Gender differences in heroin addiction and treatment: results from the VEdeTTE cohort

Gender Differences in Heroin Addiction and Treatment: Results from the VEdeTTE Cohort

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Abstract

Background: Gender differences strongly affect heroin addiction, from risk factors to patterns of consumption, access to treatments, and outcomes. Objectives: To investigate gender differences in the VEdeTTE cohort of heroin addicts.

Methods: VEdeTTE is a cohort of 10,454 heroin users enrolled between 1998 and 2001 in 115 public drug treatment centres in Italy. Clinical and personal information were collected at intake through a structured interview. Treatments were recorded using a standardized form. Gender differences were explored with regard to characteristics at intake, treatments, and retention in methadone maintenance and therapeutic community. Cox Proportional models were carried out to identify risk factors for treatment abandon.

Results: Compared with men, at their first access to treatment women with drug addiction were younger, more frequently married, legally separated, divorced or widow, unemployed though better educated, HIV+; more frequently they lived with their partner and sons. They reported a higher use of sedatives, but a lower use of alcohol; more frequently they had psychiatric comorbidity, including depression, self-injuries, and suicide attempts. Psychotherapy was more frequently prescribed to women, pharmacological treatments to men. Methadone maintenance was less frequently abandoned by women. Drug abuse severity factors predicted abandon of methadone among women. High methadone doses and the combination with psychotherapy improved treatment retention in both genders. Low education level and severity factors among women and young age among men predicted abandon of therapeutic community.

Conclusions: Gender differences in the VEdeTTE cohort suggest the need of a gender sensitive approach to improve treatment outcomes among heroin addicts.

Introduction

Gender differences strongly affect heroin addiction, from risk factors to patterns of consumption, access to Health Services, treatments, and even outcomes.

Differences in pre-treatment characteristics are well document ed. Sexual abuse and violence episodes in the childhood or in the adulthood are more frequently reported by heroin addicts females (Blume, 1994; Brady& Randall, 1999; Green, Poelen, Dickinson, Lynch, & Bennett, 2002; National Institute on Drug Abuse [NIDA], 1994; Pirard, Sharon, Kang, Angarita, & Gastfriend, 2005; Shand, Degenhardt, Slade, & Nelson, 2011) and increase their risk of developing drug dependence (Winhusen & Kropp, 2003), as well as early problems in the family (Colton, 1980; Ellinwood, Smith, & Vaillant, 1966; Graeven & Schaef, 1978; Moise, Reed, & Ryan, 1982).

Initiation of heroin use is related among males to group experience and socialization, among females to cope with stress and reduce anxiety (Haseltine, 2000; Hser, Anglin, & McGlothlin, 1987a; Marsh & Miller, 1985), and frequently is a partner-related behavior, a characteristic observed in many studies (Brady & Randall, 1999; Evans at al., 2003; Marsh & Miller, 1985; Powis, Griffiths, Gossop, & Strang, 1996; Rosenbaum, 1981; Shand et al., 2011) and recognized as peculiar of the female gender (Hser et al., 1987a; Hser, Anglin, & Booth, 1987b; Riehman, Iguchi, Zeller, Morral, 2003; Stocco, Llopis Llacer, de Fazio, Calafat, & Mendes, 2000; Taylor, 1993). Indeed, a drug dependent partner is more frequently reported by women (Grella, Joshi, & Anglin, 2003; Puigdollers et al., 2004; Stewart, Gossop, Marsden, Kidd, & Treacy, 2003; Winhusen & Kropp, 2003).

Age at first use is similar among males and females, but the access to drugs can be more limited among females, resulting in a later and less frequent use (Brady & Randall, 1999; Freeman, Rodriguez, & French, 1994; Haseltine, 2000; Marsh&Miller, 1985). After developing addiction, however, their amount of use is not different from that of men (Almog, Anglin, & Fisher, 1993; Bretteville-Jensen, 1999; Rosenbaum, 1981). On the contrary, differences are observed in the type of concurrent drugs: men use alcohol and marijuana (Anglin, Hser, & McGlothlin, 1987; Brady, Grice, Dustan, & Randall, 1993; Freeman et al., 1994; Green et al., 2002; Grella et al., 2003; Hser, Huang, Teruya, & Douglas Anglin, 2003; Marsh & Miller, 1985; Shand et al., 2011; Suffet, 1976; Wu et al., 2010), while women use benzodiazepines (Bretteville-Jensen, 1999; Chambers, Hinesley, & Moldestad, 1970; Darke, 1994; Freeman et al,. 1994; Hser et al., 1987b; Marsh & Miller, 1985; Wechsberg, Craddock, & Hubbard, 1998; Wu et al., 2010).

At treatment intake, women more frequently have children and live with them (Chatham, Hiller, Rowan-Szal, Joe, & Simpson, 1999; European Monitoring Centre for Drugs and Drug Addiction [EMCDDA], 2005; Freeman et al., 1994; Green et al., 2002; Grella & Joshi, 1999; Hser et al., 2003; Hser et al., 1987b; Stewart et al., 2003; Wechsberg et al., 1998).More frequently they are married (Acharyya & Zhang, 2003; Grella & Joshi, 1999; Schottenfeld, Pakes, & Kosten, 1998; Shand et al., 2011; Wechsberg et al., 1998), divorced or widow (Acharyya & Zhang, 2003; Marsh & Miller, 1985). They have a lower income and are frequently unemployed or have an unstable job (Acharyya & Zhang, 2003; Brady et al., 1993; Callaghan & Cunningham, 2002; Chatham et al., 1999; EMCDDA, 2005; Freeman et al., 1994; Grella & Joshi, 1999; Green et al., 2002; Grella et al., 2003; Hser et al., 1987b; Hser, Huang, Teruya, & Anglin, 2004; Kelly et al., 2009; Marsh & Miller, 1985; Marsh & Simpson, 1986; Petry & Bickel, 2000; Puigdollers et al., 2004; Riehman et al., 2003; Schottenfeld et al., 1998; Shand et al., 2011; Stocco et al., 2000; Wechsberg et al., 1998; Winhusen & Kropp, 2003). On the contrary, more frequently than women, men commit crimes or have legal problems, while among female drug addicts prostitution (with unprotected sexual intercourses) is more frequent (Anglin et al., 1987; Chatham et al., 1999; Grella et al., 2003; Grella & Joshi, 1999; Hser et al., 1987a; Hser et al., 2003; Hser et al., 2004;Joe & Simpson, 1995; Marsh & Miller, 1985; Marsh & Simpson, 1986; Mino, Page, Dumont, & Broers, 1998; Powis et al, 1996; Rowan-Szal, Chatham, Joe, & Simpson, 2000; Shand et al., 2011; Stewart et al., 2003; Wechsberg et al., 1998; Wu et al., 2010). Women share needles or other injection instruments more frequently than men (Bennett, Velleman,

