Substitution treatment of opioid dependent Patients in Routine Care in Germany: Retention Rates after 12 Months of Follow-up (COBRA*)

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COBRA
Substitution im Focus

*Cost-Benefit and Risk Appraisal of Substitution Treatment in Routine Care

Background

- Keeping the patient in substitution treatment is a core challenge.
- Retention rates are a crude measure for indicating how well the substitution treatment works.
- In controlled clinical trials the retention rates vary between 30 to 80% depending upon type of substitution drug and duration of treatment.
- Little is known about the retention rates and their determinants in routine care.
- In routine care the influences of
  - the type of substitution drug (methadone vs. buprenorphine)
  - the type of provider model (small, medium, large size of facility) and
  - the intensity of care

  on the retention rates are clearly understudied.

Objectives

To describe over a period of 12 months…

1. If the retention rates differ by…
   - type of substitution drug (methadone vs. buprenorphine)?
   - type of provider model (small [<10 patients/day], medium [10-40 patients/day], large [>40 patients/day] scale setting) and
   - duration of current substitution therapy (newly adjusted [up to 1 month in substitution therapy], medium duration [2-6 months in substitution therapy], long running [>6 months in substitution therapy])
2. What are the most common reasons for dropout of substitution treatment?

Methods

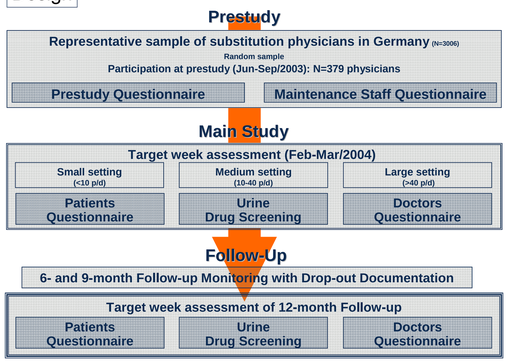
The COBRA baseline sample of N = 2,694 patients of an overall of N = 223 substitution doctors was followed-up over a period of 12 months with two short assessments in-between.

Retention rates are based on the subset of patients that were still eligible (N = 2,187). Patients who finished substitution therapy successfully (n = 100) or changed to drugfree therapy (clean, n = 174) are not included in the survival analyses. This results will be presented separately.

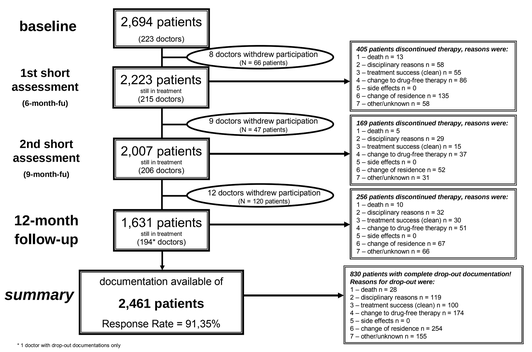
In addition to the categories “clean” and “change to drugfree therapy” the following drop-out reasons were accounted: “death”, “disciplinary reasons”, “change of residence/doctor”, “imprisonment” and “other/unknown reasons”.

Statistical analyses were done by STATA 9.

Design



Study Flow Chart



* 1 doctor with drop-out documentations only

Results

Retention rates by substitution drug (N = 2.187)

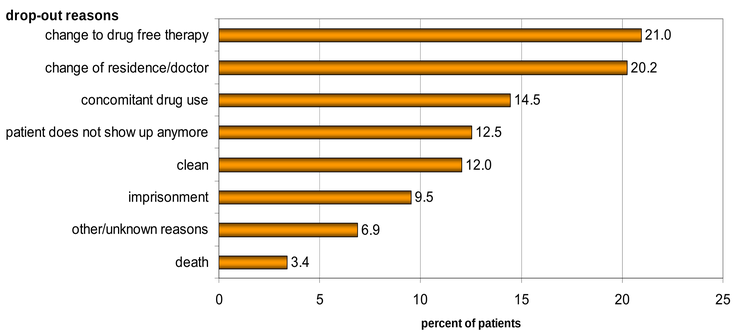
Retention rates by provider model (N = 2.187)

Retention rates by substitution drug and duration of current substitution therapy at baseline (N = 2.187)

