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Effectiveness of inpatient withdrawal and residential rehabilitation interventions for alcohol use disorder: A national observational, cohort study in England **

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ABSTRACT

BACKGROUND: This was a national English observational cohort study to estimate the effectiveness of inpatient withdrawal (IW) and residential rehabilitation (RR) interventions for alcohol use disorder (AUD) using administrative data.

METHODS: All adults commencing IW and/or RR intervention for AUD between April 1 2014 and March 31 2015 reported to the National Drug Treatment Monitoring System (n=3,812). The primary outcome was successful completion of treatment within 12 months of commencement, with no re-presentation (SCNR) in the subsequent six months, analysed by multi-level, mixed effects, multivariable logistic regression.

RESULTS: The majority (70%, n=2,682) received IW in their index treatment journey; one-quarter (24%, n=915) received RR; 6% (n=215) received both. Of treatment leavers, 59% achieved the SCNR outcome (IW: 57%; RR: 64%; IW/RR: 57%). Positive outcome for IW was associated with older age, being employed, and receiving community-based treatment prior to and subsequent to IW. Patients with housing problems were less likely to achieving the outcome. Positive outcome for RR was associated with paid employment, self/family/peer referral, longer duration of RR treatment, and community-based treatment following discharge. Community-based treatment prior to entering RR, and receiving IW during the same treatment journey as RR, were associated with lower likelihood of SCNR.

CONCLUSIONS: In this first national effectiveness study of AUD in the English public treatment system for alcohol-use disorders, 59% of patients successfully completed treatment within 12 months and did not represent for more treatment within six months. Longer duration of treatment and provision of structured continuing care is associated with better treatment outcomes.

KEYWORDS: alcohol; inpatient; residential; treatment; alcohol use disorder

1. Introduction

Alcohol use is a leading risk factor for morbidity and mortality (World Health Organisation, 2014). An estimated 3.6% of the global population aged 15-64 years meet criteria for alcohol use disorder each year (AUD; American Psychiatric Association, 2013), with relatively higher rates estimated for Europe (5.5%; Rehm et al., 2009). Negative health, social and economic consequences are higher among the population with AUD (Hasin, Stinson, Ogburn, & Grant, 2007; Odlaug et al., 2016). In Europe, it is estimated that AUDs are responsible for 60% of alcohol-related mortality (Rehm, Shield, Gmel, Rehm, & Frick, 2013). There are concerns that only a minority of people with AUD access treatment services (United Nations, 2015). For example, in England just 6% of those with AUD in England receive treatment (National Institute for Health and Care Excellence, 2011; UK Home Office, 2012).

The goal of AUD treatment is to help patients quit drinking or prevent harmful consumption, thereby reducing the health, social and economic harms (Haber, Lintzeris, Proude, & Lopatko, 2009; Rahhali et al., 2015). In the English public healthcare system, structured AUD treatment is mainly delivered by National Health Service or third-sector providers in the outpatient/community setting, offering psychosocial interventions (including motivational, cognitive behavioural, family/social network modalities and facilitation of access to 12-step groups) and pharmacotherapies (including acamprosate and naltrexone for approximately 6 months).

This is complemented by a relatively small number of inpatient withdrawal (IW) and residential rehabilitation (RR) services. Patients are treated in the community or inpatient/residential setting based on a clinical assessment of problem severity and complexity; patient preference; and service availability (National Institute for Health and Care Excellence, 2011). There is some provision of detoxification management in the community over 7-10 days typically using benzodiazepines (National Institute for Health and Care Excellence, 2011).

IW or RR are usually indicated for people with greater AUD severity (e.g. those drinking more than 30 standard drinks per typical drinking day), or instances of complexity due to unstable housing; comorbid psychiatric/physical conditions; or a history of seizures. IW is usually 5-7 nights in a controlled hospital environment with pharmacological interventions for medical management of withdrawal (National Institute for Health and Care Excellence,

2011). RR is usually a 6-12 weeks stay in a structured, residential facility which provides a phased, structured programme of psychosocial interventions. Detoxification support may be provided as needed. RR programmes usually follow an underlying therapeutic philosophy, including 12-step; therapeutic community; faith-based practice; cognitive behavioural therapy and social learning; personal and skills development; or an eclectic/integrated approach (Moos, Moos, & Andrassy, 1999).

