

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...
- 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])
 - What are the most common reasons for dropout of substitution treatment?

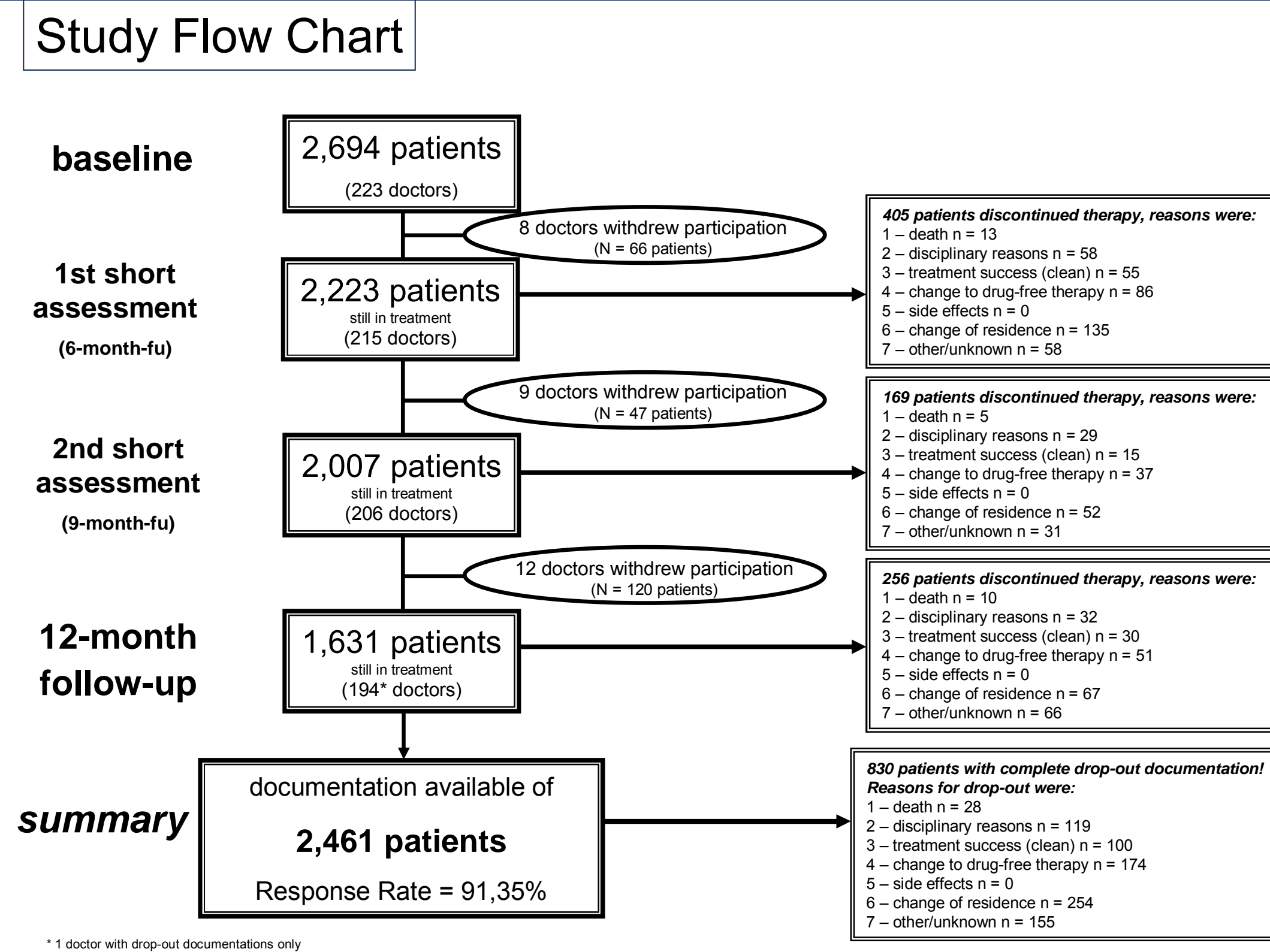
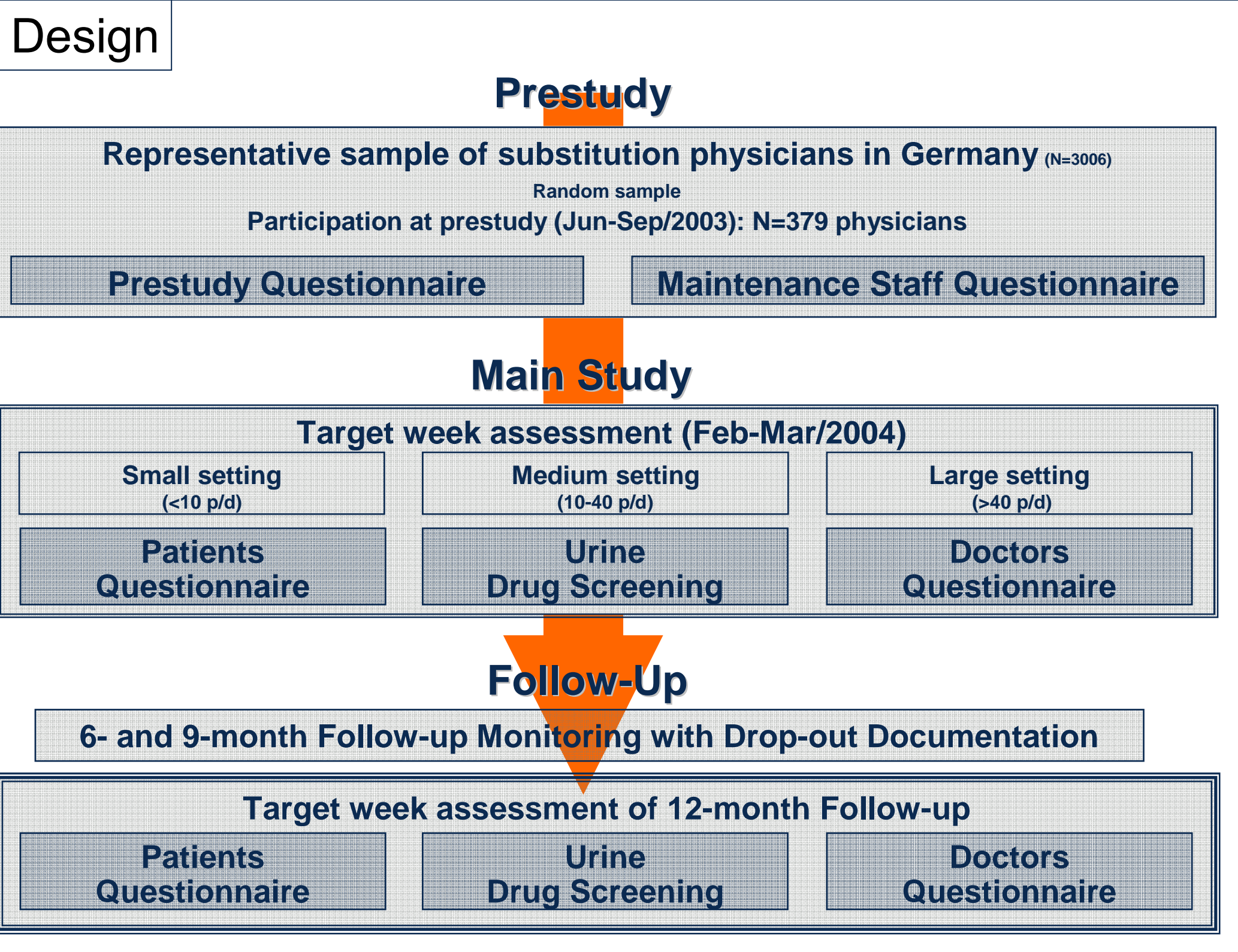
Methods

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.

