Original

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Perception of Spanish professionals on Therapeutic Adherence of Dual Diagnosis Patients

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Objective: The aim of this study is to determine the health professional's perspective about the therapeutic adherence among dual diagnosis patients. It also analyzed the most frequently used pharmacological and non-pharmacological treatments. The aim is to learn the professional's perception regarding the reasons for non-adherence and to identify the type of strategies that may improve adherence.

Methodology: We performed an on-line survey that was answered by 169 health professionals (79.8%, doctors or psychologists) who were working in centers where the dual diagnosis patients could be treated (Mental Health Centers, Drug Outpatients Clinics, Inpatient Unit, private practice).

Results: A majority of the mental health professionals perceive the existence of non-compliance of dual diagnosis patients and they consider that 29.8% have no compliance and 39.15% have partial compliance. In addition, 96.2% believe that treatment nonadherence can be related with poor evolution in a severe or very severe degree. The reasons for the nonadherence to treatment are the poor disease awareness, side effects, low efficacy and complicated posologies. No differences were found regarding the difficulties and reasons for non-compliance between professionals or centers. It is proposed that using drugs with low side effects drugs and easy-to-manage can improve compliance. It is also proposed to use motivational techniques, psychoeducation and psychological treatment.

Conclusions: The perception exists that a high proportion of dual patients have poor treatment adherence, which affects the therapeutical process. Efforts should be

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Keywords: Adherence, Perception of the professional, Dual diagnosis, Dual pathology, Compliance, Evolution, Relapse, Decompensation

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Percepción de los profesionales Españoles sobre la Adherencia Terapéutica en Patología Dual

Objetivo: Evaluar la percepción de los profesionales sobre el grado de importancia de la adherencia terapéutica de los pacientes con patología dual y valorar los tratamientos farmacológicos y no farmacológicos más utilizados. Se pretende averiguar cual es la percepción de los clínicos sobre las causas del incumplimiento y el tipo de estrategias que pueden facilitar una buena adherencia.

Metodología: Se realizó una encuesta on-line que fue contestada por 169 profesionales (79,8% médicos o psicólogos) que trabajan en los diferentes tipos de centros españoles que atienden pacientes duales (ambulatorios de drogodependencias, centros de salud mental, hospitalización psiquiátrica, unidades de desintoxicación y centros privados).

Resultados: La percepción de existencia de incumplimiento de los pacientes duales es mayoritaria, los profesionales creen que un 29,8% incumplen y un 39,15% cumplen parcialmente. Además el 96,2% percibe que el incumplimiento está relacionado con una mala evolución, de manera grave o muy grave. Ello se relaciona principalmente con la baja conciencia de enfermedad, la presencia de efectos secundarios, la falta de eficacia y las posologías complicadas. No existen diferencias en función del tipo de recurso en el que trabaja el profesional. Para mejorar el cumplimiento se propone utilizar fármacos con pocos efectos secundarios y fáciles de manejar. También se plantea utilizar psicoeducación, técnicas motivacionales y tratamiento psicológico individual.

Conclusiones: Existe la percepción de que un alto porcentaje de pacientes duales presentan mala adherencia y que esto influye en el proceso terapéutico. Se deben realizar esfuerzos en el tratamiento farmacológico y no farmacológico.

Palabras clave: Adherencia, Percepción del profesional, Patología dual, Cumplimiento, Evolución, Recaída, Descompensación

INTRODUCTION

Patients with mental disorders have a greater risk of substance abuse disorder (SAD), especially in those who have more severe mental conditions.^{1,2} In psychiatry admission units, patients with psychotic disorders and SAD represent a large proportion (53% schizophreniform disorder and 28% schizophrenia).² It is also known that addict patients very frequently have other psychiatric disorders.³⁻⁵ In the population of addicted Spanish patients, it is calculated that affective disorders are the most frequent (21.6%), followed by anxiety disorders (11.7%) and by schizophrenia (3%).⁵ The coexistence of a mental disorder and SAD has been called dual diagnosis.^{6,7} It is calculated that approximately 30-50% of the population receiving psychiatric treatment have an associated SAD.^{1,8} However, the number varies depending on the type of patients studied,^{9,10} the center where the study is performed¹¹ or the research methodology used.¹²

