Prevalence morbidity and mortality among heroin users and methadone patients
Buster, M.C.A.

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PREVALENCE

PMAMA
HUAMP
Marcel C.A. Buster  
Department of Epidemiology, Documentation and Health Promotion EDG, 
Municipal Health Service, Amsterdam

Giel H.A. van Brussel  
Department of Social and Mental Health, Municipal Health Service, Amsterdam.

Wim van den Brink  
Amsterdam Institute for Addiction Research AIAR, Amsterdam.
European Journal Of Epidemiology 2001; 17: 935-94

Abstract

One of the objectives of Amsterdam's methadone maintenance treatment is maximising its coverage among problematic opiate users. In order to evaluate what proportion is reached, the capture-recapture method is conducted to estimate the prevalence of problematic opiate use. Samples of opiate users in contact with police, hospital or treatment are used. The treatment sample is limited to the low-threshold treatment sample - treatment with minimal requirements to the clients - based on differences of log likelihood ratio, Akaike's and Bayesian Information Criteria, log linear models are selected. The size of the population of problematic opiate users in 1997 is estimated to be 4130 - 95% confidence interval CI: 3753-4566. Within three months 50% was registered: 16% at the police, 2.5% at the hospital and 40% at treatment. This study shows that the Amsterdam methadone treatment programmes succeed in reaching a high proportion of problematic opiate users. The estimation of the prevalence of problematic opiate users is considered to be valid. However, if, instead of the low-threshold treatment, the total treatment sample had been used, the population of interest and the sampled population would not match correctly, and prevalence would have been overestimated.

Introduction

Large scale methadone programmes exist in Amsterdam since 1981. A treatment system with three different treatment modalities is designed in order to contact all heroin users; particularly those heroin users who could not be reached with abstinence-oriented treatment programmes. Until now, no adequate estimation of the num-
ber of opiate users is described in the scientific literature. The estimation that is generally used is based on a two sample Capture Recapture C/RC method in which the annual sample of opiate users arrested by the police and receiving methadone at the police station is compared with the annual sample of opiate users receiving methadone at the Municipal Health Service MHS. This way, the number of opiate users was estimated as 5177 at 1997.

However, the C/RC method is vulnerable for biases as there are several assumptions that can be violated. First, it is assumed that the capture probabilities for different sources are not all dependent. Thus, if only two sources are used they are assumed to be independent. In this study three samples - hospital, police and methadone treatment - are used and it is, therefore, possible to adjust for potential dependencies by using log-linear methods. Second, the population must be closed; i.e. the same individuals must be present throughout the period in which samples are taken. In this study we try to minimise the effect of violation of the closed population assumption by using a three months sampling period. Third, all true matches and only true matches are identified. In this study the linkage of the samples is facilitated because two of the three samples - police and treatment - are extracted from the same register with unique identification codes. The hospital sample is extracted from another register but sufficient information is available to match the individuals of different samples accurately. The fourth assumption is that registration probabilities should be homogeneous across all individuals in the population. This seems less of a problem, in previous studies in Glasgow, Scotland, and Barcelona, Spain, it was concluded that the observed heterogeneity in sex and age groups did not affect the results. The fifth assumption is of special importance if C/RC is used in epidemiological studies. This assumption is related to case definition: there needs to be correct matching between the population of interest and the population appearing on the lists. In this study we focus on the latter assumption.

The primary goal of this study is to estimate the size of the population of problematic opiate users and the extent to which methadone treatment is reaching this population. Furthermore, to contribute to the discussion on the use of the C/RC method in epidemiology. By repeating the C/RC method with different treatment samples we describe the effect of incorrect matching of the population of interest and the sampled population.