Routine delivery of AUD treatment interventions is remarkably under-researched. Our group has previous reported reductions in offending associated with AUD treatment (Willey et al., 2016), but there have been no national outcome studies. Addressing this gap is important because treatment outcomes in the clinic cannot be assumed to be the same as randomised controlled trials. AUD intervention trials are often designed to answer questions of efficacy; with participants selected on restricted characteristics (Witkiewitz, Finney, Harris, Kivlahan, & Kranzler, 2015); using very detailed research assessment procedures (Epstein et al., 2005); and implemented with complex intervention exposures that are not routinely available in the healthcare system (Allen et al., 1997).

The National Drug Treatment Monitoring System (NDTMS; Public Health England, 2015b) evaluates all public AUD treatment services in England (NDTMS; Public Health England, 2015b). NDTMS has been in operation since 2005/06 and had an initial focus on services providing structured treatment and care for people with drug use disorders. All operational public alcohol and drug treatment services who deliver treatment interventions now report to the system, and ~98% of patients consent to the use of their administrative and clinical data for local treatment system needs assessment and national research (Marsden et al., 2009; Marsden et al., 2012; White et al., 2015; Willey et al., 2016)

In 2008/09, NDTMS was enhanced to monitor outcomes from all public treatment services for AUD. Elsewhere, we report on the effectiveness of community-based AUD interventions (Peacock et al., under review). In this report, we estimate the clinical effectiveness of IW and RR interventions for AUD in the English public healthcare system.

2. Materials and Methods

2.1 Design

This was an observational, follow-up study of all individuals accessing publicly funded, IW and/or RR treatment for AUD in England. The study included all 152 upper-tier local authorities within England, and all specialist AUD services. The study is reported according to the STROBE and RECORD guidelines for cohort research (Benchimol et al., 2015).

2.2 Patient and treatment information

NDTMS records were accessed on patient-demographic, behavioural, clinical and treatment outcome variables for each episode of treatment, including the dates of starting and finishing specific treatment interventions and the treatment exit date (Public Health England, 2015a, 2015b).

Reflecting national reporting standards (Public Health England, 2015b), individual treatment episodes were concatenated into 'treatment journeys', whereby multiple episodes (community-based or residential program) are subsumed under a single journey. AUD intervention episodes were allocated to the same journey if fewer than 21 days elapsed between the date of ending one treatment modality and the date of starting a subsequent one. In this way, a treatment journey for a patient could comprise a single intervention episode; concurrent episodes provided by more than one agency; or a continuing care package of consecutive episodes provided by one or more service providers.

2.3 Study cohort

The study population was adults (aged ≥18 years) who commenced IW and/or RR treatment for primary AUD between 1 April 2014 and 31 March 2015 (N=3,861). Patients were not included in the study cohort if they: (1) reported problematic use of other psychoactive substances at assessment; (2) had missing information on drinks per drinking day (DDD) at both triage and treatment admission; or (3) had missing information on clinical status at discharge were not considered for inclusion.

Analyses were based on the patient's first treatment journey during the period (hereafter 'index journey'). The observation period commenced from the date of starting IW or RR and ended: (1) six months after the date of discharge from the index journey, if discharge occurred within 12 months of starting IW or RR, or (2) 12 months after starting IW or RR if the patient was not yet discharged (the latter group was excluded from analysis of the primary outcome). Periods in community-based treatment subsequent but not prior to IW or RR,

contributed to the observation time, with discharge date adjusted accordingly. If the index journey involved progression from IW or RR, or vice versa, it was categorised as involving both.

2.4 Outcome measure

The study outcome measure is the English national outcome standard, defined as the proportion of the cohort that successful completed treatment within 12 months of commencement with no representation within six months (SCNR; Public Health England, 2015b).

The proportion of patients treated who complete treatment successfully has been used before in the AUD treatment literature (Alterman, Langenbucher, & Morrison, 2001). This outcome may be associated with improvements in personal and social functioning (Finigan, 1996), but it does not identify sustained benefit. This is important given the relapsing nature of AUD. In the present context, re-presentation for further AUD treatment within six months of discharge is taken to be an indicator of remission.

Treatment journeys were categorised according to clinical assessment of the patient's discharge status, as: (1) successfully completed treatment within 12 months; (2) retained in the same treatment journey at 12 months from entry; or (3) withdrawn from treatment journey within 12 months of entry (unsuccessful transfer between agencies; treatment terminated due to incarceration; patient dropped out treatment died during treatment). Successful treatment was defined as the patient being discharged having: completed their care plan, with no AUD (and either abstinent or no heavy drinking), and no re-presentation to any service for further AUD treatment within six months of concluding their treatment journey (Eastwood, Strang, & Marsden, 2017; Peacock et al., under review; Public Health England, 2016).

