Road traffic accidents have been decreasing over the years, probably due to strict road safety measures. Males and adults were more affected by assaults, while females and elderly people present a higher prevalence of falls.

The year 2020 shows an evident decrease in injuries compared to the remaining years due to the current pandemic situation. As for dental injuries, the upper incisors were frequently affected by uncomplicated crown fractures. The prescription of painkillers is the most used therapy, followed by surgical treatment.

Ethics committee and informed consent

Study performed was approved and realized in accordance with the ethical standards specified by the Health Ethics Committee of the Faculty of Dental Medicine, University of Lisbon, Lisbon, Portugal.

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Journal of Statistics on Health Decision

EXTENDED ABSTRACT

Purpose in life and caregiver burden in kidney failure: Preliminary results from a hierarchical multiple regression analysis

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Introduction:

Hemodialysis (HD) is the most common renal therapy for kidney failure; however, it is highly demanding due to inflexible treatment schedules, complex medical recommendations (e.g., dietary and fluid restrictions), and serious complications (e.g., cardiovascular and/or pulmonary disease, electrolyte imbalances, fatigue), all of which increase patients' dependence on family caregivers [1]. Therefore, caring for a family member on HD has been described as one of the most burdensome experiences, marked by adjustment struggles, social isolation, and psychological distress [2,3].

According to Pearlin's Stress Process Model [4], caregiver burden can be affected by caregiving stressors (e.g., caregiving daily demands) and caregiver's background/context (e.g., gender, kinship with the patient); nonetheless, resources like social support and/or coping, can buffer the impacts of caregiver stress and improve well-being [4,5]. Previous research has evidenced that purpose in life can help promote dementia caregivers' ability to regulate negative emotions, persevere despite obstacles, and increase engagement in self-care activities [6,7]. However, purpose in life as a psychological resource remains largely unexplored in the caregiving literature and, to the best of our knowledge, has not yet been examined in the context of HD caregiving demands.

This study aimed to explore the role of purpose in life in the caregiver burden of family members of patients undergoing HD, after accounting for social support and coping.

Methods:

A cross-sectional study was conducted with a convenience sample of family caregivers of patients undergoing HD. Participants completed an online assessment protocol with validated self-report measures to assess caregiver burden, social support, coping, and purpose in life (Table 1). A hierarchical multiple regression (HMR) analysis was performed to explore the role of purpose in life as a potential predictor of caregiver burden, after controlling for social support and coping. The set of predictors was entered in a sequence of two blocks; Block 1 contained social support and coping dimensions and Block 2 included purpose in life. To ascertain whether the HMR could be used and guarantee the validity of the results, some first-line tests were performed [12] (Supplementary Data 1). All statistics were computed using SPSS 28.0. Statistical significance was set at $p<0.05$.

Results:

The sample consisted of 77 family caregivers with a mean age of 60.4 years old (SD=13.3). Most were female (76.6%), married to the cared-for person (51.9%), and caring for less than four years (58.4%); 41.6% reported high levels of caregiver burden (Table 2). Pearson's R coefficients (Table 3) showed significant associations between caregiver burden and social support ($r=-0.249$, $p=0.029$), purpose in life ($r=-0.584$, $p<0.001$) and the following coping dimensions: positive reframing ($r=-0.317$, $p=0.005$), acceptance ($r=-0.289$, $p=0.011$), self-blame ($r=0.235$, $p=0.040$), and denial ($r=0.316$, $p=0.005$). Regarding the HMR analysis (Table 4), Model 1 with social support and the aforementioned coping dimensions predicted approximately 28.4% of the variance of caregiver burden ($R^2=0.284$, $F(5,71)=5.63$, $p<0.001$). After the inclusion of purpose in life, Model 2 explained an additional 14.4% ($\Delta R^2=0.144$) predicting approximately 42.8% of the variance of caregiver burden ($R^2=0.428$, $F(6,70)=8.73$, $p<0.001$). Purpose in life was the significant predictor with the highest contribution ($\beta=-0.493$, $p<0.001$).

Keywords:
Caregiver; Caregiver Burden; Chronic Kidney Disease; Dialysis; Hemodialysis; Kidney Failure; Multiple Regression; Renal Therapy; Purpose in Life

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Supplementary material:
SousaH_SuppMat.pdf

Conflict of interest:
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Table 1 - Self-report measures used to assess caregiver burden, social support, coping, and purpose in life.

Variables	Self-report measures	Brief description
Caregiver Burden	Zarit Burden Interview [8]	Scale composed of 22 items, considered a reference measure to assess caregiver burden. Each item is rated on a 5-point Likert scale (1 = never; 5 = almost always). The global score ranges from 22 to 110; higher scores correspond to higher levels of burden. Three benchmarks allow a better interpretation of caregiver burden levels: (i) scores below 46 = no burden; (ii) scores between 46-56 = mild burden; and (iii) scores above 56 = intense burden. In this study sample, this scale presented good psychometric qualities (α=0.89).
Social support	Medical Outcomes Study-Social Support Survey [9]	Questionnaire with 19 items that assesses the perception of social support rated on a 5-point Likert scale (1 = never; 5 = always). The scoring range is from 0 to 100, with a higher score indicating better perceived social support. In this study sample, this questionnaire showed excellent psychometric qualities (α=0.96).
Coping	Brief Cope [10]	Instrument composed of 28 items that evaluates the strategies that each individual adopts to deal with different life situations. Each item is rated on a 4-point Likert scale (0 = I never do that; 3 = I almost always do that) distributed over 14 subscales: use of instrumental support, use of emotional support, self-distraction, active coping, substance use, behavioral disengagement, venting, planning, humor, religion, positive reframing, self-blame, acceptance, and denial. There is no total score, since only a profile of the individual should be presented. In this study sample, this instrument has good psychometric qualities (α=0.78).
Purpose in life	Purpose in Life Test Revised [11]	A 20-item questionnaire that aims to assess the goals and ambitions that support a sense and purpose of personal life. Respondents rate each item on a 7-point Likert scale that is specifically designed for that item. The minimum score is 20 (lowest purpose) and the maximum is 140 (highest purpose). In this study sample, this questionnaire revealed good psychometric qualities (α=0.84).

Table 2 - Sociodemographic and caregiving characteristics of the study sample

Characteristics	Family caregivers (n = 77)
Gender	
Female, n (%)	59 (76.6)
Age (years old), M ± SD	60.4 ± 13.3
Kinship with the patients, n (%)	
Spouse (legally or otherwise)	40 (51.9)
Other (siblings and adult children)	37 (48.1)
Caregiving (years), M ± SD	
< 4	45 (58.4)
> 4	32 (41.6)
Classification of caregiver burden, n (%)	
No burden (<46)	22 (28.6)
Mild burden (46 – 56)	23 (29.9)
Intense burden (> 56)	32 (41.6)

Notes: M=mean; SD=standard deviation.

Table 3 - Pearson's R coefficients (and p-values) for the associations of caregiver burden (dependent variable) with social support, coping dimensions (positive reframing, self-blame, acceptance, and denial), and purpose in life (potential predictors).

	Caregiver burden
Social Support	-0.249* (0.029)
Positive reframing	-0.317* (0.005)
Self-blame	0.235* (0.040)
Acceptance	-0.289* (0.011)
Denial	0.316* (0.005)
Purpose in life	-0.584* (0.001)

Notes: * p<0.05. The remaining coping dimensions (self-distraction, active coping, substance use, use of emotional support, use of instrumental support, behavioral disengagement, venting, planning, humor, and religion), did not present statistically significant associations with caregiver burden and, therefore, were excluded from the HMR analysis. To consult all Pearson's R coefficients and p-values, see Supplementary Data 2.

Table 4 - Results from the HMR analysis.

		B	β	p-value
Model 1	Social support	-0.179	-0.226*	0.040
	Positive reframing	-4.634	-0.237	0.061
	Self-blame	8.144	0.211*	0.044
	Acceptance	-3.395	-0.142	0.263
	Denial	5.595	0.196	0.077
	R^2	0.284		
	$R^{2adjusted}$	0.233		
	F	5.63		
	p value	<0.001		
Model 1	Social support	-0.001	-0.002	0.988
	Positive reframing	-1.959	-0.100	0.394
	Self-blame	6.713	0.174	0.065
	Acceptance	-0.266	-0.011	0.925
	Denial	5.791	0.202*	0.043
	Purpose in life	-0.463	-0.493*	<0.001
	R^2	0.428		
	$R^{2adjusted}$	0.379		
	ΔR^2	0.144		
	F	8.73		
	p value	<0.001		

Notes: * p<0.05. β=beta coefficient; B=unstandardized coefficient; ΔR^2=the change in R^2 values from Model 1 to Model 2.

Discussion:

The results showed that the perception of purpose in life among family caregivers of patients on HD seems to have a protective role against burden, even after accounting for social support and several coping dimensions. This finding has crucial implications for the development of psychological interventions aimed at facilitating caregivers' adjustment to dialysis care demands, suggesting that purpose in life is a key target. Future studies are needed to better comprehend the benefits of integrating meaning-making strategies into these interventions, in order to maximize caregivers' understanding of their life priorities, pursuits, personal, family, and social roles, beyond (and including) caregiving demands [6,7]. This study also expands Pearlin's Stress Process Model [4,5] of caregiving by identifying purpose in life as an important psychological resource in the context of hemodialysis caregiving.

Limitations

This is a cross-sectional study with a small preliminary sample and, therefore, causal associations and interpretations should be made with caution.

Ethics committee and informed consent:

The current research was approved by an independent ethics committee (UICISA:E_669_05-2020) and subjects gave their informed consent before they were enrolled in the study.

Acknowledgments:

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Journal of Statistics on Health Decision

EXTENDED ABSTRACT

The COVID-19 impact on family caregivers' mental health in the Municipality of Aveiro

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Introduction:

Portugal had the first Covid case on March 2nd, 2022. In the following month, 81.087 new cases and 266 deaths were reported [1]. Directorate-General for Health (DGS) took some measures to control the pandemic, including social distancing, and other methods. Social distancing, adds to the disruption on Family Caregivers' (FCs) routines, challenging their abilities to adopt new procedures, reconciling them with the existing ones. This caused increased tension, distress, and overload to caregivers[2][3], which in turn may have affected caregiver's mental health, triggering feelings of loneliness, insomnia, anxiety, and depression.

In this context, social distancing associated with other existing factors, may have contributed to further weakening of caregivers' physical and mental health.

The purpose of this study is to identify the effects of social distancing on family caregivers' (of elderlies and/or dependent people) mental health resulting from the COVID-19 pandemic.

Methods:

A quantitative study was conducted, using a convenience sampling of 36 FC's, indicated by several Private Institutions of Social Solidarity (IPSS), in the Municipality of Aveiro, from June 2020, until March 2022.

Data collection was performed with a structured questionnaire, consisting of three parts: (i) the first part related to sociodemographic and clinical data, and the following two composed of scales (ii) Psychological Wellbeing Manifestation Measure Scale - EMMBEP (Psychological Wellbeing Scale) [4], with 25 items divided into 6 subscales: self-esteem, balance, social involvement, sociability, self and event control, and happiness; and (iii) the Reliability and Factor Structure of the 10-item Kessler Psychological Distress Scale [5], on a 5-point Likert scale.

Data analysis was performed using SPSS V 28. Descriptive statistics were used to describe sociodemographic and clinical characteristics of the sample, and inferential statistics were used to test the relationships between distress and well-being psychosocial variables. Pearson's Correlation Coefficient was used, given that normally distributed variables were verified.

Results:

Family caregiver's sociodemographic profile

Family caregivers' mean age observed (Table 1) is 60.03 (SD= 15.20), ranging from 28 to 85, 30 (83.3%) female and 6 (16.7%) male, mostly married, 20 (55.6%), and retired 15 (42.9%). Most caregivers are daughters 10 (27.8%), followed by husband/wife 8 (22.2%), or mother/father 7 (19.4%). Of this sample, 25 (69.4%) report that it is the first time they take care of someone (Table 1).

Clinical and Psychosocial Characterization

In this sample, during the period of social distancing, 10 felt sadness (27.8%), 12 fatigue, depression, and stress (33.3%), 14 fear (38.9%), 16 future uncertainty (44.4%), and 17 lack of socializing and being with the family (47.2%) (Table 2).

It should be noted that 8 FC (22.2%) were in confinement, infected with SARCOV 2, and positive for COVID 19.

Keywords:
Aged; Caregiver Burden; Covid-19; Elderly; Family Caregivers; Mental Health; Social DISTANCING

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Conflict of interest:
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Table 1 - Family caregiver's sociodemographic profile

Sociodemographic Characterization (N = 36)				
	Min	**Max**	**Mean**	**SD**
Age	28	85	60.03	15.20
			N	**%**
Sex	Male		6	16.7
	Female		30	83.3
Marital Status	Married		20	55.6
	Other marital state		16	44.4
Other characteristics	Retired		15	42.9
	Child caregiver		10	27.8
	Husband/wife caregiver		8	22.2
	Mother/father caregiver		7	19.4
	First time caregiver		27	75

Table 2 - Impacts caused by social distancing on family caregivers' mental health

Clinical and Psychosocial Characterization of the Sample (N = 36)		
Psychosocial Variables	**N**	**%**
Sadness	10	27.8
Fatigue/ Depression/ Stress	12	33.3
Fear	14	38.9
Future uncertainty	16	44.4
Lack of socializing and being with the family	17	47.2
Clinical Variables		
Had COVID-19	8	22.2

Table 3 - Distress and psychological well-being manifestation

Relation between distress and psychological well-being

	(N=32)	
	1	2
1. Distress	1	**-.365***
2. Well-being		1
M	22.16	93.91
DP	8.44	15.15

$^{**}p < .01$, $^{*}p < .05$

Distress and psychological well-being manifestation

Regarding the association between psychological well-being and distress (Table 3), evaluated through the EMMBEP scales, and the Psychological Distress Scale - Kessler (K10), it was found that distress is negatively correlated with well-being, r=- -.36, p = .028, thus, the greater the distress, the lower the psychological well-being.

Discussion:

The FC's sociodemographic profile agrees with other studies [6-7].

Social distancing (relevant for reducing the spread of the virus and reducing the number of COVID-19 cases and deaths) had implications on FCs' mental health [8].

COVID-19 pandemic led FCs to face numerous difficulties to conciliate existing routines with the new rules, particularly mandatory social distancing, increasing the current feeling of isolation, and add to the negative impact on their mental health.

The main distress symptoms manifested by the FCs were fear, loneliness, future uncertainty, stress, fatigue, depression, and sadness. Other studies reported, also, fear of being infected, fear of getting sick, and fear of having financial losses [9]. Thus, may have led to a decrease on psychological well-being perception [2].

It is, thus, considered that social distancing contributed to further weakening of FCs' mental health, compromising their health and psychological well-being.

This study has two main limitations, the reduced sample due to difficulties on study dissemination, and the focus on Aveiro's region. A larger and more comprehensive sample is needed to extrapolate results.

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EXTENDED ABSTRACT

Caregiver burden and family functioning – the moderating effect of educational level

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Introduction:

Demographic aging in Portugal continued to increase significantly, with the population aging index, an indicator that compares the population 65 or more years old over the population aged 0 to 14, being equal to 182 - this index was 128 in 2011 and 102 in 2001 (1). This fact not only puts pressure on the functioning of health and social support services but also on the definition of strategies that promote the quality of life of all those who deal daily with the consequences of an aging population, particularly in the informal caregiver's force (2). Informal caregivers are usually family, friends, or neighbors who provide assistance without financial remuneration (3), constituting the biggest pillar of long-term care in the European Union, despite the tenuous initiatives of public policies (4). Studying the factors that influence caregiver burden may lead to better intervention practices including from family nursing. The aim of this research was to study caregiver burden and family functioning, and explore possible moderation effects of personal factors.

Methods:

A cross-sectional study was conducted in the Aveiro region, Portugal. Recruitment occurred through primary care centers which invited potential participants. After the explanation of the aims and procedures of the study, the participants were informed about ethical and data protection aspects. Inclusion criteria were: (i) be an informal caregiver of an adult person, (ii) having 18 or more years old, and (iii) be fluent in Portuguese. Exclusion criteria was: (i) person cared for has undergone surgery for less than six months.

The caregiver burden was assessed through a self-reported instrument – Questionário de Avaliação da Sobrecarga do Cuidador Informal - QASCI (5), which consists of 32 items where higher values reflect a greater burden on the caregiver (range 32-160). Personal factors (sex, age, educational level, number of years as caregiver) were obtained directly from participants and the functional independence level (Barthel Index) of the person cared for was retrieved from digital clinical records. Family functioning was self-reported through the Family APGAR scale (6).

Data analysis was conducted via JASP, version 0.14.0 (7). Statistical significance was defined for α=0.5. Association analysis included Pearson correlation for continuous variables and independent t-test for assessing differences between means. Moderation effects were tested using linear regression by enter method, presenting under this work only those that were statistical significative.

Results:

Two hundred and twenty-four participants (female: n= 195, 87.1%) with a mean age of 61y10m±12y3m were included in the study - Table 1. The caregiver burden mean was 101.2±15.3. The mean for Barthel Index (functional independence) was 73.9±27.1.

Associations with caregiver burden were found for educational level ($r=-0.193$, $p<0.01$), number of years as a caregiver ($r=0.203$, $p<0.001$), functional independence level ($r=0.195$, $p<0.01$), and family functioning ($r=-0.234$, $p<0.001$), but not for other personal factors like age or sex.

In the first linear regression model using enter method included all the four variables that correlated with caregiver burden were statistical significative [ANOVA $F(4,219) = 8.64$, $p<0.001$] explaining 13.6% of the variance. Considering the interaction between family functioning and educational level on caregiver burden (Figure 1) the linear regression model by enter method showed a small improvement [ANOVA $F(5,218)=7.90$, $p<0.001$; $r^2=15.3\%$] for the explained variance (Table 2).

Keywords:
Caregiver burden, Personal factors, Family Health, Nursing

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Conflict of interest:
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Table 1 – Participants' characteristics

Variables	
Sex, n(%)	
Female	195 (87.1)
Male	29 (12.9)
Age, mean±sd	61y10m±12y3m
Education level, n(%)	
No formal education	16 (7.1)
Elementary school - 1st cycle, 4 years	108 (48.2)
Elementary school - 2nd or 3rd cycle, 6-9 years	58 (25.9)
Secondary, 12 years	30 (13.4)
University education	12 (5.4)
Years as caregiver, mean±sd	7y1m±6y7m

Table 2 – Regression models for caregiver burden

Model 1	**β**	**SE**	**p-value**
(Intercept)	101.491	3.890	<0.001
Family_apgar	-0.918	0.293	0.002
Years as Caregiver	0.327	0.148	0.028
Barthel Index	0.094	0.036	0.009
Educational level	-2.301	0.990	0.021
Model 2	**β**	**SE**	**p-value**
(Intercept)	95.543	4.796	<0.001
Family_apgar	0.067	0.554	0.904
Years as Caregiver	0.306	0.147	0.039
Barthel Index	0.088	0.036	0.014
Educational Level	2.236	2.383	0.349
Fm_apgar * Edu_lev	-0.669	0.320	0.038

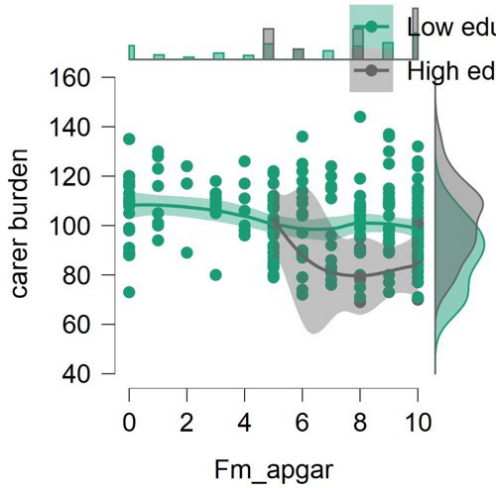

Figure 1 - Scatter plot for the moderator effect of education level between caregiver burden and family functioning

Discussion:

The evidence demonstrated that some factors influencing caregiver burden could lead to an individualized intervention. A previous study (8) showed the relevance of educational level in caregiver burden perception. These results are as those presented in this work, with a higher educational level revealing lower caregiver burden values. The same is possible be observed for the association between the functional independence level or for the number of years as a caregiver and the caregiver burden, which is transversal to different health conditions (9–12). Family functioning also plays an important role in

caregiver burden experience but has a close relationship with educational level. This relationship is quite evident in this study, and their interaction seems to contribute with more relevance to the caregiver burden perception than just their individual influence. Future studies may confirm these results in other population samples, and explore the relationship with other constructs, namely those related to the quality of life and social participation.

Ethics committee and informed consent:

The ethics committee of the Health Regional Administration of Center approved this study. All participants signed an informed consent form.

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EXTENDED ABSTRACT

Real-world data from an online health education program for pregnancy and transition to parenthood: process indicators.

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Introduction:

The SARS-COV-2 pandemic emergency had a significant impact on the dynamics of health institutions, leading to the suspension of programs for preparation for childbirth and parenthood with couples and families deprived of this essential accompaniment for this transition period. The preparation courses for childbirth and parenthood acquire an added importance, providing women and men with improved knowledge and skills in the field of procreation, namely the exercise of informed consent during pregnancy, childbirth, and postpartum [1]. To fill the gap caused by the suspension of these health education activities, the School of Health Sciences of Aveiro - Portugal in collaboration with professionals from the area, developed a project UaCuida (Caring for families in a friendly university) using Internet based information and communication tools. The branch for accompanying pregnant women and their families was made through e-colloquia with the generic designation of 'Barriguitas' ('little potbellies').

The aim of this work is to describe process indicators of the participation of pregnant women/couples in health education sessions of 'Barriguitas' at UaCuida project.

Methods:

The development of the project was grounded on the theoretical foundations of an action research methodology [2], with public e-colloquia delivery weekly using the ZOOM Platform-Colibri V3-FCCN Videoconference, approaching over time thirteen different themes like 'Preparing for delivery (birth)', 'Care for the baby at the hospital' or' Pain management & relief during delivery (birth)'. A specialized team of health professionals (nurses, primary care physicians, therapists) were responsible for preparation and for conducting e-colloquia sessions which included slide presentation, videos and time for answers to questions from de audience. The participants include women or couples in pregnancy, or puerperium, which self-identified with needs of support in the process of preparation for parenthood.

The dissemination of the e-colloquia was carried out through the social networks (like Facebook), through the agenda section of the website uacuida.com and through Health Care Units of Aveiro Region. Data was retrieved from the Zoom Platform at the end of each session held from April 9, 2020, to April 15, 2021, and analyzed using descriptive and inferential statistics [3].

Results:

During the period under review, 52 e-colloquia were held with the participation of 138 different pregnant women / couples. The total participations were 1674 of which 1539 (91.9%) from women. On average, 33±10 pregnant women / couples participated per session, with a minimum of eight participants in the first session (open topic) and a maximum of 51 participants in sessions 47th (care for the new-born at home) and 52nd (non-pharmacological methods for pain management in the child-birth labour) - Figure 1. These data reveal that participants attended different e-colloquia with a minimum of 1 session and some of them 21sessions, repeating themes (Figure 2). The average time of participation in the sessions was 101m36s ± 38m58s, ranging from a minimum of 10 minutes to a maximum of 186 minutes with a high dis-

Keywords: Public participation, Digital Health; eHealth Strategy; Health Education; Nurse Midwives; Parenting Education.

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Clinical study registration number: This project was registered in CIDTFF

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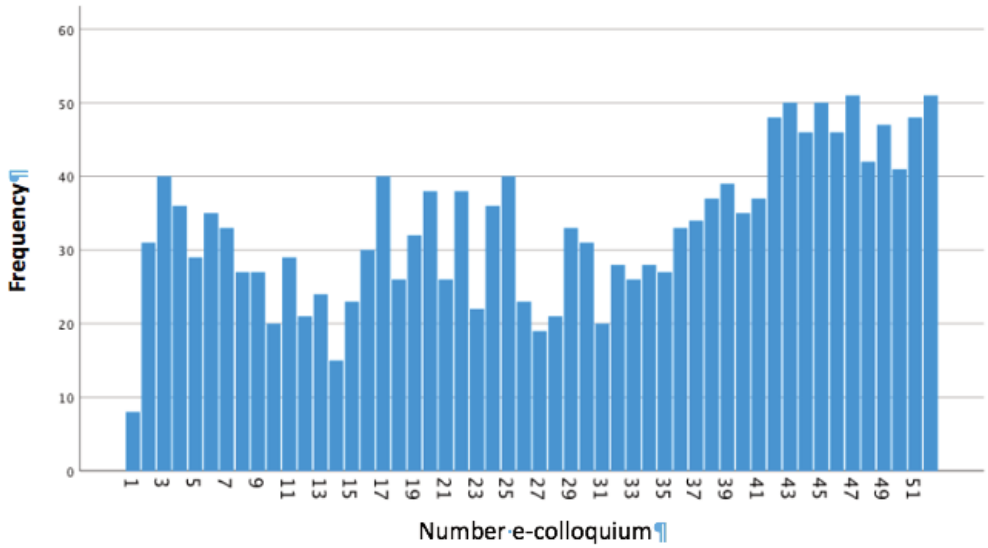

Figure 1 - Participants by e-colloquium

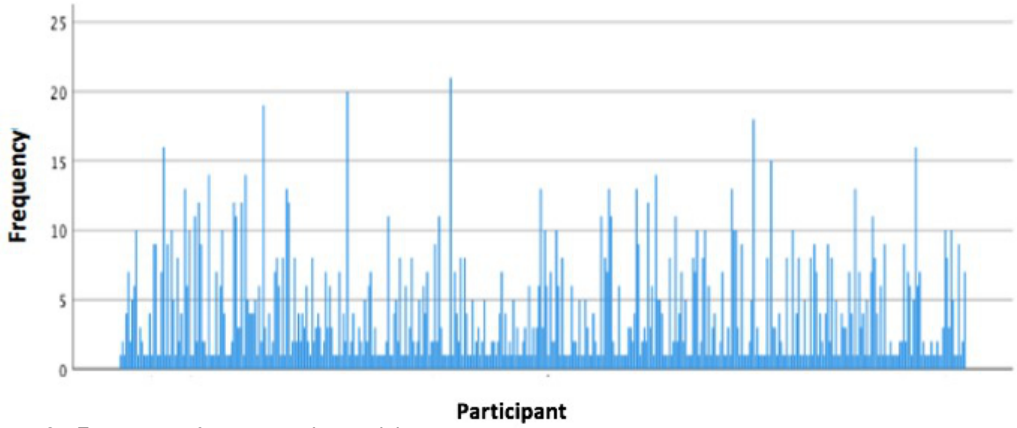

Figure 2 - Frequency of presences by participant

Table 1 - Time of participation by sex

	n	min-max	Mean (sd)	CV (%)
Male	135	10-160	92m3s±42m0s	45,62
Female	1539	10-186	102m33s±38m32s	37,57
Total	1674	10-186	101m36s±38m58s	38,29

persion around the mean (CV=38.3%), (Table 1). Male participants recorded lower mean times than females (92m3s±42m0s vs 102m33s±38m32s; U Mann-Whitney=98344.000; p<0.01).

The e-colloquium that presented the shortest mean time of participation was the 35th (child-birth labour pain management), with a mean of 56m13s ± 11m58s (minimum-maximum, 23m-66m). On the other hand, the e-colloquium that presented a higher average time of participation was the 51st, with an average of 141m57s± 40m54s (minimum-maximum, 19m-173m).

Discussion:

This project, although planned to be carried out in a non-pandemic context, was forced to adapt to the conditions imposed by the national authorities but sought to overcome the restrictions on health promotion activities given that primary health care focused its action on monitoring of people flagged with SARS-COV-2 infection and their risk contacts.

A first note for the number of participation units (female/couple) that can be considered substantial, given its proportion in relation to the number of births that took place in the region of Aveiro during the years 2020 and 2021 (2841 and 2737, respectively), which leads to a minimum of 2.4% of participants, perhaps more, as the data period considered did not extend to all months.

As expected, the participation of female elements was considerably higher, which is relevant for the continuity of the dissemination of equality policies and the promotion of the role of men in parenthood, namely those with origin from the employers themselves.

If the first session revealed a timid start in terms of the number of participants, it is possible to verify a relationship with the different phases of the pandemic, visible with the decrease in participation during moments of deflation and increase in mandatory periods of restriction of movements. Another reason for this variation could be point out to the program from home avoiding unnecessary risks for the course of pregnancy [4]. A last note to raise that participation in these e-colloquiums can help to provide relatively affordable medical services, reducing inequality in the accessibility of health care.

Ethics committee and informed consent:

The project was submitted to the Ethics Council of the University of Aveiro, obtaining a favorable opinion and all the requirements inherent to the RGPD were met, and subjects gave their informed consent before they were enrolled in the study.

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Journal of Statistics on Health Decision

EXTENDED ABSTRACT

Charlson Comorbidity Index Score and the odds of death in COVID-19 patients

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Introduction:

The Charlson Comorbidity Index Score (CCIS) was developed by Charlson et al. in 1987 [1]. This was developed based on the relative risk of death and measures the severity of disease using morbidities with different impacts on prognosis. Each morbidity is associated with a score. For example, a metastatic solid tumor is associated with a score of 6 and diabetes with target organ damage is associated with a score of 2. The sum of the scores associated with each morbidity results in a final morbidity score. This score has been widely used as a predictor of prognosis and long-term survival [2] – [4].

This work aims to understand if the assessment of the morbidities of the patients hospitalized due to COVID-19 and consequent stratification by CCIS, allows obtaining any association with this index and the occurrence of death.

Methods:

This study included the patients hospitalized in Baixo Vouga Hospital Centre due to COVID-19 who were admitted since 18th March 2020 and who were discharged until 21st October 2021.

The morbidities of the patients with COVID-19 were assessed on patient admission and the values of CCIS were calculated and divided into four categories: $0, 1-2, 3-4$ e ≥ 5. The study began with a descriptive analysis (absolute and relative frequencies). Then, binary logistic regression models were used. The outcome of interest was the death (yes or no), the predictor variable was the CCIS category and the covariate considered was the gender (male or female). The performance of the model was assessed considering the following performance metric: area under the curve (AUC).

All analyses were performed with a significance level of 5% and using the software R (version 4.1.0).

Results:

A total of 1026 patients were included in this study. During the period of study 276 (26.9%) patients died. The number of patients within the categories of CCIS 0, 1-2, 3-4 e ≥ 5 are 99 (9.7%), 190 (18.5%), 350 (34.1%) e 387 (37.7%), respectively. The most frequent morbidities are the following: uncomplicated diabetes (269, 26.2%), dementia (172, 16.8%) and chronic obstructive pulmonary disease (85, 8.3%). The age group ≥ 80 years is the one with the most patients (409, 39.9%).

Regarding the multivariate logistic regression model, the odds of death are significantly higher in the patients who belong to the category CCIS $3-4$ (OR = 9.27, 95%CI = [3.74, 30.90]) and CCIS ≥ 5 (OR = 17.8, 95%CI = [7.22, 59.00]) compared to those who belong to the category CCIS 0. Although the association is not significant, there is a trend for the odds of death being higher in the patients who belong to the category CCIS $1-2$ (OR = 2.03, 95%CI = [0.71, 7.29]) compared to those who belong to the category CCIS 0. These results are depicted in table 1 and figure 1. The model has a moderate capacity of discrimination (AUC = 0.71, 95%CI = [0.68, 0.74]).

Discussion:

The use of scores can help doctors to identify patients on admission who are at greater risk of developing more severe forms of the disease. CCIS is commonly used to evaluate the impact of comorbidities on mortality prediction. In this study, an increased risk of mortality was found in patients with higher scores, showing the weight of comorbidities and age in the prognosis of COVID-19. CCIS can remove some of the unpredictability of the infection, identifying patients at higher risk at the time of diagnosis. With the increase in knowledge, new scores will be needed for better patient management.

Keywords:
Charlson Comorbidity Index Score, COVID-19, Logistic regression

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Conflict of interest:
The authors declare no conflict of interests.

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Table 1 – Multivariate logistic regression model.

Predictor variables	Multivariate analysis		
	OR [1]	95%CI [2]	p-value
Gender (Male)	1.67	1.24, 2.26	<0.001
CCIS [3] category (ref. 0)			
1 – 2	2.03	0.71, 7.29	0.220
3 – 4	9.27	3.74, 30.90	<0.001
≥ 5	17.8	7.22, 59.00	<0.001

[1] Odd Ratio; [2] 95% Confidence Interval; [3] Charlson Comorbidity Index Score.

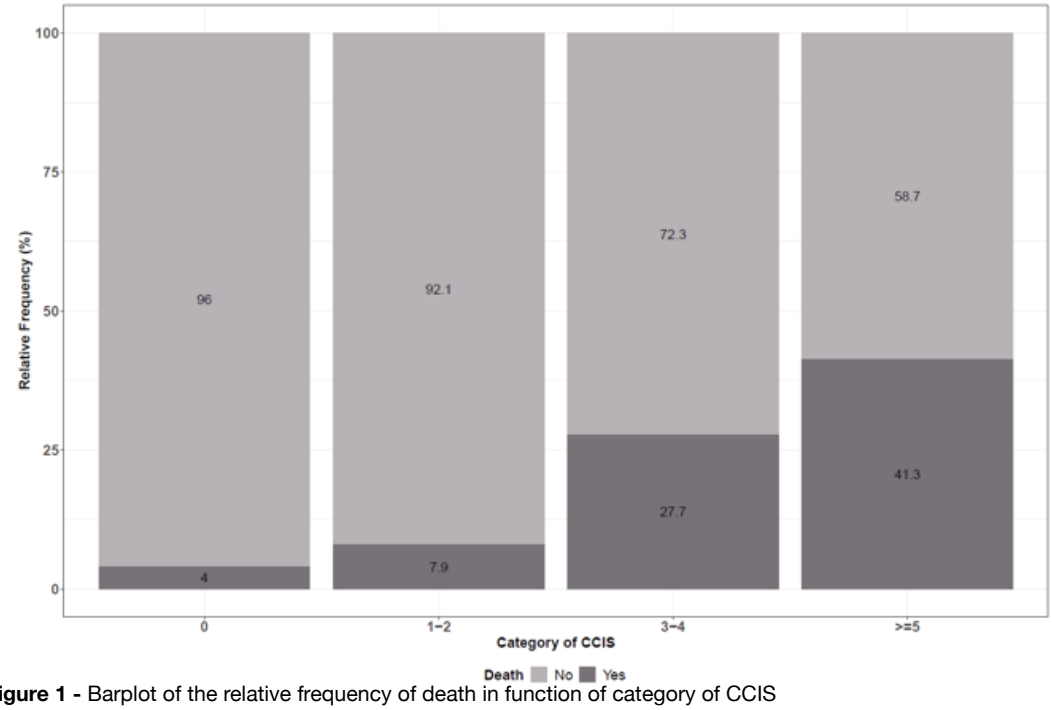

Figure 1 - Barplot of the relative frequency of death in function of category of CCIS

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Journal of Statistics on Health Decision

EXTENDED ABSTRACT

Content validation index of an interdisciplinary intervention plan to support informal caregivers in Autonomous Region of Azores

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Introduction:

Caring for dependent persons includes supporting or performing essential activities for survival such as personal hygiene, dressing, feeding, and control of elimination, or mobility, which are frequently assured by informal caregivers (1). Numerous informal caregivers perform these functions full-time or part-time for affective, sentimental, kinship, or friendship reasons (2). The growing complexity of the phenomena implies accompanying these caregivers and developing intervention plans adjusted with interdisciplinary responses to their needs(3). Thus, based on a literature review, an intervention plan was prepared for the informal caregiver, implemented in a Portuguese region, in 19 municipalities by several multidisciplinary teams.

