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Regular article

Heroin Addict Relat Clin Probl 20xx; xx(x): xx-xx

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Opioid Maintenance in Primary Care: a case register based comparison

Barbara Broers¹, Ignazio Cassis², and Bernard Cerutti³

1 Division for Primary Care, University Hospitals, Geneva, Switzerland

2 Department of Health and Social Affairs, Republic and Canton of Ticino, Switzerland

3 Faculty of Medicine, University of Geneva, Switzerland

Summary

Background: In Switzerland, opioid maintenance prescription for heroin dependence is possible since the seventies, by all licensed physicians, in specialized centers or primary care, and reimbursed by basic health insurance. Every treatment must be declared to the cantonal public health officer. **Aim:** The aim of our study was to compare basic facts, trends, and outcomes of mainly primary care based opioid maintenance treatment in two areas in Switzerland (Ticino, Geneva) with different health care organizations. **Methods:** Historical cohort study with data-collection (start, every 6 months, end) through standardized administrative databases. **Results:** Overall 3,824 patients (28% females) were included over a 3.5 years period. Of all treatment episodes 97% concerned methadone prescription. We observed an aging population, with no significant canton effect on retention in treatment. Prescribers practicing in or close to specialized centers were more compliant with methadone guidelines. Female patients were better retained in primary care settings. **Conclusion:** This study adds evidence for the effectiveness of opioid maintenance treatment in primary care, especially for female patients. Continuous education should be encouraged to increase congruence with guidelines.

Key Words: Opioid replacement treatment; methadone; buprenorphine; health care structures; primary care

1. Introduction

Methadone, prescribed as maintenance treatment, has been proven an effective treatment for opiate addiction since the first studies published by Dole and Nyswander [1]. It can be prescribed in specialized centers or in private practice, depending on national or local regulations but also according to the existing policies and health care systems.

Very few studies found in the literature concern the organizational aspects of methadone maintenance treatment or of addiction medicine in general. Also, most studies on maintenance treatment concern patients treated in specialized centers, and few studies concern methadone prescriptions by family physicians. This even if, at least part of, methadone pre-

scriptions take place in primary care in several countries as the United Kingdom, the Netherlands, or Switzerland [16, 5].

The Swiss authorities have allowed maintenance treatment prescription since the seventies. Methadone can be prescribed by all licensed physicians in all 26 cantons. No special training in addiction medicine is required and about 60% of prescriptions take place in private practice. A special authorization from the cantonal public health officer is needed for the prescriptions. Details of the treatment (supervised intake, take-home and holidays, galenic form, maximum of methadone maintained patients per physician) vary from one canton to another. As a general procedure, every beginning or end of treatment must be declared to the cantonal public health officer, who may also

request a follow-up form every six months.

Since the early nineties, with the emerging HIV epidemic, the Swiss Federal Office of Public Health, within the context of a comprehensive drug policy, tried to encourage access to methadone treatment. Different initiatives to improve training and supervision for private physicians were taken. There has been also an increase of treatment slots in public and private methadone treatment centers mostly in the big cities [14]. Experimental heroin (diacetylmorphine) prescription was made available in specialized centers in 1994, and there are currently about 1,400 slots [4]. High dosage buprenorphine has been available since 2001. The whole opiate maintenance treatment is covered by the basic medical insurance.

Currently, about 17,000 patients receive opiate maintenance treatment in Switzerland most concern methadone prescriptions (about 90% [3]). The birth cohorts between 1965 and 1969 were the most affected by opioid use [13]. Of them, around 2,500 are treated in two Swiss cantons with different organizational structures for maintenance treatment: Ticino (TI, population 320,000) is mainly a semi-urban canton, with only primary care physicians prescribing methadone at the time of the study, whereas the urban canton of Geneva (GE, population 427,000) has methadone prescription in primary and secondary care (private and public specialized centers). Geneva has also granted access to a diacetylmorphine prescription program since 1995 (about 50 treatment slots).