Barter, & Bradbury, 2000; Chatham et al., 1999; Evans et al., 2003; Puigdollers et al., 2004; Sherman, Latkin, & Gielen, 2001), often with their partner (Evans et al., 2003; Freeman et al., 1994).

Psychopathologic problems, such as anxious depressive syndrome and personality disorders are more frequent and more severe among females heroin addicts (Brady et al., 1993; Brady & Randall, 1999; Chathamet al., 1999; Darke et al., 2009; El-Guebaly, 1995; Green et al., 2002; Grella et al., 2003; Grella & Joshi, 1999; Haseltine, 2000; Petry&Bickel, 2000; Rowan-Szal et al., 2000; Shand et al., 2011; Stewart et al., 2003; Wechsberg et al., 1998; Wu et al., 2010; Zilberman, Tavares, Blume, & el-Guebaly, 2003), as well as suicide attempts and self-damaging behaviors (Darke, Ross, Lynskey, & Teesson, 2004; Haseltine, 2000; Luthar, Cushing, & Rounsaville, 1996; Shand et al., 2011;Wechsberg et al., 1998).

Women seem to access to treatment earlier (Avila, Perez, & Rodriguez, 1996; Brady & Randall, 1999; Chathamet al., 1999; El-Guebaly, 1995; Green et al., 2002; Greenfield et al., 2007; Grella & Joshi, 1999; Haseltine, 2000; Hser et al., 1987a; Hser et al., 1987b; Hser et al., 2004; Marsh & Simpson, 1986; Rosenbaum, 1981; Shand et al., 2011; Wechsberg et al., 1998), but only a low proportion of them access to treatment (National Institute on Drug Abuse [NIDA], 1996; Stevens, Arbiter, & Glider, 1989; Montanari et al., 2011): when asking for a treatment, they wait longer than men before getting it (Downey, Rosengren, & Donovan, 2003).

With regard to treatment outcomes, the results of studies that examined gender differences in retention and completion are inconsistent (Greenfield et al., 2007). According to some studies, women abandon substance abuse treatment more frequently than men (Mino et al., 1998; Petry & Bickel, 2000; Simpson et al., 1997; Taylor, 1995); however, others did not find differences (Del Rio, Mino, & Perneger, 1997; Gerstein & Johnson, 2000; Green et al., 2002; Schottenfeld et al., 1998; Stewart et al., 2003). Low socioeconomic status among women, young age among men and severity of dependence in both genders seemed to be associated with a low treatment retention (Green et al., 2002).

Adding child and family components favors retention and completion of therapeutic community program (Grella, Joshi & Hser, 2000; McComish, Greenberg, Ager, Chruscial, & Laken, 2000; Szuster, Rich, Chung, & Bisconer, 1996). High education and low level of legal problems are predictors of therapeutic community completion among women (Knight, Logan, & Simpson, 2001; Messina,Wish, & Nemes, 2000).

The explanations of the observed gender differences in heroin addiction, however, are not clear (EMCDDA, 2005; Roberts, Mathers, & Degenhardt, 2010) warranting new studies investigating mechanisms of gender differences.

VEdeTTE is the largest study of heroin addicts conducted in Italy, involving more than 10,000 heroin addicts of whom 14.4%women; given the large number of addicts enrolled, it gives the possibility to explore gender differences. The objective of this paper is to investigate differences in risk factors, characteristics at intake, and treatment outcomes between heroin addicted women and men enrolled in the VEdeTTE cohort.

Methods

Study design and data collection

VEdeTTE is a cohort study of heroin addicts admitted to 115 (out of 554, 21%) NHS addiction treatment centers throughout Italy. From September 1998 through March 2001, 15,779 heroin addicts were asked to participate in the study: 3876 refused (24.6%) and 11,903 were recruited (75.4%). Complete information was available for 10,454 participants.

The study was approved and monitored by an ethical committee. All patients were formally asked to participate in the study after being informed of the objectives and methods of the study, and provided informed consent.

Upon enrolment, clinical history and personal information were collected by center personnel through a structured interview according to a standardized questionnaire. Information on treatment was registered along 18 months from the start of the study. Using a standardized form, detailed information was collected on each in- and outpatient treatment episode: methadone maintenance, methadone and non-opiate drugs detoxification, naltrexone, psychotropic drugs, psychotherapy, counseling, job guidance, social advice, and residential and day-residential treatments. All treatments were generally provided on an outpatient basis, except for residential and semi-residential treatments and in some cases of inpatient detoxification. Type of treatment, mean dose (where applicable), starting and closing dates were registered for each treatment.

For further details on the study design and population, see Bargagli et al. (2006).

Statistical analysis

The enrolled population was described according to gender with regard to sociodemographic characteristics, drug-addiction related issues, risk behaviors at intake, and psychiatric symptoms before and after the first heroin use. Gender differences were explored through logistic regression models.