2.5 Covariates

Following our general evaluation approach (Willey et al., 2016), the analysis included patient socio-demographics; indicators of clinical severity/case complexity; and summary measures of treatment journey exposure. Possible covariates were identified from reviews of predictors of treatment outcome (Adamson et al., 2009; Brorson, Arnevik, Rand-Hendriksen, & Duckert, 2013). Patient-level measures were recorded at triage assessment at the first admission to the index journey. The following covariates were included:

2.5.1 Socio-demographics. Analyses were adjusted for: age (years), gender, ethnic origin, housing problems (homeless, in short-term hostel provision, or at risk of eviction in the past 28 days); and employment (whether in paid work in past 28 days). Analyses were also adjusted for an indicator of social deprivation, imputed by assigning patients to their electoral ward of residence, based on the partial postal code recorded by NDTMS, categorised according to the Department for Communities and Local Government ward-level Indices of Multiple Deprivation (IMD; Department for Communities and Local Government, 2015). If the partial postcode could be located in more than one electoral ward the median IMD score was assigned. The IMD score for the first treatment service address within the treatment journey was assigned if partial postcode was missing. Following UK local government reporting convention (Public Health England, 2015a), IMD scores were grouped by quintile.

2.5.2 Clinical characteristics. Analyses were adjusted based on patients' self-report of the number of days on which they consumed alcohol; and the number of standard DDD in the previous 28 days. These were recorded via the Treatment Outcomes Profile (TOP; Marsden et al., 2008). TOP is the national clinical outcome measure in NDTMS, administered as a face-to-face structured clinical interview, with timeline follow-back technique to maximise recall accuracy (Sobell, Sobell, Leo, & Cancilla, 1988). Reflecting National Institute for Health and Care Excellence (2011) guidelines, DDD were categorised as: *abstinent* (i.e. zero drinks in the past 28 days); *low to high* (1 to 15 DDD); *high to extreme* (16 to 30 DDD); and *extreme* (≥ 31 DDD). We also adjusted for source of treatment referral (health service; self/friend/family; criminal justice system), and whether the patient had previously received AUD treatment as recorded in NDTMS (i.e., from 2006 onwards).

2.5.3 Treatment exposure. Analyses were adjusted based on receipt within the index treatment journey involving: (1) community-based treatment that started prior to the RR or IW component; (2) community-based treatment that ended following cessation of RR /IW; and (3) recovery support (treatment agency provision or referral for: facilitated access to mutual aid; peer support involvement, family, parenting, support groups; housing, employment, education and training support; and complementary therapies). The total duration of treatment exposure, IW exposure, and RR exposure was recorded in days (IW) or weeks (RR) from the start of the index journey to discharge, right censored at 365 days and

computed using the triage and discharge date for the specific intervention. Pharmacological intervention provided during residential rehabilitation was indicator coded (0,1).

2.6 Statistical analysis

In this national treatment population study, with a hierarchical design and participants grouped in treatment services, our statistical power concerns reflected control of clustering effects and minimising bias of model coefficients. We note that multi-level simulation studies have concluded that power is increased by adding groups rather than the number of cases per group. In the event, our sample well exceeded the minimum recommended for multi-level designs (e.g. 50 groups for random effects models; Maas & Hox, 2005).

Stata (Stata version 13.1; Stata Corporation, College Station, TX, USA) was used for analyses. All estimates were computed with associated 95% confidence intervals (CI). A multi-level approach to analysis was chosen given that individuals were nested within agencies. Multinomial logistic regression (command: *mlogit*) with robust standard errors was used to adjust for clustering of participants within treatment services and to identify correlates of IW and RR (i.e., '*IW group'*, '*RR group'*, '*IW and RR group*'). The analysis of SCNR excluded those individuals who did not leave treatment within 12 months of initiation.

Missing data for employment, housing status, days of alcohol use and DDD from standard assessment procedures were replaced with data from the initial TOP assessment interview where available. Despite this, missing values were recorded for covariates ethnicity (n=82), paid employment (n=159), unstable housing (n=46 cases), and referral source (n=19). With evidence that data loss was not missing-at-random (Little & Little, 2002), we used a multiple imputation via chained equations procedure (command: *mi: impute chained*). An all-case multivariate logistic model was run to check on potential bias and loss of precision (Sterne et al., 2009). To achieve a relative efficiency above 98% (Rubin, 1987) and to ensure that reduction in power was less than 1% (Graham, Olchowski, & Gilreath, 2007), 20 datasets of probabilistic values were created, each analysed separately, and then combined using Rubin's rules.

