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Estimation of Cocaine Consumption in the Community: A Critical Comparison of the Results from Three Complimentary Techniques

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ABSTRACT

Objectives: Increases in the prevalence of cocaine use are shadowed by the growing concern to public health. A range of approaches are now available to estimate the level of drug use in the community so it is desirable to critically compare results from the differing techniques. This paper presents a comparison of the results from three methods for estimating the level of cocaine use in the general population for the purpose of validating the resulting data-set.

Design: The comparison applies to; a set of regional-scale sample survey questionnaires, a representative sample survey on drug use among drivers, and an analysis of the quantity of cocaine related metabolites in sewage.

Setting: 14,438 participants provided data for the set of regional-scale sample survey questionnaires; 2,341 drivers provided oral-fluid samples; and untreated sewage from 570,000 people was analysed for biomarkers of cocaine use. All data was collected in Oslo, Norway.

Results: 0.70 (0.36 – 1.03) % of drivers tested positive for cocaine-use which suggest a prevalence that is higher than the 0.22 (0.13 – 0.30) % (per day) figure derived from regional-scale survey questionnaires. Despite the comparatively low prevalence figure the survey questionnaires did provide estimates of the volume of consumption that are comparable with the amount of cocaine related metabolites in sewage. Per-user consumption estimates are however highlighted as a significant source of uncertainty, and the degree to which cocaine consumption in the driver-population follows the general population is an unanswered question.

Conclusions: The comparison carried out in the present study can provide an excellent means of checking the quality and accuracy of the three measurement techniques because they each approach the problem from a different viewpoint. Together the three complimentary techniques provide a well-balanced assessment of the drug-use situation in a given community and identify areas where more research is needed.

49 **ARTICLE SUMMARY**

50 **Article Focus**

51 • Estimation of the prevalence of cocaine use is important for; the assessment of the needs of public health; the

52 development of appropriate drug strategies to reduce health effects; and the subsequent monitoring of the

53 effectiveness of such strategies.

54 • It is generally accepted that there is a lack of information with respect to the dynamics and scale of illicit drug

55 markets, and the validity or reliability of estimates are questionable.

56 • This paper presents a critical comparison of the results from three different methods for estimating the level of

57 cocaine use in the general population for the purpose of validating the resulting data.

58 **Key Messages**

59 • 0.70 (0.36 – 1.03) % of drivers tested positive for cocaine use compared with 0.22 (0.13 – 0.30) % (per day)

60 as derived from regional-scale survey questionnaires.

61 • Direct comparison of prevalence estimates with the amount of drug related metabolites in sewage is difficult

62 because accurate data on per-user consumption estimates is lacking.

63 • Such a comparison as carried out here helps to identify key short-falls in the respective datasets and highlights

64 where further research is needed.

65 **Strengths and Limitations of this Study**

66 • A rigorous ecological approach to the present study would require that the comparison was based on exactly

67 the same population, and at the same time, but the logistics of sampling and the vastly different time-scales

68 involved in each of the three techniques make this difficult.

69 • No similar comparisons of the three drug epidemiology techniques have been carried out before so it is

70 difficult to relate the present findings to other study populations.

71

1. Introduction

Cocaine is the second most commonly used illicit drug in Europe and the United States, and use of the drug is associated with numerous health problems including cardiovascular disorders, neurological impairment and death [1]. Increases in the prevalence of cocaine use over recent years are shadowed by the growing concern to public health, so quantification and the estimation of the prevalence of cocaine use are important for assessing the needs of public health, developing appropriate drug strategies to reduce health effects, and in the subsequent monitoring of the effectiveness of such strategies. It is generally accepted that there is a lack of information with respect to the dynamics and scale of illicit drug markets, and the validity or reliability of estimates are questionable [2]. The estimation of drug use patterns in society is currently reliant on questionnaire based data-collection at the population level, and among groups of drug users, together with statistics from hospital admissions, registered drug-overdose deaths, treatment services and the records from police seizures [3–8]. Validation of drug use statistics derived from individual self-reporting has previously been attempted by drawing comparisons between the self-reported use and measurements of samples taken from hair, urine and blood [9–13]. This technique has shown that despite the use of an array of methods to increase the level of accuracy of self-reporting, under-reporting is still apparent. Recently, additional data on the level of drug use at the community level have also been acquired through the implementation of anonymous road-side testing studies [14,15], and also through the measurement of drug metabolites in sewage water [16–22]. With a range of different approaches now available to estimate the level of community drug use it is highly desirable to critically compare the results they provide. For the first time this paper presents a critical comparison of the results from three different methods for estimating the level of cocaine use in the general population for the purpose of validating the resulting data-set. The comparison was performed on three studies in Oslo, Norway and applies to; a combination of user group and representative population sample survey questionnaires, a representative sample survey on drug use measured in saliva among drivers, and an analysis of the quantity of drugs and drug related metabolites in sewage.

2. Materials and Methods

2.1. Background - Cocaine Use in Norway

Life time prevalence of cocaine use in the general population 15 years and over was reported as 2.7 percent in 2004 and 2.5 percent in 2009 [23]. Results from both these studies (combined) show the prevalence of recent cocaine use (within the last year) in the total population was as low as 0.6 percent. A separate study on young adults (21-30 years)

100 [24] reports higher rates of cocaine use in these age groups: prevalence of use within the last 6-months was 4.3 percent

101 in 2002 and 4.9 percent in 2006.

102 Cocaine use in Norway is dominated by recreational intranasal use. Crack use has been rare. Among young adult

103 cocaine users less than one in a hundred reported crack use and crack is seldom seized by the police/customs. A

104 survey among the prison population [25] identified 6 percent of inmates report daily or almost daily use of cocaine in

105 the 6 months leading up to imprisonment, but frequent cocaine use is lower among marginalized and injecting drug

106 user groups [26].

107 Purity of cocaine will vary from batch to batch, by place of production, and by level of sale (such as street-level or

108 whole-sale market level). The purity of cocaine in Norway is measured in conjunction with seizures of the drug by the

109 police and customs. Data from the period 2007 – 2009 shows a trend of decreasing purity over time; lately 39% in

110 2007 compared to 25% in 2009 [27]. This degree of variation is consistent with data from other nations [28–31].

2.2. Methodology for the survey of drug-use amongst the driver population

112 Data collection was performed in the greater Oslo area in cooperation with two National Mobile Police Service (MPS)

113 districts from April 2008 to March 2009 as part of the DRUID Project [32]. Drivers of motor vehicles were selected

114 using a stratified two-stage cluster sampling procedure. In the first stage, random road sites and time intervals were

115 selected according to a table of random sampling numbers [33] which covered all days and times of the week and all

116 seasons of the year. Sampling periods of 5 consecutive days were first selected. Roads were then chosen by randomly

117 selecting map co-ordinates, then choosing the closest roads. For each day, two consecutive two-hour periods were

118 randomly selected for sample collection at two different road sites. The MPS then selected the exact time and place

119 allowing for practical considerations (e.g., choosing sites suitable as checkpoints, and ensuring a driving time of less

120 than 40 minutes between consecutive checkpoint sites). If the chosen time intervals did not comply with working hour

121 regulations for police officers; the intervals had to be cancelled and replaced by new intervals as close as possible to

122 the original interval.

123 The second stage consisted of randomly stopping drivers within the defined two hour period. The number of data

124 collection personnel was related to the expected traffic density. When the data collection personnel were ready for a

125 new driver, the MPS stopped the first approaching car or motorcycle and carried out their own routine controls (e.g.,

126 breath alcohol testing or driver's licence control). Afterwards the drivers were asked to proceed to the study team, who

6

127 requested voluntary and anonymous participation in the project. Oral and written information about the project was

128 given to each driver. If informed consent was given, a sample of oral fluid was collected and the following data

129 recorded: gender, age, day of the week, time interval, and geographical site. In general, the sampling procedure was

130 designed in a way that should ensure that the drivers rendering samples should give a representative picture of the total

131 driver population. Saliva samples were collected using the Statsure Saliva Sampler (Saliva Diagnostic Systems,

132 Framingham, MA, USA). The saliva collection pad was placed under the tongue until the indicator turned blue, or

133 until five minutes has passed and transferred to a capped vial labelled with a bar code label corresponding to the bar

134 code of the questionnaire. The sample was kept in a plastic bag at a temperature of approximately 5°C for a maximum

135 of 6 hours, and then stored at -20°C.

136 Concentrations of cocaine and benzoylecgonine in oral fluid-buffer mixtures were determined by liquid

137 chromatography – tandem mass spectrometry [34] and concentrations in un-diluted oral fluid were calculated. The

138 cut-off thresholds in oral fluid-buffer mixture were 0.9 and 3.6 ng/mL for cocaine and benzoylecgonine, respectively.

139 The combined prevalence of cocaine or benzoylecgonine was estimated by a weighted average, using weights adjusted

140 for under- or over-sampling of the data compared to overall population statistics [35]. This weighting took into

141 account the age and gender of drivers with respect to the general population, together with an appropriate weighting

142 for the days of the week and time of the day (Table 2).

2.3. Methodology for the analysis of drugs and related metabolites is sewage

144 Sample collection was carried out in the greater Oslo area in cooperation with the region's largest sewage treatment

145 plant (Vestfjorden Avløpselskap). This plant processes sewage from a metropolitan and suburban population of

146 approximately 500 000 people. An Isco 6712 portable automatic wastewater sampler (Teledyne, Nebraska USA) was

147 used to collect 6-hour time-proportional composite sewage effluent samples (total volume 1000 mL), continuously

148 throughout the course of September 2009. Deuterated internal standards were spiked at the time of collection (1mL of

149 benzoylecgonine-d3, cocaine-d3, cocaethylene-d8, methamphetamine-d5, metoprolol acid-d5 and ceterizine-d8 at 50

150 ng/mL to give a final working concentration of 50 ng/L of each standard in sewage) and samples were stored at 4°C

151 until analysis.

152   Concentrations of cocaine and benzoylecgonine in the sewage water composites were determined by liquid

153   chromatography – tandem mass spectrometry [21]. The limit of quantification for the analytes in raw sewage was 5

154   ng/L.

155   Careful consideration of the urinary excretion rates of cocaine and its metabolites allows for back-calculation of the

156   total mass of cocaine consumed during the sampling period. Benzoylecgonine is the primary urinary metabolite of

157   cocaine and accounts for 30 (15 – 45) percent of the recoverable dose in urine [36–40] so it is assumed that the total

158   mass of benzoylecgonine in the sewage accounts for 30 percent of the total mass of cocaine consumed by the

159   community group. (Note that cocaine use in Norway is dominated by intranasal administration so the

160   pharmacokinetic parameters used in this study are focused on this route of administration). The total mass of

161   benzoylegonine passing through the sewage treatment processes in the Oslo region over the sampling period was

162   calculated by scaling the measured sewage concentration of the metabolite (ng/L) by the total volume of sewage

163   treated (L). The resulting mass-transport rate of benzoylecgonine (g / week) was then multiplied by the factor 3.5

164   (which accounts for the 30 % excretion rate, and the molar-ratio of cocaine to benzoylecgonine) to give the total mass

165   of consumed cocaine (g/week, or g/month).

2.4. Combined Population and User-Group Survey Methodology

167   The population of cocaine users was divided into two groups; socially integrated individuals (experimental,

168   recreational and heavy users), and marginalized individuals (light, medium or heavy users). The two groups were

169   reached by differing survey-types [41–44]. Data on the socially integrated users was acquired in three different

170   population surveys, each for a different age segment, and averaged over two or three survey years to increase N and

171   reduce statistical uncertainty (Table 1). Data on marginalized users was collected from surveys of prison inmates and

172   the Oslo homeless or street population attending a needle exchange. Note that the estimated number of marginalized

173   cocaine users was reduced to 80 percent of the sum from the two surveys because of a likely overlap between the

174   prison and the street population. Population rates were based on the general population aged 15-64 years provided by

175   government statistics correct to 31 December 2009 [35].

176   A "bottom up" method was used to estimate community cocaine use in Oslo. This method multiplies the number of

177   users by the reported frequency of use and reported amount (mass) of cocaine used [45–48]. Frequency was

178   established from the surveys (Table 1) while average values of amounts were based on self-report (last survey in Table

8

179 1) and existing literature (39). The amount varied with frequency of use such that the higher the frequency the higher

180 the dose (see Table 3).

181 Estimates of the prevalence of cocaine use derived from the survey among the driving population provides data on

182 cocaine use within a short period of time (within the last 24 hours). The combined survey method, however, acquires

183 data on the prevalence of consumption within the last 12 months. To be able to compare the roadside and the

184 combined survey method, the prevalence of use on a single day was estimated based on the frequency of use.

185 Frequency of use, measured as the number of days used in a year, yields the probability of use on a single day for each

186 level of frequency (see Table 3). This probability, multiplied by the number of users in the frequency group, yields the

187 expected number of users on a single day. Summing up expected number of daily users over frequency groups and

188 diving by the population figure yields the prevalence of users per day.

189 **3. Results**

190 ### *3.1. Survey of drug-use amongst the driver population*

191 Cocaine was detected in 14 out of 2341 samples from the greater Oslo area, and benzoylecgonine was detected in 9

192 samples, none were positive for benzoylecgonine only. Therefore, only the results for cocaine were used in the

193 estimations below. A weighted average of 0.7% of the driver population was found to be positive for cocaine using the

194 weights presented in Table 2.

195 The concentration of cocaine and benzoylecgonine in oral fluid depends on the dilution of oral fluid during sampling

196 and the recovery from the sampling device. For the samples found to be positive for cocaine, the average collection

197 volume of oral fluid was 0.74 ml, giving an average dilution of 1:2.4. A recovery for cocaine of 85.6% has been

198 reported [49]. Thus, the analytical cut-off corresponded to a cocaine concentration of 2.5 ng/ml in native (undiluted)

199 oral fluid.

200 ### *3.2. Results of the analysis of drugs and related metabolites is sewage*

201 Benzoylecgonine (the urinary metabolite of cocaine) was detected in all sewage samples collected in the Oslo region.

202 Measurements of the flow of this cocaine metabolite in sewage indicate an average load of 428 g/week (CV= 0.07, n =

203 4 weeks). Benzoylecgonine recovered in urine accounts for 30 (15 – 45) % of the initial cocaine dose, so the

204 measured mass of this metabolite in the sewage is equivalent to 30 % of the total mass of cocaine consumed by the

205 community group. The measured flow of benzoylecgonine in the Oslo sewage system is therefore indicative of a

206 community-wide cocaine consumption rate of 1498 (997 – 2992) g/week (pure cocaine) which is equivalent to 78 (52

207 – 156) kg/year if we assume the rate of cocaine consumption remains constant throughout the year.

3.3. Combined population and user-group survey results

209 Socially integrated users (aged 15-64 years) in Oslo reporting at least one instance of cocaine use in the last 12 months

210 constituted 2.7 % (CI 2.4-3.1) of the total population (15-64 years) in Oslo. Proportions were highest in the age

211 groups 20 to 24 years (4.0 – 7.6 %). Marginalized cocaine users in Oslo constitute an additional 0.2 % (CI 0.0-0.4) of

212 the total population (15-64 years), so the proportion of the total population that admits at least one instance of cocaine

213 use in the last 12 months is 2.9 % (CI 2.6-3.2) in Oslo.

214 An estimated 0.22 (CI 0.13-0.30) % of the population (15-64 years) use cocaine on a given day in Oslo.

215 Approximately 80 % of self-reported cocaine users (aged 15-64 years) used cocaine less than 10 times per year. The

216 remaining proportion of the user population (20 %) have taken more cocaine more frequently and are subsequently

217 responsible for in excess of 90% of the total daily cocaine consumption (g/day). In terms of user-group population,

218 the vast majority (73 %) of cocaine was consumed by the socially integrated population, while marginalized users

219 (including injecting drug users and prison inmates) consumed 27 % of the total.

3.4. Comparison of Results

221 The three methods provide two distinct measures of cocaine use; the prevalence of cocaine use in terms of the

222 proportion of the community that use the drug, and a quantitative measure (mass) of the total amount of cocaine that is

223 consumed by the entire community.

224 Comparison of the prevalence estimates derived from the combined population survey (0.22 (0.13 – 0.30) % per day)

225 and the road-side testing (0.70 (0.36 – 1.03) %) indicates that under reporting and possible under-representation of

226 users is apparent within the combined population surveys.

227 The combined population survey also provided an estimate for the total amount of cocaine that is consumed which can

228 be directly compared with the results of sewage measurements (Table 4). The estimated annual consumption rate

229 from the combined population survey (117 (70 – 165) kg/year, pure cocaine) is perhaps slightly higher than the 78 (52

230 – 156) kg/year figure from measurements of cocaine metabolites in sewage. The confidence intervals for these figures

231 are large however, and it cannot be concluded that they are different.

232 With this data it is also possible to calculate an estimated per-user consumption rate by combining the annual

233 prevalence of cocaine use (2.9 %) with the measured annual consumption from the sewage (78 kg/year). Such

234 analysis implies a per-user cocaine consumption rate of 6.5 (3.5 – 9.6) g/user/year (pure cocaine). For comparison, a

235 per-user consumption estimate of 30.2 g/year from The United Nations Office on Drugs and Crime [50] was also

236 applied (to Table 4), but it is immediately apparent that this UNODC consumption estimate does not fit well with the

237 measured results of the present study. If 2.9 % of the population used an average of 30.2 g/user/year then the

238 measured mass of cocaine metabolites in sewage would equate to a combined (city-wide) consumption of 361 (321 –

239 401) kg/year. This is far in excess of the measured value. Similarly, dividing the measured annual city-wide

240 consumption (kg/year) provided by analysis of sewage by the UNODC per-user consumption rate would imply an

241 annual prevalence of 0.6 (0.4 – 2.7) % which is again not in agreement with the measured results.