This study aimed to describe the content validity testing of the interdisciplinary intervention plan (IIP) for informal caregivers in the Autonomous Region of Azores (ARA), Portugal

Methods:

About fifty potential participants were invited by electronic mail. These potential participants are health professionals from local teams supporting informal caregivers at ARA who have implemented the IIP.

The instrument comprises 49 items divided in six domains: 'Caregiver role empowerment' – 11 items; "Material & equipment resources' – 5 items; 'Physical resources accessibility' – 5 items; 'Social support' – 19 items; 'Individual & family support needs' – 6 items; 'Caregiver health support' – 3 items.

An online survey with two questions for each of the items of the instruments was conducted between April 27th, 2022, and May 10th, 2022. The first question of the survey was related to the inclusion in the instrument of each of the intervention plan items, with three response options: strongly agree; relevant, but not essential; strongly disagree. The second question asked about the clarity and ease of understanding of the wording of the item with two options, 'yes' or 'no'.

An item content validity index (I-CVI) and a modified kappa coefficient (K), following recommendation from Polit & colleagues (4), was computed for the instrument's items using Microsoft Excel (for the first question only 'strongly agree' option was considered relevant).

Results:

Fifteen health professionals fulfilled the online survey during the period under consideration.

Two items were classified as 'poor' for relevance: the item related to the existence of 'information and communication technology devices' in the domain of material & equipment resources was the one that obtained the lowest value, with an I-CVI of 29% and a modified k value of 0.24, followed by the item 'other rooms in the house' in the field of accessibility (I-CVI=43%; modified k value of 0.30). Another two items were classified as 'fair' for relevance: in the domain of caregiver role empowerment the item 'socialization activities promotion' (I-CVI=57%; modified k value of 0.48) and in the domain of social support the item 'volunteering' (I-CVI=54%; modified k value of 0.42). All the other items were classified as 'Excellent' - Table 1.

The interpretation of the results regarding the clarity and ease of understanding of the items places three items with the classification of 'Good' (socialization activities promotion': I-CVI=73%, modified k value of 0.72; 'information and communication technology devices': I-CVI=67%, modified k value of 0.63; 'need to redefine family roles': I-CVI=73%, modified k value of 0.72) and all others as 'Excellent' - Table 1.

Keywords:
Caregiver; needs assessment; health plan

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Conflict of interest:
The authors declare no conflict of interests

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Table 1 – Results of Item Content Validity Testing of the Interdisciplinary Intervention Plan

	Important to measure?				Clear and easy to understand?			Item relevance			Item comprehensibility		
	Strongly agree	Relevant, but not essential	Strongly disagree	No answer	Yes	No	No answer	I-CVI	k*	Evaluation *	I-CVI	k*	Evaluation **
Caregiver role empowerment													
Feeding	14	0	0	1	15	0	0	100%	1,00	Excellent	100%	1,00	Excellent
Mobility	14	0	0	1	14	1	0	100%	1,00	Excellent	93%	0,93	Excellent
Hygiene care	14	0	0	1	15	0	0	100%	1,00	Excellent	100%	1,00	Excellent
Toileting	12	2	0	1	12	3	0	86%	0,86	Excellent	80%	0,80	Excellent
Dressing	13	1	0	1	14	1	0	93%	0,93	Excellent	93%	0,93	Excellent
Changing & maintaining body position	14	0	0	1	15	0	0	100%	1,00	Excellent	100%	1,00	Excellent
Transferring	14	0	0	1	15	0	0	100%	1,00	Excellent	100%	1,00	Excellent
Medication management	14	0	0	1	15	0	0	100%	1,00	Excellent	100%	1,00	Excellent
Socialization activities promotion	8	5	1	1	11	4	0	57%	0,48	Fair	73%	0,72	Good
Health surveillance	14	0	0	1	15	0	0	100%	1,00	Excellent	100%	1,00	Excellent
Autonomy promotion	12	2	0	1	14	1	0	86%	0,86	Excellent	93%	0,93	Excellent
Material & equipment resources													
Comfort and positioning	14	0	0	1	13	0	2	100%	1,00	Excellent	100%	1,00	Excellent
Hygiene and personal care	14	0	0	1	14	0	1	100%	1,00	Excellent	100%	1,00	Excellent
Mobility and transferring	14	0	0	1	14	0	1	100%	1,00	Excellent	100%	1,00	Excellent
Meals and household activities	12	1	0	2	13	2	0	92%	0,92	Excellent	87%	0,87	Excellent
Information and communication technologies	4	10	0	1	10	5	0	29%	0,24	Poor	67%	0,63	Good
Physical resources acessibility													
Bedroom	14	0	0	1	15	0	0	100%	1,00	Excellent	100%	1,00	Excellent
Kitchen	12	2	0	1	15	0	0	86%	0,86	Excellent	100%	1,00	Excellent
Bathroom	14	0	0	1	15	0	0	100%	1,00	Excellent	100%	1,00	Excellent
External areas	11	3	0	1	14	1	0	79%	0,78	Excellent	93%	0,93	Excellent
Other room in the house	6	7	1	1	13	2	0	43%	0,30	Poor	87%	0,87	Excellent
Social support													
Home Support Service: Hygiene care	14	0	0	1	15	0	0	100%	1,00	Excellent	100%	1,00	Excellent
Home Support Service: Meals	14	0	0	1	15	0	0	100%	1,00	Excellent	100%	1,00	Excellent
Home Support Service: Housing cleaning	14	0	0	1	15	0	0	100%	1,00	Excellent	100%	1,00	Excellent
Home Support Service: Clothes management	14	0	0	1	15	0	0	100%	1,00	Excellent	100%	1,00	Excellent
Home Support Service: Support for Informal Caregivers	14	0	0	1	14	1	0	100%	1,00	Excellent	93%	0,93	Excellent
Psychological support	14	0	0	1	14	0	1	100%	1,00	Excellent	100%	1,00	Excellent
Transport for the person cared for	14	0	0	1	15	0	0	100%	1,00	Excellent	100%	1,00	Excellent
Day center	14	0	0	1	15	0	0	100%	1,00	Excellent	100%	1,00	Excellent
Complementary finantial subsidy	13	1	0	1	14	1	0	93%	0,93	Excellent	93%	0,93	Excellent
Dependency finantial subsidy	13	1	0	1	14	1	0	93%	0,93	Excellent	93%	0,93	Excellent
Pension finantianal supplement	13	1	0	1	14	1	0	93%	0,93	Excellent	93%	0,93	Excellent
Third person assistance subsidy	13	1	0	1	14	1	0	93%	0,93	Excellent	93%	0,93	Excellent
Social Benefit for Inclusion	12	2	0	1	14	1	0	86%	0,86	Excellent	93%	0,93	Excellent
Financial support to the caregiver	14	0	0	1	15	0	0	100%	1,00	Excellent	100%	1,00	Excellent
Respite services	14	0	0	1	13	2	0	100%	1,00	Excellent	87%	0,87	Excellent
Compamid	13	0	0	2	15	0	0	100%	1,00	Excellent	100%	1,00	Excellent
Neighborhood / family network	12	1	0	2	14	1	0	92%	0,92	Excellent	93%	0,93	Excellent
Volunteering	7	5	1	2	13	2	0	54%	0,42	Fair	87%	0,87	Excellent
Tele-assistance	10	3	0	2	13	2	0	77%	0,76	Excellent	87%	0,87	Excellent
Individual & Family support needs													
Need for support in providing care	14	0	0	1	14	1	0	100%	1,00	Excellent	93%	0,93	Excellent
Difficulty in organizing care	14	0	0	1	13	2	0	100%	1,00	Excellent	87%	0,87	Excellent
Difficulty managing household activities	12	2	0	1	14	1	0	86%	0,86	Excellent	93%	0,93	Excellent
Difficulty setting time for yourself	14	0	0	1	14	1	0	100%	1,00	Excellent	93%	0,93	Excellent
Need to redefine family roles	13	0	1	1	11	4	0	93%	0,93	Excellent	73%	0,72	Good
Need to participate in activities of personal interest	13	1	0	1	12	2	1	93%	0,93	Excellent	86%	0,86	Excellent
Caregiver health support													
Health promotion: Introducing healthy lifestyles	13	1	0	1	14	1	0	93%	0,93	Excellent	93%	0,93	Excellent
Health surveillance	12	1	0	2	13	2	0	92%	0,92	Excellent	87%	0,87	Excellent
Health problems	12	2	0	1	14	1	0	86%	0,86	Excellent	93%	0,93	Excellent

I-CIV Item content validation index; k* - modified kappa ; ** Poor k*: <40; Fair k*: .40 to .59; Good k*: .60–.74; Excellent k* > .74.

Discussion:

This work presents the preliminary quantitative results of the content validation phase of an interdisciplinary intervention plan to support informal caregivers. The results seem to support the option for items defined based on the literature, with most items being rated 'Excellent' for relevance (45 out of 49) and for their formulation (47 out of 49). While it may be understandable that the item 'other rooms in the house' may be redundant in the assessment of the accessibility of physical resources, the classification obtained by the item relating to 'information and communication devices' is somewhat surprising, especially in a geographical context where support at distance could be one of the resource optimization strategies. All items presented acceptable comprehensibility. Future works should include qualitative data to deepen the reasons for the results obtained.

Ethics committee and informed consent:

Ethical precepts safeguarded, with authorization by the Ethics Committee of the Portuguese Society of Mental Health Nursing.

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Journal of Statistics on Health Decision

Transition to parenthood recognition and accepting the maternal role.

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Introduction:

Pregnant women experience, an ambivalence feelings and emotions during pregnancy, causing a significant impact on the transition to parenthood and adjustment process to the maternal role [1]. Our qualitative research will allow pregnant women to describe their experience and the main difficulties in this transition, allowing us to develop appropriate interventions facilitating the transition to parenthood. Our aim is describe the pregnancy experience, recognition and accepting the maternal role.

Methods:

The qualitative study with descriptive phenomenological approach it was performed at a purposive sample consisting of 35 women, in the third trimester of pregnancy. The interviews occur in two center hospitals from Portugal and were conducted by two experienced researchers in the field of expertise. The researcher's relation with the interviewees were strictly professional. The eligibility criteria that we use in this research was: inclusion criteria - maternal age ≥ 35A; primiparity; pregnant/healthy fetus and exclusion criteria - multiple pregnancy; mental/psychiatric illness. Curiously no one refused to participate in this study. After informed consent, the interview was conducted by two questions: "What is your pregnancy experience?" and "what were the main feelings and emotions that you experienced in pregnancy?". Data were analyzed according to the descriptive phenomenological method of Amedeo Giorgi [2]. From data analysis of the qualitative study, we proceed to the transformation of the units of meaning, perceiving the meaning of the phenomenological reduction and the imaginative variation, being important in the identification of the essential structures of the phenomenon.

Results:

From the data, 35 women are more representative between 35 and 39 years old. We also show that there is less representation of the sample between 40 and 45 years, a fact that may be related to the decline in fertility after 35 years [3]. Our sample includes pregnant women with ≥35 years, and it´s curious that the interviewees refer, that in this age they are more mature and prepare to be a mother, which reflects a better acceptance of the maternal role. In the analysis of the speech the maternal experiences of the transition to parenting during pregnancy emerged as an essential structure the context: Transition to parenthood and the awareness to the maternal role. In this context, emerge the following key constituents: (i) Pregnancy experience; (ii) Pregnancy feelings; (iii) Feel prepared to be a mother; (iiii) Changes and discomforts in pregnancy:

(i) Pregnancy experience

"It´s a very positive experience and allows me to experience and discover new sensations and emotions (…) feel the baby's movements for the first time, see him on the ultrasound, hear his heart (…) feel that we have a baby growing inside us, it is wonderful…" G6

(ii) Pregnancy feelings

" I'm experiencing pregnancy with a great happiness, but at the same time, very calmly, to enjoy every moment, it is a unique experience!" G3

(iii) Feel prepared to be a mother

"we decided to wait until now because (…) we see the arrival of a baby, in a different way, with more responsibly and maturity." G15

Keywords:
Health Transition; Parenting; Pregnancy; Qualitative Research

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Conflict of interest:
The author declare that there is no conflict of interest.

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(iiii) Changes and discomforts in pregnancy

"There are many changes, physical and psychological, everything happens at the same time (…) nauseas, see our body change… it's not easy, we stay a little fragile with everything, sometimes when I realize I'm crying." G7

Discussion:

After analysing the contexts in pregnancy, we found that the living and experience of motherhood are involved in a mix of emotions and sensations. Our interviewees referred to fetal movements and ultrasound visualization as a remarkable experience, considering motherhood a realization of a dream, allowing their personal fulfilment. Motherhood is seen as something unique and special in a woman's life, implying the combination of positive and negative aspects, reward and sacrifices. Woman cannot hide the desire to be a mother and even through some difficulties, she advances towards the realization of her dream [4].

Our participants mentioned that there are many changes and discomforts in pregnancy, which agrees with other authors who mention that pregnancy is a complex event, involving physical, physiological and emotional changes in a woman's life, interfering with her daily life and the entire family [5].

This research allows us to understand how motherhood is lived and experienced by these women, evidencing their concerns and feelings. The sample was carried out only in central region hospitals, but it could have been beneficial, if we apply this study to the north and south of Portugal.

Ethics committee and informed consent:

This research was submitted to the Ethics Council of the selected institutions. All the requirements inherent to the RGPD were met. Participants gave their informed consent to participate in the research.

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Journal of Statistics on Health Decision

EXTENDED ABSTRACT

The impact of Intensive Care Unit admission, sex and vaccination on COVID-19 death

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Introduction:

On March 2nd, 2020, the first case of Sars-Cov-2 was detected in Portuguese territory [1]. The disease set off by this virus, Covid-19, has reportedly been known to affect the respiratory system and cause higher fatality rates. [2][3]

The employed database for this study was provided by the Baixo Vouga ACeS, and it includes data gathered during the epidemiological investigation of all COVID-19 confirmed cases reported in this area, between March 2020 and January 2022. [4]

We aimed to find significant correlations between various variables and death from COVID-19, as well as a subsequent appropriate regression model.

Methods:

All reported cases of COVID-19 from March 8, 2020 until January 31, 2022 in Baixo Vouga region were the subjects of a retrospective study. The incidence per 1,000,000 population was estimated by habitants residing in each county using PORDATA data of Census 2021 Population description. Employing R software 33 variables were analyzed with 42746 observations. To evaluate daily incidence of COVID-19 a seasonal plot was elaborated (EpiEstim package) showcasing the standardized incidence of the viral disease by county, using packages tmap, Tcpp, sp, raster, rgdal, terra and rgeos, and the design was exported from government data site. [5] To select the interesting variables it was performed a Welch two-sample t-test for the variable Age, a 4-point z-test for equality of proportions without continuity correction for the variable Sex and a 2-point z-tests for equality of proportions for the variables Comorbidities, COVID-19 Symptoms and Intensive Care. A logistic regression model for death was performed and the odds ratio for each explanatory variable was calculated. The assumptions, quality and significance of the model were validated. The significance level was set at 0.05.

Results:

The incidence of COVID-19 during its inception until January 2022 had several oscillations. It is evident that there are five observable peaks of incidence, firstly when COVID-19 cases started appearing in Portugal and the last coinciding with the highest number of cases ever in regional Baixo Vouga, it seems that this region follows the national peaks (Figure 1). It's interesting to note that cases dropped during months of stricter lockdowns in the country, the beginning of Spring in 2020 and 2021. More cases seem to be reported since the beginning of Autumn and end of Winter in both years analyzed, rather than during Spring and Summer, which is supported by global literature. Perhaps climate, lockdowns and self-protection interventions can explain the variations.

Ovar, Ílhavo, Sever do Vouga, Águeda and Anadia were the most affected (between 120,000 and 140,000 cases per 1,000,000 habitants), in Aveiro district (Figure 2).

In univariate statistical analysis, tests were applied to the variables of interest for the outcome "Death". All tests revealed a p-value less than 0.05. They were therefore all included in the logistic regression model.

From the multivariate analysis, p-values less than 0.05 appear for the variables Age, Intensive Care and Vaccinated. These are also the only variables whose 95% CI of the ORs do not include the value 1. VIFs were obtained with values between 1.00 and 1.15, and the likelihood-ratio test applied reached a p-value of 3.54 x 10-8. The deviance and AIC values in table 1 of our model are lower than the values of the null model.

Keywords:
Covid-19, logistic regression model, Covid-19 mortality, Baixo Vouga ACeS, incidence

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Conflict of interest:
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Table 1 - Death Regression Models

Predictors	Normal Model			Null Model		
	Odds Ratios	Conf.Int (95%)	P-Value	Odds Ratios	Conf.Int (95%)	P-Value
(Intercept)	0.000	0.000 - 0.004	**<0.001**	0.174	0.128 - 0.236	**<0.001**
Age	1.066	1-035 - 1.103	**<0.001**			
Sex (Male)	1.645	0.842 - 3.270	0.148			
Comorbidities	3.501	0.614 - 67.177	0.249			
Symptoms COVID-19	1.907	0.740 - 5.940	0.216			
Intensive Care	5.212	1.401 - 19.518	**0.013**			
Vaccination	0.360	0.163 - 0.744	**0.008**			
Observations		324			324	
Deviance		226.213			271.825	
AIC		240.213			273.825	

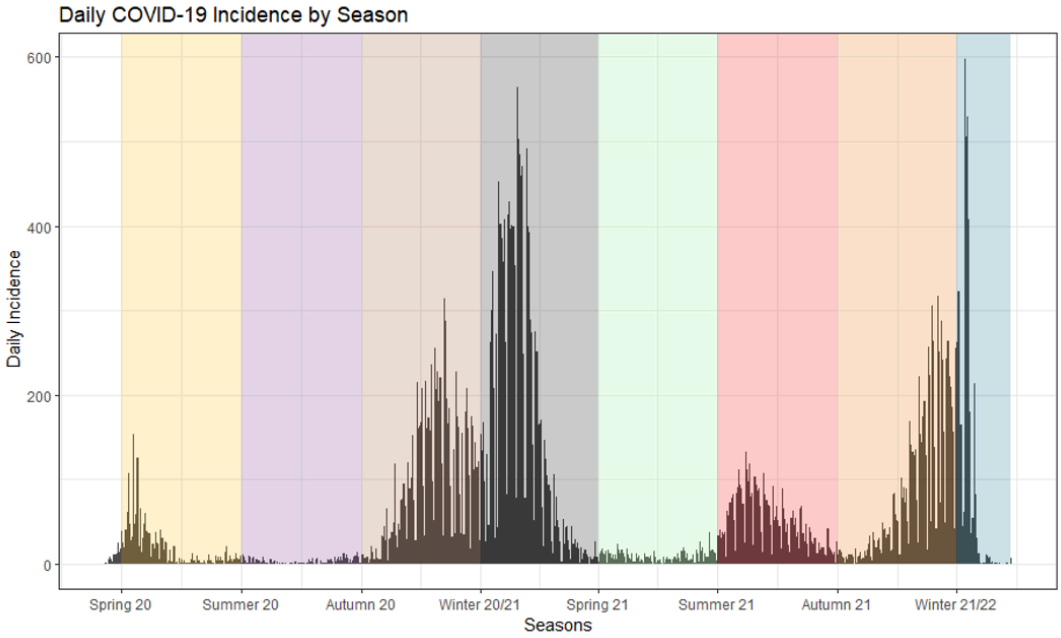

Figure 1 - Daily COVID-19 incidence across time, with seasons highlighted in different colors.

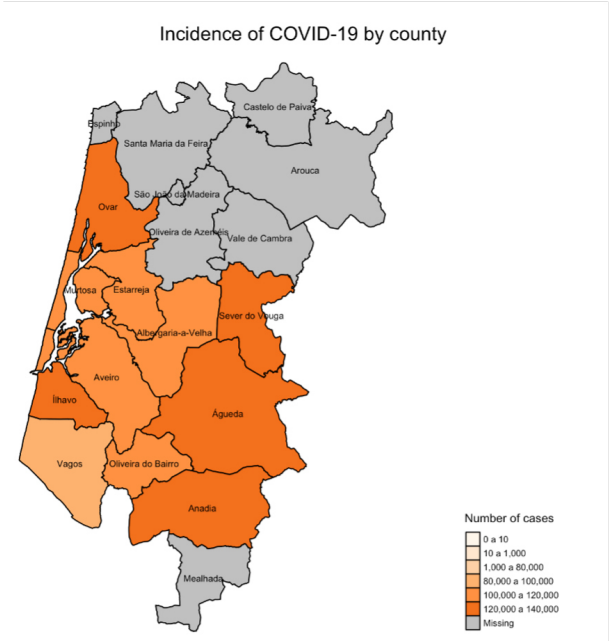

Figure 2 - Heatmap of Covid-19 cases in Baixo Vouga ACeS, from March 2020 to January 2022, standardized by population per county.

Discussion:

The Aveiro region, like Portugal, has suffered the surge of infection cases and death caused by this virus, alongside the rest of the world. In this study we have explored how the incidence varied by season and county, although the incidence may vary according to air temperature and lockdowns.

In Figure 2 the area that covers the Baixo Vouga ACeS can be marked (area in orange).

From multivariate analysis, the p-values from the variables Age, Intensive Care and Vaccinated indicate that these are significant for obtaining the outcome.

The ORs values show that the odds of dying increase 6.6% per one year older, are increased by 421.2% for patients in an ICU, and are decreased by 277.8% when the vaccination is present.

The VIFs values tell us that there is no multicollinearity between regressors, and the p-value of the likelihood ratio test demonstrates that the model is statistically different from the null model. Lastly, AICs and deviances measures mentioned reveal that our model has higher quality than the null model.

Acknowledgements:

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Journal of Statistics on Health Decision

EXTENDED ABSTRACT

Features related to respiratory disability and performance of inhaler technique in COPD population.

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Introduction:

Chronic obstructive pulmonary disease (COPD) is one of the most common respiratory diseases treated in the community setting [1]. If not appropriately managed can result in poorer health, negative societal and economic effects, with a significant burden on patients' quality of life [1].

COPD cannot be cured, but treatment can help slow down disease progression and control of the symptoms. Treatments may include non-pharmacological approaches as smoking cessation, or pharmacological inhaled therapy, pulmonary rehabilitation, and in very few cases surgery or lung transplant [2], depending on medical doctor assessment of each individual case to provide tailored therapy.

This work aimed to explore which features of patients with COPD can be related with respiratory disability and the performance of inhaler technique in Portugal.

Methods:

Data for this work were obtained from the Pilot Project INspira – Study of inhaler use in asthma and COPD (January to November 2019) patients. A cluster randomized controlled trial, was conducted in the community pharmacies affiliated to National Association of Pharmacies to improve inhalation technique among COPD patients with inhaled therapy [3, 4]. Eligible patients were adults aged 18 years or older using at least 1 of the targeted inhalers (both chronic or first user), and a self-reported diagnosis of COPD. The self-reported diagnosis was checked by the pharmacist, using a differential algorithm [4].

Data on sociodemographic features (i.e., sex, age, educational level, occupational status, tobacco exposure), body mass index (BMI), number of comorbidities, number of different medicines and inhalators used by patients to control the disease, respiratory disability, and performance of inhaler technique, were collected prior to any education have been provided. Respiratory disability was quantified according to the modified Medical Research Council dyspnea (mMRC) scale [5, 6]. This tool comprises five statements describing the entire range of respiratory disability from none (score 0) to almost complete incapacity (score 4). Values of mMRC ≥ 2 were classified as more symptomatic. Inhaler technique was considered well performed when all steps (100%) of the inhalation process were executed correctly, and not well performed if patient failed at least one step.

For purposes of descriptive statistics, continuous variables were summarized by median and interquartile range and categorical variables by counts and percentages. Quantitative variables were analysed through the Mann-Whitney Wilcoxon Test and qualitative ones through Fisher's exact test.

Univariate logistic regression was used to select all candidate variables ($p \leq 0.25$) to enter in multivariate logistic regression. Multimodel inference was performed and the models with lowest AIC were proposed as final models. Odds ratios (OR) and 95% confidence intervals (CI) were calculated.

Results were considered statistically significant at $p < 0.05$.

Results and conclusions:

A sample of 84 patients with available mRMC scores and inhaler technique scores was analysed. Patients' main features are summarised in Table 1. The number of medicines taken to control the disease and the educational level, were significantly associated with the respiratory disability and the performance of inhaler technique, respectively.

From the univariate logistic regressions (Table 2), BMI, number of medicines and number of comorbidities were selected to integrate the respiratory disability multivariate logistic regression. Sex, tobacco exposure and educational level were selected to integrate the performance of the inhaler technique multivariate logistic regression.

Keywords:
Chronic disease, COPD, Dyspnea, Inhaler technique, Modeling, Respiratory disability

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Support statement:
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Conflict of interest:
The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: ZM, SR and ATR are/were employees of Infosaúde, a company owned by Portuguese National Association of Pharmacies. SM and VA declare no conflict of interests.

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Table 1 – Descriptive Statistics of the chronic obstructive pulmonary disease (COPD) sample by respiratory disability and by performance of inhaler technique.

Variable	Respiratory disability			Performance of inhaler technique		
	More symptomatic	Less symptomatic	p-value	Not well performed inhaler technique	Well performed inhaler technique	p-value
	N (%)	N (%)		N (%)	N (%)	
Sex						
Male	18 (40)	27 (60)	0.384	32 (84)	6 (16)	0.050
Female	19 (50)	19 (50)		18 (62)	11 (38)	
Age						
<65 years old	12 (44)	15 (56)	1.000	16 (70)	7 (30)	0.560
≥ 65 years old	25 (45)	31 (55)		34 (77)	10 (23)	
Educational level						
Primary	14 (47)	16 (53)	0.878	20 (91)	2 (9)	**0.007****
Sixth or ninth grades	8 (50)	8 (50)		14 (88)	2 (13)	
Secondary or university	15 (42)	21 (58)		16 (55)	13 (45)	
Occupational status						
Employed	5 (36)	9 (64)	0.562	8 (73)	3 (27)	1.000
Retired or Unemployed	32 (46)	37 (54)		42 (75)	14 (25)	
Tobacco exposure						
Never smoked	8 (53)	7 (47)	0.790	7 (58)	5 (42)	0.377
Ex-smoker	20 (43)	27 (57)		29 (76)	9 (24)	
Active smoker	9 (43)	12 (57)		14 (82)	3 (18)	
Respiratory disability						
More symptomatic	-	-	-	22 (71)	9 (29)	0.587
Less symptomatic	-	-		27 (77)	8 (23)	
Inhaler technique						
Not well performed	22 (45)	27 (55)	0.587	-	-	-
Well performed	9 (53)	8 (47)		-	-	
	Median (IQR)	Median (IQR)		Median (IQR)	Median (IQR)	
Body mass index (BMI)	27.68 (6.07)	26.18 (5.42)	0.140	27.65 (6.52)	26.64 (5.43)	0.757
Number of inhalators	1.00 (0.00)	1.00 (0.00)	0.565	1.00 (0.00)	1.00 (0.00)	0.599
Number of medicines	2.00 (2.00)	1.00 (1.00)	0.018*	1.00 (1.00)	1.00 (1.00)	0.550
Number of comorbidities	2.00 (3.00)	2.00 (2.00)	0.088	2.00 (2.00)	2.00 (1.00)	0.813

IQR – Interquartile Range; * p-value < 0.05; **p-value < 0.01.

Table 2 – Univariate Logistic regression results for respiratory disability and performance of inhaler technique outcomes.

Variable	Respiratory disability			Performance of inhaler technique		
	OR	CI	p-value	OR	CI	p-value
Sex (Male)	1.50	0.63-3.62	0.362	0.31	0.09-0.94	**0.044***
Age (>=65)	0.99	0.39-2.50	0.986	0.67	0.22-2.15	0.493
Body mass index (BMI)	0.90	0.81-0.99	**0.038***	0.99	0.89-1.09	0.807
Number of inhalers	0.71	0.25-1.87	0.493	0.83	0.21-2.40	0.759
Number of medicines	0.63	0.40-0.94	**0.031***	0.90	0.53-1.41	0.650
Number of comorbidities	0.73	0.52-0.98	**0.046***	0.93	0.62-1.36	0.726
Respiratory disability	-	-	-	0.72	0.23-2.20	0.568
Performance of inhaler technique	0.72	0.23-2.20	0.568	-	-	-
Tobacco exposure (Active Smoker)	0.99	0.35-2.85	0.981	0.69	0.14-2.74	0.618
Tobacco exposure (Never smoked)	0.65	0.20-2.09	0.467	2.30	0.56-9.15	**0.233***
Occupational status (Retired or Unemployed)	0.64	0.18-2.06	0.467	0.89	0.22-4.48	0.874
Educational level (Sixth or ninth grades)	0.88	0.26-2.98	0.829	1.43	0.16-13.10	0.736
Educational level (Secondary or University)	1.23	0.46-3.28	0.684	8.13	1.89-57.00	**0.012***

OR – Odds Ratio; CI – confidence interval; * p-value ≤ 0.25

Due to the existence of incomplete cases in the initial data set, the multivariate logistic regression analysis was performed with 66 COPD patients. In the respiratory disability multivariate model, only the number of medicines showed to be significant ($p = 0.044$), when adjusted to BMI. As the number of medicines used increases, the respiratory disability increases. In the performance of the inhaler technique multivariate model, only the educational level showed to be significant ($p = 0.005$), when adjusted to tobacco exposure. Patients with a secondary or university degree were 14 times more likely to perform the inhalation technique correctly than individuals with primary school (Table 3).

The positive association between the number of medicines used by patients and the respiratory disability is an interesting result, since the prescription of a greater number of medicines by the doctors will have

Table 3 – Multivariate logistic final models of respiratory disability and performance of the inhaler technique in people with chronic obstructive pulmonary disease (COPD).

	Coefficients Estimate	SE	OR	95% CI	p-value
Respiratory disability					
(Intercept)	3.33	1.56	28.01	1.62-785.42	0.032*
Body mass index (BMI)	-0.09	0.05	0.92	0.82-1.01	0.094
Number of medicines	-0.49	0.24	0.61	0.37-0.96	**0.044***
Performance of Inhaler technique					
(Intercept)	-2.79	0.89	0.06	0.00-0.26	0.002**
Tobacco exposure (Active Smoker)	-0.85	0.82	0.43	0.08-1.99	0.300
Tobacco exposure (Never smoked)	1.72	0.95	5.60	0.96-46.82	0.070
Educational level (Sixth or ninth grades)	0.19	1.14	1.20	0.11-12.33	0.870
Educational level (Secondary or University)	2.71	0.95	14.97	2.86-140.00	**0.005****

* p-value < 0.05; ** p-value < 0.01

the objective of greater effectiveness in controlling the disease or reduce its severity. However, it is known that polypharmacy tends to increase poor medication adherence [7, 8], and thus reducing the effectiveness of the medication, and consequently worsening disease.

On the other hand, as expected, according to previous literature [9–13], our results show that educational level is significantly associated to the performance of the inhaler technique. The correct inhaled technique favors therapeutic effectiveness and consequently better outcomes, namely better symptom control, lower risk of exacerbations, and improved quality of life [14, 15].

Ethics committee and informed consent:

The current research was approved by an independent ethics committee and patients gave their informed consent before they were enrolled in the study. Ethics compliant 10/12/2018, Ethics Committee Institute of Bioethics of Universidade Católica Portuguesa (Instituto de Bioética, Universidade Católica Portuguesa, Porto, Rua de Diogo Botelho, 1327, 4169-005 Porto, Portugal).

Clinical study registration number: ISRCTN10844309 https://doi.org/10.1186/ISRCTN10844309

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EXTENDED ABSTRACT

Thyroid Cancer Incidence in North Region of Portugal: A Spatial Analysis using Moran's Index

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Introduction:

Cancer incidence has been increasing worldwide and is one of the most important causes of morbidity and mortality [1]. In 2020, approximately 19 million new cases of cancer and almost 10 million deaths due to cancer were estimated [2]. Consistently, there is a growing trend in cancer incidence in the North Region of Portugal, highly supported by the rising number of cases of thyroid cancer, particularly among women [3]. Regional differences were found in the incidence of thyroid cancer, which is higher in the North of Portugal compared to other regions [3,4]. The regional and sex differences reported in Portugal seem to line up with what is happening in other countries [5].

Monitoring the trends and patterns in cancer incidence is relevant at regional and national levels for cancer prevention and control [2,3,6,7]. In this context, spatial data analysis is especially useful when the geographic location can play an important role in the development of the phenomenon under study [8]. The study of spatial patterns of thyroid cancer incidence has been carried out in different countries, allowing the identification of regional differences [9,10,11]. Disease mapping is a popular tool in cancer's spatial epidemiology. Spatial distribution patterns have been studied using distinct methods (e.g. Moran's I, Bayesian models) [7].

Our main goal is to map thyroid cancer incidence and investigate the existence of spatial distribution patterns in the North Region of Portugal.