The main objective of this study was to compare data on maintenance treatment prescriptions in both cantons over a 3.5 year period (February 1, 2000 - July 31, 2003) using the available cantonal administrative registers that were similar at that time. We considered patient and prescriber characteristics, sequences of episodes of treatment in terms of duration, treatment interruptions, changes in methadone provider and methadone doses.

2. Methods

In both cantons the Health Officer collects basic information about the patient and the treatment in order to avoid parallel illicit multiple prescription. Further questionnaires used to be regularly sent for the evaluation of the substitution treatment (when the treatment started, every semester or yearly, and whenever the treatment ended or was interrupted). The treatment questionnaires were filled in by the treating

physician and the patient; the data were entered in a local electronic database system that had been used in both cantons since February 1, 2000.

2.1. Sample

All patients in opioid substitution treatment in Geneva and Ticino for at least one day during the 3.5 year period (February 1, 2000 to July 31, 2003) were included in the study (N=3,284).

2.2. Measures

An episode of treatment was defined as a period for which the patient was treated by the same physician or center. The end of an episode could be the end of substitution (with success or not), the transfer to another physician or center (with or without common agreement), a hospitalization, an imprisonment, a transfer of residence to another geographic area, or the death of the patient.

2.3. Data analysis

By default, all the data were analyzed sequentially on a semester basis. Seven consecutive cross sectional analyses were thus done. Missing values were treated as missing at random.

To estimate the retention in treatment, a subset of so called naïve patients (N=2,100) was considered: it included those patients who had started a new treatment without any other substitution treatment reported in the six preceding months. Kaplan Meier models were used, and a Cox proportional hazards model was fitted to take into account different covariates: canton (Geneva, Ticino), gender, age and daily dosage of methadone (taken as continuous variables: we use natural cubic splines with three degrees of freedom to allow more flexibility in the model), prescriber (private physician, private center, public center), level of social integration (very low, low, acceptable, high, very high), nationality (Swiss, other), heroin intake (no intake, occasional, frequent, daily), cocaine intake, cannabis intake, benzodiazepine intake, and alcohol intake. For the Cox proportional hazards model we used a dataset in which there were no missing values (n=1,050), and a stepwise iteration procedure was used. All data analyses were done with S+ TIBCO, TIBCO Software Inc, palo Alto, CA, USA.

Table 1. Characteristics of the maintenance treatment, by quarter, during the study period (February 2000 to July 2003)

Semester	1	2	3	4	5	6	7	Trend
Number of patients in treatment								
GE Total	1613	1569	1526	1529	1497	1457	1439	<.001
new	102	66	64	78	48	44	46	.018
TI Total	986	988	956	930	884	869	856	<.001
new	48	35	34	41	18	25	21	<.001
All	2598	2557	2482	2459	2380	2324	2295	<.001
new	150	101	98	119	66	69	67	.016
Age (median)								
GE	35	35	36	35	36	36	37	<.001
TI	33	33	34	34	35	35	36	<.001
All	34	34	35	35	36	36	37	<.001
Number of treatments per type of providers (and %per canton)								
GE public institutions	330 (19.5%)	306 (18.7%)	298 (18.8%)	301 (18.9%)	301 (19.5%)	273 (17.9%)	274 (18.3%)	.005
GE private centers	645 (38.1%)	619 (37.9%)	585 (36.8%)	603 (37.9%)	589 (38.1%)	594 (38.9%)	581 (38.9%)	.028
GE family physicians	720 (42.5%)	709 (43.4%)	706 (44.4%)	687 (43.2%)	655 (42.4%)	661 (43.3%)	640 (42.8%)	<.001
TI	1014 (100%)	1027 (100%)	975 (100%)	949 (100%)	904 (100%)	772 (100%)	932 (100%)	.054
All	2709	2661	2564	2540	2449	2300	2425	.003
Median (average) daily dosage of methadone (in mg)								
GE	60 (74.9)	60 (75.9)	60 (76.3)	60 (76.3)	60 (75.8)	60 (77.2)	60 (77.2)	.034
GE family physicians	55 (66.5)	55 (66.8)	55 (69.0)	55 (69.5)	56.5 (69.8)	57.9 (72.3)	58.2 (72.4)	<.001
TI	43.3 (47.9)	45.0 (45.0)	43.8 (48.6)	43.8 (49.1)	45.0 (50.5)	46.5 (51.1)	46.3 (51.2)	<.001
ALL	52.5 (64.5)	53.3 (65.1)	52.9 (65.4)	52.1 (65.2)	53.1 (66.2)	53.7 (67.1)	54.3 (67.2)	<.001

