



Validity of the EQ-5D as a generic health outcome instrument in a heroin-dependent population

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Abstract

Objective: To evaluate the validity of the EuroQol (EQ-5D) in a population of chronic, treatment-resistant heroin-dependent patients.

Methods: The EQ-5D is studied relative to the Maudsley Addiction Profile (MAP), the Symptom Checklist (SCL-90) and the European Addiction Severity Index (EuropASI) which were used to assess the participant's physical functioning, mental health and social integration, respectively. Data were gathered from 430 patients participating in the Dutch heroin trials with an intended 12-month treatment period. The EQ-5D was used as a separate health outcome measure. Statistical analyses were conducted using Spearman's and Pearson's correlations.

Results: The EQ-5D dimensions mobility, self-care and usual activities generally showed low correlations with relevant parameters of the MAP-HSS, SCL-90 and EuropASI ($r=0.132$ – 0.369). The EQ-5D dimension pain/discomfort showed low to moderate hypothesized correlations with all disease-specific measures ($r=0.153$ – 0.496). The EQ-5D dimension anxiety/depression showed moderate to high correlations with the SCL-90 (including the sum score) and some of the EuropASI parameters ($r=0.133$ – 0.615). The EQ-5D utility scores were moderately correlated with the MAP-HSS ($r=-0.468$) and the SCL-90 ($r=-0.491$) total score and with response to treatment at month 12.

Conclusion: The majority of hypothesized associations between the EQ-5D and the disease or domain-specific measures could be confirmed. The validity of the EQ-5D-based utility score appears to be suitable in the evaluation of chronic, heroin-dependent populations.

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1. Introduction

Nowadays, many proven effective interventions are available for the treatment of heroin-dependent patients (van den Brink and van Ree, 2003). The interventions differ in their target populations, effectiveness and in the costs per treatment. It is common to evaluate new treatments not only in terms of effectiveness or direct health benefit for the patient (clinical outcome), but also in terms of efficiency integrating the costs and changes in health status and comparing it with the best available alternative(s) (Gold et al., 1996). To compare the cost-effectiveness of different interventions and to compare the results with the

cost-effectiveness of interventions in other domains of medicine, general and standardized comparable indicators of effect are needed, such as measures assessing health status. One of the most frequently applied general health status measures is the EuroQol questionnaire (EQ-5D, The EuroQol Group, 1990). The EQ-5D is a brief, simple and easy-to-use self-completion questionnaire. It is often used in economic evaluations of health care as a complement to disease-specific outcome measures. The EQ-5D is available in many languages and its use and qualities are described for a growing number of different populations and settings. To our knowledge the EQ-5D, which is an instrument of choice in economic evaluations, has not been used in (randomized) studies in drug-dependent populations, hence, little is known about its validity in these populations (Dijkgraaf et al., 2005).

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This paper attempts to establish the validity of the EQ-5D in a population of chronic, treatment-resistant heroin-dependent patients participating in the Dutch heroin trials. The EQ-5D is studied relative to three disease-specific instruments commonly used in addiction research: the Maudsley Addiction Profile (MAP, Marsden et al., 1998), the Symptom Checklist (SCL-90, Arrindell and Ettema, 1986) and the European Addiction Severity Index (EuropASI, Kokkevi and Hartgers, 1995).

2. Methods

2.1. Trials, treatments and patients

In two recent Dutch trials, medically co-prescribed heroin in addition to methadone maintenance treatment was compared to methadone maintenance treatment only ($n = 549$). These trials were conducted among inhaling ($n = 375$) and injecting ($n = 174$) heroin-dependent patients and were carried out simultaneously (van den Brink et al., 2003). Participants were chronic heroin-dependent patients who had been treated unsuccessfully in methadone maintenance programs. The trials were multi-centred with treatment centres at six locations in The Netherlands.

A standard methadone maintenance program was considered the reference treatment. Participants in the control group received methadone once a day in existing treatment centres. The participants in the experimental condition received their heroin, under supervision, three times a day (maximum) and methadone once a day in newly established units. All participants had access to a similar offer of additional psychosocial care. Details on the randomized controlled trials, the inclusion and exclusion criteria, as well as the treatment characteristics are published elsewhere (Central Committee on the Treatment of Heroin Addicts, 2002; van den Brink et al., 2003).

Health outcome data to be used in a cost-utility analysis were gathered from all patients with an intended 12-month treatment period in both trials ($n = 430$). These data were gathered between 15 July 1998 and 1 October 2001.

