

Study to determine relevant health outcome measures in opioid use disorder: Multicriteria decision analysis

Estudio para la determinación de medidas de resultados en salud relevantes en el trastorno por consumo de opiáceos. Análisis de decisión multicriterio

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Abstract

The aim of the current study was to establish the most relevant health outcomes to assess opioid substitution treatment programmes (OSP) in patients with opioid use disorder (OUD) in Spain. A multicriteria decision analysis was applied in 3 phases: 1) concepts and criteria definitions; 2) criteria screening and weighting by means of a discrete choice experiment; 3) deliberative process. Criteria established in phase 1 were: substance use (opioids, alcohol, tobacco, stimulants and cannabis), other mental disorders (affective/anxiety disorder, psychosis, attention deficit hyperactivity disorder, borderline personality disorder, antisocial personality disorder, gambling disorder and other impulse control disorders), level of disability, adherence, medical illnesses (medical comorbidities, risk behaviours, infectious and sexually transmitted diseases), psychosocial aspects (hostile and/or violent behaviour and work problems), functional disability (quality of life, treatment and service satisfaction, social functionality). In phase 2, the most relevant factors in OSP were determined, and subsequently assessed in the deliberative process: remission of substance use (opioids, alcohol and stimulants), improvement of other mental disorders (psychosis and borderline personality disorder), improvement in comorbidity management, and improvement in social functionality, with a weighting of 56.5%, 21.9%, 11.0%, and 10.7%,

Resumen

El objetivo fue establecer los resultados en salud con mayor relevancia en la evaluación de programas de tratamiento de sustitución de opiáceos (PTSO) en pacientes con trastorno por consumo de opiáceos (TCO) en España. Se realizó un análisis de decisión multicriterio con 3 fases: 1) definición de conceptos y criterios a evaluar; 2) cribado y ponderación de criterios mediante un experimento de elecciones discretas; 3) proceso deliberativo. Los criterios de la fase 1 fueron: consumo de sustancias (opiáceos, alcohol, tabaco, estimulantes y cannabis), trastornos mentales (trastorno afectivo ansioso, psicosis, trastorno por déficit de atención e hiperactividad, trastorno límite de personalidad, trastornos de personalidad antisocial, trastorno por juego y otras alteraciones del control de los impulsos), nivel de discapacidad, adherencia, enfermedades médicas (comorbilidades, conductas de riesgo, enfermedades infecciosas y de transmisión sexual), aspectos psicosociales (conducta hostil y/o violenta, presencia de problemas laborales), discapacidad funcional (calidad de vida, satisfacción con el tratamiento y servicio, funcionamiento social). En la fase 2 se determinaron los factores fundamentales en la elección de un PTSO, revisados en el proceso deliberativo: remisión del consumo de sustancias (opiáceos, alcohol y estimulantes), mejoría en el manejo de otros trastornos mentales (psicosis y trastorno límite de la personalidad),

Received: November 2018; Accepted: May 2020.

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respectively. The current analysis defines the main health outcomes in OSP in patients with OUD in Spain, supporting decision making and socio-health management of existing resources.

Keywords: Opioid use disorder; Opioid substitution programmes; Multicriteria decision analysis; Health outcomes; Discrete choice experiment.

The management of opioid use disorders (OUD) represents a major challenge both from healthcare and social perspectives. A series of pharmacological and psychological approaches defined by professional experts in mental health and addictions have been consolidated to manage OUDs in different healthcare contexts (Pilling, Strang & Gerada, 2007; Socidrogalcohol, 2016). Nevertheless, it has been estimated that opioid users in Europe have a probability of mortality at least 5-10 times greater compared to the rest of the population of same age and gender, with overdose being the main cause of death. It is estimated that in 2015 at least 7,585 overdose deaths associated with the use of at least one illegal drug occurred in European Union member states, with opioids detected in 81% of these overdose deaths (European Monitoring Centre for Drugs and Drug Addiction, 2017). Similarly, an increase in the problems derived from opioid use and from deaths associated with overdoses of heroin and synthetic and legal and illegal opioids has been detected in the United States in recent years (Hedegaard, Warner & Miniño, 2017).

