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ESTIMATION OF THE RESOURCES AND DIRECT HEALTH
COSTS FOR THE MANAGEMENT OF PATIENTS WITH
OPIOID USE DISORDER TREATED WITH
BUPRENORFINE/NALOXONE AND METHADONE IN
ROUTINE CLINICAL PRACTICE IN SPAIN:
COSTEDOPIA STUDY

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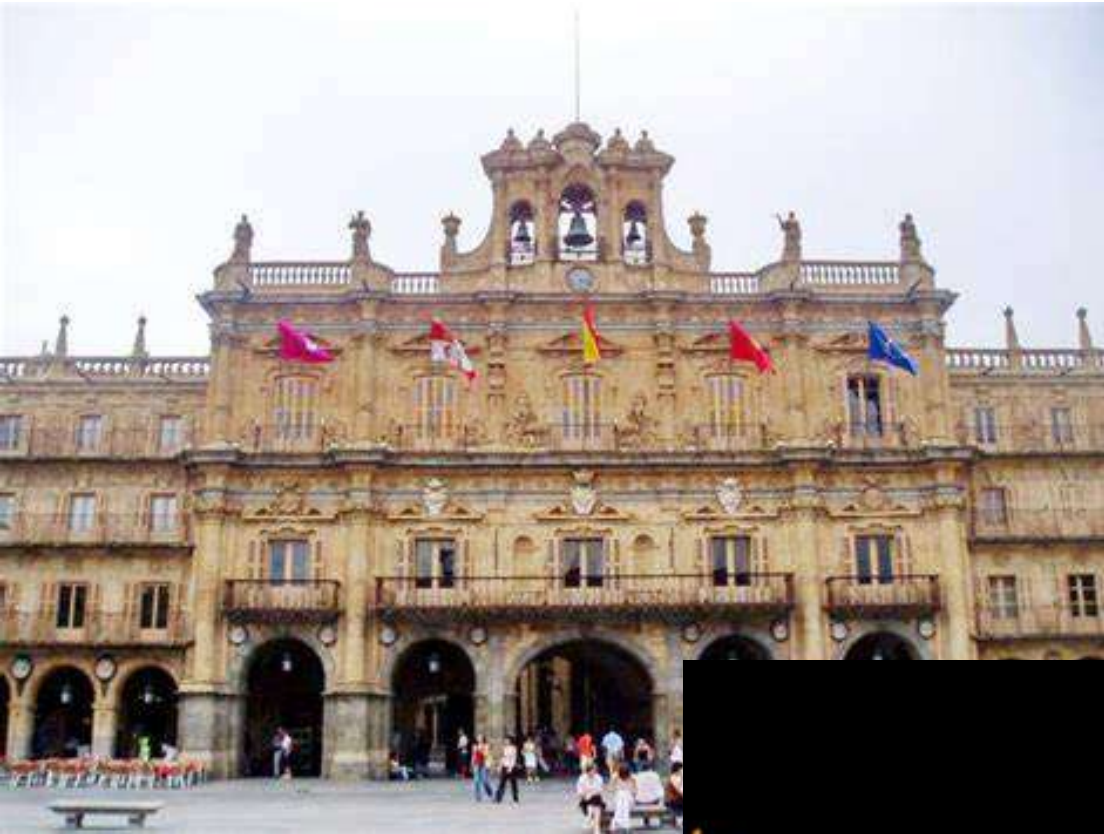




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Conflict of Interest/Disclosure

- Dr Carlos Roncero has received fees to give lectures for Janssen-Cilag, Ferrer-Brainfarma, Indivior, Lundbeck, Otsuka, Servier, GSK, Astra, Gilead, MSD, Sanofi, Exceltis, Abbvie, Takeda Rubio and Casein. He has received financial compensation for his participation as consultant or a board member of Lundbeck, Gilead, MSD, Mundipharma, INDIVIOR, Exceltis, Martindale, Camurus, Gebro and Abbvie board.
- Dr Carlos Roncero has been the PI of PROTEUS project, which was funded by a grant from Reckitt-Benckiser/Indivior and the COSTEDOPIA project, which was funded by Indivior. He received two medical education grants by Gilead.

Role of funding

- COSTEDOPIA study was sponsored by Indivior UK Ltd.