242 **4. Discussion**

243 A comparison was performed on three independent methods for estimating the use of cocaine in Oslo, Norway. The

244 comparison applies to; a combined sample survey questionnaire approach, a representative sample survey on drug use

245 among drivers, and a survey of the mass of cocaine-related metabolites in sewage. The estimated prevalence of use on

246 a single day was higher in the survey among drivers than using the combined survey approach, while the estimated

247 amount used (mass) in the latter was not significantly different than in the sewage approach.

248 The comparison identified a higher prevalence of cocaine use in the representative sample survey among drivers than

249 in the combined sample survey questionnaire approach. Under-reporting is not unexpected in the survey

250 questionnaires because the subject was drug use and the level of response was low, but this discrepancy may be even

251 larger than is immediately apparent from the present study. Firstly, marginalised drug users were included in the

252 combined population survey but they are far less likely to own or drive motor vehicles and therefore less likely to be

253 detected in the road-side testing surveys. Secondly, the detection time for cocaine in oral fluid depends upon the

254 analytical cut-off, sampling method, method of cocaine administration, dose used, acute or chronic cocaine use, and

255 other factors. In controlled studies of administration of 25-45 mg cocaine by intravenous injection, snorting or

256 smoking, cocaine was detected in oral fluid for more than 12 hours in only about 25% of the experiments [51,52].

11

257   However, cocaine may be detected in oral fluid from chronic cocaine users for up to 118 hours after last dose in

258   extreme cases [53]. Finally, the measured prevalence (0.7 %) of cocaine or metabolites in the oral fluid of drivers is

259   also considered a minimum because it is expected that many cocaine users refrain from driving for some hours after

260   cocaine administration, and further, approximately 10% of drivers declined to participate in the study. It is possible

261   that the group of drivers that refused to offer a saliva sample have a higher prevalence of recent drug consumption

262   than that of drivers who volunteered a sample.

263   Interestingly although the combined population survey appears to underestimate the prevalence of cocaine use, this

264   method did result in a combined consumption estimate (kg/year) that was not significantly different to the results of

265   sewage analysis. This may mean that self-reported amounts of cocaine used were actually too high, but it is important

266   to remember that the accuracy of the sewage estimate is strongly affected by the accuracy of the clinical

267   pharmacokinetic data on cocaine. The present study used the pharmacokinetic parameters that apply for intra-nasal

268   cocaine use because this is the most relevant for study population. This implies that a degree of back-ground

269   information from combined population surveys with regard to the proportion of differing routes of administration are

270   required before accurate sewage measurements are feasible. For example, the use of the intra-nasal pharmacokinetic

271   parameters would not be appropriate if the study was carried out in a region with extensive crack-cocaine use as the

272   excretion patterns differ for differing routes of administration.

273   No similar comparisons of the three drug epidemiology techniques have been carried out before so it is difficult to

274   relate the present findings to other study populations. It was however necessary, with the present study, to make some

275   general assumptions with regard to the average amount of cocaine used per individual in order to adequately compare

276   the prevalence estimates with that of the measured mass of cocaine metabolites in sewage. The combined population

277   surveys indicated an average per-user consumption rate of 9.8 g/user/year (pure cocaine) which is much lower than the

278   30.2 g/user/year (in Europe) proposed by The United Nations Office on Drugs and Crime (2010). While it is possible

279   that the average per-user consumption rate in Oslo may actually be lower than in the areas included in the UNODC

280   estimate, the UNODC does state that their estimate is a considerable approximation as little or no data on the

281   quantities consumed by individuals is available, and much of the existing data is contradictory [54]. Similar concerns

282   were also expressed in the report on Drug Availability Estimates in the United States [55] in which the authors note

283   that the figures rely on "manipulating a number of estimated variables which themselves require acceptance of some

284   heroic assumptions and are subject to substantial margins of error".

285 The UNODC defines the lack of information on the per-capita consumption of illegal drugs as the largest constraint

286 with respect to the interpretation of international drug markets [54], but the results of the present study do strongly

287 suggest that combining accurate measurements of the total drug consumption in the population (via sewage analysis)

288 with reliable prevalence figures acquired through rigorous survey of the population could provide a significant

289 improvements in the accuracy of average per-user consumption figures in the future.

290 The comparison carried out in the present study has provided an excellent means for checking the quality and

291 accuracy of each the three measurement techniques because they each approach the problem from different angels.

292 The results do however highlight the difficulties associated with performing such a comparison. A rigorous ecological

293 approach to the present study would require that the comparison was based on exactly the same population, and at the

294 same time, but the logistics of sampling and the vastly different time-scales involved in each of the three techniques

295 make this difficult. It is possible, for example, that the population of drivers that took part in the road-side study

296 included individuals that were in transit and therefor from outside the region covered by the combined population

297 survey. Similarly, results of the sewage analysis are based on a one-month period and an assumption is made that

298 combined cocaine use (by the total population) remains relatively constant throughout the year. These problems do

299 however allow more precise research questions to be formulated: How can we better combine surveys to better cover

300 all segments of the population? Does cocaine use in the population of drivers follow the same pattern as cocaine use

301 in the general population? How can we better estimate the amounts used? How can we better estimate frequency of

302 use? Short-falls have been identified in each of the three epidemiology techniques when used in isolation, but together

303 the three complimentary techniques provide a well-balanced assessment of the drug-use situation in a given

304 community with limited reliance on derived estimates.

5. Conclusion

306 Under-reporting is apparent in prevalence estimates provided by the combined population surveys when compared

307 with the proportion of motor-vehicle drivers with detectable levels of cocaine or cocaine metabolites in oral-fluid, but

308 an unanswered question is whether cocaine use in the population of drivers follows the same pattern as cocaine use in

309 the general population. Direct measurements of sewage from a defined population provide data on the size of the

310 cocaine market in a particular region (with some uncertainty). These measurements indicate that self-reported cocaine

311 consumption may be over-exaggerated and highlight the large degree of uncertainty with respect to per-user

312 consumption estimates. Each of the three techniques has significant short-falls when used in isolation, but together

313 they deliver complimentary data which provides a well-balanced assessment of the drug-use situation in a given

314 community and identify areas where more research is needed.

Acknowledgements

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Table 1. Combined population and user group survey parameters including study population, study dates and sample size.

Target Population	Survey Year	Type of survey	Sample Size (n=)	Publication
15 – 20 years, Oslo [1]	2006, 2007, 2008	Postal	5104	(Vedøy and Skretting, 2009)
21 – 30 years, Oslo [2]	2006, 2010	Postal	3468	(Lund et al., 2007)
31 – 64 years, Oslo [3]	2004, 2009	Questionnaire completed in private	899	(Nordlund, 2010)
Prison Inmates, Norway (national, applied to Oslo) [4]	2002	Questionnaire completed in private	1093	(Odegard, 2008)
Injecting drug users, Oslo [3]	2000-2004	Face to face	3829	(Bretteville-Jensen and Amundsen, 2009)
Marginalized Users, Arendal [3]	2010	Face to face	45	Unpublished pilot

Response rates: [1] 35 percent, [2] 40-50 percent, [3] not recorded or applicable, [4] 41 percent.

Table 2. Weights for under- or over-sampling associated with the road-side saliva study.

Characteristics	Distribution among drivers (%)	Distribution in the total population of Oslo (%)	Weight
Age (years)			
16-24	9.4	10.6	1.13
25-34	18.1	20.9	1.15
35-44	24.3	16.2	0.67
45-54	21.4	12.2	0.57
55-64	16.4	10.2	0.62
65+	10.4	11.7	1.13
Total	100.0	81.8	-
Gender			
Female	29.8	50.6	1.70
Male	70.2	49.4	0.70
Total	100.0	100.0	-
Day of the week			
Mon-Thu	48.0	57.1	1.19
Fri	8.6	14.3	1.66
Sat	31.0	14.3	0.46
Sun	12.4	14.3	1.15
Total	100.0	100.0	-
Time of day (h)			
00.00-05.59	3.4	25.0	7.35
06.00-11.59	30.1	25.0	0.83
12.00-17.59	43.0	25.0	0.58
18.00-23.59	23.5	25.0	1.06
Total	100.0	100.0	-

Table 3. Parameters for combined survey method estimates of community cocaine consumption: Self-reported frequency of use categories with the resulting number of usage-days per unit time, the probability of use on a given day[1], the estimated proportion of users in the total survey population, frequency of use in terms of the prevalence of differing usage rates amongst the user population, and average self-reported weekly consumption

Survey - Population 15-30 years

Frequency of use categories for Self-report (per half year)	Never	1-4 times	5-10 times	11-25 times	25-50 times	50+ times	Total/average (CI)
Frequency of use parameter for subsequent calculations (usage-days per half year)	0	2.5	7.5	18	38	116.5	-
Probability of use on any given day (%)	0	1.4	4.1	9.9	20.8	63.7	-
Distribution of frequency of use among total age-group population (%)	95.3 (94.8-95.7)	3.0	0.9	0.4	0.2	0.2	100
Distribution of frequency of use among users (%)	-	63	20	9	4	5	100
Average per-user consumption, mg (pure) / week	-	6	43	156	585	2240	154 (71-237)

Survey - Population 31-64 years

Frequency of use categories for Self-report (per year)	Never	1-4 times	Monthly	Weekly	Daily, almost daily	Total/average (CI)
Frequency of use parameter for subsequent calculations (Usage-days per year)[2]	0	2.5	12	52	182.5	-
Probability of use on any given day (%)	0	0.7	3.3	14.8	50.0	-
Distribution of frequency of use among total age-group population (%)	98.3 (97.2-99.4)	0.9	0.5	0.3	0.1	100
Distribution of frequency of use among users (%)	-	50	30	15	5	100
Average per-user consumption, mg (pure) / week	-	4	42	270	2106	160 (37-283)

Survey - Prison population

Frequency of use categories for Self-report (per half year prior to incarceration)	Never	1-3 times per month or less	Weekly	Daily, almost daily	Total/average (CI)
Frequency of use parameter for subsequent calculations (Usage-days per year)[2]	0	12	52	182.5	-
Probability of use on any given day (%)	0	3.3	14.2	50.0	-
Distribution of frequency of use proportional to total population 15-64 years (%)	99.9 (99.7-100)	0.06	0.03	0.01	100
Distribution of frequency of use among user-group (%)	-	63	23	13	100
Average per-user consumption, mg (pure) / week	-	138	900	3510	767 (487-1048)

Survey - Injectors/marginalized users

Frequency of use categories for Self-report (per year)	Never	Less than once a month	Monthly	Weekly	Daily, almost daily	Total/average (CI)
Frequency of use parameter for subsequent calculations (Usage-days per year)[2]	0	6	12	52	182.5	-
Probability of use on any given day (%)	0	1.6	3.3	14.2	50.0	-
Distribution of frequency of use proportional to total population 15-64 years (%)	99.9 (99.6-100)	0.06	0.01	0.01	0.02	100
Distribution of frequency of use among user-group (%)	-	55	12	12	21	100
Average per-user consumption, mg (pure) / week	-	21	42	270	2106	491 (217-765)

[1] Defined as a usage-day or a single 24-hour period in which cocaine is consumed.
[2] Assumes 6 usage-months per year

Table 4. Prevalence and scale of cocaine use in Oslo as determined by combined population surveys and measurements of a cocaine metabolite in sewage. (Direct measurements or estimates in **bold**. Derived estimates in *italics*).

Method	*Annual Prevalence % (CI)* [a]	*Cocaine Consumption (Pure)*	
		Per-user g/year (CI)	*Total population kg/year (CI)*
Combined Population Survey (CPS)			
Per-user consumption from CPS	**2.9 (2.6 – 3.2)**	9.8 (5.6 – 14.1)	*117 (70 – 165)*
Per-user consumption from UNODC	**2.9 (2.6 – 3.2)**	30.2	*361 (321 – 401)* [b]
Sewage Analysis			
Prevalence from CPS	**2.9 (2.6 – 3.2)**	*6.5 (3.5 – 9.6)*	**78 (52 – 156)**
Per-user consumption from CPS	*1.9 (1.4 – 3.4)*	9.8 (5.6 – 14.1)	**78 (52 – 156)**
Per-user consumption from UNODC	*0.6 (0.4 – 2.7)* [c]	30.2	**78 (52 – 156)**

[a] Population 15 – 64 years of age, 410 000 (source Statistics Norway)

[b] CI from uncertainty in prevalence only

[c] CI from uncertainty in sewage estimate of total cocaine consumption (kg/year) only

Estimation of Cocaine Consumption in the Community: A Critical Comparison of the Results from Three Complimentary Techniques

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Estimation of Cocaine Consumption in the Community: A Critical Comparison of the Results from Three Complimentary Techniques

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ABSTRACT

Objectives: Increases in the prevalence of cocaine use are shadowed by the growing concern to public health. A range of approaches are now available to estimate the level of drug use in the community so it is desirable to critically compare results from the differing techniques. This paper presents a comparison of the results from three methods for estimating the level of cocaine use in the general population.

Design: The comparison applies to; a set of regional-scale sample survey questionnaires, a representative sample survey on drug use among drivers, and an analysis of the quantity of cocaine related metabolites in sewage.

Setting: 14,438 participants provided data for the set of regional-scale sample survey questionnaires; 2,341 drivers provided oral-fluid samples; and untreated sewage from 570,000 people was analysed for biomarkers of cocaine use. All data was collected in Oslo, Norway.

Results: 0.70 (0.36 – 1.03) % of drivers tested positive for cocaine-use which suggest a prevalence that is higher than the 0.22 (0.13 – 0.30) % (per day) figure derived from regional-scale survey questionnaires. Despite the comparatively low prevalence figure the survey questionnaires did provide estimates of the volume of consumption that are comparable with the amount of cocaine related metabolites in sewage. Per-user consumption estimates are however highlighted as a significant source of uncertainty, and the degree to which cocaine consumption in the driver-population follows the general population is an unanswered question.

Conclusions: The comparison carried out in the present study can provide an excellent means of checking the quality and accuracy of the three measurement techniques because they each approach the problem from a different viewpoint. Together the three complimentary techniques provide a well-balanced assessment of the drug-use situation in a given community and identify areas where more research is needed.

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50 **ARTICLE SUMMARY**

51 **Article Focus**

52 • Estimation of the prevalence of cocaine use is important for; the assessment of the needs of public health; the

53   development of appropriate drug strategies to reduce health effects; and the subsequent monitoring of the

54   effectiveness of such strategies.

55 • It is generally accepted that there is a lack of information with respect to the dynamics and scale of illicit drug

56   markets, and the validity or reliability of estimates are questionable.

57 • This paper presents a critical comparison of the results from three different methods for estimating the level of

58   cocaine use in the general population.

59 **Key Messages**

60 • 0.70 (0.36 – 1.03) % of drivers tested positive for cocaine use compared with 0.22 (0.13 – 0.30) % (per day)

61   as derived from regional-scale survey questionnaires.

62 • Direct comparison of prevalence estimates with the amount of drug related metabolites in sewage is difficult

63   because accurate data on per-user consumption estimates is lacking.

64 • Such a comparison as carried out here helps to identify key short-falls in the respective datasets and highlights

65   where further research is needed.

66 **Strengths and Limitations of this Study**

67 • A rigorous ecological approach to the present study would require that the comparison was based on exactly

68   the same population, and at the same time, but the logistics of sampling and the vastly different time-scales

69   involved in each of the three techniques make this difficult.

70 • No similar comparisons of the three drug epidemiology techniques have been carried out before so it is

71   difficult to relate the present findings to other study populations.

72

1. Introduction

Cocaine is the second most commonly used illicit drug in Europe and the United States, and use of the drug is associated with numerous health problems including cardiovascular disorders, neurological impairment and death [1]. Increases in the prevalence of cocaine use over recent years are shadowed by the growing concern to public health, so quantification and the estimation of the prevalence of cocaine use are important for assessing the needs of public health, developing appropriate drug strategies to reduce health effects, and in the subsequent monitoring of the effectiveness of such strategies. It is generally accepted that there is a lack of information with respect to the dynamics and scale of illicit drug markets, and the validity or reliability of estimates are questionable [2]. The estimation of drug use patterns in society is currently reliant on questionnaire based data-collection at the population level, and among groups of drug users, together with statistics from hospital admissions, registered drug-overdose deaths, treatment services and the records from police seizures [3–7]. Validation of drug use statistics derived from individual self-reporting has previously been attempted by drawing comparisons between the self-reported use and measurements of samples taken from hair, urine and blood [8–12]. This technique has shown that despite the use of an array of methods to increase the level of accuracy of self-reporting, under-reporting is still apparent. Recently, additional data on the level of drug use at the community level have also been acquired through the implementation of anonymous road-side testing studies [13,14], and also through the measurement of drug metabolites in sewage water [15–20]. With a range of different approaches now available to estimate the level of community drug use it is highly desirable to critically compare the results they provide. For the first time this paper presents a critical comparison of the results from three different methods for estimating the level of cocaine use in the general population. The comparison was performed on three studies in Oslo, Norway and applies to; a combination of user group and representative population sample survey questionnaires, a representative sample survey on drug use measured in saliva among drivers, and an analysis of the quantity of drugs and drug related metabolites in sewage.

2. Materials and Methods

2.1. Background - Cocaine Use in Norway

Life time prevalence of cocaine use in the general population 15 years and over was reported as 2.7 percent in 2004 and 2.5 percent in 2009 [21]. Results from both these studies (combined) show that the prevalence of recent cocaine use (within the last year) in the total population was as low as 0.6 percent. A separate study on young adults (21-30 years) [22] reports higher rates of cocaine use in these age groups: prevalence of use within the last 6-months was 4.3

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101   percent in 2002 and 4.9 percent in 2006. Also, lifetime prevalence of cocaine use among young people (15 - 20 years)

102   in Oslo has remained very stable in the years 2003 to 2008.