3. Results

3.1. Patient's characteristics

A total of 3,284 patients were in treatment for at least one day during the study period: 1,986 in Geneva, 1,292 in Ticino, and 6 in both cantons. Around 28% of the patients were women (29% in Geneva and 26% in Ticino). Table 1 shows the number of patients in treatment every semester. There was a steady and significant decline over time in active patient files in both cantons: -13.2% in Ticino and -10.8% in Geneva. The overall median age increased from 34 in 2000 (first and third quartiles: 29, 39) to 37 in 2003 (first and third quartiles: 32, 42), showing a rapidly ageing population. Swiss nationals represent 73% of the patients: they are over represented when compared to the general population (p GE<.001, p TI =.021).

During the last quarter of the study period, 36.2% of the patients were employed (fully or regu-

lar part time): in Ticino 42.6% of patients were employed, versus 32% in Geneva. No significant trend over time was observed in Ticino (p=.328), whereas in Geneva the employment rate decreased from 35% in 2000 to 32% in 2003 (p<.001).

Overall 670 patients started a maintenance treatment for the first time during the study period. There was a significant decline in number of new patients (Table 1). The median age of these patients was around 30 years.

3.2. Treatment providers

During the period of observation, 314 prescribers were identified: 152 in Geneva and 162 in Ticino. There were six private centers (all from the same foundation) and six public institutions in Geneva, all considered as one prescriber, and no specialized centers in Ticino. The 302 remaining prescribers were mostly family physicians and a few psychiatrists.

Female prescribers were respectively 23% in Geneva and 11% in Ticino. These percentages were similar to the gender distribution of medical doctors in the two considered cantons at the time of the study.

In Geneva the number of patients decreased by 17% in public institutions, by 10% in private centers, by 11% for those treated by family physicians. The median number of patients per provider remained stable over time. During the last quarter of observation, private physicians looked after a median number of three patients (average 6.5) with a significant difference between Geneva (median 2, average 5.7) and Ticino (median 4, average 7.3).

In Ticino a majority (89%) of patients received the substitution medication in a pharmacy and 11% directly in the physician's practice. In Geneva the distribution was equally split between pharmacies and specialized centers.

3.3. Treatment episodes and prescriptions

A large majority of treatment episodes (total 5,634) concerned methadone prescriptions (97.3% of treatment episodes). In Ticino (1,824 episodes), where there was no medical prescription of heroin, other prescriptions concerned buprenorphine (0.2%) and morphine (0.1%). In Geneva (3,810 episodes) other prescriptions included diacetylmorphine (heroin, 1.8%), buprenorphine (1.4%) and morphine (0.7%). The median daily dose for those substituted with methadone increased from 52.5 mg to 54.3 mg.

During the same period the average daily methadone dose increased from 64.5 mg to 67.2 mg. The trend is more pronounced in Ticino (40.6 mg per quarter) than in Geneva (+0.3 mg per quarter). However, for every quarter the median daily dosages in Geneva were significantly higher than in Ticino, with a difference between 14 and 17 mg (20 mg for the means). If we considered the family physicians only, the differences (between 10 mg and 12 mg) would have remained highly significant ($p < .001$). This striking difference of means may be ascribed to the presence of high dose prescriptions in Geneva (up to 600 mg daily, see Figure 1). In Ticino, no patient received over 200 mg in the last period considered versus 59 patients in Geneva. For buprenorphine (total 184 treatment episodes) the mean daily dose was 6.09 mg with a median dose of 4 mg, with no time trend and no difference between cantons.