When the patients with dual diagnosis (co-occurring disorders) seen in the mental health network and in drug dependent network were studied in Spain, it was observed that there was a greater percentage of patients with dual diagnosis within the drug dependent network.¹³ However, other studies did not find differences between the patients of the two care networks.¹⁴ Nonetheless, the great prevalence of patients with dual diagnosis in both contexts has been confirmed in all the works.^{13,14}

Improving the care services for these patients should be a priority because abuse of alcohol and other drugs is associated to adverse consequences, such as greater noncompliance, relapse, suicide, HIV, HCV, lack of basic resources, unemployment, legal problems, etc.¹⁵⁻¹⁸ Furthermore, the burden on the families is elevated and there is great need for social resources. This would be related with the fact that dual diagnosis patients have worse adherence and treatment compliance and therefore more relapses, worse evolution, frequent visits to emergency services and to other care services.^{16,19-21}

Because the epidemiology and clinical characteristics of the dual diagnosis patients are not totally known,^{22,23} the great complexity of the treatment,¹² frequent treatment abandonment¹⁹ and because the treatment protocols are provisional, ²⁴ it is important to know the opinion of the professionals on the difficulties in treatment adherence. In addition, it is fundamental for the professional to indicate the solutions or beneficial changes¹² in order to avoid treatment abandonment and its consequences. On the other hand, this type of information is very useful for obtaining consensuses or protocols on the approach to patients with dual diagnosis.^{10,24}

The objectives of this study are to evaluate the professionals' perception on the degree of compliance, the causes for non-compliance, the importance of treatment compliance, pharmacological and non-pharmacological factors that hinder adherence, type of drugs used, strategies that can facilitate good adherence in patients with dual diagnosis and the training of the professionals in this field. It can be hypothesized that the professionals will detect the existence of non-compliance and its consequences and can propose strategies to improve compliance. In addition, there may be differences based on the professional profile or work center.

METHODOLOGY

A survey on adherence and compliance in dual diagnosis (Annex) was designed by a group of different experts in dual diagnosis from different work and academic origins. The questionnaire was presented online for a 4-week period between September and October 2010. It was aimed at different professionals who worked in the centers in which patients with dual diagnosis could be attended.

To cover the greatest possible number of participants, a message was sent by mail to all the members of the three scientific societies that collaborated in the study: the Spanish Society of Dual Diagnosis (Sociedad Española de Patología Dual), Spanish Scientific Society for Research on Alcohol, Alcoholism and Other Drug Addictions (Socidrogalcohol) and Spanish Society on Drug Addiction (Sociedad Española de Toxicomanías). Furthermore, the survey could be answered on the web page of the societies and was publicized on the psychiatry webpage <u>www.psiquiatría.com</u>. It was possible to answer the survey after the person had identified him/ herself as a mental health professional who was working in Spain. The participants did not receive any payment for answering the questionnaire.

The population addressed by the questionnaire was not a closed one. There is no official census of professionals who work in drug addiction²⁵ or in facilities for dual diagnosis. It could be estimated that approximately 900-1000 medical professionals work in the drug addict network. Approximately 50% of these state they are general practitioners.²⁵ On the other hand, there are about 4500-5000 psychiatrist in Spain, including those in training.²⁶ However, it is unknown how many work in facilities that may attend to dual diagnosis patients.