Models were run separately for participants of each treatment setting (i.e., IW versus RR) for analysis of the SCNR outcome (command: *meqrlogit* with 7 integration points), with patient-level covariates were included as fixed effects. Simulation studies suggest a minimum of 10

or more events per covariate in logistic regression analyses; this criteria was satisfied in the current analyses (Peduzzi, Concato, Kemper, Holford, & Feinstein, 1996). For the purpose of these analyses, those participants who had received both IW and RR were included in analyses for the RR model, and a covariate identifying receipt of IW was included in the model. Models based on imputation are reported in-text; complete-case analyses are available in supplementary materials.

3. Results

3.1 Socio-demographic and clinical characteristics

The majority of patients were male (65%) and the median age was 46 years (**Table 1**). Half (53%) had a history of structured AUD treatment prior to their index journey. Median drinking days at triage was 28 (i.e., daily in the past month), and the majority were classified as '*High to Extreme'* (49%) or '*Extreme'* (30%) based on DDD.

3.2 Treatment exposure and status

Most patients (70%, n=2,682) received IW treatment ('*IW group'*); one-quarter (24%, n=915) received RR treatment ('*RR group')*; and 6% (n=215) received both ('*Combined group*'). Compared to the '*IW group'* (referent), patients in the '*RR'* and '*Combined'* groups were slightly younger and less likely to be male. The '*RR group'* were more likely to report: housing problems; self, family, or peer referral to treatment; and to report abstinence at triage (**Table 2**).

The cohort accessed 171 specialist IW and RR treatment services (median of 7 clients per agency, IQR 2-23). Median duration of treatment exposure for the '*Combined group'* (25 weeks; IQR 13-41) was greater than that of the '*IW group'* (6 weeks, IQR 2-20), with the '*RR group'* reporting a median of 13 weeks (IQR 6-24) in treatment.

Half (53%) of the cohort received structured community-based treatment prior to the earliest IW or RR admission within their index treatment journey (**Table 1**). The relative risk of prior community-based treatment was lower for the '*RR group'* relative to the '*IW group'*. A similar proportion (52%) received community-based treatment subsequent to IW or RR cessation, although delivery was less likely for the '*RR'* and '*Combined'* groups. Two-thirds (66%) received recovery support within their treatment journey.

Three-fifths of the sample (60%) successfully completed their index treatment journey within 12 months of admission to IW or RR; nearly one-fifth (17%) were unsuccessfully referred to an agency, one-sixth (15%) had an unplanned discharge, and less than one-tenth (7%) were still in their index treatment journey at the end of observation (**Table 3**).

Relative to the '*IW group'*, the '*RR group'* were less likely to be recorded as having an unsuccessful transfer between agencies (RR 0.51, 95%CI 0.27, 0.96, p=0.037). Further, the '*RR group'* had a lower risk ratio (RR 0.60, 95%CI 0.36, 0.98, p=0.041), and the '*Combined group'* had a higher risk ratio (RR 1.78, 95%CI 1.07, 2.96, p=0.028), of being retained in the index treatment journey 12 months post-admission.

3.3 SCNR outcome

Three-fifths (59%) of those who left treatment within 12 months of commencement (i.e., excluding those still in treatment) achieved SCNR (IW: 57%; RR: 64%; Combined: 57%).

A multi-level, mixed effects, multivariable logistic model for the '*IW group*' showed that being older, engaged in paid employment, and receiving community-based treatment prior and subsequent to IW were associated with greater likelihood of the SCNR outcome (**Table 4**). Having a housing problem was a negative predictor of the SCNR outcome. Notably, the odds of the SCNR outcome were 59% higher for those who received community-based treatment prior to IW, and 47% higher for those who received community-based treatment subsequent to IW. No such association was evident for provision of recovery support throughout the treatment journey.

For the RR analysis, a multi-level, mixed effects, multivariable logistic model (i.e., '*RR group'* and '*Combined group*') showed that being engaged in paid employment, self/family/peer referral to treatment, a longer duration of RR treatment exposure, and receipt of community-based treatment subsequent to RR were associated with greater likelihood of achieving the SCNR outcome. Receiving community-based treatment prior to RR, and IW in the same treatment journey as RR, were associated with a lower likelihood of this outcome (**Table 4**). Notably, the odds of SCNR were 69% higher for those who received structured outpatient intervention after RR; no such association was evident for provision of recovery support.