Methods
Three modalities of outpatient methadone treatment can be distinguished in Amsterdam. The first modality is the "low-threshold" methadone maintenance programme of the MHS. In this programme,
Figure 1 Opiate users in Amsterdam: different subgroups referred to in this study

abstinence of illegal drugs is not a precondition to be treated and demands on participants are limited to those considered essential for the health status of the clients - e.g. registration, X-thorax screening and a periodical medical check up. Several times a week, clients receive methadone and, if necessary, additional medication at the clinics or methadone bus. The second modality is a general practitioners GPs methadone maintenance programme. Opiate users treated with methadone at their GP receive methadone at the pharmacist for 7-14 days. They are expected to be able to control their addiction - i.e. not to sell their methadone at the black market, or swap it for heroin. The MHS advises GPs to limit methadone prescription to relatively stable heroin users stable housing, insurance, limited illicit drug use etc. and to refer 'difficult' patients to the MHS. The third modality is an abstinence-oriented methadone reduction programme and consists of opiate users motivated to quit the use of opiates. Treatment at the GP or the abstinence oriented programme is not possible for all opiate users and is referred to as 'high-threshold methadone treatment'. In addition, specialised physicians and nurses of the MHS visit opiate users incarcerated at Amsterdam police stations and opiate users admitted in hospitals of Amsterdam. This assistance is needed because craving, withdrawal and behavioural problems often compli-
cate hospital admissions and incarceration of opiate users.

The Amsterdam policy of discouragement limits treatment possibilities for heroin users without a residence permit. Opiate users born in the Netherlands, Surinam or the Dutch Antilles further called 'Dutch and Surinam opiate users' generally have a residence permit and maximal access to treatment. Therefore this subgroup is described separately.

In this study we attempt to estimate the total population of problematic opiate users. To estimate this number, the C/RC analysis is limited to samples with problematic opiate users only. Opiate users committing criminal offences and those with serious health problems 'those at high risk to be arrested by the police or admitted in a hospital' are considered as problematic opiate users. Furthermore, opiate users who would participate in a low-threshold treatment programme if they demand for treatment are considered as problematic opiate users since they would be referred to high-threshold treatment programmes otherwise. The purple surface within the inner dotted circle represents the hidden number of problematic opiate users that we attempt to estimate.

Calculating the coverage of treatment, all clients of low-threshold methadone treatment and an unknown proportion of high-threshold methadone treatment participants are considered as problematic opiate users. Outside the bold circle non-problematic opiate users are shown. Part of them are stable high-threshold methadone treatment participants. The C/RC analysis is repeated with the use of the total treatment sample and the high treatment sample only. In the discussion section the question is raised whether the results obtained from these analyses represent the prevalence of the total population of opiate users or not.

* Data sources and matching

Three lists are used to estimate the number of opiate users in the city of Amsterdam: a list of participants of the methadone programmes, a list of arrested opiate users who received methadone at police stations, and a list of opiate users admitted to a hospital. The period of observation is limited to the first three months of 1997.

Methadone prescriptions of treatment centres and police stations are all centrally registered at the Central Methadone Register CMR. Within this register each individual has its own unique identification code independent of location of prescription. Hospital admissions are registered separately.

Both CMR and the register of hospital admissions provide sufficient information to identify individual opiate users: surname, forename initials, date of birth, country of birth and gender. Initially, both registers were matched using the SPSS 9.0 merge procedure with
The size of the study population

During the first three months of 1997, a total of 2429 opiate users participated in the three outpatient methadone treatment modalities: 1325 at the MHS, 198 at an abstinence oriented programme and 981 at the GP. Sixty-five patients attended both high-threshold programmes. The number of high-threshold patients is 1179. Seventy-five high-threshold participants also participated in a low-threshold programme. The mean and median percentage of days of treatment participation during these first three months of 1997 was 70% and 89%, respectively. Moreover, 102 opiate users had a registered hospital admission and 648 opiate users received methadone at the police office.

An opiate user can either be in methadone treatment or not, be arrested or not and be admitted in a hospital or not. If three samples are used, eight different combinations are possible. These combinations vary from appearing in all three samples to appearing in none of the samples. The number of people appearing in none of the samples is unknown. This is the hidden population that can be estimated using the C/RC method. If all samples are independent, the expected frequencies of the different cells are the product of the size of the estimated total population and the chances to appear, or not to appear, in
the different samples during the sampling period. The number of unique persons appearing in the seven known cells are described in Table 1. A distinction is made between low-threshold, high-threshold and total treatment samples.