Methods:

We analyzed thyroid cancer cases, diagnosed between 2001 e 2015, in the North Region of Portugal. Thyroid cancer was classified according to the International Statistical Classification of Diseases and Related Health Problems 10th Revision (C73). The study area comprised the following five districts: Braga, Bragança, Porto, Viana do Castelo, and Vila Real. The municipality was considered the geographical unit of analysis. The number of cancer cases was retrieved from the North Region Cancer Registry (RORENO), by sex, age (5-year age-groups), municipality, and year of diagnosis. Population estimates were acquired from Statistics Portugal (INE).

Age-standardized incidence rates (ASIR), for each municipality were calculated by the direct method using the European standard population, adjusted by age-group and sex. The administrative boundary of the municipalities was obtained from the Portuguese Public Administration's open data portal.

R software version 4.0.2 was used for geospatial analyses and map visualization [12]. The ASIR of thyroid cancer mapping was performed at a municipality level, for men and women. We computed a spatial neighborhood matrix of the municipalities, using the queen criterion of contiguity. Spatial distribution patterns were studied using Moran's I method, which estimates spatial autocorrelation based on data by area and the location of the study units.

Results:

Between 2001 and 2015, there were 9,726 cases of thyroid cancer in the North Region, 82% of them in women. The median age was 50 (IQR = 22). The ASIR at a municipality level was presented in choropleth maps, for women, for men, and for both sexes (Figures 1-3). The ASIR varies across municipalities, with the highest rate of 55.63/100000 in women (Vila do Conde), and of 15.74/100000 in men (Póvoa do Varzim).

Keywords:
Disease mapping, Moran's I, North Region, Spatial Analysis, Thyroid Cancer Incidence

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Conflict of interest:
The authors declare no conflict of interests.

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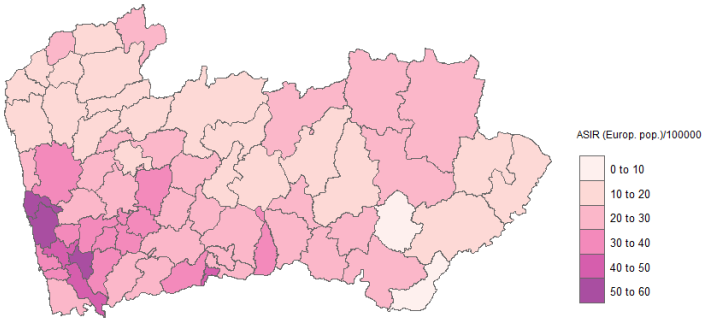

Figure 1 - North Region of Portugal map, representing women's Age-standardized incidence rates (ASIR), for each municipality, calculated by the direct method using European standard population, adjusted by age group and sex, per 100000.

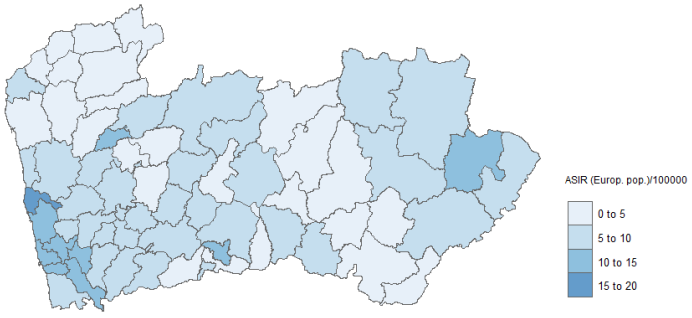

Figure 2 - North Region of Portugal map, representing men's Age-standardized incidence rates (ASIR), for each municipality, calculated by the direct method using European standard population, adjusted by age group and sex, per 100000.

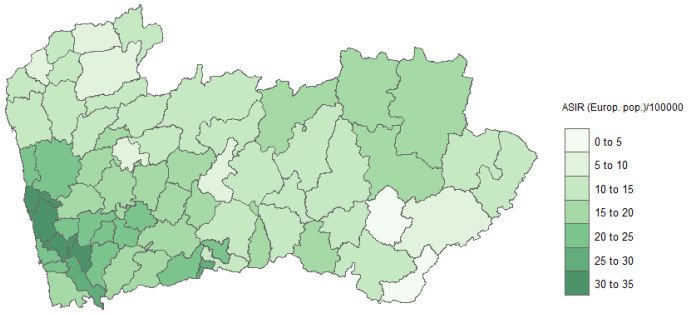

Figure 3 - North Region of Portugal map, representing Age-standardized incidence rates (ASIR), for each municipality, calculated by the direct method using European standard population, adjusted by age group and sex, per 100000.

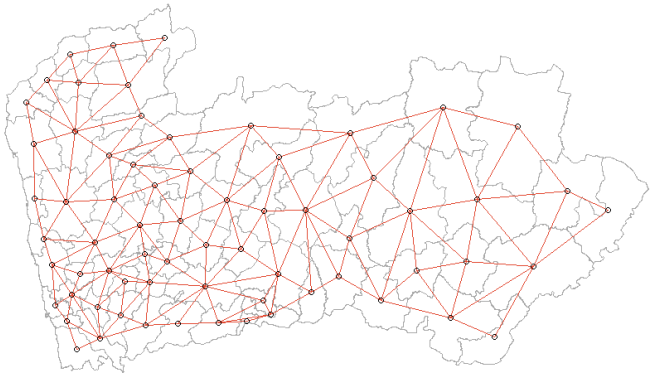

Figure 4 - North Region of Portugal map, representing the spatial neighborhood matrix based on the queen criterion of contiguity.

The spatial neighborhood matrix based on the queen criterion of contiguity can be visualized in Figure 4. A spatial distribution pattern was found for ASIR of cancer thyroid in the North Region. For ASIR in both sexes, we estimated a Moran's I of 0.59 ($p < 0.001$), for ASIR in women a Moran's I of 0.56 ($p < 0.001$), and in men 0.41 ($p < 0.001$).

Discussion:

Portugal presents higher estimates of ASIR than Europe and world average, mainly because of the high incidence rates in the North Region [4]. In this region, the incidence of thyroid cancer is much higher in women, in line with European and world tendencies. We found patterns in incidence rates. Moran's I method revealed a significant spatial association of data. There were two spots of high incidence in the North Region, one of them at the central coast and the other located at the northeast area. In future studies, we aim to compare these findings with other methods used in spatial epidemiology, such as the Bayesian approach [7]. Regional differences found are line up with what is happening in other countries [5].

The identification of regional differences may be relevant for future investigation, cancer prevention, and control.

Ethics committee and informed consent:

The study was approved by the Ethics Committee of the Portuguese Institute of Oncology of Porto (Ref. CES IPO: 69/022).

Acknowledgements:

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Journal of Statistics on Health Decision

EXTENDED ABSTRACT

Do Variant Histologies of Urothelial Carcinoma change the survival outcome in patients managed with radical cystectomy?

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Introduction:

The tenth most common type of cancer worldwide is bladder cancer, with urothelial carcinoma (UC) being the most common histology.1 Besides pure urothelial carcinoma (PUC), which is the most common UC, a wider spectrum of variant histologies (VH) has been recognized by the 2004 World Health Organization (WHO) classification of tumors of the urinary system, due to its known propensity for differentiation.2 These variants show urothelial differentiation mixed with specific morphological phenotypes, with the squamous, glandular and micropapillary being the most common, with an incidence of 20-40%, 18% and 2-5% respectively.3

Although the presence of VH, compared to the presence of pure urothelial carcinoma has been associated with more aggressive behavior4,5, conclusive data on their effect on survival outcomes are currently not well established.

One of this work's aims was to increase the awareness of the identification of those variants on pathology specimens and, in that way, better understand its clinical and therapeutic impact. VH have been reported in 7-81% of bladder cancer.6

Methods:

From 2013 to 2019, data from 181 patients (Table 1) with urothelial carcinoma (UC) treated with radical cystectomy was retrospectively collected at a single tertiary care referral center. Overall survival (OS), disease-specific survival (DSS), and recurrence-free survival (RFS) were evaluated using the Kaplan-Meier methodology and the Cox proportional hazards regression.

Descriptive statistical analysis was performed using Pearson chi-square test to compare categorical variables and Mann-Whitney-U (2 categories) or Kruskal-Wallis (3 or more categories) tests to compare continuous variables.

Statistical analysis was conducted using SPSS Statistics® v. 24.0 (IBM Corp., Armonk, New York, United States of America) and RStudio v. 1.4.1 (Integrated Development for R. RStudio, PBC, Boston, United States of America), and a p-value < 0.05 was considered significant.

Results:

Of 181 patients, 43.1% (n = 78) had VH, with the most common being squamous differentiation (n = 29), followed by mixed variants (n = 18), micropapillary variant (N=10) and other subtypes (n = 21). The median (range) follow-up was 35 (18-59) months. Kaplan-Meier survival analysis shows that median OS (Figure 1) and DSS (Figure 2) were significantly worse for VH patients (78 vs 31 months, p = 0.038; Not Reached vs 42 months; p = 0.016). At 5 years, VH was associated with a 12% and 14% decrease in OS and DSS, respectively. No significant statistical difference between the two groups was reached regarding RFS (Figure 3). However, after adjusting for confounders, such as demographic characteristics, comorbidities, and pathological features, VH were not associated with both survival outcomes (Table 2).

Discussion:

The study revealed that the incidence of bladder cancers with VH was high. Although these variants are associated with features of more aggressive behavior, the study's results did not show a significant impact on the survival expectations of the patients when all confounders were adjusted in multivariate analysis.

Keywords:
Urothelial Carcinoma, Variant Histology, Radical Cystectomy, Survival Analysis

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Conflict of interest:
The authors declare no conflicts of interest.

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Table 1 - Clinicopathological characteristics of the cohort.

	PUC (n=103; 57%)	VH (n=78; 43%)	P value
Age, median, range (years)	69 (62-74)	69 (62-75)	0,659
Male gender	88 (85%)	67(86%)	0,930
BMI 25	58 (56%)	38 (49%)	0,311
Estimated 10-year survival according CCI	21% (2-53)	21% (2-53)	0,220
TURBT muscle invasive	79 (76,7%)	65 (83,3%)	0,542
NAC	44 (42,7%)	20 (25,3%)	**0,017**
Time to RC, median, range (weeks)	19 (10-27)	16 (10-22)	0,094
Pathological stage			
T0	22 (21,3%)	5 (6,4%)	
pTa-T1-cis	31 (30,1%)	4 (5,1%)	**<0,0001**
T2	15 (14,6%)	11 (14,1%)	
T3-T4	35 (34,0%)	58 (74,4%)	
pN+	24 (23,3%)	29 (37,2%)	**0,042**
PSM	7 (6,8%)	14 (17,9%)	**0,020**
LVI	34 (33,0%)	47 (60,3%)	**<0,0001**

Legend: BMI – Body mass index; CCI – Charlson comorbidity index; LVI – Lymphvascular invasion; NAC – Neoadjuvant chemotherapy; PSM – Positive surgical margins; PUC – Pure urothelial carcinoma; RC – Radical cystectomy; VH – Variant histology

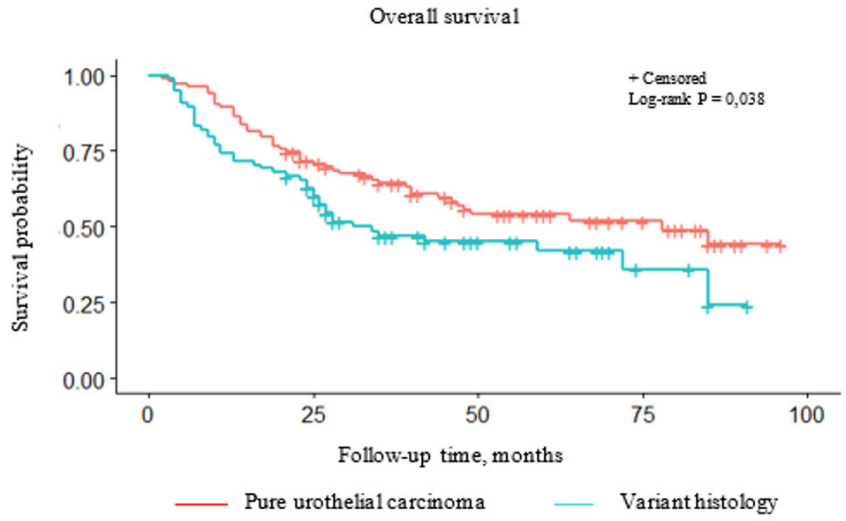

Figure 1 - The Kaplan Meier analysis assessing overall survival.

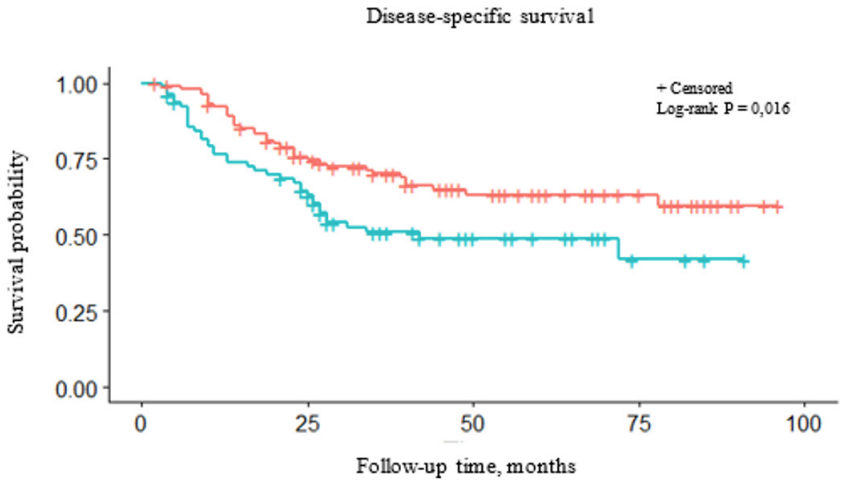

Figure 2 - The Kaplan Meier analysis assessing disease-specific survival.

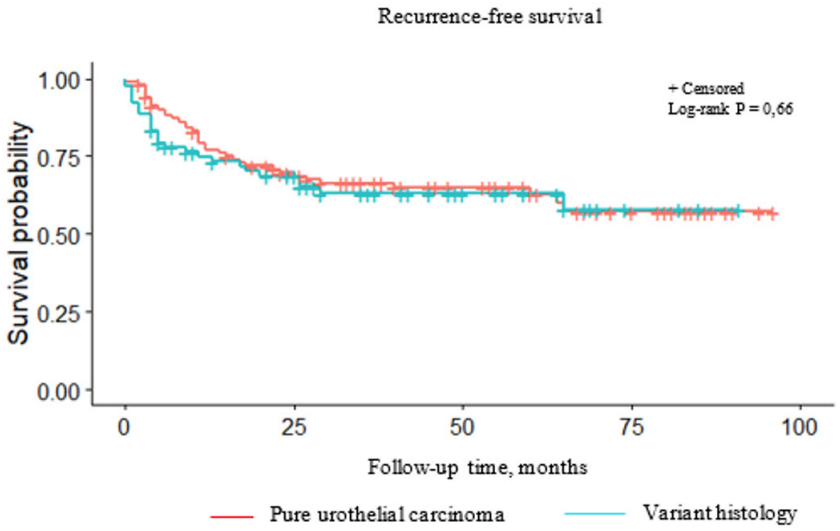

Figure 2 - The Kaplan Meier analysis assessing recurrence-free survival.

Table 2 - Multivariable Cox regression analyses predicting de risk of overall mortality (OM), disease-specific mortality (DSM), and recurrence

	OM		DSM		Recurrence	
	HR [95% CI]	**P value**	**HR [95% CI]**	**P value**	**HR [95% CI]**	**P value**
Age	0.99 [0.95;1.03]	0.55	0.99 [0.95;1.04]	0.76	0.98 [0.93;1.02]	0.34
Gender (male ref.)	0.74 [0.37;1.50]	0.41	0.86 [0.41;1.79]	0.68	0.92 [0.39;2.16]	0.85
BMI 25						
(<25.0 ref.)	0.65 [0.42;1.02]	0.06	0.63 [0.38;1.04]	0.07	0.71 [0.42;1.24]	0.23
Time to RC	1.00 [0.99;1.01]	0.18	1.00 [0.99;1.01]	0.65	1.00 [0.99;1.01]	0.79
NAC	0.76 [0.45;1.30]	0.32	0.80 [0.44;1.46]	0.47	0.95 [0.51;1.80]	0.88
Estimated 10-y survival CCI	0.99 [0.98;1.01]	0.27	0.99 [0.98;1.01]	0.69	0.99 [0.98;1.01]	0.26
pT3 (pT0-T2 ref)	3.30 [1.81;6.01]	< 0.001	4.67 [2.24;9.78]	< 0.001	3.51 [1.77;6.93]	< 0.001
pN+	1.97 [1.16;3.34]	0.01	1.93 [1.07;3.47]	0.03	32.54 [1.41;4.60]	< 0.001
PSM	1.99 [1.10;3.61]	0.02	2.35 [1.26;4.39]	0.007	0.08 [0.01;0.61]	0.01
LVI	1.54 [0.88;2.68]	0.13	2.03 [1.17;3.71]	0.02	1.93 [1.05;3.55]	0.03
PUC (ref)	-	-	-	-	-	-
VH	0.83 [0.52; 1.33]	0.44	0.91 [0.54; 1.53]	0.72	0.75 [0.42; 1.35]	0.33
Squamous	0.68 [0.36;1.31]	0.25	0.77 [0.38; 1.56]	0.47	0.72 [0.32; 1.59]	0.41
Micropapillary	0.58 [0.24;1.42]	0.23	0.63 [0.25; 1.58]	0.32	0.78 [0.28; 2.18]	0.64
Mixed	0.86 [0.41;1.81]	0.69	1.01 [0.46;2.24]	0.97	0.66 [0.35; 2.14]	0.38
Others	1.24 [0.64;2.41]	0.52	1.40 [0.46; 2.24]	0.39	0.66 [0.26; 1.69]	0.75
	Concordance (SE): 0.761 (0.026) Likelihood ratio test: p < 0.001 Wald test: p < 0.001 Score test: p < 0.001		**Concordance (SE): 0.795 (0.026)** Likelihood ratio test: p < 0.001 Wald test: p < 0.001 Score test: p < 0.001		**Concordance (SE): 0.779 (0.031)** Likelihood ratio test: p < 0.001 Wald test: p < 0.001 Score test: p < 0.001	

Legend: BMI – Body mass index; CCI – Charlson comorbidity index; LVI – Lymphvascular invasion; NAC – Neoadjuvant chemotherapy; PSM – Positive surgical margins; PUC – Pure urothelial carcinoma; RC – Radical cystectomy; VH – Variant histology

References:

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Journal of Statistics on Health Decision

EXTENDED ABSTRACT

Evolution of diet patterns over time in European countries from 1963 to 2013: an exploratory analysis using PCA for compositional data vectors.

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Introduction:

The study of the evolution of the diet of populations, namely in Europe, is crucial for decision-making by public authorities to promote healthy nutrition and prevent diet related noncommunicable diseases [1]. In fact, for instance, European Commission food law impacts the transformative potential of alternative proteins [2]. Composition food consumption in terms of each macronutrient, i.e., protein (animal and vegetal), fat and carbohydrate, has been usually investigated separately by nutrient [3]. However, these macronutrients constitute the whole diet of each individual and so, add up to a constant sum (in general 100% or 1 if the constitution of macronutrients in a diet is evaluated in percentage or proportion, respectively). Hence, it seems crucial that any analysis of diet compositions must take the constrained or compositional nature of the data. A set of several procedures has been developed in Statistics and applied in many fields to handle with this type of data structure, i.e., with compositional data [4,5].

Compositional data are multivariate observations that represent quantitative descriptions of the parts of some whole, conveying only relative information between parts. In mathematical notation, a p-multivariate observation corresponds to a sample unit described by a vector with p components. When all the components of this vector are positive numbers and contain relative information of parts of a whole (e.g, proportions, percentages), the nature of multivariate observation is compositional. This means that the important information between components is given by ratio rather difference. For instance, while the difference between 0.05 and 0.10 and between 0.45 and 0.50 are the same, in a compositional perspective, the number 0.05 should be considered as half of 0.10 while 0.45 forming a fraction 0.9 of 0.50. In mathematical notation, a D-part compositional observation is expressed as $\mathbf{x} = [x_1 x_2 \cdots x_D]$ with $x_j > 0$, for $j = 1, 2, ..., D$, and subject to the so-called unit-sum constraint, $\Sigma_{j=1}^{D} x_j = 1$.

In this paper, composition food consumption by both country and decade will be analyzed. In this context, a $(p \times D)$-multivariate observation is described by p variables each one with D-part compositional components. This type of multivariate observation is referred to as a (p-dimensional) compositional data vector as, for instance, the quantity of four macronutrients (p=4: animal protein, vegetal protein, fat, carbohydrate) across six years (D=6: 1963, 1973, 1983, 1993, 2003, 2013) by country). In [6], the operations in the space of the p-dimensional compositional data vectors were deduced: $\bigoplus$ for the "addition" (called perturbation) and $\bigotimes$ for the multiplication by a scalar (called powering) (for details see Equation 14 and 15 in [7]).

Recently, principal component analysis (PCA) [8] for modeling compositional data vectors was developed in [7]. In this study, this statistical procedure is explored to reduce the dimensionality of the evolution of diet patterns of ten countries in Europe during five decades. The main focus is on a temporal composition of the consumption in the diet of the four macronutrients.

Methods:

Daily caloric supply derived from each of the four macronutrients by country has been produced by Our World in Data and are freely accessible in [9]. For this study, data related to ten European countries (see Table 2) 10-by-10 years from 1963 to 2013 were collected. Hence, the data set includes ten observations featured by four 6-dimensional compositional variables: animal protein (**U1**), vegetal protein (**U2**), fat (**U3**), carbohydrate (**U4**). Given the structure of the data and following [7], a set of instructions in R were constructed to perform the PCA method on the correlation matrix for compositional data vectors (for more details see [10]).

Keywords:
Compositional data vectors, Diet pattern, Macronutrient shares, Principal component analysis.

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The authors declare no conflict of interest.

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Results:

The unit-loading and the variance of each principal component (PC) are displayed in Table 1 and the compositional scores of PC1 for the ten observations are shown in Table 2. PC1 accounts for 60.9% of the total variance and

$$PC1 = 0.475 \bigotimes \mathbf{U1} \bigoplus (-0.526) \bigotimes \mathbf{U2} \bigoplus 0.545 \bigotimes \mathbf{U3} \bigoplus (-0.448) \bigotimes \mathbf{U4}.$$

Table 1 - Coefficients of the PCs and the percentage of variance explained by each PC.

Components	PC1	PC2	PC3	PC4
Animal protein	0.475	-0.562	0.285	0.614
Vegetal protein	-0.526	-0.421	-0.661	0.330
Fat	0.545	-0.400	-0.464	-0.572
Carbohydrate	-0.448	-0.589	0.515	-0.432
Variance (%)	60.9	31.7	5.2	2.2

Table 2 - Score of the first PC.

Country	PC1 scores (%)
Finland	[24.0 24.2 21.0 13.6 8.8 8.3]
France	[9.0 18.8 16.7 19.5 22.1 13.9]
Germany	[36.7 19.8 12.4 13.6 9.6 7.9]
Greece	[11.1 12.6 11.9 14.7 18.4 31.4]
Italy	[5.9 6.3 18.5 23.9 21.2 24.2]
Norway	[28.5 36.3 13.2 8.1 7.3 6.5]
Portugal	[3.5 4.7 8.5 13.9 27.3 42.1]
Spain	[2.8 4.3 10.3 18.4 36.2 28.1]
Sweden	[40.1 19.8 14.3 8.7 9.1 8.0]
United Kingdom	[40.8 23.3 15.0 10.4 5.0 5.6]

Then, considering the coefficient signals, PC1 represents a balance of consumption of animal protein and fat comparatively with vegetal protein and carbohydrate such that higher the score of PC1, the greater the fraction consumption of animal protein and fat compared with those of vegetal protein and carbohydrate.

It is clearly observed in Table 2 that there existed a higher percentage of consumption of animal protein and fat in the first decade in Finland, Germany, Norway, Sweden and United Kingdom, while this percentage is higher, in general, for the other countries in the last two decades.

Discussion:

PCA can be applied on data sets that can be arranged into compositional vector. In terms of macronutrient diet pattern, PCA revealed different shares of animal protein and fat between countries further Mediterranean region and further north in Europe from 1963 to 2013.

Acknowledgements:

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Journal of Statistics on Health Decision

EXTENDED ABSTRACT

Mortality prediction scores in burn patients – a comparative analysis

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Introduction:

The aim of this study was to assess and to compare the accuracy of different mortality prediction models used in the burn population from a tertiary Burn Unit (BU), taking in account the clinical and demographic characteristics.of survivors and non-survivors.

Methods:

A retrospective study of adult burn patients admitted to a BU in a 5-year period was performed. Toxic epidermal necrolysis and polytraumatized patients were not included. Mortality rate was assessed. Survivors and non-survivors clinical and sociodemographic characteristics were analyzed and compared. Four models were included, namely Abbreviated Burn Severity Index (ABSI), Belgian Outcome in Burn Injury (BOBI), revised-Baux and Ryan model. Observed and predicted mortality were compared using Hosmer-Lemeshow test for models goodness-of-fit, receiver operating curves (ROC) and area under curve (AUC) for discriminative performance evaluation.

Results:

The sample was composed by 641 patients, from which 58,2% were male. Patients mean age was 60.02 ± 18.97 years and total burned surface area (TBSA) was 12.94 ± 15.11 %. Third degree burns were present in 71% and inhalation injury in 12.3%. Observed mortality rate was 9.4% (n=60). Non-survivors were significantly older (73 vs. 60 years; $p<0.001$), had a larger TBSA (27.75 vs. 7%; $p<0.001$), higher frequency of third-degree burns (96.7 vs. 68.3%; $p<0.001$) and inhalation injury (31,7% vs. 10,3%; $p<0.001$), but no gender significant difference was verified. All models demonstrated an adequate goodness-of-fit, all with p-values >0.05 in Hosmer-Lemeshow test assessment. Revised-Baux (AUC 0.870 ± 0.025), ABSI (AUC 0.850 ± 0.026) and BOBI (AUC 0.831 ± 0.026) have demonstrated good discriminative power and Ryan model (0.774 ± 0.030) was only moderate.

Discussion:

The four models revealed proper predictive performance, with revised-Baux presenting as the most accurate model for mortality prediction. Their use in the BU represents a practical and valuable tool for risk stratification, treatment appropriateness and improve the burns care quality control.

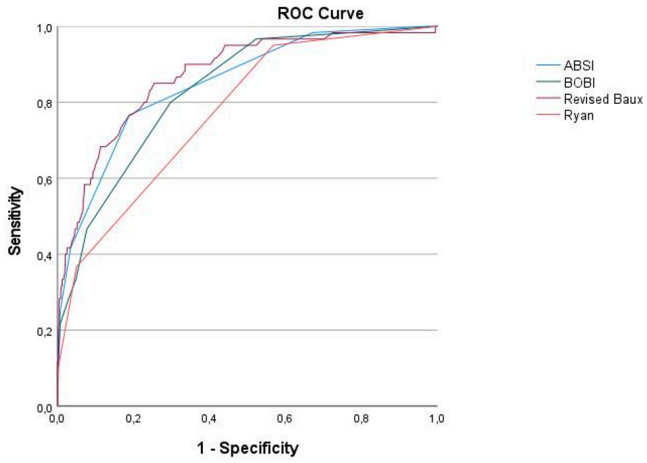

Figure 1 - Mortality Prediction Models ROC Curve

Keywords:
Burns, Mortality, Injury Severity Score

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EXTENDED ABSTRACT

Applying machine learning methods to predict the Parkinson´s Disease Questionnaire-39 Summary Index

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Introduction:

Health-related quality of life (HRQoL) gained importance in the last decades and is considered to be an important outcome measure in chronic diseases studies. HRQoL disease specific instruments reflect the consequences of that disease to a particular person and are sensitive to change in perceived HRQoL. In Parkinson's disease (PD) several disease specific HRQoL instruments have become available in the past few years. A 2002 systematic review of HRQoL instruments in PD concluded that in many situations the Parkinson´s Disease Questionnaire -39 (PDQ-39) is the most appropriate HRQoL instrument, because it is the scale that has been tested most thoroughly, has adequate clinimetric characteristics, has been used in the largest number of studies, and is available in many languages [1].

The PQD-39 is a 39-item self-report questionnaire, which assesses PD specific health related quality over the last month. It assesses how often patients experience difficulties across the 8 quality of life dimensions and the impact of PD on specific dimensions of functioning and well-being [2]. Its summary index (PDQ-39SI) is a widely used patient-reported clinical trial endpoint. Peter Hagell and Maria H. Nilsson assessed the unidimensionality of the PDQ-39 and PDQ-39SI using Rasch and confirmatory factor analysis and concluded its multidimensional nature [3].

The objective of this study is to do an exploratory analysis on the multidimensional nature of the PDQ-39SI using machine learning methods to improve the interpretability of the score and obtain a model to predict the perceived quality of life of people with PD.

Methods:

Data analysis was completed with R version 4.1.1. Data used in the preparation of this article were obtained from the Parkinson's Real-World Impact assesSMent (PRISM) database. PRISM study and database was funded by BIAL – Portela & C[a], S.A., designed in collaboration with The Cure Parkinson's Trust, an advocacy group based in the United Kingdom (UK), and reviewed by the PRISM steering committee.

The PRISM database contains data from 861 people from 5 European countries with PD collected in the context of an observational study with cross-sectional design [4].

PDQ-39SI multivariable nature was first assessed using the Expectation-Maximization (EM) algorithm (Figure 1). Based on the latent classes, a transformation of PDQ-39SI from continuous to binomial outcome was performed: mild vs severe symptoms impacting their quality of life.

Clinically relevant variables for modeling the PDQ-39SI were initially selected from the PRISM database. Univariate logistic regressions were created with the PDQ-39SI as a function of each of the previously selected variables. The variables presenting a p-value below 0.05 were ordered according to their impact on the odds ratio and included in the machine learning models by forward selection based on the resulting AUC values. Incomplete observations were then removed resulting in a dataset with 615 patients

Before training the models, 20% of the dataset was saved to be used as independent validation data. With the remaining 80% of the dataset (training set), several models were trained to predict the classes obtained through EM. A repeated 10-fold cross validation was performed on this training set to estimate the respective ROC curves (Figure 2). Additionally, the performance of each model obtained with the 20% independent validation set was also assessed through the plotting of ROC curves (Figure 3).

Keywords:
Health-Related Quality of Life, Machine Learning, Parkinson Disease, Parkinson´s Disease Questionnaire -39, Parkinson´s Disease Questionnaire -39 Summary Index

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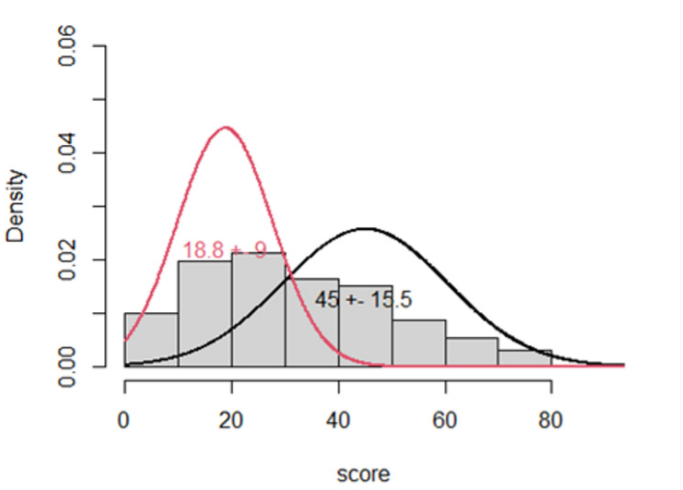

Figure 1 - Latent classes on Parkinson´s Disease Summary Index. ***Legend:*** With the use of Expectation Maximization algorithm (2 kernels) 2 latent classes are described: **(i)** red distribution with mean of 18.8 and standard deviation of ± 9, and **(ii)** black distribution with mean of 45 and standard deviation of 15.5. Interception of the two distributions at the 31 value.

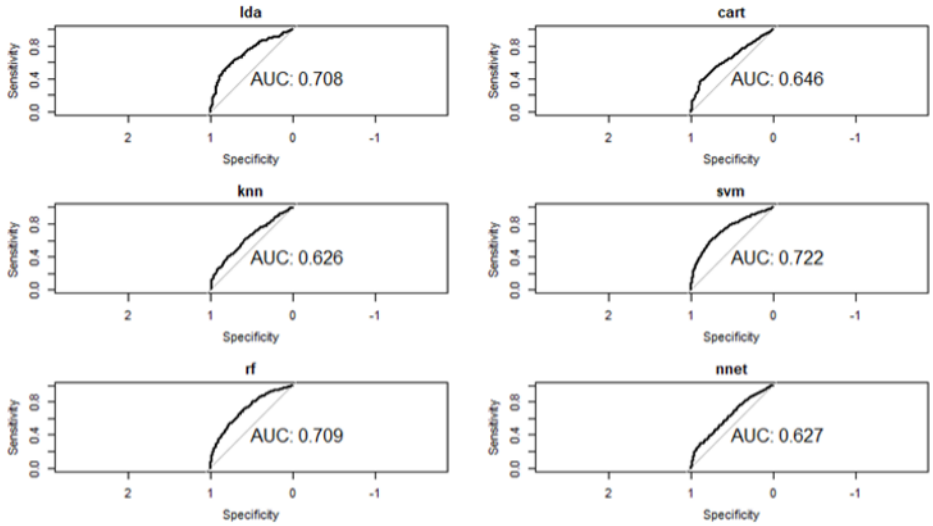

Figure 2 - Performance estimation of different machine learning methods for PDQ-39SI modeling on the training set using repeated 10-fold cross validation. ***Legend:*** ROC curves (receiver operating characteristic curves) of the repeated 10-fold cross validation training set (80% of the dataset) with **(i)** lda (Linear Discriminant Analysis), **(ii)** cart (Classification and Regression Tree, splitting index: gini), **(iii)** knn (K-nearest Neighbors, K=3), **(iv)** svm (Support Vector Machine, kernel: radial basis function), **(v)** rf (Random Forest, number of trees = 500), **(vi)** nnet (Feedforward Neural Network, 1 hidden layer with 5 neurons). AUC (area under the curve)

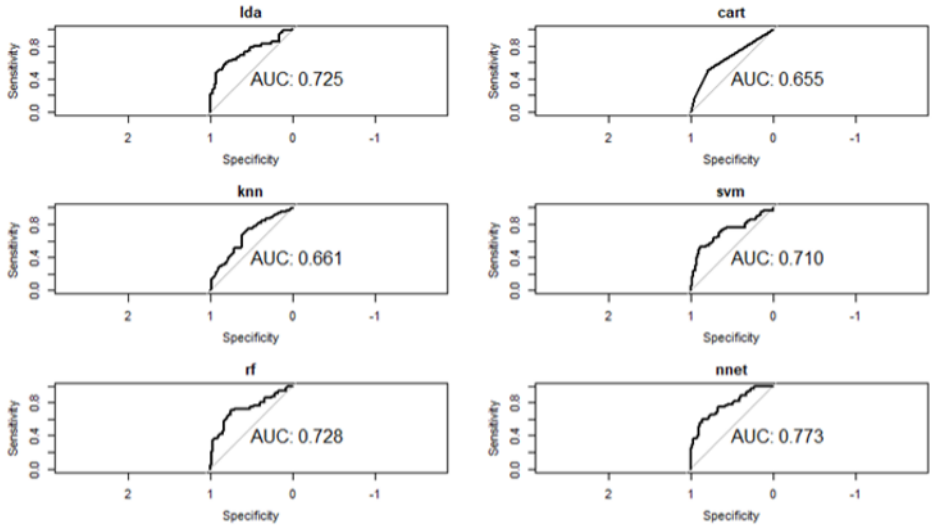

Figure 3 - Performance of different machine learning methods for PDQ-39SI modeling on the independent validation set. ***Legend:*** ROC curves (receiver operating characteristic curves) of the independent validation set (20% of the dataset) with **(i)** lda (Linear Discriminant Analysis), **(ii)** cart (Classification and Regression Tree, splitting index: gini), **(iii)** knn (K-nearest Neighbors, K=3), **(iv)** svm (Support Vector Machine, kernel: radial basis function), **(v)** rf (Random Forest, number of trees = 500), **(vi)** nnet (Feedforward Neural Network, 1 hidden layer with 5 neurons). AUC (area under the curve)

Results:

The PDQ-39SI was converted from a continuous outcome into two categories based on the impact on the quality of life of the person with PD: mild (with a PDQ-39SI below 31) and severe (PDQ-39SI above 31).

