

Efficacy of the inpatient alcohol rehabilitation program with the use of naltrexone for the years 1997-2010

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Summary

This study aims to present the results of our 3-Month Inpatient Alcohol Rehabilitation Program with the use of naltrexone, during the years 1997-2010, at the Psychiatric Hospital of Attica at Dafni. We examine the percentage of abstinence among patients who completed our program and their demographic and clinical characteristics.

Our sample comprises of 859 patients, 542 of whom completed the final psychological rehabilitation phase of our inpatient program (317 either dropped out or were excluded upon decision of the therapeutic team). Out of the 859 patients, we managed to gather information from 339 of them (the rest could not be contacted), whereas 4 patients declined to respond.

Our data suggests a statistically significant correlation of lower future abstinence rates ($p=0.004$) and lower future death rates ($p=0.007$) with the completion of our inpatient program. The level of education was also found to have a statistically significant correlation to the completion of our inpatient program within the group of secondary and tertiary education patients, married patients and patients with children (respectively at $p=0.0005$, $p=0.045$, $p=0.015$). In terms of abstinence levels, patients who completed our full Rehabilitation Program at a range of 53.95 – 55.77% and patients who completed our Inpatient Program at a range of 46.31 – 50% remained abstinent, without relapse of alcohol use.

As far as chronic alcoholism and psychiatric comorbidities are concerned, our patient sample showed such comorbidities at a cumulative 50.78%,

with psychotic disorders at 5.04%, bipolar disorder at 3.15%, unipolar depression at 21.76% and drug abuse at 11.98%.

Keywords: alcohol abuse/alcohol dependence, chronic alcohol abuse, alcohol rehabilitation programs, naltrexone

Introduction

Alcohol dependence is a complex phenomenon determined by numerous interacting factors including both individual (biological, psychological, psychiatric) and environmental factors (family relationships, cultural habits).

Alcohol abuse and alcohol dependence are contributing factors to disease globally and are ranked as the fifth leading risk factor for premature death and disability in the world (WHO 2007). Alcohol is identified for causing more than 60 types of diseases and injuries, while alcohol-attributable neuropsychiatric disorders account by themselves for more than 1/3 (34%) of the disease and disability burden associated with alcohol (WHO 2009). In 2005, it is estimated that 5.4% of all men and 1.5% of all women aged 18 to 64 in the EU suffered from alcohol dependence (Rehm et al.¹).

Among the Greek population 12.2% report at least one incident of insobriety within the past year (Greek Documentation and Monitoring Centre for Drugs Annual Report, 2010). Furthermore, in 2010 there has been significant increase in the weekly alcohol consumption rates among Greek 15-year-old students which raised to 35.3% compared to 27.6% in 2006 (Greek Documentation and Monitoring Centre for Drugs Annual Report, 2011), while 41.4% of the individuals receiving treatment in 2012 mentioned that they had suffered a severe problem of mental or physical health (Greek Documentation and Monitoring Centre for Drugs Annual Report, 2013).

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In Greece, there are (I) seven outpatient programs: (a) the two-year Outpatient Program at the Psychiatric Hospital of Attica at Dafni (PHA), (b) the DANAE Outpatient Day Treatment Program (PHA), (c) the ATHENA Treatment Program of the Athens University Psychiatric Clinic and OKANA anti-drug centers, (d) the Counseling Station and the Rehabilitation Unit for people with alcohol, drug and gambling addiction at the Thessaloniki Psychiatric Hospital (TPH), (e) the METHEXIS Outpatient Psychiatric Treatment Centre, Rehabilitation Unit for people with alcohol, drug and gambling addiction at TPH, (f) the ALFA Treatment Program for alcohol and gambling addiction (KETHEA - Therapy Center for Dependent Individuals), (g) the KIVOTOS Counseling Center for drug addicts in Thrace (KETHEA - Therapy Centre for Dependent Individuals), and (II) two inpatient programs: (a) the Alcoholic Rehabilitation Community, Psychological Support Alcohol Dependence Treatment Unit 18 ANO (PHA), (b) the Short Duration Inpatient Alcohol Rehabilitation Program with the use of naltrexone at the 10th ward of alcoholics (PHA). In 2010, a total of 1,389 individuals addicted to alcohol participated in the afore-mentioned treatment programs displaying a steady increase in the rates of those who entered their main therapeutic phase within the past three years (2010, 2009, 2008) (Greek Documentation and Monitoring Centre for Drugs Annual Report, 2011). In 2012, a total of 1,348 people with alcohol dependence attended the counseling centers with the overwhelming majority (92.4%) attending the Psychiatric Hospital of Attica at Dafni (Greek Documentation and Monitoring Centre for Drugs Annual Report, 2013).