2.2. Health status measurement

The primary outcome measure of the trials was a dichotomous, multi-domain outcome index with response covering three domains: physical functioning, mental health and social integration. Improvement at month 12 of 40% compared to baseline in at least one domain with no deterioration of 40% or more in any of the other domains was the criterion for response. The improvement had to take place in an area in which the patients functioned poorly at the start of the study. Besides the minimum improvement needed and maximum deterioration allowed in the domains mentioned, participants were only defined as responder when they had not been in a controlled environment (e.g. hospital, detention) for more than 7 days in the month prior to the outcome assessment, with a maximum increase of 6 days cocaine and/or amphetamine use compared to baseline.

Several instruments were used to measure changes in health outcome (van den Brink et al., 2003). During baseline and

bi-monthly follow-up interviews, the participants completed the Health Symptom Scale of the Maudsley Addiction Profile (MAP-HSS), the Symptom Checklist, the European version of the Addiction Severity Index and the EQ-5D. The MAP-HSS, SCL-90 and EuropASI were used to assess the participant's physical functioning, mental health and social integration, respectively, and subsequently, to derive the primary outcome index of response. The EQ-5D was used as an independent health outcome measure.

Only one section of the Maudsley Addiction Profile was used in the trials. Of the four domains present in the MAP one focuses on health symptoms and only the 10 items measuring *physical* health were used, leaving out the other 10 items measuring emotional or psychological symptoms. The 10 items on physical health are adapted from the Opiate Treatment Index (Darke et al., 1992) and each item is scored on a five-point scale ranging from 0 to 4 ('symptom never [0]/always [4] present in the previous 30 days'). The item sum score results in a scale score ranging from 0 to 40. In this population, the MAP-HSS had a Cronbach's alpha of 0.81.

The Dutch version of the SCL-90 is a multidimensional instrument that is sensitive to mental health problems expressed as complaints (Meeuwesen et al., 1992). It consists of 90 items to be self-scored on a five-point scale [0–4]. Besides a total scale score for psychoneuroticism, ranging from 0 to 360, scores of prespecified items can be summed to calculate scores for different dimensions. The following dimensions (Cronbach's alpha) of the SCL-90 are used in this analysis: depression (0.94), hostility (0.86), agoraphobia (0.86), anxiety (0.91), insufficiency of thought and action (0.90) and somatization (0.89).

The EuropASI is a semi-structured interview that is primarily used to measure treatment outcome. It provides a multidimensional profile and the questions cover the following seven domains: medical, employment, alcohol use, drug use, legal status, family/social and psychiatric status. In addition, both the patient and the interviewer rate the severity of the problems and the need for additional help [0–9] in each domain. A selection of single item questions has been made for use in this paper. During the trials, all interviewers were extensively trained with regular booster sessions and under these conditions, good reliability and validity can be expected (Hendriks et al., 1989).

The EQ-5D is a generic instrument, consisting of five three-level items, representing various aspects of health: mobility, self-care, usual activities, pain/discomfort and anxiety/depression (mood) (Brooks, 1996; EuroQol Group, 1990, 2005). Respondents can value their health in each domain by reporting whether they are experiencing none [1], some [2] or extreme [3] problems. These scores result in a health profile, e.g. a patient with profile 12113 has no problems with mobility, usual activities and pain/discomfort, some problems with self-care and extreme problems with anxiety/depression. Data of a visual analogue scale, also included in the EQ-5D and used by patients to rate their health status between worst imaginable health state (score 0) to best imaginable health state (score 100), are beyond the scope of this paper and were ignored. A utility index score was calculated for each participant's EQ-5D health status by applying the time trade-off-based valuations from a general

Table 1
Hypothesized associations between the EQ-5D dimensions and the dimensions of MAP-HSS, SCL-90 and EuropASI items

| EQ-5D dimensions | | | | | | |
|------------------|-------------------------------------|------------------|------------------|------------------|-----------------|--------------------|
| Instrument | Dimension/item | Mobility | Self-care | Usual activities | Pain/discomfort | Anxiety/depression |
| MAP-HSS | Poor appetite | | | | + | + |
| | Tiredness/fatigue | + | + | + | + | + |
| | Nausea (feeling sick) | | | | + | |
| | Stomach pains | | | | + | |
| | Difficulty breathing | + | | | + | |
| | Chest pains | (+) | | | + | |
| | Joint/bone pains | + | | | + | |
| | Muscle pains | (+) | | | + | |
| | Numbness/tingling | | | | + | |
| | Tremors/shakes | | | | + | + |
| Sum score | + | | | + | + | |
| SCL-90 | Agoraphobia | + | | | | + |
| | Depression | | | | | + |
| | Hostility | | | + | | |
| | Somatization | + | | | + | |
| | Anxiety | | | | | + |
| | Insufficiency of thought and action | | | + | | |
| Sum score | + | | + | + | + | |
| EuropASI | Alcohol and drugs | | + | | | |
| | Employment | | | (+) | | |
| | Family/social | | –/+ ^a | + | | |
| | Legal | | | (+) | | |
| | Medical | (–) ^b | | | + | |
| | Psychiatric | | | (+) | | + |

Note: Parentheses point to non-significant correlations (see Section 3).