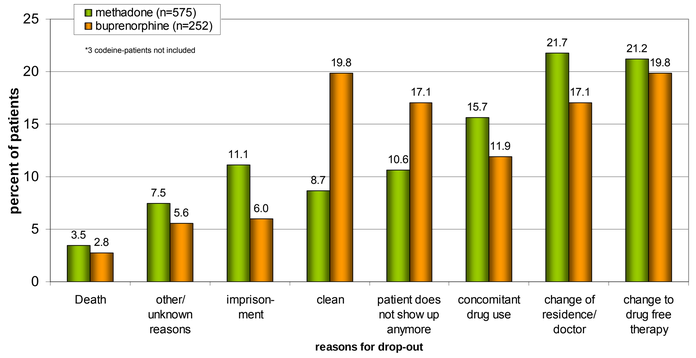
Differences of selected patients characteristics (N = 2.442)

		substitution drug: methadone (N=1.823)	buprenorphine (N=619)	signif.
Sex	male	68.8	68.2	ref.
	female	31.2	31.8	1.03 (0.85-1.25)
Mean age (sd)		35.47 (7.99)	32.75 (8.11)	t=7.299***
Mean yrs of education (sd)		10.04 (1.69)	10.13 (2.0)	t=-1.062
Professional status	employed	20.0	29.0	ref.
	unemployed	57.4	46.5	0.56*** (0.45-0.70)
	homemaker	8.1	7.3	0.62* (0.43-0.91)
	other	14.6	17.1	0.81 (0.61-1.08)
Marital status	single	55.3	57.4	ref.
	married	12.3	13.4	1.05 (0.79-1.39)
	sep./dev./wid.	20.7	16.3	0.76* (0.59-0.98)
	other	11.7	12.8	1.05 (0.79-1.4)
Mean BMI (sd)		24.14 (4.35)	23.34 (4.18)	t=3.847***
Mean yrs of opiate use (sd)		15.67 (8.22)	12.73 (7.96)	t=7.581***
Mean yrs since 1st maintenance treatment (sd)		5.89 (5.24)	4.62 (4.49)	t=5.397***
Mean no. of maintenance treatments (sd)		2.38 (1.94)	2.32 (1.4)	t=0.725
Mean no. of months of current treatment (sd)		19.14 (28.52)	8.75 (10.69)	t=8.852***
Mean of total of severity rating (sd)		2.83 (1.49)	2.44 (1.4)	t=5.693***
Comorbid illnesses	HIV infection	7.0	3.1	0.42*** (0.24-0.71)
	HCV infection	68.7	53.7	0.53*** (0.43-0.64)
	cardiovascular disease	13.6	12.8	0.93 (0.58-1.5)
	pulmonary disease	24.9	19.4	0.72 (0.49-1.07)
	other somatic disorders	78.1	76.0	0.89 (0.61-1.29)
	depressive disorders	55.9	57.9	1.09 (0.86-1.37)
	anxiety disorders	27.7	20.5	0.67** (0.51-0.89)
	psychotic disorders	5.4	3.4	0.61 (0.33-1.12)
	sleep disorders	20.0	21.6	1.1 (0.83-1.46)
	PTSD/acute stress disorders	11.8	10.9	0.91 (0.63-1.31)
	personality disorders	34.9	26.5	0.67** (0.52-0.87)
	other mental disorder	18.3	17.1	0.92 (0.68-1.25)
Mean of total score quality of life (EQ5D)		70.99 (20.21)	73.56 (19.74)	t=-2.637**

Drop-out reasons (N = 830)



Selected drop-out reasons by substitution drug (N = 827*)