Management of opioid-dependent patients: comparison of the cost associated with use of buprenorphine/naloxone or methadone, and their interactions with concomitant treatments for infectious or psychiatric comorbidities

Manejo de pacientes dependientes de opiáceos: Comparación del coste asociado al uso de buprenorfina/naloxona o metadona, y sus interacciones con tratamientos concomitantes para comorbilidades infecciosas o psiquiátricas

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Abstract

The objective was to estimate the annual interaction management cost of agonist opioid treatment (AOT) for opioid-dependent (OD) patients with buprenorphine-naloxone (Suboxone®) (B/N) or methadone associated with concomitant treatments for infectious (HIV) or psychiatric comorbidities. A costs analysis model was developed to calculate the associated cost of AOT and interaction management. The AOT cost included pharmaceutical costs, drug preparation, distribution and dispensing, based on intake regimen (healthcare center or take-home) and type and frequency of dispensing (healthcare center or pharmacy), and medical visits. The cost of methadone also included single-dose bottles, monthly costs of custody at pharmacy, urine toxicology drug screenings and nursing visits. Potential interactions between AOT and concomitant treatments (antivirals, antibacterials/antifungals, antipsychotics, anxiolytics, antidepressants and anticonvulsants), were identified to determine the additional use of healthcare resources for each interaction management. The annual cost per patient of AOT was €1,525.97 for B/N and €1,467.29 for methadone. The average annual cost per patient of interaction management was €257.07 (infectious comorbidities), €114.03 (psychiatric comorbidities) and €185.55 (double comorbidity) with methadone and €7.90 with B/N in psychiatric comorbidities. Total annual costs of B/N were €1,525.97, €1,533.87 and €1,533.87 compared to €1,724.35, €1,581.32 and €1,652.84 for methadone per patient with infectious, psychiatric or double comorbidity respectively.

Compared to methadone, the total cost per patient with OD was lower with B/N (€47.45-€198.38 per year). This is due to the differences in interaction management costs associated with the concomitant treatment of infectious and/or psychiatric comorbidities.

Key Words: costs analysis, buprenorphine-naloxone, methadone, comorbidities, opioid dependence.

Background

Abstract

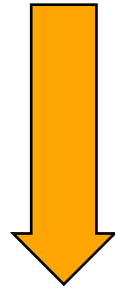
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Key Words: costs analysis, buprenorphine-naloxone, methadone, comorbidities, opioid dependence.

What about the real-world patients & treatments?

What about the real-world patients & treatments?



The COSTEDOPIA study

Study characteristics

- **Study design:** observational, retrospective and multicenter study
- **Treatment groups:**
 - Buprenorphine/naloxone (B/N)
 - Methadone
- **Study population:** Patients on opioid agonist therapy with B/N or methadone for at least 12 months before the inclusion in the analysis
- **Sample size:** 203 patients have been included in the analysis
 - 101 patients treated with B/N
 - 102 patients treated with methadone

Selection criteria

▪ Inclusion criteria:

- Patients older than 18 years
- Patients diagnosed with opioid use disorder (OUD) according to the DSM-IV/5
- Patients who were in the same opioid agonist therapy (OAT) for at least 12 month.
- Informed consent obtained

▪ Exclusion criteria:

- Patient's difficulty to read and to understand informed consent or patient's diary
- Patient with severe uncontrolled systemic disease
- Absence of relevant data in the clinical history
- Patient with severe physical disability not related to opioid dependence, according investigator's opinion
- Lack of willingness or inability to comply with the study procedures

Aim of the study

- **To estimate and compare the annual direct health costs of the management of OUD patients with different OAT (methadone or B/N)**
- To determine and compare the number of hospitalizations, resources utilization related to OUD and relapses in patients treated with B/N or methadone
- To estimate the annual health cost of comorbidities (infections and psychiatric) associated with OUD in patients on OAT

- To study the sociodemographic and clinical characteristics of patients with OUD in real world setting
- To evaluate and compare adherence to treatment in patients with OUD treated with B/N or methadone
- To evaluate the psychological well-being of patients with OUD
- To evaluate and compare satisfaction with treatment and quality of life related to the health status