Around 53% of the patients had one single episode of treatment during the study, but there was a difference between cantons ($p < .001$). Patients in Geneva had significantly more treatment episodes than patients in Ticino (38% had two episodes, 14% had three episodes, 7% had four and more episodes, respectively 21%, 6.5%, and 2% in Ticino). There was no gender difference with regard to the number of periods of treatment ($p = .269$). In Ticino prescriptions concerned almost exclusively family physicians and methadone (except for four prescriptions of buprenorphine or morphine). This is reason why the treatment switches (substance, prescriber) summarized in Table

Table 2. Treatment interruption and switch of substance and provider during opioid substitution treatment, Geneva (February 2000 to July 2003)

Substance	To methadone	To heroin	To buprenorphine
From Methadone n=1,772§	97% n=1720	1% n=15	1% n=22
From heroin n=15	67% n=10	33% n=5	0%
From buprenorphine n=25	64% n=16	0%	36% n=9
Provider	To family physician	To private institution	To public institution
From family physician n=592	78% n=461	11% n=66	11% n=65
From private institution n=857	7% n=62	87% n=748	6% n=47
From public institution n=373	26% n=97	16% n=59	58% n=217

§ among these 1,772 changes, there were 15 switches from methadone to morphine.

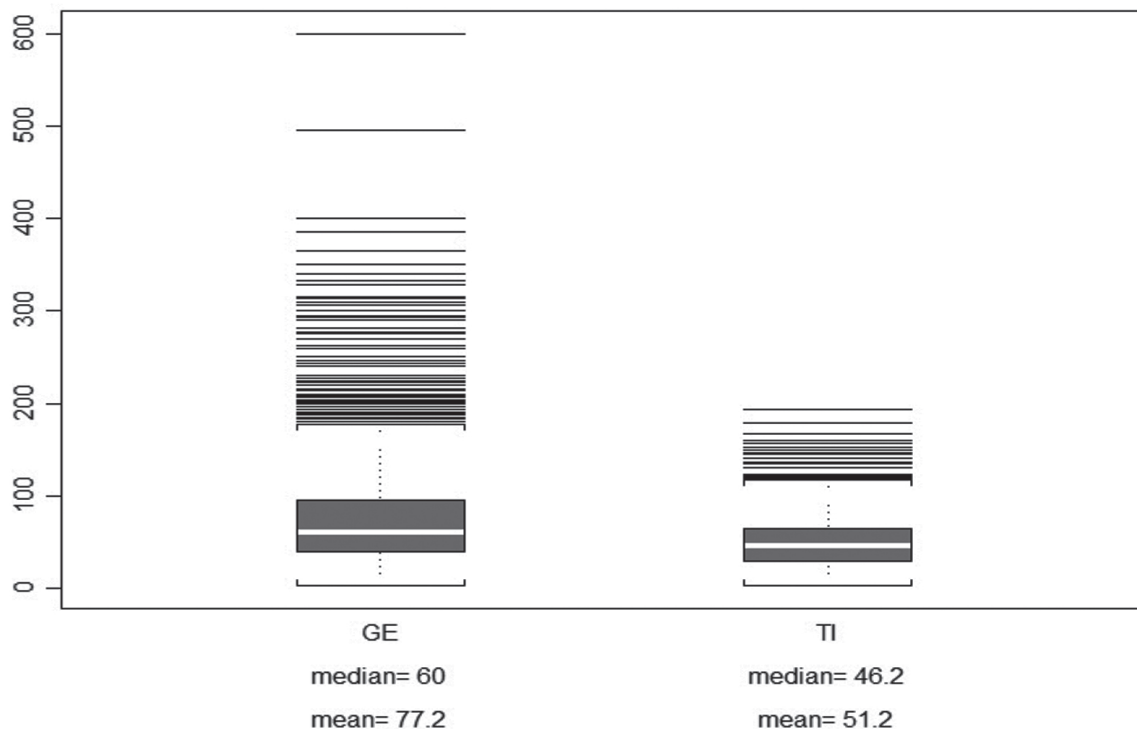


Figure 1 Boxplot of the daily dosage (mg) for the patient in substitution treatment with methadone during the last semester of observation (February to July 2003)

2 deal with Geneva only.