**Applied formulas**

Two sample Capture-Recapture: If \( a \) is the number of individuals appearing in both samples and \( b \) and \( c \) are unique individuals within each sample.

Total population: \( N = \frac{((a+b)(a+c))/a}{b} \)

Variance: \( \text{VAR}(N) = \frac{((a+b) x (a+c) x (b) x (c))/a^3}{b} \)

**Information Criteria**

Aikake's Information Criterion: \( \text{AIC} = C^2 - 2 \times (\text{df}) \)

Bayesian Information Criterion: \( \text{BIC} = C^2 - (\ln N_{\text{observed}}) x (\text{df}) \)

\( C^2 \) = likelihood ratio
\( \text{df} = \) degrees of freedom

**Estimating the population size**

General log linear analysis · SPSS · 9.0 · is used to perform a three-sample C/RC analysis.\(^{114}\) This method analyses the frequency counts of observation in each cross-classification category in a cross-tabulation · i.e. Table 1 · A structural zero for incomplete tables is defined by a cell structure variable.\(^{113}\) Different models are compared in order to find the best fitting model. The aim of model selection is to select a model that adequately describes the data with as few parameters as possible. Rival models were compared using the Log Likelihood ratio \( C^2 \) for models with different degrees of freedom, the Aikake's Information Criterion \( \text{AIC} \) and the Bayesian Information criterion as proposed by Schwarz \( \text{BIC} \) are used for models with the same degrees of freedom.\(^{114}\) The simplest model with the lowest \( \text{AIC} \), \( \text{BIC} \) score was selected in the absence of a more complex model with a significantly lower Log likelihood ratio.

Before conducting a three sample C/RC analysis, two sample C/RC estimations are presented to illustrate the relations between different samples. Formulas to perform the two sample C/RC analysis and information criteria are shown in the Box.\(^{115}116\)

**Estimating the coverage among problematic opiate users.**

To calculate the coverage of health services among problematic opiate users, the percentage of opiate users covered by low-threshold methadone treatment, police and hospitals can be deduced directly from the estimation of the size of problematic opiate users and its 95%
Table 2 Size of the population estimated by a two-sample capture recapture method

P = Police sample  
H = Hospital sample  
T = treatment sample  
SD = Standard Deviation

<table>
<thead>
<tr>
<th>Samples used</th>
<th>H/T</th>
<th>SD</th>
<th>P/T</th>
<th>SD</th>
<th>P/H</th>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Low-threshold</td>
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<td>343</td>
<td>4069</td>
<td>462</td>
<td>4721</td>
<td>1159</td>
</tr>
<tr>
<td>High-threshold</td>
<td>7507</td>
<td>1778</td>
<td>16637</td>
<td>4069</td>
<td>4721</td>
<td>1159</td>
</tr>
<tr>
<td>Total treatment</td>
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<td>351</td>
<td>6197</td>
<td>595</td>
<td>4721</td>
<td>1159</td>
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<tr>
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<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Low-threshold</td>
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<td>372</td>
<td>2694</td>
<td>379</td>
<td>4490</td>
<td>1597</td>
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<tr>
<td>High-threshold</td>
<td>3945</td>
<td>935</td>
<td>9575</td>
<td>2393</td>
<td>4490</td>
<td>1597</td>
</tr>
<tr>
<td>Total Treatment</td>
<td>2996</td>
<td>298</td>
<td>3980</td>
<td>438</td>
<td>4490</td>
<td>1597</td>
</tr>
</tbody>
</table>

Cl. However, an unknown part of the participants of high-threshold programmes is considered as problematic opiate user - as shown in Figure 1. This part contributes to the coverage of the problematic opiate users by health services as well. Because no specific client information is available, the proportion of problematic opiate users among high-threshold treatment can only be determined indirectly. To estimate this proportion, the proportion problematic opiate users that is admitted in a hospital or captured by the police is estimated first. The proportion of high-threshold treatment participants that is admitted in a hospital or captured by the police is expected to be lower. The quotient of the two proportions is used to indicate the proportion of problematic opiate users within high-threshold programmes.