Addiction management is particularly complex given its multidimensional impact, which significantly compromises the lifestyles of people who suffer it and of the communities in which they live (Barrio et al., 2016; Fernández Miranda, 2001; Gedeon et al., 2019; Jiménez-Treviño et al., 2011; Martínez-Luna et al., 2018; Pedrero-Pérez & Grupo MethaQoL, 2017; Torrens, Mestre-Pintó, Montanari, Vicente & Domingo-Salvany, 2017). Therefore, when assessing the health outcomes of interventions used in the initiation and maintenance of opioid substitution treatment programs in patients with OUD, psychiatric, psychological, biological, and socioeconomic indicators should be considered. While the key measure of the effectiveness of these interventions has traditionally been abstinence, undoubtedly a very important factor, it is not enough to ensure patient recovery (Cloud & Granfield, 2008).

Other indicators have also been used, such as treatment program retention, reduction in the use of non-prescribed opioids or other secondary drugs, or decrease in crime and morbimortality (Iraurgi, 2000). In addition, a number of factors have been incorporated into the assessment of opioid substitution treatment programs, such as satisfaction with and perception of treatment in studies of healthcare

mejoría en manejo de comorbilidades médicas y mejoría en el funcionamiento social, con un peso del 56,5%, 21,9%, 11,0% 10,7% respectivamente. Este análisis define los resultados sanitarios más relevantes en PTSO en pacientes con TCO en España, favoreciendo la toma de decisiones y la gestión socio-sanitaria de los recursos existentes.

Palabras clave: Trastorno por consumo de opiáceos; Programas de tratamiento de sustitución de opiáceos; Análisis de decisión multicriterio; Medidas de resultados en salud; Experimento de elecciones discretas.

quality and effectiveness (Bobes, Casas & Gutiérrez, 2011; Pérez de los Cobos et al., 2004; Sociedad Española de Toxicomanías, 2006; Stahler & Cohen, 2000; Treolar, Fraser & Valentine, 2007; Trujols & Pérez de los Cobos, 2005). Patients who are more satisfied with the intervention have been shown to have greater acceptance of treatment programs, in turn resulting in better adherence and retention to these programs (Bilbao Acedos, Lozano Rojas, Ballesta Gómez & González-Saiz, 2009; Fan, Burman, McDonnell & Fihn, 2005; World Health Organization, United Nations International Drug Control Program and European Monitoring Centre on Drugs and Drug Addiction, 2000). The great challenge for decision-making based on health outcomes arises when integrating and weighting all the indicators to help decision-makers (healthcare professionals and managers, political and social administrators) to establish the safest, most effective and efficient strategy, without oversimplifying the problem. Multicriteria decision analysis (MCDA) offers a suitable approach for decision making in complex environments since it allows the systematization of the decision in different stages, establishing and estimating the preferences of the decision makers explicitly (Marsh et al., 2016; Thokala et al., 2016; Thokala & Duenas, 2012).

The number of MCDAs at international level is low and have been focused, among other things, on specific pathologies, such as rare diseases or HIV/AIDS (Goetghebeur et al., 2008; Paulden, Stafinski, Menon & McCabe, 2015; Schlander et al., 2016; Sussex et al., 2013; Wagner, Khoury, Willet, Rindress & Goetghebeur, 2015; Youngkong, Teerawattananon, Tantivess & Baltussen, 2012), on the application of the EVIDEM evaluation framework for assessing interventions in ultra-rare diseases by health systems (Goetghebeur et al., 2011), such as the Catalan Health Service (Spain) (Gilabert-Perramon et al., 2017), on the incorporation of innovations in certain geographic areas, such as Lombardy (Italy) (Radaelli et al., 2014) and on the prioritization of health interventions in Norway (Defechereux et al., 2012).

The aim of this study is therefore to generate a framework for assessing health outcomes with greater relevance in opioid substitution treatment programs for patients with OUD in Spain, using MCDA methodology, which facilitates the objective assessment of these interventions from the point of view of clinical management.

Method

The MCDA process was carried out following international recommendations which define the necessary steps (Marsh et al., 2016; Thokala et al., 2016; Thokala et al., 2012). The study comprised three distinct phases based on the tasks to be performed: 1) a first phase in which concepts and criteria were defined for use in the assessment of opioid substitution treatment programs in patients with OUD; 2) a second phase in which these criteria were screened and weighted; 3) a deliberative process to reach a final conclusion on the entire process (Bobes et al., 2018).