3.4. Treatment outcomes: substance use, treatment duration and retention

Physicians in Ticino considered their patients, when compared to those in Geneva, to be slightly more often abstinent from cocaine (85% versus 69%, last quarter) and cannabis (51% versus 48%) and less from heroin (65% versus 66%), alcohol (43% versus 52%), and benzodiazepine (65% versus 70%). Percentage of missing values in the data from Geneva is high (up 19.8% for the parallel intake of benzodiazepine), so data should be interpreted with caution. Considering potential trends over time, the intake of heroin or cocaine was considered stable.

A significant percentage of patient remained continuously in treatment during the whole study period (1,238, that is, 37.7% of the patients). Treatment interruptions represented about 10 to 14% of all the ongoing treatments every quarter. There were no significant trends over time ($p_{GE}=.076$, $p_{TI}=.731$). A straightforwardly computed ratio given by the cumulative duration of treatment for every patient divided by the duration of the study showed that a median

patient opted out his or her treatment for about two months every year (abstinence, residential treatment, hospitalization, relapse, transfer of residence...).

A specific subset analysis was made with the naïve patients who started a new episode treatment during the period of observation, and who had no other substitution treatment in the last 6 months ($n=2,100$). After 425 days, half of the patients were still in treatment (almost exactly 14 months, 95% confidence interval 397 – 453). Figure 2 shows the retention curve split by canton ($n=2,100$). The median duration of treatment was 336 days in Ticino (95% Confidence Interval 288 – 399), and 458 days in Geneva (95% CI 427 – 488; $p=.001$).

The median duration of treatment for the patients treated by a private institution was 543 days (95% CI 486 – 732), 384 days (95% CI 348 – 426) for those treated by a family physician, and 274 days (95% CI 237 – 328) for those treated by a public institution ($p<.001$). The median duration of treatment split by level of cocaine intake at the beginning of the treatment ($n=1'217$) was 370 days (95% CI 322 – 405) for the abstinent patients, 237 days (95% CI 195 – 313) for those with occasional intake, 222 days (95% CI 154 – 293) for those with frequent intake, and 179