It is interesting to examine the efficacy of these alcohol rehabilitation programs since various intervention methods are recommended (treatment communities, behavioural-knowledge interventions, special pharmaceutical treatment, outpatient programs, day centers etc.).

A study of the inpatient alcohol dependence treatment program 18 Ano (where inpatient treatment lasts at least 8 months) showed that in the period 1996-2008, 486 patients were treated in the program while 87 (17.9%) of them completed it successfully. Of those 87, 49 patients (56.3%) continue to abstain since the completion of the program averaging around 5 years of abstinence (SD=3.4 years) to date. The number of relapses after the completion of the program reached 5.5 (SD=2.8) lasting on average 5.5 months (SD=4.5 months) (Mitsonis et al.²).

This study aims to present the results of the only

Short Duration Inpatient Alcohol Rehabilitation Program in Greece using naltrexone, during the years 1997-2010 at the Psychiatric Hospital of Attica at Dafni.

PRESENTATION OF THE SHORT DURATION INPATIENT ALCOHOL REHABILITATION PROGRAM AT THE PSYCHIATRIC HOSPITAL OF ATTICA AT DAFNI

The program recommends a treatment for alcohol dependence taking into consideration both mental and physical factors. Naltrexone is used at a 50mg dose daily. There is a Counseling Station operating on an outpatient basis while the inpatient treatment takes place in independent facilities on the premises of the Psychiatric Hospital of Attica at Dafni. The treatment lasts three months and admission takes place only on a voluntary and group basis every 1.5 month.

The patient goes through the stage of physical recovery as an outpatient while receiving medical and psychological treatment, as well as pharmaceutical treatment to overcome the withdrawal syndrome and any psychiatric comorbidity. Abstinence is verified through breath and urine testing.

During the inpatient treatment, individuals have no contact with their family environment whatsoever. Provided that liver function is normal, naltrexone is administered for a period of 12 months and liver enzymes are checked every other month. The daily schedule determines the patients' activities and responsibilities. A combination of therapeutic approaches is used: supportive individual and group psychotherapy, drama therapy and occupational therapy.

The third stage of the program concerns the individuals' social rehabilitation and takes place on an outpatient basis at the Counseling Station. This stage lasts three months and includes weekly group and individual sessions.

Naltrexone

Naltrexone is an opioid receptor antagonist used as a complementary treatment in alcohol dependence management programs. It suspends the effect of endogenous opioids (endorphins, enkephalines), believed to be released after high consumption of alcohol, and is considered to play a significant role in

regulating the hypothalamic-pituitary-adrenal axis' reaction to stress (Besirli et al.³).

It reduces the craving for alcohol, lowering the levels of produced alcohol-induced dopamine in the ventral striatum (Myrick et al.³). According to meta-analyses, the oral administration of naltrexone can reduce the number of relapses in heavy drinkers (Maisel et al.⁵, Garbutt⁶), but is less effective in promoting abstinence. Despite the fact that naltrexone seems to have a positive effect on abstinence from alcohol, the effect size is average ranging from .15 to .2 (Garbutt⁶).

According to the COMBINE study, patients treated with naltrexone or receiving cognitive behaviour intervention (CBI) or both displayed better results. Nevertheless, no combination of drugs proved more efficient than naltrexone or CBI separately. Further focus on the sex of the patients showed that there are no statistically significant differences in the response to naltrexone (Greenfield et al.⁷)

In review studies based on organised psychotherapy models, the number of relapses by patients treated with naltrexone and patients treated with placebo were the same. In contrast, in studies using ordinary psychotherapy, the number of relapses was lower in the naltrexone group compared to the control group (Agosti et al.⁸, Jarosz et al.⁹).

RESEARCH DESIGN

PURPOSE

This research aims to investigate the efficacy of the Short Duration Inpatient Alcohol Rehabilitation Program with the use of naltrexone at the Psychiatric Hospital of Attica at Dafni during the years 1997-2010. We will examine the percentage of abstinence among the patients who completed the aforementioned program over these years, taking into consideration their demographic and clinical characteristics.