A panel of 20 Spanish experts of national and international standing in the clinical management of mental health and addictive behaviours took part in the project, alongside representatives of scientific societies and health-care policy administrators.

Phase 1: Definition of criteria and levels

The main aim of this phase was to establish the criteria with which to assess the suitability of the interventions in the treatment of OUD. To this end, we called on five experts in the treatment of OUD. First, they were sent a questionnaire with a series of criteria and outcome measures and a proposal with different patient profiles for consideration in choosing a program for OUD treatment. After completing and processing the responses to this first questionnaire, a consensus was established with the five experts during a face-to-face meeting on the criteria and levels to be considered. In this consensus, a performance matrix was drawn up for use in the next phase.

Phase 2: Screening and weighting of criteria

The main aim of this phase was the screening of those criteria considered important in decision-making and the weighting of each one. Thus, a questionnaire was designed based on Discrete Choice Experiment (DCE) methodology, in accordance with international recommendations for good practice (Bridges et al., 2011; Reed Johnson et al., 2013). This questionnaire was completed by 15 experts who participated exclusively in this phase, in addition to three experts from phase 1.

The questionnaire items comprised pairs of hypothetical interventions and patient profiles. The interventions were configured based on the combination of the levels of each of the criteria agreed on in phase 1 (Table 1). Based on these criteria, it was necessary to generate 72 intervention pairs to calculate the weighting of each of the criteria. To facilitate completion of the DCE, two versions of the questionnaire with 36 items each were generated. For the design of the interventions shown in the items, an orthogonal design was chosen using the "Support.Ces" package (Aizaki, 2012).

The patient profiles included in the questionnaire were designed on the basis of the characteristics considered rel-

evant by the panel of experts in phase 1 with the aim of evaluating whether the characteristics of these patients influenced the assessment of the interventions, based on the established criteria. Twenty-one patient profiles were generated using a fractional factorial design algorithm with Fedorov optimization. To obtain the patient profiles, the "AlgDesign" package was used (Wheeler, 2004).

On obtaining the completed questionnaire, two statistical analyses were performed using multinomial logistic regression models, one to screen criteria and the other to estimate weights.

The selection criterion in the screening analysis required the coefficient to have a statistically significant value ($p < 0.05$). The screened variables were subject to a second multinomial logistic regression model to calculate the weight of the screened criteria. The following formula was used for weighting the criteria:

$$WD_i = \frac{e^{\beta_i D_i}}{\sum_{D_1}^{D_n} e^{\beta_D}} * 100$$

D_i = Domain

WD_i = Domain i weight percentage

β_i = Domain i model coefficient for

In addition, a qualitative analysis of the response pattern was also carried out to assess the influence that patient characteristics may have had on the choice of an intervention. The method of analysis is detailed in Appendix 1.

All statistical analyses were performed with R software, version 3.2.3.

Phase 3: Deliberative process

In this phase, the aim was to reflect on and interpret the screened criteria and their weights. Furthermore, we reviewed which patient profile characteristics had a notable influence on decision criteria in the choice of intervention. This phase involved the five experts from phase 1.

Results

Definition of criteria and levels

The criteria and levels agreed on by the experts for assessing opioid substitution treatment programs in patients with OUD, after the consensus meeting with the phase 1 experts, are shown in Table 1. In terms of *substance use*, it was assessed whether there was a remission (total or partial) after the intervention in the use of opioids, alcohol, tobacco, stimulants and cannabis, according to DSM-5 criteria (American Psychiatric Association, 2013). In the *mental disorders* section, it was considered whether the intervention led to an improvement in psychopathology based on DSM-5 criteria (American Psychiatric Association, 2013). Mental disorders considered were affective/anxiety disorder, psychosis, attention deficit hyperactivity

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Table 1. *Criteria and levels assessed.*