The questionnaire used was made up of 27 blocks of questions.²⁷ The professionals were asked to answer aspects about the treatment of their patients with dual

pathology (2 units), their perception on compliance (1 unit), evolution (1 unit), disease awareness (1 unit), consequences of non-compliance (1 unit), pharmacological problems that can hinder treatment adherence (1 unit) and non-pharmacological factors that hinder or can improve adherence (2 units). Drugs commonly used (8 units) and number used (1 unit) were evaluated. Finally, there was a unit of one question on the training needs of the professionals. There were 8 blocks of sociodemographic questions that were answered by choosing a response or providing information.

In eleven units, the professionals had to sort the options presented by order of importance/frequency of use. Four questions were answered using Likert type scales having different intervals (from 0 to 3: Compliant, Partial, Non-Compliant, from 0 to 4: None, little, A lot, Much, or Very used, Used, Little used or not at all used and finally 0 to 5: Very low, Low, Middle, Elevated, Very elevated). The unit in which the use of drugs was questioned had 7 subsections, based on the pharmacological families.²⁷

The centers in which the professionals carried out their work were: Outpatient clinics specialized in Drug Addictions, Private Centers, Hospitalization Units for Drug Addictions, Mental Health Centers (MHC) and Psychiatric Hospitalization Units.

A descriptive statistics analysis was made with the information collected using the SPSS v.15 statistical program.

The sample was made up of 169 professionals, 58.5% of whom were women and 41.5% were men. A total of 93.5% had Spanish nationality and 50.5% were older than 45 years. Almost half (41.5%) had more than 15 years of experience in the field of drug addictions. The professionals belonged to different branches within the health care settings: 57.1% were physicians (22% were psychiatrists, 30% specialists in drug addictions, 2.9% were general practitioners and 2.2% were doing residency in psychiatry), 27.8% were psychologists, 4.3% were nurses and 10.8% were social workers and other types of professionals. The physicians and psychologists accounted for 79.8% of the sample. Because of this extensive majority, only the evaluations of these professionals were analyzed. To be able to explain the results of the analysis clearly and operatively, all the professionals were grouped into 3 groups: Physicians who worked in drug addiction, Psychiatrists and Psychologists. The work centers were studied in 4 groups: Centers specialized in Drug Addictions (outpatient and desintoxication units), MHC, Psychiatric Hospitalization and Private Center.

Collaboration of professionals from all the regional communities (including the regional city of Ceuta and Melilla) was achieved. The communities having the largest number of participants were Catalonia, the Regional Community of Madrid and Andalucía (Table 1).

Table 1	Percentage of participants divided by Regional Communities				
Regional Community		Percentage	Number of Participants		
Andalusia		12.3	34		
Aragon		1.4	4		
Balearic Islands		2.9	8		
The Canary Islands		2.9	8		
Cantabria		0.7	2		
Castilla y León		8.3	23		
Castilla-La Mancha		1.4	4		
Cataluña		20.2	56		
Ceuta y Melilla		1.4	4		
Community of Madrid		14.1	39		
Navarre Community		2.2	6		
Valencian Community		8.7	24		
Extremadura		4	11		
Galicia		8.7	24		
La Rioja		0.7	2		
Basque Count	try	2.5	7		
Principality o	f Asturias	3.2	9		
Region of Mu	ircia	4.3	12		

The professionals who worked in specialized centers for drug addiction (56.7% of the sample) accounted for the largest group.

RESULTS

According to the professionals, 47.2% of the patients attended were dual patients. Of these, it was observed that cocaine was the main abuse drug used (Table 2).

Treatment compliance

In the questionnaire, the professionals were asked to evaluate grade of therapeutic compliance of their patients with dual diagnosis. To classify the perception on compliance, following the international recommendations²⁸ it was considered that the patients who complied more than 80% of the times were total compliers. Those who complied 20 to 80% of the times were defined as partial compliers. Finally, those who took the treatment less than 20% of the times were considered non-compliers.