^a Correlation direction depends on specific item.

^b Item 'improvement of physical health' is expected to correlate negatively with mobility problems.

UK population sample to the observed EQ-5D score profile (Dolan, 1997).

Baseline data were used to study the associations between the EQ-5D and the MAP-HSS, SCL-90 and EuropASI. To investigate whether these associations are sensitive to changes in the specific scores, all analyses were performed on the month 12 data as well.

2.3. Hypothesized associations and statistical analysis

Table 1 shows the a priori hypothesized associations between the dimensions of MAP-HSS, SCL-90, EuropASI and the EQ-5D dimensions. We based the a priori hypothesized associations on face validity and expert opinion (WvdB) and thus the associations are subjective. We further hypothesized that the sum scores of the MAP-HSS and SCL-90 correlate positively with some of the EQ-5D dimensions and correlate negatively with the EQ-5D-based utility estimate.

Based on the ordinal scoring ranges and the hypothesized, potentially non-linear associations, we calculated Spearman's rank-order correlation coefficients for the associations between the EQ-5D and other instruments. We calculated Pearson product-moment correlation coefficients (Pearson's r) for the associations between the (continuous) sum scores of MAP-HSS and SCL-90 on one hand and the EQ-5D-based health utility index on the other hand, because the utility index is considered parametric though based on ordinal data. Testing

was done one- or bi-directionally, depending on the particular hypothesis.

Although we hypothesized associations before analysis and correction for multiple testing is not inevitable, we considered only a p -value of less than 0.01 statistically significant in all cases. The interpretation of the magnitude of the observed correlations is based on Cohen (1988). In absolute sense, significant correlations below 0.3 are considered low, between 0.3 and 0.5 moderate, and 0.5 or above high. We calculated confidence intervals using Fisher's transformations for correlation coefficients.

We used the chi-square test (with a standard significance level of 0.05) to analyse differences between responders and non-responders on EQ-5D scores, dichotomized by 'no problems' versus 'any problems' at month 12.

This paper evaluates the criterion-related convergent validity of the EQ-5D in comparison with the disease-specific measures and the concurrent validity of the EQ-5D-based utility index with the response to treatment.

3. Results

Table 2 shows socio-demographic data and baseline substance abuse characteristics of the study population. Most patients were male, of Dutch/Western-European ethnicity with a mean age of 39 years and of low education. More than two-thirds of all patients lived independently (alone or with partner). About 60% of all patients used heroin predominantly by inhala-

Table 2
Socio-demographics and substance abuse characteristics at baseline

| Variable | n = 430 |
|--|-----------------|
| Male (%) | 80.2 |
| Age (mean) | 39.2 (S.D. 5.7) |
| Dutch/Western-European ethnicity (%) | 87.4 |
| Education (%) | |
| Low | 73.7 |
| Middle | 21.0 |
| High | 5.4 |
| Usual employment status, past 2 months (%) | |
| Working regularly | 11.6 |
| Other | 88.4 |
| Major source of income, past month (%) | |
| Work | 6.8 |
| Other | 93.2 |
| Usual housing arrangement, past month (%) | |
| Own house, rented room | 69.2 |
| Other | 30.8 |
| Injecting heroin (%) | 40.5 |
| Years of regular use (mean) | |
| Heroin | 16.4 (S.D. 5.8) |
| Methadone | 12.4 (S.D. 6.3) |
| Cocaine (90.2%) | 10.1 (S.D. 6.2) |
| Poly drug use | 17.3 (S.D. 6.6) |
| Alcohol (≥ 5 units/day) (63.7%) | 10.0 (S.D. 8.2) |
| MAP-HSS [0–40]: median sum score (IQR) | 11 (10) |
| SCL-90 [0–360]: median sum score (IQR) | |
| Males (n = 345) | 49.0 (69) |
| Females (n = 84) | 74.5 (93) |

tion. Mean number of years of heroin use on a regular basis was over 16 years.