In order to study treatment retention and its determinants, the analysis was conducted on the first Methadone Maintenance treatment and the first Therapeutic Community episode started in the first 6 months of the study period. For the purposes of the survival analysis, treatments were considered abandoned accordingly to the classification given by the clinician in the registration form. Treatments still ongoing at the end of the study period (18 months) were treated as right-censored. Kaplan-Meier product-limit estimator was applied for each group stratification, and log-rank test was used to assess statistical significance. A Cox Proportional Hazard model was built for the maximum likelihood estimation of the risk of drop-out (Kleinbaum&Klein, 1996). Models were fitted following a backward procedure from a saturated model, including all the most relevant information collected in the interview and considered possible determinants of treatment abandon. Likelihood-ratio test was used to assess the fitness of models. For the purposes of the present analysis, all models were fitted separately for males and females.

Results

Of 10,454 heroin addicts included in the analysis, 8,953 were males (85.6%) and 1,501 were females (14.4%).

Differences in sociodemographic characteristics, use of drugs and drug-related patterns, and psychiatric symptoms before and after the first heroin use are described in Tables 1, 2 and 3.

Sociodemographic characteristics (Table 1)

Women enrolled in the VEdeTTE cohort were born in the north and center of Italy, and they were married, divorced or widow more frequently than men (12.1% of women vs 7.8% of men were divorced and 3.8% vs 0.5% were widow). A lower proportion of women lived with their family of origin (38.2% vs 57.9% of men), while a larger proportion lived with their partner (23.7% vs 9.6% of men) or their children but without the partner (3.5% vs only 0.3% of men). A higher proportion of women had no fixed abode (2.2% vs 1.5%). Education level was higher among women (26.6% had

more than 13 years of education, compared to 15.1% of men). However, they had a stable job less frequently than men (23.3% vs 35.7%), and they were more often unemployed (42.9% vs 34.3%) or in a "nonprofessional condition" (8.7% vs 2.5%) including housewives, retired persons, disabled persons, conscripts. Women had recent legal problems or imprisonment less frequently than men (68.0% vs 74.0%).

For all the above mentioned variables gender differences were statistically significant, both in univariate and multivariate analysis (data not shown).

Use of drugs and drug-related patterns (Table 2)

Women were more frequently younger than 17 or older than 22 at first heroin use, while men were more frequently 18–21 years old (41.5% vs 35.3%). Also the age at first access to treatment was younger among women (36.4% were younger than 21 years old vs 28.6% of men). As a consequence, they had been addicted for a shorter period of time (less than 7 years for 33.5% of women and 26.1% of men). Men were sent to treatment by Justice System more frequently than women (4.3% vs 2.8%), while women were more frequently referred by the Health System (6.4% vs 4.0%) or by their family (7.9% vs 6.2%).

With regard to other substances concurrently used with heroin, women used amphetamines or ecstasy (3.0% vs 1.7% of men), or benzodiazepines more frequently (25.2% vs 16.2% of men). By contrast, men used alcohol (54.6% vs 44.0% of women).

Women shared needles or injection instruments more than men (22.1% vs 17.2%), but they had unprotected intercourses less frequently than men (9.6% vs 14.9%).

As reported by patients or registered in clinical records, more women than men were affected by HIV/AIDS and hepatitis C (respectively, 17.8% vs 11.0% and 74.0% vs 70.2%). Also psychiatric comorbidity was more frequently registered among women (21.9% vs 15.9% of men).

For all the above-mentioned variables gender differences were statistically significant, both in univariate and multivariate analysis including sociodemographic characteristics (data not shown).

Psychiatric symptoms before and after first heroin use (Table 3)

Gender differences were detected in the occurrence of psychiatric symptoms affecting heroin addicts either before or after their first heroin use.

All symptoms were reported as already occurring before the first heroin use in a higher proportion of women than men: bad mood/depression (65.9% of women vs 46.4% of men), self-damaging behaviors (29.0% vs 11.6%), aggressive behaviors (31.8% vs 26.7%), suicide attempts (20.9% vs 4.3%), psychotic thinking and hallucinations (7.4% vs 4.9%), and psychiatric hospital admissions (10.6% vs 4.4%). Gender differences were statistically significant for all symptoms in the univariate analysis. In multivariate analysis including sociodemographic characteristics, gender differences were statistically significant for bad mood/depression, self-damaging behaviors and suicide attempts, while the differences attenuated and lost significance for aggressive behaviors, psychotic thinking and hallucinations, and psychiatric hospital admissions (data not shown).

After starting heroin use, the rate of psychiatric symptoms increased in both genders, but differences generally decreased: bad mood/depression after the first heroin use was reported by 90.0% of women versus 85.6% of men. The same pattern affected all other symptoms: self-damaging behaviors (39.2% of women vs 25.8% of men), aggressive behaviors (44.0% vs 38.2%), suicide attempts (21.1% vs 11.3%), psychotic thinking and hallucinations (18.5% vs 15.0%), and psychiatric admissions (13.4% vs 8.6%). Again, gender differences were statistically significant for all symptoms in the univariate analysis. In multivariate analysis gender differences were statistically significant for self-damaging

behaviors and suicide attempts, while the differences attenuated and lost significance for bad mood/depression, aggressive behaviors, psychotic thinking and hallucinations, and psychiatric hospital admissions (data not shown).

Treatments (Table 4)

Throughout the 18 months of enrolment, a total of 16,499 therapeutic interventions were administered to 10,315 patients as first treatment (alone or combined with others): 13,925 to 8,830 men and 2,574 to 1,485 women.

Therapeutic community was the first treatment upon enrolment for 8.1% of men and 6.9% of women, and methadone maintenance for 46.9% of men and 49.5% of women. Methadone at tapered doses was administered as first treatment to 22.8% of men and 21.6% of women. A statistically significant difference was observed in the proportion of psychotherapies administered to men and women, alone or concurrent with other first treatments: 9.0% among men and 14.3% among women ($p < 0.001$). Also the proportion of counselling interventions was significantly higher among women (38.7% vs 33.1%, $p <0.001$), as well as the job guidance (6.1% vs 4.5%, $p = 0.006$).