The professionals indicated that most (68%) of the patients did not adequately adhere to the treatment (Figure 1). All the professionals, regardless of the professional

Table 2	Drugs demanded for treatment by patients with dual diagnoses		
Ab	use Substance	Percentage	
Cocaine		56%	
Alcohol		26%	
Heroin		10%	
Cannabis		6%	
Benzodiazepi	nes	2%	
Others		1%	

profile, indicated that about 70% of their dual patients did not adequately take their treatment.

Evolution of the patient

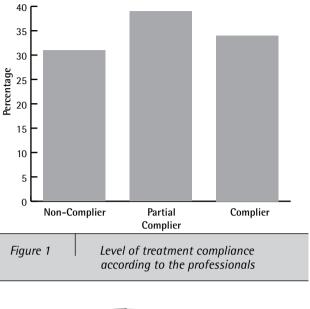
The professionals perceived that lack of treatment compliance affects the course of the patient. In 96.2% of the cases, they considered that disease deteriorated a lot or much (Figure 2). The psychiatrists as well as the psychologists considered that lack of compliance in the treatment was severe or very severe. When it was analyzed based on type of center where the professionals carried out their care activity, all of the groups considered that the lack of compliance was very severe.

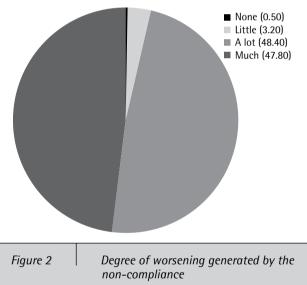
Degree of disease awareness

A total of 68.3% of the patients, according to all the group of professionals, have a low or very low degree of disease awareness. Approximately 60% of the physicians and psychologists considered that the awareness level of their patients with dual diagnosis was low or very low. Those who perceived less disease awareness were the psychiatrists, followed by the physicians in the drug addiction network and psychologists, When the responses were analyzed based on work center, the first cause indicated in every case was that *insight* was low.

Pharmacological factors that hinder adherence

Those surveyed were asked to indicate three pharmacological type factors that could favor the presentation of difficulties for treatment adherence of a patient. All stated that the main cause related with lack of adherence are the side effects of the psychopharmaceuticals. Furthermore, they coincided in the order of the other factors: lack of efficacy, complicated regimes, administration route

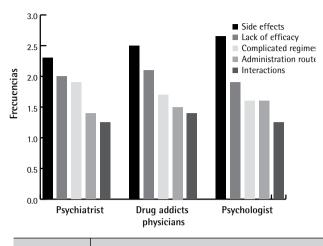


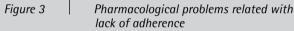


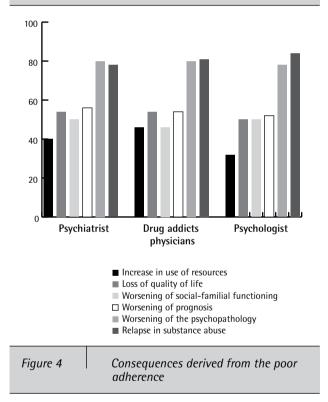
and interactions. All the groups studied classified the factors in the same order (Figure 3).

Non-pharmacological factors that hinder adherence

The subjects were asked to choose the three factors that most hindered adherence to non-pharmacological treatments. Lack of disease awareness was described as the first option in the three groups of professionals. In the group of psychiatrists, this was followed by lack of belief and expectations and problems to access the service. In the case of the medical specialists in drug addictions, this was followed by lack of family/social support and by beliefs and expectations by the patients. In the case of the group of







psychologists, the second option was cognitive deterioration and lack of memory and finally lack of family/social support.

Use of pharmacological treatments

The perception of the use of pharmacological treatments was only studied in the group of professionals formed by the physicians (N=96). The professionals reported that most of the patients were receiving multiple medications. Sixty percent of the professionals indicated that the patients received three drugs, 25% that they received two and 10%

that they received four, the mean being 2.85. The option of more than five drugs was chosen. When questioned about the drugs used, all indicated that those used the most were antidepressants and antipsychotics, followed by anticraving drugs.