3.4 Sensitivity analyses

Models for IW and RR groups were repeated using complete-case data (**Table S1**) and were comparable. We calculated the E-value for a common outcome (where the outcome >15%). The E-value is an estimate of the minimum strength of association that an unmeasured confounder would need to account for a treatment-outcome association, conditional on the included covariates (VanderWeele & Ding, 2017).

For the IW model, the magnitude of the observed AOR for prior structured community-based treatment (1.59) and for subsequent structured community-based treatment (1.47) was relatively protected from influence of unmeasured confounding. The E-value indicated that these treatment-outcome associations could be explained away by an unmeasured confounder, but only one that that was associated with both the treatment and the outcome with a risk ratio of 1.83 and 1.72, respectively. Weaker unmeasured confounding could not do so, although the confidence intervals could be moved towards the null with smaller risk ratios (1.38 and 1.29, respectively). For the RR model, the observed AORs of 0.67 for prior community-based treatment and 1.69 for subsequent community-based treatment could be explained away by E-values of 1.74 and 1.92, respectively and with relative modest impact of the confidence intervals towards the null (1.08 and 1.28, respectively).

4. Discussion

The aim of this study was to estimate the clinical effectiveness of publicly-funded IW and RR treatment for AUD in England. In this national cohort, categorisation of patients who entered a form of accommodation-based treatment revealed that the majority received treatment in an IW setting; less than one-third entered a RR facility. IW is recommended where individuals are at risk of alcohol withdrawal seizures or delirium tremens, and thus require medically-assisted alcohol withdrawal and 24 hour assessment and monitoring (National Institute for Health and Care Excellence, 2011). RR is typically recommended where the individual may not have stable housing and/or may require intensive treatment longer-term (National Institute for Health and Care Excellence, 2011). Whilst pharmacological intervention may be offered in some RR facilities, abstinence on treatment commencement can be a requirement. Indeed, the current study showed that those who received RR were more likely to be homeless or at housing risk, had a longer duration of treatment exposure, and were more likely to report abstinence at triage, relative to those who received IW.

Notably, half the sample had received outpatient treatment prior to IW/RR, with greater prevalence amongst IW patients. Outpatient-based community-assisted withdrawal programs with psychosocial intervention and a medication regime where necessary are recommended as the first-line response to AUD (National Institute for Health and Care Excellence, 2011). Half the sample received structured outpatient treatment after discharge from accommodation-based treatment, and two-thirds received some form of recovery support, showing general support for recommendations regarding engagement in continuing care in outpatient settings (National Institute for Health and Care Excellence, 2011).

Over half of those who left treatment (planned or unplanned) achieved SCNR, with a higher rate amongst those who received RR versus IW. The present study is not able to shed light on the relative efficacy of treatment here given that participants were not randomly allocated to settings. However, IW is often considered the first step in the treatment journey, focused purely on withdrawal, whilst RR is often focused on maintenance of abstinence (National Institute for Health and Care Excellence, 2011). Further, IW is typically a week or so in duration, and RR several months. Longer duration of treatment, as opposed to treatment intensity, is associated with better short and long-term outcomes, including abstinence, severity of dependence and broader psychosocial wellbeing (Moos & Moos, 2003).

The analysis of correlates of SCNR for those who received IW and RR revealed that longer duration of exposure to IW or RR predicted greater likelihood of SCNR after covariate control. Previous AUD treatment exposure was associated with lower odds of SCNR, aligning with current understanding of AUD as a chronic, remitting condition (Grahn, Chassler, & Lundgren, 2014). Receipt of community-based treatment following discharge from IW or RR, what we would term here ‘continuing care’, was associated with greater odds of SCNR across both subsamples. Continuing care has been defined as treatment which follows a period of more intensive care, typically IW/RR or intensive outpatient care, intended to maintain progress and provide support for continued engagement in other recovery activities (McKay, 2009). Whilst there is considerable variability in patient response, there is evidence to support a positive effect of continuing care in enhancing positive short- and long-term treatment outcomes (McKay, 2002, 2009). Indeed, several studies have shown increased rates of abstinence over time with provision of structured outpatient psychosocial treatment following RR and IW for problematic alcohol and other

drug use (Gossop et al., 2003; Gossop, Stewart, & Marsden, 2008; Kim et al., 2012; Ouimette, Moos, & Finney, 1998).