Study variables



Treatment adherence

Morisky-Green
Questionnaire



Resources* utilization and Associated costs

Pharmacological
treatment

Comorbidities
Psychiatric and Infectious

Relapses

Overdoses

Patients monitoring

*hospitalizations, visits to
specialists, medical tests and
concomitant medication



Patients Reported Outcomes (PRO)

Service Satisfaction
VSSS-MT

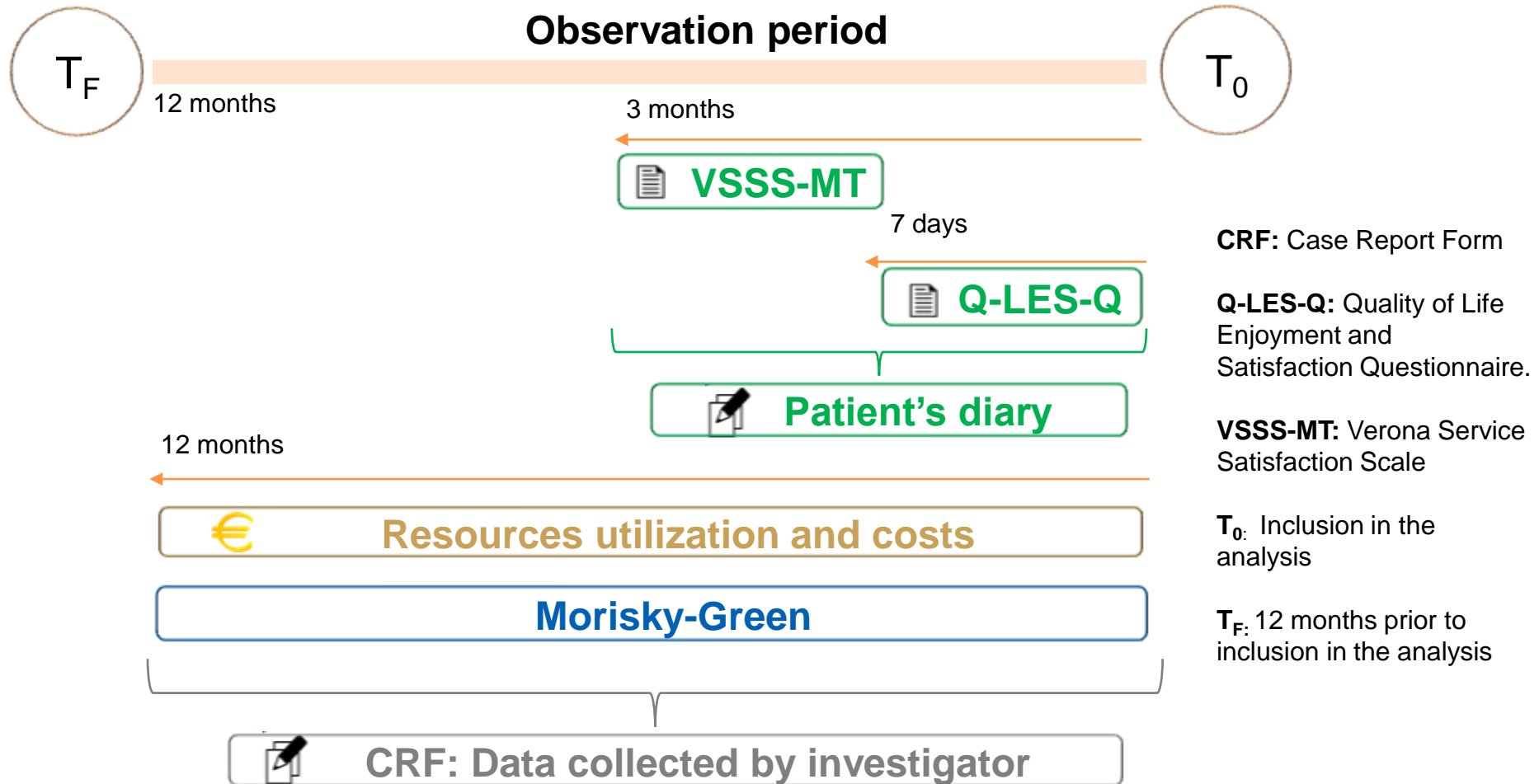
HRQL and
Patient Satisfaction
Q-LES-Q

VSSS-MT: Verona Service Satisfaction Scale.