Criteria	Levels
Substance use	Opioids No remission Partial remission//early total remission (according to DSM-5 at least 3 months and less than 12 months) Prolonged total remission (according to DSM-5 more than 12 months)
	Alcohol No remission Partial remission//early total remission (according to DSM-5 at least 3 months and less than 12 months) Prolonged total remission (according to DSM-5 more than 12 months)
	Tobacco No remission Partial remission//early total remission (according to DSM-5 at least 3 months and less than 12 months) Prolonged total remission (according to DSM-5 more than 12 months)
	Stimulants No remission Partial remission//early total remission (according to DSM-5 at least 3 months and less than 12 months) Prolonged total remission (according to DSM-5 more than 12 months)
	Cannabis No remission Partial remission//early total remission (according to DSM-5 at least 3 months and less than 12 months) Prolonged total remission (according to DSM-5 more than 12 months)
Mental disorders	Affective / anxious disorders No improvement in psychopathology determined according to DSM-5 criteria Improvement in psychopathology determined according to DSM-5 criteria
	Psychosis No improvement in psychopathology determined according to DSM-5 criteria Improvement in psychopathology determined according to DSM-5 criteria
	Attention deficit and hyperactivity disorder No improvement in psychopathology determined according to DSM-5 criteria Improvement in psychopathology determined according to DSM-5 criteria
	Borderline personality disorder No improvement in psychopathology determined according to DSM-5 criteria Improvement in psychopathology determined according to DSM-5 criteria
	Antisocial personality No improvement in psychopathology determined according to DSM-5 criteria Improvement in psychopathology determined according to DSM-5 criteria
	Other compulsive behaviours (gambling ...) No improvement in psychopathology determined according to DSM-5 criteria Improvement in psychopathology determined according to DSM-5 criteria
Level of disability	No improvement in social functioning assessed using the WHO_DAS II questionnaire Improvement of social functioning assessed using the WHO_DAS II questionnaire
Intervention adherence	Attending less than 70% of visits Attending more than 70% of visits
Medical diseases	Comorbidities: Clinical picture derived from substance use (or not). No improvement in medical comorbidities Improvement in medical comorbidities
	Risk behaviour (sex, hygiene, etc.) Reduction of risk behaviours No reduction of risk behaviours
	Infectious diseases (viral hepatitis, HIV) Therapeutic benefits in the management of infectious diseases. No therapeutic benefits in the management of infectious diseases.
	Sexually transmitted diseases Therapeutic benefits in the management of sexually transmitted diseases No therapeutic benefits in the management of sexual transmission
Psychosocial	Hostile and/or violent behaviour No effect on hostile and violent behaviour Reduction of behaviour frequency
	Presence of work problems No effect on work problems Reduction of work problems
Functional capacity	Quality of life No improvement based on SF-36 questionnaire Improvement based on SF-36 questionnaire
	Satisfaction with treatment and service No improvement based on Verona Service Satisfaction Scale (VSSS-32) Improvement based on Verona Service Satisfaction Scale (VSSS-32)
	Social functioning No improvement based on Duke-UNC Social Support Scale Improvement based on Duke-UNC Social Support Scale

disorder, borderline personality disorder, antisocial personality disorders, gambling disorder, and other compulsive behaviours. Using the WHODAS II questionnaire (World Health Organization, 2010; Üstün et al., 2010), the extent to which the intervention produced a decrease in the *level of disability* was assessed. An additional important factor was *intervention adherence*, for which the criteria was attending 70% of visits.

Regarding *medical illnesses*, the question was whether the intervention could have beneficial effects on the awareness regarding the care of other comorbidities (whether linked to substance use or not), on the reduction of risk behaviours (sex, hygiene, etc.), improvement in the management of infectious diseases (viral hepatitis and HIV), as well as in the adoption of preventive behaviours to avoid sexually transmitted diseases (STDs). Hostile and/or violent behaviour (measured by the reduction in the frequency of this type of behaviour) and the presence of work problems (decrease in work problems) were considered under *psychosocial aspects*.

Functional disability was assessed in terms of quality of life (improvement based on the SF-36 questionnaire (Fernández Miranda, 2003; Fernández Miranda, González G^a-Portilla, Saiz Martínez, Gutiérrez Cienfuegos & Bobes García, 1999; Fernández Rodríguez, Fernández Sobrino & López Castro, 2016; Iraurgi Castillo, 2008; Ware & Sherbourne, 1992)), satisfaction with treatment and service (improvement based on the Verona Service Satisfaction Scale (Pérez de los Cobos et al., 2004)). Whether or not there was a post-intervention improvement in social functioning was also considered (based on the Duke-UNC Social Support Scale (Ayala et al., 2012; Bellón Saameño, Delgado Sánchez, Luna del Castillo & Lardelli Claret, 1996; de la Revilla et al., 1991)).