3.1. Baseline EQ-5D scores

Fig. 1 shows the functional status at baseline according to EQ-5D. Almost 20% of the patients experienced any problems (score 2 or 3) with mobility at baseline. Less than 10% reported any

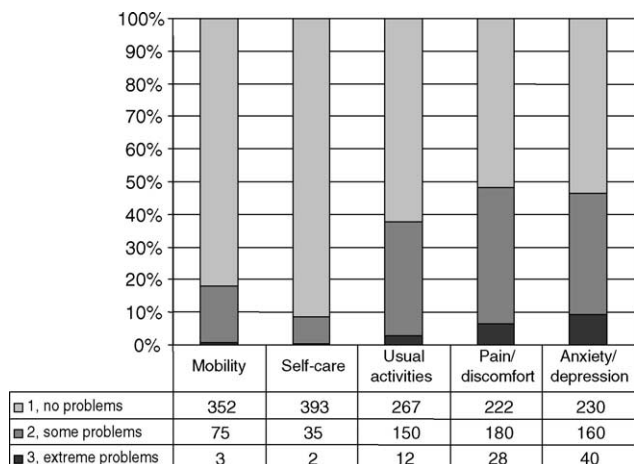


Fig. 1. EQ-5D score distributions (n = 430).

problems with self-care. Many patients reported any problems with usual activities (37.8%), pain or discomfort (48.4%) and anxiety or depression (46.5%).

Based on the EQ-5D scoring patterns, 60 of the 243 (3^5) possible health states were present in the study population at baseline (n = 430): from state 11111 (no problems at all: n = 111, 25.8%) to state 32233 (some problems with self-care and usual activities and extreme problems with mobility, pain and depression: n = 1, 0.2%). At baseline, 66 patients (15.3%) reported extreme problems (score 3) on at least one EQ-5D dimension.

3.2. Baseline EQ-5D associations

The hypothesized associations between the MAP-HSS, SCL-90 and EuropASI and each of the five EQ-5D scores are reported in Table 3 if correlations were significant at the 0.01 level. Hypothesized, but non-significant correlations are given in Table 1 within parentheses.

All correlations of the presented items with EQ-5D dimension *mobility* in Table 3 are significant, but rather low ($\rho < 0.3$).

Some expected associations of the dimensions with *self-care* actually turn up. The highest significant correlation of a EuropASI item with self-care was found for the frequency of drug overdoses. As with mobility, all significant correlations with self-care are in the expected direction, but their magnitude is small ($\rho < 0.3$).

Few of the EuropASI items correlate significantly with the EQ-5D dimension *usual activities*. The SCL-90 dimensions ‘insufficiency of thought and action’ and ‘hostility’ are related significantly with usual activities, but the correlations are only low ($\rho < 0.3$) to moderate ($\rho = 0.3–0.5$).

All hypothesized correlations with *pain/discomfort* are significant. The majority of the items from the MAP-HSS, SCL-90 and EuropASI show moderate ($\rho = 0.3–0.5$) correlations with the pain/discomfort dimension of the EQ-5D. The answers to the question ‘how many days have you experienced medical problems in the past 30 days?’ (EuropASI) correlates best with pain/discomfort ($\rho = 0.496$).

Except for ‘suicidal thoughts’, all pre-selected SCL-90 and EuropASI items correlate significantly with the EQ-5D score *anxiety/depression*. The SCL-90 dimensions anxiety and depression show a high correlation with the similar EQ-5D dimension ($\rho > 0.5$). The EuropASI items referring to depression and psychological problems according to the patient correlate moderately ($\rho = 0.3–0.5$).

Significant Pearson product-moment correlation coefficients were calculated for the sum scores of the SCL-90 and MAP-HSS in association with the *EQ-5D-based utility index* (Dolan) on baseline: -0.468 (MAP-HSS) and -0.491 (SCL-90).

3.3. Month 12 EQ-5D associations

All hypothesized associations were analysed with month 12 data as well. The correlations were in the same direction and of similar magnitude as observed at baseline. All 95% confidence intervals of the correlation coefficients at baseline and month 12 overlapped. Few correlation coefficients did not meet the