We did not observe a significant association between provision of recovery support and SCNR for IW or RR subsamples. Recovery support can be delivered and recorded outside structured treatment, and comprises activities targeted at relapse prevention (e.g., periodic contact between provider and client regarding recovery progress) and supports for broader functioning (e.g., employment, housing, parenting, family). It should be noted that non-structured recovery support is not captured within NDTMS, nor is services offered outside of reporting agencies, so rates of engagement in recovery support may be under-ascertained.

5.1 Strengths and limitations

Past research exploring outcomes following AUD treatment within IW and RR settings is typically restricted to prospective cohort studies, focusing on achievement of abstinence, as well as retention and successful completion of treatment (Gossop et al., 2003). To the best of our knowledge, this is the first study of IW and RR treatment outcomes, as conceptualised, using a national monitoring system.

We acknowledge several study limitations. Firstly, the sample was restricted to those who reported only problematic alcohol use. Whilst existing research indicates high comorbidity between AUD and other substance disorders (Stinson et al., 2005), annual 2014/15 NDTMS data (Public Health England, 2015a) indicated that alcohol only patients formed 30% of the total treatment population, and patients with comorbid alcohol and non-opiate problematic use only 10%. Second, NDTMS lacks research measures of self-efficacy, personality traits and specific co-existing mental health conditions, so there is relatively limited opportunity for confounder control and evaluation of outcome mediation, and these are recognised as potential unmeasured confounders (Adamson et al., 2009). However, we included an analysis of the strength of unmeasured confounding (using the E-value) and found that this was not likely to represent a threat to the adjusted models; although the assessment of unmeasured confounding for the RR model did point to some imprecision in the confidence intervals for the intervention-outcome associated identified.

Third, we were not able to link treatment records to national deaths registry or the national prisons system, meaning that we could not censor data for barriers to treatment re-presentation, and privately-funded treatment may not be captured in NDTMS. Given that only 1.2% of the sample ceased treatment within 12 months of admission due to mortality, we do not anticipate that the rate of SCNR would decrease substantially accounting for these factors.

Fourth, SCNR outcome is a proxy for remission. It does not include people who have relapsed but not, for whatever reason, not re-presented to treatment. This sub-group are detectable by research studies with research follow-up, but are not detectable by data registries such as NDTMS. Fifth, whilst our definition of SCNR matched national reporting standards (Public Health England, 2015b), further research using longer period to identify relapse (≥12 months) could evaluate benefit in the longer-term. Finally, it should be emphasised that this study does not comprise a comparison of treatment outcomes for IW versus RR given that patients were not randomised to setting.

5.2 Conclusion

In this first national effectiveness study of AUD in the English public treatment system for alcohol-use disorders, 59% of patients successfully completed treatment within 12 months and did not represent for more treatment within six months. Greater likelihood of SCNR with longer treatment exposure aligns with current literature suggesting that the duration of treatment may be critical in determining outcomes. Further, provision of continuing care in the form of structured outpatient intervention was associated with greater likelihood, and previous history of AUD treatment was associated with lower likelihood, of successful completion without re-presentation. Taken together, these findings reinforce current conception of AUD as a chronic condition, whereby continued provision of support over time may delay the time until relapse.

Contributors

The design and statistical analysis plan for this study was developed and implemented by A.P., J.M. and B.E. Data validation was implemented by B.E, P.H., T.L and P.W. The analysis was implemented by A.P., B.E and J.M. A.P. wrote the first draft of the manuscript, with J.M. and B.E. drafting further versions. All authors reviewed and approved the final manuscript.

Conflict of Interests

B.E. is enrolled at a part-time PhD programme at King's College London. He is employed full-time at Public Health England with the Evidence Application Team, Alcohol, Drugs and Tobacco Division, Public Health England.

A.P. is supported by a National Health and Medical Research Council Early Career Fellowship (#APP1109366). A.P. works at the National Drug and Alcohol Research Centre, which is funded by the Australian Government as part of the National Drug Strategy. She has received untied educational grants from Mundipharma and Seqirus for post-marketing surveillance of pharmaceutical opioid formulations.