The ROC curves obtained with repeated cross-validation for each of the trained models are presented in figure 2 while the ROC curves obtained with the independent validation data set are presented in figure 3.

Discussion:

The obtention of a binomial classification for the PDQ-39SI can facilitate its interpretation and harmonize its utilization by different health care providers (HCP). Additionally, machine learning models applied to clinical variables can be used to predict to which of these classes a person with Parkinson's disease would belong. This information would allow HCPs to predict which of the patients are expected to have a lower quality of life.

The PDQ-39SI is based on the patient's interpretation about several dimensions measuring his/her perceived quality of life. The subjectivity of the information collected through a survey is considered a limitation of this study.

The results obtained demonstrate a good performance of Linear Discriminant Analysis, Support Vector Machine and Random Forest methods. Future work will focus on hyperparameters optimization and on studying a wider range of variables to accommodate possible confounding factors.

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Journal of Statistics on Health Decision

EXTENDED ABSTRACT

Assessment of the stability of a procedure for variables selection in high dimensionality data: an application to genomic data - Alzheimer's Disease

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Introduction:

Alzheimer's disease (AD) is a neurodegenerative disease and a complex disorder caused by a combination of environmental and genetic factors [1]. One of the main goals of modern genetics has been unraveling the genetic background of common complex disorders, so Genome-Wide Association Studies have been conducted with large-scale data sets of genetic variants (Single Nucleotide Polymorphisms - SNPs). Most of these studies have relied on approaches that consist of a univariate analysis of the association of each SNP with the phenotype. Consequently, the possibility of a correlational and interactional structure between SNPs is not considered [2]. The challenge in finding a plausible method to apply to genetic data is due to its high dimensionality.

This work aims to assess the stability of a procedure that identifies association between relevant SNPs and AD in a structure where the number of SNPs (p) is much more than the number of individuals (n), ($p >>> n$ problem).

Methods:

The genotypic data used in this study was obtained from the Alzheimer's Disease Neuroimaging Initiative (ADNI) – 1 study (adni.loni.usc.edu). In this work, were considered 451 individuals (163 cognitively normal - 36.1%; 288 AD – 63.9%) and 518257 SNPs [3]. A hundred prediction models were constructed using Least Absolute Shrinkage and Selection Operator (LASSO) and applied a feature selection and explanation procedure [3]. A weight based on Akaike's Information Criterion (AIC) was calculated for each SNP. The criteria for classifying a SNP as important was its weight being at least 0.8 and only these SNPs were part of the final model proposed (original model). We re-run the analysis excluding one selected variable at a time to measure how sensitive the findings were. In addition, we also re-run the analysis after removing from the data SNPs selected by LASSO but not considered important according to our procedure (weight < 0.8). For this purpose, three SNPs, classified as non-important, were randomly chosen. The sensitivity of the resulting models to the removal of these SNPs was also evaluated.

Results:

The procedure that gave rise to the original model led to the choice of 11 SNPs (the first row of the heatmap represented in Fig. 1). The removal of the SNPs rs12054808, rs4391167 and rs1052242 from the data had no impact on the selected variables, but the weights of the remaining SNPs increased. The removal of the SNPs rs11625567 and rs6090754 also had no considerable impact: only the SNP rs4391167 became unimportant, but the removal of the SNP rs6090754 caused the weight of the remaining SNPs to increase. Contrariwise, removing the SNPs rs486512, rs2075650, rs6427160, rs4982401 and rs11906462 made all the SNPs unimportant. The removal of the SNP rs573399 also made changes: only three SNPs remained important. Regarding the SNPs that are not part of the original model, their removal did not have a considerable impact on the selected variables: only the SNP rs4391167 became unimportant with the removal of the SNPs rs1387089 and rs1582317. A summary of the results presented is in Fig. 1.

Keywords:
Alzheimer's Disease, Single Nucleotide Polymorphisms, Akaike's Information Criterion, Least Absolute Shrinkage and Selection Operator, Stability

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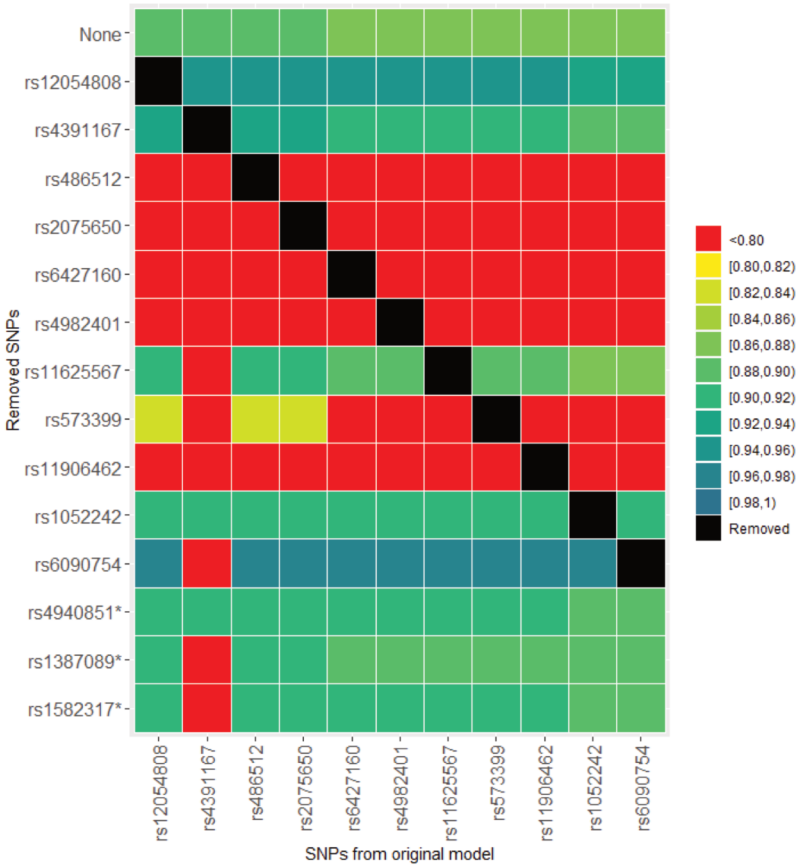

Figure 1 - Scheme of the SNPs selected in the original model (row "None") and after removal of these SNPs from the data one by one. The SNPs assigned with * are not part of the original model. The SNPs are colored according to their weight.

Discussion:

It is possible that the SNPs that when removed cause substantial changes in the selection of SNPs compared to the original model are the really important ones. An argument that can support this hypothesis is that the removal from the data of almost all SNPs tested makes the SNP rs4391167 unimportant and the removal of this SNP from the data had no impact on the selection of the SNPs. Another argument is that the removal of the SNPs that are not included in the original model did not have a substantial considerable impact on the selection of SNPs. In the future, testing the sensitivity of the model to the removal of more SNPs like this will be important.

Acknowledgements:

We thank ADNI for supplying us with their databases.

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Journal of Statistics on Health Decision

EXTENDED ABSTRACT

Exploratory Analysis based on Relative Risk on the incidence of different causes of death in mortality in the Region of Aveiro

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[2]Public Health Unit – ACES Baixo Vouga
[3]Department of Mathematics – University of Aveiro (UA)

Introduction:

The Baixo Vouga Group of Health Centers (ACES) is one of the six ACES belonging to the Regional Health Administration of the Center. According to 2018 data from the National Statistics Institute (INE), ACES Baixo Vouga covers a resident population of 362,100 inhabitants, in which the average life expectancy of this population was estimated at 81.5 years, in the triennium 2015-2017 – lower than the value of ARS Centro (81.7) and equal to that of Portugal.

This work emerged with the aim of understanding which causes of death present a higher risk of death between the years 2015 and 2019. For this, the Relative Risk was used as a measure to evaluate and compare the mortality of the different municipalities with national mortality in order to obtain statistical conclusions regarding the behavior of the different municipalities. [1,2]

Methods:

The data used were first taken from the INE, according to the indicator "Deaths (No.) by Place of residence (NUTS - 2013), Sex, Age group and Cause of death (European Shortlist); Yearly". These data are according to age and sex and divided by county. The aforementioned indicator had many variables, that is, causes of death, and those that did not have relevant data, that is, had missing or few records, were excluded.

Subsequently, PORData was used to obtain the population of each of the municipalities, in order to standardize the same via excel. Having standardized the data, we moved on to statistical analysis through line graphs for each variable / cause of death, to observe the counties with the highest risk for a given variable.

In the same way, national population data were obtained with the objective of statistically comparing the data of each municipality with the national data, and visually it was possible to observe statistically significant differences.

Then, the relative risk of each board was calculated for all variables, in the different biennia and a cohort study was carried out, in which a significance of 0.05% was defined. [2,3]

The entire analysis was carried out using R, including epiR package.

Results:

The results obtained, taking into account the p-value, can be classified into: lower risk of death, if the RR value is less than 1; without association between variables, if the value of RR is equal to 1; and at higher risk of death, if the RR value is greater than 1. According to the Relative Risk values and the p-values, 2 of the municipalities stand out from the others as they present more significant results.

On the one hand, it was possible to observe that the municipality that has a relative risk greater than 1, in a greater number of variables, was the municipality of Anadia. The data relating to this municipality can be seen in Table 1.

On the other hand, the municipality of Aveiro proved to be the one with the highest number of variables with a relative risk of less than 1. The data relating to this municipality can be seen in Table 2.

In addition, the municipality of Murtosa, despite not showing statistical significance in the relative risks, their tendency is to increase. The data relating to this municipality can be seen in Table 3.

Keywords:
Mortality, Relative Risk, Aveiro, Statistical Analysis

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Table 1 - Relative Risk Values for the municipality of Anadia

Anadia	**2015/2016**		**2016/2017**		**2017/2018**		**2018/2019**	
Variables	**RR**	**p-value**	**RR**	**p-value**	**RR**	**p-value**	**RR**	**p-value**
All causes of death	1.12	*	1.15	*	1.27	*	1.26	*
Circulatory system diseases	1.22	*	1.26	*	1.32	*	1.31	*
Digestive system diseases	1.24		1.26		1.67	*	2.03	*
Abnormal symptoms, signs and laboratory and clinical examination findings not elsewhere classified	1.45		1.26		1.53	*	1.49	*

Table 2 - Relative Risk Values for the municipality of Aveiro

Aveiro	**2015/2016**		**2016/2017**		**2017/2018**		**2018/2019**	
Variables	**RR**	**p-value**	**RR**	**p-value**	**RR**	**p-value**	**RR**	**p-value**
All causes of death	0.88	*	0.89	*	0.89	*	0.86	*
Endocrine, nutritional and metabolic diseases	0.59	*	0.66	*	0.66	*	0.53	*
Diabetes mellitus	0.58	*	0.6	*	0.6	*	0.49	*
Circulatory system diseases	0.81	*	0.82	*	0.82	*	0.87	*
Other sudden deaths of unknown cause, unassisted deaths, other ill-defined and non-specific causes	0.35	*	0.22	*	0.22	*	0.36	*

Table 3 - Relative Risk Values for the municipality of Murtosa

Murtosa	**2015/2016**		**2016/2017**		**2017/2018**		**2018/2019**	
Variables	**RR**	**p-value**	**RR**	**p-value**	**RR**	**p-value**	**RR**	**p-value**
Endocrine, nutritional and metabolic diseases	2.09	*	1.82		2.02	*	1.743	
Abnormal symptoms, signs and laboratory and clinical examination findings not elsewhere classified	1.59		2.21	*	2.48	*	2.39	*
Other sudden deaths of unknown cause, unassisted deaths, other ill-defined and non-specific causes	0.72		1.18		1.75		1.91	*

Discussion:

Certain variables were observed that presented a greater risk in certain municipalities. These higher risks could be associated with factors such as age-related comorbidities, other disease-specific risk factors or even misclassification.

The municipality of Anadia has a statistically significant relative risk greater than 1 in several variables, which may be indicative of the wrong use of data insertion protocols, used by professionals of health. These data can be used to determine the causes of these risks of death in order to reduce them in the near future.

Even though the municipality of Murtosa does not have significant relative risk values, as its tendency is to increase, measures similar to those of the municipality of Anadia should be applied. The data can be used to discover the reason for this growth in order to reverse the effect and decrease the risk of death over the next few years.

In the municipality of Aveiro, the relative risk is less than 1 in several variables, which may have clinical use because because understanding the factors behind this lower risk might allow us to change the mortality dynamic in other municipalities with climatic, financial conditions, among others, similar to those of Aveiro.

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Journal of Statistics on Health Decision

EXTENDED ABSTRACT

Prognostic predictors in stroke patients undergoing thrombectomy with recanalization

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Introduction:

Stroke is a major cause of morbidity and mortality. Thrombectomy is a highly effective and approved treatment for patients with ischemic stroke and large vessel occlusion of the anterior circulation [1] . However, despite effective recanalization, a considerable proportion of patients remains with significant neurological damage. The aim of this study was to evaluate outcome predictors in ischemic stroke patients undergoing thrombectomy with effective recanalization.

Methods:

A consecutive sample of patients with acute ischemic stroke due to large vessel occlusion, submitted to endovascular treatment with effective recanalization at a comprehensive stroke center in the north of Portugal was analyzed. Clinical, demographic, and laboratory variables (age, gender, hypotension, diabetes mellitus, heart disease, dyslipidemia, previous CVA, cardioembolic stroke, systolic blood pressure, diastolic blood pressure, glycemia, initial NIH Stroke Scale (NIHSS) and D-dimer) were obtained from the initial evaluation. The outcome of interest was good functional outcome defined as a value of 0-2 on the modified Rankin scale at 3 months. A descriptive analysis was performed using absolute and relative frequencies for qualitative variables and mean and standard deviation or median and interquartile range for quantitative variables. The normality of quantitative variables was available by the Shapiro-Wilk test. Variables with a p 0.20 in the univariable logistic regression analysis were included in a logistic regression model to determine the independent predictors [2]. Performance of multivariable model displayed as area under the receiver operating curve (AUC) and corresponding 95 % confidence interval. Residual analysis and the diagnosis of influential cases was performed through the graphical analysis. Only two observations were candidate outliers, but these were included in the final model, their removal did not improve the significance and quality of the model fit. Values of $p<0.05$ were considered statistically significant. All analyses were performed with R software (version 4.0.3).

Results:

A total of 116 patients were included in the analysis, and 63 had a favorable outcome. In the univariable analysis, age, diabetes, blood glucose, and stroke severity measured by the NIHSS scale showed an association with unfavorable outcome. In multivariable analysis, only age and NIHSS scale were statistically significant (Table 1).

Discussion:

Despite effective recanalization, a significant proportion of patients in this cohort failed to achieve functional independent (46%, n=53). Univariate analysis demonstrated that older age, diabetes, elevated blood sugar and higher NIHSS score were associated with lower odds of achieving functional independence at 3 months. These results are in accordance to the literature [3]. In multivariate analysis, however, only age and NIHSS maintained the association. This suggests that the association between diabetes/glycemia and unfavorable outcome is due, at least in part, to a confounding effect, as diabetes is more frequent in elderly patients [4]. This study has an important limitation that should be acknowledged: time to recanalization was not available for analysis, and this factor has been shown to be a major predictor of outcome in stroke [5].

Keywords:
Stroke, thrombectomy, modelling

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Conflict of interest:
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Table 1 - Logistic regression analysis of predictors of favorable outcome

	Univariate Logistic Regression		Multivariate Logistic Regression	
Characteristics	**OR (95% CI)**	***p***	**OR (95% CI)**	***p***
Age (years)	0.93 (0.89 – 0.96)	0.0002	0.92 (0.86 – 0.97)	0.003
Gender (Male)	0.82 (0.39 – 1.72)	0.6010	–	–
Hypertension	0.47 (0.19 – 1.08)	0.0828	1.49 (0.38 – 6.01)	0.563
Diabetes mellitus	0.16 (0.06 – 0.41)	0.0002	0.27 (0.06 – 1.07)	0.070
Heart disease	0.73 (0.34 – 1.56)	0.4200	–	–
Dyslipidemia	0.51 (0.24 – 1.07)	0.0760	0.39 (0.12 – 1.11)	0.085
Previous CVA	0.50 (0.18 – 1.31)	0.1630	0.39 (0.09 – 1.45)	0.166
Cardioembolic stroke	0.55 (0.24 – 1.19)	0.1339	1.90 (0.60 – 6.34)	0.278
SBP	0.99 (0.97 – 1.01)	0.2970	–	–
DBP	1.01 (0.98 – 1.03)	0.6020	–	–
Glycemia	0.98 (0.97 – 0.99)	0.0024	0.99 (0.97 – 1.00)	0.107
Initial NIHSS	0.82 (0.39 – 1.72)	<0.001	0.10 (0.83 – 0.96)	0.002
D-dimer	0.89 (0.75 –1.00)	0.0894	0.97 (0.76 – 1.19)	0.818

CI: confidence interval; SBP: Systolic blood pressure; DBP: Diastolic blood pressure

In conclusion, age and higher NIHSS score are important predictors of poor functional outcome despite recanalization in stroke patients submitted to thrombectomy. More therapeutic options are required for these patients to optimize outcome.

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EXTENDED ABSTRACT

(Dis)similarities of primary health care indicators, a special case of USF Arte Nova

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Introduction:

Primary Health Care (PHC) are focused on the needs of people and communities and focuses on aspects of physical, mental, social and well-being health, and therefore it is necessary to monitor whether services are being well provided to the community [1,2].

In recent years, PHC have been undergoing a reform that aims to transform it organizationally, allowing greater proximity to communities and better service delivery [3]. In this sense, there has been the implementation of health indicators whose objective is for the health unit team to manage it and improve its worst points according to the results of the indicators. The indicators are divided into 22 Dimensions (e.g., Personalization). Their results are used for the weighted calculation of the Global Performance Index which gives an indication, as the name implies, of the overall performance of that unit [5].

This study aims to explore the indicators to find a possible correlation and proximity between them and to obtain more knowledge about the behavior of the indicators.

Methods:

The statistical analysis was performed using R (version 4.1.3), most of which was presented in shiny app format [4].

The data were collected from the Primary Health Care Identity Card - Contracting, Indicators website [5]. The database is composed of monthly results of 117 indicators for 41 Health Care Units of the Baixo Vouga ACES from 2017 to 2021. The repeated measure correlation between the different indicators with all Units was evaluated (package rmcorr). The correlation between the indicators only with the data of the USF Arte Nova was also performed and, from this point on, the analysis was restricted to this Unit. An exploratory analysis was performed using ggplot2 and scales packages to assess whether the behavior (indicator result over time) of the different indicators of the same dimension was similar, with subsequent consistency analysis of the different dimensions with cls.scatt.data from clv packages. Finally, a hierarchical time series clustering using Shape-based distance (based on coefficient-normalized cross-correlation), with the dtwclust package, was performed for all dimensions.

Results:

The pairs of indicators 2013.035.01 FL/2013.261.01 FL and 2013.006.01 FL/2013.100.01 FL correspond to the two highest positive correlations in both analysis (all Units and only USF Arte Nova). Nevertheless, the correlations of the other pairs of indicators are different between the two approaches. Regarding the 10 highest negative correlations, the scenario observed is already different, the pairs of indicators are very diversified (Table 1).

The most consistent dimensions were "Distribuição de Consultas Presenciais no Dia" (Table 2). There are seven dimensions whose distance is 0 because they only have one indicator associated and the dimensions consisting of only 2 indicators are unsuitable for clustering.

From the cluster analysis, it was found that indeed the consistency of the dimensions influences the results of the cluster analysis. When we analyze the most consistent dimension just from the graphic visualization there are two different behaviors in the indicators, three indicators with very similar behavior and another with an opposite behavior. This ended up also being reflected in the clusters, that is, the clusters formed followed this distinction in behavior visible graphically (Figure 1).

Keywords:
Health indicators, health care unit, association analysis

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Table 1 - Ten highest positive and negative correlations between Health Indicators in all Units and USF Arte Nova data.

Repeated Measures		USF Arte Nova	
Correlation	**Indicators**	**Correlation**	**Indicators**
Positive			
0.9997	2013.035.01 FL/2013.261.01 FL	1.0000	2013.035.01 FL/2013.261.01 FL
0.9841	2013.006.01 FL/2013.100.01 FL	0.9980	2013.006.01 FL/2013.100.01 FL
0.9784	2013.053.01 FL/2018.395.01 FL	0.9940	2013.037.01 FL/2013.100.01 FL
0.9780	2013.047.01 FL/2013.053.01 FL	0.9930	2013.053.01 FL/2013.100.01 FL
0.9650	2013.015.01 FL/2013.296.02 FL	0.9921	2013.006.01 FL/2013.037.01 FL
0.9357	2013.297.01 FL/2018.409.01 FL	0.9902	2013.015.01 FL/2013.296.02 FL
0.9349	2017.352.01 FL/2017.353.01 FL	0.9884	2013.037.01 FL/2013.053.01 FL
0.9318	2013.031.01 FL/2013.063.01 FL	0.9883	2013.023.01 FL/2013.053.01 FL
0.9232	2018.339.01 FL/2018.410.01 FL	0.9875	2013.006.01 FL/2013.053.01 FL
0.9174	2013.017.01 FL/2013.269.01 FL	0.9859	2013.032.01 FL/2013.054.01 FL
Negative			
-0.8423	2013.020.01 FL/2015.314.01 FL	-0.9861	2013.054.01 FL/2013.276.01 FL
-0.8029	2015.314.01 FL/2015.316.01 FL	-0.9853	2013.032.01 FL/2013.276.01 FL
-0.7890	2013.039.01 FL/2015.314.01 FL	-0.9786	2017.346.01 FL/2017.349.01 FL
-0.7754	2013.261.01 FL/2015.314.01 FL	-0.9754	2017.346.01 FL/2017.348.01 FL
-0.7742	2013.035.01 FL/2015.314.01 FL	-0.9674	2017.331.01 FL/2017.346.01 FL
-0.7737	2013.019.01 FL/2015.314.01 FL	-0.9557	2013.015.01 FL/2017.346.01 FL
-0.7487	2013.018.01 FL/2015.314.01 FL	-0.9554	2013.001.01 FL/2013.032.01 FL
-0.7279	2013.037.01 FL/2015.314.01 FL	-0.9534	2013.296.02 FL/2017.346.01 FL
-0.6780	2013.038.01 FL/2015.314.01 FL	-0.9521	2013.001.01 FL/2013.054.01 FL
-0.6577	2013.091.01 FL/2015.314.01 FL	-0.9285	2013.046.01 FL/2017.346.01 FL

Table 2 - Consistency intra Dimensions of USF Arte Nova based on centroids.

Dimension (number os indicators)	**Intra Cluster Distance**
Distribuição das Consultas Presenciais no Dia (4)	0.007029137
Tempos Máximos de Resposta Garantidos (2)	0.007809507
Prescrição MCDT (2)	0.007895714
Personalização (2)	0.009009222
Consulta no Próprio Dia (6)	0.042651585
Prescrição Farmacoterapêutica (9)	0.453415056
Saúde da Mulher (15)	0.573905393
Saúde do Idoso (3)	0.650924029
Saúde do Adulto (12)	0.685108403
Doenças Aparelho Respiratório (2)	0.693297328
Cobertura ou Utilização (7)	0.695591546
Hipertensão Arterial (8)	0.716080569
Saúde Infantil e Juvenil (14)	0.742260558
Diabetes Mellitus (15)	0.788553885
Multimorbilidade e Outros Tipos de Doenças (2)	0.982404119
Acesso (1)	0.000000000
Atividades de Governação Clínica no ACES (1)	0.000000000
Formação da Equipa Multiprofissional (1)	0.000000000
Formação de Internos e Alunos (1)	0.000000000
Programas de Melhoria Contínua de Qualidade e Processos Assistenciais Integrados (1)	0.000000000
Segurança de Utentes (1)	0.000000000
Serviços de Carácter Assistencial (1)	0.000000000

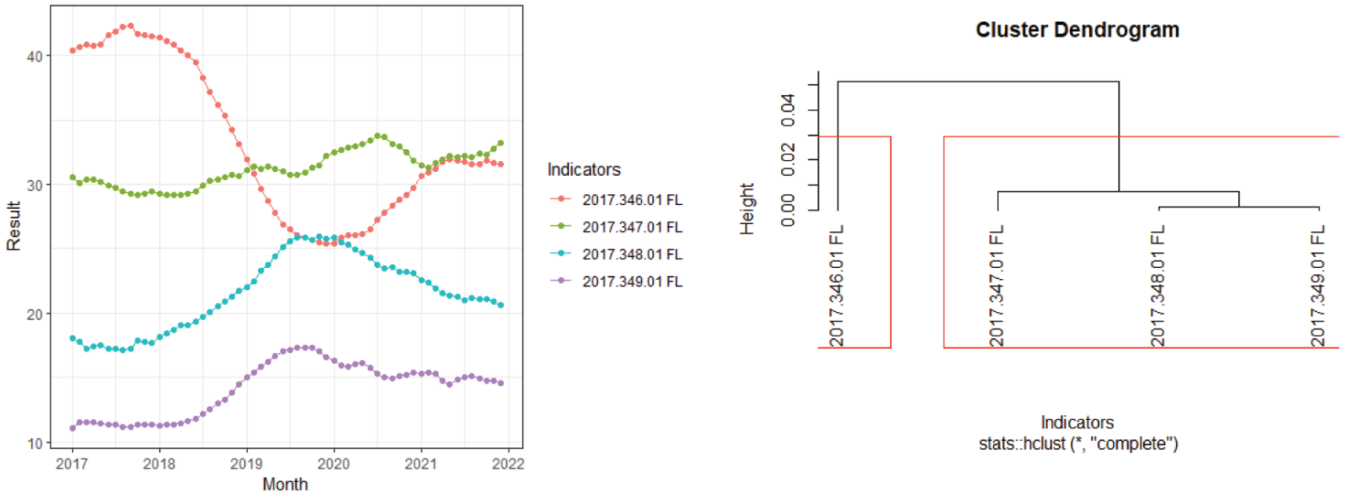

Figure 1 - Visualization of the Indicators of the "Distribuição de Consultas Presenciais no Dia" dimension and respective dendrogram of USF Arte Nova.

Discussion:

The results show that there are pairs of indicators with a clear correlation. This happens, for example, in the first pair of indicators in which both are related to screening or assessment of diabetic foot ulcers, which is expected to be directly proportional. It is not advisable to assume that the correlations obtained only with USF Arte Nova are the same as when using all units (repeated measures). This is explained by the fact that the different types of units have different management and operation.

By the analysis of consistencies and clusters, it is possible to identify groups of similar indicators in some dimensions, while in others this did not prove to be a reality.

The analysis performed allows for more detailed knowledge about the indicators and thus better planning for continuous improvement of the quality of health services. In other words, the more knowledge there is, the better health services can become.

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Journal of Statistics on Health Decision

EXTENDED ABSTRACT

Antimicrobial susceptibility profile of bacteria associated with urinary tract infections in Aveiro, 2021

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Introduction:

Urinary tract infections (UTIs) are among the most common bacterial infections. These affect around 150 million people per year globally [1], [2]. UTI diagnosis and treatment at an early stage is essential, as it allows the reduction of morbidity rates [3]. However, this implies that in many cases antimicrobial therapy is prescribed empirically. To administer an appropriate empirical therapy, it is essential to know the main bacteria involved in UTIs, as well as their susceptibility profiles. This knowledge allows for the control of increased antimicrobial resistance (AMR) [3], which has reached alarming levels in pathogens associated with UTIs and beyond, resulting from the generalized and indiscriminate use of antimicrobial agents [4].

This work aims to assess the antimicrobial susceptibility profiles of the most frequent bacterial isolates associated with UTIs in the community of the district of Aveiro, to establish appropriate empirical therapies.

Methods:

The data used in this work included the results of the antimicrobial susceptibility testing (AST) performed on urine samples from patients with UTI, that is, with a positive urine culture. These samples were collected in the collection points of the medical clinical analysis laboratory Avelab between 02/01/2021 and 31/12/2021. The identification of bacteria and AST were performed with the automated system BD Phoenix™ and the European Committee on Antimicrobial Susceptibility Testing (EUCAST) recommendations were considered. According to EUCAST, there are three interpretative categories: a bacteria can be resistant (R), susceptible with increased exposure (I) or susceptible with a standard dosing regimen (S) to an antimicrobial agent [5].

The process of cleaning, analyzing and presenting the data was based on the guidelines proposed by the Clinical and Laboratory Standards Institute (CLSI) [6] and carried out using the package AMR of the software R [7]. The data was filtered to correspond to the samples collected in sites in the district of Aveiro that do not correspond to nursing centers. Only the first isolate of a given bacteria specie per patient was considered, to avoid the calculation of susceptibilities estimates biased in favor of isolates from patients that appear more frequently [6]. Only bacteria species associated with at least 30 samples were considered, to reduce misinterpretations of susceptibility estimates, since the smaller the sample size, the greater the uncertainty associated with the estimate [6], [8]. For each combination of microorganism / antimicrobial agent, the percentage of susceptibility was calculated: S+I/S+I+R [6]. Only the results of the combinations with clinical relevance were presented [6]. For each bacteria comparisons between all the relevant antimicrobial agents were performed using the Cochran's Q test. The significance level used was 5%.

Results:

During the period of study, were performed 17842 bacteriological examinations to urine, of which 3256 (18.2%) resulted in a positive culture. In this study were considered a total of 2538 bacterial isolates. The isolates of Escherichia coli are the most frequent (1702, 67.1%), followed by Klebsiella pneumoniae (293, 11.5%). For example, it is observed that the susceptibility estimate of Escherichia coli to amoxicillin (61%) is lower than the susceptibility estimate to cefuroxime (92%). Thus, for the empirical treatment of uncomplicated UTIs, the second antimicrobial agent should be chosen. Regarding all bacteria, except for Streptococcus agalactiae, were found significant differences in the susceptibility estimates between at least two antimicrobial agents. All of these results are depicted in figure 1.

Keywords:
Bacteria, Susceptibility, Urinary tract infections

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		Beta - lactams									Aminoglycosides		Others					
	Microorganism	Amoxicillin	Amoxicillin / Clavulanic acid	Aztreonam	Cefotaxime	Ceftazidime	Cefuroxime	Imipenem	Meropenem	Piperacillin / Tazobactam	Amikacin	Tobramycin	Ciprofloxacin	Fosfomycin	Levofloxacin	Nitrofurantoin	Trimethoprim / Sulfamethoxazole	p**
		Antimicrobial agent																
Gram Negative Bacteria	*Escherichia coli* (n = 1702)	61	72	–	–	–	92*	–	–	–	–	–	87	98*	–	99*	82	<0.001
	Klebsiella pneumoniae (n = 293)	R	56	–	–	–	67*	–	–	–	–	–	70	–	–	–	72	<0.001
	Proteus mirabilis (n = 179)	60	86	–	–	–	91*	–	–	–	–	–	74	–	–	R	75	<0.001
	Pseudomonas aeruginosa (n = 53)	R	R	81	R	85	R	92	96	85	94	88	70	–	65	–	–	<0.001
	Klebsiella oxytoca (n = 39)	R	77	–	–	–	82*	–	–	–	–	–	100	–	–	–	97	<0.001
	Citrobacter koseri (n = 38)	R	89	–	100	–	–	–	–	–	–	–	100	–	–	–	100	0.029
Gram Positive Bacteria	*Staphylococcus saprophyticus* (n = 130)	–	–	R	–	R	–	–	–	–	–	–	100	R	–	100*	83	<0.001
	Enterococcus faecalis (n = 72)	100	100	R	R	R	R	–	–	–	–	–	79*	–	–	100*	–	<0.001
	Streptococcus agalactiae (n = 32)	100	–	R	–	R	100	–	–	–	–	–	–	–	94	97*	–	0.300

> 80% of susceptibility; between 50 and 80% of susceptibility; < 50% of susceptibility

– > Antimicrobial agent not tested or not reported

R Intrinsic resistance

* Only use this antimicrobial agent in case of uncomplicated urinary tract infections

** Cochran's Q test

Figure 1 - Antimicrobial susceptibility profile of the most frequent bacterial isolates associated with UTIs in the community of the district of Aveiro.