HRQL: Health-Related Quality of Life

Q-LES-Q: Quality of Life Enjoyment and Satisfaction Questionnaire.

Data collection



RESULTS - recruitment

Recruited patients **B/N** **Methadone**
 204 102 102

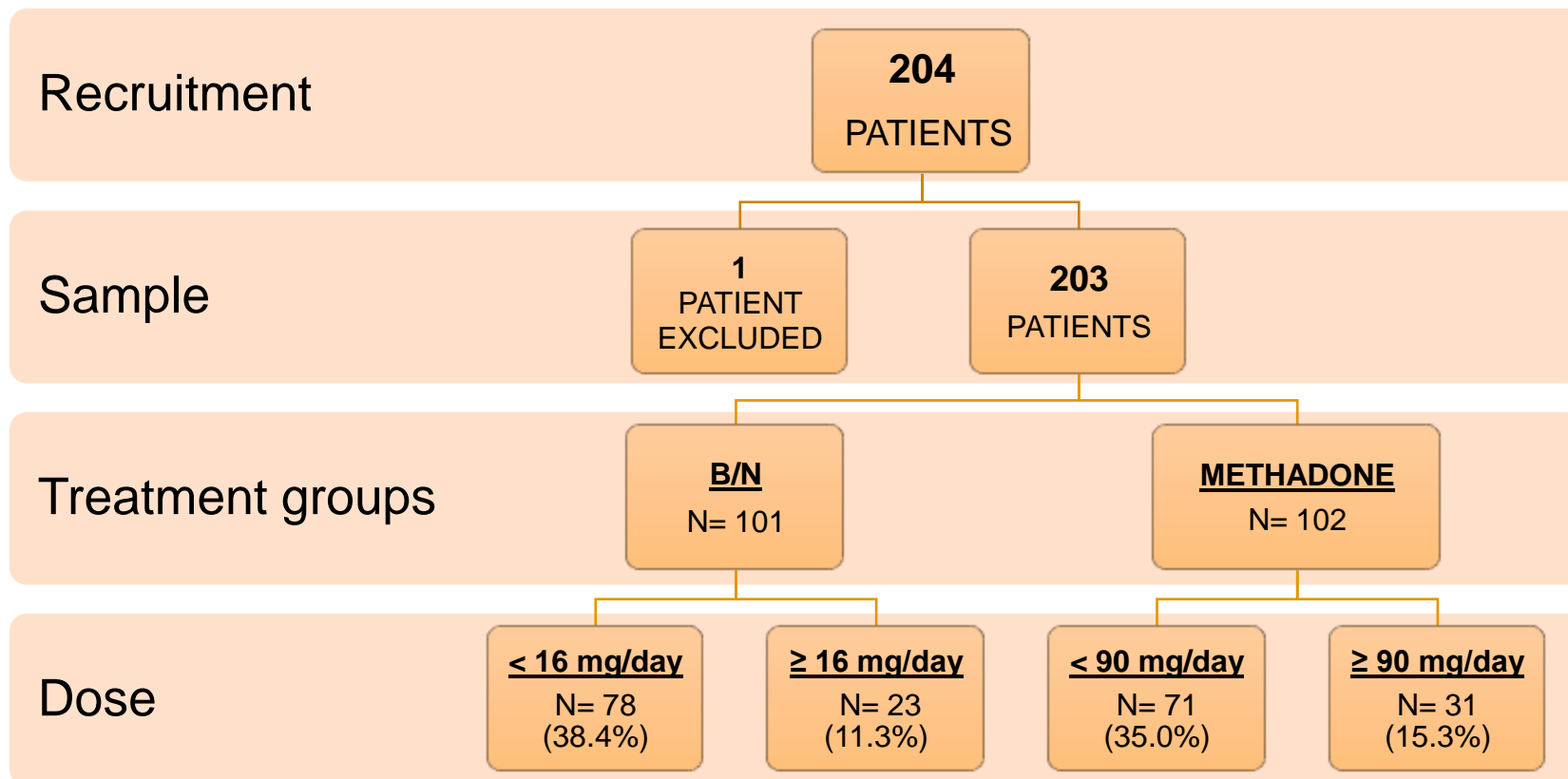
Analyzed **B/N** **Methadone**
 203 101 102