		provider model: small (N=780)	medium (N=1.151)	large (N=511)	signif. medium vs. small	signif. large vs. small
Sex	male	70.3	68.4	66.7	ref.	ref.
	female	29.7	31.6	33.3	1.09 (0.90-1.33)	1.18 (0.93-1.50)
Mean age (sd)		35.39 (8.16)	34.29 (8.18)	34.95 (7.8)	t=2.912**	t=0.965
Mean yrs of education (sd)		10.2 (1.67)	10.01 (1.77)	9.98 (1.92)	t=2.328*	t=2.164*
Professional status	employed	28.8	20.6	15.9	ref.	ref.
	Unemployed	49.0	57.3	57.2	1.63*** (1.31-2.04)	2.11*** (1.57-2.84)
	Homemaker	7.3	8.0	8.6	1.53* (1.05-2.23)	2.13** (1.34-3.41)
	Other	14.8	14.1	18.3	1.33 (0.99-1.8)	2.24*** (1.54-3.25)
Marital status	single	54.8	57.7	53.3	ref.	ref.
	Married	13.9	11.3	13.7	0.77 (0.58-1.02)	1.02 (0.72-1.42)
	sep./dev./wid.	19.1	19.6	20.2	0.98 (0.77-1.24)	1.09 (0.81-1.46)
	Other	12.2	11.4	12.8	0.89 (0.66-1.19)	1.07 (0.75-1.52)
Mean BMI (sd)		24.14 (4.52)	23.89 (4.07)	23.74 (4.54)	t=1.241	t=1.505
Mean yrs of opiate use (sd)		15.31 (8.37)	14.57 (8.21)	15.07 (8.15)	t=1.878	t=0.496
Mean yrs since 1st maintenance treatment (sd)		5.84 (4.94)	5.57 (5.34)	5.13 (4.71)	t=1.146	t=2.592**
Mean no. of maintenance treatments (sd)		2.29 (1.45)	2.34 (2.08)	2.56 (1.68)	t=-0.556	t=-3.011**
Mean no. of months of current treatment (sd)		18.29 (26.99)	17.37 (27.14)	11.84 (18.46)	t=0.727	t=4.721***
Mean of total of severity rating (sd)		2.61 (1.44)	2.66 (1.49)	3.07 (1.46)	t=-0.75	t=-5.444***
Comorbid illnesses	HIV infection	4.9	6.2	7.5	1.27 (0.82-1.98)	1.57 (0.92-2.66)
	HCV infection	63.2	64.6	68.3	1.06 (0.87-1.29)	1.25 (0.97-1.62)
	cardiovascular disease	10.4	15.6	14.2	1.6* (1.01-2.54)	1.42 (0.84-2.41)
	pulmonary disease	24.2	23.3	23.6	0.95 (0.67-1.36)	0.97 (0.64-1.45)
	other somatic disorders	77.7	75.6	81.1	0.89 (0.62-1.27)	1.24 (0.8-1.91)
	depressive disorders	56.9	57.2	54.2	1.01 (0.8-1.28)	0.89 (0.68-1.17)
	anxiety disorders	24.0	27.0	26.3	1.17 (0.89-1.53)	1.13 (0.83-1.54)
	psychotic disorders	4.1	4.7	6.3	1.15 (0.65-2.03)	1.58 (0.85-2.91)
	sleep disorders	23.6	20.4	16.5	0.83 (0.63-1.1)	0.64** (0.45-0.9)
	PTSD/acute stress disorders	14.5	11.1	9.1	0.74 (0.52-1.04)	0.59** (0.38-0.91)
	personality disorders	29.9	28.9	44.1	0.95 (0.74-1.23)	1.85*** (1.4-2.45)
	other mental disorder	16.5	15.7	24.3	0.95 (0.69-1.3)	1.63** (1.16-2.28)
Mean of total score quality of life (EQ5D)		71.9 (19.2)	72.84 (19.86)	68.61 (21.75)	t=-0.986	t=2.719**

Summary

The retention rates in the COBRA study do not describe the retention since the 1st prescription of the substitution drug! They rather indicate for a representative cross-section of substitution patients in routine care, how well patients are retained in treatment in general.

- The retention rates are quite similar irrespective of the type of setting (small, medium, large practice) studied. But there is a clear tendency towards higher retention rates with small-scale, primary care based settings.
- Methadone and buprenorphine patients show similar retention rates in the 12-month follow-up, if accounting for prior treatment duration.
- The retention rate is lowest among patients who just started the substitution treatment (≤1 month at baseline) and highest among those who were receiving the substitution drug already for a longer time (>6 months at baseline).

Reasons for drop-out/discontinuation:

- Referring to all patients (*N* = 2,694), the mortality rate was only 1% in the COBRA study (*n* = 27).
- There is a remarkably high proportion of patients who switched from substitution to in- or outpatient drug-free therapy.
- Often, physicians did not know where their patients were and why they did not appear anymore.
- The data indicate differences in drop-out reasons among methadone and buprenorphine patients: More buprenorphine patients remained with their physicians, more of them became clean, fewer of them had significant concomitant drug use and fewer of them were imprisoned compared to methadone patients.

Conclusion

- The study confirms an overall effectiveness of agonist maintenance treatments in routine care.
- Small-scale, primary care based settings perform as well or better as large-scale substitution centres...
- ...suggesting that these primary care based settings might be a promising alternative to improve access to maintenance therapy in underserved areas.
- Further analyses of the found patient' differences between substitution drugs and settings are necessary.
- Analyses with baseline and 6-,9- and 12-month follow-up data to examine predictors for high retention are under way.

BMBF - Suchtforschungsverbund Sachsen – Bayern Allocating Substance Abuse Treatments to Patient Heterogeneity
This work has been prepared in the context of the project F8 “Allocation in substitution treatments – COBRA” (*PI*) within the Addiction Research Network ASAT. Contact information: asatkoordination@mpipsykl.mpg.de (www.asat-verbund.de).
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