Both among men and women, the most frequent sequence of treatments was methadone maintenance followed by methadone at tapered doses followed by another attempt with methadone maintenance. Different sequences of substitution treatments characterized the treatment choices among men. By contrast, after a certain number of substitution treatments women engaged psychotherapies and psychosocial treatments. They were able to come to an agreement about the treatment outcome with the clinical staff more than men, and they remained in contact with the NHS centre longer, asking for new and different treatments, especially psychosocial treatments, counselling, job advices and psychotherapy (data not shown).

Retention in methadone maintenance (Figure 1, Table 5)

In the first 6 months of the study, 1,984 patients (1,727 men and 257 women) received a methadone maintenance as their first treatment. Among them, 28.3% of men (n = 488), and 21.8% of women (n = 56) left the treatment in the following 12 months, with an abandon rate of 520/1000 person years among men and of 346/1000 person years among women. The difference in the abandon rate was statistically significant, with a HR = 0.71 ($p = 0.015$) in favour of women; Figure 1 shows that the outdistance begun at the sixth month of treatment.

Results of the Cox model showed that a short duration of addiction was predictive of abandon of Methadone Maintenance among men (HR = 1.40, $p = 0.005$) but not among women. Among women, a lower education level was predictive of treatment abandon but the HR was not statistically significant. No fixed abode was a risk factor for abandon in both genders (men: HR = 1.93, $p = 0.009$, women: HR = 11.0, $p = 0.009$), as well as an unstable job (men: HR = 1.38, $p = 0.004$, women: HR = 2.03, $p = 0.090$). Sharing needles was a risk factor for leaving treatment for women (HR = 2.22, $p = 0.007$), while heroin use at the time of the interview and recent legal problems or imprisonment acted as risk factors among men (HR = 1.62, $p < 0.0001$; HR = 1.53, $p < 0.0001$). High methadone dosages were protective towards the abandon both in men (HR=0.62, $p<0.0001$) and in women, among whom the effect was stronger (HR = 0.32, $p = 0.017$). The combination of treatments was protective towards the abandon, both among men (HR = 0.47, $p < 0.0001$) and women (HR = 0.55, $p = 0.047$); in particular, the association of methadone treatment with psychotherapy had a strong protective effect both among men (HR = 0.30, $p < 0.0001$) and among women (HR = 0.33, $p = 0.073$).

Retention in therapeutic community (Figure 2, Table 5)

In the first six months of the study, 514 patients (433 men and 81 women) received a therapeutic community treatment as their first treatment. In the following 12 months, 51.0% of men (n=221), and 55.6% of women (n=45) left the treatment, with an abandon rate of 818/1000 person years among men and of 1,253/1000 person years among women. The difference in abandon rate was in favour of men but not statistically significant (HR=1.28, p=0.128, Figure 2).

A younger age was a predictor of abandon of therapeutic community among men (HR = 1.42, p = 0.050) but not among women (Table 4). A lower education level was a risk factor for the abandon of the community in both genders (men: HR = 1.43, p = 0.062; women: HR = 1.92, p = 0.055), as well as sharing needles (men: HR = 1.44, p = 0.012; women: HR = 1.90, p = 0.049). To be under psychotherapy treatment was associated with abandon of the community among men (HR = 1.39, p = 0.049), but not among women. Previous episodes of therapeutic community in the last 12 months predicted abandon among men (HR = 1.46, p = 0.023).

Discussion

The analysis of gender differences in the Italian VEdeTTE cohort of heroin addicts confirms the findings of previous studies, at least on sociodemographic characteristics and drug-related patterns:

• at intake in the VEdeTTE cohort, women had a higher education level, but they had a stable job less frequently than men, and were more frequently unemployed, consistently with previous studies (Acharyya & Zhang, 2003; Brady et al., 1993; Callaghan & Cunningham, 2002; Chatham et al., 1999; Freeman et al., 1994; Grella et al., 2003; Grella & Joshi, 1999; Green et al., 2002; Hser et al., 1987b; Hser et al., 2004; Kelly et al., 2009; Marsh & Miller, 1985;Marsh & Simpson, 1986; Petry & Bickel, 2000; Riehman et al., 2003; Schottenfeld et al., 1998; Stocco et al., 2000; Wechsberg et al., 1998; Winhusen & Kropp, 2003);

• compared with men, women lived with their partner, or alone with their children more frequently (Chatham et al., 1999; Freeman et al., 1994; Green et al., 2002; Grella & Joshi, 1999; Hser et al., 1987b; Hser et al., 2003; Rowan-Szal et al., 2000; Stewart et al., 2003; Wechsberg et al., 1998), and were more frequently divorced or widowed (Acharyya & Zhang, 2003; Marsh&Miller, 1985);

• age at first heroin use was younger among women, as well as the age of first treatment, with a shorter addiction career at intake (Avila et al., 1996; Chatham et al., 1999; El-Guebaly, 1995; Green et al., 2002; Grella & Joshi, 1999; Haseltine, 2000; Hser et al., 1987a; Hser et al., 1987b; Hser et al., 2004; Marsh & Simpson, 1986; Rosenbaum, 1981; Rowan-Szal et al., 2000; Shand et al., 2011; Wechsberg et al., 1998);

• psychiatric symptoms were more frequent and more severe among women, including depression, self-damaging behaviors and suicide attempts (Chatham et al., 1999; Brady et al., 1993; Darke et al., 2009; El-Guebaly, 1995; Green et al., 2002; Grella et al.,2003; Grella & Joshi, 1999; Haseltine, 2000; Luthar et al., 1996; Petry & Bickel, 2000; Shand et al., 2011; Rowan-Szal et al., 2000; Stewart et al., 2003; Wechsberg et al., 1998; Wu et al., 2010; Zilberman et al., 2003); consistently withATOS findings, female heroin users were far more likely to attempt suicide prior to the initiation of heroin use (Darke et al., 2004);