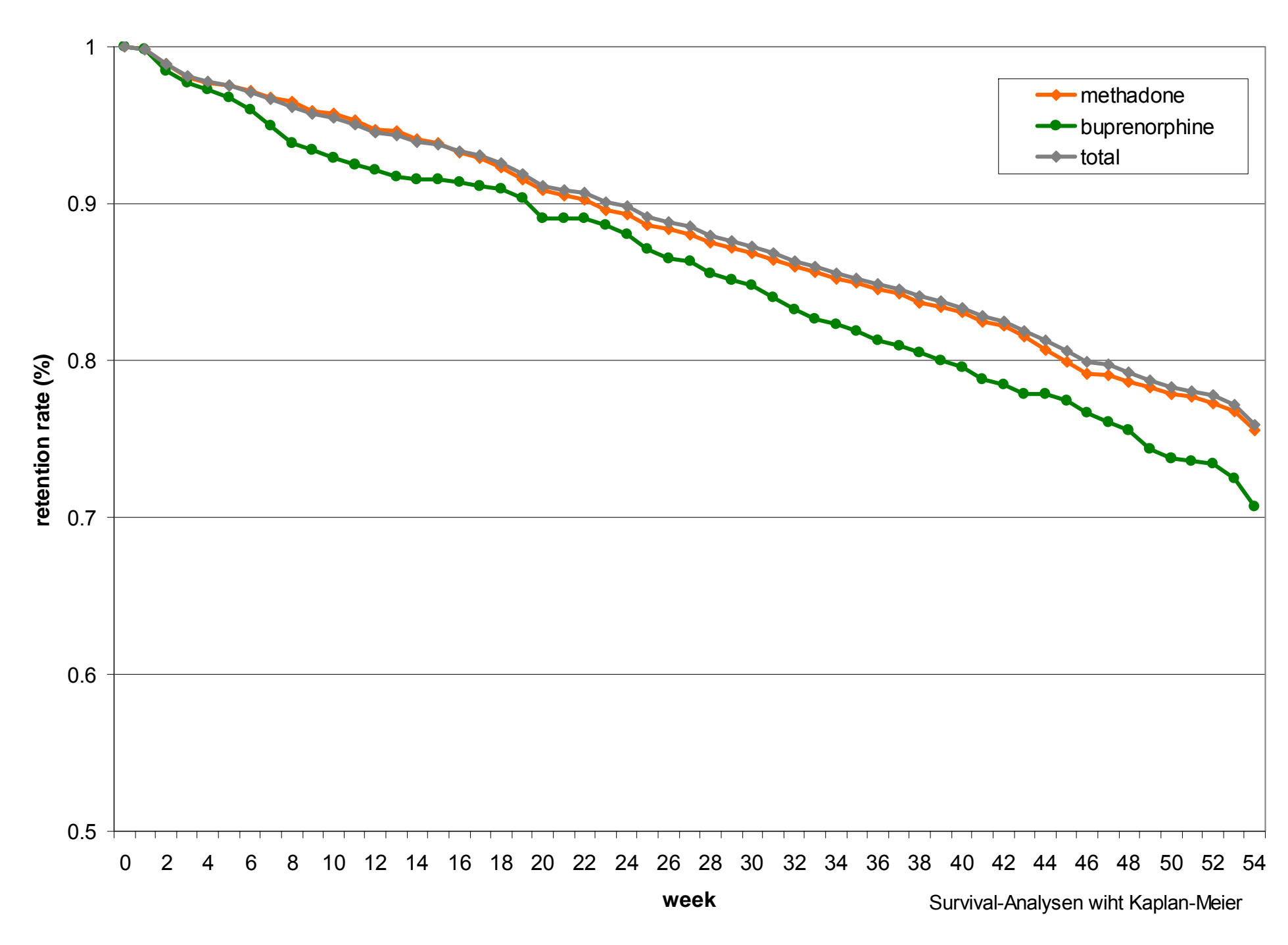
In addition to the categories "clean" and "change to drugfree therapy" the following drop-out reasons were accounted: "death", "disciplinary reasons", "change of residence/doctor", "imprisonment" and "other/unknown reasons".

Statistical analyses were done by STATA 9.