J.M. works in an integrated university and National Health Service academic health sciences centre (Institute of Psychiatry, Psychology and Neuroscience [IoPPN], King's College London and King's Health Partners). He is supported by research grants from the Department of Health, Institute for Health Research (NIHR), and the NIHR Biomedical Research Centre for Mental Health at South London and Maudsley NHS Mental Health Foundation Trust (SLaM MHFT) and has part-time employment as Senior Academic Advisor for the Alcohol, Drugs and Tobacco Division, Health and Wellbeing Directorate, Public Health England. He declares untied educational grant funding from the pharmaceutical industry at IoPPN and SLaM MHFT for a study of psychological interventions in opioid maintenance (2010-2016; Indivior PLC via Action on Addiction). In the past three years he has received honoraria from Merck Serono in 2015 (clinical oncology medicine) and from Indivior via PCM Scientific in relation to the Improving Outcomes in Treatment of Opioid Dependence conference (co-chair, 2015; 2016; chair: 2017). He holds no stocks in any company.

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Appendix A. Supplementary materials

Supplementary material related to this article can be found, in the online version, at: XXXXXXX.

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Table 1
Socio-demographic, clinical/treatment characteristics of the cohort (n=3,812)

Characteristic	IW (n=2,682)	RR (n=915)	Combined (IW + RR; n=215)	Total (n=3,812)
Socio-demographic [a]				
No. (%) male	1792 (66.8)	569 (62.2)	129 (60.0)	2490 (65.3)
Age (M, IQR)	47 (40, 54)	45 (37, 51)	45 (37, 52)	46 (39, 53)
No. (%) Black or minority ethnic group	309 (11.7)	86 (9.9)	22 (10.4)	417 (11.2)
No. (%) deprivation quintile				
1 (least deprived)	508 (18.9)	212 (23.2)	33 (15.3)	753 (19.8)
2	442 (16.5)	219 (23.9)	47 (21.9)	708 (18.6)
3	494 (18.4)	143 (15.6)	54 (25.1)	691 (18.1)
4	550 (20.5)	168 (18.4)	49 (22.8)	767 (20.1)
5 (most deprived)	688 (25.7)	173 (18.9)	32 (14.9)	893 (23.4)
No. (%) with housing problems	358 (13.5)	196 (21.8)	39 (18.2)	593 (15.7)
No. (%) in paid employment	438 (17.1)	160 (18.2)	37 (17.5)	635 (17.4)
Clinical [a]				
Days alcohol use (M, IQR)	28 (28, 28)	28 (14, 28)	28 (28, 28)	28 (28, 28)
No. (%) DDD group: [b]				
Abstinent	113 (4.2)	122 (13.3)	11 (5.1)	246 (6.5)
Low-High	408 (15.2)	110 (12.0)	28 (13.0)	546 (14.3)
High-Extreme	1340 (50.0)	438 (47.9)	103 (47.9)	1881 (49.3)
Extreme	821 (30.6)	245 (26.8)	73 (34.0)	1139 (29.9)
No. (%) previous treatment for AUD	1458 (54.4)	442 (48.3)	129 (60.0)	2029 (53.2)
No. (%) referral route:				
Health service	897 (33.5)	409 (45.4)	81 (37.7)	1387 (36.6)
Self/family member/friend	33 (1.2)	12 (1.3)	5 (2.3)	50 (1.3)
Criminal justice	1748 (8.6)	479 (53.2)	129 (60.0)	2356 (62.1)
Treatment exposure				
Total weeks in treatment (M, IQR)	6 (2-20)	13 (6-24)	25 (13-41)	9 (2-23)
No. (%) prior structured community-based treatment	1526 (56.9)	359 (39.2)	144 (67.0)	2029 (53.2)
Total days community-based treatment (M, IQR)	62 (35-104)	84 (50-133)	83 (49-132)	67 (38-111)
No. (%) subsequent structured community-based treatment	1627 (60.7)	252 (27.5)	84 (39.1)	1963 (51.5)
No. (%) recovery support	1,952 (69.6)	453 (49.1)	184 (87.6)	2,589 (65.7)

IW, inpatient withdrawal; RR, residential rehabilitation; IW + RR, inpatient withdrawal and residential rehabilitation; M, median; IQR, inter-quartile range; DDD, drinks per drinking day; AUD, alcohol use disorder.

[a] Recorded at triage assessment with reference to the preceding 28 days as appropriate; [b] Recoded at treatment commencement with reference to the preceding 28 days were appropriate.