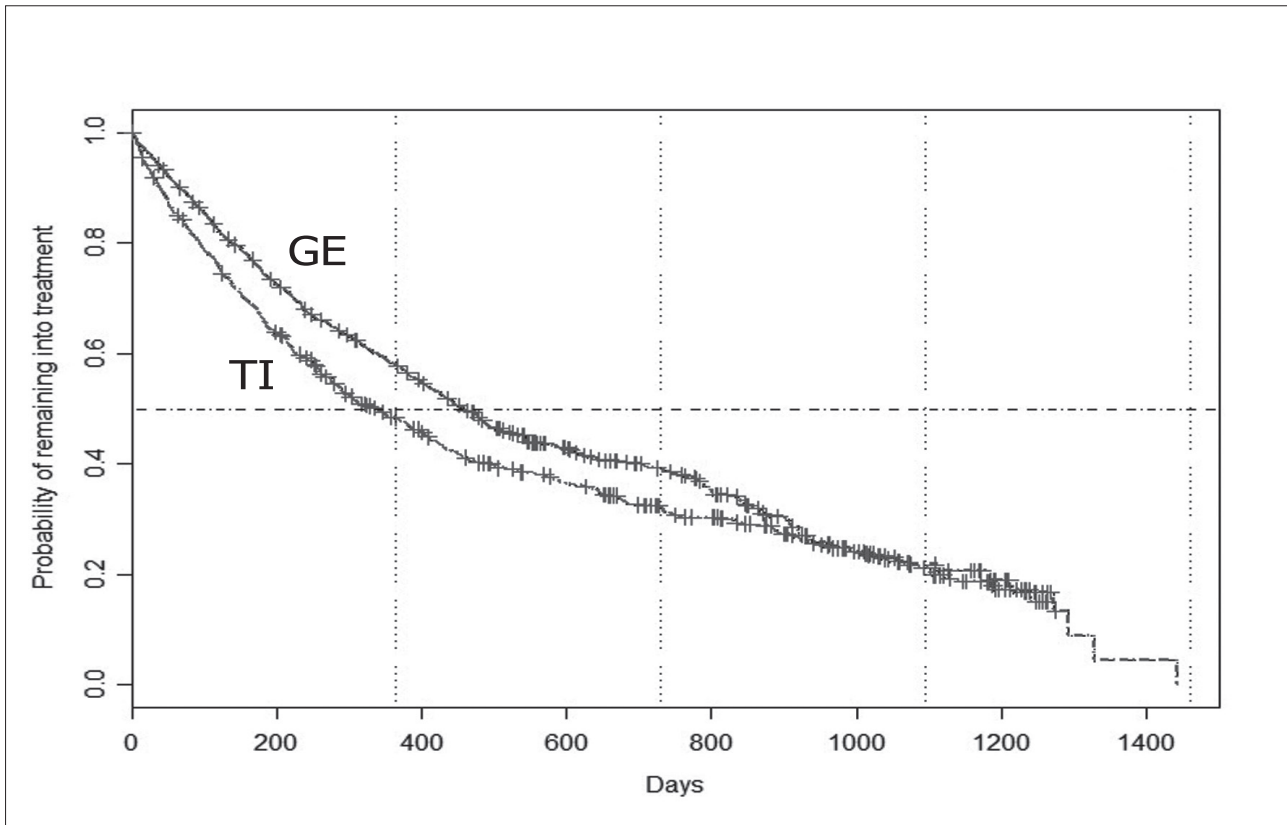


Figure 2 Retention in treatment split by canton for all patients who started a new treatment (without previous substitution treatment in the last 180 days) during the study period of observation (n = 2100).

days (95% CI 124 – 301) for the patients who took cocaine daily ($p < .001$).

A stepwise procedure used with a Cox-proportional hazards model identified the following significant covariates associated with the duration of treatment: men tended to have shorter treatment than women (HR (estimated Hazard Ratio) 1.22; $p=.020$); foreign citizenship (HR 1.28; $p=.003$), cocaine intake (HR 1.52 daily intake when compared to abstinence; $p=.001$), and lower dosage of methadone ($p=.002$) were all predictors of shorter treatment.

There was also weaker evidence that a low level of social integration (HR 1.22 lower level when compared to upper level of social integration; $p=.065$), and being followed up by an institution (HR 0.81 when compared to family physician; $p=0.286$) were also predictor of a shorter treatment. There was no evidence of any underlying geographical effect regarding a difference between the two cantons ($p=.683$).

4. Discussion

This historical cohort study, based on case registers covering all opioid maintenance prescriptions in a semi-urban area (Ticino) and urban area (Geneva),

was a rare opportunity to evaluate exhaustively the treatments, as they effectively result from the mix of research, medical practice, and coverage of the target population for opioid maintenance treatment. Regarding the coverage, it is usually considered that there is no waiting delay to access a maintenance treatment in Geneva and Ticino, though the thresholds may be different.

We observed in both cantons similar trends of an aging population of methadone maintained patients and a decrease in active patient files with few young drug users entering treatment. These trends have been described elsewhere in Switzerland [12, 13] and in Western Europe [2]. The fact that these patients are aging can probably be considered a positive outcome of treatment, since treatment retention, improved health status and less premature deaths are related [2, 15]. The decrease in young patients seems mainly due to a real decrease in opiate use among young drug users, as suggested by Nordt and Stohler [13], and not to a barrier for treatment for this group.