103   Cocaine use in Norway is dominated by recreational intranasal use. Crack use has been rare. Among young adult

104   cocaine users less than one in a hundred reported crack use and crack is seldom seized by the police/customs. A

105   survey among the prison population [23] identified 6 percent of inmates report daily or almost daily use of cocaine in

106   the 6 months leading up to imprisonment, but frequent cocaine use is lower among marginalized and injecting drug

107   user groups [24].

108   Purity of cocaine will vary from batch to batch, by place of production, and by level of sale (such as street-level or

109   whole-sale market level). The purity of cocaine in Norway is measured in conjunction with seizures of the drug by the

110   police and customs. Data from the period 2007 – 2009 shows a trend of decreasing purity over time; lately 39% in

111   2007 compared to 25% in 2009 [25]. This degree of variation is consistent with data from other nations [26–29].

2.2. Methodology for the survey of drug-use amongst the driver population

113   Data collection was performed in the greater Oslo area in cooperation with two National Mobile Police Service (MPS)

114   districts from April 2008 to March 2009 as part of the DRUID Project [30]. Drivers of motor vehicles were selected

115   using a stratified two-stage cluster sampling procedure. In the first stage, random geographical areas and time periods

116   of five consecutive days were selected using a table of random sampling numbers [31]. All days and times of the week

117   and all seasons of the year were covered. Roads were chosen by randomly selecting map co-ordinates, then choosing

118   the closest roads. For each day the police selected two study sites along the chosen roads. The sites had to be suitable

119   as checkpoints (possibility to stop a number of cars at the same time on the roadside without causing traffic

120   congestion) and they had to be located within about 30-45 minutes' drive from each other. For each day, the starting

121   time for roadside sampling was also randomly selected. However, a few of the selected time periods had to be changed

122   to comply with working time regulations for police officers.

123   The second stage of the sampling procedure consisted of randomly stopping drivers within the defined two hour

124   period. The police officers were instructed to stop cars at random, rather than stopping old cars, young drivers or other

125   possible suspects of impaired driving. The number of data collection personnel at each site was related to the expected

126   traffic density. When one of the data collection personnel were ready for a new driver, the MPS stopped the first

127   approaching car or motorcycle and carried out their own routine controls (breath alcohol testing or driver's licence

128 control). Afterwards the driver was asked to proceed to the study team, who requested voluntary and anonymous

129 participation in the project. Oral and written information about the project was given to each driver. If verbal informed

130 consent was given, a sample of oral fluid was collected and the following data recorded: gender, age, day of the week,

131 time interval, and geographical site. It was thus impossible to trace a given sample to a specific donor or motor

132 vehicle. In general, the sampling procedure was designed in a way that should ensure that the drivers rendering

133 samples should give a representative picture of the total driver population. Saliva samples were collected using the

134 Statsure Saliva Sampler (Saliva Diagnostic Systems, Framingham, MA, USA). The saliva collection pad was placed

135 under the tongue until the indicator turned blue, or until five minutes has passed and transferred to a capped vial

136 labelled with a bar code label corresponding to the bar code of the questionnaire. The sample was kept in a plastic bag

137 at a temperature of approximately 5°C for a maximum of 6 hours, and then stored at -20°C.

138 Concentrations of cocaine and benzoylecgonine in oral fluid-buffer mixtures were determined by liquid

139 chromatography – tandem mass spectrometry [32], which specifically measured the substances in question. The

140 amount of collected oral fluid was determined by weighing the sample, and concentrations of substances in un-diluted

141 oral fluid were calculated. The cut-off thresholds in oral fluid-buffer mixture were 0.9 and 3.6 ng/mL for cocaine and

142 benzoylecgonine, respectively. The combined prevalence of cocaine or benzoylecgonine was estimated by a weighted

143 average, using weights adjusted for under- or over-sampling of the data compared to overall population statistics [33].

144 This weighting took into account the age and gender of drivers with respect to the general population, together with an

145 appropriate weighting for the days of the week and time of the day (Table 2).

2.3. Methodology for the analysis of drugs and related metabolites in sewage

147 Sample collection was carried out in the greater Oslo area in cooperation with the region's largest sewage treatment

148 plant (Vestfjorden Avløpselskap). This plant processes sewage from a metropolitan and suburban population of

149 approximately 570 000 people. An Isco 6712 portable automatic sampler (Teledyne, Nebraska USA) was used to

150 collect samples of wastewater every hour throughout the course of September 2009. The hourly samples were pooled

151 to produce 6-hour composites (n = 120) with mid-points corresponding to 2 am, 8 am, 2 pm and 8 pm for each day of

152 the month. Deuterated internal standards were spiked at the time of collection (1mL of benzoylecgonine-d3, cocaine-

153 d3, cocaethylene-d8, methamphetamine-d5, metoprolol acid-d5 and ceterizine-d8 at 50 ng/mL to give a final working

154 concentration of 50 ng/L of each standard in sewage) and samples were acid stabilised and stored at 4°C until analysis.

7

155 Concentrations of cocaine and benzoylecgonine in the sewage water composites were determined by liquid

156 chromatography – tandem mass spectrometry [18]. The limit of quantification for the analytes in raw sewage was 5

157 ng/L.

158 The total mass of benzoylegonine passing through the sewage treatment processes in the Oslo region over the

159 sampling period was calculated by scaling the measured sewage concentration of the metabolite (ng/L) in each of the

160 120 samples (each representing 6-hours of sewage) by the total volume of sewage (L) for that 6-hour period. The

161 uncertainty with this estimate is associated with errors in sampling (5% RSD), flow measurements (1% RSD),

162 chemical analysis (5% RSD) and biotransformation of cocaine and benzoylecgonine in the sewer system which is

163 typically less than 10 % [34,35].

164 Careful consideration of the urinary excretion rates of cocaine and its metabolites are then needed for back-calculation

165 of the total mass of cocaine consumed during the sampling period. Benzoylecgonine is the primary urinary metabolite

166 of cocaine and accounts for 30.8±7.7 % of the recoverable dose of nasally insufflated cocaine in urine [36]. (Note that

167 cocaine use in Norway is dominated by intranasal administration so the pharmacokinetic parameters used in this study

168 are focused on this route of administration). It is therefore assumed that the total mass of benzoylecgonine in the

169 sewage accounts for 30.8±7.7 % of the total mass of cocaine consumed by the community group. As such, the

170 measured mass-transport rate of benzoylecgonine (g / week) is multiplied by a factor 3.5 to account for the 30.8±7.7

171 % excretion rate and the molar-ratio of cocaine to benzoylecgonine to give the total mass of consumed cocaine

172 (g/week, or g/month).

2.4. Combined Population and User-Group Survey Methodology

173

174 The population of cocaine users was divided into two groups; socially integrated individuals (experimental,

175 recreational and heavy users), and marginalized individuals (light, medium or heavy users). It was assumed that the

176 two groups could be reached by differing survey-types [37–40]. Data on the socially integrated users was acquired in

177 three different population surveys, each for a different age segment. Two or three surveys were employed to increase

178 N and reduce statistical uncertainty (Table 1). Since cocaine use could be seen as stable and that sampling frames,

179 mode of administration and data collection were the same for surveys in each age segment, estimates were averaged

180 over the surveys, Data on marginalized users was collected from surveys of prison inmates and the Oslo homeless or

181 street population attending a needle exchange. Note that the estimated number of marginalized cocaine users was

8

182   reduced with 20 percent because of a likely overlap between the prison and the street population [41,42]. Population

183   rates were based on the general population aged 15-64 years provided by government statistics correct to 31 December

184   2009 [33].

185   A "bottom up" method was used to estimate community cocaine use in Oslo. This method multiplies the number of

186   users by the reported frequency of use and reported amount (mass) of cocaine used [43–46]. Frequency was

187   established from the surveys (Table 1) while average values of amounts were based on self-report (last survey in Table

188   1) and existing literature (39). The amount varied with frequency of use such that the higher the frequency the higher

189   the dose (see Table 3).

190   Estimates of the prevalence of cocaine use derived from the survey among the driving population provide data on

191   cocaine use within a short period of time (within the last 24 hours). The combined survey method, however, acquires

192   data on the prevalence of consumption within the last 12 months. To be able to compare the roadside and the

193   combined survey method, the prevalence of use on a single day was estimated based on the frequency of use.

194   Frequency of use, measured as the number of days used in a year, yields the probability of use on a single day for each

195   level of frequency (see Table 3). This probability, multiplied by the number of users in the frequency group, yields the

196   expected number of users on a single day. Summing up expected number of daily users over frequency groups and

197   dividing by the population figure yields the prevalence of users per day.

3.   Results

3.1. Survey of drug-use amongst the driver population

200   Cocaine was detected in 14 out of 2341 samples from the greater Oslo area, and benzoylecgonine was detected in 9

201   samples, none were positive for benzoylecgonine only. Therefore, only the results for cocaine were used in the

202   estimations below. A weighted average of 0.7% of the driver population was found to be positive for cocaine using the

203   weights presented in Table 2.

204   The concentration of cocaine and benzoylecgonine in oral fluid depends on the dilution of oral fluid during sampling

205   and the recovery from the sampling device. For the samples found to be positive for cocaine, the average collection

206   volume of oral fluid was 0.74 ml, giving an average dilution of 1:2.4. A recovery for cocaine of 85.6% has been

207   reported [47]. Thus, the analytical cut-off corresponded to a cocaine concentration of 2.5 ng/ml in native (undiluted)

208   oral fluid.

9

3.2. Results of the analysis of drugs and related metabolites in sewage

210   Benzoylecgonine (the urinary metabolite of cocaine) was detected in all sewage samples collected in the Oslo region.

211   Measurements of the flow of this cocaine metabolite in sewage indicate an average load of 428 (CI 355 – 500)

212   g/week). Benzoylecgonine recovered in urine accounts for 30.8±7.7 % of the initial cocaine dose, so the measured

213   mass of this metabolite in the sewage is equivalent to 30.8±7.7 % of the total mass of cocaine consumed by the

214   community group. The measured flow of benzoylecgonine in the Oslo sewage system is therefore indicative of a

215   community-wide cocaine consumption rate of 1458 (CI 1181 – 1735) g/week (pure cocaine) which is equivalent to 76

216   (CI 61 – 90) kg/year if we assume the rate of cocaine consumption remains constant throughout the year.

3.3. Combined population and user-group survey results

218   Socially integrated users (aged 15-64 years) in Oslo reporting at least one instance of cocaine use in the last 12 months

219   constituted 2.7 % (CI 2.4-3.1) of the total population (15-64 years) in Oslo. Proportions were highest in the age

220   groups 20 to 24 years (4.0 – 7.6 %). Marginalized cocaine users in Oslo constitute an additional 0.2 % (CI 0.0-0.4) of

221   the total population (15-64 years), so the proportion of the total population that admits at least one instance of cocaine

222   use in the last 12 months is 2.9 % (CI 2.6-3.2) in Oslo.

223   An estimated 0.22 (CI 0.13-0.30) % of the population (15-64 years) use cocaine on a given day in Oslo.

224   Approximately 80 % of self-reported cocaine users (aged 15-64 years) used cocaine less than 10 times per year. The

225   remaining proportion of the user population (20 %) have taken more cocaine more frequently and are subsequently

226   responsible for in excess of 90% of the total daily cocaine consumption (g/day). In terms of user-group population,

227   the vast majority (73 %) of cocaine was consumed by the socially integrated population, while marginalized users

228   (including injecting drug users and prison inmates) consumed 27 % of the total.

3.4. Comparison of Results

230   The three methods provide two distinct measures of cocaine use; the prevalence of cocaine use in terms of the

231   proportion of the community that use the drug, and a quantitative measure (mass) of the total amount of cocaine that is

232   consumed by the entire community.

10

233   Comparison of the prevalence estimates derived from the combined population survey (0.22 (0.13 – 0.30) % per day)

234   and the road-side testing (0.70 (0.36 – 1.03) %) indicates that under reporting and possible under-representation of

235   users is apparent within the combined population surveys.

236   The combined population survey also provided an estimate for the total amount of cocaine that is consumed which can

237   be directly compared with the results of sewage measurements (Table 4). The estimated annual consumption rate

238   from the combined population survey (117 (70 – 165) kg/year, pure cocaine) is comparable with the 76 (CI 61 – 90)

239   kg/year kg/year figure from measurements of cocaine metabolites in sewage.

240   With this data it is also possible to calculate an estimated per-user consumption rate by combining the annual

241   prevalence of cocaine use (2.9 %) with the measured annual consumption from the sewage (76 kg/year). Such

242   analysis implies a per-user cocaine consumption rate of 6.4 (4.6 – 8.4) g/user/year (pure cocaine).

243   **4. Discussion**

244   A comparison was performed on three independent methods for estimating the use of cocaine in Oslo, Norway. The

245   comparison applies to; a combined sample survey questionnaire approach, a representative sample survey on drug use

246   among drivers, and a survey of the mass of cocaine-related metabolites in sewage. The estimated prevalence of use on

247   a single day was higher in the survey among drivers than using the combined survey approach, while the estimated

248   amount used (mass) in the latter was not significantly different than in the sewage approach.

249   The comparison identified a higher prevalence of cocaine use in the representative sample survey among drivers than

250   in the combined sample survey questionnaire approach. Under-reporting is not unexpected in the survey

251   questionnaires because the subject was drug use and the level of response was low, but this discrepancy may be even

252   larger than is immediately apparent from the present study. An earlier roadside study [48] found that the use of

253   medicinal drugs was under-estimated by 17-59% when using data from a survey of drivers compared to actually

254   dispensed amounts in the studied area. For the use of cannabis the results from a roadside survey were similar to self-

255   reported data. We therefore expect that data from a roadside survey will under-estimate the use of cocaine in the adult

256   population somewhat. In the present study marginalised drug users were included in the combined population survey

257   but they are far less likely to own or drive motor vehicles and therefore less likely to be detected in the road-side

258   testing surveys. Secondly, the detection time for cocaine in oral fluid depends upon the analytical cut-off, sampling

259   method, method of cocaine administration, dose used, acute or chronic cocaine use, and other factors. In controlled

260 studies of administration of 25-45 mg cocaine by intravenous injection, snorting or smoking, cocaine was detected in

261 oral fluid for more than 12 hours in only about 25% of the experiments [49,50]. However, cocaine may be detected in

262 oral fluid from chronic cocaine users for up to 118 hours after last dose in extreme cases [51]. Finally, the measured

263 prevalence (0.7 %) of cocaine or metabolites in the oral fluid of drivers is also considered a minimum because it is

264 expected that many cocaine users refrain from driving for some hours after cocaine administration, and further,

265 approximately 10% of drivers declined to participate in the study. It is possible that the group of drivers that refused

266 to offer a saliva sample have a higher prevalence of recent drug consumption than that of drivers who volunteered a

267 sample. This would give an even higher prevalence of use on a single day.

268 Interestingly although the combined population survey appears to underestimate the prevalence of cocaine use, this

269 method did result in a combined consumption estimate (kg/year) that was not significantly different to the results of

270 sewage analysis. This may mean that self-reported amounts of cocaine used were actually too high. Estimates of the

271 amount of cocaine used were the weakest part of the combined population survey, however, and the frequency

272 categories were also rather coarse. If there was a non-accounted overlap between the population survey and the

273 surveys among marginalized users to cover the cocaine user population, this would reduce both the estimated

274 proportion of users and the estimated amount. In addition, it is important to remember that the accuracy of the sewage

275 estimate is strongly affected by the accuracy of the clinical pharmacokinetic data on cocaine. The present study used

276 the pharmacokinetic parameters that apply for intra-nasal cocaine use because this is the most relevant for study

277 population. This implies that a degree of back-ground information from combined population surveys with regard to

278 the proportion of differing routes of administration are required before accurate sewage measurements are feasible.

279 For example, the use of the intra-nasal pharmacokinetic parameters would not be appropriate if the study was carried

280 out in a region with extensive crack-cocaine use as the excretion patterns differ for differing routes of administration.

281 No similar comparisons of the three drug epidemiology techniques have been carried out before so it is difficult to

282 relate the present findings to other study populations. It was however necessary, with the present study, to make some

283 general assumptions with regard to the average amount of cocaine used per individual in order to adequately compare

284 the prevalence estimates with that of the measured mass of cocaine metabolites in sewage. The combined population

285 surveys indicated an average per-user consumption rate of 9.8 g/user/year (pure cocaine) which is much lower than the

286 30.2 g/user/year (in Europe) proposed by The United Nations Office on Drugs and Crime (2010). While it appears

287 that the average per-user consumption rate in Oslo may actually be lower than in many other European regions [20],

288 the UNODC does state that their estimate (which is based on empirical data from a small number of locations and

289 makes significant assumptions with regard to the importance of drug availability and the effectiveness of law

290 enforcement) is a considerable approximation as little or no data on the quantities consumed by individuals is

291 available, and much of the existing data is contradictory [53]. The results of the present study do suggest that

292 combining accurate measurements of the total drug consumption in the population (via sewage analysis) with reliable

293 prevalence figures acquired through rigorous survey of the population could provide improvements to the accuracy of

294 average per-user consumption figures in the future.

295 The comparison carried out in the present study has provided an excellent means for checking the quality and

296 accuracy of each the three measurement techniques because they each approach the problem from different angels.