Discussion:

The most frequent bacterial isolates found in this study were the same as those found in the literature [9]. One of the limitations of this study was that only samples collected from Avelab collection centers were considered. However, it was assumed that the sample considered is representative of the district of Aveiro: Avelab is the largest medical clinical analysis laboratory in this region; this study considered approximately 55 collection points spread across it. Similar to this study, it is important that in future works rules for the description of antimicrobial susceptibility profiles of bacteria are followed (e.g. CLSI guidelines), as it increases the credibility of the results obtained, as well as makes them comparable between institutions and even within the same institution.

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Journal of Statistics on Health Decision

EXTENDED ABSTRACT

Hydroxychloroquine reports to EudraVigilance database during COVID-19

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Introduction:

Hydroxychloroquine is an antimalarial drug that belongs to the 4-aminoquinolone group. [1] Besides this property, it presents several immunomodulatory and anti-inflammatory characteristics [1,2]. In 2020, with the emergence of the COVID-19 pandemic, researchers used existing drugs with potential for the treatment of COVID-19, including hydroxychloroquine, which ended up being used off-label [3,4]. Clinical trials show that hydroxychloroquine has many adverse effects that can increase risk for the SARS-COV-2 patients health. Common adverse effects are related to gastrointestinal and cardiovascular systems, neurotoxicity and retinopathy [2,5]. The objective of this research was to describe the adverse effects profile of hydroxychloroquine in COVID-19 patients and to characterize the risks associated with off-label use of hydroxychloroquine.

Methods:

An observational, retrospective and descriptive study was conducted. Information collected from the "Eudravigilance" database was analyzed using descriptive statistics with R Studio® software. Information about the source of reporting, patient sex, serious adverse reactions, deaths and off-label cases and their outcome, were evaluated and compared in the pre-pandemic and pandemic period, from January 2017 to December 2021. All cases in which hydroxychloroquine was a suspected drug were considered.

Results:

The number of reports of adverse reactions to hydroxychloroquine increased significantly during the pandemic period (increase of 310.3%), with health professionals reporting the most (92.0%). The off-label administration of hydroxychloroquine has increased as well as incidence and severity of adverse reactions during pandemic period. Serious outcomes, as deaths, presented an increased number during the pandemic. The total number of suspected adverse drug reactions reports increased from a mean of 7.7 reports per month, pre-pandemic, to 114.5 reports during the pandemic. Serious outcomes also increased during the pandemic: a total of 6.8% (n=361) reactions were considered serious before the pandemic, and 26.6% (n=2740) in pandemic period. Finally, deaths associated with the use of hydroxychloroquine were also evaluated, of which 67.0% are described in off-label use cases.

Discussion:

The profile of safety of hydroxychloroquine appears to have changed during the pandemic with the off-label use. Hydroxychloroquine presents different adverse reactions, which should be reported whenever possible. Its off-label use for COVID-19 has been shown to be a risk for patients, as it causes them more risks than usual use. In short, hydroxychloroquine appears to not bring benefits to COVID-19 and it ends up bringing several complications when it is administered.

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Keywords:
hydroxychloroquine, adverse effects, COVID-19, EudraVigilance

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EXTENDED ABSTRACT

Impact of the Covid-19 pandemic on dispensing of anticoagulant therapy

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Introduction:

On the 11th of March 2020, the World Health Organization (WHO) declared a pandemic due to the disease caused by the novel coronavirus, Sars-Cov-2 [1]. Governments implemented many measures to decrease the incidence of COVID-19 cases and control the spread of this disease like social distancing, periods of lockdown, etc. Such measures affected people's lives and may have reduced access to health care and services. In this regard, we want to understand whether the pandemic had an immediate and or long-term impact on dispensing of novel oral anticoagulants (NOAC) drugs, which are drugs used to help prevent blood clots. To answer this research question, we used interrupted time series analysis (ITS) [2], a method proposed to evaluate the effectiveness of population-level interventions or health events that have been implemented at a defined point in time.

Methods:

Data collection was carried out at the level of consumption of NOACs (WHO ATC class: B01AA03, B01AA07, B01AE07, B01AF01, B01AF02 and B01AF03) on an outpatient basis in Portugal, it was collected from the hmR Information System, which is a national database that provides national and regional estimates representative of drug dispensing data for all medicines, from about 84% of all Portuguese community pharmacies. The data used was from January 2017 to December 2021.

For the analysis, the measure of interest was the DHD (DDD per 1000 inhabitants per day). The DDD is the assumed the average maintenance dose per day for a drug used for its main indication in adults [3]. To obtain an estimate of the resident population in Portugal, the INE Portal was used. The DHD was calculated using the formula: total DDD / (number of days in the period under analysis * population) *1000. For the analysis of the interrupted time series, four variables of interest were used. The dependent variable was the total DHD per month and the independent variables were time; the intervention as a dummy variable (0-pre-intervention; 1-post-intervention); and the trend – time since the start of the intervention. Results will be stratified by substance. A segmented linear regression model was built, adjusted with ARIMA (Autoregressive Integrated Moving average) errors. $Y = \beta0 + \beta1 * Time + \beta2*Intervention + \beta3* Trend + \epsilon t$, with $\epsilon t \sim ARIMA\ (p, d, q)$ [4]. In this model, $\beta0$ estimates the baseline level of the outcome, mean number of DHD per month, at time zero;, $\beta1$ estimates the change in the average number of DHD per month before the intervention; $\beta2$ estimates the level variation in the mean number of DHD immediately after the intervention (immediate effect), and $\beta3$ estimates the change in the trend of the average monthly number of DHD per month after the threshold compared to the monthly trend before the threshold (long-term effect). Statistical analysis was performed in R. Significance level adopted was 0.05.

Results:

According to the results of the exploratory analysis, the data appear to have an increasing linear trend over the years and do not show seasonality. In addition, in the series graph, there is a peak in March 2020 that can be explained due to the implementation of the quarantine in which there was a considerable increase in demand for treatment stocking. The data of March was considered an outlier, so it was excluded from the modeling analysis of the models in order not to bias the analysis results. Figure 1 represents the graph of the trend before and after the intervention. To select the orders of ARIMA (p and q), we inspected the graphs of the sample autocorrelation and partial autocorrelation functions and for order d, we use the first difference. Through the result, some models were proposed that fit the data, the best model found was ARIMA (2,1,1) with an AIC of 109.44 and the coefficients were all statistically significant. The values of the time, intervention, and trend coefficients were 0.164, -1.128, and 0.051 respectively. Figure 2 shows the graph of the distribution of residuals, autocorrelation, and partial autocorrelation respectively of the

Keywords:
Pandemic, Interrupted Times Series, ARIMA, Segmented regression, Anticoagulant drugs

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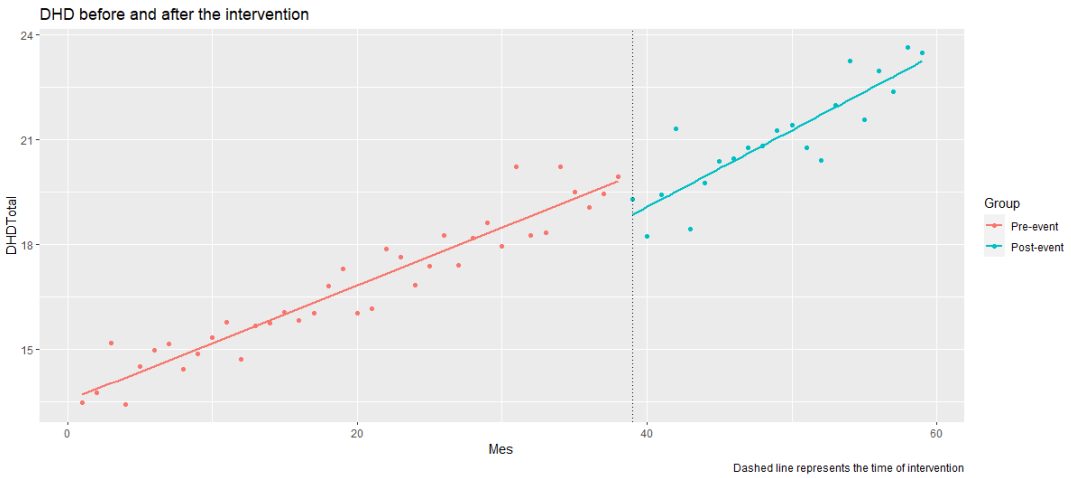

Figure 1 - Distribution of the Interrupted Time Serie

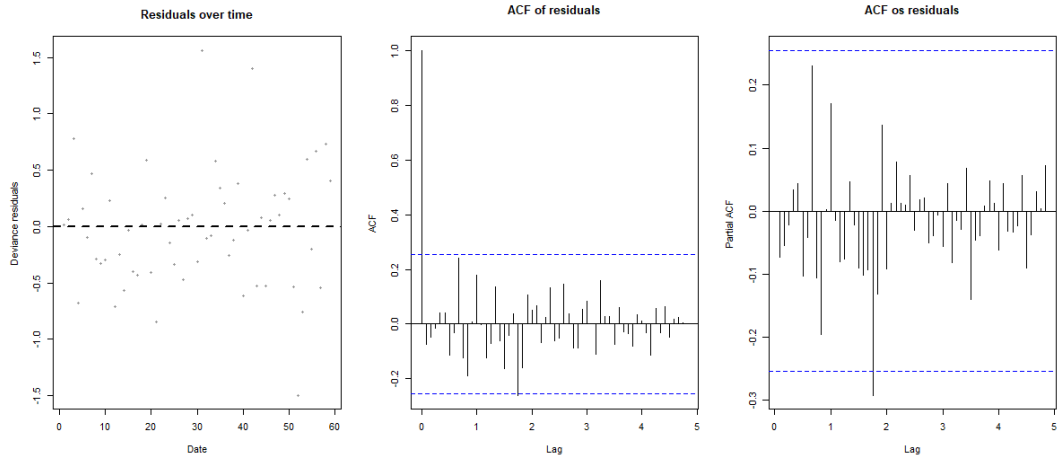

Figure 2 - Distribution of residuals, autocorrelation, and partial autocorrelation of residuals from ARIMA

ARIMA model. The residuals appear to be randomly distributed and the Ljung-Box test does not reject the hypothesis that the residuals are random (p-value =0.07). The autocorrelation graph does not show significant autocorrelation however, we have a lag that reaches the marginal of the interval.

Conclusion:

The analysis suggested that the COVID 19 pandemic had an immediate and significant impact on NOAC consumption (a decrease of 1,128 DHD), with the absolute effect of the intervention being 11,7 patients and the relative change in DHD associated with the intervention was of -5.8%). Also, a long-term impact seen by a positive and significant change in trend after the start of the pandemic period (+0.051 DHD per month) compared to the pre-pandemic period.

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Journal of Statistics on Health Decision

EXTENDED ABSTRACT

Development and validation of COVID-19 mitigation measures instrument: Application of Hierarchical Principal Components Analysis and Building Shiny app

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Introduction

On March 11, 2020, the World Health Organization (WHO) declared a pandemic state caused by the SARS-CoV2 virus [1].

Two years after, the study of each mitigation measures adopted is important, in order to understand the effectiveness of their application on the infection incidence, on the response of health services and on the disease prognosis.

However, many of the mitigation measures were applied aggregated in time and within countries therefore a development of mitigation measures instrument that identifies the major patterns of this measures is the extreme importance [2].

This work aims to develop a COVID-19 mitigation measures instrument, obtained through Hierarchical Principal Components Analysis, that allows tracking the mitigation measures application and that can lead to improve the responses by the governments of the European Union (EU) countries. This work also intends to compare the proposed instrument with the Stringency Oxford Index given by Oxford University [3]. The Stringency Index was developed by a panel of experts from the University of Oxford, with the aim of understanding the effect of mitigation measures on the incidence of the virus. In this work we develop an instrument with same purpose, but using a data driven approach, and the objective was to compare both to understand which one explain better the effect on incidence number of cases of SARS-CoV2 infection at 14 days per 100 000 inhabitants.

Methods

This study included the information from the 27 countries of the EU, provided by the European Center for Disease Control and Prevention (ECDC) [4]. Data were collected on the implementation of 66 mitigation measures, as well as their start and end dates, by country and by week, from February 2020 to March 2022. In order to simplify the data, and considering that several measures were only different levels from same measure, a variables restructuring was carried out, resulting in 31 mitigation measures with Likert scale (ranged from 0: no measure applied to 3: maximum level implemented).

Taking into account that many of the mitigation measures were applied simultaneously, a principal component analysis was performed, with Oblimin rotation, applied to the correlation matrix to identify how the measures were aggregated. Considering the scree plot, two different solutions were selected with 1 and 7 subdimensions (components).

The principal components analysis was again applied to the 7 scores extracted from to obtain a general dimension. This method is called Hierarchical principal components analysis and it is more advantageous than the traditional because it allows to determine the existence of a general dimension. The existence of this general dimension is one of the main objectives of this work. To obtain reparameterization of the general dimension, a Schmid-Leiman rotation was applied. To evaluate the internal consistency the alpha and the omega T and H values were determined.

Three separated (not nested) linear regressions models were estimated, stratified by country, between the cumulative incidence number of cases of SARS-CoV2 infection at 14 days per 100 000 inhabitants (dependent variable) and the general score (model 1), the Stringency Index (model 2) and the 7 subdimensions Scores (model 3).

The comparison of the variance explained (R^2) and information criteria (AIC and BIC) of the 3 models was performed considering that the models were not nested.

At the end it was developed a Shiny app https://inesviseu.shinyapps.io/Covid-19/# .

All analyses were performed using the software R (version 4.0.2).

Keywords:
COVID-19, Principal Components Analysis, Mitigation Measures, Hierarchical Factor Analysis, Shiny

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Conflict of interest:
The authors declare no conflict of interests

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Results

A total of 31 mitigation measures has different proportions of applications in each country. The 7 components explained 55% of total variance. Considering the measures with highest correlations and that contribute most to the formation of each subdimension, the following components were identified: 1st represented Closure of educational institutions, 2nd represented Indoor/Outdoor interventions, 3rd represented Closure of non-essential shops, 4th represented Ban on all events, 5th represented Closure of hotels/accommodation services, 6th represented Masks Mandatory and 7th represented Stay Home Order. The Cronbach's alpha value was approximately or higher 0.7 for all subdimensions (except component 7).

Hierarchical principal components analyses were performed to obtain the general dimension. This factor explained 22% of total variance and omega H 0.54.

The R^2, AIC and BIC values showed that the general factor is similar to the Stringency Index and none of them explains the incidence with R^2 ranging from 0.0 to 0.22. The model 3 has higher R^2 values, ranging from 0.16 to 0.88. All AIC and the majority of BIC values of model 3 are lower compared to model 1 and 2. For example, for Germany the R^2 values for model 1 was 0.03, for model 2 was 0.11 and for model 3 was 0.60. And to Belgium the R^2 values for model 1 was 0.07, for model 2 was 0.04 and for model 3 was 0.59.

Discussion

The study showed that was possible to identify an aggregation of mitigation measures in time, with existence of strong general factor. The use of 7 subdimensions to evaluate the effect of mitigation measures in incidence showed more explanatory capacity. Country differences were identified on the explanatory capacity, this could be explained by differences of the population adherence to these measures, also to the implementation program of the vaccination.

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Journal of Statistics on Health Decision

EXTENDED ABSTRACT

Functional Status in People with COPD: A Cluster Analysis with Bootstrap Resampling

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Introduction:

Functional status of people with chronic obstructive pulmonary disease (COPD) is heterogeneous, complex, and highly meaningful to their daily life. It is also a strong predictor of acute exacerbations of COPD (AEOPD), healthcare utilisation and mortality (1, 2). Nevertheless, it has been overlooked by treatment options. Understanding the heterogeneity of this important health domain, might contribute to better personalised care. This study sought to identify clusters based on functional status of people with COPD.

Methods:

A secondary analysis of socio-demographic, lung function, activity-related dyspnoea (modified Medical Research Council (mMRC)), impact of the disease (COPD Assessment Test (CAT)) and functional status data collected between 2017-2021 in GENIAL (PTDC/DTP-PIC/2284/2014), PRIME (PTDC/SAU-SER/28806/2017), 3R (SAICT-POL/23926/2016), and CENTR(AR) (POISE-03-4639-FSE-000597) was conducted.

People (aged ≥ 18 years old) diagnosed with COPD, according to GOLD criteria, and clinically stable in the previous month (i.e., no hospital admissions, AECOPD, or changes in medication) were included. Those with the presence of other respiratory diseases or any clinical condition which could have hindered test performance were excluded.

The six-minute walk test (6MWT), one-minute sit-to-stand test (1-min STS), quadriceps muscle voluntary contraction (QMVC) and handgrip muscle strength have been rescaled using the z-score formula. A principal component analysis was performed on scaled data; components extracted were used to group individuals with the K-means clustering algorithm. Principal components (PCs) were retained until cumulative percentage of total variance reached 70% minimum (3). Multivariate outliers were detected by comparing the Mahalanobis distance to a chi-square distribution (with a critical value set at 0.999) and removed from the analysis. The total within-cluster sum of squares was computed for different values of k; the optimum number of clusters was taken as the inflexion point on the curve.

Functional status differences between clusters were explored using one-way Multivariate Analysis of Variance (MANOVA), followed by one-way Analysis of Variance (ANOVA) with Bonferroni adjusted p-values and post-hoc multiple pairwise comparison tests. Multivariate skew and kurtosis were evaluated with Mardia's test for multivariate normality, and chi-square quantile-quantile plot. Homogeneity of variance-covariance matrices was assessed with Box's M test. Cluster stability was measured by bootstrap resampling methods (999 resampling runs) (4, 5). The Jaccard coefficient was used as a cluster-wise measure of cluster stability, allowing to quantify the quality of the clustering solution (4).

One-way ANOVA was used for continuous variables followed by pairwise comparisons with Bonferroni correction, and the Pearson's Chi-square or Fisher-exact test for categorical variables, to characterise clusters with regard to socio-demographic data, lung function, activity-related dyspnoea, and impact of the disease. Normality and homoscedasticity were assessed with Shapiro-Wilk and Bartlett's test, respectively.

All statistical analysis were performed using R Statistical Software (4.2.0), with a significance level set at 0.05.

Results:

In total, 132 people with COPD (107 (81.06%), 68.15 ± 7.82 yrs, FEV1 56.25 ± 19.27 %predicted) were included for analysis. Two PCs were retained (PC1 56% (2.22); PC2 21% (0.82)), and four clusters were identified (depicted in Fig. 1, 2). Differences between clusters for the combined dependent variables were

Keywords:
Cluster Analysis; COPD; Functional Status

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Table 1 - Socio-demographic and clinical characteristics of people with chronic obstructive pulmonary disease for the total sample and per cluster.

	Total (n=132)	Cluster 1 (n=45)	Cluster 2 (n=29)	Cluster 3 (n=27)	Cluster 4 (n=31)	p
Age, years	68.15 ± 7.82	71.0 ± 6.60b,d	65.45 ± 6.85a,c	70.89 ± 7.05b,d	64.16 ± 8.58a,c	<0.001
Sex [male]	107 (81.1)	33 (73.3)	27 (93.1)	17 (63.0)	30 (96.8)	0.001
FEV1 %pred	56.25 ± 19.27	54.56 ± 16.36	59.9 ± 18.28	52.0 ± 19.41	59.0 ± 23.44	0.346
mMRC [≥2]	75 (56.8)	26 (57.8)	15 (51.7)	22 (81.5)	12 (38.7)	0.011
CAT [≥10]	87 (65.9)	32 (71.1)	18 (62.1)	23 (85.2)	14 (45.2)	0.011
6MWT, m	408.8 ± 113.22	411.64 ± 62.29c,d	440.38 ± 67.54c,d	247.74 ± 92.41a,b,d	515.39 ± 50.64a,b,c	<0.001
1-min STS, reps	23.30 ± 7.17	23.49 ± 3.85c,d	22.28 ± 3.98c,d	14.11 ± 3.27a,b,d	31.97 ± 4.93a,b,c	<0.001
QMVC, kg/F	31.34 ± 9.94	26.73 ± 5.53b,d	40.64 ± 12.14a,c	23.43 ± 5.83b,d	36.2 ± 4.83a,c	<0.001
Handgrip strength, kg	34.14 ± 9.22	29.53 ± 6.65b,d	42.24 ± 7.27a,c	26.63 ± 7.39b,d	39.77 ± 5.52a,c	<0.001

Continuous variables are presented as mean ±standard deviation and categorical variables as counts and percentages. Legend: 6MWT, 6-minute walk test; 1-min STS, 1-minute sit-to-stand test; QMVC, Quadriceps maximum voluntary contraction. a – p<0.05 vs cluster 1; b – p<0.05 vs cluster 2; c – p<0.05 vs cluster 3; d – p<0.05 vs cluster 4

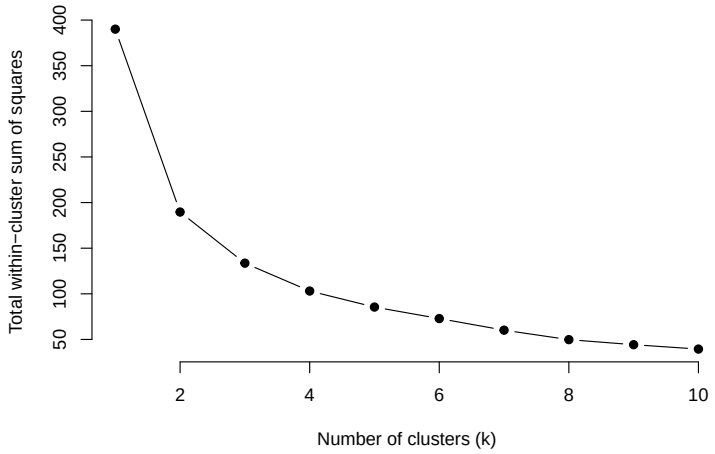

Figure 1 - Scree plot (elbow criterion) for determining the optimum number of clusters (k = 4).

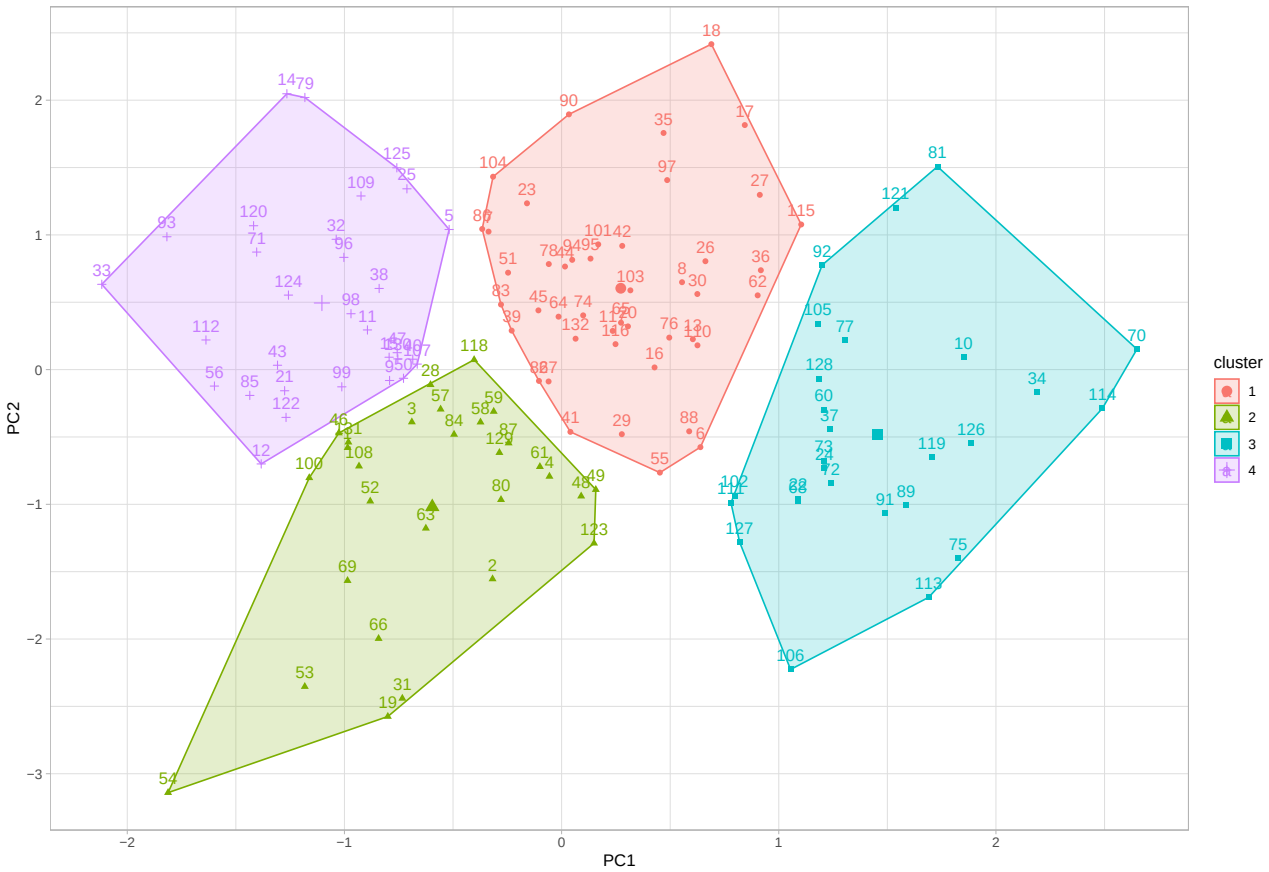

Figure 1 - Two-dimensional, graphical representation of the four clusters based on functional status of people with chronic obstructive pulmonary disease. X-axis or PC1 is the first rank component with the variance percentage of 56%, and Y-axis or PC2 is the second rank component with the variance percentage of 21%.

statistically significant, $F(12, 331.01) = 44.39$, $p < 0.001$; Wilks' $\Lambda = .079$; partial $\eta 2 = .45$. Follow-up univariate ANOVAs showed that all variables were significantly different between clusters, using a Bonferroni adjusted α level of 0.0125: 6MWT ($F(3, 128) = 77.27$, $p < 0.001$; partial $\eta 2 = 0.64$); 1-min STS ($F(3, 128) = 94.17$, $p < 0.001$; partial $\eta 2 = 0.69$); QMVC ($F(3, 128) = 35.62$, $p < 0.001$; partial $\eta 2 = 0.45$); handgrip strength ($F(3, 128) = 39.74$, $p < 0.001$; partial $\eta 2 = 0.48$). Comparisons between clusters are presented in Table 1. The Jaccard coefficients for nonparametric bootstrap were 0.78, 0.59, 0.88, and 0.72, for cluster 1, 2, 3, and 4, respectively.

Conclusion:

Four clusters were identified in people with COPD, which were significantly different in all variables of functional status, activity-related dyspnoea, and impact of the disease. Nevertheless, additional phenotypic characterisation based on treatable clinical traits is needed, which may guide tailored treatment regimens to improve this meaningful outcome. Cluster validity, their behaviour over time and differential response to treatment needs further investigation.

Ethics committee and informed consent:

All studies were approved by several Ethics Committees (CHMA 09/2016-10/2018; ULS Matosinhos 10/CES/JAS 17/02/2017-73/CE/JAS 12/10/2018; CHBV 777638-086892-15/05/2019; HDFF 1807/2017-27/05/2019; ARS Centro 64/2016-73/2016-85/2018-16/2020; UICISA-E P620-10/2019) and subjects gave their informed consent before they were enrolled in the studies.

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EXTENDED ABSTRACT

Characterization of mental health issues in the region of Aveiro — A retrospective analysis

Filipa S. Rocha[1], Cristiana J. Silva[1,2], Miguel M. Felgueiras[3], Rui Pedro R.P. Leitão[4], Sofia J. Pinheiro[1,2], Vera M.A. Afreixo[1,2]

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Introduction:

The world has acknowledged the important role of mental health. However, in the last decade, mental health disorders increased by 13%, being Depression and Anxiety the most common issues [1]. Portugal has Europe's 2nd-highest prevalence of psychiatric illnesses and further studies show that 57% of the Portuguese population presents psychological distress [2,3]. This study was conducted to investigate the registered psychological problems between 2009 and 2021 in the region of Aveiro.

Methods:

Data was imported to RStudio with 5 common variables: County, Sex, GroupAge, ICPC and Problem. The remaining record the number of registered psychological problems in each year. All data was filtered according to ICPC variable and lines with a psychological ICPC2 code below 70 were deleted as they represent signs and symptoms. The GroupAge variable was aggregated to obtain 5 groups (0-14, 15-24, 25-44, 45-65, +65 years). All 11 counties from ACeS Baixo Vouga were present. Columns concerning the number of reported problems per year were merged, lines reporting 0 problems were deleted, data was aggregated to sum the total of problems of duplicated entries and the Year variable was created. To study Cancer, Obesity and Diabetes, counts of registered psychological problems in the presence of these comorbidities were imported and processed as described. To obtain the final dataset, columns referring to the number of reported psychological problems in the presence of each comorbidity were added to the first one. Exploratory data analysis began with the number of problems per year, comparing it to the number of problems for each comorbidity. Secondly, the number of problems per year for each county, gender, age group and for each psychological problem was accessed. Further analysis was only conducted with the County variable. To visually compare the number of registered problems, interactive maps of the district of Aveiro were built, where the counties belonging to the ACeS Baixo Vouga were colored through a gradient coded in parallel with the number of issues registered; a standardization was performed according to the number of resident populations. Clusters analysis was performed to find which counties were similar. Ward's method was used, Spearman correlations were calculated and turned into a dissimilarity measure. To assess the association between psychological problems and its occurrence in the counties (two nominal variables), Cramer's V measure was used.

Results:

A total of 1092760 psychological problems were reported between 2009 and 2021 in the ACeS Baixo Vouga. Of all years, 2021 had more reports and this number has been increasing. Women had more than twice as many problems compared to men (Figure 1). The county with the most psychological problems registered in 2021 was Ovar; Anadia stands out because it reported the least psychological problems per 100000 habitants. Figure 2 shows that the most reported problems were Depressive and Anxiety Disorders. Figure 3 shows the result of a cluster analysis between counties for the time considered; Murtosa, Ovar, Estarreja and Anadia formed one cluster, and Sever do Vouga, Oliveira do Bairro, Ílhavo, Aveiro, Albergaria-a-Velha, Vagos and Águeda formed another. The silhouette coefficient of 0.5 revealed a reasonable structure. The results of the association between psychological issues and its occurrence in the counties reveal that Somatization has the highest association with a Cramer's V value of 0.11.

Keywords:
Mental health services; health promotion; regional differences; ACeS Baixo Vouga.

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Conflict of interest:
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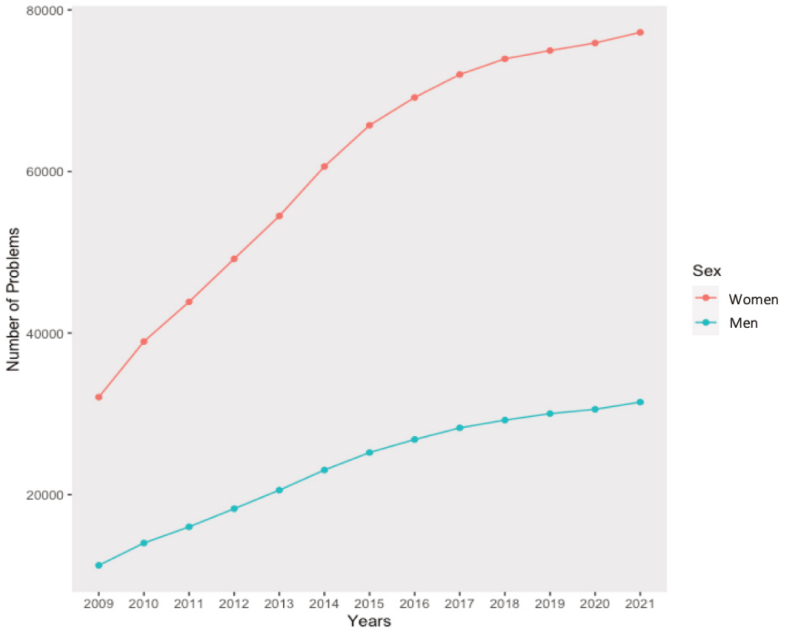

Figure 1 - Line graph showing the number of problems reported by males and females over the years.

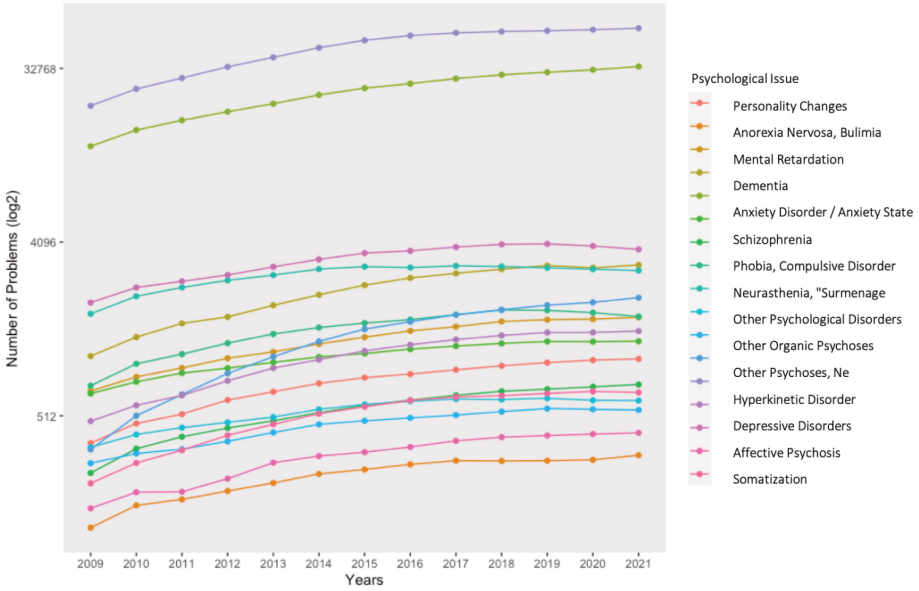

Figure 2 - Line graph showing the number of problems reported by type of psychological issue over the years, with a log2 transformation in the y axis.