In regards to the antidepressants, the professionals reported that those taken most by the patients were the SSRIs, followed by dual antidepressants and dopaminergic/ noradrenergic antidepressants. This coincided in both the physicians working in drug addictions as in the group of psychiatrists.

In relation to the antipsychotics, those surveyed were asked to classify the drugs received the most by the patients. Those reported the most were olanzapine, oral and long acting injectable risperidone, conventional neuroleptics, above all oral and quetiapine, the latter being chosen, above all, by the psychiatrists. The use pattern was very similar taking the type of center into consideration, except for the MHC where neuroleptics, both oral and deport, were the most used.

Of the so-called "anticraving" drugs, disulfiram and naltrexone were cited the most, in a very similar way. Use of acamprosate and cyanamide was also reported, although mention was made of their use clearly less. Among the opiate agonists, methadone was used the most. With the group of "other medications" generally used, antiseizuresmood stabilizers generally appeared, topiramate being that used the most in all the settings. This was followed gabapetine and lithium in the professionals of the drug addiction networks, which was followed by valproate and lithium in the psychiatrist group. When the patients have Attention Deficit Hyperactivity Disorders, the professionals consulted considered that the treatment most used was long-acting release methylphenidate. Finally, it should be stressed that benzodiazepines are used or very used in dual patients according to 50% of the professionals.

Consequences derived from treatment noncompliance

The most important consequences caused by treatment non-compliance were studied. Both the physician and psychologist group considered that relapse in substance abuse was the main consequence, followed by worsening of the psychopathological symptoms and social-familial problems. When this was analyzed on the basis of the three groups, minimum differences existed (Figure 4).

When the consequences were evaluated based on work centers, differences were found. The options mentioned the most by the professionals from the centers specialized in drug addictions were, on the same level, worsening of the psychopathological symptoms and relapse in substance abuse. These were followed, much farther behind, by loss of quality of life. On the other hand, for the MHC professionals, the two most chosen options were relapse in consumption and worsening of the prognoses and, in the third place, worsening of the psychopathology. In the psychiatric hospitalization centers, the responses were first of all worsening of the psychopathology. In the second place, the responses were relapse in consumption and in the third, deterioration in quality of life. Finally, the first option in the private centers was relapsing consumption, the second one being worsening of the psychopathology and in the third place worsening in the prognoses.

Adherence improvement

The three non-pharmacological interventions that improve the adherence to treatment of dual pathology patients cited the most were psychoeducation, motivational strategies and individualized treatment. However, among the professionals, there were minimum differences in the classification. All coincided in indicating psychoeducation as the first option to improved treatment adherence. Differences were not detected based on type of center.

Training of the professionals

The professionals were consulted about the type of training resources they needed to improve their clinical practice. From the list of strategies that could be beneficial to improve the management of these patients (manuals, guidelines, courses, monographs and workshops), the workshops (30.5%) and courses (30.6%) were evaluated as being the most efficient.

DISCUSSION

The purpose of this study was to evaluate, the degree of compliance and factors associated to the non-adherence to treatment of patients with tool diagnoses in accordance with the perception of the clinicians. Knowing the perception of the professionals is important since they are the ones who really prescribe and apply the different treatments.^{29,30} They detect when a patient is noncompliant²⁸ and what is more important, they can provide reasons, based on experience, which help to improve adherence. The professionals perceived that approximately 50% of the patients attended in the different facilities have dual diagnoses, information that is close to that described in the epidemiological studies.^{14,13}

The dual diagnosed patient, associated to cocaine consumption, was perceived as being mainly noncompliant, with a complicated evolution, in which the noncompliance worsened the disease. The association of dual patients with cocaine consumption was detected in the target epidemiological studies.¹³ Therefore, this could account for the frequent presence of serious psychopathological disorders in cocaine dependence,^{3,31} as well as its frequent consumption in patients with severe mental disorders.^{16,18,24}