297 The results do however highlight the difficulties associated with performing such a comparison. A rigorous ecological

298 approach to the present study would require that the comparison was based on exactly the same population, and at the

299 same time, but the logistics of sampling and the vastly different time-scales involved in each of the three techniques

300 make this difficult. It is possible, for example, that the population of drivers that took part in the road-side study

301 included individuals that were in transit and therefor from outside the region covered by the combined population

302 survey. Similarly, results of the sewage analysis are based on a one-month period and an assumption is made that

303 combined cocaine use (by the total population) remains relatively constant throughout the year. These problems do

304 however allow more precise research questions to be formulated: How can we better combine surveys to better cover

305 all segments of the population? Does cocaine use in the population of drivers follow the same pattern as cocaine use

306 in the general population? How can we better estimate the amounts used? How can we better estimate frequency of

307 use? Short-falls have been identified in each of the three epidemiology techniques when used in isolation, but together

308 the three complimentary techniques provide a well-balanced assessment of the drug-use situation in a given

309 community with limited reliance on derived estimates.

5. Conclusion

311 Under-reporting is apparent in prevalence estimates provided by the combined population surveys when compared

312 with the proportion of motor-vehicle drivers with detectable levels of cocaine or cocaine metabolites in oral-fluid, but

313 an unanswered question is whether cocaine use in the population of drivers follows the same pattern as cocaine use in

314 the general population. Direct measurements of sewage from a defined population provide data on the size of the

315 cocaine market in a particular region (albeit with a degree of uncertainty). These measurements indicate that self-

316 reported cocaine consumption may be over-exaggerated and highlight the large degree of uncertainty with respect to

317 per-user consumption estimates. Each of the three techniques has significant short-falls when used in isolation, but

318 together they deliver complimentary data which provides a well-balanced assessment of the drug-use situation in a

319 given community and identify areas where more research is needed.

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Estimation of Cocaine Consumption in the Community: A Critical Comparison of the Results from Three Complimentary Techniques

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ABSTRACT

Objectives: Increases in the prevalence of cocaine use are shadowed by the growing concern to public health. A range of approaches are now available to estimate the level of drug use in the community so it is desirable to critically compare results from the differing techniques. This paper presents a comparison of the results from three methods for estimating the level of cocaine use in the general population.

Design: The comparison applies to; a set of regional-scale sample survey questionnaires, a representative sample survey on drug use among drivers, and an analysis of the quantity of cocaine related metabolites in sewage.

Setting: 14,438 participants provided data for the set of regional-scale sample survey questionnaires; 2,341 drivers provided oral-fluid samples; and untreated sewage from 570,000 people was analysed for biomarkers of cocaine use. All data was collected in Oslo, Norway.

Results: 0.70 (0.36 – 1.03) % of drivers tested positive for cocaine-use which suggest a prevalence that is higher than the 0.22 (0.13 – 0.30) % (per day) figure derived from regional-scale survey questionnaires. Despite the comparatively low prevalence figure the survey questionnaires did provide estimates of the volume of consumption that are comparable with the amount of cocaine related metabolites in sewage. Per-user consumption estimates are however highlighted as a significant source of uncertainty, and the degree to which cocaine consumption in the driver-population follows the general population is an unanswered question.

Conclusions: The comparison carried out in the present study can provide an excellent means of checking the quality and accuracy of the three measurement techniques because they each approach the problem from a different viewpoint. Together the three complimentary techniques provide a well-balanced assessment of the drug-use situation in a given community and identify areas where more research is needed.

3

ARTICLE SUMMARY

Article Focus

- Estimation of the prevalence of cocaine use is important for; the assessment of the needs of public health; the development of appropriate drug strategies to reduce health effects; and the subsequent monitoring of the effectiveness of such strategies.

- It is generally accepted that there is a lack of information with respect to the dynamics and scale of illicit drug markets, and the validity or reliability of estimates are questionable.

- This paper presents a critical comparison of the results from three different methods for estimating the level of cocaine use in the general population.

Key Messages

- 0.70 (0.36 – 1.03) % of drivers tested positive for cocaine use compared with 0.22 (0.13 – 0.30) % (per day) as derived from regional-scale survey questionnaires.

- Direct comparison of prevalence estimates with the amount of drug related metabolites in sewage is difficult because accurate data on per-user consumption estimates is lacking.

- Such a comparison as carried out here helps to identify key short-falls in the respective datasets and highlights where further research is needed.

Strengths and Limitations of this Study

- A rigorous ecological approach to the present study would require that the comparison was based on exactly the same population, and at the same time, but the logistics of sampling and the vastly different time-scales involved in each of the three techniques make this difficult.

- No similar comparisons of the three drug epidemiology techniques have been carried out before so it is difficult to relate the present findings to other study populations.

4

1. Introduction

Cocaine is the second most commonly used illicit drug in Europe and the United States, and use of the drug is associated with numerous health problems including cardiovascular disorders, neurological impairment and death [1]. Increases in the prevalence of cocaine use over recent years are shadowed by the growing concern to public health, so quantification and the estimation of the prevalence of cocaine use are important for assessing the needs of public health, developing appropriate drug strategies to reduce health effects, and in the subsequent monitoring of the effectiveness of such strategies. It is generally accepted that there is a lack of information with respect to the dynamics and scale of illicit drug markets, and the validity or reliability of estimates are questionable [2]. The estimation of drug use patterns in society is currently reliant on questionnaire based data-collection at the population level, and among groups of drug users, together with statistics from hospital admissions, registered drug-overdose deaths, treatment services and the records from police seizures [3–7]. Validation of drug use statistics derived from individual self-reporting has previously been attempted by drawing comparisons between the self-reported use and measurements of samples taken from hair, urine and blood [8–12]. This technique has shown that despite the use of an array of methods to increase the level of accuracy of self-reporting, under-reporting is still apparent. Recently, additional data on the level of drug use at the community level have also been acquired through the implementation of anonymous road-side testing studies [13,14], and also through the measurement of drug metabolites in sewage water [15–20]. With a range of different approaches now available to estimate the level of community drug use it is highly desirable to critically compare the results they provide. For the first time this paper presents a critical comparison of the results from three different methods for estimating the level of cocaine use in the general population. The comparison was performed on three studies in Oslo, Norway and applies to; a combination of user group and representative population sample survey questionnaires, a representative sample survey on drug use measured in saliva among drivers, and an analysis of the quantity of drugs and drug related metabolites in sewage.

2. Materials and Methods

2.1. Background - Cocaine Use in Norway

Life time prevalence of cocaine use in the general population 15 years and over was reported as 2.7 percent in 2004 and 2.5 percent in 2009 [21]. Results from both these studies (combined) show that the prevalence of recent cocaine use (within the last year) in the total population was as low as 0.6 percent. A separate study on young adults (21-30 years) [22] reports higher rates of cocaine use in these age groups: prevalence of use within the last 6-months was 4.3

percent in 2002 and 4.9 percent in 2006. Also, lifetime prevalence of cocaine use among young people (15 - 20 years) in Oslo has remained very stable in the years 2003 to 2008.

Cocaine use in Norway is dominated by recreational intranasal use. Crack use has been rare. Among young adult cocaine users less than one in a hundred reported crack use and crack is seldom seized by the police/customs. A survey among the prison population [23] identified 6 percent of inmates report daily or almost daily use of cocaine in the 6 months leading up to imprisonment, but frequent cocaine use is lower among marginalized and injecting drug user groups [24].

Purity of cocaine will vary from batch to batch, by place of production, and by level of sale (such as street-level or whole-sale market level). The purity of cocaine in Norway is measured in conjunction with seizures of the drug by the police and customs. Data from the period 2007 – 2009 shows a trend of decreasing purity over time; lately 39% in 2007 compared to 25% in 2009 [25]. This degree of variation is consistent with data from other nations [26–29].

2.2. Methodology for the survey of drug-use amongst the driver population

Data collection was performed in the greater Oslo area in cooperation with two National Mobile Police Service (MPS) districts from April 2008 to March 2009 as part of the DRUID Project [30]. Drivers of motor vehicles were selected using a stratified two-stage cluster sampling procedure. In the first stage, random geographical areasroad sites and time periodsintervals of five consecutive days were selected usingto a table of random sampling numbers [31]. All days and times of the week and all seasons of the year were covered. Sampling periods of 5 consecutive days were first selected. Roads were then chosen by randomly selecting map co-ordinates, then choosing the closest roads. For each day the police selected two study sites along the chosen roads. The sites had to be suitable as checkpoints (possibility to stop a number of cars at the same time on the roadside without causing traffic congestion) and they had to be located within about 30-45 minutes' drive from each other. For each day, the starting time for roadside sampling was also randomly selected. However, a few of the selected time periods had to be changed to comply with working time regulations for police officers.For each day, two consecutive two-hour periods were randomly selected for sample collection at two different road sites. The MPS then selected the exact time and place allowing for practical considerations (e.g., choosing sites suitable as checkpoints, and ensuring a driving time of less than 40 minutes between consecutive checkpoint sites). If the chosen time intervals did not comply with working hour regulations for

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~~police officers; the intervals had to be cancelled and replaced by new intervals as close as possible to the original interval.~~

The second stage <u>of the sampling procedure</u> consisted of randomly stopping drivers within the defined two hour period. <u>The police officers were instructed to stop cars at random, rather than stopping old cars, young drivers or other possible suspects of impaired driving.</u> The number of data collection personnel <u>at each site</u> was related to the expected traffic density. When <u>one of</u> the data collection personnel were ready for a new driver, the MPS stopped the first approaching car or motorcycle and carried out their own routine controls (~~e.g.,~~ breath alcohol testing or driver's licence control). Afterwards the driver was asked to proceed to the study team, who requested voluntary and anonymous participation in the project. Oral and written information about the project was given to each driver. If <u>verbal</u> informed consent was given, a sample of oral fluid was collected and the following data recorded: gender, age, day of the week, time interval, and geographical site. <u>It was thus impossible to trace a given sample to a specific donor or motor vehicle.</u> In general, the sampling procedure was designed in a way that should ensure that the drivers rendering samples should give a representative picture of the total driver population. Saliva samples were collected using the Statsure Saliva Sampler (Saliva Diagnostic Systems, Framingham, MA, USA). The saliva collection pad was placed under the tongue until the indicator turned blue, or until five minutes has passed and transferred to a capped vial labelled with a bar code label corresponding to the bar code of the questionnaire. The sample was kept in a plastic bag at a temperature of approximately 5°C for a maximum of 6 hours, and then stored at -20°C.

Concentrations of cocaine and benzoylecgonine in oral fluid-buffer mixtures were determined by liquid chromatography – tandem mass spectrometry [32], <u>which specifically measured the substances in question. The amount of collected oral fluid was determined by weighing the sample, and concentrations of substances</u> in un-diluted oral fluid were calculated. The cut-off thresholds in oral fluid-buffer mixture were 0.9 and 3.6 ng/mL for cocaine and benzoylecgonine, respectively. The combined prevalence of cocaine or benzoylecgonine was estimated by a weighted average, using weights adjusted for under- or over-sampling of the data compared to overall population statistics [33]. This weighting took into account the age and gender of drivers with respect to the general population, together with an appropriate weighting for the days of the week and time of the day (Table 2).

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2.3. Methodology for the analysis of drugs and related metabolites ~~is~~ _in_ sewage

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Sample collection was carried out in the greater Oslo area in cooperation with the region's largest sewage treatment plant (Vestfjorden Avløpselskap). This plant processes sewage from a metropolitan and suburban population of approximately ~~500~~ 570 000 people. An Isco 6712 portable automatic ~~wastewater~~ sampler (Teledyne, Nebraska USA) was used to collect samples of wastewater every hour ~~6-hour time-proportional composite sewage effluent samples (total volume 1000 mL), continuously~~ throughout the course of September 2009. The hourly samples were pooled to produce 6-hour composites (n = 120) with mid-points corresponding to 2 am, 8 am, 2 pm and 8 pm for each day of the month. Deuterated internal standards were spiked at the time of collection (1mL of benzoylecgonine-d3, cocaine-d3, cocaethylene-d8, methamphetamine-d5, metoprolol acid-d5 and ceterizine-d8 at 50 ng/mL to give a final working concentration of 50 ng/L of each standard in sewage) and samples were acid stabilised and stored at 4°C until analysis.

Concentrations of cocaine and benzoylecgonine in the sewage water composites were determined by liquid chromatography – tandem mass spectrometry [18]. The limit of quantification for the analytes in raw sewage was 5 ng/L.

The total mass of benzoylegonine passing through the sewage treatment processes in the Oslo region over the sampling period was calculated by scaling the measured sewage concentration of the metabolite (ng/L) in each of the 120 samples (each representing 6-hours of sewage) by the total volume of sewage (L) for that 6-hour period. The uncertainty with this estimate is associated with errors in sampling (5% RSD), flow measurements (1% RSD), chemical analysis (5% RSD) and biotransformation of cocaine and benzoylecgonine in the sewer system which is typically less than 10 % [34,35].

Careful consideration of the urinary excretion rates of cocaine and its metabolites are then needed for back-calculation of the total mass of cocaine consumed during the sampling period. Benzoylecgonine is the primary urinary metabolite of cocaine and accounts for 30.8±7.7 % ~~(15 – 45) percent~~ of the recoverable dose of nasally insufflated cocaine in urine [36]. (Note that cocaine use in Norway is dominated by intranasal administration so the pharmacokinetic parameters used in this study are focused on this route of administration). It is therefore assumed that the total mass of benzoylecgonine in the sewage accounts for 30.8±7.7 % of the total mass of cocaine consumed by the community group. As such, the measured mass-transport rate of benzoylecgonine (g / week) is multiplied by a factor 3.5 to account for the 30.8±7.7 % excretion rate and the molar-ratio of cocaine to benzoylecgonine to give the total mass of consumed cocaine (g/week, or g/month).

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2.4. Combined Population and User-Group Survey Methodology

The population of cocaine users was divided into two groups; socially integrated individuals (experimental, recreational and heavy users), and marginalized individuals (light, medium or heavy users). It was assumed that the two groups were could be reached by differing survey-types [37–40]. Data on the socially integrated users was acquired in three different population surveys, each for a different age segment. Two or three surveys were employed to increase N and reduce statistical uncertainty (Table 1). Since cocaine use could be seen as stable and that sampling frames, mode of administration and data collection were the same for surveys in each age segment, estimates were averaged over the surveys, Data on marginalized users was collected from surveys of prison inmates and the Oslo homeless or street population attending a needle exchange. Note that the estimated number of marginalized cocaine users was reduced to 80 percent of the sum from the two surveys with 20 percent because of a likely overlap between the prison and the street population [41,42]. Population rates were based on the general population aged 15-64 years provided by government statistics correct to 31 December 2009 [33].

A "bottom up" method was used to estimate community cocaine use in Oslo. This method multiplies the number of users by the reported frequency of use and reported amount (mass) of cocaine used [43–46]. Frequency was established from the surveys (Table 1) while average values of amounts were based on self-report (last survey in Table 1) and existing literature (39). The amount varied with frequency of use such that the higher the frequency the higher the dose (see Table 3).

Estimates of the prevalence of cocaine use derived from the survey among the driving population provide data on cocaine use within a short period of time (within the last 24 hours). The combined survey method, however, acquires data on the prevalence of consumption within the last 12 months. To be able to compare the roadside and the combined survey method, the prevalence of use on a single day was estimated based on the frequency of use. Frequency of use, measured as the number of days used in a year, yields the probability of use on a single day for each level of frequency (see Table 3). This probability, multiplied by the number of users in the frequency group, yields the expected number of users on a single day. Summing up expected number of daily users over frequency groups and dividing by the population figure yields the prevalence of users per day.

3. Results

3.1. Survey of drug-use amongst the driver population

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Cocaine was detected in 14 out of 2341 samples from the greater Oslo area, and benzoylecgonine was detected in 9 samples, none were positive for benzoylecgonine only. Therefore, only the results for cocaine were used in the estimations below. A weighted average of 0.7% of the driver population was found to be positive for cocaine using the weights presented in Table 2.

The concentration of cocaine and benzoylecgonine in oral fluid depends on the dilution of oral fluid during sampling and the recovery from the sampling device. For the samples found to be positive for cocaine, the average collection volume of oral fluid was 0.74 ml, giving an average dilution of 1:2.4. A recovery for cocaine of 85.6% has been reported [47]. Thus, the analytical cut-off corresponded to a cocaine concentration of 2.5 ng/ml in native (undiluted) oral fluid.

3.2. Results of the analysis of drugs and related metabolites ~~is~~ in sewage

Benzoylecgonine (the urinary metabolite of cocaine) was detected in all sewage samples collected in the Oslo region. Measurements of the flow of this cocaine metabolite in sewage indicate an average load of 428 (CI 355 – 500) g/week). Benzoylecgonine recovered in urine accounts for 30.8±7.7 % of the initial cocaine dose, so the measured mass of this metabolite in the sewage is equivalent to 30.8±7.7 % of the total mass of cocaine consumed by the community group. The measured flow of benzoylecgonine in the Oslo sewage system is therefore indicative of a community-wide cocaine consumption rate of 1458 (CI 1181 – 1735) g/week (pure cocaine) which is equivalent to 76 (CI 61 – 90) kg/year if we assume the rate of cocaine consumption remains constant throughout the year.

3.3. Combined population and user-group survey results

Socially integrated users (aged 15-64 years) in Oslo reporting at least one instance of cocaine use in the last 12 months constituted 2.7 % (CI 2.4-3.1) of the total population (15-64 years) in Oslo. Proportions were highest in the age groups 20 to 24 years (4.0 – 7.6 %). Marginalized cocaine users in Oslo constitute an additional 0.2 % (CI 0.0-0.4) of the total population (15-64 years), so the proportion of the total population that admits at least one instance of cocaine use in the last 12 months is 2.9 % (CI 2.6-3.2) in Oslo.

An estimated 0.22 (CI 0.13-0.30) % of the population (15-64 years) use cocaine on a given day in Oslo. Approximately 80 % of self-reported cocaine users (aged 15-64 years) used cocaine less than 10 times per year. The remaining proportion of the user population (20 %) have taken more cocaine more frequently and are subsequently

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responsible for in excess of 90% of the total daily cocaine consumption (g/day). In terms of user-group population, the vast majority (73 %) of cocaine was consumed by the socially integrated population, while marginalized users (including injecting drug users and prison inmates) consumed 27 % of the total.