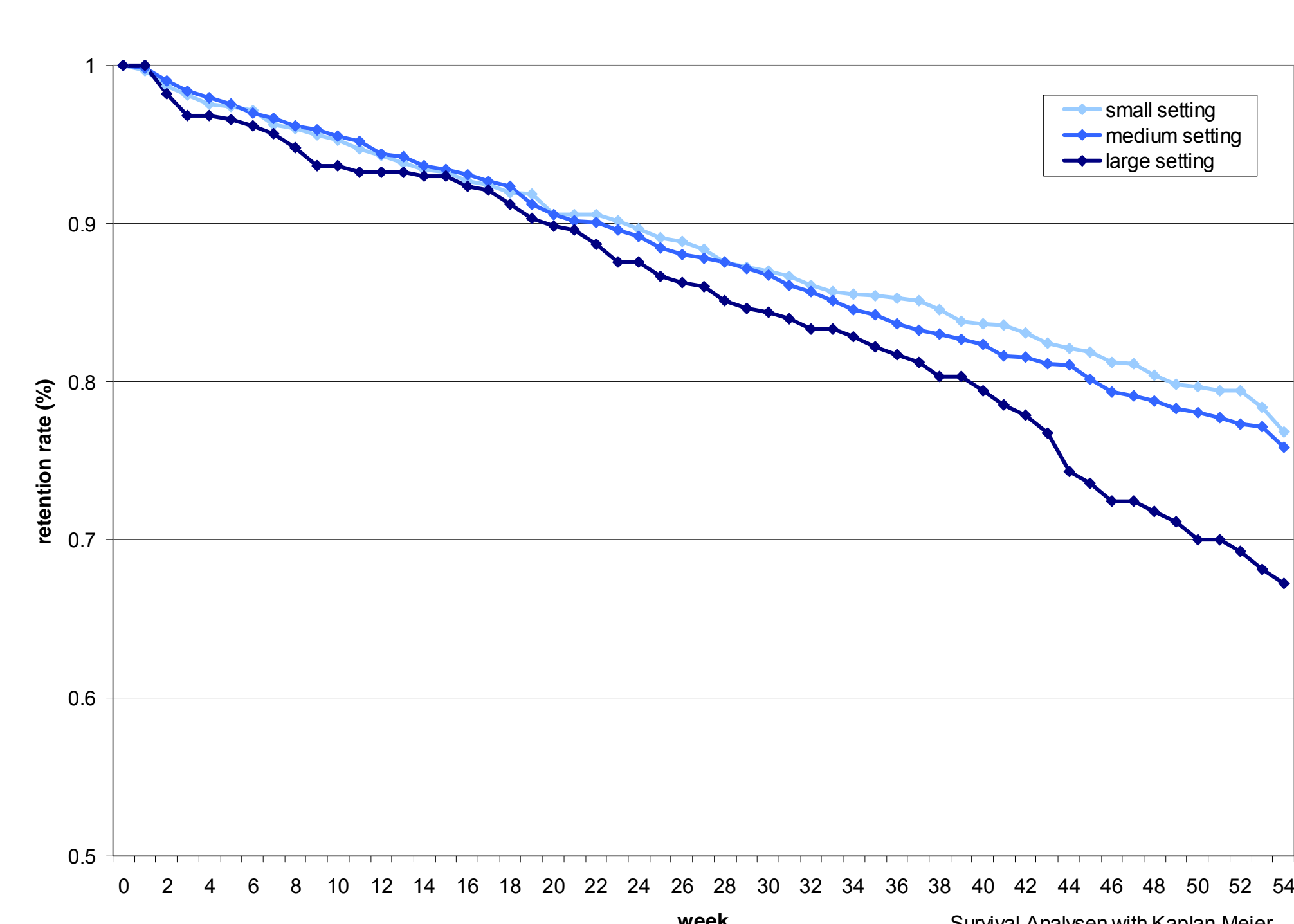


Results

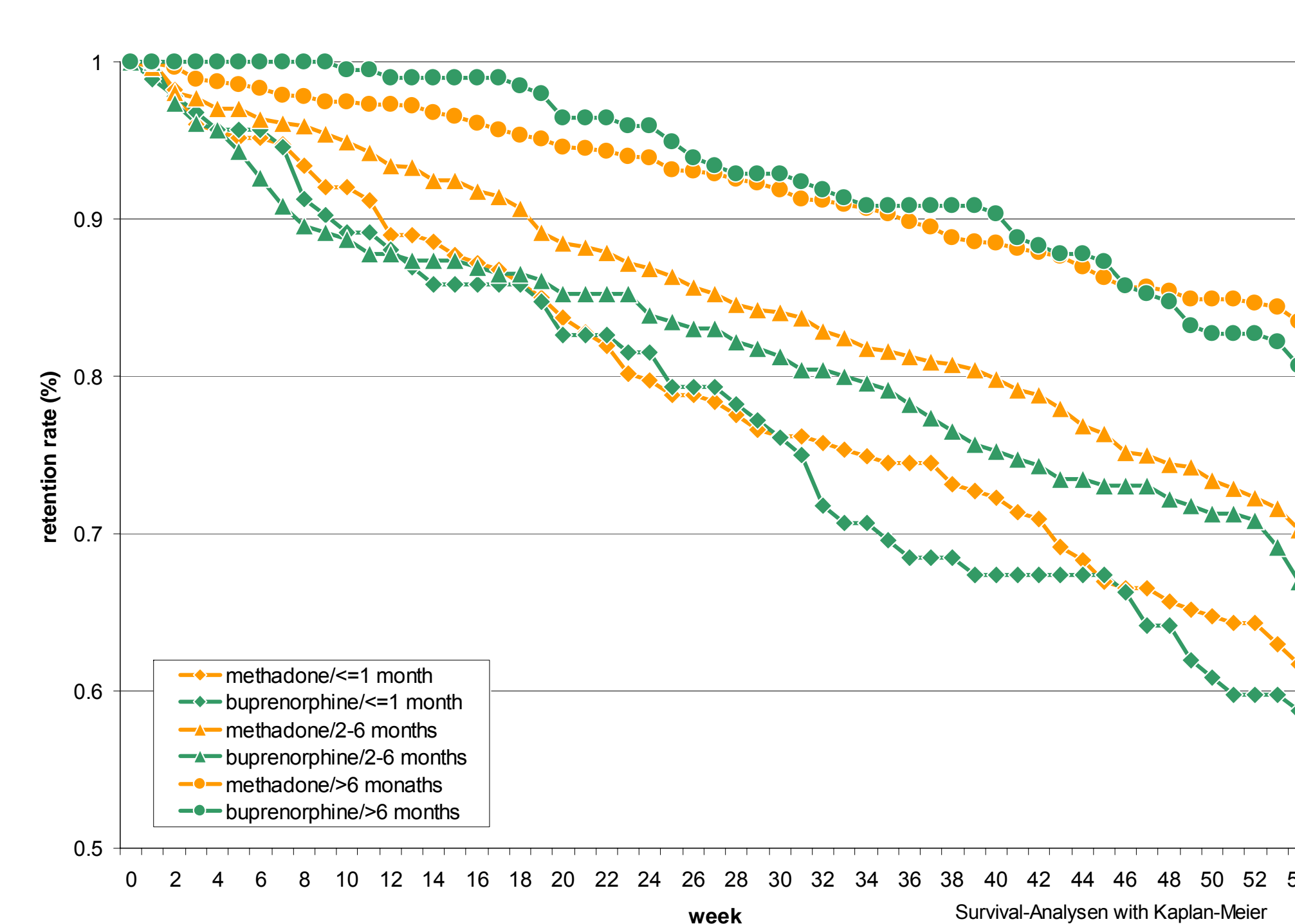
Retention rates by substitution drug (N = 2.187)