Sample characteristics

The collection of information was done via the telephone. The names and telephone numbers of the patients who had participated in the program were randomly allocated to four therapists at the program. Our first aim was to contact the patients themselves

but where this was not feasible, the information was provided by a relative. The fact that the telephone communication was made by therapists in the program contributed, at least in most cases, to higher intimacy and facilitated the collection of reliable information.

Data collection procedure

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Instruments

Through the telephone communication, the therapists completed a structured questionnaire with demographic and clinical data for the patients. More specifically, they included information such as: sex, age, place of residence, level of education, family status, existence of children, occupational status, completion or not of the inpatient program and of the rehabilitation phase, existence of physical illness (during the time of the interview), type of illness, existence of psychiatric comorbidity and/or use of substances, hospital admissions, relapses and the substance in question (alcohol/drugs), duration of relapses, participation in different programs or therapies, deaths, status of the interviewee (the patients themselves or a relative) and credibility of the interviewee.

Statistical processing

The statistical method used for the categorical variables under investigation was the chi-square (χ^2) test applying Fisher's exact test for calculating statistical significance. The level of statistical significance was set at $p=0.05$.

OUTCOME

Demographic characteristics of patients

In terms of age, 54.5% of patients were under and 45.5% were over 50 years old.

The majority were from Attica, at a percentage of 66.4%, while the remaining 33.6% were from rural areas of the country.

As far as the education level is concerned, 40.5% of the patients had completed the compulsory education, 43.5% had moved on and graduated from secondary education, while 16% were tertiary education or university graduates.

In terms of family status, 37.3% were not married while the other 62.7% were married, and 64.4% of the patients had children leaving a percentage of 35.6% without children.

As far as their occupational status is concerned, 41% were working at the time whereas 59% were unemployed (Table 1).

Clinical characteristics of patients regarding somatic and psychiatric comorbidities

During the interview, patients mentioned the existence of a somatic comorbidity at a percentage of 32.2%. Some common somatic comorbidities were: liver disorders (15.7%), gastrointestinal diseases (6.5%), neurological disorders (8.3), neoplasms (19.4%), and other disorders (50%).

Of the total number of patients, 35.5% mentioned they had been admitted to hospital with physical symptoms, while in 16.7% of the cases, relatives informed us of the death of the patient.

The sampled patients also displayed psychiatric comorbidities at a percentage of 50.78%. In particular, 5.04% suffered from psychotic disorder, 3.15% from bipolar disorder, 21.76% displayed unipolar depression while 11.98% made use of substances.

Only 10% of the patients had entered another rehabilitation program (Table 2).

Statistically significant findings

1. Completion of the rehabilitation program

Examining the characteristics of the patients who

had completed the rehabilitation program (Table 3), it was noted that achieving this milestone was statistically significant and correlated with:

- lower relapse percentage in the future ($p=1.01 \times 10^{-8}$),

- lower percentage of hospital admission for physical symptoms in the future ($p=0.001$)

- The age tended to correlate with the completion of the rehabilitation program (statistical significance $p=0.087$), where a high percentage of patients over 50 years of age tended to complete the rehabilitation phase.

- The family status also tended to correlate with the completion of the rehabilitation program (statistical significance $p=0.062$), with higher completion rates among married patients.

- The shortest relapse duration tended to correlate with the completion of the rehabilitation phase (tendency towards statistical significance $p=0.057$), with relapses lasting less than 6 months being more often.

2. Completion of the inpatient program

Analyzing the characteristics of the patients who completed only the inpatient program (Table 4), it was noted that achieving this milestone was statistically significant and correlated with:

- Lower relapse percentage in the future ($p=0.004$)

- Lower death rates in the future ($p=0.007$)

- The level of education; patients who had attended the secondary and tertiary level of education were more likely to complete the inpatient program, $p=0.0005$

Moreover:

- The family status; married patients were more likely to complete the program ($p=0.045$)

- The existence of children; patients who had children were more likely to complete the program ($p=0.015$)

- The occupational status; unemployed patients were more likely to complete the program ($p=0.013$)

- The time period after treatment; patients whose treatment had started more than 5 years ago were more likely to complete the inpatient program ($p=0.026$)

As far as the incidents of relapse among the patients who participated in the research is concerned, 53.95-55.77% of the patients who completed the rehabilitation phase, and 46.31-50% of the

patients who completed the inpatient program remain abstinent without relapse of alcohol use. The percentages and the respective time periods since the treatment are detailed in Table 5.