Table 3
Correlations of MAP-HSS, SCL-90 and EuropASI items with EQ-5D dimensions

| | Dimension/item | Spearman's rho (95% CI); $n_{\min} = 402$ |
|---------------------------|-------------------------------------|--|
| Mobility | | |
| MAP-HSS | Tiredness/fatigue | 0.178 (0.067 to 0.284) |
| | Difficulty breathing | 0.161 (0.050 to 0.268) |
| | Joint/bone pains | 0.282 (0.175 to 0.382) |
| | Sum score | 0.226 (0.117 to 0.330) |
| SCL-90 | Agoraphobia | 0.235 (0.126 to 0.338) |
| | Somatization | 0.255 (0.147 to 0.357) |
| | Sum score | 0.243 (0.134 to 0.346) |
| Self-care | | |
| MAP-HSS | Tiredness/fatigue | 0.210 (0.100 to 0.315) |
| EuropASI | Frequency of drug overdoses | 0.222 (0.113 to 0.326) |
| | Satisfaction with living condition | -0.161 (-0.268 to -0.050) |
| | Treatment for addiction problems | 0.132 (0.020 to 0.241) |
| Usual activities | | |
| MAP-HSS | Tiredness/fatigue | 0.325 (0.221 to 0.422) |
| SCL-90 | Insufficiency of thought and action | 0.369 (0.268 to 0.462) |
| | Hostility | 0.239 (0.130 to 0.342) |
| | Sum score | 0.335 (0.231 to 0.431) |
| EuropASI | Satisfaction with leisure time | -0.221 (-0.325 to -0.112) |
| Pain/discomfort | | |
| MAP-HSS | Poor appetite | 0.153 (0.042 to 0.261) |
| | Tiredness/fatigue | 0.244 (0.136 to 0.347) |
| | Nausea (feeling sick) | 0.196 (0.086 to 0.301) |
| | Stomach pains | 0.306 (0.201 to 0.404) |
| | Difficulty breathing | 0.352 (0.250 to 0.447) |
| | Chest pains | 0.303 (0.198 to 0.401) |
| | Joint/bone pains | 0.405 (0.307 to 0.495) |
| | Muscle pains | 0.329 (0.225 to 0.426) |
| | Numbness/tingling | 0.280 (0.173 to 0.380) |
| | Tremors/shakes | 0.303 (0.198 to 0.401) |
| | Sum score | 0.474 (0.382 to 0.557) |
| SCL-90 | Somatization | 0.450 (0.356 to 0.535) |
| | Sum score | 0.330 (0.226 to 0.426) |
| EuropASI | Treatment of physical complaints | 0.229 (0.120 to 0.333) |
| | Suffering from physical complaints | 0.496 (0.406 to 0.576) |
| Anxiety/depression | | |
| MAP-HSS | Poor appetite | 0.279 (0.172 to 0.379) |
| | Tiredness/fatigue | 0.327 (0.223 to 0.424) |
| | Tremors/shakes | 0.345 (0.242 to 0.440) |
| | Sum score | 0.427 (0.331 to 0.514) |
| SCL-90 | Agoraphobia | 0.442 (0.347 to 0.528) |
| | Anxiety | 0.589 (0.511 to 0.658) |
| | Depression | 0.615 (0.540 to 0.680) |
| | Sum score | 0.602 (0.525 to 0.669) |
| EuropASI | Experienced depression | 0.530 (0.441 to 0.609) |
| | Experienced anxiety or tension | 0.472 (0.377 to 0.557) |

Table 3 (Continued)

| Dimension/item | Spearman's rho (95% CI); $n_{\min} = 402$ |
|--|--|
| Medication for any psychological problem | 0.141 (0.029 to 0.249) |
| Thoughts of suicide | 0.231 (0.118 to 0.338) |
| Frequency of psychological problems | 0.466 (0.373 to 0.550) |
| Burden of psychological problems | 0.507 (0.419 to 0.586) |
| Patient is obviously depressed | 0.215 (0.105 to 0.320) |
| Patient is obviously anxious/nervous | 0.167 (0.056 to 0.274) |
| Treatment of psychological problems | 0.133 (0.021 to 0.242) |
| Improvement of mental status | -0.375 (-0.469 to -0.273) |

$p < 0.01$ significance level at month 12 in contrast to baseline and vice versa.

3.4. EQ-5D and treatment response

In addition, we observed the changes in the EQ-5D dimensions between baseline and month 12 split by treatment response as shown in Fig. 2. Dichotomized by 'any problems' versus 'no problems' (EQ-5D), responders did not significantly differ from non-responders at baseline on any EQ-5D dimension. At month 12, responders differed significantly from non-responders ($p < 0.05$) on all EQ-5D dimensions. For instance, 308 patients reported no problems with mobility and 44% (135/308) were treatment responder, while among patients who did report any problems with mobility, response amounted to 24% (22/91). Finally, the group was split in half by the EQ-5D-based utility index score with the median (0.803) as cut-off value, resulting in 33% responders (70/215) with a utility index score below the median and 44% in the group above the median (95/215, $\chi^2 = 6.1$, $p = 0.013$).