3.4. Comparison of Results

The three methods provide two distinct measures of cocaine use; the prevalence of cocaine use in terms of the proportion of the community that use the drug, and a quantitative measure (mass) of the total amount of cocaine that is consumed by the entire community.

Comparison of the prevalence estimates derived from the combined population survey (0.22 (0.13 – 0.30) % per day) and the road-side testing (0.70 (0.36 – 1.03) %) indicates that under reporting and possible under-representation of users is apparent within the combined population surveys.

The combined population survey also provided an estimate for the total amount of cocaine that is consumed which can be directly compared with the results of sewage measurements (Table 4). The estimated annual consumption rate from the combined population survey (117 (70 – 165) kg/year, pure cocaine) is comparable with ~~is perhaps slightly higher than~~ the 76 (CI 61 – 90) kg/year kg/year figure from measurements of cocaine metabolites in sewage. ~~The confidence intervals for these figures are large however, and it cannot be concluded that they are different.~~

With this data it is also possible to calculate an estimated per-user consumption rate by combining the annual prevalence of cocaine use (2.9 %) with the measured annual consumption from the sewage (76 kg/year). Such analysis implies a per-user cocaine consumption rate of 6.4 (4.6 – 8.4) g/user/year (pure cocaine). ~~For comparison, a per-user consumption estimate of 30.2 g/year from The United Nations Office on Drugs and Crime [50] was also applied (to Table 4), but it is immediately apparent that this UNODC consumption estimate does not fit well with the measured results of the present study. If 2.9 % of the population used an average of 30.2 g/user/year then the measured mass of cocaine metabolites in sewage would equate to a combined (city-wide) consumption of 361 (321 – 401) kg/year. This is far in excess of the measured value. Similarly, dividing the measured annual city-wide consumption (kg/year) provided by analysis of sewage by the UNODC per-user consumption rate would imply an annual prevalence of 0.6 (0.4 – 2.7) % which is again not in agreement with the measured results.~~

4. Discussion

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A comparison was performed on three independent methods for estimating the use of cocaine in Oslo, Norway. The comparison applies to; a combined sample survey questionnaire approach, a representative sample survey on drug use among drivers, and a survey of the mass of cocaine-related metabolites in sewage. The estimated prevalence of use on a single day was higher in the survey among drivers than using the combined survey approach, while the estimated amount used (mass) in the latter was not significantly different than in the sewage approach.

The comparison identified a higher prevalence of cocaine use in the representative sample survey among drivers than in the combined sample survey questionnaire approach. Under-reporting is not unexpected in the survey questionnaires because the subject was drug use and the level of response was low, but this discrepancy may be even larger than is immediately apparent from the present study. An earlier roadside study [48] found that the use of medicinal drugs was under-estimated by 17-59% when using data from a survey of drivers compared to actually dispensed amounts in the studied area. For the use of cannabis the results from a roadside survey were similar to self-reported data. We therefore expect that data from a roadside survey will under-estimate the use of cocaine in the adult population somewhat. In the present study marginalised drug users were included in the combined population survey but they are far less likely to own or drive motor vehicles and therefore less likely to be detected in the road-side testing surveys. Secondly, the detection time for cocaine in oral fluid depends upon the analytical cut-off, sampling method, method of cocaine administration, dose used, acute or chronic cocaine use, and other factors. In controlled studies of administration of 25-45 mg cocaine by intravenous injection, snorting or smoking, cocaine was detected in oral fluid for more than 12 hours in only about 25% of the experiments [49,50]. However, cocaine may be detected in oral fluid from chronic cocaine users for up to 118 hours after last dose in extreme cases [51]. Finally, the measured prevalence (0.7 %) of cocaine or metabolites in the oral fluid of drivers is also considered a minimum because it is expected that many cocaine users refrain from driving for some hours after cocaine administration, and further, approximately 10% of drivers declined to participate in the study. It is possible that the group of drivers that refused to offer a saliva sample have a higher prevalence of recent drug consumption than that of drivers who volunteered a sample. This would give an even higher prevalence of use on a single day.

Interestingly although the combined population survey appears to underestimate the prevalence of cocaine use, this method did result in a combined consumption estimate (kg/year) that was not significantly different to the results of sewage analysis. This may mean that self-reported amounts of cocaine used were actually too high. Estimates of the amount of cocaine used were the weakest part of the combined population survey, however, and the frequency

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categories were also rather coarse. If there was a non-accounted overlap between the population survey and the surveys among marginalized users to cover the cocaine user population, this would reduce both the estimated proportion of users and the estimated amount. In addition, it is important to remember that the accuracy of the sewage estimate is strongly affected by the accuracy of the clinical pharmacokinetic data on cocaine. The present study used the pharmacokinetic parameters that apply for intra-nasal cocaine use because this is the most relevant for study population. This implies that a degree of back-ground information from combined population surveys with regard to the proportion of differing routes of administration are required before accurate sewage measurements are feasible. For example, the use of the intra-nasal pharmacokinetic parameters would not be appropriate if the study was carried out in a region with extensive crack-cocaine use as the excretion patterns differ for differing routes of administration.

No similar comparisons of the three drug epidemiology techniques have been carried out before so it is difficult to relate the present findings to other study populations. It was however necessary, with the present study, to make some general assumptions with regard to the average amount of cocaine used per individual in order to adequately compare the prevalence estimates with that of the measured mass of cocaine metabolites in sewage. The combined population surveys indicated an average per-user consumption rate of 9.8 g/user/year (pure cocaine) which is much lower than the 30.2 g/user/year (in Europe) proposed by The United Nations Office on Drugs and Crime (2010). While it appears that the average per-user consumption rate in Oslo may actually be lower than in many other European regions [20]the areas included in the UNODC estimate, the UNODC does state that their estimate (which is based on empirical data from a small number of locations and makes significant assumptions with regard to the importance of drug availability and the effectiveness of law enforcement) is a considerable approximation as little or no data on the quantities consumed by individuals is available, and much of the existing data is contradictory [53]. Similar concerns were also expressed in the report on Drug Availability Estimates in the United States [55] in which the authors note that the figures rely on "manipulating a number of estimated variables which themselves require acceptance of some heroic assumptions and are subject to substantial margins of error".

The UNODC defines the lack of information on the per-capita consumption of illegal drugs as the largest constraint with respect to the interpretation of international drug markets , but tThe results of the present study do suggest that combining accurate measurements of the total drug consumption in the population (via sewage analysis) with reliable prevalence figures acquired through rigorous survey of the population could provide improvements to the accuracy of average per-user consumption figures in the future.

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The comparison carried out in the present study has provided an excellent means for checking the quality and accuracy of each the three measurement techniques because they each approach the problem from different angles. The results do however highlight the difficulties associated with performing such a comparison. A rigorous ecological approach to the present study would require that the comparison was based on exactly the same population, and at the same time, but the logistics of sampling and the vastly different time-scales involved in each of the three techniques make this difficult. It is possible, for example, that the population of drivers that took part in the road-side study included individuals that were in transit and therefor from outside the region covered by the combined population survey. Similarly, results of the sewage analysis are based on a one-month period and an assumption is made that combined cocaine use (by the total population) remains relatively constant throughout the year. These problems do however allow more precise research questions to be formulated: How can we better combine surveys to better cover all segments of the population? Does cocaine use in the population of drivers follow the same pattern as cocaine use in the general population? How can we better estimate the amounts used? How can we better estimate frequency of use? Short-falls have been identified in each of the three epidemiology techniques when used in isolation, but together the three complimentary techniques provide a well-balanced assessment of the drug-use situation in a given community with limited reliance on derived estimates.

5. Conclusion

Under-reporting is apparent in prevalence estimates provided by the combined population surveys when compared with the proportion of motor-vehicle drivers with detectable levels of cocaine or cocaine metabolites in oral-fluid, but an unanswered question is whether cocaine use in the population of drivers follows the same pattern as cocaine use in the general population. Direct measurements of sewage from a defined population provide data on the size of the cocaine market in a particular region (albeit with a degree of some uncertainty). These measurements indicate that self-reported cocaine consumption may be over-exaggerated and highlight the large degree of uncertainty with respect to per-user consumption estimates. Each of the three techniques has significant short-falls when used in isolation, but together they deliver complimentary data which provides a well-balanced assessment of the drug-use situation in a given community and identify areas where more research is needed.

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Table 1. Combined population and user group survey parameters including study population, study dates and sample size.

Target Population	Survey Year	Type of survey	Sample Size (n=)	Publication
15 – 20 years, Oslo [1]	2006, 2007, 2008	Postal	5104	(Vedøy and Skretting, 2009)
21 – 30 years, Oslo [2]	2006, 2010	Postal	3468	(Lund et al., 2007)
31 – 64 years, Oslo [3]	2004, 2009	Questionnaire completed in private	899	(Nordlund, 2010)
Prison Inmates, Norway (national, applied to Oslo) [4]	2002	Questionnaire completed in private	1093	(Odegard, 2008)
Injecting drug users, Oslo [3]	2000-2004	Face to face	3829	(Bretteville-Jensen and Amundsen, 2009)
Marginalized Users, Arendal [3]	2010	Face to face	45	Unpublished pilot

Response rates: [1] 35 percent, [2] 40-50 percent, [3] not recorded or applicable, [4] 41 percent.

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Table 2. Weights for under- or over-sampling associated with the road-side saliva study.

Characteristics	Distribution among drivers (%)	Distribution in the total population of Oslo (%)	Weight
Age (years)			
16-24	9.4	10.6	1.13
25-34	18.1	20.9	1.15
35-44	24.3	16.2	0.67
45-54	21.4	12.2	0.57
55-64	16.4	10.2	0.62
65+	10.4	11.7	1.13
Total	100.0	81.8	-
Gender			
Female	29.8	50.6	1.70
Male	70.2	49.4	0.70
Total	100.0	100.0	-
Day of the week			
Mon-Thu	48.0	57.1	1.19
Fri	8.6	14.3	1.66
Sat	31.0	14.3	0.46
Sun	12.4	14.3	1.15
Total	100.0	100.0	-
Time of day (h)			
00.00-05.59	3.4	25.0	7.35
06.00-11.59	30.1	25.0	0.83
12.00-17.59	43.0	25.0	0.58
18.00-23.59	23.5	25.0	1.06
Total	100.0	100.0	-

Table 3. Parameters and estimates of community cocaine consumption for combined survey method by frequency of use categories in four surveys. Mean number of usage-days per unit time and the probability of use on a given day. Estimates of the proportion of users in the total survey population, frequency of use among users, and average weekly consumption

Survey - Population 15-30 years

Frequency of use categories (per half year)	Never	1-4 times	5-10 times	11-25 times	25-50 times	50+ times	Total/average (CI)
Mean number of usage days per half year[1]	0	2.5	7.5	18	38	116.5	-
Probability of use on any given day (%)[2]	0	1.4	4.1	9.9	20.8	63.7	-
Proportion of users among total age-group population (%)[3]	95.3 (94.8-95.7)	3.0	0.9	0.4	0.2	0.2	100
Frequency of use among users (%)[4]	-	63	20	9	4	5	100
Average per-user consumption, mg (pure) / week[5]	-	6	43	156	585	2240	154 (71-237)

Survey - Population 31-64 years

Frequency of use categories (per year)	Never	1-4 times	Monthly	Weekly	Daily, almost daily	Total/average (CI)
Mean number of usage-days per year[6]	0	2.5	12	52	182.5	-
Probability of use on any given day (%)[2]	0	0.7	3.3	14.8	50.0	-
Proportion of users among total age-group population (%)[3]	98.3 (97.2-99.4)	0.9	0.5	0.3	0.1	100
Frequency of use among users (%)[4]	-	50	30	15	5	100
Average per-user consumption, mg (pure) / week[5]	-	4	42	270	2106	160 (37-283)

Survey - Prison population

Frequency of use categories (per half year prior to incarceration)	Never	1-3 times per month or less	Weekly	Daily, almost daily	Total/average (CI)
Mean number of usage-days per year[6]	0	12	52	182.5	-
Probability of use on any given day (%)[2]	0	3.3	14.2	50.0	-
Proportion of users among total population 15-64 years (%)[3]	99.9 (99.7-100)	0.06	0.03	0.01	100
Frequency of use among users (%)[4]	-	63	23	13	100
Average per-user consumption, mg (pure) / week[5]	-	138	900	3510	767 (487-1048)

Survey - Injectors/marginalized users

Frequency of use categories (per year)	Never	Less than once a month	Monthly	Weekly	Daily, almost daily	Total/average (CI)
Mean number of usage-days per year[6]	0	6	12	52	182.5	-
Probability of use on any given day (%)[2]	0	1.6	3.3	14.2	50.0	-
Proportion of users among total population 15-64 years (%)[3]	99.9 (99.6-100)	0.06	0.01	0.01	0.02	100
Frequency of use among users (%)[4]	-	55	12	12	21	100
Average per-user consumption, mg (pure) / week[5]	-	21	42	270	2106	491 (217-765)

[1] Midpoint of frequency category reported in each survey, set to 116.5 for those using more than 50 times per half year. [2] Defined as a usage-day or a single 24-hour period in which cocaine is consumed. Number of usage days per user, divided by 182.6 for half year periods and 365.25 for one year periods [3] Number of users in each category divided by population figures of relevant age group [4] Number of users in each category divided by the total number of users [5] For each category the total consumption of pure cocaine equals number of users * mean number of usage days * mean dose size * mean number of doses per day * purity. Average per user consumption per week of pure cocaine equals this amount divided by the number of users and 26 for half year period and 52 for one year period. Mean dose size and mean number of doses per day vary from 0.1 gram and 2.5 doses in categories of lowest frequency to 0.25 gram and 8 doses in categories of highest frequency. [6] Midpoint of frequency category, but assuming 6 usage-months per year

Table 4. Prevalence and scale of cocaine use in Oslo as determined by combined population surveys and measurements of a cocaine metabolite in sewage. (Direct measurements or estimates in **bold**. Derived estimates in *italics*).

Method	Annual Prevalence % (CI) [a]	Cocaine Consumption (Pure)	
		Per-user g/year (CI)	Total population kg/year (CI)
Combined Population Survey (CPS)	**2.9 (2.6 – 3.2)**	9.8 (5.6 – 14.1)	*117 (70 – 165)*
Sewage Analysis			
Prevalence from CPS	**2.9 (2.6 – 3.2)**	*6.4 (4.6 – 8.4)*	**76 (61 – 90)**
Per-user consumption from CPS	*1.9 (1.1 – 3.9)*	9.8 (5.6 – 14.1)	**76 (61 – 90)**

[a] Population 15 – 64 years of age, 410 000 (source Statistics Norway)

Estimation of Cocaine Consumption in the Community: A Critical Comparison of the Results from Three Complimentary Techniques

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Estimation of Cocaine Consumption in the Community: A Critical Comparison of the Results from Three Complimentary Techniques

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ABSTRACT

Objectives: A range of approaches are now available to estimate the level of drug use in the community so it is desirable to critically compare results from the differing techniques. This paper presents a comparison of the results from three methods for estimating the level of cocaine use in the general population.

Design: The comparison applies to; a set of regional-scale sample survey questionnaires, a representative sample survey on drug use among drivers, and an analysis of the quantity of cocaine related metabolites in sewage.

Setting: 14,438 participants provided data for the set of regional-scale sample survey questionnaires; 2,341 drivers provided oral-fluid samples; and untreated sewage from 570,000 people was analysed for biomarkers of cocaine use. All data was collected in Oslo, Norway.

Results: 0.70 (0.36 – 1.03) % of drivers tested positive for cocaine-use which suggest a prevalence that is higher than the 0.22 (0.13 – 0.30) % (per day) figure derived from regional-scale survey questionnaires, but the degree to which cocaine consumption in the driver-population follows the general population is an unanswered question. Despite the comparatively low prevalence figure the survey questionnaires did provide estimates of the volume of consumption that are comparable with the amount of cocaine related metabolites in sewage. Per-user consumption estimates are however highlighted as a significant source of uncertainty as little or no data on the quantities consumed by individuals is available, and much of the existing data is contradictory.

Conclusions: The comparison carried out in the present study can provide an excellent means of checking the quality and accuracy of the three measurement techniques because they each approach the problem from a different viewpoint. Together the three complimentary techniques provide a well-balanced assessment of the drug-use situation in a given community and identify areas where more research is needed.

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ARTICLE SUMMARY

Article Focus

- Estimation of the prevalence of cocaine use is important for; the assessment of the needs of public health; the development of appropriate drug strategies to reduce health effects; and the subsequent monitoring of the effectiveness of such strategies.

- It is generally accepted that there is a lack of information with respect to the dynamics and scale of illicit drug markets, and the validity or reliability of estimates are questionable.

- This paper presents a critical comparison of the results from three different methods for estimating the level of cocaine use in the general population.

Key Messages

- 0.70 (0.36 – 1.03) % of drivers tested positive for cocaine use compared with 0.22 (0.13 – 0.30) % (per day) as derived from regional-scale survey questionnaires.

- Direct comparison of prevalence estimates with the amount of drug related metabolites in sewage is difficult because accurate data on per-user consumption estimates is lacking.

- Such a comparison as carried out here helps to identify key short-falls in the respective datasets and highlights where further research is needed.

Strengths and Limitations of this Study

- A rigorous ecological approach to the present study would require that the comparison was based on exactly the same population, and at the same time, but the logistics of sampling and the vastly different time-scales involved in each of the three techniques make this difficult.

- No similar comparisons of the three drug epidemiology techniques have been carried out before so it is difficult to relate the present findings to other study populations.