• women engaged risk behaviors (needle sharing) more frequently than men (Bennett et al., 2000; Chatham et al., 1999; Evans et al., 2003; Sherman et al., 2001), but they experienced crimes and imprisonment less frequently (Anglin et al., 1987; Chatham et al., 1999; Grella et al., 2003; Grella & Joshi, 1999; Hser et al., 1987a; Hser et al., 2003; Marsh & Miller, 1985; Marsh & Simpson, 1986; Powis et al., 1996; Shand et al., 2011; Wechsberg et al., 1998; Wu et al., 2010);

• heroin addicted women used amphetamines and benzodiazepines as secondary drugs, while men used alcohol more frequently (Bretteville-Jensen, 1999; Chambers et al., 1970; Darke, 1994; Shand

et al., 2011; Freeman et al., 1994; Grella et al., 2003; Hser et al., 1987b; Marsh & Miller, 1985; Rowan-Szal et al., 2000; Wechsberg et al., 1998; Wu et al., 2010).

Most of the observed differences among males and females do not appear to be related to the condition of heroin addiction: they are a common finding of studies on gender differences in the general population. In Italy, females reach higher education level but they find a stable job less frequently than men, and they get a lower salary (ISTAT 2011, 2012). They live with children and old parents more frequently than men (ISTAT 2011). Certain psychiatric diseases are more frequent among females: depression affects 5.9% of Italian males and 12.8% of females (PASSI, 2007); anxiety disturbances affect only 0.8% of males and 3.0% of females (de Girolamo et al., 2003); 5.3% of males>65 years of age and 7.2% of females develop dementia (Ministero della Salute, 2003). Population surveys show that alcohol use is more frequent among males, while sedative use is more frequent among females, since adolescence (Scafato, Massari, Russo, & Bartoli, 2002; EMCDDA 2006; ESPADItalia 2011; Hibell et al., 2012). These findings could be related with the higher depression and anxiety symptoms affecting girls since early ages, and to the use of alcohol and drugs to socialize among boys (Haseltine, 2000; Hser, Anglin, & McGlothlin, 1987a).

With regard to treatments, in the VEdeTTE cohort women were more willing to ask and receive psychosocial treatments, counselling, job advices and psychotherapy (Rowan-Szal et al., 2000). They retained better in Methadone Maintenance, and worst in Therapeutic Community. Indicators of poor socioeconomic situation and severe addiction, such as bad housing conditions, an unstable job and sharing needles were risk factors among women for leaving methadone treatment. By contrast, a recent addiction, heroin use at the time of the interview, and recent legal problems or imprisonment were risk factors for abandon among men. High methadone dosages were strongly protective towards abandon among women, while the protection given by combined treatments was similar for males and females. Lower education and sharing needles were risk factors for the abandon of therapeutic community in both genders, while the young age, to be in psychotherapy treatment and previous episodes of therapeutic community predicted abandon among men only.

It is difficult to compare our findings on treatment retention with previous literature, since studies on gender differences in treatment outcomes are quite rare. Our findings on higher treatment retention in methadone maintenance among women do not confirm the results of two previous studies (Mino et al., 1998; Simpson et al., 1997; Taylor, 1995), which had the opposite direction. However, other studies did not find differences in treatment retention between genders (Alterman, Randall, & McLellan, 2000; Gerstein & Johnson, 2000; Stewart et al., 2003). On the contrary, the young age among men and the low socioeconomic status among women were risk factors for treatment abandon also in a previous study (Green et al., 2002).

Our study on gender differences has both strength and limitations. Enrolling more than 10,000 heroin addicts in 15 Italian regions, the VEdeTTE cohort allowed the investigation of gender differences in heroin addiction. However, since the study was not intended to investigate risk factors for heroin addiction, the possibility to study this research question was very limited. On the contrary, the amount of information collected at intake, and the detailed and standardized registration of treatments allowed analyzing gender differences both at intake and in the effectiveness of treatments. All the same, due to the prospective observational design of the study, the female sample accounted only for 14% of the entire sample. Despite ensuring the representativeness of the sample, this relatively low female sample limited the statistical power of subgroup analysis, and it may account for some of the not statistically significant associations we observed in the retention analysis. Moreover, the study refers to 1998–2001, and this could limit the generalizability of the findings to nowadays practice. However, the characteristics of heroin addicts treated at NHS addiction centers are not very changed. The main changes that occurred in the last 15 years regard characteristics of the treatment (e.g., MMT dosages), and the treatment typology (Presidenza del Consiglio dei Ministri, 2011), variables that do not decrease the validity of our results, that are quite independent by the context and by the time period. For example, we show that high MMT dosages are very protective towards abandon, and more on

female that on males, and that the associations of treatments are protective: these results are independent by the time period, and can still give suggestions to the practitioners in the field.

Despite the limitations, clear gender differences in heroin addiction and its treatment emerged, that can lead to some guidance for differential treatment of women versus men. Women experienced a worst socioeconomic condition: in all pretreatment variables they were disadvantaged towards men. Since this could indicate a higher severity of the general condition, the first recommendation is to consider socioeconomic factors in the choice and combination of treatments. The higher prevalence of psychiatric symptoms among women underline the need of take into account comorbidity when the patient firstly access the treatment, as pointed out also by Zilberman et al. (2003). High methadone dosages are highly recommended in the literature (Faggiano, Vigna-Taglianti, Versino, & Lemma, 2003). Also in this case, the stronger protective effect of high dosages among women should be taken into account in the practice. The higher protection of high methadone dosages towards abandon among women could be also due to a possible effect of methadone in lowering psychiatric symptoms, a suggestion that could apply and should be taken into account when treating men, too.

From a general point of view, since many features both of the patient and of the treatment can influence treatment outcomes differently in men and women, a gender specific approach in addiction treatment and relapse prevention should always be applied.