Retention rates by provider model (N = 2.187)



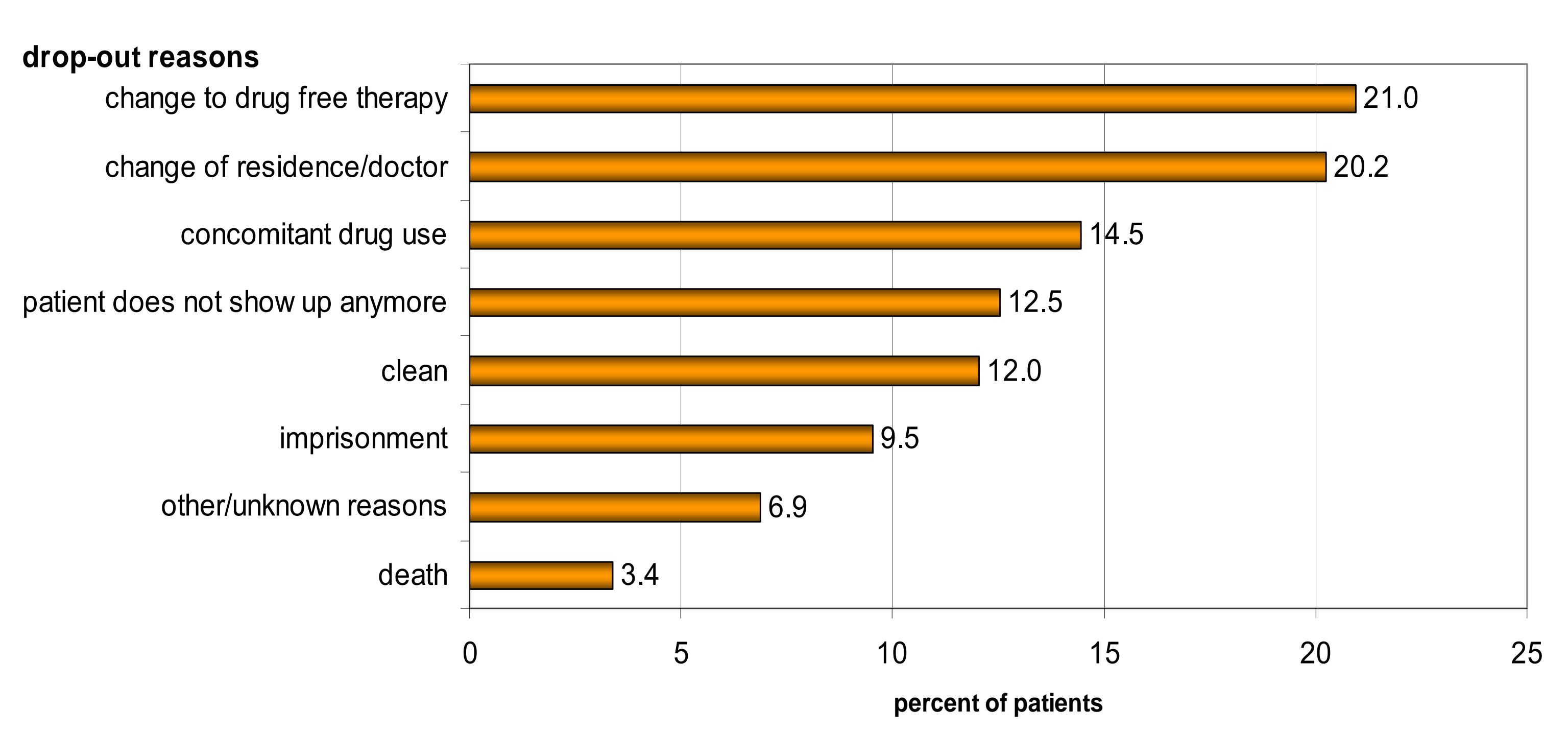
Retention rates by substitution drug and