Major differences between cantons concerned a better social integration of patients in Ticino, where there was a higher number of patients per prescriber in average, and in Geneva a higher daily dose of

methadone and more treatment episodes.

Taking into account the gender and nationality of the patients, the type of institution, the cocaine intake, the social integration, and the dosage when the treatment starts, we can conclude that, apart from the objective indicators above mentioned, there did not seem to be other “intrinsic” differences between the two areas regarding the retention in treatment, since the covariate “canton” was not significant. This result may thwart the assumption of some professionals involved in addictions who still use the pretext of unclear Cantonal specificities to defend some local practices.

Episode of treatment followed by the specialized centers tended to be shorter than treatment followed by family physicians: patients had probably been referred to the family physicians once they were in a more stable situation. However, it could also be beneficial for the patients to stay with a family physician because it was easier for them to take more distance from the drug scene (they did not meet other drug users, daily or regularly, in or around the specialized centers [9]). Our findings of higher retention among family physicians confirm the result of Stohler et al. in Zurich [11], although their median retention time was slightly shorter than the ones we observed in our study (12 months versus 14 for the family physicians; 8 versus 9 for public institutions), and was higher than reported in other settings [8].

An important difference between cantons laid in the prescription of higher daily doses of methadone in Geneva (median 60 mg, mean 77 mg), especially in specialized centers, but also among Geneva family physicians (median 58 mg, mean 72 mg) compared to their colleagues in Ticino (median 46 mg, mean 51 mg). Data from another Swiss canton (Vaud, 2001-2003) show intermediate results [7]: median daily dose of methadone 50 mg (mean 67 mg). Relatively low dose methadone prescription in Ticino could be partially explained by a higher proportion of well integrated patients needing less methadone (as has been suggested in the Vaud survey), but also by the total absence of high dosage prescriptions, suggesting that dosages were not always adapted to individual needs and “heroin addiction stages”. Compliance with current methadone guidelines seemed to be lower in Ticino suggesting the need for continuous education and supervision in addiction medicine. This desire had been expressed [7, 10]. We think this is even more important since we can expect more complex methadone treatments in the future with increasing age-related morbidity, HCV-related hepatic failure

and drug interactions.

We found that the profile of the person with best retention in treatment was: a Swiss woman treated by family physicians, with a relatively high dosage of methadone, well socially integrated and abstinent from cocaine when starting the treatment. The only “surprise” among these variables was the more positive outcome for women [17, 6]. A private practice may be particularly appropriate for female drug addicts, because it tends to offer a calmer, more secure and more confidential care environment than drug treatment centers.

Family physicians in Switzerland can prescribe different opioids for maintenance treatment, including methadone, buprenorphine or morphine. Only heroin (diacetylmorphine) can be prescribed exclusively in specialized centers. Although there is in principle a free choice of substance a very large majority of treatments (97%) concerned methadone. We did not investigate the reason of this choice preference, but hypothesize that Swiss physicians and patients are more at ease and confident with methadone treatment (buprenorphine treatment had been allowed since 2001 only, methadone since 1976), to economic considerations (buprenorphine and morphine are far more expensive), and to initial official recommendations that proposed prescription of buprenorphine to a restricted group of patients (young, non-injecting, low level of heroin use) [3]. It is interesting to note also that, in Geneva, after a treatment switch, most patients opted for methadone treatment again. Only 1% of patients opted for heroin treatment, and 1% for buprenorphine. However, after a treatment episode with buprenorphine, one third of patients chose this medication again, and the two thirds switched for methadone (the sample was however small). This finding may rise the question of both patient and physician satisfaction with buprenorphine treatment.

Strong points of this study include the large sample size, the relatively long-term follow-up, and the absence of major selection bias and of selective follow-up, since all methadone treatment declarations were, and are still, mandatory in both cantons. Of course patients can buy methadone on the “black market” and we cannot reject the hypothesis of undeclared methadone treatments, but we expect that this concerns a very small minority of prescriptions. For example, the hospital of Geneva hardly has to deal with patients with unannounced methadone treatments [11].