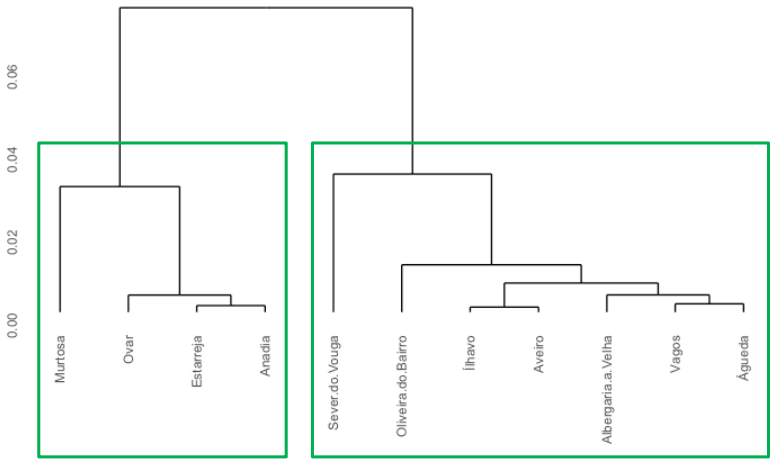

Figure 3 - Result of the cluster analysis performed for the County variable.

Discussion:

This study showed that some counties behave similarly when taking the report of psychological problems into account. Cluster analysis results are supported by the grouping of the counties with more reported psychological problems, which might be explained by a greater presence of the elderly population or better primary care services. In Portugal, there's still mental health stigma and discrimination [4] and this might explain men's lack of reported issues. Anxiety and Depression are the most reported issues in the Aveiro region. These results are consistent with country and world's results. The weak, although significant association of Somatization with the County variable could be related to genetic influence. The importance of mental health is highlighted in the main mental health strategies and action plans. However, interventions in the area are done in isolation and are not sustained over time [4]. This study might alert the population and its doctors to be more aware of the Portuguese's needs. These findings could help doctors identify mental health issues' risk factors and act to prevent them in time. This study revealed limitations as only aggregated data was studied, where duplicates are present but impossible to resolve.

Acknowledgements:

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Journal of Statistics on Health Decision

EXTENDED ABSTRACT

Graph Theory approach to COVID-19 transmission across adjacent municipals

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Introduction:

The spread of the "Severe Acute Respiratory Coronavirus 2" (SARS-CoV-2), responsible for the coronavirus disease (COVID-19), was first recognized as a pandemic by the World Health Organization (WHO) in March 2020, considering its rapid dissemination over the world in a short period of time, rendering it a global health emergency. [1,2]

Given the importance of understanding how this infection flows are represented in real life and how relevant COVID19 is on a global scale, represented in a conceptual model, this study used graph theory to try to understand it.

Graphs may be used to represent many different types of relationships and processes in physical, biological, social, and information systems. [3–5] Ultimately graph theory is about connections networks and thus it can be used to model and answer, different kinds of questions. In this work graph theory will be used to emulate COVID-19 virus transition chain between municipalities in the district of Aveiro.

Methods:

All COVID-19-related test results in ACES BV reported to the Public Health Unit (PHU) between January 30, 2020, and January 14, 2022 (N = 17.568) were used in this investigation. However, due to missing numbers and/or insufficient information in the data for 2022, only the first two years of data were considered. Since the study's focus was on the dynamics between municipalities, the database was filtered to contain just the IDs (person identification number) and each relevant ID county, as well as COVID results and test dates. The dataset was filtered to eliminate missing and repetitive items.

Contact matrices, being those matrixes that display the transmission between the infector (line) and the infected (column) [6], were created using the resulting dataset for the years 2020 and 2021. These matrices were then used to generate graphs. To each of these graphs, the following centrality metrics were applied: Closeness Centrality, Betweenness Centrality, Eigencentrality, Degree Centrality. Closeness centrality reflects how near a node is to all other nodes in the network. It is determined as the average of the shortest path lengths from the node to every other node in the network, and so indicates the transmission speed. Betweenness centrality quantifies how much influence a node has on the flow of information in a network. Eigencentrality is a measure of a node's impact in a network, but it excludes information about ego's changes and so evaluates the strength of each node's neighbors in the proximity network. The number of connections occurring at a node is known as its degree centrality (i.e., the number of ties that a node has). Some of these measures are based on the shortest paths between a vertex and all others, so the smaller the edge weight, the shorter the distance, and thus for the measures of Closeness Centrality and Betweenness Centrality the inverse of the matrices were used for the calculations.

The study of the dynamics of the COVID-19 disease was then understood by comparing the evolution of this measures across the calculated time periods.

Results:

The contact matrices (Tab.1) for the time intervals related to 2020 and 2021 are similar, having both the majority of transmissions within the diagonal, hence they occur within the municipality.

As for the measures of centrality (Fig. 1), it can be said that they all remained relatively constant between the two years.

Aveiro had the greatest value for Closeness Centrality, with Águeda and Ílhavo coming in second and third, respectively, in the first interval and shifting positions in the second interval. In both intervals of the

Keywords:
Graph theory, Betweenness centrality, Centrality measures, Closeness centrality, COVID-19, Degree centrality, Eigencentrality.

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Conflict of interest:
The authors declare no conflict of interests.

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Table 1 – Contact matrices

Contact Matrix of 2020

	A. Velha	Águeda	Anadia	Aveiro	Estarreja"	Ílhavo	Murtosa	O. Bairro	Ovar	S. Vouga	Vagos
A. Velha	268	6	0	8	0	1	0	0	0	1	1
Águeda	2	517	16	13	2	0	0	6	1	0	0
Anadia	0	5	460	4	0	0	0	9	0	0	0
Aveiro	5	5	4	972	6	38	1	0	5	3	6
Estarreja	0	2	1	6	400	1	33	0	10	0	1
Ílhavo	1	2	0	46	0	472	0	2	1	1	2
Murtosa	0	0	0	2	54	0	236	0	3	1	0
O. Bairro	0	5	10	3	2	5	0	96	1	0	2
Ovar	0	0	0	10	5	0	4	0	1022	0	2
S. Vouga	0	3	0	0	0	0	1	0	0	160	0
Vagos	0	1	3	13	0	11	0	1	0	0	208

Contact Matrix of 2021

	A. Velha	Águeda	Anadia	Aveiro	Estarreja"	Ílhavo	Murtosa	O. Bairro	Ovar	S. Vouga	Vagos
A. Velha	864	14	0	23	4	6	0	0	2	3	0
Águeda	36	1222	11	25	0	3	0	15	0	4	2
Anadia	1	15	873	11	0	3	0	20	0	1	0
Aveiro	32	19	16	2520	13	89	1	38	2	3	12
Estarreja	8	3	0	14	850	0	14	0	8	0	0
Ílhavo	5	6	2	104	2	1313	2	10	0	0	16
Murtosa	0	0	0	6	14	2	402	0	4	0	0
O. Bairro	6	23	11	37	0	3	0	528	0	0	2
Ovar	2	4	0	8	25	1	6	0	1841	1	0
S. Vouga	0	4	3	2	0	3	0	0	1	349	2
Vagos	1	4	3	34	1	12	0	4	0	1	630

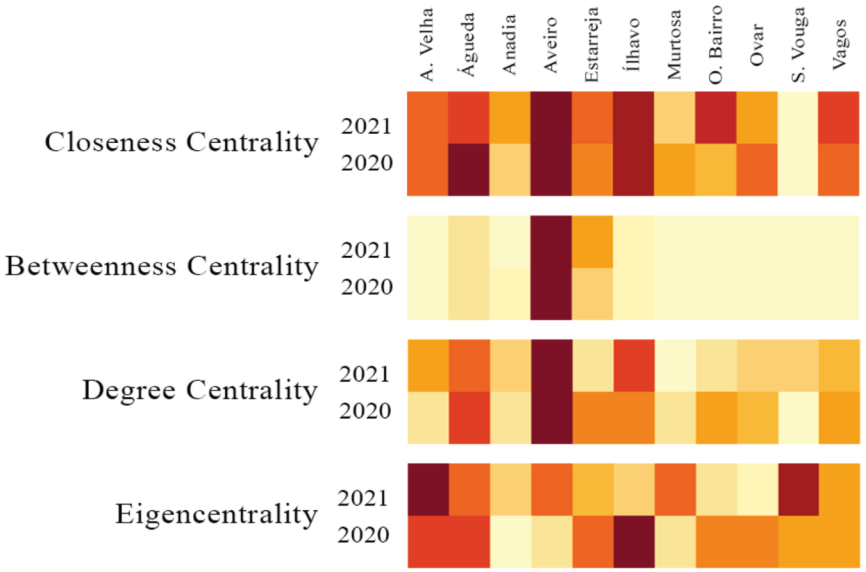

Figure 1 - Centrality measures heatmaps

betweenness centrality measure, the municipality of Aveiro is the strongest node, with Estarreja and Águeda coming in second and third, respectively. The nodes showed about the similar strength for the Degree Centrality measure (for both time intervals), with only the Aveiro node outperforming the others, although the general values are all high. In terms of Eigencentrality, the first interval is dominated by S.Vouga and A.Velha, whereas the second interval is dominated by Ílhavo, however, it still has A.Velha with high values.

Discussion:

The measurements of centrality were largely stable over the two years, showing that the COVID-19 dynamics were similar in these two periods, even while vaccination practically only occurred in 2021 and the prophylactic isolation of Ovar occurred in 2020. Analyzing the Closeness and Betweenness Centrality, it is concluded that in both years, Aveiro was the strongest node in both measures, and so, it was the municipality that infected other nodes the fastest and had the most influence. For the Eigencentrality, the time intervals appear to be shifting. A. Velha, on the other hand, has been shown to be the overall node with the strongest neighbors. Regarding the Degree Centrality, all the nodes appear to be linked to the majority of nodes.

Ethics committee and informed consent:

The current research was approved by an independent ethics committee and subjects gave their informed consent before they were enrolled in the study.

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Journal of Statistics on Health Decision

EXTENDED ABSTRACT

Can exercise training reduce central systolic blood pressure among patients with resistant hypertension?

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Introduction:

Resistant hypertension is a problematic phenotype marked by the limited efficacy of available blood pressure-lowering treatments [1], such as antihypertensive medicines and kidney denervation [2-4]. Given its health-related and economic impact, it is an important medical and societal issue. Patients with resistant hypertension have a higher risk of myocardial infarction, stroke, heart failure, chronic renal disease, and death, in addition to the cost of multiple drugs [5,6]. Cardiovascular disease risk is associated to central blood pressure. Central blood pressure seems to better relate with target organ damage and long-term cardiovascular outcomes, compared to traditional brachial blood pressure [7,8]. Increased aortic stiffness, assessed by carotid-femoral pulse wave velocity, is also an independent predictor of cardiovascular risk [9]. However, there are few studies on exercise interventions to improve these markers in people with resistant hypertension.

The EnRicH (The Exercise Training in the Treatment of Resistant Hypertension) was a prospective, single-blinded randomized clinical trial. The current analysis details the effect of aerobic exercise training intervention or usual care on central blood pressure and carotid–femoral pulse wave velocity.

Methods:

Patients with resistant hypertension were randomized 1:1 to a 12-week moderate-intensity aerobic exercise program (added to usual care) or usual care. Exercise training sessions were supervised and took place three times per week. Each session included a 10-min warm-up and cool-down period, and 40 minutes of aerobic exercise. Walking and cycling were the main chosen exercises and intensity was 50-70% of maximum oxygen uptake (VO2 max). Secondary outcome measures included central blood pressure and carotid–femoral pulse wave velocity. The Complior Analyse (Alam Medical, Saint Quentin Fallavier, France) and the SphygmoCor (AtCor Medical, Sydney, NSW, Australia) were used to measure central blood pressure and carotid–femoral pulse wave velocity. The two devices offer highly correlated measurements and similar outcomes. The carotid–femoral pulse wave velocity measurements were taken in accordance with Van Bortel et al. [10] expert's consensus document. SPSS version 28.0 was used for all statistical analyses (SPSS Inc., Chicago, Illinois, USA). Student's independent t-test was used to compare between-group differences at baseline, following the exercise program, and between changes in continuous variables from baseline to the end of the study. Student's paired t-tests were performed for within-group comparisons from baseline to the end of the study. The level of significance was set as $P \leq 0.05$.

Results:

Fifty-three patients (exercise n = 26, mean age 59.3 ± 8.2; control n = 27, mean age 60.8 ± 9.2) completed the study. No differences were found between groups at baseline. The change in central systolic blood pressure was significantly different between groups by -12.2 (95% CI, -22.6to -1.9, P = 0.022), with a mean change of -11.3 ± 19.2 mm Hg in the exercise arm vs 0.9 ± 11.8 mm Hg in the control arm. There were no differences in carotid–femoral pulse wave velocity between groups (P = 0.197).

Discussion:

Keywords: Central systolic pressure, Cardiac rehabilitation, hypertension, arterial stiffness

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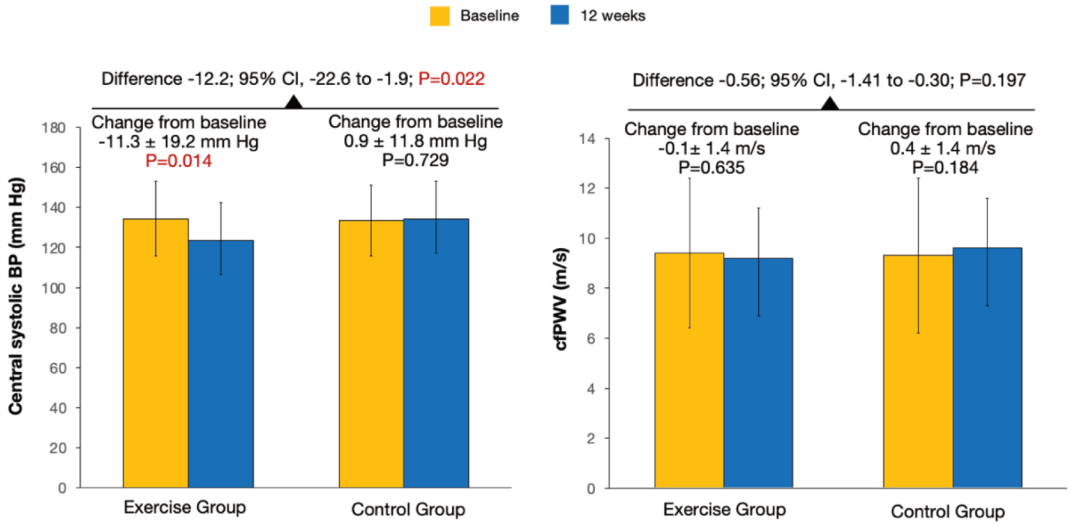

Figure 1 - Change from baseline to the end of treatment in central blood pressure and carotid-femoral pulse wave velocity in both study groups.

This study demonstrated that a 12-week exercise training program reduces central systolic blood pressure among patients with resistant hypertension. However, no significant changes were found for carotid-femoral pulse wave velocity. Our study agrees with previous evidence of aerobic exercise with similar programs in patients with prehypertension and hypertension [11,12]. Possibly, higher exercise intensities or longer duration programs may be necessary to induce changes to arterial stiffness.

A limitation of this study is that exercise training program consisted of moderate-intensity aerobic exercises. Therefore, other types of exercise and intensities need future investigation.

This trial demonstrated a benefit of 12-week of moderate-intensity aerobic exercise training on reducing central blood pressure in patients with resistant hypertension. The central blood pressure reduction is clinically promising as this indicator is associated with target organ damage, cardiovascular risk, and mortality.

Ethics committee and informed consent:

All patients provided written informed consent. The study was approved by the Ethics Committee of the Centro Hospitalar do Baixo Vouga

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Journal of Statistics on Health Decision

EXTENDED ABSTRACT

What are the predictors of clinical improvement in adolescents with chronic neck pain after pain neuroscience education and exercise? – secondary analysis of a randomized controlled trial

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Introduction:

Among the different painful chronic musculoskeletal conditions that affect adolescents, neck pain (NP) has emerged as one of the most prevalent, reaching up to 29.5% of adolescents aged 16 to 18 years old [1,2]. Several factors such as female gender, older age and high levels of disability have been associated with NP persistence and disability in this age group [3,4], raising doubts as to whether they influence the improvement of adolescents with NP in response to rehabilitation. Studies exploring NP management in adolescents are scarce [5]. A recent study by our team [6] suggested that interventions based on pain neuroscience education (PNE) and exercise are similarly effective. However, we were unable to find any studies that explored factors of treatment response in adolescents with NP. Thus, this study aimed to explore whether sociodemographic data, pain characteristics, physical activity, psychosocial factors, sleep, symptoms of central sensitization, pressure pain thresholds and neck muscles endurance at baseline predicted clinical improvement when using different standards: the Patient Global Impression of Change (PGIC) scale and the minimal change in the Numeric Pain Rating Scale (NPRS) for pain intensity and the Functional Disability Inventory (FDI) for disability, at post-intervention and 6-month follow-up.

Methods:

This study is a secondary analysis of a randomized controlled trial (6) conducted with 127 adolescents with chronic NP. Pain intensity, disability, physical activity, sleep, catastrophizing, fear of movement, and self-efficacy were assessed at baseline, post-intervention, and 6-month follow-up. Pressure pain thresholds and neck muscles endurance were assessed only at baseline and post-intervention. Impression of change (PGIC scale) was assessed at post-intervention and 6-month follow-up. To classify adolescents who improved from baseline to post-intervention and 6-month follow-up, different clinical improvement criteria were used: i) reporting a PGIC≥5 (moderately better, better, or a great deal better), ii) ≥50% reduction of pain intensity in the NPRS, iii) ≥50% reduction of disability in the FDI, and iv) ≥50% reduction in the NPRS and in the FDI, from baseline levels. Independent logistic-regression analyses were used to examine univariable and multivariable associations between the independent and dependent (clinical improvement) variables. The multivariable analyses were performed using Forward LR method and the significance level was set at $p<0.10$ and $p<0.05$ for univariable and multivariable analyses, respectively. The Nagelkerke R2 statistic was reported as an indication of the proportion of variance in the odds of a clinical improvement, which is explained by all of the significant variables in each multivariable model. The reported analyses were repeated for post-intervention and 6-month follow-up. All statistical analyses were performed using SPSS Software, version 22.0.

Results:

The characterization of adolescents with chronic neck pain is shown in table 1. At post-intervention, 72%(n=91) of the adolescents were classified as PGIC≥5, 52%(n=66) with improvements in the NPRS, 39%(n=50) with improvements in the FDI and 26%(n=33) with improvements in both NPRS and FDI. In the univariable models, i) older age was associated with decreased likelihood of improvement (OR=0.57, OR=0.70, $p<0.05$) using the PGIC and FDI scales, respectively and ii) moderate physical activity (OR=1.00, $p<0.10$) was associated with increased likelihood of improvement using the FDI. A multivariable model was found for the improvement of 50% in the FDI in which older age (OR=0.64, $p<0.05$) and

Keywords:
Adolescents; Pain neuroscience education; Exercise; Predictors; Clinical improvement

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Conflict of interest:
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moderate physical activity (OR=1.00, p<0.05) remained associated with decreased and increased likelihood of improvement, respectively (Nagelkerke R2 =0.12) (Table 2).

At 6-month follow-up, 69%(n=88) of the adolescents were classified as PGIC≥5, 54%(n=68) with improvements in the NPRS, 45%(n=57) with improvements in the FDI and 32%(n=40) with improvements in both NPRS and FDI. In the univariable models, i) older age (OR=0.70, p<0.10) was associated with decreased likelihood of improvement using the PGIC, ii) longer pain duration (OR=0.08, p<0.05), higher disability (OR=0.94, p<0.05) and more symptoms of central sensitization (OR=0.97, p<0.10) were associated with decreased likelihood of improvement and higher pressure pain thresholds (OR=1.04, p<0.10) was associated with increased likelihood of improvement using the NPRS, iii) having pain often (OR=0.21, p<0.05) was associated with decreased likelihood of improvement and higher neck flexors endurance (OR=1.07, p<0.10) with increased likelihood of improvement using the FDI, iv) having pain sometimes and often (OR=0.28 and OR=0.26, p<0.05) was associated with a decreased likelihood of improvement using NPRS and FDI. A multivariable model was found for the improvement of 50% in the NPRS ((Table 3) in which higher disability (OR=0.94, p<0.05) remained associated with decreased likelihood of improvement (Nagelkerke R2 =0.05) and for the improvement of 50% in the FDI (Table 2) in which having pain often (OR=0.23, p<0.05) and higher neck flexors endurance (OR=1.07, p<0.05) were associated with decreased and increased likelihood of improvement, respectively (Nagelkerke R2 =0.11).

Conclusions:

Taken together, our findings suggest that there are different factors associated with clinical improvement depending on the outcome used to categorize this improvement, but factors such as age, pain characteristics, disability, symptoms of central sensitization, pressure pain thresholds and neck muscle endurance seem to be relevant in the improvement of neck pain in adolescents at post-intervention and 6-month follow-up. However, considering the low explanatory percentage of the models found, other factors not included in this study should be considered in the assessment of these adolescents, such as parental factors.

Table 1 - Characterization of adolescents with chronic neck pain at baseline, post-intervention, and 6-month follow-up.

		Baseline (N=127)	**Post-intervention** (N=118)	**6-month follow-up** (N=117)
Sex	Female	109 (85.8%)	101 (85.6%)	99 (84.6%)
	Male	18 (14.2%)	17 (14.4%)	18 (15.4%)
Age (years)	Mean (SD)	16.06 (1.8)	16.44 (1.08)	16.92 (1.16)
BMI (Kg/m^2)	Mean (SD)	22.3 (4.0)	22.42 (4.1)	22.54 (3.8)
Scholar level (N, %)	10th	41 (32.3%)	39 (33.1%)	38 (32.5%)
	11th	52 (40.9%)	48 (40.7%)	48 (41.0%)
	12th	34 (26.8%)	31 (26.3%)	31 (26.5%)
Pain frequency (N, %)	Never	17 (13.4%)	26 (22.0%)	49 (41.9%)
	Sometimes	61 (48.0%)	59 (50.0%)	32 (27.4%)
	Oftentimes	36 (28.3%)	23 (19.5%)	29 (24.8%)
	Always	13 (10.2%)	10 (8.5%)	7 (6.0%)
Pain duration (N, %)	3 to 6 months	31 (24.4%)	--	--
	6 months to 1 year	24 (18.9%)		
	1 to 2 years	41 (32.3%)		
	2 to 5 years	24 (18.9%)		
	>5 years	7 (5.5%)		
Moderate PA (minutes/week)	Mean (SD)	197.05 (286.18)	185.00(198.02)	198.68 (237.08)
Vigorous PA (minutes/week)	Mean (SD)	137.65 (233.28)	140.85 (224.19)	166.45 (281.49)
NPRS (0-10)	Mean (SD)	4.51 (1.86)	2.44 (2.07)	2.24 (1.96)
FDI (0-60)	Mean (SD)	10.34 (6.55)	7.47 (7.02)	6.25 (6.92)
BaSIQS (0-28)	Mean (SD)	11.71 (4.63)	11.08 (4.72)	10.97 (4.72)
PCS (0-52)	Mean (SD)	13.48 (8.54)	11.29 (9.14)	9.63 (8.02)
TSK (13-52)	Mean (SD)	25.80 (5.52)	23.78 (5.96)	23.02 (5.90)
CSES (7-35)	Mean (SD)	17.17 (5.06)	15.83 (5.24)	15.50 (5.42)
CSI (0-100)	Mean (SD)	36.31 (12.90)	32.65 (13.55)	30.44 (13.94)
NPQ (0-12)	Mean (SD)	4.25 (1.84)	6.24 (2.32)	5.83 (2.50)
PPT (N/cm^2)	Right articular pillar C5/C6	21.10 (10.03)	--	--
	Left articular pillar C5/C6	19.37 (9.64)		
	Tibialis anterior	38.22 (13.89)		
Endurance tests (seconds)	Neck flexors	10.33 (6.00)		
	Neck extensors	116.54 (74.23)		
	Scapular stabilizers	33.56 (24.59)		

BMI, Body Mass Index; PA, Physical Activity (assessed with the International Questionnaire of Physical Activity for Adolescents); NPRS, Numeric Pain Rating Scale; FDI, Functional Disability Inventory; BaSIQS, Basic Scale on Insomnia complaints and Quality of Sleep; PCS, Pain Catastrophizing Scale; TSK, Tampa Scale of Kinesiophobia; CSES, Child Self-Efficacy Scale; CSI, Central Sensitization Inventory; NPQ, Pain Neurophysiology Questionnaire; PPT, Pressure Pain Thresholds

Table 2 - Results from univariable and multivariable models predicting ≥50% improvement in disability.

Predictors	Univariable models				Multivariable models			
	Post-intervention N=117		6-month follow-up N=118		Post-intervention Nagelkerke R^2=0.12		6-month follow-up Nagelkerke R^2=0.11	
	OR (95%CI)	*p*	OR (95%CI)	*p*	OR (95%CI)	*p*	OR (95%CI)	*p*
Female sex	1.42 (0.49-4.12)	0.53	0.55 (0.20-1.54)	0.26				
Age	0.70 (0.49-1.01)	0.05*	0.82 (0.59-1.15)	0.26	0.64 (0.44-0.93)	0.02**		
BMI	1.02 (0.93-1.12)	0.69	0.95 (0.87-1.05)	0.30				
Pain frequency								
Sometimes	1.43 (0.48-4.29)	0.53	0.39 (0.12-1.25)	0.11				
Oftentimes	0.51 (0.15-1.76)	0.29	0.24 (0.07-0.84)	0.03**			0.23 (0.06-0.82)	0.02**
Always	1.71 (0.37-7.92)	0.49	0.50 (0.10-2.43)	0.39				
Pain duration								
6 months to 1 year	0.93 (0.32-2.77)	0.90	0.63 (0.21-1.88)	0.40				
1 to 2 years	1.05 (0.39-2.78)	0.93	0.81 (0.31-2.14)	0.68				
2 to 5 years	0.98 (0.32-3.03)	0.97	0.81 (0.26-2.54)	0.72				
>5 years	0.52 (0.09-3.14)	0.48	0.33 (0.05-1.96)	0.22				
NPRS	0.91 (0.74-1.11)	0.33	1.04 (0.85-1.26)	0.72				
Moderate PA	1.00 (0.99-1.00)	0.07*	1.00 (0.99-1.00)	0.71	1.00 (1.00-1.01)	0.04**		
Vigorous PA	1.00 (0.99-1.00)	0.35	1.00 (0.99-1.00)	0.58				
FDI	0.99 (0.94-1.05)	0.84	0.96 (0.91-1.01)	0.14				
BaSIQS	1.04 (0.96-1.13)	0.35	0.99 (0.92-1.07)	0.84				
PCS	0.96 (0.92-1.01)	0.11	1.00 (0.96-1.05)	0.87				
TSK	0.98 (0.92-1.05)	0.58	0.99 (0.92-1.06)	0.69				
CSES	0.97 (0.90-1.05)	0.49	1.01 (0.94-1.09)	0.73				
CSI	1.00 (0.98-1.03)	0.79	0.99 (0.96-1.02)	0.46				
NPQ	1.16 (0.95-1.41)	0.15	1.00 (0.82-1.21)	0.96				
PPT-Right articular pillar C5/C6	1.00 (0.96-1.03)	0.90	1.01 (0.98-1.05)	0.48				
PPT-Left articular pillar C5/C6	1.00 (0.96-1.04)	0.91	1.03 (0.99-1.07)	0.17				
PPT-Tibialis anterior	0.99 (0.96-1.02)	0.44	1.00 (0.98-1.03)	0.77				
Endurance tests								
Neck flexors	1.05 (0.98-1.12)	0.14	1.07 (0.99-1.14)	0.06*			1.07 (1.00-1.15)	0.046**
Neck extensors	1.00 (0.99-1.01)	0.24	1.00 (0.99-1.01)	0.13				
Scapular stabilizers	1.00 (0.99-1.02)	0.74	1.01 (0.99-1.03)	0.22				

*p ≤ 0.1, **p<0.05. OR, Odds Ratio; CI, Confidence Interval; BMI, Body Mass Index; PA, Physical Activity (assessed with the International Questionnaire of Physical Activity for Adolescents); NPRS, Numeric Pain Rating Scale; FDI, Functional Disability Inventory; BaSIQS, Basic Scale on Insomnia complaints and Quality of Sleep; PCS, Pain Catastrophizing Scale; TSK, Tampa Scale of Kinesiophobia; CSES, Child Self-Efficacy Scale; CSI, Central Sensitization Inventory; NPQ, Pain Neurophysiology Questionnaire; PPT, Pressure Pain Thresholds

Table 3 - Results from univariable and multivariable models predicting ≥50% improvement in pain intensity

Predictors	Univariable models				Multivariable models	
	Post-intervention N=117		6-month follow-up N=118		6-month follow-up Nagelkerke R^2=0.05	
	OR (95%CI)	*p*	OR (95%CI)	*p*	OR (95%CI)	*p*
Female sex	0.87 (0.31-2.47)	0.80	0.65 (0.23-1.88)	0.43		
Age	0.88 (0.63-1.23)	0.45	0.80 (0.57-1.13)	0.21	0.64 (0.44-0.93)	0.02**
BMI	1.00 (0.91-1.10)	0.99	1.00 (0.91-1.09)	0.97		
Pain frequency						
Sometimes	1.37 (0.46-4.10)	0.57	0.52 (0.16-1.66)	0.27		
Oftentimes	0.70 (0.22-2.26)	0.55	0.39 (0.11-1.36)	0.14		
Always	2.37 (0.46-12.14)	0.30	1.88 (0.29-11.97)	0.51		
Pain duration						
6 months to 1 year	0.77 (0.26-2.25)	0.63	0.49 (0.16-1.53)	0.22		
1 to 2 years		0.55	0.77 (0.28-2.15)	0.62		
2 to 5 years	0.70 (0.23-2.13)	0.53	0.55 (0.17-1.79)	0.32		
>5 years	1.02 (0.19-5.37)	0.98	0.08 (0.01-0.72)	0.03**		
NPRS	1.09 (0.89-1.33)	0.40	1.08 (0.89-1.32)	0.44		
Moderate PA	1.00 (0.99-1.00)	0.45	1.00 (0.99-1.00)	0.81		
Vigorous PA	1.00 (0.99-1.00)	0.19	1.00 (0.99-1.00)	0.67		
FDI	0.98 (0.93-1.04)	0.54	0.94 (0.89-1.00)	0.05*	0.94 (0.89-1.00)	0.049**
BaSIQS	1.02 (0.94-1.10)	0.68	0.95 (0.88-1.03)	0.22		
PCS	1.00 (0.96-1.05)	0.94	0.97 (0.93-1.02)	0.23		
TSK	0.96 (0.90-1.03)	0.27	0.97 (0.91-1.04)	0.42		
CSES	0.95 (0.88-1.03)	0.21	0.94 (0.87-1.02)	0.14		
CSI	0.98 (0.95-1.01)	0.14	0.97 (0.94-1.00)	0.06*		
NPQ	1.05 (0.87-1.28)	0.62	0.89 (0.73-1.09)	0.27		
PPT-Right articular pillar C5/C6	1.01 (0.98-1.05)	0.51	1.04 (0.996-1.08)	0.08*		
PPT-Left articular pillar C5/C6	1.01 (0.97-1.05)	0.56	1.04 (0.996-1.08)	0.08*		
PPT-Tibialis anterior	1.01 (0.99-1.04)	0.34	1.02 (0.995-1.05)	0.12		
Endurance tests						
Neck flexors	1.02 (0.96-1.08)	0.62	1.04 (0.97-1.11)	0.28		
Neck extensors	1.00 (0.99-1.00)	0.20	1.00 (0.99-1.01)	0.52		
Scapular stabilizers	1.00 (0.99-1.02)	0.86	1.00 (0.99-1.02)	0.71		

*p ≤ 0.1, **p<0.05. OR, Odds Ratio; CI, Confidence Interval; BMI, Body Mass Index; PA, Physical Activity (assessed with the International Questionnaire of Physical Activity for Adolescents); NPRS, Numeric Pain Rating Scale; FDI, Functional Disability Inventory; BaSIQS, Basic Scale on Insomnia complaints and Quality of Sleep; PCS, Pain Catastrophizing Scale; TSK, Tampa Scale of Kinesiophobia; CSES, Child Self-Efficacy Scale; CSI, Central Sensitization Inventory; NPQ, Pain Neurophysiology Questionnaire; PPT, Pressure Pain Thresholds

Ethics committee and informed consent:

The current research was approved by an independent ethics committee and subjects gave their informed consent before they were enrolled in the study.

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Journal of Statistics on Health Decision

EXTENDED ABSTRACT

Study of associations between COVID-19 and bacterial infections: a retrospective study

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Introduction:

The COVID-19 pandemic disease, caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (Sars-CoV-2), has affected millions of people worldwide. Clinical practice highlights that the number of patients with COVID-19 diagnosed with bacterial infections during periods of hospitalization is increasing. Rapid characterization of co-infection is essential in the treatment of most patients with COVID-19, as it can result in failure of antimicrobial therapy. Some studies report the prevalence of variable coinfection among patients with COVID-19, however, it can be up to 50% in patients who did not survive. [1, 2]

The present study aims:

- To assess the occurrence of associations between COVID-19 and bacterial infections in patients hospitalized at Centro Hospitalar Baixo Vouga – Aveiro between April 1, 2020 and December 31, 2021.

- Contribute to the definition of pharmacological therapy strategies in patients with mixed, bacterial and Sars-CoV-2 infections.

Methods:

A total of 9194 Sars-CoV-2 test results (Abbott molecular) and 3374 clinical isolates (MALDI Biotyper® - Bruker), from various clinical sources, obtained between April 1, 2020 and October 31, 2021 from Centro Hospitalar Baixo Vouga – Aveiro, Portugal, were studied. Bacterial infections on hospitalized patients which had a positive COVID-19 test (n = 183) in a period of in a period of -30 and +30 days, were selected. The most prevalent bacteria in patients COVID-19 positive were determined and associations between occurrence of COVID-19 infection and occurrence of each bacterial infection, analysed. The association strength was evaluated through Odds Ratio (OR) and it 95% confidence interval. The chi-square testing with P values <0.05 were considered as significant association effect. All statistical analyses were performed using R software, using epiR package.

Results:

We studied 183 hospitalized patients that had positive COVID-19 test and bacterial infections. The percentage of infection was 9,8%. There are several isolates per patient (average 1,7 per patient). The most prevalent bacteria in patients COVID-19 positive are *Escherichia coli* (19,03%), *Klebsiella pneumoniae* (14,84%), *Staphylococcus aureus* (10,65%), *Pseudomonas aeruginosa* (7,42%), *Proteus mirabilis* (7,74%), *Staphylococcus epidermidis* (4,52%), *Candida albicans* (5,16%) and *Enterococcus faecalis* (4,84%). In patients COVID-19 negative (n = 1668) the most prevalent are *Escherichia coli* (21,57%), *Klebsiella pneumoniae* (13,84%), *Enterococcus faecalis* (7,25%), *Staphylococcus aureus* (6,63%), *Staphylococcus epidermidis* (6,49%), *Pseudomonas aeruginosa* (6,20%), *Candida albicans* (5,22%), *Proteus mirabilis* (3,82%). There is a significant association of occurrence between COVID-19 infection and five bacteria (Table 1).