duration of current substitution therapy at baseline (N = 2.187)



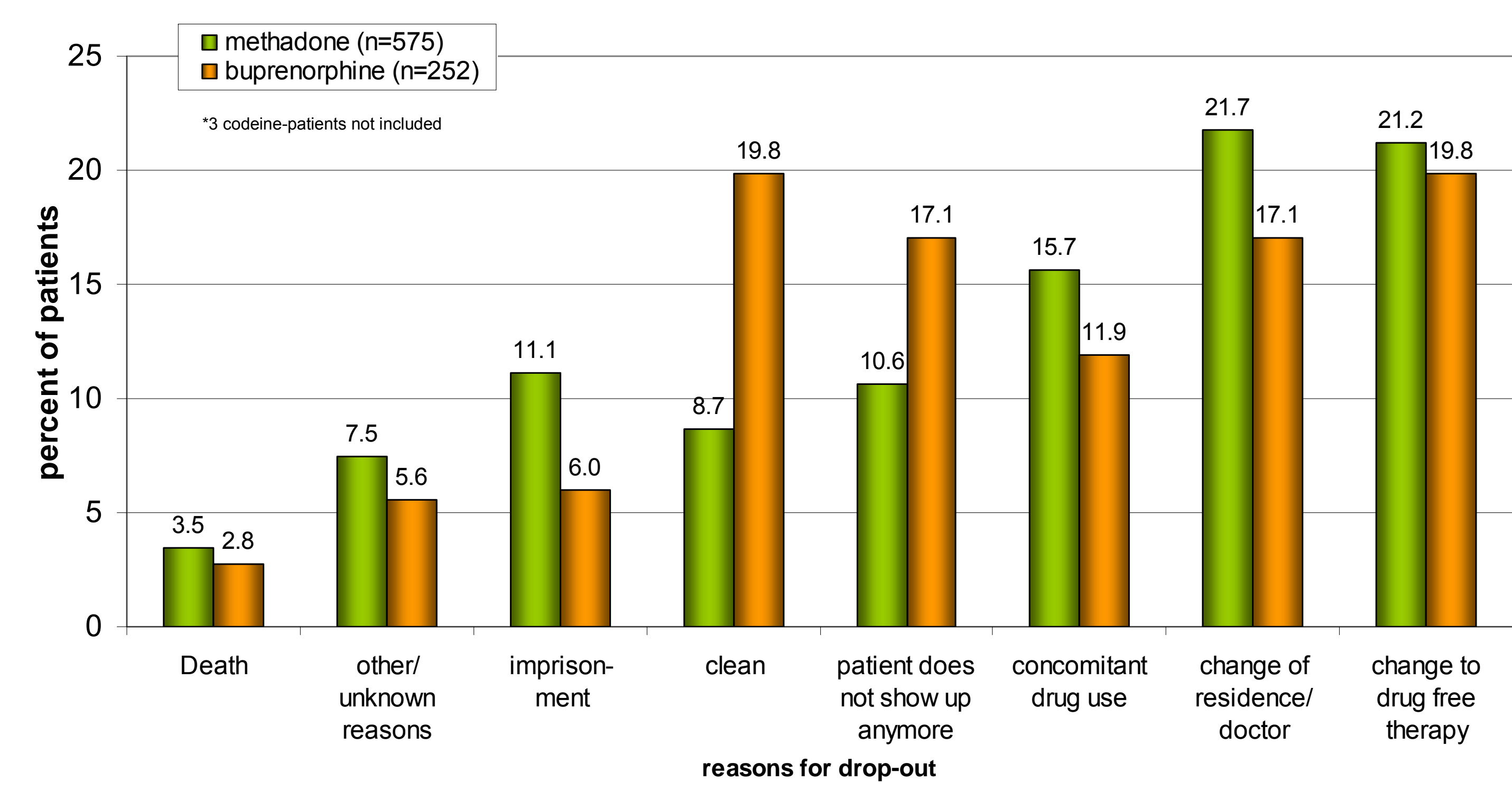
Differences of selected patients characteristics (N = 2.442)

	substitution drug		signif.
	methadone (N=828)	buprenorphine (N=1614)	
Sex	male 68.8 female 31.2	68.2 31.8	ref.