DISCUSSION

This study examines the aggregate results of patients who joined an inpatient alcohol rehabilitation program at a psychiatric hospital and received combined treatment (administration of naltrexone and individual psychological counseling, group therapy, drama therapy and occupational therapy). Besides examining the results from this particular program, the study also investigates the efficacy of similar programs and the demographic variables that may correlate with the outcomes. It does this because it is deemed necessary to explore the different methods and means which can prevent relapse to alcohol use.

In the EU, the 2/3 of treatments for alcohol dependence include psychotherapeutic interventions either exclusively or in combination with pharmaceutical treatment. Pharmaceutical treatment is used in 50% of the cases while 60% of the drugs are prescribed along psychotherapy (Rehm et al.¹⁰)

Various studies support different therapeutic approaches according to Lesch typology. According to Kiefer et al., the use of acamprosate is more efficient in type 1 patients, while naltrexone in type 3 and 4 patients based on the Lesch typology (Kiefer et al.¹¹, Hillemacher & Bleich¹²). However, although meta-analyses have shown that no significant difference is observed in terms of efficacy between naltrexone and acamprosate (Jonas et al.¹³), acamprosate is slightly more efficient in promoting abstinence while naltrexone in reducing heavy consumption and craving (Maisel et al.⁵). The identification of

naltrexone-responsive alcohol-dependent patients is still in development. Studies to date point to two potential moderators: family history and presence of the OPRM1 Asn40Asp polymorphism (Garbutt et al.¹⁴, Enoch¹⁵).

Meta-analyses on the benefits of naltrexone have demonstrated that naltrexone is superior to placebo. Patients treated with naltrexone displayed fewer relapses and remained abstinent for more time, after 12 weeks of treatment. They also consumed considerably smaller quantities of alcohol during the period of the study. Concerning the number of individuals who relapsed at least once or the number of people who stopped the study because of relapse, no statistically significant difference was observed between the group who was treated with naltrexone and the control group (Streeton & Whelan¹⁶).

Thus, the results of the program under investigation, namely the inpatient alcohol rehabilitation program with the use of naltrexone, are deemed rather satisfactory: 53.95-55.77% ⁽¹⁾ of the patients who completed the rehabilitation phase and 46.31-50% ⁽²⁾ of those who only completed the inpatient program remain fully abstinent. Particularly in the five-year period, abstinence rates among the patients who completed the rehabilitation phase reached 55.77%, and 46.31% for those who only completed the inpatient program. The relapse rates among patients who completed the program within the past 2 years, although equally quantitatively significant, are not statistically significant when compared to those of patients who had completed the program in the previous years, possibly due to the small size of the sample.

The completion of the inpatient program correlates with lower relapse rates in the future in terms of statistical significance ($p=0.004$)

In addition, the shortest relapse duration tended to correlate with the completion of the rehabilitation phase ($p=0.057$), with relapses lasting less than 6 months being more often.

There are few studies on the efficacy of inpatient rehabilitation programs. Most studies deal with individuals following daily or weekly outpatient treatment (Beasley et al.¹⁷, Ehrenreich et al.¹⁸, Stinchfield et al.¹⁹, Vuoristo-Myllys et al.^{20,21}). We came across one study dealing with admitted patients (Neto et al.²²) whose authors describe the results on 124 sequentially admitted patients, after the first year has elapsed following the completion of the program at the Southern Regional Alcohol-Abuse Treatment

(1) In particular, the rates acquired are the following: 53.95% for individuals who completed rehabilitation 2-5 years ago, 55.77% for individuals who completed rehabilitation 5 or more years ago, and 55.00% for individuals who completed rehabilitation less than 2 years ago.

(2) More specifically, they included information such as: 46.31% for individuals who completed the inpatient program 5 or more years ago, 46.34% for individuals who completed the inpatient program 2-5 years ago, and 50.00% for individuals who completed the inpatient program less than 2 years ago.

Centre in Lisbon. The patients were admitted and treated for 5-7 weeks. According to the study, at the end of year 44.3% of the patients abstained, 40.3% consumed alcohol and 15.4% did not respond.

As different therapy approaches are used in various alcohol treatment programs, it is difficult to attempt a comparison and the results vary.

In this study, we noted that the correlation between a higher educational level, marriage and the existence of children, and the completion of the inpatient program is statistically significant ($p=0.000$, $p=0.045$, $p=0.015$ respectively). Furthermore, age tended to correlate with the completion of the rehabilitation program, with the age group over 50 tending to display higher rates in the completion of the rehabilitation phase ($p=0.087$).