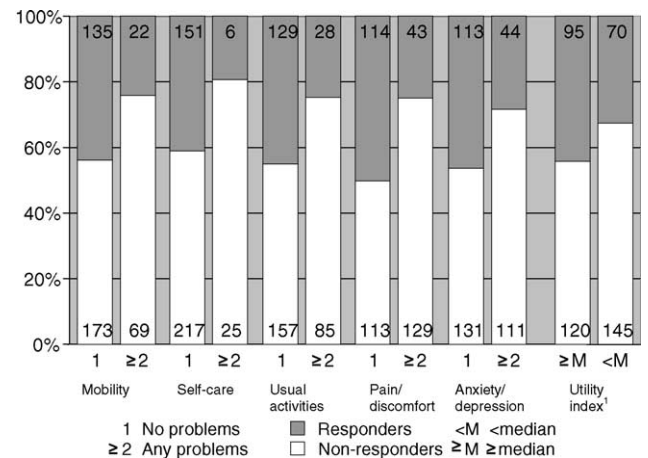


Fig. 2. Dichotomized EQ-5D score distributions at month 12 and utility by treatment outcome (n in bars). Superscript (1) denotes group split by EQ-5D-based utility index score with median (0.803) as cut-off value.

4. Discussion

4.1. Summary of the results

The EQ-5D dimensions mobility and self-care generally showed low correlations with the disease-specific items or dimensions from the MAP-HSS, SCL-90 and EuropASI, whereas usual activities showed low to moderate correlations. The pain/discomfort dimension showed low to moderate correlations with all disease-specific measures and a moderate correlation with the MAP-HSS sum score. The anxiety/depression dimension showed moderate to high correlations with the SCL-90 (including the sum score) and some high hypothesized correlations with the EuropASI. The anxiety/depression dimension also correlated moderately with the MAP-HSS sum score. Finally, the EQ-5D utility index score was moderately correlated with the MAP-HSS and the SCL-90 total score. The associations between the measures were stable over time: correlation coefficients at baseline and month 12 data did not vary significantly. EQ-5D scores on month 12 differed on all dimensions between responders and non-responders.

4.2. Interpretation of results

Overall, the highest correlation was found between the anxiety/depression dimension of the EQ-5D and the SCL-90 depression dimension, 0.615. Many explanations can be given why we did not find more correlations of a similar magnitude. The explanations that may be relevant here are: (a) lack of score variance; (b) difference in constructs; (c) difference in time frames.

4.2.1. Lack of score variance

In- and exclusion criteria of the trial possibly restricted the observed variation of the scale scores, thus, prohibiting high correlations (Dorman et al., 1999). Patients had to score above 8 on the MAP-HSS and above 41 (males) or 60 (females) on the SCL-90 at baseline in order to be included. Further, the observed strengths of the correlations coincided with the extent to which patients differed at the individual EQ-5D dimensions. Data from a general UK population sample showed that the percentage of respondents with any problems with self-care and mobility was around 5 and 2%, respectively (Kind, 1996). Although the corresponding percentages in our study population were somewhat higher, we found that heroin-dependent patients were noticeably homogeneous with less than 20% of patients reporting any problems with self-care and mobility. Whether this represents the actual health status of patients or results from an optimistic perception of one's status can be debated. From a bystander perspective, the patients may have reported their mobility level accurately. Doubts can be raised concerning their self-care, which may actually be lower (worse) than reported. Hurst et al. (1997) pointed out that 'self-perceptions of health-related quality of life may represent the gap between an individual's reality and their expectations in those aspects of their life affected by their health,' and that there is an adjustment of expectations over time. From the data presented in Table 2, it can be concluded that this is a treatment-resistant, malfunctioning group of chronic

heroin-dependent patients. For patients of a heroin-dependent population with a mean of over 16 years of drug abuse, the perception of adequate self-care may have shifted over the years. Moreover, looking at all dimensions together, nearly 26% of the patients achieved the best possible health at baseline, which seems remarkably high given the inclusion criteria. In a comparably bothersome, schizophrenic population this percentage was only 5.9% at the first visit (Prieto et al., 2004).

4.2.2. Difference in constructs

Another explanation for the relatively low correlations can be the difference in constructs; domains look similar, but measure different aspects or details of a disease or health status (Dorman et al., 1999). Unfortunately, comparable results published elsewhere on the EQ-5D and disease-specific measures are lacking. Only Schrag et al. (2000) compared disease-specific measures with the EQ-5D for patients with Parkinson's disease resulting in significant Spearman's rhos in the range from 0.41 to 0.70. The EQ-5D as a general health outcome and utility measure has, however, been compared with other general health status measures like the SF-36. The SF-36 is a general quality of life measure that has been used in some studies in the field of addiction research (Falck et al., 2000; Millson et al., 2004; Ryan and White, 1996).