AUTONOMOUS COMMUNITIES	CENTRES		RECRUITED PATIENTS			
			Patients	Patients by treatment		% by treatment
Catalonia	001	Hospital Universitari de la Vall d'Hebrón	51	Methadone	34	16.67%
				B/N	17	8.33%
Valencia Community	002	Hospital Clínico Universitario de Valencia	46	Methadone	17	8.33%
				B/N	29	14.22%
	003	Hospital General Universitario de Valencia	39	Methadone	17	8.33%
Murcia	004	Hospital General Universitario Santa Lucía de Cartagena	68	Methadone	34	16.67%
				B/N	34	16.67%

B/N: buprenorphine-naloxone

RESULTS – Study population



Results



Results - Sociodemographic characteristics (I)

	B/N (n=101)	Methadone (n=102)	Total (n=203)	p-value
Age. Mean, years (SD)	46.38 (8.77)	46.93 (8.21)	46.66 (8.47)	0.284
Gender. Number of patients (%)				
Men	78 (77.22)	75 (73.53)	153 (75.37)	0.625
Level of education. Number of patients (%)				
No education	5 (4.95)	11 (10.78)	16 (7.88)	0.200
Primary education	46 (45.55)	46 (45.10)	92 (45.32)	1
Secondary education	41 (40.59)	40 (39.22)	81 (39.90)	0.954
University education	9 (8.91)	5 (4.90)	14 (6.90)	0.395
Work situation. Number of patients (%)				
Work: employed	31 (30.69)	17 (16.67)	48 (23.64)	0.028
Unpaid work	4 (3.97)	2 (1.96)	6 (2.96)	0.669
Unemployed	25 (24.75)	40 (39.21)	65 (32.02)	0.039
Other	2 (1.98)	1 (0.98)	3 (1.48)	0.993

Sociodemographic characteristics

Clinical characteristics - comorbidities

Clinical characteristics - treatment

Relapses and dose

Adherence and dose

Costs

HRQL

Results - Sociodemographic characteristics (II)

	B/N (n=101)	Methadone (n=102)	Total (n=203)	p-value
Family situation. Number of patients (%)				
Stable	89 (88.12)	70 (68.63)	159 (78.3%)	0.001
Unstable	12 (11.88)	32 (31.37)	44 (22.67)	-
Legal situation:				
Crimes in the last year. N. of patients (%)	33 (32.67)	50 (49.01)	83 (40.88)	0.026
Co-occurrent consumption of other substances. Number of patients (%) *				
Alcohol	78 (77.22)	75 (73.53)	153 (75.37)	0.625
Cannabis	5 (4.95)	11 (10.78)	16 (7.88)	0.200
Cocaine	46 (45.55)	46 (45.10)	92 (45.32)	1
Sedative drugs	41 (40.59)	40 (39.22)	81 (39.90)	0.954

B/N: buprenorphine/naloxone

* Some patients could have met the criteria for addiction to other substances

Sociodemographic characteristics

Clinical characteristics - comorbidities

Clinical characteristics - treatment

Relapses and dose

Adherence and dose

Costs

HRQL

Results - Clinical characteristics - comorbidities

	B/N (n=101)	Methadone (n=102)	Total (n=203)	p-value
Psychiatric comorbidities. Number of patients (%)				
Depression	25 (24.75)	19 (18.62)	44 (21.67)	0.308
Induced psychosis	7 (6.93)	11 (10.78)	18 (8.86)	0.460
Other personality disorders	38 (37.62)	33 (32.35)	71 (34.97)	0.377
Infectious comorbidities. Number of patients (%)				
Tuberculosis	4 (3.96)	5 (4.90)	9 (4.43)	1
Hepatitis B	5 (4.95)	20 (19.60)	25 (12.31)	0.003
Hepatitis C	45 (44.55)	60 (58.82)	105 (51.72)	0.058
B/N: buprenorphine/naloxone HIV	14 (13.86)	30 (29.41)	44 (21.57)	0.010

Results - Clinical characteristics - treatment (I)