The perception on the difficulties of treatment agrees with the studies that indicate the complexity of the treatment and the need to approach both the psychopathological disorders and the addiction to avoid poor evolution and lower response to the treatment.¹⁰

Regardless of the type of professional or center where they worked, important differences were not found in the perception of the existence of poor compliance and treatment adherence. This would coincide with the reviews of the target studies.^{19,32} The professionals who worked in the mental health network had greater perception of poor compliance. This could be explained due to the fact that professionals working in the drug addiction network, because of the profile of their non-dual patients, frequently contemplate the scarce adherence of their patients.^{19,32}

Lack of compliance is clearly related to poor evolution. This once again coincides with the reviews of the target studies.^{16,20} One of the main causes that would explain lack of adherence would be the limited capacity of these patients to obtain awareness of their disease (*insight*). This has also been indicated as very important when research has been done on the opinion of the nursing professionals about the causes of noncompliance.³³ In dual patients, all the groups of professionals: side and perceived disease awareness as low or very low in 68.3% of the cases. This is slightly superior to the target studies carried out in heroin dependent dual patients, which is approximately 55%.³⁴

The problems of adherence to non-pharmacological treatments have been related with lack of disease awareness, coinciding with the general explanations on the perception of poor adherence.^{12,33} According to the professionals, poor compliance of pharmacological treatment would be very related with the side effects. This would coincide with previous studies on that reported by the patients themselves.35 The other most cited factors are the lack of efficacy and complicated dosage regimes, the importance of one factor or another varying based on the work center. The association between perception of lack of efficacy and noncompliance is a factor that has already been described in our setting.³⁵ In relation to prescription, Douglas et al. (2005) described that the use of simple dosage regimes was one of the main factors affecting good compliance of pharmacological treatment in dual patients.¹⁰ On the contrary, multiple medication is a factor associated to poor compliance.^{30,35} Thus, it is to be expected that within the drugs cited as most useful, those having a long half life appear since these have a simple dosage and their utility

has been proposed in patients with severe mental disorders and poor compliance.³⁶ This agrees with the idea that the easier and simpler the dosage, the greater likelihood that the evolution will be good³⁰ and that the compliance and adherence will be adequate.¹⁶ Finally, those cited the least are administration route and pharmacological interactions. Few studies are found on the importance of the administration route. It has been described that aspects such as preference for the administration zone may vary in accordance with the geographic area used to question the patients.³⁷ Therefore, it could be hypothesized that the administration route could be a factor having less importance. Due to the influence of multiple factors, all of the aspects related with effectiveness of the drugs in dual patients should be permanently investigated.³⁸

When those surveyed were questioned about the number of drugs used, it was perceived that most received almost 3 drugs. This coincides with the target studies in which it was described that these patients were treated with multiple drugs^{5,21} and that they received more drugs than the non-dual patients.¹² In addition, it should not be overlooked that the use of too many medications is a factor associated to noncompliance.³⁵ Regarding the type of medication the dual patient receives, the distribution of the drugs that were reported to be used (great use of antidepressants and antipsychotics), coincided with prescription studies carried out in Spain.⁵ It is notable that, according to the professionals, benzodiazepines are widely used in dual patients. However, the prescription of these drugs should be used with caution because of the great risk of abuse.³⁹ The phenomenon of the important use of benzodiazepines has been described in dual³⁹ and drug addict patients.40,41 In Spain, approximately 75% of the hospitalized drug addicts consumed benzodiazepines, both prescribed and nonprescribed.⁴⁰ In addition, in patients with in a methadone maintenance program, 46% consumed benzodiazepines abusively.⁴¹ All this in spite of the facts that it has been recommended to avoid and control its use in dual patients.24,39

In relation to the consequences of noncompliance, the clinicians do not agree on whether psychopathological decompensation or the reinitiation of substance abuse occur more frequently. Although it is known that both situations can evolve towards relapse,^{7,21} this information has not been sufficiently clarified in the target studies. There are small differences on the perception of the consequences based on the type of work center. In the MHC, it is perceived that the relapsing consumption causes the worsening. However in the drug addict centers, the consequences are divided among relapse in consumption and decompensation.