Results
Two sample capture recapture estimations
Table 2 shows the two sample C/RC estimations. The estimations vary widely - from 3072 till 16637. Highest estimations are calculated if a high-threshold treatment sample is used. This may be attributed to a negative dependency. High-threshold treatment clients probably are at lower risk to be arrested by the police or to be admitted in a hospital than other opiate users. In this case the overlap is small and the estimated size of the population is probably too large. Lowest estimations are calculated if treatment and hospital samples are compared. This may be attributed to a positive dependency. Foreign opiate users can only receive methadone treatment if they are sex workers.
Prevalence of problematic opiate users

$N_{obs}$ = number of registered opiate users
$C^2$ = likelihood ratio
AIC = Akaike’s Information Criterion
BIC = Bayesian Information Criterion proposed by Schwarz
$N$ = estimated size of the total population
Bold; best fitting model

### Samples used

<table>
<thead>
<tr>
<th>Model</th>
<th>DF</th>
<th>$C^2$</th>
<th>AIC</th>
<th>BIC</th>
<th>$N$</th>
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<td>0.00</td>
<td>0.00</td>
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<tr>
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<td>1.64</td>
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<tr>
<td>HT, HP</td>
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<td>1.28</td>
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<td>-6.22</td>
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<tr>
<td>HT</td>
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<td>-13.4</td>
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</tr>
<tr>
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<td>1.42</td>
<td>-9.59</td>
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</tr>
<tr>
<td>HP</td>
<td>2</td>
<td>6.00</td>
<td>2.00</td>
<td>-9.01</td>
<td>3948</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>6.55</td>
<td>0.55</td>
<td>-16.0</td>
<td>3976</td>
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### Low-threshold treatment

- Police, Hospital
  - $N_{obs} = 1814$

<table>
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<th>BIC</th>
<th>$N$</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>10120</td>
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</table>

### High-threshold treatment

- Police, Hospital
  - $N_{obs} = 1783$

<table>
<thead>
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<th>$C^2$</th>
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<th>BIC</th>
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</thead>
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<tr>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>7302</td>
</tr>
</tbody>
</table>

### Total treatment

- Police, Hospital
  - $N_{obs} = 2861$

<table>
<thead>
<tr>
<th>$C^2$</th>
<th>AIC</th>
<th>BIC</th>
<th>$N$</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>7302</td>
</tr>
</tbody>
</table>

### Table 3

Using different treatment samples for three months of 1997, in a three sample capture recapture method leads to different estimations of the number of opiate users.

- Public health reasons or if they have severe illnesses.
- Humanitarian reasons.

In case the number of people appearing in the overlap cell is low, standard deviations will be large. As a consequence, largest standard deviations are found if the hospital and police samples are compared and if the high-threshold treatment sample is compared to the hospital or police sample.

Three-sample estimation of the population of opiate users.
Table 3 shows the results of the three sample C/RC analyses of the total population. If the low-threshold treatment sample is used, the estimated size of problematic opiate users is 4130. 95% CI: 3753-4586.
If the high-threshold treatment sample is applied, the model with adjustment for the negative dependency between the treatment and police sample is selected - lower part Table 3. This leads to an estimated number of 6226 - 95% CI 4647-8688. Similar to the two sample estimations the CI is large because of small overlaps between samples. Due to a sparse sensitive cell of individuals appearing within high-threshold treatment and police and hospital sample both the estimation as confidence intervals are inflated if the saturated model is used. If the total treatment sample is used, the selected model is similar to the model with the low-threshold treatment sample. The estimated number of opiate users, however, increases to 6185 - 95% CI: 5697-6766. The size of the population is comparable to that of the high-threshold treatment. If the sample population is limited to the Dutch and Surinam and the low-threshold treatment sample is used, the crude
Prevalence of problematic opiate users

<table>
<thead>
<tr>
<th>Sample</th>
<th>Total population</th>
<th>Dutch and Surinam only</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Number</td>
<td>%</td>
</tr>
<tr>
<td><strong>N1</strong> total no. problematic opiate users</td>
<td>4130</td>
<td>100%</td>
</tr>
<tr>
<td><strong>N2</strong> hospital or police</td>
<td>736</td>
<td>18%</td>
</tr>
<tr>
<td><strong>N3</strong> high-threshold treatment</td>
<td>1104</td>
<td>100%</td>
</tr>
<tr>
<td><strong>N4</strong> N2 - N3</td>
<td>57</td>
<td>5%</td>
</tr>
<tr>
<td>Problematic opiate users within N3*</td>
<td>320</td>
<td>29%</td>
</tr>
</tbody>
</table>

Table 5: Estimation of problematic opiate users among the high-threshold treatment sample - first three months of 1997.