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1. Introduction

Cocaine is the most commonly used illicit stimulant drug in Europe and consumption remains high in the United States despite a recent decline in annual prevalence [1]. Use of the drug is associated with numerous health problems including cardiovascular disorders, neurological impairment and death [2]. Accurate and timely information on the prevalence of cocaine use   are therefore important for assessing the needs of public health, developing appropriate drug strategies to reduce health effects, and in the subsequent monitoring of the effectiveness of such strategies. Whilst official statistics indicate that cocaine use is relatively stable in Europe and may be dropping in the United States, it is generally accepted that there is a lack of information with respect to the dynamics and scale of illicit drug markets, and the validity or reliability of estimates are questionable [3]. The estimation of drug use patterns in society is currently reliant on questionnaire based data-collection at the population level, and among groups of drug users, together with statistics from hospital admissions, registered drug-overdose deaths, treatment services and the records from police seizures [4–8]. Validation of drug use statistics derived from individual self-reporting has previously been attempted by drawing comparisons between the self-reported use and measurements of samples taken from hair, urine and blood [9–13]. This technique has shown that despite the use of an array of methods to increase the level of accuracy of self-reporting, under-reporting is still apparent. Recently, additional data on the level of drug use at the community level have also been acquired through the implementation of anonymous road-side testing studies [14,15], and also through the measurement of drug metabolites in sewage water [16–21]. With a range of different approaches now available to estimate the level of community drug use it is highly desirable to critically compare the results they provide. For the first time this paper presents a critical comparison of the results from three different methods for estimating the level of cocaine use in the general population. The comparison was performed on three studies in Oslo, Norway and applies to; a combination of user group and representative population sample survey questionnaires, a representative sample survey on drug use measured in saliva among drivers, and an analysis of the quantity of drugs and drug related metabolites in sewage.

2. Materials and Methods

2.1. Background - Cocaine Use in Norway

Life time prevalence of cocaine use in the general population 15 years and over was reported as 2.7 percent in 2004 and 2.5 percent in 2009 [22]. Results from both these studies (combined) show that the prevalence of recent cocaine use (within the last year) in the total population was as low as 0.6 percent. A separate study on young adults (21-30

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101 years) [23] reports higher rates of cocaine use in these age groups: prevalence of use within the last 6-months was 4.3

102 percent in 2002 and 4.9 percent in 2006. Also, lifetime prevalence of cocaine use among young people (15 - 20 years)

103 in Oslo has remained very stable in the years 2003 to 2008.

104 Cocaine use in Norway is dominated by recreational intranasal use (where the term "recreational" is defined as regular

105 occasional/infrequent use as opposed to dependent use). Crack use has been rare. Among young adult cocaine users

106 less than one in a hundred reported crack use and crack is seldom seized by the police/customs. A survey among the

107 prison population [24] identified 6 percent of inmates report daily or almost daily use of cocaine in the 6 months

108 leading up to imprisonment, but frequent cocaine use is lower among marginalized and injecting drug user groups

109 [25].

2.2. Methodology for the survey of drug-use amongst the driver population

111 Data collection was performed in the greater Oslo area in cooperation with two National Mobile Police Service (MPS)

112 districts from April 2008 to March 2009 as part of the DRUID Project [26]. Drivers of motor vehicles were selected

113 using a stratified two-stage cluster sampling procedure. In the first stage, random geographical areas and time periods

114 of five consecutive days were selected using a table of random sampling numbers [27]. All days and times of the week

115 and all seasons of the year were covered. Roads were chosen by randomly selecting map co-ordinates, then choosing

116 the closest roads. For each day the police selected two study sites along the chosen roads. The sites had to be suitable

117 as checkpoints (possibility to stop a number of cars at the same time on the roadside without causing traffic

118 congestion) and they had to be located within about 30-45 minutes' drive from each other. For each day, the starting

119 time for roadside sampling was also randomly selected. However, a few of the selected time periods had to be changed

120 to comply with working time regulations for police officers.

121 The second stage of the sampling procedure consisted of randomly stopping drivers within the defined two hour

122 period. The police officers were instructed to stop cars at random, rather than stopping old cars, young drivers or other

123 possible suspects of impaired driving. The number of data collection personnel at each site was related to the expected

124 traffic density. When one of the data collection personnel were ready for a new driver, the MPS stopped the first

125 approaching car or motorcycle and carried out their own routine controls (breath alcohol testing or driver's licence

126 control). Afterwards the driver was asked to proceed to the study team, who requested voluntary and anonymous

127 participation in the project. Oral and written information about the project was given to each driver. If verbal informed

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128   consent was given, a sample of oral fluid was collected and only the following data recorded: gender, age, day of the

129   week, time interval, and geographical site. It was thus impossible to trace a given sample to a specific donor or motor

130   vehicle. In general, the sampling procedure was designed in a way that should ensure that the drivers rendering

131   samples should give a representative picture of the total driver population. Saliva samples were collected using the

132   Statsure Saliva Sampler (Saliva Diagnostic Systems, Framingham, MA, USA). The saliva collection pad was placed

133   under the tongue until the indicator turned blue, or until five minutes has passed and transferred to a capped vial

134   labelled with a bar code label corresponding to the bar code of the questionnaire. The sample was kept in a plastic bag

135   at a temperature of approximately 5°C for a maximum of 6 hours, and then stored at -20°C.

136   Concentrations of cocaine and benzoylecgonine in oral fluid-buffer mixtures were determined by liquid

137   chromatography – tandem mass spectrometry [28], which specifically measured the substances in question. The

138   amount of collected oral fluid was determined by weighing the sample, and concentrations of substances in un-diluted

139   oral fluid were calculated. The cut-off thresholds in oral fluid-buffer mixture were 0.9 and 3.6 ng/mL for cocaine and

140   benzoylecgonine, respectively. The combined prevalence of cocaine or benzoylecgonine was estimated by a weighted

141   average, using weights adjusted for under- or over-sampling of the data compared to overall population statistics [29].

142   This weighting took into account the age and gender of drivers with respect to the general population, together with an

143   appropriate weighting for the days of the week and time of the day (Table 2).

2.3. Methodology for the analysis of drugs and related metabolites in sewage

145   Sample collection was carried out in the greater Oslo area in cooperation with the region's largest sewage treatment

146   plant (Vestfjorden Avløpselskap). This plant processes sewage from a metropolitan and suburban population of

147   approximately 570 000 people. An Isco 6712 portable automatic sampler (Teledyne, Nebraska USA) was used to

148   collect samples of wastewater every hour throughout the course of September 2009. The hourly samples were pooled

149   to produce 6-hour composites (n = 120) with mid-points corresponding to 2 am, 8 am, 2 pm and 8 pm for each day of

150   the month. Deuterated internal standards were spiked at the time of collection (1mL of benzoylecgonine-d3, cocaine-

151   d3, cocaethylene-d8, methamphetamine-d5, metoprolol acid-d5 and ceterizine-d8 at 50 ng/mL to give a final working

152   concentration of 50 ng/L of each standard in sewage) and samples were acid stabilised and stored at 4°C until analysis.

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153 Concentrations of cocaine and benzoylecgonine in the sewage water composites were determined by liquid

154 chromatography – tandem mass spectrometry [19]. The limit of quantification for the analytes in raw sewage was 5

155 ng/L.

156 The total mass of benzoylegonine passing through the sewage treatment processes in the Oslo region over the

157 sampling period was calculated by scaling the measured sewage concentration of the metabolite (ng/L) in each of the

158 120 samples (each representing 6-hours of sewage) by the total volume of sewage (L) for that 6-hour period. The

159 uncertainty with this estimate is associated with errors in sampling (an estimated 5% RSD based on an uncertainty

160 analysis performed by Lai et al, 2011), flow measurements (4.2% RSD), chemical analysis (5% RSD) and

161 biotransformation of cocaine and benzoylecgonine in the sewer system which is typically less than 10 % [30,31].

162 Careful consideration of the urinary excretion rates of cocaine and its metabolites are then needed for back-calculation

163 of the total mass of cocaine consumed during the sampling period. Benzoylecgonine is the primary urinary metabolite

164 of cocaine and accounts for 30.8±7.7 % of the recoverable dose of nasally insufflated cocaine in urine [32]. (Note that

165 cocaine use in Norway is dominated by intranasal administration so the pharmacokinetic parameters used in this study

166 are focused on this route of administration). It is therefore assumed that the total mass of benzoylecgonine in the

167 sewage accounts for 30.8±7.7 % of the total mass of cocaine consumed by the community group. As such, the

168 measured mass-transport rate of benzoylecgonine (g / week) is multiplied by a factor 3.5 to account for the 30.8±7.7

169 % excretion rate and the molar-ratio of cocaine to benzoylecgonine to give the total mass of consumed cocaine

170 (g/week, or g/month).

171 ***2.4. Combined Population and User-Group Survey Methodology***

172 The population of cocaine users was divided into two groups; socially integrated individuals (experimental,

173 recreational and heavy users), and marginalized individuals (light, medium or heavy users). It was assumed that the

174 two groups could be reached by differing survey-types [33–36]. Data on the socially integrated users was acquired in

175 three different population surveys, each for a different age segment. Two or three surveys were employed to increase

176 N and reduce statistical uncertainty (Table 1). Since cocaine use could be seen as stable and that sampling frames,

177 mode of administration and data collection were the same for surveys in each age segment, estimates were averaged

178 over the surveys, Data on marginalized users was collected from surveys of prison inmates and the Oslo homeless or

179 street population attending a needle exchange. Note that the estimated number of marginalized cocaine users was

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180 reduced by 20 percent because of a likely overlap between the prison and the street population [37,38]. Population

181 rates were based on the general population aged 15-64 years provided by government statistics correct to 31 December

182 2009 [29].

183 A "bottom up" method was used to estimate community cocaine use in Oslo. This method multiplies the number of

184 users by the reported frequency of use and reported amount (mass) of cocaine used [39–42]. Frequency was

185 established from the surveys (Table 1) while average values of amounts were based on self-report (last survey in Table

186 1) and existing literature (39). The amount varied with frequency of use such that the higher the frequency the higher

187 the dose (see Table 3). Note also that consumption estimates are purity adjusted. The purity of cocaine in Norway is

188 measured in conjunction with seizures of the drug by the police and customs. Data from the period 2007 – 2009

189 shows a trend of decreasing purity over time; lately 39% in 2007 compared to 25% in 2009 [43]. This degree of

190 variation is consistent with data from other nations [44–47].

191 Estimates of the prevalence of cocaine use derived from the survey among the driving population provide data on

192 cocaine use within a short period of time (within the last 24 hours). The combined survey method, however, acquires

193 data on the prevalence of consumption within the last 12 months. To be able to compare the roadside and the

194 combined survey method, the prevalence of use on a single day was estimated based on the frequency of use.

195 Frequency of use, measured as the number of days used in a year, yields the probability of use on a single day for each

196 level of frequency (see Table 3). This probability, multiplied by the number of users in the frequency group, yields the

197 expected number of users on a single day. Summing up expected number of daily users over frequency groups and

198 dividing by the population figure yields the prevalence of users per day.

3. Results

3.1. Survey of drug-use amongst the driver population

201 Cocaine was detected in 14 out of 2341 samples from the greater Oslo area, and benzoylecgonine was detected in 9

202 samples, none were positive for benzoylecgonine only. Therefore, only the results for cocaine were used in the

203 estimations below. A weighted average of 0.7% of the driver population was found to be positive for cocaine using the

204 weights presented in Table 2.

205 The concentration of cocaine and benzoylecgonine in oral fluid depends on the dilution of oral fluid during sampling

206 and the recovery from the sampling device. For the samples found to be positive for cocaine, the average collection

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207 volume of oral fluid was 0.74 ml, giving an average dilution of 1:2.4. A recovery for cocaine of 85.6% has been

208 reported [48]. Thus, the analytical cut-off corresponded to a cocaine concentration of 2.5 ng/ml in native (undiluted)

209 oral fluid.

3.2. Results of the analysis of drugs and related metabolites in sewage

211 Benzoylecgonine (the urinary metabolite of cocaine) was detected in all sewage samples collected in the Oslo region.

212 Measurements of the flow of this cocaine metabolite in sewage indicate an average load of 428 (CI 347 – 510)

213 g/week). Benzoylecgonine recovered in urine accounts for 30.8±7.7 % of the initial cocaine dose, so the measured

214 mass of this metabolite in the sewage is equivalent to 30.8±7.7 % of the total mass of cocaine consumed by the

215 community group. The measured flow of benzoylecgonine in the Oslo sewage system is therefore indicative of a

216 community-wide cocaine consumption rate of 1458 (CI 1158 – 1758) g/week (pure cocaine) which is equivalent to 76

217 (CI 60 – 91) kg/year if we assume the rate of cocaine consumption remains constant throughout the year.

3.3. Combined population and user-group survey results

219 Socially integrated users (aged 15-64 years) in Oslo reporting at least one instance of cocaine use in the last 12 months

220 constituted 2.7 % (CI 2.4-3.1) of the total population (15-64 years) in Oslo. Proportions were highest in the age

221 groups 20 to 24 years (4.0 – 7.6 %). Marginalized cocaine users in Oslo constitute an additional 0.2 % (CI 0.0-0.4) of

222 the total population (15-64 years), so the proportion of the total population that admits at least one instance of cocaine

223 use in the last 12 months is 2.9 % (CI 2.6-3.2) in Oslo.

224 An estimated 0.22 (CI 0.13-0.30) % of the population (15-64 years) use cocaine on a given day in Oslo.

225 Approximately 80 % of self-reported cocaine users (aged 15-64 years) used cocaine less than 10 times per year. The

226 remaining proportion of the user population (20 %) have taken more cocaine more frequently and are subsequently

227 responsible for in excess of 90% of the total daily cocaine consumption (g/day). In terms of user-group population,

228 the vast majority (73 %) of cocaine was consumed by the socially integrated population, while marginalized users

229 (including injecting drug users and prison inmates) consumed 27 % of the total.

3.4. Comparison of Results

231   The three methods provide two distinct measures of cocaine use; the prevalence of cocaine use in terms of the

232   proportion of the community that use the drug, and a quantitative measure (mass) of the total amount of cocaine that is

233   consumed by the entire community.

234   Comparison of the prevalence estimates derived from the combined population survey (0.22 (0.13 – 0.30) % per day)

235   and the road-side testing (0.70 (0.36 – 1.03) %) indicates that under reporting and possible under-representation of

236   users is apparent within the combined population surveys.

237   The combined population survey also provided an estimate for the total amount of cocaine that is consumed which can

238   be directly compared with the results of sewage measurements (Table 4). The estimated annual consumption rate

239   from the combined population survey (117 (70 – 165) kg/year, pure cocaine) is comparable with the 76 (CI 60 – 91)

240   kg/year kg/year figure from measurements of cocaine metabolites in sewage.

241   With this data it is also possible to calculate an estimated per-user consumption rate by combining the annual

242   prevalence of cocaine use (2.9 %) with the measured annual consumption from the sewage (76 kg/year). Such

243   analysis implies a per-user cocaine consumption rate of 6.4 (4.6 – 8.5) g/user/year (pure cocaine).

244   **4. Discussion**

245   A comparison was performed on three independent methods for estimating the use of cocaine in Oslo, Norway. The

246   comparison applies to; a combined sample survey questionnaire approach, a representative sample survey on drug use

247   among drivers, and a survey of the mass of cocaine-related metabolites in sewage. The estimated prevalence of use on

248   a single day was higher in the survey among drivers than using the combined survey approach, while the estimated

249   amount used (mass) in the latter was not significantly different than in the sewage approach.

250   The comparison identified a higher prevalence of cocaine use in the representative sample survey among drivers than

251   in the combined sample survey questionnaire approach. Under-reporting is not unexpected in the survey

252   questionnaires because the subject was drug use and the level of response was low, but this discrepancy may be even

253   larger than is immediately apparent from the present study. An earlier roadside study [49] found that the use of

254   medicinal drugs was under-estimated by 17-59% when using data from a survey of drivers compared to actually

255   dispensed amounts in the studied area. For the use of cannabis the results from a roadside survey were similar to self-

256   reported data. We therefore expect that data from a roadside survey will under-estimate the use of cocaine in the adult

257   population somewhat. In the present study marginalised drug users were included in the combined population survey

258   but they are far less likely to own or drive motor vehicles and therefore less likely to be detected in the road-side

259   testing surveys. Secondly, the detection time for cocaine in oral fluid depends upon the analytical cut-off, sampling

260   method, method of cocaine administration, dose used, acute or chronic cocaine use, and other factors. In controlled

261   studies of administration of 25-45 mg cocaine by intravenous injection, snorting or smoking, cocaine was detected in

262   oral fluid for more than 12 hours in only about 25% of the experiments [50,51]. However, cocaine may be detected in

263   oral fluid from chronic cocaine users for up to 118 hours after last dose in extreme cases [52]. Finally, the measured

264   prevalence (0.7 %) of cocaine or metabolites in the oral fluid of drivers is also considered a minimum because it is

265   expected that many cocaine users refrain from driving for some hours after cocaine administration, and further,

266   approximately 10% of drivers declined to participate in the study. It is possible that the group of drivers that refused

267   to offer a saliva sample have a higher prevalence of recent drug consumption than that of drivers who volunteered a

268   sample. This would give an even higher prevalence of use on a single day.

269   Interestingly although the combined population survey appears to underestimate the prevalence of cocaine use, this

270   method did result in a combined consumption estimate (kg/year) that was not significantly different to the results of

271   sewage analysis. This may mean that self-reported amounts of cocaine used were actually too high. Estimates of the

272   amount of cocaine used were the weakest part of the combined population survey, however, and the frequency

273   categories were also rather coarse. If there was a non-accounted overlap between the population survey and the

274   surveys among marginalized users to cover the cocaine user population, this would reduce both the estimated

275   proportion of users and the estimated amount. In addition, it is important to remember that the accuracy of the sewage

276   estimate is strongly affected by the accuracy of the clinical pharmacokinetic data on cocaine. The present study used

277   the pharmacokinetic parameters that apply for intra-nasal cocaine use because this is the most relevant for study

278   population. This implies that a degree of back-ground information from combined population surveys with regard to

279   the proportion of differing routes of administration are required before accurate sewage measurements are feasible.