Research into the correlation between demographic characteristics and relapses demonstrate that being married increases the possibilities for better prognosis (Waisberg et al.²³). Ornstein et al.²⁴ conclude that the factors with higher correlation rates with improved prognosis are age, occupation and married life. Neto et al.²², on the other hand, maintain that these factors are married life, professional security and the continuation of treatment after admission.

The percentage of deaths in our sample amounts to 16.70%. Of the patients who had died 64.20% had completed the inpatient program, while the percentage rises to 81.10% among survivors. Moreover, the completion of the inpatient program displays statistically significant correlation with lower death rates in the future ($p=0.007$).

Alcohol consumption is responsible for 3.4% of deaths worldwide and strongly related to mortality from cirrhosis, chronic pancreatitis and hypertension. In the EU, one in 7 men and one in 13 women, aged between 15 and 64 years, die of alcohol-attributable causes. In 2004, alcohol dependence accounted for more than 70% of the overall alcohol-attributable mortality (Rehm et al.¹)

In the European population aged 20-64 years,

the absolute number of alcohol-attributable deaths is greater later in adult life, despite the highest percentage occurring in the 20-44 age group (approx. one in five) rather than the 45-64 age group (approx. one in nine). More than two-thirds of all alcohol-attributable deaths in the 20-64-year-old population occur in the 45-64 age group (Rehm et al.¹).

This study concluded that the percentage of comorbidity between chronic alcoholism and psychiatric disorders in the patient sample was 50.78%. In specific, 5.04% of the sample showed schizophrenia, 3.15% bipolar disorder, 21.76% unipolar depression, and 11.98% substance abuse.

The percentage of comorbidity in literature can reach 70% (Mellos²⁵, Regier et al.²⁶, Schuckitt et al.²⁷, Kessler & Walters²⁸).

Based on the results from the Epidemiological Catchment Area Survey (ECA), among the patients with bipolar disorder, 44% suffered from alcohol abuse, 4% of alcohol-dependent patients met the criteria for schizophrenic psychosis, while 5% of men and 19% of women suffered from major depression. Furthermore, other clinical trials also conclude that 80% of alcohol-dependent patients display depressive symptoms with 1/3 of those suffering from major depression (Mellos²⁵, Schuckitt et al.²⁷, Kessler et al.²⁹, Roy et al.³⁰, Kandel et al.³¹).

The limitation of the study is that it was not possible to collect data from more patients of those who participated in the rehabilitation program over the years 1997-2010, and the sample consisted of only a small percentage (41.6%).

Regarding future perspectives, it would be interesting to conduct more research on relapse to alcohol abuse and how this potentially correlates with various demographic or clinical data. Such information could allow us to identify and assess factors relating to higher improvement percentages. Equally interesting would also be to identify which patient groups who have been diagnosed are more suitable for inpatient monitoring and administration of naltrexone.

Table 1.

DEMOGRAPHIC CHARACTERISTICS OF PATIENTS	
AGE	%
<50 years of age	54.50
>50 years of age	45.50
PLACE OF RESIDENCE	
Attica	66.40
Countryside	33.60
EDUCATION	
Primary	40.50
Secondary	43.50
Tertiary	16.00
FAMILY STATUS	
Single	37.30
Married	62.70
CHILDREN	
No children	35.60
Children	64.40
OCCUPATIONAL STATUS	
Employed	41.00
Unemployed	59.00

Table 2.

CLINICAL CHARACTERISTICS OF PATIENTS	
OTHER PROGRAM	
Yes	10.00
No	90.00
SOMATIC COMORBIDITY	
Yes	32.20
No	67.80
TYPE	
Liver disorder	15.70
Gastrointestinal disease	6.50
Neurological disorder	8.30
Neoplasms	19.40
Other	50.00
ADMISSION FOR PATHOLOGICAL CONDITIONS	
Yes	35.50
No	64.50
DEATHS	
Yes	16.70
No	83.30
COMORBIDITY	
No	49.22
Yes	50.78
Schizophrenia	5.04
Bipolar Disorder	3.15
Depression	21.76
Substance use	11.98
Other disorders	8.85

Table 3. Clinical and demographic characteristics of all patients who completed the rehabilitation phase