Model is selected and the estimated number of opiate users is 2807 - 95% CI: 2568-3048 - Table 4. If high-threshold and total treatment samples are used, selected models are equal to those of the total population presented in Table 3. Again, the estimated sizes are comparable to each other but significantly higher than the estimation with the low-threshold treatment sample. A C/RC analysis with the total treatment sample results in an estimated number of 4005 - 95% CI: 3653-4425.

Problematic opiate users in high-threshold samples

As shown in Figure 1, part of the high-threshold treatment sample belongs to the problematic opiate users. Table 5 shows that the percentage of high-threshold treatment participants has been deduced indirectly. The 18% - 95% CI: 16-20% - opiate users appearing in the hospital or police sample among the estimated population of problematic opiate users is compared to the 5% observed among the high-threshold treatment sample. This results in an estimated percentage of problematic opiate users among the high-threshold sample of 5/18 x 100% = 29% - 95% CI: 26-32%. A similar calculation among Dutch and Surinam opiate users only, leads to an estimated percentage of problematic opiate users among high-threshold treatment participants of 35% - 95% CI: 32-38%.

Coverage of the population

Data of the coverage of the problematic opiate users are presented in Table 6. Among problematic opiate users, the percentage that appeared in the police sample within three months is 16%, the percentage that appeared in the hospital sample was 2.5% and the
percentage appearing in methadone treatment is estimated to be 40%. Within three months, 50% of the problematic opiate users comes into contact with health services. If the population is limited to Dutch and Surinam opiate users, coverage by methadone treatment is higher 44% and total coverage increases to 54%.

**Discussion**

To estimate the size of the population of problematic opiate users in Amsterdam a C/RC analysis was performed using three samples of opiate users, all registered during the first three months of 1997: opiate users participating in low-threshold methadone treatment, arrested opiate users who received methadone at a police office and opiate users admitted in a hospital. The prevalence was estimated as 4130 - 95% CI: 3753-4566. A repeated analysis using the total methadone treatment sample - *both high and low-threshold* - resulted in an estimated number of 6185 - 95% CI: 5697-6786 - opiate users. Restriction of the treatment sample to high-threshold methadone treatment, resulted in a comparable estimation but larger confidence interval.

How should this difference be interpreted? If we limit the samples to the low-threshold treatment, police and hospital sample, all sampled opiate users match correctly with the population of problematic opiate users that we intend to estimate - *i.e. the fifth assumption mentioned in the introduction*. Hospitalised opiate users will have medical problems, arrested opiate users judicial problems. Opiate
users treated at the low-threshold methadone treatment of the MHS are generally unable to control their addiction. Otherwise, they would be referred to high-threshold methadone treatment and receive treatment at their GP or abstinence oriented treatment centre.

However, if the treatment sample is enlarged with opiate users participating in high-threshold treatment, the sample will partly consist of non-problematic methadone clients. We could argue that the population we intend to estimate is extended to all opiate users and therefore meet the fifth assumption too - see Figure 1. However, the population of non-problematic opiate users consists of two different populations; non-problematic heroin users outside treatment and non-problematic methadone clients inside treatment. In case non-problematic methadone clients have always used heroin without additional problems this assumption may have been met. However, many of these clients will not use heroin anymore and may be socially stabilised due to methadone treatment. Probably, they gradually turned from problematic heroin users into non-problematic methadone clients. If methadone treatment is successful, the proportion of non-problematic methadone clients will be high. As a consequence, if a C/RC-method would be applied, the number of non-problematic heroin users outside treatment appears to be higher. Most probably, this is an artefact. Although all sampled individuals are opiate users, the samples do not match correctly with the population of interest. Therefore, by using the C/RC method with the total treatment or high-threshold treatment samples, it is impossible to estimate the size of the total non-problematic and non-problematic population of opiate users and we have to limit our pronouncements to the size of the population of problematic opiate users only.