Discussion:

For five bacteria the OR association strength can be considered moderated. There are differences in bacterial infections between positive and negative COVID-19 patients, mainly in *Staphylococcus aureus*. These results strength the importance to further studies on this association including the evaluation of co-morbidities, microbiological distribution, probable increase of nosocomial infection and patient mortality during hospital admission. Agents like *Staphylococcus epidermidis* could be colonisations and is need

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careful to understand this data. This analysis may contribute to help in the definition of empirical therapies in patients with mixed COVID-19 and bacterial infections.

Table 1 - Associations between COVID-19 infection and each bacterial infection.

	COVID + n = 405	**COVID -** n = 8790	**OR**	**LBCI95%**	**UBCI95%**	**p-value***
Escherichia coli	59	661	2.10	1.57	2.79	<0.001
Klebsiella pneumoniae	46	424	2.53	1.83	3.49	<0.001
Staphylococcus aureus	33	203	3.75	2.56	5.50	<0.001
Pseudomonas aeruginosa	23	190	2.73	1.75	4.25	<0.001
Proteus mirabilis	24	117	4.67	2.97	7.33	<0.001
Staphylococcus epidermidis	15	226	1.55	0.89	2.68	0.952
Candida albicans	16	160	2.22	1.31	3.75	0.016
Enterococcus.faecalis	15	226	1.55	0.89	2.68	1.000

* adjusted to simultaneous testing (Bonferroni correction)

Ethics committee and informed consent:

The current research was approved by CHBV ethics committee.

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Journal of Statistics on Health Decision

EXTENDED ABSTRACT

Technology-mediated intervention and cognitive functioning: a systematic review and meta-analysis

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Introduction:

Mild cognitive impairment (MCI) is usually defined as an early stage of cognitive decline with a risk of progressing to Alzheimer's disease or dementia[1, 2]. Interventions to prevent MCI as well as to delay its progression are important. Research has shown a significant and consistent protective effect for all levels of physical activity against the occurrence of cognitive decline [3-5]. Despite evidence on the benefits of physical activity, a recent study has shown that only 55,5% of the European older adults meet WHO's recommendations, and older adults with MCI presented higher odds of not performing this recommended level of physical activity [6, 7]. Identifying pleasant ways of performing physical activity might help them achieve the recommended levels. A potentially attractive way of performing physical activity is through technology. There are several types of physical activity activities that are mediated by technology, including sports [8-10] or dancing [11-14]. These activities are believed to require both physical and cognitive abilities and have been used to improve physical and cognitive functions in older adults [15-17]. To our knowledge there is no systematic review that aimed at synthetizing and evaluating existing evidence on the impact of technology-mediated physical activity on cognitive functioning of older adults with clinical conditions, therefore this study aims to assess the impact of technology-mediated physical activity on the cognitive function of older adults with clinical conditions.

Methods:

The literature search was carried out independently by one of the authors. Four databases (PubMed, SCOPUS, SciELO and Web of Science) were searched using a combination of words related to interventions mediated by technology, physical exercise, and older adults. There were no restrictions on date of publication. We included studies published in English, Portuguese, and Spanish languages, randomized or quasi-randomized clinical trials, including participants 55 years or older with no to mild cognitive impairment.

Risk of bias of the included studies was assessed using Rob 2 [18], and quality of evidence was assessed using the GRADE [19].

A meta-analysis was performed using R packages meta and metafor in RStudio Version 1.4.1103 (Rstudio Team, 2020) running R version 4.0.5 (R Core Team, 2021). As cognitive function was measured on different scales, the standardized mean difference (SMD) was used to measure the effect size. Heterogeneity was evaluated using I2 statistic that ranges from 0 to 100%, which reflect low (25%), moderate (50%), and high (75%) statistical heterogeneity [20]. A random-effect model was used, and forest plots were used to present the SMD.

Cognitive function was classified into six domains, (1) general cognition (2) immediate verbal memory, (3) delayed verbal memory, (4) working memory, (5) attention, and (6) inhibition.

Results:

Eight studies were included in this systematic review [10, 15, 21-26]. Of these, five studies assessed general cognition [15, 21, 23-25], three assessed immediate verbal memory [15, 23, 26], three assessed delayed verbal memory [15, 23, 26], two assessed working memory [10, 26], three assessed attention [22, 23, 26], and two assessed inhibition [23, 26]. Very low quality of evidence indicates that the intervention mediated by technology was superior to combined exercise (cognitive + physical activity) [15, 23] and traditional physical exercise [26] for delayed verbal memory (SDM 0.42, 95% CI 0.01 – 0.83, p=0.04, I2=

Keywords:
Technology; older adults; cognition.

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0%, p=0.47). For the remaining comparisons no difference was found between the technology intervention and traditional physical exercise [21, 22, 24, 26], combined exercise [15, 23], and receiving a booklet with information and illustration outlining the benefits and risks of physical activities [25].

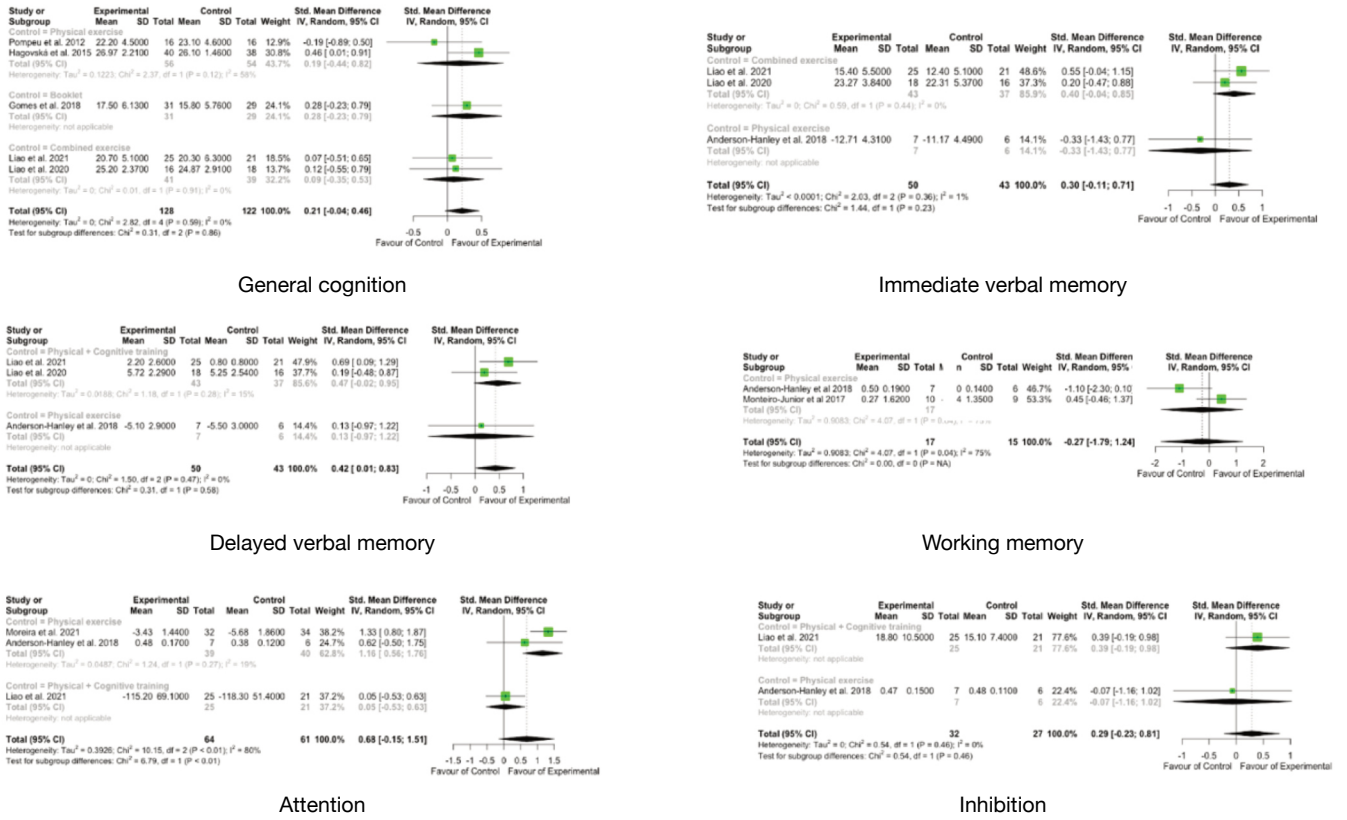

Figure 1 - Metanalysis of cognitive function for older adults with clinical conditions

Discussion:

Results suggest no difference between interventions mediated by technology and the other interventions (i.e. physical exercise and combined physical and cognitive exercise) on the cognition of older adults with clinical conditions. The small sample size of the studies, and the diversity of the design of the included studies, which vary in duration of the intervention, number of sessions, duration of session, and interventions used can explain the obtained results. For the result presented in delayed verbal memory, it might be due to the pattern of the interventions. In all studies that assessed this domain included greater demand on the cognitive component (such as X-box, VR bicycle), and in the control group, one of the studies [23], the authors did not include a cognitive component, and in the other (26), the cognitive component was of very low demand (virtual scenic bike tour: physical exercise interactive with relatively passive and low cognitive load).

In conclusion, very low quality of evidence indicates no difference between intervention mediated by technology and the other intervention in cognition of older adults with clinical conditions. The first limitation of this meta-analysis is the methodological quality of the included studies, which presented high risk of bias, and the second one is the heterogeneity of the studies. Given the potential benefits of interventions mediated by technology, more research is needed to establish the effective components for cognition and physical function and apply this understanding to the development of evidence-based interventions and stablished guidelines for the best prevention or treatment of cognitive decline.

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Journal of Statistics on Health Decision

EXTENDED ABSTRACT

Modelling the impact of the disease on people with COPD – a comparison of feature selection methods

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Introduction:

Linear models (LMs) aim to predict outcomes given p features [1]. The following measure can be used to quantify the fit: (i) mean squared error (MSE); (ii) coefficient of determination (R^2); (iii) adjusted R^2; (iv) Akaike's information criterion (AIC) [2]; (v) Bayesian information criterion (BIC) [3].

Criteria to choose the most appropriate methods to select features in datasets are unclear [4–6]. One approach is the automatic stepwise selection which removes one feature at a time. Another is the Least Absolute Shrinkage and Selection Operator (LASSO) which adds a penalty term λ that reduces the magnitude of coefficients [7].

Information theory provides criteria for setting up probability distributions on the basis of partial knowledge [8]. Normalized entropy [9] measures the information content of a particular model or feature. It was defined based on the consistent and asymptotically normal generalized maximum entropy estimator [10]. Features with normalized entropy approximately equal to one should be excluded from the model.

Chronic obstructive pulmonary disease (COPD) is a progressive, treatable and preventable respiratory disease [11]. The 2020 imposed lockdown due to the Coronavirus Disease 2019 (COVID-19) pandemic is likely to have influenced the daily life of people with COPD.

We aimed to compare feature selection (FS) methods and describe the effect of the COVID-19 lockdown, sociodemographic and clinical features on the impact of the disease on people with COPD.

Methods:

Sociodemographic, anthropometric and clinical data from stable people with COPD recruited in GENIAL (PTDC/DTP-PIC/2284/2014) and PRIME (PTDC/SAU-SER/28806/2017) projects were used.

The COPD assessment test (CAT) was performed at baseline and 5 month after (post) and evaluated the disease impact [12, 13]. The minimal clinically important difference (MCID) is 2 points [14]. Change of CAT score (dCAT) was considered the outcome.

FS was performed in numeric data standardized by subtracting the mean and dividing by the standard deviation: (i) the λ used in LASSO was the one that produced the lowest 5-fold cross-validation MSE from a grid of 15000 values; (ii) the AIC/BIC based stepwise automatic selection consisted of a backward elimination of terms from a LM with all features in order to obtain the lowest AIC/BIC [15]; (iii) normalized entropy procedure with optimization of the supports [10].

Ordinary least squares (OLS) LMs and fit measures were applied with the features selected. A LM with the features selected by the entropy algorithm that returned the highest leave-one-out cross-validation R^2 (LOOCV R^2) was computed with non-standardized data. An α=0.05 was considered.

Results:

A total of 42 participants with mean age 66.3 years (sd 7.8), 3 to 4 comorbidities (64.3%) and a median CAT score of 9.0 ([Q1,Q3]=[5.3,11.0]) were included, 24 (57.1%) of whom in the pre-lockdown group. No significant differences were found between groups (Table S1) nor median CAT scores at different assessments (Figure 1).

The MSE in LASSO was minimized with λ=1.26 and selected CCI and respiratory emergencies (Figure S1, Table 1).

The AIC algorithm removed 18 features. With decreasing order of importance CCI, AECOPD and SGRQ were kept. Using BIC, CCI and respiratory emergencies remained (Table 1).

CCI had the lowest normalized entropy (0.901) followed by the SGRQ (0.929). Respiratory emergencies, pack-years and BMI registered a value under 0.95 (Table 1, Figure S2).

Keywords: COPD, COVID-19, Feature Selection, LASSO, Normalized Entropy, Stepwise Selection

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Table 1 - Feature's importance according to LASSO, AIC based stepwise automatic selection (StepAIC), BIC based stepwise automatic selection (StepBIC) and entropy estimation algorithms.

Features	LASSO	StepAIC	StepBIC	Entropy (NE)	Mean Importance
CCI	1	1	1	1 (0.901)	1
SGRQ	4	3	4	2 (0.929)	3.25
Respiratory emergencies	2	11	2	3 (0.941)	4.5
AECOPD	3	2	3	13 (0.990)	5.25
FEV1 % predicted	5	4	5	9 (0.974)	5.75
Group	7	6	7	16 (0.996)	9
mMRC	11	9	10	8 (0.972)	9.5
Respiratory hospitalizations	6	13	13	6 (0.963)	9.5
FEV1/FVC	12	5	6	18 (0.997)	10.25
BORG Fatigue	9	7	8	19 (0.997)	10.75
LTOT	8	8	9	20 (0.999)	11.25
Sex	10	10	11	15 (0.995)	11.5
Age	14	12	12	12 (0.987)	12.5
NIV	13	15	15	7 (0.965)	12.5
Body mass index	19	16	16	5 (0.944)	14
Pack years	17	20	20	4 (0.943)	15.25
Smoking no. of years	18	14	14	17 (0.997)	15.75
BPAAT Moderate	21	17	17	10 (0.981)	16.25
Smoking status	15	21	21	11 (0.987)	17
BORG Dyspnoea	16	19	19	14 (0.993)	17
BPAAT Vigorous	20	18	18	21 (1.000)	19.25

Abbreviations: AECOPD, acute exacerbation of COPD; BPAAT, brief physical activity assessment tool; BMI, body mass index; CCI, Charlson comorbidity index; COPD, chronic obstructive pulmonary disease; FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity; LTOT, long-term oxygen therapy; mMRC, modified medical council dyspnoea scale; NIV, non-invasive ventilation; SGRQ, St. George's respiratory questionnaire; NE, normalized entropy. Green indicates that features were selected.

The LM using the features selected by LASSO and the BIC method was the same and had the lowest AIC and highest and LOOCV R^2 (0.12). The LM generated by the AIC method and the entropy algorithm with 3 features achieved the highest R^2 (0.27). No significant differences between models were found (Table 2).

The LM with 3 features from the entropy algorithm shows that participants with severe CCI are expected to have a decreased dCAT by 6.47 point when compared with participants with mild CCI (CI95=[2.49,10.45]). Participants with respiratory emergencies tend to have an increased dCAT by 3.22 points. If, at the same time, they have a mild or moderate CCI score, they tended to recover above the MCID. Those without emergencies but with a severe CCI are expected to worsen above the MCID (Figure 2).

Table 2 - Linear model's coefficients and p values for the COPD assessment test score difference using as predictors the features selected by LASSO, AIC based stepwise automatic selection (StepAIC), BIC based stepwise automatic selection (StepBIC) and entropy estimation algorithms (n=42).

	LASSO		StepAIC		StepBIC		Entropy 1 feature		Entropy 2 features		Entropy 3 features		Entropy 4 features		Entropy 5 features	
	Beta	*p*	*Beta*	*p*	*Beta*	*p*	*Beta*	*p*	*Beta*	*p*	*Beta*	*p*	*Beta*	*p*	*Beta*	*p*
AECOPD	-	-	0.32	**0.035**	-	-	-	-	-	-	-	-	-	-	-	-
CCI	-0.42	**0.003**	-0.45	**0.002**	-0.42	**0.003**	-0.41	**0.006**	-0.41	**0.007**	-0.43	**0.003**	-0.43	**0.004**	-0.43	**0.007**
BMI	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	0.01	0.941
Pack Years													0.00	0.978	0.00	0.987
Emergencies	0.29	**0.038**			0.29	**0.038**	-	-			0.30	**0.035**	0.30	**0.038**	0.30	**0.041**
SGQR			-0.23	0.120	-	-	-	-	-0.12	0.398	-0.13	0.339	-0.13	0.376	-0.13	0.381
R^2	0.254		0.271		0.254		0.167		0.182		0.271		0.271		0.271	
adjusted R^2	0.216		0.215		0.216		0.147		0.141		0.215		0.194		0.173	
LOOCV R^2	0.124		0.082		0.124		0.073		0.040		0.091		0.063		0.033	
AIC	111.892		112.889		111.892		114.490		115.730		112.894		114.893		116.887	
AICc	112.524		113.970		112.524		114.798		116.362		113.975		116.560		119.287	
BIC	117.105		119.839		117.105		117.966		120.943		119.845		123.581		127.313	
log-L	-52.946		-52.444		-52.946		-55.245		-54.865		-52.447		-52.447		-52.443	

Abbreviations: AECOPD, acute exacerbation of COPD; BMI, body mass index; CCI, Charlson comorbidity index; COPD, chronic obstructive pulmonary disease; SGRQ, St. George's respiratory questionnaire; *p, p* value; log-L, log-likelihood; LOOCV, leave-one-out cross-validation.

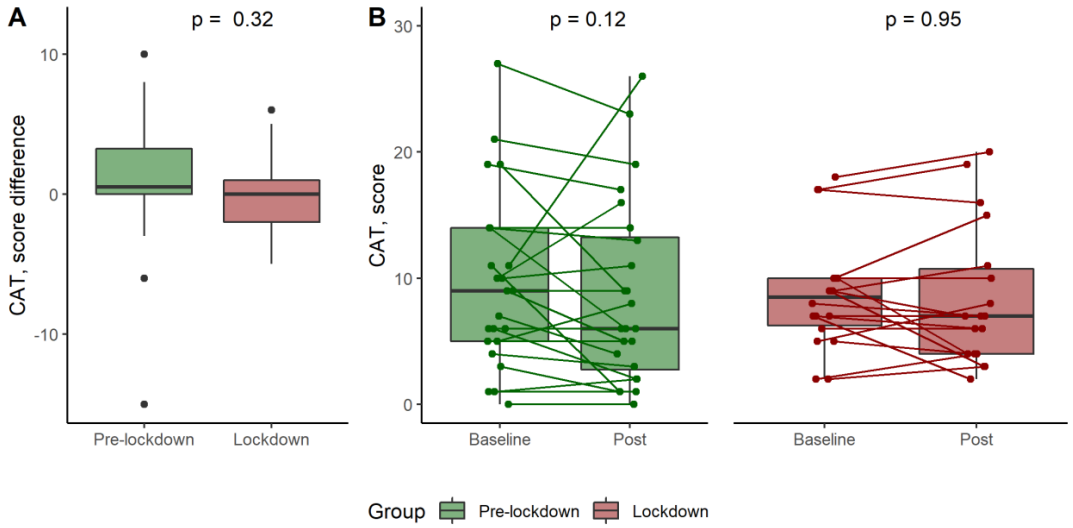

Figure 1 - Distribution of the participants' COPD assessment test (CAT) score: (A) score difference according to the group; (B) scores in the different assessments according to the group. p, p value for the Wilcoxon rank sum test (A) or Wilcoxon signed rank test (B).

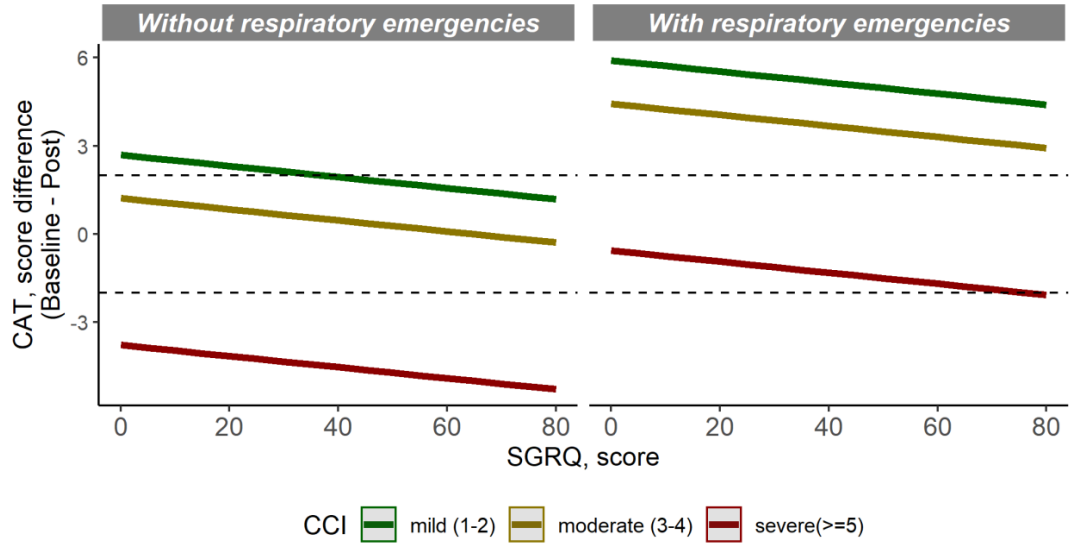

Figure 2 - Predicted difference between baseline and post COPD assessment test (CAT) score according to the Charlson comorbidity index (CCI), the existence of respiratory emergencies in the previous year and the St. George respiratory questionnaire' score (SGRQ). Dashed line represents the minimal clinically important difference.

Discussion:

In regression models with many features where does not exist relationships between features and dependent variable, some features can be considered relevant by significance tests [16]. Elimination algorithms can overestimate the effect size of features and should not be used if $p > n$ [17,18]. OLS may be biased [19] and may lead to unstable solutions because it cannot properly deal with limited information, small samples and collinearity. Normalized entropy estimation is appealing because it imposes no structure on data [10]. Nevertheless, the LM obtained with 3 features selected by the entropy approach was at least not worse than the remaining.

Our model suggests that lockdown had no influence in COPD impact but those with comorbidities but no emergencies tended to recover poorly from the pandemic.

Ethics committee and informed consent:

Five independent Ethics Committees (Centro Hospitalar do Médio Ave ref. 09/2016 and 10/2018; Unidade Local de Saúde de Matosinhos ref. 10/CES/JAS 17/02/2017 and 73/CE/JAS 12/10/2018; Centro Hospitalar Baixo Vouga ref. 777638 and 086892; Hospital Distrital da Figueira da Foz ref. 1807/2017 and 27/05/2019; Administração Regional de Saúde do Centro ref. 64/2016 and 85/2018) approved the study. Written informed consent was obtained from all participants before data collection. Data protection was ensured by the National Committee for Data Protection (no. 7295/2016) and followed the General Data Protection Regulation.

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Journal of Statistics on Health Decision

EXTENDED ABSTRACT

Comparison of comorbidities prevalence in patients with HIV vs non HIV

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Introduction:

USF Arte Nova (USFAN) is inserted in the Baixo Vouga ACES and serves a population of 13086 users. In this population, 29 people have been diagnosed with Human Immunodeficiency Virus (HIV) based on data collected in 2021.

HIV infection can contribute to the development of complications related to both the disease and its treatment, such as mental health, sexually transmitted diseases, obesity, hypertension, neoplasms, heart disease, and social problems. [1,2,3]

Therefore, this study's purpose was to explore the association of being HIV positive with different medical complications, as the ones mentioned before.

Methods:

All the comorbidities presented before were analyzed as binary variables using the R tool version 4.2.0 and the significance level used was 0.05.

The prevalences of the different variables by group (HIV vs non-HIV) were calculated and tested through the chi-square test. The association effect was assessed using Odds Ratio (OR) and its confidence interval. If the variables are directly associated, the OR is greater than 1; if the variables are inversely associated, the OR is less than 1; if the OR is equal to 1, the association effect is null. [4]

Results:

In the HIV population, the comorbidities with lower prevalence compared to the non-HIV population were Depressive Disorder and Sleep Disorder, whose OR<1. However, the decreased prevalence of these two was not statistically significant, as shown in Table 1.

Based on the p-values obtained, it was observed that the prevalence of feeling anxious/nervous/tension, ne/other psychosis, male syphilis, altered lipids, obesity, Hodgkin's disease/lymphoma, malignant skin neoplasm, ischemic heart disease without angina, acute myocardial infarction and tuberculosis were statistically significant in HIV population.

Discussion:

Comparing the prevalence of comorbidities between the HIV and non-HIV population, it was found that the HIV population had a higher incidence in most comorbidities under study. However, Depressive and Sleep Disorder had the lowest prevalence in the HIV population. This observation is not in accordance with the current literature. [3,5,6,7,8,9]

However, the data analyzed was from 2021, so levels of Depressive and Sleep Disorder may be increased in the general population due to the pandemic.

The events assessed are rare for the non-HIV population which becomes a limitation of this study as it leads to imprecise estimates of the association effect and in order to improve the accuracy of the results, the sample size could be increased.

Keywords:
HIV, comorbidities, USF Arte Nova, comorbidity prevalence

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Table 1 - Comparison of prevalence among the various comorbidities

	HIV (n=92)	Non-HIV (n= 13057)	Prevalence ratio	CI (95%)	Attribute prevalence	CI (95%)	OR	CI (95%)	P-Value
DEPRESSIVE DISORDER	2	997	0.91	0.24, 3.48	-0.66	-9.90, 8.57	0.91	0.22, 3.81	1.000
ANXIETY DISORDER/ANXIETY STATE	2	737	1.22	0.32, 4.66	1.25	-7.98, 10.48	1.24	0.29, 5.22	0.678
SLEEP DISTURBANCE	1	481	0.94	0.14, 6.44	-0.24	-6.88, 6.41	0.93	0.13, 6.88	1.000
FEELING ANXIOUS/NERVOUS/ TENSION	2	49	18.38	4.69, 72.04	6.52	-2.70, 15.74	19.66	4.55, 84.97	0.006
NEUROSIS/OTHER PSYCHOSIS	1	4	112.56	12.97, 976.81	3.42	-3.22, 10.06	116.54	12.63, 1075.70	0.011
PERSONALITY DISORDER	1	26	17.32	2.43, 123.41	3.25	-3.39, 9.89	17.90	2.35, 136.48	0.058
HEPATITIS B	1	34	13.24	1.87, 93.54	3.19	-3.45, 9.83	13.68	1.81, 103.42	0.075
CERVICAL DISEASE NE	1	89	5.06	0.73, 35.10	2.77	-3.88, 9.41	5.20	0.70, 38.66	0.182
MALE SYPHILIS	4	2	900.48	171.59, 4725.56	13.78	1.23, 26.33	1044.40	182.92, 5963.04	<0.001
HTN	7	2544	1.24	0.65, 2.36	4.65	-10.94, 20.24	1.31	0.56, 3.08	0.486
ALTERATION IN LIPIDS	8	160	22.51	12.24, 41.41	26.36	10.09, 42.63	30.71	13.40, 70.36	<0.001
OBESITY	5	163	13.81	6.13, 31.10	15.99	2.24, 29.74	16.48	6.21, 43.73	<0.001
NON-INSULIN DEPENDENT DIABETES	1	167	2.70	0.39, 18.61	2.17	-4.47, 8.81	2.76	0.37, 20.38	0.313
MALIGNANT COLON/ RECTUM NEOPLASM	1	49	9.19	1.31, 64.33	3.07	-3.57, 9.71	9.48	1.26, 71.06	0.241
HODGKIN'S DISEASE/ LYMPHOMA	2	18	50.03	12.16, 205.87	6.76	-2.46, 15.98	53.66	11.87, 242.63	<0.001
MALIGNANT SKIN NEOPLASM	2	51	17.66	4.51, 69.14	6.51	-2.72, 15.73	18.89	4.38, 81.54	<0.001
ISCHEMIC HEART DISEASE WITHOUT ANGINA	2	107	8.42	2.18, 32.48	6.08	-3.15, 15.30	8.97	2.11, 38.18	0.010
ACUTE MYOCARDIAL INFARCTION	2	57	15.80	4.05, 61.68	6.46	-2.76, 15.68	16.89	3.92, 72.72	<0.001
PROBLEM DUE TO ILLNESS OF FATHER/MOTHER/ FAMILY MEMBER	1	42	10.72	1.53, 75.30	3.13	-3.52, 9.77	11.07	1.47, 83.22	0.091
POVERTY / ECONOMIC PROBLEM	1	28	16.08	2.26, 114.28	3.23	-3.41, 9.88	16.62	2.19, 126.39	0.062
TUBERCULOSIS	2	16	56.28	13.55, 233.79	6.77	-2.45, 16.00	60.38	13.24, 275.41	<0.001

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Journal of Statistics on Health Decision

EXTENDED ABSTRACT

Changes in consumer habits in community pharmacies in Portugal during the SARS-CoV-2 pandemic using Market Basket Analysis and Network Diagrams

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Introduction:

The sales of over-the-counter (OTC) products in community pharmacies in Portugal is analogous to standard retail business. Several techniques such as cross-selling have been used to increase sales in this segment by encouraging customers to purchase complementary products or services. This technique analyzes transactional data using different methodologies, such as market basket analysis (MBA), which explores associations between items within transactions to uncover customer buying habits and trends. The pairings are supported by measures of interestingness such as the exclusivity of associations of items, lift [1].

OTC products are divided in hierarchical categories, such as beauty, hygiene, and body care, all which include sublevels (e.g. skin, face and hair). Previous works explored the use of network diagrams to group categories based on interpretation of the association rules as links between items [2].

This work explores the association of product categories through generation of rules using MBA in yearly transactional data prior to and during the SARS-CoV-2 pandemic period (2019 and 2020-2021, respectively) to uncover changes in basket purchasing behavior.

Methods:

Data comprising transactions from 1st January 2019 through 31st December 2021 were collected from 2519 community pharmacies in Portugal (approximately 86,2% of all community pharmacies country-wide) and divided in three yearly subsets. Each set was analyzed using the MBA apriori algorithm [3] to extract association rules composed of one antecedent and one consequent product category. Lift measures of the resulting rules were compared across the 3 years to conclude about changes in basket associations. Results were filtered considering absolute variation in lift higher than 10 from 2019 to 2020, and lower than 10 from 2020 to 2021. Moreover, minimum support of 300 occurrences in any of the subsets was imposed. Changes in OTC groups were interpreted by visualizing the networks of product categories produced by the association rules calculated for each subset (year).

Results:

The total number of transactions analyzed from 2019, 2020 and 2021 were 65.232.346, 58.374.315 and 63.858.049, respectively, and a total of 54 associations were considered for analysis. Among these, three use cases stand out: (i) the occurrence of iron supplements and products containing vitamin D in the same transaction was observed in only 19 transactions in 2019. In 2020 and 2021 the support was 613 and 784, respectively, and lift increased from 1.46 to 19.55 and 20.42 in the same years. Figure 1 shows strong association of iron supplements with breastfeed products in 2019. The lack of solar exposition can explain the purchase increase of products containing vitamin D during the pandemic lockdowns (Figure 2); (ii) contrarily, the lift of the association of appetite suppressants and female anti-cellulite products reduced from 63.09 (2019) to 9.51 (2020) and 4.90 (2021). Also, a significant decreased was observed in the number of transactions with the association from pre to the pandemic period, from 353 (2019) to 35 (2020) and 24 (2021). The seasonality of weight loss purchases coupled with the decrease in social and summer activities in 2020 and 2021 decreased the strengths of associations of these products overall (Figures 3 and 4); (iii) the sales of surgical masks, previously highly coupled with various disposable material (e.g. gloves, tissues and bags) stand out as a mixture of effects of both previous use cases. Though the lift reduced from 15.98 (2019) to 3.17 (2020) and 5.37 (2021), the support increased from 740 (2019) to 5053 (2020) and 2293 (2021). Surgical masks were very likely to be bought with almost any product in community pharmacies during the pandemic, which decreased the exclusivity of this association.

Keywords:
Association Rules, Community Pharmacies, SARS-CoV-2, Market Basket Analysis, Network Diagrams, Portugal

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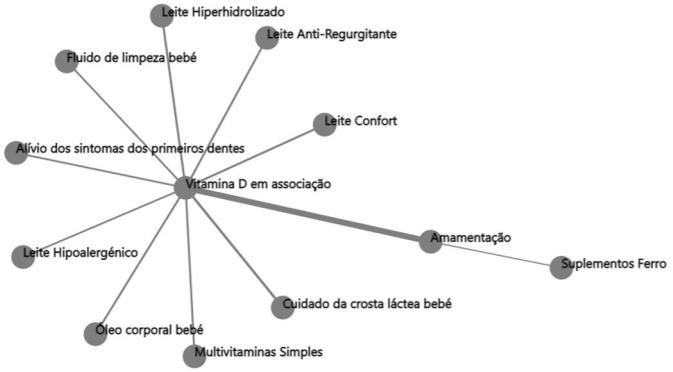

Figure 1 - Network diagram of top 15 associations, by lift, involving iron supplements and products containing vitamin D in 2019.

Figure 2 - Network diagram of top 15 associations, by lift, involving iron supplements and products containing vitamin D in 2020 and 2021.