		COMPLETION OF REHABILITATION		NON COMPLETION OF REHABILITATION		TOTAL	x2	df	p
		N	(%)	N	(%)				
AGE	<50 years of age	105	63.30%	61	36.70%	166	2.198	1	0.087
	>50 years of age	97	71.30%	39	28.70%	136			
PLACE OF RESIDENCE	Athens	134	67.70%	64	32.30%	198	0.324	1	0.328
	Countryside	67	64.40%	37	35.60%	104			
EDUCATION	Primary	73	61.90%	45	38.10%	118	2.622	2	0.27
	Secondary	93	71.50%	37	28.50%	130			
	Tertiary	31	67.40%	15	32.60%	46			
FAMILY STATUS	Single	51	59.30%	35	40.70%	86	2.853	1	0.062
	Married	97	70.30%	41	29.70%	138			
CHILDREN	Children	133	69.30%	59	30.70%	192	1.374	1	0.148
	No children	67	62.60%	40	37.40%	107			
OCCUPATIONAL STATUS	Employed	79	66.40%	40	33.60%	119	0.182	1	0.381
	Unemployed	121	68.80%	55	31.30%	176			
TIME PERIOD AFTER TREATMENT	Treatment before >5 years	104	75.90%	33	24.10%	137	3.249	2	0.197
	Treatment before 2-5 years	76	84.40%	14	15.60%	90			
	Treatment before <2 years	20	71.40%	8	28.60%	28			
SOMATIC COMORBIDITY	Somatic comorbidity	59	65.60%	31	34.40%	90	0.103	1	0.424
	No somatic comorbidity	143	67.50%	69	32.50%	212			
ADMISSION FOR PHYSICAL ILLNESS	Physical illness	54	53.50%	47	46.50%	101	11.881	1	0.001
	No physical illness	148	73.30%	54	26.70%	202			
RELAPSES	Relapses	91	53.50%	79	46.50%	170	31.335	1	0.000
	No relapses	111	84.10%	21	15.90%	132			
DURATION OF RELAPSES	Relapse for <6 months	49	62.00%	30	38.00%	79	3.648	1	0.054
	Relapse for < 2 years	11	55.00%	9	45.00%	20			
	Relapse for >2 years	33	46.50%	38	53.50%	71			
DEATH	Dead	28	66.70%	14	33.30%	42	0.001	1	0.562
	Alive	174	66.40%	88	33.60%	262			

Table 4. Clinical and demographic characteristics of all patients who completed the inpatient program

		COMPLETION OF INPATIENT PROGRAM		NON COMPLETION OF INPATIENT PROGRAM		TOTAL			
		N	(%)	N	(%)	N	x2	df	p
AGE	<50 years of age	134	76.10%	42	23.90%	176	1.03	1	0.19
	>50 years of age	118	80.80%	28	19.20%	146			
PLACE OF RESIDENCE	Athens	168	78.50%	46	21.50%	214	0.232	1	0.364
	Countryside	83	76.10%	26	23.90%	109			
EDUCATION	Primary	82	66.10%	42	33.90%	124	15.306	2	0.000
	Secondary	110	82.70%	23	17.30%	133			
	Tertiary	44	89.80%	5	10.20%	49			
FAMILY STATUS	Single	63	70.00%	27	30.00%	90	3.472	1	0.045
	Married	120	80.50%	29	19.50%	149			
CHILDREN	Children	169	82.00%	37	18.00%	206	5.385	1	0.015
	No children	80	70.80%	33	29.20%	113			
OCCUPATIONAL STATUS	Employed	92	72.40%	35	27.60%	127	5.64	1	0.013
	Unemployed	153	83.60%	30	16.40%	183			
TIME PERIOD AFTER TREATMENT	Treatment before >5 years	152	95.00%	8	5.00%	160	7.27	2	0.026
	Treatment before 2-5 years	82	87.20%	12	12.80%	94			
	Treatment before <2 years	24	82.80%	5	17.20%	29			
SOMATIC COMORBIDITY	Somatic comorbidity	85	81.00%	20	19.00%	105	0.569	1	0.273
	No somatic comorbidity	170	77.30%	50	22.70%	220			
ADMISSION FOR PHYSICAL ILLNESS	Physical illness	87	75.70%	28	24.30%	115	0.436	1	0.299
	No physical illness	164	78.80%	44	21.20%	208			