An earlier estimation of the size of the population resulted in a higher estimation than this study 5177. This estimation was based on the annual police and the annual low-threshold treatment samples of 1997 and can be considered as an overestimation. This overestimation is mainly due to the violation of the closed-population assumption; a similar two sample C/RC estimation with three months samples resulted in an estimated size of 4069 opiate users - Table 2. The estimation given in this article reflects the size of the Amsterdam population of problematic opiate users at risk to be captured by the police, admitted in a hospital or low-threshold methadone treatment. An unknown proportion of problematic opiate users residing in prison during the sample period has not been taken into account.

The validity of the estimations depends on the success on meeting the other assumptions. We were able to adjust for some dependencies by performing a three sample C/RC. The fact that all registers are constructed at the MHS facilitated matching, but may imply the risk of a positive dependency between all samples. However, hospitals and
police stations take the initiative to ask the MHS for assistance when an opiate user is admitted or arrested. The short sampling period prevented a serious violation of the closed population assumption. This is of special importance to estimate the population of opiate users including the foreign opiate users that show a higher mobility. Moreover, the small sampling period prevents a cumulating number of wrongly registered persons that can not be matched. The fourth assumption, 'registration probabilities of the samples should be homogeneous for all individuals' appears to be violated. Male problematic opiate users for example, are at higher risk of being arrested, older opiate users are at higher risk of being admitted in a hospital. However, as mentioned earlier, this kind of heterogeneity does not seem to lead to biased results.18 In epidemiology, homogeneity refers to the correct matching of the samples and the population of interest - mentioned earlier as the fifth assumption. In this study all sampled persons are 'drawn' from the referent population of problematic opiate users. If, for example, people who only used cannabis had been included in the hospital sample, the samples would be heterogeneous in the sense that some individuals belong to a different referent population. Because the other samples are limited to those who receive methadone, the cannabis users will neither appear in the treatment sample - even if they demand for treatment - nor in the police sample - even if they are arrested. As a result of this kind of heterogeneity, prevalence estimations will be severely biased.

Similarly, estimated prevalence increases if a C/RC analysis is performed with the total treatment sample. This increase is considered to be an artefact and not to refer to a broader target population. This is of major importance when a C/RC analysis is conducted in regions with one treatment centre or high-threshold treatment only. In that case additional information is needed to distinguish problematic opiate users and stabilised non-problematic opiate users in order to have a correct match between the sampled individuals and the population of interest.

The C/RC analysis is an attractive method because existing registers can be used. We had the opportunity to perform and compare various analyses. We conclude that with the registers we used it is not possible to estimate the total population of opiate users and that we have to limit our prevalence estimation to the problematic opiate users. This population, however, is the target population of a public health related measures concerning opiate users. To answer the question to what extent health services are reaching problematic opiate users we have to limit our pronouncements to the problematic opiate users as well. Among this population, 2.5% appeared in the hospital sample, 16% in the police sample and 32% is treated at the low-threshold methadone treatment of the MHS within three months. Besides, an
unknown percentage of high-threshold treatment clients is assumed to be a problematic opiate user. Based on the prevalence of hospital admissions and police arrests among these clients we estimated that 29% of them are problematic opiate users. Including these clients, forty percent of the problematic opiate users participates in methadone treatment, within three months. Coverage among the Surinam and Dutch population was higher: 44% - 95% CI: 40-48% - participates in methadone treatment. This may be explained by the policy of discouragement of Amsterdam; in order to prevent a cumulating number of foreign heroin users in Amsterdam, treatment possibilities for heroin users without a residence permit are limited. Although the estimated coverage is based on a three months period, it is high compared to other European or American cities. Therefore, we can conclude that the Amsterdam treatment programmes have succeeded in reaching a large proportion of the population of problematic opiate users of Amsterdam.

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