	B/N (n=101)	Methadone (n=102)	Total (n=203)	p-value
Dispensation treatment. Number of patients (%)				
Hospital pharmacy	6 (5.94)	0 (0)	6 (2.96)	0.037
Retail pharmacy	58 (57.43)	5 (4.90)	63 (31.03)	<0.001
Health center/outpatient drug clinics	37 (36.63)	79 (77.45)	116 (57.14)	<0.001
Mobile treatment vans	0 (0)	3 (2.9%)	3 (2.94)	0.248
Methadone dispensary center	0 (0)	15 (14.71)	15 (14.71)	<0.001
Treatment phase, Number of patients (%)				
Maintenance	95 (94.06)	95 (93.14)	190 (93.60)	1
Medically supervised withdrawal	6 (5.94)	7 (6.86)	13 (6.40)	1
Treatment dose, mg				
B/N: buprenorphine/naloxone; SD: standard deviation Mean (SD)	8.86 (6.02)	71.31 (48.28)	-	-

Sociodemographic characteristics

Clinical characteristics - comorbidities

Clinical characteristics - treatment

Relapses and dose

Adherence and dose

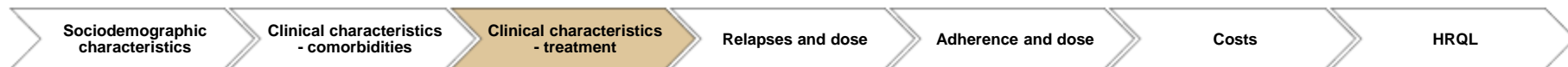
Costs

HRQL

Results - Clinical characteristics - treatment (II)

	B/N
Treatment phase, %	
Induction	0%
Maintenance	94%
Dose reduction	6%
Doses, %	
Daily dose < 16 mg	77%
Daily dose ≥ 16 mg	23%

	Methadone
Treatment phase, %	
Induction	0%
Maintenance	92%
Dose reduction	8%
Doses, %	
Daily dose ≤ 90 mg	70%
Daily dose ≥ 90 mg	30%



Results - Clinical characteristics - treatment (III)

	B/N (n=101)	Methadone (n=102)	Total (n=203)	p-value
Positive UDS of unprescribed opioids in urine (use on top)				
Patients with positive detections (%)	9 (8.91)	28 (27.45)	37 (18.22)	0.001
Total number of positive detections (%)	18 (10.23)	158 (89.77)	176 (100.00)	-
Mean number of positive detections (SD)	2 (1.12)	5.6 (6.46)	4.76 (5.84)	0.086

B/N: buprenorphine/naloxone; SD: standard deviation; UDS: Urine drug screen

- In B/N group, 9 out of 101 patients had positive urine drug screen (UDS).
- We detected lower illicit opioid use among patients treated with B/N, which was statically significant compared to methadone.

Results – Relapses and dose

	B/N (n=101)		Methadone (n=102)		p-value
	Relapse	No relapse	Relapse	No relapse	
Number of patients (%)	30 (29.70)	71 (70.30)	46 (45.10)	56 (54.90)	0.02
Dose, mg					
	Patients with relapse		Patients without relapse		p-value
B/N dose (SD)*	6.60 (3.69)		9.82 (6.56)		0.04
Methadone dose (SD)*	65.43 (37.56)		76.14 (55.45)		0.551

B/N: buprenorphine/naloxone; SD: standard deviation

- In B/N group, there was a statically significant difference in dosage of patients who relapsed Vs. those who didn't.
- Higher dosage are associated to lower relapses.

Sociodemographic characteristics

Clinical characteristics - comorbidities

Clinical characteristics - treatment

Relapses and dose

Adherence and dose

Costs

HRQL

Results – Adherence and dose

Adherence measured by Morisky-Green Test

	B/N		Methadone		p-value
	(n=101)		(n=102)		
	Adherent patients	Non adherent patients	Adherent patients	Non adherent patients	
Number of patients (%)	64 (63.37)	37 (36.63)	52 (50.98)	50 (49.02)	0.1
B/N					
	Adherent (n=64)		Non adherent (n=37)		p-value
Dose; Mean (SD)	8.39 (5.47)		9.69 (6.89)		0.412
Methadone					
	Adherent (n=52)		Non adherent (n=50)		p-value
Dose; Mean (SD)	62.02 (42.26%)		80.98 (52.54)		0.065