Characteristics of the patients

The patient profile characteristics to be taken into account when choosing an intervention were established by the experts participating in phase 1. An important characteristic was patient age, divided into 5 categories based on a recent study carried out in Spain (Carrera et al., 2016): children under 18 years of age, adults aged 18 to 24, 25 to 34, 35 to 44, and over 45. Other relevant characteristics were patient relapse (return to the habitual pattern of use) in a binary response (yes/no) and the length of addiction (< 1 year, 1-2 years, and > 2 years). The following were considered treatment-related variables: the number of previous treatments (none, 1, 2 or ≥ 3 treatments received), the type of treatment previously received (treatment with opioid antagonists, treatment with opioid agonists and drug-free treatment) and the location of administration of previous treatments (outpatient, day centre and residential withdrawal unit (therapeutic community)). Another important question for the experts was to find out if pa-

tients had a criminal history (crimes related to substance use, whether prosecuted or not).

Criteria screening

Table 2 shows the coefficients of the adjusted multinomial logistic regression model in the screening of criteria. In a first model including all criteria, the most important factor in choosing an intervention for the treatment of patients with OUD is remission (both total and partial) from opioid use. Likewise, total remission from alcohol and/or stimulant use was established as a relevant factor in the choice. Other general criteria with statistically significant coefficients were mental disorders (psychosis and borderline personality disorder), medical illnesses (comorbidities) and functional disability (social functioning).

Criteria weighting

Based on the screened criteria (with statistically significant coefficient values), a multinomial logistic regression model was fitted to estimate the weight of each criterion in deciding on an intervention for the treatment of OUD patients. The values of the resulting model are shown in Figure 1. The factor with the greatest weight was the remission from substance use, with 56.5% of the total weight in making the choice; the presence of mental disorders was second, with 21.9%; the presence of medical diseases was third, with 11.0% and functional disability was fourth, with 10.7%.

Analysis by patient profiles

These models and their weights are shown in Figure 2. In the analysis by profiles, it was found that an additional recommended criterion to consider in patients aged 25-34 years was that the intervention should reduce the appearance of sexually transmitted diseases.

In addition, the choice of an intervention for patients prosecuted for crimes related to substance use should take into account whether or not it reduces hostile and/or violent behaviour.

Discussion

MCDAs are very versatile tools since they allow the complexity of decision making to be dealt with in a transparent and reproducible way. Furthermore, they enable the integration of different profiles of decision-makers, clinicians, pharmacists, nurses, managers and directors, regional and national public administrations, and even patients. In this way, a dialogue framework can be established to integrate the different interests, facilitating decision-making based on the preferences of all the agents involved.

From the perspective of the clinical experts who participated in this study, the fundamental factor in the choice of an intervention and subsequent recovery of a patient with

Table 2. Coefficients of the multinomial logistic regression screening model.

Criteria		coef	exp(coef)	se(coef)	z	p	
Substance use	Opioids	Partial remission	0.571	1.770	0.115	4.98	<.001*
		Total remission	0.727	2.069	0.112	6.52	<.001*
	Alcohol	Partial remission	0.184	1.202	0.107	1.72	.085
		Total remission	0.281	1.325	0.104	2.69	.007*
	Tobacco	Partial remission	0.104	1.110	0.103	1.02	.309
		Total remission	0.012	1.012	0.105	0.12	.907
	Stimulants	Partial remission	0.038	1.039	0.108	0.35	.725
		Total remission	0.262	1.299	0.104	2.53	.012*
	Cannabis	Partial remission	0.097	1.101	0.103	0.93	.351
		Total remission	0.052	1.053	0.104	0.49	.622
Mental disorders	Affective / anxious disorders	0.057	1.059	0.084	0.68	.496	
	Psychosis	0.211	1.235	0.085	2.50	.013*	
	Attention deficit and hyperactivity disorder	0.134	1.144	0.084	1.59	.111	
	Borderline personality disorder	0.165	1.180	0.084	1.96	.049*	
	Antisocial personality	-0.002	0.998	0.084	-0.03	.979	
	Other compulsive behaviours (gambling ...)	0.046	1.047	0.084	0.55	.583	
Level of disability		0.121	1.129	0.084	1.44	.150	
Intervention adherence		0.062	1.064	0.084	0.74	.461	
Medical diseases	Comorbidities	0.183	1.201	0.085	2.17	.030*	
	Risk behaviour	-0.118	0.889	0.084	-1.40	.163	
	Infectious diseases	-0.056	0.946	0.084	-0.66	.510	
	Sexually transmitted diseases	0.150	1.161	0.084	1.77	.076	
Psychosocial	Hostile and/or violent behaviour	0.059	1.060	0.084	0.70	.485	
	Presence of work problems	0.103	1.108	0.084	1.22	.224	
Functional capacity	Quality of life	0.010	1.010	0.084	0.11	.910	
	Satisfaction with treatment and service	0.061	1.063	0.084	0.73	.468	
	Social functioning	0.175	1.192	0.084	2.08	.037*	