It is recognized that female drug addicts have different needs that arise from the role of the woman in the society and the expectations of the society, firstly related to the need of taking care of children, partner and family. This can be a stimulus but also a barrier to both outpatient and residential treatment (UNODC 2004; EMCDDA, 2009; Roberts, Mathers, & Degenhardt, 2010). A debate on the best way of organizing treatment for female addicts is currently under way. It is still unclear if the best strategy for substance use and misuse is to set dedicated services and special treatment groups for females, or to apply a gender-oriented approach in a gender-mixed treatment context (Green 2006). Whether at low-threshold or at structured treatment services, it is necessary to ensure that the treatment environment is safe for women, and that staff have the necessary skills for training and support. Although some women require residential services, community-based outpatient services have many advantages in terms of being more accessible and less costly. Aftercare and social reintegration components, particularly skill development, employment training and housing, are critical for many women (UNODC 2004; EMCDDA, 2006; Roberts, Mathers, & Degenhardt, 2010).

A 2003 review found that gender sensitive programs improved treatment completion, length of stay, birth outcomes, employment, self-reported health status, and decreased substance use and HIV risk (Ashley, Marsden, & Brady, 2003). Furthermore, a study on cost-effectiveness of mixed-gender programs for substance abuse found that those programs standardized irrespectively of gender are less cost-effective for women: they show less improvement than men in the outcomes and are more costly (Yeom & Shepard, 2007). In line with these results, the Commission on Narcotic Drugs of Unites Nations approved in 2012 a Resolution to promote “strategies and measures addressing specific needs of women in the context of complete and integrated drug demand reduction programmes and strategies” encouraging the integration of “essential female specific services in the overall design, implementation, monitoring and evaluation of policies and programs addressing drug abuse and dependence” (UN-CND, 2012).

A last recommendation addressing future research naturally emerges from our study: the exploration of gender differences needs a specific care at the study design level, to overcome the low sample of female heroin addicts in the general population. The enrolment of a larger sample of women must be planned to study gender differences.

Declaration of interest

The authors declare that they have no conflict of interest. The authors alone are responsible for the content and writing of the paper.

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Glossary

Addiction: A chronic, relapsing disease, characterised by the effects of the prolonged use of the drug itself and by the behavioral disorder due to its compulsive seeking.

Cohort study: A study design where subjects (cohort) are followed prospectively collecting detailed information on exposures (risk factors) and outcomes in order to study causal relationships between them.

Cox Proportional Hazard model: A statistical survival analysis method used to investigate the effect of several variables upon the time a specified event takes to happen, under the assumption that the effects of the predictor variables on survival are constant over time. The hazard function is the probability that if a person survives to time t, they will experience the event in the next instant.

Gender differences: Differences due to biological, psychological, and social factors influencing the development of social constructs of male and female, not limited to sexual contents but deeply related to symbols, values and health, including characteristics that make up male and female identity and their representation which changes across time and generations.

Methadone maintenance: Methadone treatment characterized by a constant dosage, with variations lower than 20 mg.

Methadone at tapered doses: Methadone treatment administered gradually decreasing the dosage, reaching a final dose of zero milligrams by no more than 180 days. NHS addiction treatment centers: Health units of the National Public Health Service aimed to prevention, treatment and rehabilitation of patients with tobacco, alcohol and drugs abuse or addiction.

Psychotherapy: Individual, family, or couple treatment aimed to the analysis of interpersonal and intra-psychic dynamics, of mechanisms of defence, and to the identification of conflicts, in order to generate awareness and motivate the patient to change.

Treatment abandon: Interruption of treatment not agreed with the clinician.

Therapeutic community: A structured residential or semi-residential program, promoting a drugfree lifestyle and based on the use of the peer community to facilitate social and psychological change.

Treatment retention: The length of stay in treatment measured by days, months, or specific time period.

VEdeTTE: Italian multicentric cohort study of heroin addicts admitted to NHS treatment centres. Acronym of “eValuation of the Effectiveness of Treatments for hEroin dependence” (Valutazione dell’Efficacia DEi Trattamenti per la Tossicodipendenza da Eroina).

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Table 1. Characteristics of the VEdeTTE study population at intake, by gender.

Characteristic		N	Men ($n = 8,953$)		Women ($n = 1,501$)	
			n	%	*n*	%
Age	18–27	3,136	2,645	29.5	491	32.7
	28–31	2,604	2,236	25.0	368	24.5
	32–35	2,283	1,978	22.1	305	20.3
	36–66	2,431	2,094	23.4	337	22.5
Place of birth	Northern Italy	3,070	2,459	27.5	611	40.7
	Central Italy	2,381	1,976	22.1	405	27.0
	Southern Italy	1,853	1,680	18.7	173	11.5
	Italian main islands	2,770	2,523	28.2	247	16.5
	Other countries	380	315	3.5	65	4.3
Marital status	Single	6,723	5,991	67.1	732	49.0
	Married	1,737	1,466	16.4	271	18.1
	Living with partner	984	730	8.2	254	17.0
	Separated/divorced	883	702	7.8	181	12.1
	Widow	98	42	0.5	56	3.8
Housing	With parents/relatives	5,734	5,165	57.9	569	38.2
	With partner and sons	1,526	1,303	14.6	223	14.9
	With partner only	1,210	857	9.6	353	23.7
	With sons only	77	25	0.3	52	3.5
	With friends	125	92	1.1	33	2.2
	Alone	961	811	9.1	150	10.1
	In therapeutic community	605	528	5.9	77	5.2
	No fixed abode	168	135	1.5	33	2.2
Years of education	<5	6,181	5,366	60.2	815	54.6
	5	95	91	1.0	4	0.3
	8	1,687	1,557	17.5	130	8.7
	9–11	704	558	6.2	146	9.8
	13	1,659	1,280	14.4	379	25.4
	17 or more	82	64	0.7	18	1.2
Employment	Stable	3,500	3,154	35.7	346	23.3
	Unstable	2,697	2,355	26.7	342	23.0
	Student	105	74	0.8	31	2.1
	Non-professional condition	350	221	2.5	129	8.7
	Unemployed	3,666	3,028	34.3	638	42.9
Legal problems/prison*	No	7,095	5,995	68.0	1,100	74.0
	Yes	3,210	2,823	32.0	387	26.0

*in the last 12 months.