280   For example, the use of the intra-nasal pharmacokinetic parameters would not be appropriate if the study was carried

281   out in a region with extensive crack-cocaine use as the excretion patterns differ for differing routes of administration.

282   No similar comparisons of the three drug epidemiology techniques have been carried out before so it is difficult to

283   relate the present findings to other study populations. It was however necessary, with the present study, to make some

284   general assumptions with regard to the average amount of cocaine used per individual in order to adequately compare

12

285 the prevalence estimates with that of the measured mass of cocaine metabolites in sewage. The combined population

286 surveys indicated an average per-user consumption rate of 9.8 g/user/year (pure cocaine) which is much lower than the

287 30.2 g/user/year (in Europe) proposed by The United Nations Office on Drugs and Crime (2010). While it appears

288 that the average per-user consumption rate in Oslo may actually be lower than in many other European regions [21],

289 the UNODC does state that their estimate (which is based on empirical data from a small number of locations and

290 makes significant assumptions with regard to the importance of drug availability and the effectiveness of law

291 enforcement) is a considerable approximation as little or no data on the quantities consumed by individuals is

292 available, and much of the existing data is contradictory [54]. The results of the present study do suggest that

293 combining accurate measurements of the total drug consumption in the population (via sewage analysis) with reliable

294 prevalence figures acquired through rigorous survey of the population could provide improvements to the accuracy of

295 average per-user consumption figures in the future.

296 The comparison carried out in the present study has provided an excellent means for checking the quality and

297 accuracy of each the three measurement techniques because they each approach the problem from different angels.

298 The results do however highlight the difficulties associated with performing such a comparison. A rigorous ecological

299 approach to the present study would require that the comparison was based on exactly the same population, and at the

300 same time, but the logistics of sampling and the vastly different time-scales involved in each of the three techniques

301 make this difficult. It is possible, for example, that the population of drivers that took part in the road-side study

302 included individuals that were in transit and therefor from outside the region covered by the combined population

303 survey. Similarly, results of the sewage analysis are based on a one-month period and an assumption is made that

304 combined cocaine use (by the total population) remains relatively constant throughout the year. These problems do

305 however allow more precise research questions to be formulated: How can we better combine surveys to better cover

306 all segments of the population? Does cocaine use in the population of drivers follow the same pattern as cocaine use

307 in the general population? How can we better estimate the amounts used? How can we better estimate frequency of

308 use? Short-falls have been identified in each of the three epidemiology techniques when used in isolation, but together

309 the three complimentary techniques provide a well-balanced assessment of the drug-use situation in a given

310 community with limited reliance on derived estimates.

311 **5. Conclusion**

312 Under-reporting is apparent in prevalence estimates provided by the combined population surveys when compared

313 with the proportion of motor-vehicle drivers with detectable levels of cocaine or cocaine metabolites in oral-fluid, but

314 an unanswered question is whether cocaine use in the population of drivers follows the same pattern as cocaine use in

315 the general population. Direct measurements of sewage from a defined population provide data on the size of the

316 cocaine market in a particular region (albeit with a degree of uncertainty). These measurements indicate that self-

317 reported cocaine consumption may be over-exaggerated and highlight the large degree of uncertainty with respect to

318 per-user consumption estimates. Each of the three techniques has significant short-falls when used in isolation, but

319 together they deliver complimentary data which provides a well-balanced assessment of the drug-use situation in a

320 given community and identify areas where more research is needed.

321 **Acknowledgements**

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Estimation of Cocaine Consumption in the Community: A Critical Comparison of the Results from Three Complimentary Techniques

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ABSTRACT

Objectives: A range of approaches are now available to estimate the level of drug use in the community so it is desirable to critically compare results from the differing techniques. This paper presents a comparison of the results from three methods for estimating the level of cocaine use in the general population.

Design: The comparison applies to; a set of regional-scale sample survey questionnaires, a representative sample survey on drug use among drivers, and an analysis of the quantity of cocaine related metabolites in sewage.

Setting: 14,438 participants provided data for the set of regional-scale sample survey questionnaires; 2,341 drivers provided oral-fluid samples; and untreated sewage from 570,000 people was analysed for biomarkers of cocaine use. All data was collected in Oslo, Norway.

Results: 0.70 (0.36 – 1.03) % of drivers tested positive for cocaine-use which suggest a prevalence that is higher than the 0.22 (0.13 – 0.30) % (per day) figure derived from regional-scale survey questionnaires, but the degree to which cocaine consumption in the driver-population follows the general population is an unanswered question. Despite the comparatively low prevalence figure the survey questionnaires did provide estimates of the volume of consumption that are comparable with the amount of cocaine related metabolites in sewage. Per-user consumption estimates are however highlighted as a significant source of uncertainty as little or no data on the quantities consumed by individuals is available, and much of the existing data is contradictory. ~~the degree to which cocaine consumption in the driver-population follows the general population is an unanswered question.~~

Conclusions: The comparison carried out in the present study can provide an excellent means of checking the quality and accuracy of the three measurement techniques because they each approach the problem from a different viewpoint. Together the three complimentary techniques provide a well-balanced assessment of the drug-use situation in a given community and identify areas where more research is needed.

3

ARTICLE SUMMARY

Article Focus

- Estimation of the prevalence of cocaine use is important for; the assessment of the needs of public health; the development of appropriate drug strategies to reduce health effects; and the subsequent monitoring of the effectiveness of such strategies.

- It is generally accepted that there is a lack of information with respect to the dynamics and scale of illicit drug markets, and the validity or reliability of estimates are questionable.

- This paper presents a critical comparison of the results from three different methods for estimating the level of cocaine use in the general population.

Key Messages

- 0.70 (0.36 – 1.03) % of drivers tested positive for cocaine use compared with 0.22 (0.13 – 0.30) % (per day) as derived from regional-scale survey questionnaires.

- Direct comparison of prevalence estimates with the amount of drug related metabolites in sewage is difficult because accurate data on per-user consumption estimates is lacking.

- Such a comparison as carried out here helps to identify key short-falls in the respective datasets and highlights where further research is needed.

Strengths and Limitations of this Study

- A rigorous ecological approach to the present study would require that the comparison was based on exactly the same population, and at the same time, but the logistics of sampling and the vastly different time-scales involved in each of the three techniques make this difficult.

- No similar comparisons of the three drug epidemiology techniques have been carried out before so it is difficult to relate the present findings to other study populations.

4

1. Introduction

75 Cocaine is the ~~second~~ most commonly used illicit stimulant drug in Europe and consumption remains high in the

76 United States despite a recent decline in annual prevalence [1]. Use of the drug is associated with numerous health

77 problems including cardiovascular disorders, neurological impairment and death [2]. Accurate and timely information

78 on the prevalence of cocaine use ~~over recent years are shadowed by the growing concern to public health, so~~

79 ~~quantification and the estimation of the prevalence of cocaine use~~ are therefore important for assessing the needs of

80 public health, developing appropriate drug strategies to reduce health effects, and in the subsequent monitoring of the

81 effectiveness of such strategies. Whilst official statistics indicate that cocaine use is relatively stable in Europe and

82 may be dropping in the United States, ~~I~~it is generally accepted that there is a lack of information with respect to the

83 dynamics and scale of illicit drug markets, and the validity or reliability of estimates are questionable [3]. The

84 estimation of drug use patterns in society is currently reliant on questionnaire based data-collection at the population

85 level, and among groups of drug users, together with statistics from hospital admissions, registered drug-overdose

86 deaths, treatment services and the records from police seizures [4–8]. Validation of drug use statistics derived from

87 individual self-reporting has previously been attempted by drawing comparisons between the self-reported use and

88 measurements of samples taken from hair, urine and blood [9–13]. This technique has shown that despite the use of an

89 array of methods to increase the level of accuracy of self-reporting, under-reporting is still apparent. Recently,

90 additional data on the level of drug use at the community level have also been acquired through the implementation of

91 anonymous road-side testing studies [14,15], and also through the measurement of drug metabolites in sewage water

92 [16–21]. With a range of different approaches now available to estimate the level of community drug use it is highly

93 desirable to critically compare the results they provide. For the first time this paper presents a critical comparison of

94 the results from three different methods for estimating the level of cocaine use in the general population. The

95 comparison was performed on three studies in Oslo, Norway and applies to; a combination of user group and

96 representative population sample survey questionnaires, a representative sample survey on drug use measured in saliva

97 among drivers, and an analysis of the quantity of drugs and drug related metabolites in sewage.

2. Materials and Methods

2.1. Background - Cocaine Use in Norway

100 Life time prevalence of cocaine use in the general population 15 years and over was reported as 2.7 percent in 2004

101 and 2.5 percent in 2009 [22]. Results from both these studies (combined) show that the prevalence of recent cocaine

5

102 use (within the last year) in the total population was as low as 0.6 percent. A separate study on young adults (21-30

103 years) [23] reports higher rates of cocaine use in these age groups: prevalence of use within the last 6-months was 4.3

104 percent in 2002 and 4.9 percent in 2006. Also, lifetime prevalence of cocaine use among young people (15 - 20 years)

105 in Oslo has remained very stable in the years 2003 to 2008.

106 Cocaine use in Norway is dominated by recreational intranasal use (where the term "recreational" is defined as regular

107 occasional/infrequent use as opposed to dependent use). Crack use has been rare. Among young adult cocaine users

108 less than one in a hundred reported crack use and crack is seldom seized by the police/customs. A survey among the

109 prison population [24] identified 6 percent of inmates report daily or almost daily use of cocaine in the 6 months

110 leading up to imprisonment, but frequent cocaine use is lower among marginalized and injecting drug user groups

111 [25].

112 Purity of cocaine will vary from batch to batch, by place of production, and by level of sale (such as street-level or

113 whole-sale market level). The purity of cocaine in Norway is measured in conjunction with seizures of the drug by the

114 police and customs. Data from the period 2007 – 2009 shows a trend of decreasing purity over time; lately 39% in

115 2007 compared to 25% in 2009 . This degree of variation is consistent with data from other nations [26-29].

116 ### *2.2. Methodology for the survey of drug-use amongst the driver population*

117 Data collection was performed in the greater Oslo area in cooperation with two National Mobile Police Service (MPS)

118 districts from April 2008 to March 2009 as part of the DRUID Project [26]. Drivers of motor vehicles were selected

119 using a stratified two-stage cluster sampling procedure. In the first stage, random geographical areas and time periods

120 of five consecutive days were selected using a table of random sampling numbers [27]. All days and times of the week

121 and all seasons of the year were covered. Roads were chosen by randomly selecting map co-ordinates, then choosing

122 the closest roads. For each day the police selected two study sites along the chosen roads. The sites had to be suitable

123 as checkpoints (possibility to stop a number of cars at the same time on the roadside without causing traffic

124 congestion) and they had to be located within about 30-45 minutes' drive from each other. For each day, the starting

125 time for roadside sampling was also randomly selected. However, a few of the selected time periods had to be changed

126 to comply with working time regulations for police officers.

127 The second stage of the sampling procedure consisted of randomly stopping drivers within the defined two hour

128 period. The police officers were instructed to stop cars at random, rather than stopping old cars, young drivers or other

6

129 possible suspects of impaired driving. The number of data collection personnel at each site was related to the expected

130 traffic density. When one of the data collection personnel were ready for a new driver, the MPS stopped the first

131 approaching car or motorcycle and carried out their own routine controls (breath alcohol testing or driver's licence

132 control). Afterwards the driver was asked to proceed to the study team, who requested voluntary and anonymous

133 participation in the project. Oral and written information about the project was given to each driver. If verbal informed

134 consent was given, a sample of oral fluid was collected and only the following data recorded: gender, age, day of the

135 week, time interval, and geographical site. It was thus impossible to trace a given sample to a specific donor or motor

136 vehicle. In general, the sampling procedure was designed in a way that should ensure that the drivers rendering

137 samples should give a representative picture of the total driver population. Saliva samples were collected using the

138 Statsure Saliva Sampler (Saliva Diagnostic Systems, Framingham, MA, USA). The saliva collection pad was placed

139 under the tongue until the indicator turned blue, or until five minutes has passed and transferred to a capped vial

140 labelled with a bar code label corresponding to the bar code of the questionnaire. The sample was kept in a plastic bag

141 at a temperature of approximately 5°C for a maximum of 6 hours, and then stored at -20°C.

142 Concentrations of cocaine and benzoylecgonine in oral fluid-buffer mixtures were determined by liquid

143 chromatography – tandem mass spectrometry [28], which specifically measured the substances in question. The

144 amount of collected oral fluid was determined by weighing the sample, and concentrations of substances in un-diluted

145 oral fluid were calculated. The cut-off thresholds in oral fluid-buffer mixture were 0.9 and 3.6 ng/mL for cocaine and

146 benzoylecgonine, respectively. The combined prevalence of cocaine or benzoylecgonine was estimated by a weighted

147 average, using weights adjusted for under- or over-sampling of the data compared to overall population statistics [29].

148 This weighting took into account the age and gender of drivers with respect to the general population, together with an

149 appropriate weighting for the days of the week and time of the day (Table 2).

150 *2.3. Methodology for the analysis of drugs and related metabolites in sewage*

151 Sample collection was carried out in the greater Oslo area in cooperation with the region's largest sewage treatment

152 plant (Vestfjorden Avløpselskap). This plant processes sewage from a metropolitan and suburban population of

153 approximately 570 000 people. An Isco 6712 portable automatic sampler (Teledyne, Nebraska USA) was used to

154 collect samples of wastewater every hour throughout the course of September 2009. The hourly samples were pooled

155 to produce 6-hour composites (n = 120) with mid-points corresponding to 2 am, 8 am, 2 pm and 8 pm for each day of

156 the month. Deuterated internal standards were spiked at the time of collection (1mL of benzoylecgonine-d3, cocaine-

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157 d3, cocaethylene-d8, methamphetamine-d5, metoprolol acid-d5 and ceterizine-d8 at 50 ng/mL to give a final working

158 concentration of 50 ng/L of each standard in sewage) and samples were acid stabilised and stored at 4°C until analysis.

159 Concentrations of cocaine and benzoylecgonine in the sewage water composites were determined by liquid

160 chromatography – tandem mass spectrometry [19]. The limit of quantification for the analytes in raw sewage was 5

161 ng/L.

162 The total mass of benzoylegonine passing through the sewage treatment processes in the Oslo region over the

163 sampling period was calculated by scaling the measured sewage concentration of the metabolite (ng/L) in each of the

164 120 samples (each representing 6-hours of sewage) by the total volume of sewage (L) for that 6-hour period. The

165 uncertainty with this estimate is associated with errors in sampling (an estimated 5% RSD based on an uncertainty

166 analysis performed by Lai et al, 2011), flow measurements (4.21% RSD), chemical analysis (5% RSD) and

167 biotransformation of cocaine and benzoylecgonine in the sewer system which is typically less than 10 % [30,31].

168 Careful consideration of the urinary excretion rates of cocaine and its metabolites are then needed for back-calculation

169 of the total mass of cocaine consumed during the sampling period. Benzoylecgonine is the primary urinary metabolite

170 of cocaine and accounts for 30.8±7.7 % of the recoverable dose of nasally insufflated cocaine in urine [32]. (Note that

171 cocaine use in Norway is dominated by intranasal administration so the pharmacokinetic parameters used in this study

172 are focused on this route of administration). It is therefore assumed that the total mass of benzoylecgonine in the

173 sewage accounts for 30.8±7.7 % of the total mass of cocaine consumed by the community group. As such, the

174 measured mass-transport rate of benzoylecgonine (g / week) is multiplied by a factor 3.5 to account for the 30.8±7.7

175 % excretion rate and the molar-ratio of cocaine to benzoylecgonine to give the total mass of consumed cocaine

176 (g/week, or g/month).

2.4. Combined Population and User-Group Survey Methodology

178 The population of cocaine users was divided into two groups; socially integrated individuals (experimental,

179 recreational and heavy users), and marginalized individuals (light, medium or heavy users). It was assumed that the

180 two groups could be reached by differing survey-types [33–36]. Data on the socially integrated users was acquired in

181 three different population surveys, each for a different age segment. Two or three surveys were employed to increase

182 N and reduce statistical uncertainty (Table 1). Since cocaine use could be seen as stable and that sampling frames,

183 mode of administration and data collection were the same for surveys in each age segment, estimates were averaged

184 over the surveys, Data on marginalized users was collected from surveys of prison inmates and the Oslo homeless or

185 street population attending a needle exchange. Note that the estimated number of marginalized cocaine users was

186 reduced ~~with~~ by 20 percent because of a likely overlap between the prison and the street population [37,38].

187 Population rates were based on the general population aged 15-64 years provided by government statistics correct to

188 31 December 2009 [29].

189 A "bottom up" method was used to estimate community cocaine use in Oslo. This method multiplies the number of

190 users by the reported frequency of use and reported amount (mass) of cocaine used [39–42]. Frequency was

191 established from the surveys (Table 1) while average values of amounts were based on self-report (last survey in Table

192 1) and existing literature (39). The amount varied with frequency of use such that the higher the frequency the higher

193 the dose (see Table 3). Note also that consumption estimates are purity adjusted. The purity of cocaine in Norway is

194 measured in conjunction with seizures of the drug by the police and customs. Data from the period 2007 – 2009

195 shows a trend of decreasing purity over time; lately 39% in 2007 compared to 25% in 2009 [43]. This degree of

196 variation is consistent with data from other nations [44–47].