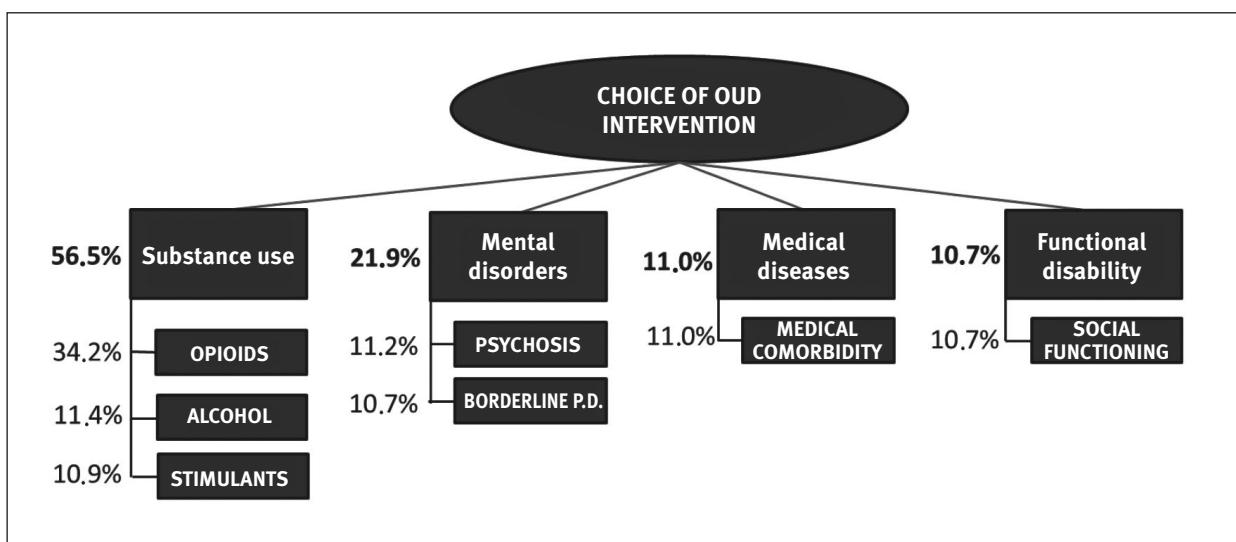


Figure 1. Results of screened criteria weighting.

ODU was confirmed to be the remission from opioid use behaviour. Other relevant factors were remission from alcohol and stimulant use behaviour. This could be the result of multiple substance use behaviour by this type of patient, so the aim of the intervention would be the cessation of addictive behaviour.

Other key factors in this study essential for the recovery of patients with OUD were improvement in psychiatric comorbidities, in the management of medical comorbidities, and in social function. The need to improve psychiatric comorbidities may be related to the fact that these patients commonly suffer some other comorbidity or relevant clinical condition in addition to opioid use disorder (Szerman et al., 2017).

Furthermore, interventions favouring an improvement in the medical comorbidities associated with this type of patients (HIV infection, HCV, etc.), would make the patients themselves adopt a greater awareness and degree of involvement in the self-care of their diseases and avoid behaviours that lead to possible complications or infection of other individuals. Lastly, the importance of an intervention

offering improved social function should be highlighted, since the final objective of clinicians is the integration of these patients into society, ensuring their ability to progress without the handicaps imposed by addictive behaviour.

The analysis of patient profiles focused on the criteria to be considered based on the characteristics of these patients. Firstly, the analysis suggests that, in patients between the ages of 25 and 34, an important criterion was reducing the risk of sexually transmitted diseases. Secondly, in patients prosecuted for criminal behaviours linked to OUD, a desirable outcome for an intervention to achieve would be a reduction in hostile and/or violent behaviour. While it is true that these results are based on the qualitative review of the response patterns, the data were confirmed by the panel of experts in the deliberative process.