B/N: buprenorphine/naloxone; SD: standard deviation

Sociodemographic characteristics

Clinical characteristics - comorbidities

Clinical characteristics - treatment

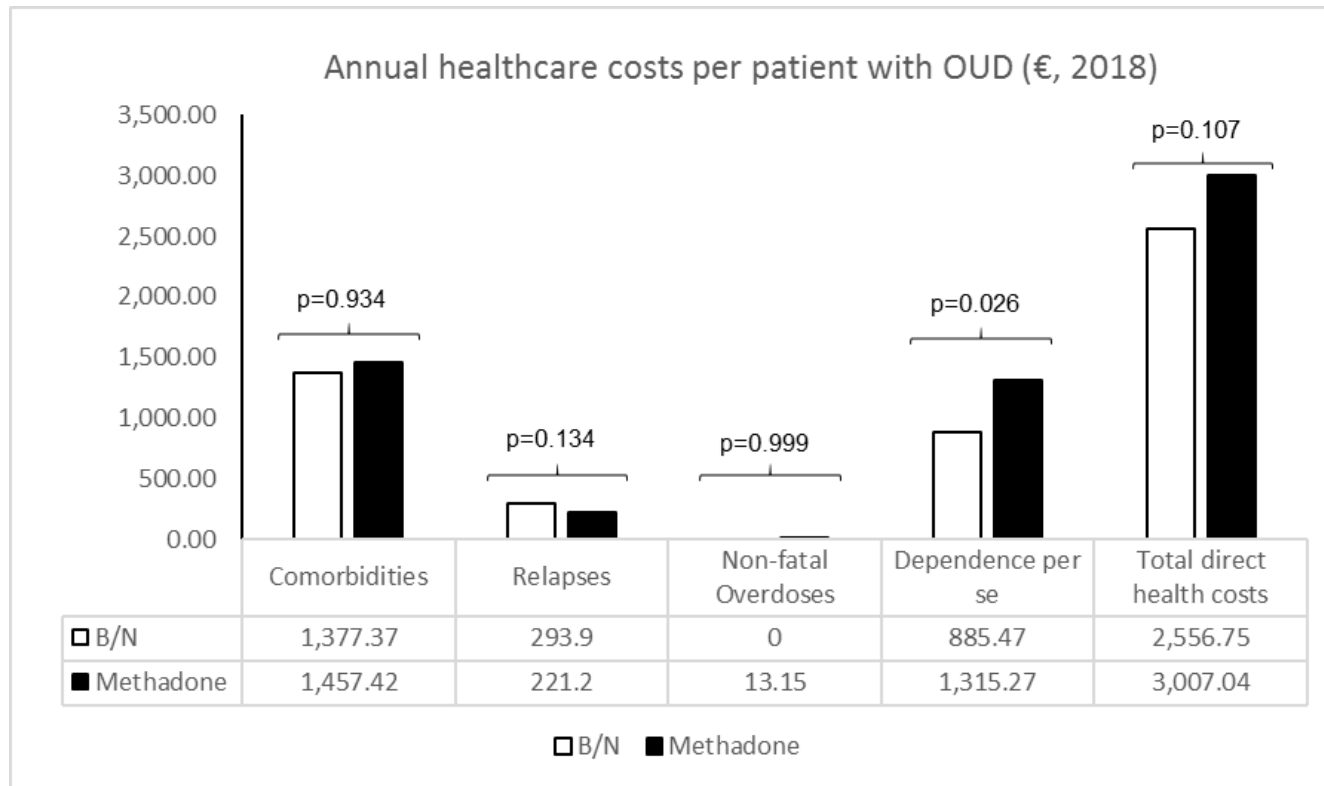
Relapses and dose

Adherence and dose

Costs

HRQL

Results - Costs



B/N: buprenorphine/naloxone

- Total direct health cost per patient for B/N and methadone was € 2,556.75 and € 3,007.04, respectively (cost savings € 450.29), with statistically significant difference in the cost of OUD “per se” (cost savings € 429.80).