Table 5. Patient relapse

PATIENTS PER THERAPEUTIC MILESTONE AND TREATMENT TIME PERIOD		NO RELAPSE	(%)	RELAPSE	(%)	TOTAL	P
> FIVE YEARS	COMPLETION OF REHABILITATION	58	55.77%	46	44.23%	104	0.001
	COMPLETION OF INPATIENT PROGRAM	69	46.31%	80	53.69%	149	NS
2 - 5 YEARS	COMPLETION OF REHABILITATION	41	53.95%	35	46.05%	76	0.072
	COMPLETION OF INPATIENT PROGRAM	38	46.34%	44	53.66%	82	NS
< 2 YEARS	COMPLETION OF REHABILITATION	11	55.00%	9	45.00%	20	NS
	COMPLETION OF INPATIENT PROGRAM	12	50.00%	12	50.00%	24	NS

References

1. Rehm J, Shield KD et al. Alcohol consumption, alcohol dependence and attributable burden of disease in Europe. Potential gains from effective interventions for alcohol dependence. Centre for Addiction and Mental Health, Canada. (2012).
2. Μητσώνης, Χ., Μουλαρογιώργου Ι., Πάλλη Ι., Δημόπουλος, Ν., Λατζουράκη, Ε., Τσακίρης, Φ. Εξαρτήσεις, Συννοσηρότητα, Πρόληψη και Θεραπεία. 2ο Μονοθεματικό Πανελλήνιο Συνέδριο Ψυχιατρικής, 5-7 Μαΐου 2010, Θεσσαλονίκη.
3. Besirli, A., Esel, E., Ozsoy, S., Turan, T. Hypothalamic-Pituitary-Adrenal Axis response to oral naltrexone in alcoholics during early withdrawal. *Pharmacopsychiatry*, 2014 Jun 17 [Epub ahead of print]
4. Myrick, H., Anton, R.F., Li, X., Henderson, S., Randall, P.K., Voronin, K. Effect of naltrexone and ondansetron on alcohol cue-induced activation of the ventral striatum in alcohol-dependent people. *Arch Gen Psychiatry*, 65(4): 466–475 (2008).
5. Maisel, N.C., Blodgett, J.C., Wilbourne, P.L., Humphreys, K., Finney, J.W. Meta-analysis of naltrexone and acamprosate for treating alcohol use disorders: when are these medications most helpful? *Addiction*, 108(2):275-93 (2013).
6. Garbutt JC. Efficacy and tolerability of naltrexone in the management of alcohol dependence. *Current Pharmaceutical Design*, 16, 2091-2097 (2010).
7. Greenfield, S.F., Pettinati, H.M., O'Malley, S., Randall, P.K., Randall, C.L. Gender Differences in Alcohol Treatment: An Analysis of Outcome from the COMBINE Study. *Alcohol Clin Exp Res*, 34(10): 1803–1812 (2010).
8. Agosti V, Nunes EV, O'Shea D. Do Manualized Psychosocial Interventions Help Reduce Relapse among Alcohol-Dependent Adults Treated with Naltrexone or Placebo? A Meta-analysis. *Am J Addict*, 21(6):501-7 (2012).
9. Jarosz, J., Miernik, K., Wachal, M., Walczak, J., Kruppl, G. Naltrexone (50mg) plus psychotherapy in alcohol-dependent patients: a meta-analysis of randomized controlled trials. *Am J Drug Alcohol Abuse*, 39(3):144-60 (2013).
10. Rehm J, Mathers C, Popova S, Thavorncharoensap M, Teerawattananon Y, Patra J. Global burden of disease and injury and economic cost attributable to alcohol use and alcohol-use disorders. *Lancet*, 27;373(9682):2223-33 (2009).
11. Kiefer, F., Helwig, H., Tarnaske, T., Otte, C., Jahn, H. and Wiedemann, K. Pharmacological relapse prevention of alcoholism: Clinical predictors of outcome. *European Addiction Research* 11, 83–91 (2005).
12. Hillemecher, T. & Bleich, S. Neurobiology and treatment in alcoholism- recent findings regarding Lesch's typology of alcohol dependence. *Alcohol & Alcoholism*, 43(3):341–346 (2008).
13. Jonas, D.E., Amick, H.R., Feltner, C., Bobashev, G., Thomas, K., Wines, R., Kim, M.M., Shanahan, E., Gass, C.E., Rowe, C.J., Garbutt, J.C. Pharmacotherapy for adults with alcohol use disorders in outpatient setting: a systematic review and meta-analysis. *JAMA*, 311(18):1889-900 (2014)