Table 2. Drug addiction-related issues and risk behaviours at intake, by gender.

Characteristic		N	Men ($n = 8,953$)		Women ($n = 1,501$)	
			n	%	*n*	%
Age of first heroin use	9–17	3,576	3,027	33.8	549	36.6
	18–19	2,459	2,134	23.8	325	21.7
	20–21	1,790	1,586	17.7	204	13.6
	22–55	2,539	2,126	23.8	413	27.5
Duration of addiction	0–7 years	2,820	2,320	26.1	500	33.5
	8–11 years	2,649	2,306	26.0	343	23.0
	12–16 years	2,592	2,251	25.4	341	22.9
	17–35 years	2,303	1,996	22.5	307	20.6
Age of first treatment	10–21	3,103	2,556	28.6	547	36.4
	22–24	2,462	2,159	24.1	303	20.2
	25–28	2,410	2,092	23.4	318	21.2
	29–65	2,094	1,820	20.3	274	18.3
Access to treatment	Voluntary	8,719	7,511	83.9	1,208	80.5
	Through family	678	559	6.2	119	7.9
	Health services	450	354	4.0	96	6.4
	Justice system	426	384	4.3	42	2.8
	Others	128	97	1.1	31	2.1
Cocaine use	No	8,281	7,088	79.8	1,193	80.1
	Yes	2,096	1,799	20.2	297	19.9
Amphetamine/ecstasy use	No	10,171	8,726	98.3	1,445	97.0
	Yes	196	151	1.7	45	3.0
Alcohol use	No	4,859	4,027	45.2	832	55.8
	Yes	5,542	4,882	54.8	660	44.2
Cannabis use	No	7,016	5,970	67.2	1,046	70.1
	Yes	3,366	2,919	32.8	447	29.9
Benzodiazepine use	No	8,544	7,430	83.8	1,114	74.8
	Yes	1,817	1,441	16.2	376	25.2
Cigarette smoking	No	308	268	3.0	40	2.7
	Yes	10,093	8,641	97.0	1,452	97.3
Needle sharing	No	8,404	7,261	82.8	1,143	77.9
	Yes	1,837	1,512	17.2	325	22.1
Unprotected sexual intercourse	No	8,698	7,380	85.1	1,318	90.4
	Yes	1,434	1,294	14.9	140	9.6
HIV/AIDS	No	6,214	5,327	89.0	887	82.2
	Yes	852	660	11.0	192	17.8
Hepatitis B	No	4,065	3,472	58.2	593	57.5
	Yes	2,935	2,497	41.8	438	42.5
Hepatitis C	No	2,120	1,838	29.8	282	26.0
	Yes	5,122	4,321	70.2	801	74.0
Psychiatric comorbidity	No	6,884	5,958	84.1	926	78.1
	Yes	1,389	1,129	15.9	260	21.9

Table 3. Psychiatric symptoms before and after the first heroin use, by gender.

Symptoms		N	Men		Women	
			n	%	n	%
Before the first heroin use						
Bad mood/depression	No	5,179	4,679	53.6	500	34.1
	Yes	5,014	4,047	46.4	967	65.9
Self-damaging behaviors	No	8,666	7,639	88.4	1,027	71.0
	Yes	1,425	1,005	11.6	420	29.0
Suicide attempts	No	9,432	8,283	95.7	1,149	79.1
	Yes	674	371	4.3	303	20.9
Aggressive behaviors	No	7,342	6,349	73.3	993	68.2
	Yes	2,774	2,310	26.7	464	31.8
Psychotic thinking/hallucinations	No	9,582	8,243	95.1	1,339	92.6
	Yes	528	421	4.9	107	7.4
Psychiatric treatments or hospitalizations	No	9,620	8,317	95.6	1,303	89.4
	Yes	533	379	4.4	154	10.6
After the first heroin use						
Bad mood/depression	No	1,403	1,256	14.4	147	10.0
	Yes	8,782	7,462	85.6	1,320	90.0
Self-damaging behaviors	No	7,252	6,368	74.2	884	60.8
	Yes	2,779	2,210	25.8	569	39.2
Suicide attempts	No	8,726	7,591	88.7	1,135	78.9
	Yes	1,272	969	11.3	303	21.1
Aggressive behaviors	No	6,119	5,312	61.8	807	56.0
	Yes	3,915	3,280	38.2	635	44.0
Psychotic thinking/hallucinations	No	8,446	7,270	85.0	1,176	81.5
	Yes	1,550	1,283	15.0	267	18.5
Psychiatric treatments or hospitalizations	No	9,110	7,853	91.4	1,257	86.6
	Yes	934	739	8.6	195	13.4

Table 4. First therapeutic treatments received by patients, by gender.

Type of treatment	N	Administered to men		Administered to women		
		n	%*	n	%*	p**
Therapeutic community	818	716	8.1	102	6.9	0.102
Methadone maintenance	4,872	4,137	46.9	735	49.5	0.059
Methadone at tapered doses	2,338	2,017	22.8	321	21.6	0.296
Residential brief detoxification	103	83	0.9	20	1.4	0.145
Psychotherapy	1,010	797	9.0	213	14.3	<0.001
Counseling	3,498	2,924	33.1	574	38.7	<0.001
Social advice	2,252	1,915	21.7	337	22.7	0.385
Job guidance	489	398	4.5	91	6.1	0.006
Naltrexone	394	350	4.0	44	3.0	0.063
Painkillers/anxiolytics	172	152	1.7	20	1.4	0.297
Other pharmacological treatments	553	436	4.9	117	7.9	<0.001
Total number of first treatments	16,499	13,925		2,574		
Total number of patients	10,315	8,830		1,485		

*Percentage out of the total number of patients.
**Pearson *p* value for the difference among proportions.