197 Estimates of the prevalence of cocaine use derived from the survey among the driving population provide data on

198 cocaine use within a short period of time (within the last 24 hours). The combined survey method, however, acquires

199 data on the prevalence of consumption within the last 12 months. To be able to compare the roadside and the

200 combined survey method, the prevalence of use on a single day was estimated based on the frequency of use.

201 Frequency of use, measured as the number of days used in a year, yields the probability of use on a single day for each

202 level of frequency (see Table 3). This probability, multiplied by the number of users in the frequency group, yields the

203 expected number of users on a single day. Summing up expected number of daily users over frequency groups and

204 dividing by the population figure yields the prevalence of users per day.

3. Results

3.1. Survey of drug-use amongst the driver population

207 Cocaine was detected in 14 out of 2341 samples from the greater Oslo area, and benzoylecgonine was detected in 9

208 samples, none were positive for benzoylecgonine only. Therefore, only the results for cocaine were used in the

209 estimations below. A weighted average of 0.7% of the driver population was found to be positive for cocaine using the

210 weights presented in Table 2.

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211　The concentration of cocaine and benzoylecgonine in oral fluid depends on the dilution of oral fluid during sampling

212　and the recovery from the sampling device. For the samples found to be positive for cocaine, the average collection

213　volume of oral fluid was 0.74 ml, giving an average dilution of 1:2.4. A recovery for cocaine of 85.6% has been

214　reported [48]. Thus, the analytical cut-off corresponded to a cocaine concentration of 2.5 ng/ml in native (undiluted)

215　oral fluid.

3.2. Results of the analysis of drugs and related metabolites in sewage

217　Benzoylecgonine (the urinary metabolite of cocaine) was detected in all sewage samples collected in the Oslo region.

218　Measurements of the flow of this cocaine metabolite in sewage indicate an average load of 428 (CI ~~355~~ 347 – ~~500~~510)

219　g/week). Benzoylecgonine recovered in urine accounts for 30.8±7.7 % of the initial cocaine dose, so the measured

220　mass of this metabolite in the sewage is equivalent to 30.8±7.7 % of the total mass of cocaine consumed by the

221　community group. The measured flow of benzoylecgonine in the Oslo sewage system is therefore indicative of a

222　community-wide cocaine consumption rate of 1458 (CI ~~1181~~ 1158 – ~~1735~~1758) g/week (pure cocaine) which is

223　equivalent to 76 (CI ~~61~~ 60 – ~~90~~91) kg/year if we assume the rate of cocaine consumption remains constant throughout

224　the year.

3.3. Combined population and user-group survey results

226　Socially integrated users (aged 15-64 years) in Oslo reporting at least one instance of cocaine use in the last 12 months

227　constituted 2.7 % (CI 2.4-3.1) of the total population (15-64 years) in Oslo. Proportions were highest in the age

228　groups 20 to 24 years (4.0 – 7.6 %). Marginalized cocaine users in Oslo constitute an additional 0.2 % (CI 0.0-0.4) of

229　the total population (15-64 years), so the proportion of the total population that admits at least one instance of cocaine

230　use in the last 12 months is 2.9 % (CI 2.6-3.2) in Oslo.

231　An estimated 0.22 (CI 0.13-0.30) % of the population (15-64 years) use cocaine on a given day in Oslo.

232　Approximately 80 % of self-reported cocaine users (aged 15-64 years) used cocaine less than 10 times per year. The

233　remaining proportion of the user population (20 %) have taken more cocaine more frequently and are subsequently

234　responsible for in excess of 90% of the total daily cocaine consumption (g/day). In terms of user-group population,

235　the vast majority (73 %) of cocaine was consumed by the socially integrated population, while marginalized users

236　(including injecting drug users and prison inmates) consumed 27 % of the total.

10

237   *3.4. Comparison of Results*

238   The three methods provide two distinct measures of cocaine use; the prevalence of cocaine use in terms of the

239   proportion of the community that use the drug, and a quantitative measure (mass) of the total amount of cocaine that is

240   consumed by the entire community.

241   Comparison of the prevalence estimates derived from the combined population survey (0.22 (0.13 – 0.30) % per day)

242   and the road-side testing (0.70 (0.36 – 1.03) %) indicates that under reporting and possible under-representation of

243   users is apparent within the combined population surveys.

244   The combined population survey also provided an estimate for the total amount of cocaine that is consumed which can

245   be directly compared with the results of sewage measurements (Table 4). The estimated annual consumption rate

246   from the combined population survey (117 (70 – 165) kg/year, pure cocaine) is comparable with the 76 (CI 61 60 –

247   90 91) kg/year kg/year figure from measurements of cocaine metabolites in sewage.

248   With this data it is also possible to calculate an estimated per-user consumption rate by combining the annual

249   prevalence of cocaine use (2.9 %) with the measured annual consumption from the sewage (76 kg/year). Such

250   analysis implies a per-user cocaine consumption rate of 6.4 (4.6 – 8.5) g/user/year (pure cocaine).

251   **4.   Discussion**

252   A comparison was performed on three independent methods for estimating the use of cocaine in Oslo, Norway. The

253   comparison applies to; a combined sample survey questionnaire approach, a representative sample survey on drug use

254   among drivers, and a survey of the mass of cocaine-related metabolites in sewage. The estimated prevalence of use on

255   a single day was higher in the survey among drivers than using the combined survey approach, while the estimated

256   amount used (mass) in the latter was not significantly different than in the sewage approach.

257   The comparison identified a higher prevalence of cocaine use in the representative sample survey among drivers than

258   in the combined sample survey questionnaire approach. Under-reporting is not unexpected in the survey

259   questionnaires because the subject was drug use and the level of response was low, but this discrepancy may be even

260   larger than is immediately apparent from the present study. An earlier roadside study [49] found that the use of

261   medicinal drugs was under-estimated by 17-59% when using data from a survey of drivers compared to actually

262   dispensed amounts in the studied area. For the use of cannabis the results from a roadside survey were similar to self-

263 reported data. We therefore expect that data from a roadside survey will under-estimate the use of cocaine in the adult

264 population somewhat. In the present study marginalised drug users were included in the combined population survey

265 but they are far less likely to own or drive motor vehicles and therefore less likely to be detected in the road-side

266 testing surveys. Secondly, the detection time for cocaine in oral fluid depends upon the analytical cut-off, sampling

267 method, method of cocaine administration, dose used, acute or chronic cocaine use, and other factors. In controlled

268 studies of administration of 25-45 mg cocaine by intravenous injection, snorting or smoking, cocaine was detected in

269 oral fluid for more than 12 hours in only about 25% of the experiments [50,51]. However, cocaine may be detected in

270 oral fluid from chronic cocaine users for up to 118 hours after last dose in extreme cases [52]. Finally, the measured

271 prevalence (0.7 %) of cocaine or metabolites in the oral fluid of drivers is also considered a minimum because it is

272 expected that many cocaine users refrain from driving for some hours after cocaine administration, and further,

273 approximately 10% of drivers declined to participate in the study. It is possible that the group of drivers that refused

274 to offer a saliva sample have a higher prevalence of recent drug consumption than that of drivers who volunteered a

275 sample. This would give an even higher prevalence of use on a single day.

276 Interestingly although the combined population survey appears to underestimate the prevalence of cocaine use, this

277 method did result in a combined consumption estimate (kg/year) that was not significantly different to the results of

278 sewage analysis. This may mean that self-reported amounts of cocaine used were actually too high. Estimates of the

279 amount of cocaine used were the weakest part of the combined population survey, however, and the frequency

280 categories were also rather coarse. If there was a non-accounted overlap between the population survey and the

281 surveys among marginalized users to cover the cocaine user population, this would reduce both the estimated

282 proportion of users and the estimated amount. In addition, it is important to remember that the accuracy of the sewage

283 estimate is strongly affected by the accuracy of the clinical pharmacokinetic data on cocaine. The present study used

284 the pharmacokinetic parameters that apply for intra-nasal cocaine use because this is the most relevant for study

285 population. This implies that a degree of back-ground information from combined population surveys with regard to

286 the proportion of differing routes of administration are required before accurate sewage measurements are feasible.

287 For example, the use of the intra-nasal pharmacokinetic parameters would not be appropriate if the study was carried

288 out in a region with extensive crack-cocaine use as the excretion patterns differ for differing routes of administration.

289 No similar comparisons of the three drug epidemiology techniques have been carried out before so it is difficult to

290 relate the present findings to other study populations. It was however necessary, with the present study, to make some

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291 general assumptions with regard to the average amount of cocaine used per individual in order to adequately compare

292 the prevalence estimates with that of the measured mass of cocaine metabolites in sewage. The combined population

293 surveys indicated an average per-user consumption rate of 9.8 g/user/year (pure cocaine) which is much lower than the

294 30.2 g/user/year (in Europe) proposed by The United Nations Office on Drugs and Crime (2010). While it appears

295 that the average per-user consumption rate in Oslo may actually be lower than in many other European regions [21],

296 the UNODC does state that their estimate (which is based on empirical data from a small number of locations and

297 makes significant assumptions with regard to the importance of drug availability and the effectiveness of law

298 enforcement) is a considerable approximation as little or no data on the quantities consumed by individuals is

299 available, and much of the existing data is contradictory [54]. The results of the present study do suggest that

300 combining accurate measurements of the total drug consumption in the population (via sewage analysis) with reliable

301 prevalence figures acquired through rigorous survey of the population could provide improvements to the accuracy of

302 average per-user consumption figures in the future.

303 The comparison carried out in the present study has provided an excellent means for checking the quality and

304 accuracy of each the three measurement techniques because they each approach the problem from different angels.

305 The results do however highlight the difficulties associated with performing such a comparison. A rigorous ecological

306 approach to the present study would require that the comparison was based on exactly the same population, and at the

307 same time, but the logistics of sampling and the vastly different time-scales involved in each of the three techniques

308 make this difficult. It is possible, for example, that the population of drivers that took part in the road-side study

309 included individuals that were in transit and therefor from outside the region covered by the combined population

310 survey. Similarly, results of the sewage analysis are based on a one-month period and an assumption is made that

311 combined cocaine use (by the total population) remains relatively constant throughout the year. These problems do

312 however allow more precise research questions to be formulated: How can we better combine surveys to better cover

313 all segments of the population? Does cocaine use in the population of drivers follow the same pattern as cocaine use

314 in the general population? How can we better estimate the amounts used? How can we better estimate frequency of

315 use? Short-falls have been identified in each of the three epidemiology techniques when used in isolation, but together

316 the three complimentary techniques provide a well-balanced assessment of the drug-use situation in a given

317 community with limited reliance on derived estimates.

318 **5. Conclusion**

319 Under-reporting is apparent in prevalence estimates provided by the combined population surveys when compared

320 with the proportion of motor-vehicle drivers with detectable levels of cocaine or cocaine metabolites in oral-fluid, but

321 an unanswered question is whether cocaine use in the population of drivers follows the same pattern as cocaine use in

322 the general population. Direct measurements of sewage from a defined population provide data on the size of the

323 cocaine market in a particular region (albeit with a degree of uncertainty). These measurements indicate that self-

324 reported cocaine consumption may be over-exaggerated and highlight the large degree of uncertainty with respect to

325 per-user consumption estimates. Each of the three techniques has significant short-falls when used in isolation, but

326 together they deliver complimentary data which provides a well-balanced assessment of the drug-use situation in a

327 given community and identify areas where more research is needed.

Acknowledgements

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Table 1. Combined population and user group survey parameters including study population, study dates and sample size.

Target Population	Survey Year	Type of survey	Sample Size (n=)	Publication
15 – 20 years, Oslo [1]	2006, 2007, 2008	Postal	5104	(Vedøy and Skretting, 2009)
21 – 30 years, Oslo [2]	2006, 2010	Postal	3468	(Lund et al., 2007)
31 – 64 years, Oslo [3]	2004, 2009	Questionnaire completed in private	899	(Nordlund, 2010)
Prison Inmates, Norway (national, applied to Oslo) [4]	2002	Questionnaire completed in private	1093	(Odegard, 2008)
Injecting drug users, Oslo [3]	2000-2004	Face to face	3829	(Bretteville-Jensen and Amundsen, 2009)
Marginalized Users, Arendal [3]	2010	Face to face	45	Unpublished pilot

Response rates: [1] 35 percent, [2] 40-50 percent, [3] not recorded or applicable, [4] 41 percent.

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Table 2. Weights for under- or over-sampling associated with the road-side saliva study.

Characteristics	Distribution among drivers (%)	Distribution in the total population of Oslo (%)	Weight
Age (years)			
16-24	9.4	10.6	1.13
25-34	18.1	20.9	1.15
35-44	24.3	16.2	0.67
45-54	21.4	12.2	0.57
55-64	16.4	10.2	0.62
65+	10.4	11.7	1.13
Total	100.0	81.8	-
Gender			
Female	29.8	50.6	1.70
Male	70.2	49.4	0.70
Total	100.0	100.0	-
Day of the week			
Mon-Thu	48.0	57.1	1.19
Fri	8.6	14.3	1.66
Sat	31.0	14.3	0.46
Sun	12.4	14.3	1.15
Total	100.0	100.0	-
Time of day (h)			
00.00-05.59	3.4	25.0	7.35
06.00-11.59	30.1	25.0	0.83
12.00-17.59	43.0	25.0	0.58
18.00-23.59	23.5	25.0	1.06
Total	100.0	100.0	-

Table 3. Parameters and estimates of community cocaine consumption for combined survey method by frequency of use categories in four surveys. Mean number of usage-days per unit time and the probability of use on a given day. Estimates of the proportion of users in the total survey population, frequency of use among users, and average weekly consumption

Survey - Population 15-30 years

Frequency of use categories (per half year)	Never	1-4 times	5-10 times	11-25 times	25-50 times	50+ times	Total/average (CI)
Mean number of usage days per half year[1]	0	2.5	7.5	18	38	116.5	-
Probability of use on any given day (%)[2]	0	1.4	4.1	9.9	20.8	63.7	-
Proportion of users among total age-group population (%)[3]	95.3 (94.8-95.7)	3.0	0.9	0.4	0.2	0.2	100
Frequency of use among users (%)[4]	-	63	20	9	4	5	100
Average per-user consumption, mg (pure) / week[5]	-	6	43	156	585	2240	154 (71-237)

Survey - Population 31-64 years

Frequency of use categories (per year)	Never	1-4 times	Monthly	Weekly	Daily, almost daily	Total/average (CI)
Mean number of usage-days per year[6]	0	2.5	12	52	182.5	-
Probability of use on any given day (%)[2]	0	0.7	3.3	14.8	50.0	-
Proportion of users among total age-group population (%)[3]	98.3 (97.2-99.4)	0.9	0.5	0.3	0.1	100
Frequency of use among users (%)[4]	-	50	30	15	5	100
Average per-user consumption, mg (pure) / week[5]	-	4	42	270	2106	160 (37-283)

Survey - Prison population

Frequency of use categories (per half year prior to incarceration)	Never	1-3 times per month or less	Weekly	Daily, almost daily	Total/average (CI)
Mean number of usage-days per year[6]	0	12	52	182.5	-
Probability of use on any given day (%)[2]	0	3.3	14.2	50.0	-
Proportion of users among total population 15-64 years (%)[3]	99.9 (99.7-100)	0.06	0.03	0.01	100
Frequency of use among users (%)[4]	-	63	23	13	100
Average per-user consumption, mg (pure) / week[5]	-	138	900	3510	767 (487-1048)

Survey - Injectors/marginalized users

Frequency of use categories (per year)	Never	Less than once a month	Monthly	Weekly	Daily, almost daily	Total/average (CI)
Mean number of usage-days per year[6]	0	6	12	52	182.5	-
Probability of use on any given day (%)[2]	0	1.6	3.3	14.2	50.0	-
Proportion of users among total population 15-64 years (%)[3]	99.9 (99.6-100)	0.06	0.01	0.01	0.02	100
Frequency of use among users (%)[4]	-	55	12	12	21	100
Average per-user consumption, mg (pure) / week[5]	-	21	42	270	2106	491 (217-765)

[1] Midpoint of frequency category reported in each survey, set to 116.5 for those using more than 50 times per half year. [2] Defined as a usage-day or a single 24-hour period in which cocaine is consumed. Number of usage days per user, divided by 182.6 for half year periods and 365.25 for one year periods [3] Number of users in each category divided by population figures of relevant age group [4] Number of users in each category divided by the total number of users [5] For each category the total consumption of pure cocaine equals number of users * mean number of usage days * mean dose size * mean number of doses per day * purity. Average per user consumption per week of pure cocaine equals this amount divided by the number of users and 26 for half year period and 52 for one year period. Mean dose size and mean number of doses per day vary from 0.1 gram and 2.5 doses in categories of lowest frequency to 0.25 gram and 8 doses in categories of highest frequency. [6] Midpoint of frequency category, but assuming 6 usage-months per year

Table 4. Prevalence and scale of cocaine use in Oslo as determined by combined population surveys and measurements of a cocaine metabolite in sewage. (Direct measurements or estimates in **bold**. Derived estimates in *italics*).

Method	Annual Prevalence % (CI) [a]	Cocaine Consumption (Pure)	
		Per-user g/year (CI)	Total population kg/year (CI)
Combined Population Survey (CPS)	**2.9 (2.6 – 3.2)**	9.8 (5.6 – 14.1)	*117 (70 – 165)*
Sewage Analysis			
Prevalence from CPS	**2.9 (2.6 – 3.2)**	*6.4 (4.6 – 8.5)*	**76 (60 – 91)**
Per-user consumption from CPS	*1.9 (1.0 – 4.0)*	9.8 (5.6 – 14.1)	**76 (60 – 91)**

[a] Population 15 – 64 years of age, 410 000 (source Statistics Norway)