14. Garbutt, J.C., Greenblatt, A.M., West, S.L., Morgan, L.C., Kampov-Polevoy, A., Jordan, H.S., Bobashev, G.V. Clinical and biological moderators of response to naltrexone in alcohol dependence: a systematic review of the evidence. *Addiction*, 2014 Mar 25. doi: 10.1111/add.12557.
15. Enoch, M.A. Genetic influences on response to alcohol and response to pharmacotherapies for alcoholism. *Pharmacol Biochem Behav.* 2013 Nov 9. pii: S0091-3057(13)00284-0. doi: 10.1016/j.pbb.2013.11.001.
16. Streeton, C., Whelan, G. Naltrexone, a relapse prevention maintenance treatment of alcohol dependence: a meta-analysis of randomized controlled trials. *Alcohol & Alcoholism*, 36;6:544-552 (2001).
17. Beasley, J.D., Grimson, R., Bicker, A.A., Closson, W.J., Heusel, C.A., Faust, F.I. Follow up of a cohort of alcoholic patients through 12 months of comprehensive behavioural treatment. *J Subst Abuse Treat*, 8:133-142 (1991).
18. Ehrenreich, H., Mangholz, A., Schmitth, M., Lieder, P., Volkel, W., Ruther, E., Poser, W. OLITA: An alternative in the treatment of therapy-resistant chronic alcoholics. First evaluation of a new approach. *Eur Arch Psychiatry Clin-Neurosci*, 247:1:51-54 (1997).
19. Stinchfield, R., Owen, P. Hazelden's model of treatment and its outcome. *Addict Behav*, 23-5:669-683 (1998).
20. Vuoristo-Myllys, S., Lipsanen, J., Lahti, J., Kalska, H., Alho, H. Outcome predictors for problem drinkers treated with combined cognitive behavioral therapy and naltrexone. *Am J Drug Alcohol Abuse*, 40(2):103-10 (2014)
21. Vuoristo-Myllys, S., Lahti, J., Alho, H., Julkunen, J. Predictors of dropout in an outpatient treatment for problem drinkers including cognitive-behavioral therapy and the opioid antagonist naltrexone. *J Stud Alcohol Drugs*, 74(6):894-901 (2013).
22. Neto, D., Xavier, M., Lucena, P., Silva, A.V. An evaluation of the therapeutic programme conducted by the southern regional alcohol-abuse treatment centre: study on the programme's results one year after discharge from inpatient care. *Eur Addict Res*, 7:61-68 (2001).
23. Waisberg, J.L. Patient characteristics and outcome of inpatient treatment for alcoholism. *Adv Alcohol Subst Abuse*, 8(3-4):9-32 (1990).
24. Ornstein, P., Cherepon, J. Demographic variables as predictors of alcoholism treatment outcome. *J Stud Alcohol*, 46:425-32 (1985).
25. Μέλλος, Ε. Συννοσηρότητα και αλκοόλ. *Εγκέφαλος* 46, 72-78 (2009).
26. Regier, D.A., Farmer, M.E., Rae, D.S. Comorbidity of mental disorders with alcohol and other drug abuse: results from the Epidemiological Catchment Area (ECA) study. *JAMA*, 264:2511-2518

(1990).

27. Schuckit, M.A., Tipp, J.E., Bergman, M., Reich, W., Hesselbrock, V., Smith, T.L. Comparison of induced and independent Major Depressive Disorders in 2,954 Alcoholics. *Am J Psychiatry*, 154(7): 948-957 (1997).

28. Kessler, R.C., Walters, E.E. The National Comorbidity Survey. In: Tsuang MT, Tohen M (eds): *Textbook in Psychiatric Epidemiology*, 2nd ed, Wiley & sons, New York: 343-362 (2002).

29. Kessler, R.C., Nelson, C.B., McGonagle, K.A., Eclund, M.J., Frank, R.G., Leaf, P.J. The epidemiology of co-occurring addictive and mental disorders. *Am J Orthopsychiatry*, 66: 17-31 (1996).

30. Roy, A., DeJone, J., Lamparski, D., George, T., Linnoila, M. Depression among alcoholics: relationship to clinical and cerebrospinal fluid variables. *Arch Gen Psychiatry*, 42: 1043-1049 (1985).

31. Kandel, D.B., Huang, F.Y., Davies, M. Comorbidity between patterns of substance use dependence and psychiatric syndromes. *Drug Alcohol Depend*, 64: 233-241 (2001).