Sociodemographic characteristics

Clinical characteristics - comorbidities

Clinical characteristics - treatment

Relapses and dose

Adherence and dose

Costs

HRQL

HRQL – Verona scale

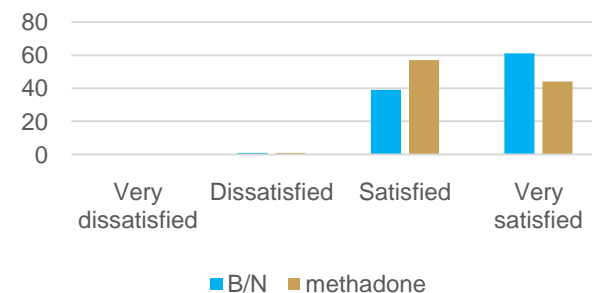
Scale from 1 (very poor) to 5 (excellent)

	B/N (n=101)	Methadone (n=102)	Total (n=203)	p-value
Verona scale:				
Satisfaction with treatment, mean (SD)				
Overall scale	3.99 (0.38)	3.97 (0.39)	3.98 (0.38)	0.221
Basic interventions	4.19 (0.41)	4.17 (0.44)	4.18 (0.43)	0.166
Specific interventions	3.53 (0.68)	3.51 (0.58)	3.52 (0.63)	0.805
Skills of social workers	3.76 (0.86)	3.87 (0.83)	3.81 (0.85)	0.568
Skills of psychologists	4.26 (0.71)	4.13 (0.85)	4.21 (0.77)	0.279

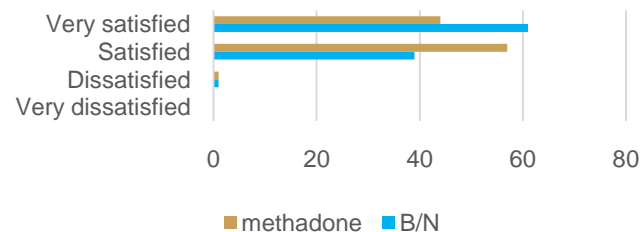
Satisfaction with treatment, n (%)

Very dissatisfied	0 (0%)	0 (0%)	0 (0%)	-
Dissatisfied	1 (0.99%)	1 (0.98%)	2 (0.99%)	1
Satisfied	39 (38.61%)	57 (55.88%)	96 (47.29%)	0.002
Very satisfied	61 (60.40%)	44 (43.14%)	105 (51.72%)	0.02

Number of patients



Number of patients



Sociodemographic characteristics

Clinical characteristics - comorbidities

Clinical characteristics - treatment

Relapses and dose

Adherence and dose

Costs

HRQL

HRQL - Q-LES-Q

Scale from 1 (very poor) to 5 (very good)

	B/N	Methadone	Total	p-value
N	101	102	203	
<hr/>				
Score, mean (SD)	3.49 (0.66)	3.28 (0.64)	3.39(0.66)	0.025

B/N: buprenorphine/naloxone; SD: standard deviation

- B/N reported statistically significant better quality of life compared with methadone

Sociodemographic characteristics

Clinical characteristics - comorbidities

Clinical characteristics - treatment

Relapses and dose

Adherence and dose

Costs

HRQL

Conclusions

- Patients with OUD are characterized by:
 - the severity of their complications
 - frequent poly-drug use
 - co-occurrent psychiatric and other comorbidities
- Based on the COSTEDOPIA Study in a real-world setting in Spain, treatment of OUD patients with **B/N results in direct healthcare cost savings**, compared to methadone.
- The health-related quality of life of patients on B/N treatment is significantly better than the one of patients treated with methadone.
- Moreover, patients on **B/N reported greater family, work and legal stability**, and had a **lower percentage of relapses** and **lower consumption of other illegal opioids. Adherence to treatment was also higher** in patients with B/N.
- At this regard, patients on methadone have a higher comorbidity, which could increase the costs of managing the OUD when compared to B/N.

HIGHLIGHTS

- B/N results in direct health cost savings, compared to methadone treatment
- B/N patients reported greater family, work, legal stability than methadone patients
- Methadone patients had a higher number of relapses than patients with B/N
- B/N patients reported a better quality of life than those treated with methadone



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