Irrespective of the disease population at hand, one might expect higher correlation coefficients for two general measures than for a general measure with disease-specific measures like the MAP-HSS and EuropASI. Yet only few studies comparing the EQ-5D with other general measures demonstrate high correlation coefficients that match or exceed the reported range from 0.13 to 0.62 in this paper. Luo et al. (2003) found correlations of 0.23–0.55 between EQ-5D and SF-36 scores in a rheumatic disease population. Stavem et al. (2001) compared the EQ-5D with the 15D, a self-administered health-related quality of life questionnaire consisting of 15 single item dimensions with 5 levels. They also assessed Spearman's rhos of associations between EQ-5D scores with 15D items as well as EQ-TTO utility with 15D sum score of persons with epilepsy and found correlations ranging from 0.34 to 0.79 for item comparisons and 0.78 for utility. Sapin et al. (2004) found correlations (Pearson) between EQ-5D utility and SF-36 items in the range 0.26–0.63 in a primary care setting of patients with major depressive disorder. In a Spanish population of schizophrenic patients, the EQ-5D Index was associated with the Clinical Global Impression score in a study by Prieto et al. (2004), the correlation coefficient at baseline was -0.34 . The EQ-5D differs from the other measures (MAP-HSS, SCL-90 and EuropASI) by comprising 5 general health domains rather than more condition-specific dimensions. Hence, the items or subscales of the three measures are more sensitive to changes than the EQ-5D. The association between an EQ-5D dimension and a sum score of a scale will therefore be stronger than with a single item.

In conclusion, the range of correlation coefficients for the EQ-5D and the disease-specific measures in the present paper matches or falls only slightly short of the ranges found elsewhere, even in case of correlations between generic measures. Hence, difference in constructs may always emerge

during comparisons and almost inevitably lead to some loss of information.

4.2.3. Difference in time frames

Finally, a difference in time frames can be a reason for the generally low to moderate associations that were found. The EQ-5D uses a time frame of 1 week, while the other questionnaires in general ask the respondent to recall a month.

4.3. Relevance of results

Besides the types of validity in this paper, normally the discriminant validity would also be of interest to establish overall validity, for example with a Multi-Trait-Multi-Method matrix (MTMM, Campbell and Fiske, 1959). A MTMM matrix contains all observed correlations between all measures (or methods) and all traits (or concepts) that should be related to each other (convergence), and all observed correlations between all measures and all traits that not should be related to each other (discrimination). The EQ-5D and the disease-specific instruments do not measure exactly the same traits, whereas the traits should overlap entirely under the MTMM approach. Furthermore, the patient population at hand shows high levels of comorbidity, which results in correlations between different traits or health domains. This has prevented us to perform a MTMM analysis. Discriminant validity has therefore not been included in the analyses.

In terms of convergent validity, our analyses showed that the majority of hypothesized associations between the EQ-5D and the three disease or domain-specific measures could be confirmed, but that the associations were not always as strong as expected. Only some EuropASI items were not associated with mobility and usual activities, and some MAP-HSS items did not associate with mobility, probably due to differences in constructs and time frames. Our analyses also showed the stability of associations over time. The ability of the EQ-5D scores to differentiate between treatment responses shows the relevance of this measure for evaluation research.

Overall, we consider the EQ-5D a general health status measure which sufficiently reflects addiction-related health impairments, with some reserve to the self-care dimension. The validity of the EQ-5D-based utility in this chronic, heroin-dependent population appears to justify its use in evaluation research.

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References

Arrindell, W.A., Ettema, J.H.M., 1986. SCL-90: Handleiding bij een Multidimensionele Psychopathologie Indicator. Swets & Zeitlinger, Lisse (Manual for a multidimensional psychopathology indicator).
Brooks, R., 1996. EuroQol: the current state of play. *Health Policy* 37, 53–72.
Campbell, D.T., Fiske, D.W., 1959. Convergent and discriminant validation by the multitrait-multimethod matrix. *Psychol. Bull.* 56, 81–105.