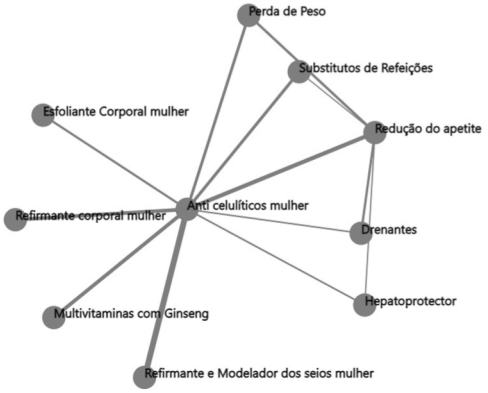

Figure 3 - Network diagram of top 15 associations, by lift, involving anti-cellulite products and appetite suppressants in 2019.

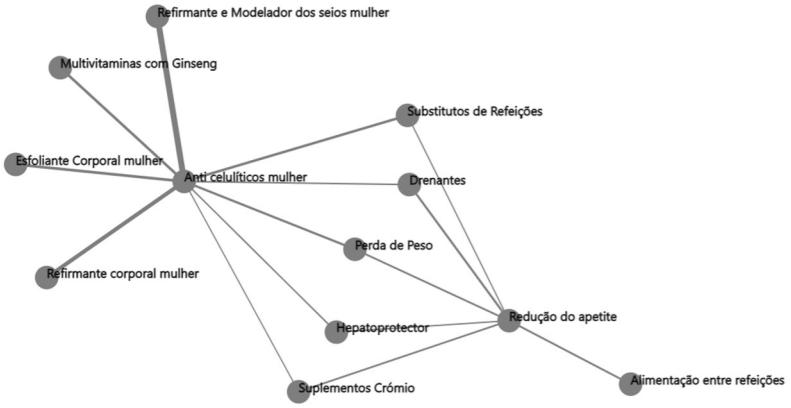

Figure 4 - Network diagram of top 15 associations, by lift, involving anti-cellulite products and appetite suppressants in 2020 and 2021.

Discussion:

The recommendations generated by analytical approaches from retail unravel a panoply of possibilities from evidence-based medicine to monetary profit. Despite the progressive adoption as a contributor to business increase in community pharmacies, the approach proposed allows fitter recommendation of products over time by considering changes in purchase patterns and in the perception of their interestingness.

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Journal of Statistics on Health Decision

EXTENDED ABSTRACT

Acute Kidney Injury after Coronary Artery Bypass Graft Surgery: The heterogeneity of the Available Real-World Data Through a Meta-analysis

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Introduction:

Meta-analysis is the method to pool data from studies that report the same event in a comparable sample and, thus, summarize information from different populations. However, data extraction is limited to the information provided in the included studies. Frequently, individual patient information is not available, hence, real world data access and data uniformization are limited.

To tackle high heterogeneity in a study-level meta-analysis, sensitivity analyses are recommended. Leave-one-out analysis is an option that evaluates the cumulative effect of each study by excluding one at a time, portraying its influence in the overall result [1].

Considering the lack of long-term data on postoperative acute kidney injury (AKI) in coronary artery bypass grafting surgery (CABG) patients, paired with the expected study heterogeneity, we intend to summarize evidence regarding its effect on early and long-term survival, evaluate heterogeneity and perform sensitivity analysis.

Methods:

Systematic searches were performed in MEDLINE and ISI Web of Science, restricted by date of publication (January 1960–April 2021). Inclusion criteria comprised observational studies reporting incidence of postoperative AKI in adult patients, submitted to isolated CABG with at least 1-year of follow-up and survival estimates.

Analyses were performed using Review Manager 5.4. and R environment. Random effects models were used to compute pooled HR and OR (95% CI), through generic inverse variance method and Mantel-Haenszel method. Generalized linear mixed-effects model and logit-transformed proportions of AKI were used for analysis of prevalence data. Heterogeneity was defined using I^2 statistics and was considered low (<49%), moderate (50-74%), or high (>75%) [2]. Between-study heterogeneity was studied using sensitivity analyses, namely, leave-one-out evaluations (metagen (meta R package)). Early and late survival were evaluated through this sensitivity analysis and were presented according to each study impact on both effect size estimates and observed I2. [3]

Results:

After screening 7369 titles and abstracts, 13 retrospective observational studies comprising 63209 patients were included, (N AKI=11366, N non-AKI=51843). AKI incidence ranged 0.6%-54% with a pooled incidence of 16%.

Postoperative AKI was associated with higher early mortality (OR (95%CI): 7.59 (3.18-18.15), $p<0.01$; I^2=94%, Chi^2=80.14, Tau^2=1.06, $p<0.01$), but also with higher long-term mortality (HR (95%CI): 2.23 (1.83-2.70), $p<0.01$), with moderate heterogeneity (I^2=74%, Chi^2=42.92, Tau^2=0.08, $p<0.01$).

In early mortality results, we observed a high effect on the leave-one-out analysis on I^2 (Figure 1) and on Baujat plot (Figure 2) by Ivert et al. [4] study which showed a relevant impact on heterogeneity. After removing this study, I^2 reduced to 0% and the pooled OR decreased and the 95% CI narrowed, (4.78 (3.74 - 6.09), $p<0.001$).

We observed the same for long-term mortality (Figures 3 and 4). The 2 most relevant studies for heterogeneity were Di Mauro et al. [5] and Lv et al. [6]. Although I^2 remained higher than 50% (I2=65%), after removing these two studies, the long-term survival pooled HR decreased and the 95% CI also narrowed, (1.98 (1.68-2.35), $p<0.001$).

Keywords:
Acute kidney injury; Coronary artery bypass; Data Analysis; Heterogeneity; Mortality; Meta-analysis; Population Characteristics; Research Design

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Conflict of interest:
The authors declare no conflict of interest.

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Figure 1 - Leave-one-out analysis for short-term mortality sorted by heterogeneity (I^2).

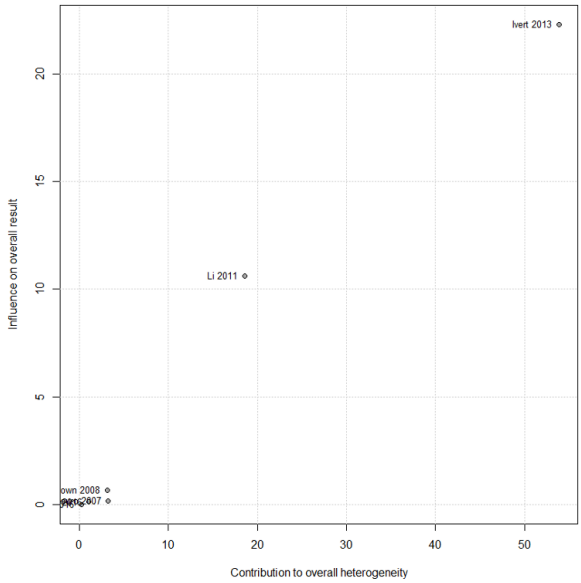

Figure 2 - Baujat plot showing the contribution of each study to the statistic for heterogeneity versus the influence of each study on short-term mortality.

Figure 3 - Leave-one-out analysis for long-term survival sorted by heterogeneity (I^2).

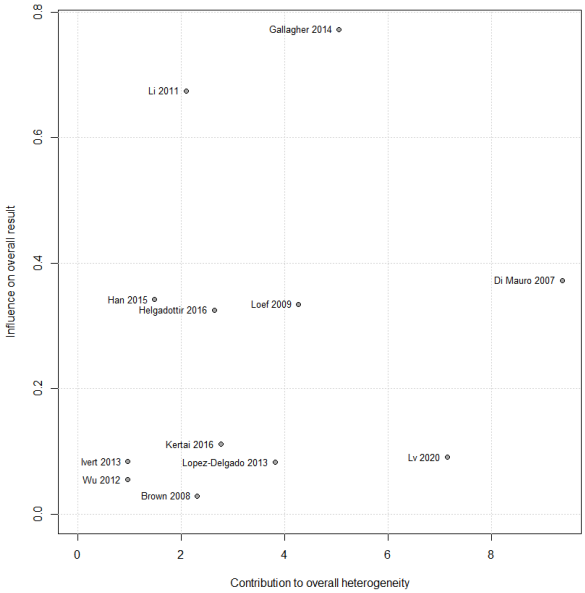

Figure 4 - Baujat plot showing the contribution of each study to the statistic for heterogeneity versus the influence of each study on long-term survival.

At meta-regression analyses, mean/median age, percentage of males, percentage of off-pump, mean/median and maximum follow-up were not found to significantly modify the effect of AKI on long-term mortality.

Discussion and Conclusion:

AKI is a frequent complication after isolated CABG surgery, being associated with higher long-term mortality.

The high heterogeneity found may be due to the different populations and variables' definitions. For instance, Ivert et al. [4] focused their analysis on patients who required postoperative dialysis, translating on a lower incidence of AKI, but also higher severity. Di Mauro et al. [7] defined AKI as an increase above 1 mg/dL or a postoperative value > 2 mg/dL according to preoperative renal function status, which differs from the most traditional criteria used by the other studies: increment of at least 0.3 mg/dL.

Leave-one-out analysis showed that one must pay attention to real-world data, since different variable definitions, namely: different AKI definitions and the samples included in each study, influence overall measures.

Acknowledgements:

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Journal of Statistics on Health Decision

EXTENDED ABSTRACT

Health status assessment through scales and questionnaires: an important tool in Public Health

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Introduction

In the physician's specialized training in Public Health, building a scale and analyzing it statistically is one of the tools to acquire the needed competencies in epidemiological research[1]. The aim is to exemplify the process of elaboration and analysis of a scale, taking as example a questionnaire developed to assess the construct "mental health" and its two domains: "stress"(S) and "eating disorders"(ED).

Methods

For the S domain, adapted items from the SF-36 scale [2] were used in our questionnaire. For the ED domain, adapted items from the Eating Questionnaire - A(EDE-A) scale [3] were used. For both domains, the same response options, in a Likert scale [4], were used: never, a little time/a few times, sometime/sometimes, a lot of time/several times, most of times/most of the time and always. The pilot questionnaire (Figure 1) included an introduction, 26 items and the consent form. A convenient sample was assessed through Google Forms, sharing it through social media. No criteria of selection of respondents were established to assess the larger and more diverse sample possible. The survey was open for three days (1st – 3th April).

Statistical analysis was performed in SPSS (significance level of 5%) to assess: the composition of the sample and responses (exploratory analysis); facial, content, construct and criterion validity; principal component analysis; analysis of the internal consistency; and floor and ceiling effects. Facial and content validity analysis was performed through peer/expert review. Criterion validity is performed using the Gold Standard(GS). As there was not a true GS to assess, convergent validation was performed through a proxy GS, the item "Do you consider yourself mentally healthy?".

Results

Exploratory Analysis: n=258 (Figure 2A, B, C, D); proportion of missings <5%(E) [6]; wide distribution of responses in the different options(F) - wide mean ($\bar{X}$) and standard deviation (SD)(G) [6]; Facial and content validity: both visual approaches used in the different domains of the survey are equally successful. Context and objectives were understood, with no apparent problems of interpretability.

Principal Components Analysis (PCA)(Figure 3): Assessment of the domains suggested by data (two as expected) and initial assessment of the construct (no construct verified). Bartlett's test of sphericity ($p<0.001$) and Kaiser-Meyer-Olkin test [0.807(>0.6)] [6], both reinforce the possibility of performing the PCA, reinforcing the findings of content validity analysis.

Internal Consistency(Figure 3): Cronbach's Alpha (CA) [0.743(0.700-0.950)] [6], item-total correlation (all>0.4) [6] and inter-item correlation (0.320, should have been>0.4, but the CA after deletion of each item increased only 0.003 just for one of the items).

Construct Validity(Table 1): Five theoretical hypothesis were proposed based on the literature to test the construct (assessed in 5 items). There is no attainment of statistically significant differences in at least >75% of the hypotheses proposed, which reinforces that there is no construct.

Criterion validity: The proxy GS has no missings, $\bar{X}$=5.72(±0.966) (respondents considering themselves mentally healthy). Spearman's Correlation(r) are significant and negative between GSxS(r=-0.433, $p<0.001$) and GSxED(r=-0.198, p=0.001), meaning the higher the self-perceived mental well-being, the lower the scores on the scales: there is agreement with the elaborated external criterion.

Floor or ceiling effects: Less than 15% selected the extreme options of response meaning there are no ceiling nor floor effect. In domain S: minimum response=18 (5%); maximum response=48(0.8%). In the ED domain: minimum response=14(0.8%); maximum response=38(0.4%).

Keywords:
Surveys and Questionnaires, Public Health, Principal Component Analysis, Epidemiologic Studies, Mental Health

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Conflict of interest:
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Questionário Inicial: ***Avaliação Stress e Perturbações Alimentares***

Este questionário está a ser divulgado no âmbito da cadeira de "Metodologias de Investigação I": Gustavo Monteiro, Ilka Rosa, Lara P. Guedes, Rachel Barbabela.
Preencha-o com a resposta que melhor se aplicar a si.
As respostas são completamente anónimas.

Parte 1 – Características Sócio Demográfica

1. **Idade:**_____

2. **Sexo**
   - ☐ Feminino:
   - ☐ Masculino:
   - ☐ Prefiro não dizer:

3. **Estado Civil:**
   - ☐ Solteiro:
   - ☐ Casado/União de Facto:
   - ☐ Divorciado:
   - ☐ Viúvo:

4. **Nível de Escolaridade:**
   - ☐ Nenhum:
   - ☐ 1º Ciclo:
   - ☐ 2º Ciclo:
   - ☐ 3º Ciclo:
   - ☐ Ensino Secundário:
   - ☐ Ensino Superior:

5. **Ocupação**
   - ☐ Profissões das Forças Armadas
   - ☐ Representantes do poder legislativo e de órgãos executivos, dirigentes, diretores e gestores executivos
   - ☐ Especialistas das atividades intelectuais e científicas
   - ☐ Técnicos e profissões de nível intermédio
   - ☐ Pessoal administrativo
   - ☐ Trabalhadores dos serviços pessoais, de proteção e segurança e vendedores
   - ☐ Agricultores e trabalhadores qualificados da agricultura, da pesca e da floresta
   - ☐ Trabalhadores qualificados da indústria, construção e artífices
   - ☐ Operadores de instalações e máquinas e trabalhadores da montagem
   - ☐ Trabalhadores não qualificados

B – Stress

As perguntas que se seguem pretendem avaliar a forma como se sentiu e como lhe correram as coisas nas últimas 4 semanas.
Quanto tempo, nas ultimas QUATRO SEMANAS ...

	Sempre	A maior parte do tempo	Bastante tempo	Algum tempo	Pouco tempo	Nunca
1. Se sentiu muito nervoso/a?	☐	☐	☐	☐	☐	☐
2. Se sentiu tão deprimido/a que nada o/a animava?	☐	☐	☐	☐	☐	☐
3. Se sentiu calmo/a e tranquilo/a?	☐	☐	☐	☐	☐	☐
	☐	☐	☐	☐	☐	☐
4. Se sentiu triste e em baixo?	☐	☐	☐	☐	☐	☐
5. Se sentiu feliz?	☐	☐	☐	☐	☐	☐
6. Sentiu que se enerva com facilidade?	☐	☐	☐	☐	☐	☐
7. Sentiu que o stress interferiu com a sua vida quotidiana?	☐	☐	☐	☐	☐	☐
8. Sentiu dificuldade em lidar com imprevistos?	☐	☐	☐	☐	☐	☐

Perturbações Alimentares

As perguntas que se seguem pretendem avaliar a forma como se sentiu e como lhe correram as coisas nas últimas 4 semanas.
Quanto tempo, nas ultimas QUATRO SEMANAS ...

	Sempre	A maior parte do tempo	Bastante tempo	Algum tempo	Pouco tempo	Nunca
1. Se sentiu descontente com o corpo?	☐	☐	☐	☐	☐	☐
2. Restringiu o teor calórico alimentar para controlar o peso / a forma do corpo?	☐	☐	☐	☐	☐	☐
3. Induziu o vómito quando comeu demais?	☐	☐	☐	☐	☐	☐
4. Realizou atividade física intensa para compensar ter comido demais?	☐	☐	☐	☐	☐	☐
5. Realizou jejum (de 8 horas ou mais), sem ingerir nenhum alimento, para controlar o peso / a forma do corpo?	☐	☐	☐	☐	☐	☐
6. Teve episódios de alimentação compulsiva e incontrolável, de grandes quantidades, em curto espaço de tempo?	☐	☐	☐	☐	☐	☐
7. Teve comportamentos de alimentação escondido/a para que os outros não vissem?	☐	☐	☐	☐	☐	☐

Parte 2 -Caracterização Stresse e Pertubações Alimentares

A – Gerais

6. **Assinale, caso se aplique, todas as atividades que realiza atualmente:**
   - ☐ Desporto de alta competição
   - ☐ Ballet
   - ☐ Modelo de fotografia / passarela
   - ☐ Representação

7. **Utiliza redes sociais (Facebook, Instagram, Twitter, chats, outros):**
   - ☐ Não utilizo
   - ☐ Pelo menos 1 vez por mês
   - ☐ Pelo menos 1 vez por semana
   - ☐ Todos os dias (menos de 2 horas por dia)
   - ☐ Todos os dias (entre 2 e 8 horas por dia)
   - ☐ Todos os dias (mais de 8 horas por dia)

8. **Já sofreu *bullying* (na escola, no trabalho, nas redes sociais, outros)?**
   - ☐ Sim, no último ano
   - ☐ Sim, há mais de um ano
   - ☐ Não

9. **Considera-se mentalmente saudável?**
   - ☐ Sempre
   - ☐ A maior parte do tempo
   - ☐ Bastante tempo
   - ☐ Algum tempo
   - ☐ Pouco tempo
   - ☐ Nunca

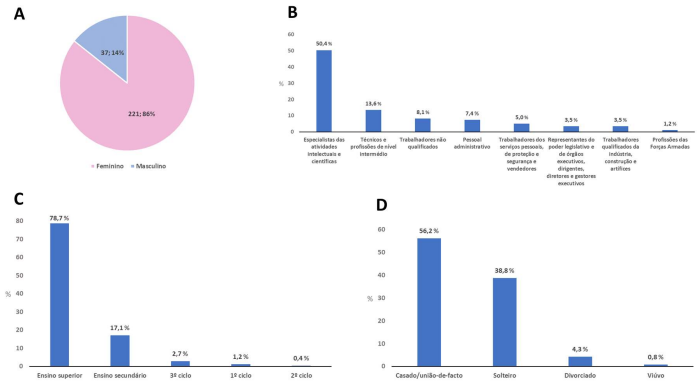
10. **No seu seio familiar, há histórico de doença mental?**
    - ☐ Sim, eu
    - ☐ Sim, em familiares de primeiro grau
    - ☐ Sim, em familiares de segundo grau ou mais afastados
    - ☐ Sim, em ambos
    - ☐ Não
    - ☐ Desconheço

Parte 3- Consentimento Informado

Declaro que dou **consentimento** para o tratamento dos meus dados pessoais, aos quais terão acesso os médicos de saúde pública mencionados e restante grupo de investigação. O período de conservação destes dados é permanente. O grupo garante a estrita confidencialidade no tratamento dos dados fornecidos, os quais não serão partilhados com terceiros e garante ao titular dos dados os direitos de aceder, actualizar, rectificar ou apagar os seus dados pessoais, através do seguinte correio electrónico: larapguedes@arsnorte.min-saude.pt

- ☐ Sim
- ☐ Não

Figure 1 - Questionnaire for epidemiological study in mental health: association of stress and eating disorders. A learning experience in Public Health. Questionnaire designed based on the SF-36 (2) scale and the EDE-A(3) scale. It includes an introduction and 26 questions and the consent form: five to assess the sample in sociodemographic terms - sex, age, marital status, level of education and work occupation; eight to assess the domain "stress" - SF-36 scale (P1 to P8); seven to assess the domain eating disorders" - original construction, from the EDE-A(P9 to P15); four specifically to assess construct validity: social activities, social networks, bullying, family history; one to assess criterion validity (gold-standard proxy question), with the self-assessment of mental state. Finally, one on the scope of informed consent, which may be the study group's judging its placement (at the beginning or end).



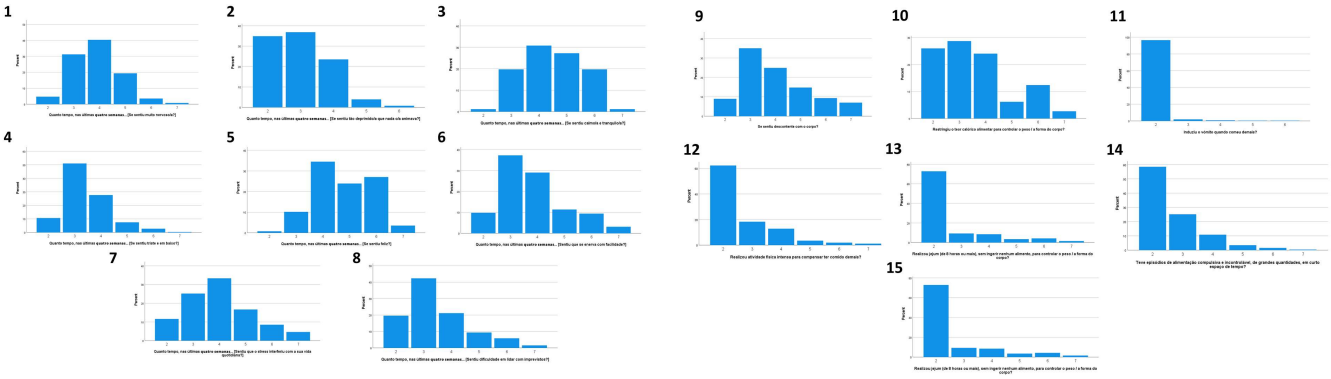
E

Question	Mean	Standard Desviation	Question	Mean	Standard Desviation
Q1	3,87	0,96	Q9	4,02	1,37
Q2	2,98	0,9	Q10	3,56	1,394
Q3	4,5	1,083	Q11	2,06	0,37
Q4	3,41	0,914	Q12	2,65	1,053
Q5	4,79	1,089	Q13	2,64	1,225
Q6	3,79	1,221	Q14	2,65	0,964
Q7	3,99	1,285	Q15	2,32	0,778
Q8	3,46	1,17			

F

Answer	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Q13	Q14	Q15
Valid	253	255	253	253	255	255	258	255	257	258	258	257	258	258	258
Missing	5	3	5	5	3	3	0	3	1	0	0	1	0	0	0
Missing (%)	1,94	1,16	1,94	1,94	1,16	1,16	0	1,16	0,39	0	0	0,39	0	0	0

G



H

Variável Original (P)	Variável Recalculada (Px_Rec)	Valor Original	Valor Recalculado
P1	P1_Rec	1	Missing
P2	P2_Rec	2	6
P4	P4_Rec	3	4
P6	P6_Rec	4	5
P8	P8_Rec	5	2
P9	P9_Rec	6	3
P12	P12_Rec	7	7

Variável Original (P)	Variável Recalculada (Px_Rec)	Valor Original	Valor Recalculado
P7	P7_Rec	1	6
P10	P10_Rec	2	4
P11	P11_Rec	3	5
P13	P13_Rec	4	2
P14	P14_Rec	5	3
P15	P15_Rec	6	7

Variável Original (P)	Variável Recalculada (Px_Rec)	Valor Original	Valor Recalculado
P3	P3_Recpos	1	Missing
		2	7
		3	6
		4	5
P5	P5_Recpos	5	4
		6	3
		7	2

Figure 2 - Exploratory analysis: of demographic data, assessment of missings, proportion of different answers, and recoding when there is inverse correlation. Analysis of socio-demographic data (A, B, C, D): mostly females (86%), specialists in intellectual and scientific activities (50.4%), with higher education as the schooling level of current or previous attendance (78.7%) and married/in a consensual union (56.2%); Distribution of answers in the different options (E): the scope is to assess the existence of problematic questions, with answers with to the left, to the right, or options with no answers; If there are no answers at the extremes, it may mean that it is a serious question and does not necessarily have to be removed from the final questionnaire, as is the case with P11 of the questionnaire. Proportion of missings (F): recommended to be less than 5%. The maximum proportion of missing (per item) was 1.9% (5 missing), and therefore do not seem to have caused any problems in perceiving the question or the answers, nor any discomfort in flagging them. Distribution of mean and standard deviation measures at the level of each item (G): of the stress domain (P1 to P8) and eating disorders (P9 to P15). P1: How long, in the last four weeks... [Have you felt very nervous?]; P2: How long in the past four weeks... [Felt so depressed that nothing could cheer you up?]; P3:How long in the last four weeks... [Felt calm and peaceful?]; P4: How long in the last four weeks... [Felt sad and down?]; P5:How long in the last four weeks... [Felt happy?]; P6: How often in the last four weeks... [Have you felt that you get on your nerves easily?]; P7: How long, in the last four weeks... [Did you feel that stress interfered with your daily life?]; P8: How often in the past four weeks... [Did you feel difficulty coping with unforeseen events?]; P9: Felt unhappy with your body?] P10: Restricted the calorie content of food to control weight/body shape?; P11: Induced vomiting when you ate too much?;P12: Undertook heavy physical activity to compensate for overeating?; P13: Have you fasted (for 8 hours or more) without eating anything to control your weight/body shape?; P14: Had episodes of compulsive and uncontrollable eating, of large quantities, in a short period of time?; P15:Have you engaged in hidden eating behaviours so that others would not see? Answers Q1 to Q15=1: never;2: not much time; 3: some time; 4: a lot of time; 5: most of the time; 6: always;P11 shows lower values, as it is a more specific item of eating disorders, so this distribution may fit the fact that we have a hypothetical sample of mostly healthy individuals and not the fact that the item is poorly constructed. Recoding of variables (H): So that all items have the same meaning, thus allowing for the calculation of the mean inter-item correlations. P3 and P5 were recoded negative for positive, since they had inverse correlations.

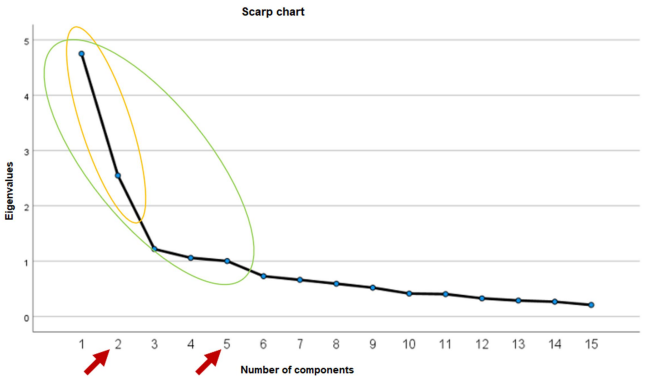
A

Total explained variance

Component	Initial Eigenvalues			Sums of squared loadings extraction			Sums of squared loadings extraction		
	Total	% of variance	Cumulative %	Total	% of variance	Cumulative %	Total	% of variance	Cumulative %
1	4,750	31,669	31,669	4,750	31,669	31,669	3,442	22,945	22,945
2	2,549	16,993	48,662	2,549	16,993	48,662	2,090	13,932	36,877
3	1,219	8,129	56,791	1,219	8,129	56,791	1,970	13,135	50,012
4	1,061	7,070	63,861	1,061	7,070	63,861	1,814	12,095	62,107
5	1,003	6,685	70,546	1,003	6,685	70,546	1,266	8,439	70,546
6	0,729	4,857	75,404						
7	0,662	4,414	79,818						
8	0,593	3,954	83,772						
9	0,521	3,476	87,248						
10	0,415	2,766	90,014						
11	0,405	2,699	92,713						
12	0,328	2,188	94,901						
13	0,289	1,923	96,825						
14	0,267	1,780	98,605						
15	0,209	1,395	100,000						

Extraction Method: Principal Component Analysis

B



C

Questions	Components Matrix		Varimax Rotation	
	Component		Componente	
	1	2	1	2
How long, in the last four weeks... [Have you felt very nervous?]	0,665	-0,282	0,718	0,073
How long in the past four weeks... [Felt so depressed that nothing could cheer you up?	0,762	-0,214	0,771	0,180
How long in the last four weeks... [Felt calm and peaceful?	-0,630	0,306	-0,700	-0,036
How long in the last four weeks... [Felt sad and down?	0,715	-0,270	0,757	0,109
How long in the last four weeks... [Felt happy?	-0,522	0,301	-0,602	0,012
How often in the last four weeks ... ... [Have you felt that you get on your nerves easily?]	0,667	-0,220	0,690	0,129
How long, in the last four weeks... [Did you feel that stress interfered with your daily life?]	0,694	-0,376	0,789	0,006
How often in the past four weeks... [Did you feel difficulty coping with unforeseen events?]	0,680	-0,194	0,689	0,158
Felt unhappy with your body?	0,498	0,420	0,233	0,608
Restricted the calorie content of food to control weight/body shape?	0,287	0,586	-0,031	0,652
Induced vomiting when you ate too much?	0,221	0,481	-0,038	0,526
Undertook heavy physical activity to compensate for overeating?	0,378	0,534	0,074	0,651
Have you fasted (for 8 hours or more) without eating anything to control your weight/body shape?	0,321	0,520	0,031	0,610
Had episodes of compulsive and uncontrollable eating, of large quantities, in a short period of time?	0,508	0,566	0,172	0,740
Have you engaged in hidden eating behaviours so that others would not see?	0,524	0,559	0,189	0,743

D

Stress" domain					Domínio "*Perturbações Alimentares*"				
Cronbach's alpha	Inter-item Correlation	Itens	Item-Total Correlation Corrected	Cronbach's alpha if item deleted	Cronbach's alpha	Inter-item Correlation	Itens	Item-Total Correlation Corrected	Cronbach's alpha if item deleted
0,863	0,450	P1_Rec	0,625	0,845	0,743	0,320	P9_Rec	0,494	0,707
		P2_Rec	0,687	0,84			P10_Rec	0,505	0,705
		P3_Recpos	0,603	0,847			P11_Rec	0,331	0,746
		P4_Rec	0,661	0,843			P12_Rec	0,45	0,714
		P5_Recpos	0,478	0,861			P13_Rec	0,448	0,715
		P6_Rec	0,606	0,848			P14_Rec	0,556	0,693
		P7_Rec	0,692	0,837			P15_Rec	0,579	0,698
		P8_Rec	0,596	0,848					

Figure 2 - Principal Components Analysis. A: Descriptive analysis of items is done to determine the natural number of constructs. The explained variance is verified, and how many components to retain. According to the eigenvalue superior to 1 criterion, we would have five components. To explain 70% of the variance, 5 components would be necessary. B: Scree plot: used in association with the evaluation of the eigenvalue criterion superior to 1, by the scree plot analysis, commonly known as the elbow rule, depending on the observer's sensibility, it is verified how many components are to be retained, and we can, in this case, aim for the two or five components, as circled. The green circle shows 5 components to be retained; the yellow one, two. Check that the distance from the first to the second point is similar to the distance from the second to the third. For there to be construct, the rule would be before the elbow, the distance between the first and the second to be greater than that from the second to the third point. This associated with the other factors explained, justifies this questionnaire not having a construct. C: Principal components matrix with and without varimax rotation: To make the final decision, we proceeded to the interpretation criterion. We found that, without rotation, there is no correlation between the items of each of the two domains under study and each of the components in specific. Not verifying a pattern of distribution, we forced to 2 domains. D: Evaluation of Internal Consistency: The items in the stress domain were found to be consistent and not redundant, justifying keeping all of them, because deletion of any of the questions would not cause an increase in Cronbach's alpha. For P11, since the increase in Cronbach's alpha was residual and, as noted above, the question is specific and measures the severity of the eating disorder domain, it would be expected that there would be this tendency to this result because not many responses would be expected. With that, it was decided not to remove it.

Table 1 - Evaluation of Construct Validity.

Theory	Hypothesis	N	Mean	Standard Desviation	*p*-value
Frequent (>8h) users of social networks are more likely to suffer from stress	Frequent users of social networks (more than 8h)	77	3,8279	0,80297	0,574
	Less frequent social network users (less than 8h)	169	3,7559	0,7613	
Frequent (>8h) social network users are more likely to suffer from an eating disorder	Frequent social network users (more than 8h)	81	2,8818	0,68541	0,527
	Less frequent social network users (less than 8h)	175	2,8294	0,66966	
Individuals who perform ballet, competitive sports, photography and catwalk modelling and acting are more likely to have an eating disorder	Individuals who do not perform the activities mentioned	232	2,8116	0,62788	0,098
	Individuals who carry out the activities mentioned	24	3,1786	0,97279	
Individuals with a family history of mental illness are more likely to have an eating disorder	Individuals with a family history	113	2,8799	0,64922	0,192
	Individuals without family history	95	2,794	0,66899	
Individuals with family history of mental illness are more likely to suffer from stress	Individuals with family history	109	3,9358	0,79086	0,001
	Individuals without a family history	92	3,5992	0,71159	
Individuals who have experienced bullying are more likely to have an eating disorder	Individuals who have experienced bullying	97	2,9087	0,63894	0,083
	Individuals who have not been bullied	159	2,8077	0,69336	
Individuals who have experienced bullying are more likely to experience stress	Individuals who have experienced bullying	91	3,9368	0,75355	0,014
	Individuals who have not been bullied	155	3,6855	0,77257	
Individuals who were female are more likely to have an eating disorder	Female	219	2,8832	0,69183	0,037
	Male	37	2,6255	0,50882	
Female report being more likely to experience stress	Female	210	3,8208	0,76155	0,02
	Female	36	3,5313	0,80809	

After ascertaining data non-normality, we performed a Mann-Whitney U-test. This scale is not consistent with 75% of the theoretical hypotheses concerning the domains (and construct) in question. After analysing the results, we found that 100% consistency was ensured in the domain of stress, but all hypothesis tests failed in the domain of eating disorders, which indicates that this result might be due to the application of the questionnaire in a healthy sample and not to the lack of validity of the scale, since it works for stress.

Discussion

The application of questionnaires is a practical tool that has the advantage of being designed for specific topics and specific populations, to assess large samples. It has the disadvantage that it needs to be analyzed and validated to guarantee its quality. In this example, our scale had: a sufficient sample, higher than 4 times the number of items, albeit healthy (the severity item, item 11, had $\bar{X}$=2,06±0.37); a low proportion of missings; a wide distribution in all the response options, except for item 11 (linked with the severity of the ED); two domains; absence of a true construct; internal consistency (S>ED); no construct validity; convergent validity; no ceiling or floor effect. As a final questionnaire proposal, we should: restructure sections and headings of the questionnaire to anonymize the domains; keep all items; reformulate some questions to increase their interpretability.

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