Table 5. Risk factors for treatment abandon: results from adjusted Cox model.*

Characteristic		Men ($n = 1,634$)			Women ($n = 246$)		
Methadone maintenance		Adj HR	95% C.I.	*p*	Adj HR	95% C.I.	*p*
Duration of addiction	>5 years	1			1		
	≤ 5 years	1.40	1.10–1.76	0.005	0.85	0.44–1.64	0.637
Years of education	>12	1			1		
	≤12	1.04	0.82–1.31	0.739	1.49	0.80–2.78	0.203
Housing	With parents/relatives	1			1		
	With partner and/or sons	1.05	0.84–1.31	0.677	1.45	0.74–2.82	0.278
	With friends/alone/in a Therapeutic community	1.23	0.91–1.66	0.174	1.27	0.54–2.98	0.587
	No fixed abode	1.93	1.18–3.17	0.009	11.0	2.11–57.4	0.004
Employment	Stable	1			1		
	Unstable	1.38	1.10–1.72	0.004	2.03	0.89–4.63	0.090
Needle sharing	No	1			1		
	Yes	1.13	0.90–1.42	0.296	2.22	1.24–3.95	0.007
Heroin use**	No	1			1		
	Yes	1.62	1.30–2.02	<0.001	1.80	0.94–3.43	0.075
Legal problems/prison***	No	1			1		
	Yes	1.53	1.26–1.86	<0.001	1.39	0.77–2.52	0.273
Methadone dosage	1–39 mg/day	1			1		
	40–59 mg/day	0.78	0.64–0.97	0.023	0.64	0.34–1.23	0.182
	≥ 60 mg/day	0.62	0.46–0.82	0.001	0.32	0.13–0.81	0.017
Concurrent treatments	no one	1			1		
	MM + other	0.47	0.39–0.57	<0.001	0.55	0.30–0.99	0.047
	MM + other + psychotherapy	0.30	0.18–0.50	<0.001	0.33	0.10–1.11	0.073
Therapeutic community			Men ($n = 422$)			Women ($n = 79$)	
Age	≥30 years	1			1		
	25–29 years	1.21	0.89–1.63	0.219	0.99	0.49–2.02	0.984
	≤24 years	1.42	1.00–2.03	0.050	1.07	0.480–2.37	0.869
Years of education	>12	1			1		
	≤12	1.43	0.98–2.08	0.062	1.98	0.98–3.99	0.055
Employment	Employed	1			1		
	Unemployed	1.10	0.83–1.45	0.500	1.12	0.58–2.18	0.736
Needle sharing	No	1			1		
	Yes	1.44	1.08–1.91	0.012	1.90	1.00–3.59	0.049
Psychotherapy***	No	1			1		
	Yes	1.39	1.00–1.94	0.049	1.01	0.46–2.21	0.970
Therapeutic community***	No	1			1		
	Yes	1.46	1.05–2.03	0.023	1.20	0.60–2.41	0.598

*Hazard Ratios are adjusted for all variables in the table.
**at interview.
***in the last 12 months.

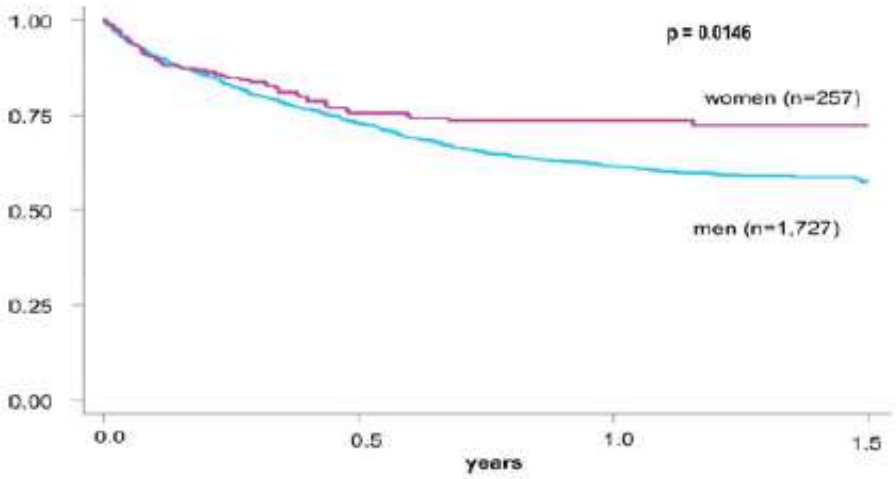

Figure 1. Retention in methadone maintenance treatment: Kaplan – Meier curve, by gender.

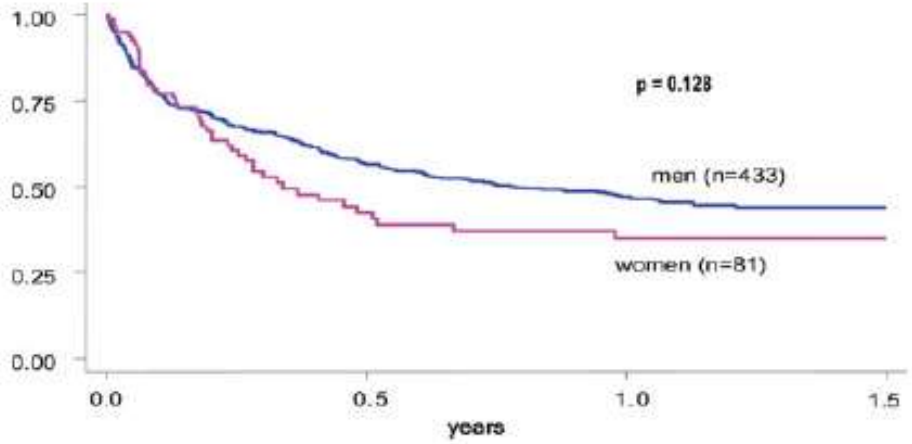

Figure 2. Retention in therapeutic community: Kaplan – Meier curve, by gender.