Central Committee on the Treatment of Heroin Addicts (Eds.), 2002. Medical Co-Prescription of Heroin: Two Randomized Controlled Trials. Central Committee on the Treatment of Heroin Addicts, Utrecht.
Cohen, J., 1988. *Statistical Power Analysis for the Behavioural Sciences*. Lawrence Erlbaum Associates, New Jersey.
Darke, S., Hall, W., Wodak, A., Heather, N., Ward, J., 1992. Development and validation of a multi-dimensional instrument for assessing outcome of treatment among opiate users: the Opiate Treatment Index. *Br. J. Addict.* 87, 733–742.
Dijkgraaf, M.G.W., van der Zanden, B.P., de Borgie, C.A.J.M., Blanken, P., van Ree, J.M., van den Brink, W., 2005. Cost utility analysis of co-prescribed heroin compared with methadone maintenance treatment in heroin addicts in two randomised trials. *BMJ* 330, 1297.
Dolan, P., 1997. Modeling valuations for EuroQol health states. *Med. Care* 35, 1095–1108.
Dorman, P.J., Dennis, M., Sandercock, P., 1999. How do scores on the EuroQol relate to scores on the SF-36 after stroke? *Stroke* 30, 2146–2151.
EuroQol Group, 1990. EuroQol—a new facility for the measurement of health-related quality of life. *Health Policy* 16, 199–208.
EuroQol Group, 2005. EQ-5D: an instrument to describe and value health. www.euroqol.org (last accessed 17th August 2005).
Falck, R.S., Wang, J., Carlson, R.G., Siegal, H.A., 2000. Crack-cocaine use and health status as defined by the SF-36. *Addict. Behav.* 25, 579–584.
Gold, M.R., Siegel, J.E., Russell, L.B., Weinstein, M.C. (Eds.), 1996. *Cost-Effectiveness in Health and Medicine*. Oxford University Press, New York.
Hendriks, V.M., Kaplan, C.D., van Limbeek, J., Geerlings, P., 1989. The Addiction Severity Index: reliability and validity in a Dutch addict population. *J. Subst. Abuse Treat.* 6, 133–141.
Hurst, N.P., Kind, P., Ruta, D., Hunter, M., Stubbings, A., 1997. Measuring health-related quality of life in rheumatoid arthritis: validity, responsiveness and reliability of EuroQol (EQ-5D). *Br. J. Rheumatol.* 36, 551–559.
Kind, P., 1996. The EuroQol instrument: an index of health-related quality of life. In: Spilker, B. (Ed.), *Quality of Life and Pharmacoeconomics in Clinical Trials*, second ed. Lippincott-Raven Publishers, Philadelphia.
Kokkevi, A., Hartgers, C., 1995. EuropASI: European adaptation of a multi-dimensional assessment instrument for drug and alcohol dependence. *Eur. Addict. Res.* 1, 208–210.
Luo, N., Chew, L.H., Fong, K.Y., Koh, D.R., Ng, S.C., Yoon, K.H., Vasoo, S., Li, S.C., Thumboo, J., 2003. A comparison of the EuroQol-5D and the Health Utilities Index mark 3 in patients with rheumatic disease. *J. Rheumatol.* 30, 2268–2274.
Marsden, J., Gossop, M., Stewart, D., Best, D., Farrell, M., Lehmann, P., Edwards, C., Strang, J., 1998. The Maudsley Addiction Profile (MAP): a brief instrument for assessing treatment outcome. *Addiction* 93, 1857–1867.
Meeuwesen, L., Arrindell, W.A., Huyse, F.J., 1992. Psychometrische kwaliteiten van de Symptom Checklist (SCL-90) bij poliklinische patiënten met buikpijn of lage rugklachten. *Tijdschr. Soc. Gezondheidsz* 70, 123–131 (Psychometric properties of the Symptom Checklist (SCL-90) for outpatient patients with abdominal pain or low back complaints).
Millson, P.E., Challacombe, L., Villeneuve, P.J., Fischer, B., Strike, C.J., Myers, T., Shore, R., Hopkins, S., Raftis, S., Pearson, M., 2004. Self-perceived health among Canadian opiate users: a comparison to the general population and to other chronic disease populations. *Can. J. Public Health* 95, 99–103.
Prieto, L., Sacristan, J.A., Hormaechea, J.A., Casado, A., Badia, X., Gomez, J.C., 2004. Psychometric validation of a generic health-related quality of life measure (EQ-5D) in a sample of schizophrenic patients. *Curr. Med. Res. Opin.* 20, 827–835.
Ryan, C.F., White, J.M., 1996. Health status at entry to methadone maintenance treatment using the SF-36 health survey questionnaire. *Addiction* 91, 39–46.
Sapin, C., Fantino, B., Nowicki, M.L., Kind, P., 2004. Usefulness of EQ-5D in assessing health status in primary care patients with major depressive disorder. *Health Qual. Life Outcomes* 2, 20.

- Schrag, A., Selai, C., Jahanshahi, M., Quinn, N.P., 2000. The EQ-5D—a generic quality of life measure—is a useful instrument to measure quality of life in patients with Parkinson's disease. *J. Neurol. Neurosurg. Psychiatry* 69, 67–73.
- Stavem, K., Bjornaes, H., Lossius, M.I., 2001. Properties of the 15D and EQ-5D utility measures in a community sample of people with epilepsy. *Epilepsy Res.* 44, 179–189.
- van den Brink, W., Hendriks, V.M., Blanken, P., Koeter, M.W.J., van Zwieten, B.J., van Ree, J.M., 2003. Medical prescription of heroin to treatment resistant heroin addicts: two randomised controlled trials. *BMJ* 327, 310–310.
- van den Brink, W., van Ree, J.M., 2003. Pharmacological treatments for heroin and cocaine addiction. *Eur. Neuropsychopharmacol.* 13, 476–487.