Some of the results of our study (especially the parallel intake of other substances) should be

interpreted with caution due to a high proportion of missing data, mainly in Geneva. Several data are also based on self-declaration. Misclassification bias could thus affect several variables, such as unprescribed substance use during the treatment, reasons to end the treatment, but also the variable “retention in treatment”: Most studies evaluating the effectiveness of maintenance treatment programs consider the patient retention in treatment as a “success” outcome [9, 15, 8]. However, in the public settings in Geneva, well stabilized patients are referred to private physicians. This is an important difference to be kept in mind compared to other treatment settings: referred patients are by definition not “retained” in treatment as such. Consequently, within the public settings in Geneva, “retained patients” are not necessarily those who have a “treatment success” but rather those who are not doing well. Reversibly, those “not retained” are a mixture of patients who dropped out (treatment failure) and those who are stabilized (referred to a family physician, treatment success).

Finally, we have tried to minimize the confounding bias with the use of multivariate analysis models, but we remember that this concerned only new, recently started treatments. Overall, we think that the Swiss administrative case registers provided a unique and interesting set of data for evaluation, but a lot of routinely collected clinical data were useless for research (and clinical) reasons because of incompleteness, absence of validation, or difference between cantons.

5. Conclusions

As has been suggested in other studies [9, 15], family physicians play an important role in the treatment of opioid dependent patients and their implication in this field should be encouraged. This study adds evidence for the “effectiveness” of opioid maintenance, essentially methadone, treatment in primary care settings; and even suggests that there might be advantages for patients (especially for females) to be treated in this particular setting. However, continuous education of the family physicians should be encouraged to increase congruence with treatment guidelines.

In both cantons health services should be prepared to deal with an increase number of chronic care patients, among them opioid maintained patients with age-related morbidity. They should question if their substance abuse treatment services are still adapted

to the changing profiles of drug users (less heroin but more alcohol and stimulant use). Also, services for particularly vulnerable groups (non-Swiss nationality, low social integration, cocaine users) should be improved. However, this still may not be a priority policy in the sub-urban area of Ticino, where the first two secondary-care centers have been opened late in 2008. The urban challenges of Geneva will probably force this State-city to earlier update its public health setting so as to meet the needs of a changing population of addicted patients.

The data collected during this study may provide some useful baseline references to measure a potential impact of both the prescription practices, and the social and health conditions of the patients.

Established administrative registers could provide specific, unique, and long term data on maintenance treatment such as overall treatment duration, treatment sequences (interruptions followed by a new treatment episode), and shifts between treatment providers, often not available through clinical studies. These complementary variables are essential for evaluation and policy making: a better governance of the system at the national level is needed to avoid costly, useless, and sometimes unethical procedures based on ambiguous and heterogeneous cantonal regulations. But, since the real power of the federal health administration is intrinsic weak (Switzerland is a strong decentralized and multilingual and –cultural federal State) major obstacles at the single State-level (Canton) are likely to be raised against a central obligation of harmonized data definition, collection and analysis. Nevertheless, we should keep the objective of a public health approach with a correct scientific evaluation that will be reached when the societal debate about addiction medicine loses the overwhelming burden of emotions and political dogmas.

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Role of the funding source

Financial support for the implementation of this study was provided by financial support of the Swiss Federal Office of Public Health (contract 03.001022 / 2.24.02.-220).

Contributors

Authors contributed equally to this work.

Conflict of interest

Authors declared no conflict of interest.

Acknowledgements

We would like to express our gratitude to Prof. Jacques Besson, Prof. Bernard Burnand, Dr Jean-Jacques Déglon, and Dr Martin Rickenbach whose help was precious during the development of the study protocol; Dr Georgette Schaller and Susan Meyer (Public Health Department, Geneva) for their collaboration in data-collection. In particular, we thank Dr Urs Künzi (Swiss Federal Office of Public Health) for his generous technical assistance.