Comparing the results of this study with others is complicated due to the novelty of incorporating MCDA in the healthcare setting. To the authors' knowledge, the few experiences of applying MCDA in the field of addictions have been carried out in works such as that of Nutt, King, Phillips and the Independent Scientific Committee on Drugs (2010)

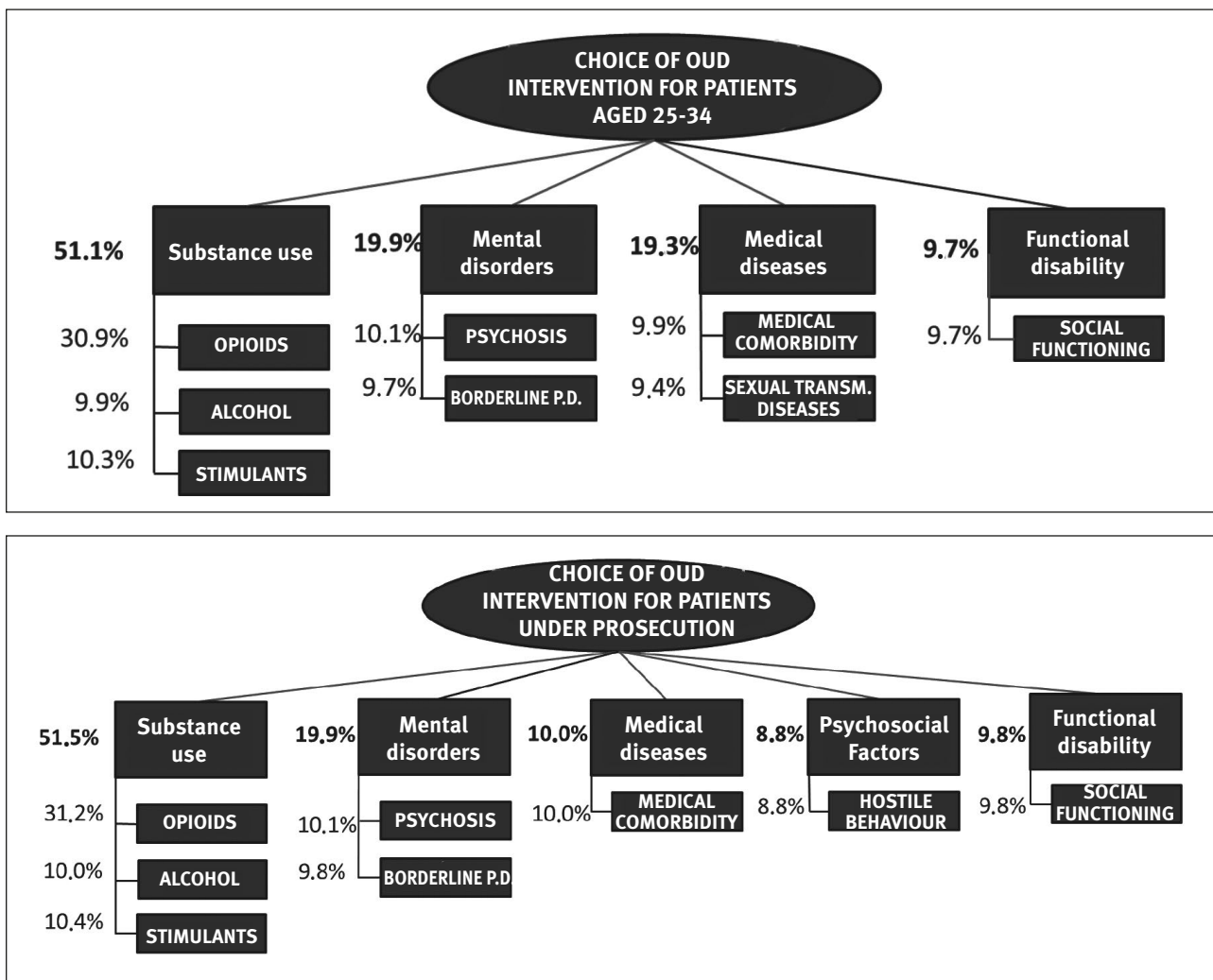


Figure 2. Alternative models according to patient profile.

in the United Kingdom, with the aim of weighting the harm arising from drug use for the user and other individuals.