The need to develop strategies to improve therapeutic adherence has been documented.³⁰ In the treatment of dual patients, it would be possible to optimize the

pharmacological treatment, psychotherapeutic attention and to increase the training of the clinicians. It would be recommendable to improve the three aspects. From the pharmacological point of view, an attempt should be made to prescribe simple dosages with good tolerability. This should be completed with psychotherapeutic interventions aimed at maintaining abstinence,¹⁰ which include promoting adherence and compliance. The most cited interventions by the professionals to achieve these objectives are psychoeducation, use of motivational strategies and individual treatment. This coincides with those indicated in the literature.⁴²

Finally, on the educational level, more than 60% of the clinicians specified the need for more information on the management of these patients by courses and workshops. This coincides with previous works that state the importance of access by the professionals to training resources in order to carry out an adequate intervention.¹⁰

Limitations to this study could be that they did not include questions about the type of psychotherapies that were performed in the centers. This point should be approached in future studies. The responses received belonged to professionals who may be motivated as well as interested in participating in a study on dual diagnoses. Thus, the responses should be compared with groups of professionals who do not have this profile. The results obtained in this pilot study may not represent the opinions of all the professionals who attend dual patients. However, given the importance of the subject, the number of persons who responded, the fact that there is representation of professionals who work in all the regional communities, that there are very few previous studies and that the difficulties under consideration to study the population of professionals who attend to the dual patients are difficult to resolve, the results provided should be considered. Furthermore, it stands out that when the perception in which target studies exist have been compared, it has been found that there is significant agreement between the perceptions found by the professionals and those found in the studies published. On the other hand, in spite of relevance of the study, the works published on the perceptions or attitudes of the professionals and compliance are extremely scarce.^{12,33}

As a final conclusion, although there are minimal differences based on the professional profile and type of work center in which they work, it can be stated that the professionals perceive that the patients with dual diagnosis have poor treatment adherence and that they consider that this affects the course and evolution. Thus, some of the strategies proposed to improve adherence to pharmacological and non-pharmacological treatment should be implemented.

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Annex 1

Survey on perception of the professionals in dual diagnosis

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Annex 1	Continuation				
21. Select according to your preference of use, 4 of the following antidepressants in your patients with Dual Pathology, ordering them from 1 to 4 (1 the most used/4 the least used).Tricyclics1 2 3 4SSRI1 2 3 4Dual1 2 3 4SNRI1 2 3 4Dopaminergic/Noradrenergic1 2 3 4		23. Select according to your preference of use, 3 of the following benzodiazepines in your patients with Dual Pathology, ordering them from 1 to 3 (1 the most used/3 the least used). Short half life1 to 3 (1 the most used/3 the least used). Short half life1 2 3 Long life24. Select according to your preference of use,		25. Select according to your preference of use, 3 of the following opiate agonists in your patients with Dual Pathology, ordering them from 1 to 3 (1 the most used/3 the least used).Methadone1 2 3 MorphineHeroin1 2 3 BuprenorphineBuprenorphine and Naloxone1 2 3	
NaSSA 1 2 3 4		3 of the following drugs used for ADHD in your patients with Dual Pathology, ordering them		Other synthetic opiates	1 2 3
22. Select according to your preference of use, 3 of the following anticraving / interdictor in your patients with Dual Pathology, ordering them from 1 to 3 (1 the most used/3 the least used).Disulfiram1 2 3 NaltrexoneDyanamide1 2 3 Acamprosate		Methylphenidate1 2 3with Dual PathoLong acting Methylphenidate1 2 31 2 3 4 5 mAtomoxetine1 2 323Bupropion1 2 327. What options to improve your patho		 2. Guides 3. Courses 4. Monographs 	most useful pment in