Mean age (sd)	35.47 (7.99)	32.75 (8.11)	$t=7.299^{***}$
Mean yrs of education (sd)	10.04 (1.69)	10.10 (2.0)	$t=-1.052$
Professional status	employed 20.0 unemployed 57.4 homemaker 8.1 other 14.6	29.0 46.6 7.3 17.1	ref. 0.06^{***} (0.45-0.70) 0.02 (0.43-0.81) 0.81 (0.61-1.08)
Marital status	single 55.3 married 12.3 separated/wid. 20.7 other 11.7	57.4 13.4 16.3 12.8	ref. 1.05 (0.78-1.39) 0.70 (0.59-0.80) 1.05 (0.79-1.4)
Mean BMI (sd)	24.14 (4.35)	23.34 (4.18)	$t=3.84^{***}$
Mean yrs of opiate use (sd)	15.67 (8.23)	12.73 (7.96)	$t=7.581^{***}$
Mean yrs since 1st maintenance treatment (sd)	5.89 (5.24)	4.62 (4.49)	$t=4.397^{***}$
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)	$t=6.693^{***}$
Comorbid illnesses	HIV infection 7.0 HCV infection 68.7 cardiovascular disease 13.6 pulmonary disease 24.9 other somatic disorders 75.1	3.1 63.7 12.8 19.4 76.0	0.42^{**} (0.24-0.71) 0.33^{**} (0.23-0.54) 0.93 (0.58-1.5) 0.72 (0.45-1.07) 0.89 (0.61-1.29)
	depressive disorders 55.9 anxiety disorders 27.7 psychotic disorders 5.4 sleep disorders 20.0 PTSD/acute stress disorders 11.8 personality disorders 34.9 other mental disorder 15.3	57.9 20.5 14.4 21.6 10.9 26.5 17.1	1.09 (0.86-1.37) 0.87^{*} (0.51-0.89) 0.61 (0.26-1.0) 1.1 (0.83-1.46) 0.81 (0.63-1.01) 0.87^{*} (0.52-0.87) 0.92 (0.61-1.29)
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			signif.
	small (N=780)	medium (N=1151)	large (N=511)	
Sex	male 70.3 female 29.7	66.4 33.6	66.7 33.3	ref. 1.09 (0.90-1.33) 1.19 (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 unemployed 49.0 homemaker 7.3 other 14.8	20.6 57.3 6.0 14.1	15.9 97.2 8.6 18.3	ref. 1.63^{**} (1.31-2.04) 2.11^{**} (1.57-2.84) 1.57 (1.05-2.23) 2.12^{*} (1.34-3.41)
Marital status	single 54.8 married 13.9 separated/wid. 19.1 other 11.4	57.7 11.3 19.8 12.2	53.3 13.7 20.2 12.8	ref. 0.77 (0.58-1.02) 1.02 (0.72-1.42) 0.96 (0.77-1.24) 1.09 (0.81-1.46)
Mean BMI (sd)	24.14 (4.32)	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 (28.99)	17.37 (27.14)	11.84 (18.48)	$t=0.727$ $t=4.721^{***}$
Mean of total of severity rating (sd)	2.61 (1.44)	2.66 (1.49)	3.07 (1.46)	$t=0.775$ $t=-5.444^{***}$
Comorbid illnesses	HIV infection 4.9 HCV infection 63.2 cardiovascular disease 10.4 pulmonary disease 24.2 other somatic disorders 77.7	6.2 64.6 15.6 23.3 75.6	7.5 68.3 14.2 23.6 81.1	1.27 (0.82-1.98) 1.57 (0.92-2.60) 1.06 (0.87-1.29) 1.25 (0.97-1.62) 1.42 (0.94-2.1)
	depressive disorders 56.9 anxiety disorders 29.0 psychotic disorders 4.1 sleep disorders 25.4 PTSD/acute stress disorders 14.5 personality disorders 28.9 other mental disorder 16.5	57.2 27.0 4.7 25.4 11.1 44.1 15.7	54.2 26.3 6.3 16.5 9.1 29.9 24.3	1.01 (0.8-1.28) 1.13 (0.83-1.54) 1.58 (0.85-2.91) 0.74 (0.52-1.04) 0.59^{*} (0.38-0.91) 1.89^{**} (1.42-2.48) 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)	$t=-0.886$ $t=2.719^{*}$

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.