One of the future strengths of MCDA is its potential use as a tool in the implementation of new forms of financing, such as results-based payment (Phelps & Madhavan, 2017; Sculpher, Claxton & Pearson, 2017). Thus, initiatives are already under way in various therapeutic areas, such as oncology, and promoted in healthcare systems (Clopes et al., 2017). A further example is the proposal developed by the United Kingdom government to measure results in the treatment of addictions and establish how results-based payment agreements could be used to pay for addiction treatment services (United Kingdom Government, 2013). In the case of our study, the results could serve as a starting point when establishing the fundamental criteria for assessing the incorporation of a new intervention for OUD patients.

A series of limitations should be noted on interpreting these results. When the results were analyzed based on patient profiles, only a qualitative analysis of the response pattern was performed given that the large number of criteria and possible profiles made it impractical to estimate the discrete choice models for each profile. Nevertheless, this analysis has allowed us to determine the situations in which the discrete choice model had worse predictive power and which factors could be involved.

Another possible limitation could be that the majority of experts on the panel had a fundamentally clinical and healthcare profile in the management of addictions. Methodologies which incorporate MCDA in the selection of health interventions favour the socio-health management of existing resources, incorporating information on health outcomes, pharmacoeconomic evidence and ethical criteria, involving all decision-makers from a multidisciplinary perspective. Therefore, future studies would be enriched by incorporating the perspective of other professionals involved in the management of OUD patients, such as psychologists, social workers and even representatives of patient associations, in order to facilitate systematic OUD-based decision-making so that better coordination of all the agents involved in the care and patient management process can be achieved.

The present study has established the bases for a bio-psycho-social assessment framework for health outcomes obtained with interventions for OUD patients, establishing a tool to systematically and transparently integrate and identify the health outcomes considered most relevant in the assessment and decision-making of opioid substitution treatment programs (OSP) in patients with OUD.

Acknowledgements

The analysis described in this paper was designed by Pharmacoeconomics & Outcomes Research Iberia (POR-

IB), a consultancy specialized in the evaluation of health interventions. The authors wish to thank Manuel Ordovás Lozano and Javier Gallardo Escudero, members of this organization, for their support and collaboration in the development of this project.

Conflicts of interest

For the development of this project, Pharmacoeconomics & Outcomes Research Iberia (PORIB), an independent consultancy specializing in the evaluation of health interventions, has received funding from Indivior Spain which was not conditional on results.

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Appendix 1

Statistical details of the analysis (Discrete Choice Experiment)

Given that the probability of choice between treatments is complementary and equal to 1, the probability of choosing treatment A would be:

$$P_{tA} = \frac{\Pr(A)}{\Pr(A) + \Pr(B)}$$

Taking into account that $\Pr(T)$ is calculated using the linear model indices of the categories contained in treatment n of item i with a total number of coefficients C_t and a number of coefficients included in the treatment of C_{in} , (cte is the intersection), then:

$$\Pr(A) = \frac{\sum_{cin=1}^{Cin} cin_i + cte}{\sum_{ct=1}^{Ct} ct + cte}$$

Example:

Suppose that the first treatment offers the options:

- partial remission of opioid consumption
- total remission of alcohol consumption.
- improvement in social functioning

Suppose the second treatment offers the options:

- total remission of opioid consumption
- improvement in social functioning

Since the rest are null or not significant categories for the model, the probability that a subject responds to each category is:

$$\Pr(A) = \frac{\sum_{cin=1}^{Cin} cin_i + cte}{\sum_{ct=1}^{Ct} ct + cte}$$

$$\Pr(T1) = \frac{1.63 + 2.49 + 1.47 + 1.58}{11.78} = 0.608$$

and

$$\Pr(T2) = \frac{1.63 + 1.35 + 3.26}{11.78} = 0.529$$

Thus the probability of selecting treatment 1 (T1) is:

$$P_{tA} = \frac{\Pr(A)}{\Pr(A) + \Pr(B)}$$

$$P_{tA} = \frac{0.608}{0.608 + 0.529} = 0.534$$

And the probability of selecting treatment 2, its complementary $1 - T1 = 0.465$.

Using these probabilities, it can be calculated whether the selection of treatments by the subjects can be considered random or based on the characteristics of the subjects.