Table 2
Likelihood of IW and RR group classification: by socio-demographic and clinical/treatment characteristics (n=3,812)

Covariate	RR (n=915)	Combined (IW + RR; n=215)
Socio-demographic [a]		
Male	0.82 (0.68, 0.99), p=0.037	0.74 (0.57, 0.97), p=0.031
Age	0.98 (0.97, 0.99), p<0.001	0.98 (0.97, 0.99), p<0.001
Black or minority ethnic group	0.84 (0.49, 1.42), p=0.507	0.88 (0.58, 1.33), p=0.541
Deprivation quintile [b]		
2	1.19 (0.90, 1.57), p=0.229	1.64 (0.95, 2.81), p=0.074
3	0.69 (0.45, 1.07), p=0.100	1.68 (0.97, 2.92), p=0.063
4	0.73 (0.45, 1.20), p=0.215	1.37 (0.81, 2.33), p=0.245
5 (most deprived)	0.60 (0.28, 1.28), p=0.186	0.72 (0.35, 1.45), p=0.353
Housing problems	1.79 (1.24, 2.59), p=0.002	1.43 (0.86, 2.36), p=0.164
Paid employment	1.08 (0.83, 1.40), p=0.564	1.03 (0.69, 1.53), p=0.903
Clinical [a]		
Days alcohol use	0.92 (0.89, 0.95), p<0.001	1.02 (0.98, 1.06), p=0.280
DDD group: [c]		
Abstinent	3.30 (1.81, 6.03), p<0.001	1.27 (0.63, 2.54), p=0.506
Low-High	0.82 (0.59, 1.15), p=0.253	0.89 (0.60, 1.32), p=0.568
Extreme	0.91 (0.70, 1.19), p=0.505	1.16 (0.87, 1.55), p=0.325
Previous treatment for AUD	0.78 (0.59, 1.04), p=0.088	1.26 (0.88, 1.80), p=0.209
Referral route: [d]		
Self/family member/friend	1.66 (1.12, 2.48), p=0.012	1.22 (0.83, 1.80), p=0.309
Criminal justice	1.33 (0.59, 2.96), p=0.490	2.05 (0.75, 5.65), p=0.164
Treatment exposure		
Total weeks in treatment	1.01 (1.00, 1.02), p=0.023	1.04 (1.03, 1.05), p<0.001
Prior structured community-based treatment	0.49 (0.28, 0.85), p=0.011	1.54 (0.87, 2.71), p=0.139
Subsequent structured community-based treatment	0.15 (0.05, 0.43), p=0.001	0.10 (0.04, 0.25), p<.001
Recovery support	0.68 (0.31, 1.47), p=0.324	2.47 (1.05, 5.81), p=0.038

IW, inpatient withdrawal; RR, residential rehabilitation; IW + RR, inpatient withdrawal and residential rehabilitation; DDD, drinks per drinking day; AUD, alcohol use disorder.

Numbers in table are relative risks (95% confidence intervals) and p-values.

Referent group in multinomial model is: Inpatient (n=2,682)

[a] Recorded at triage assessment with reference to the preceding 28 days as appropriate; [b] Referent category: Deprivation first quartile; [c] Referent category: High-Extreme, recoded at treatment commencement with reference to the preceding 28 days were appropriate; [d] Referent category: Health service.

Table 3
Treatment status and outcome at 6-month follow-up (n=3,812)

Status/outcome	IW (n=2,682)	RR (n=915)	Combined (IW + RR; n=215)	Total (n=3,812)
Treatment status				
No. (%) successfully completed	1560 (58.2)	595 (65.0)	123 (57.2)	2278 (59.8)
No. (%) unsuccessful agency transfer	504 (18.8)	97 (10.6)	34 (15.8)	635 (16.7)
No. (%) still in treatment	207 (7.7)	47 (5.1)	29 (13.5)	283 (7.4)
No. (%) dropped out	369 (13.8)	175 (19.1)	27 (12.6)	571 (15.0)
No. (%) prison terminated treatment	1 (0)	0 (0)	0 (0)	1 (0)
No. (%) died in treatment	41 (1.5)	1 (0.1)	2 (0.9)	44 (1.2)
Outcome (excluding those still in treatment; n=3,529)				
No. (%) SCNR outcome	1417 (57.3)	554 (63.8)	105 (56.5)	2076 (58.8)

SCNR, successful completion of treatment and no representation within 6 months; IW, inpatient withdrawal; RR, residential rehabilitation; IW + RR, inpatient withdrawal and residential rehabilitation

Table 4
Multi-level, mixed effects, multivariable logistic model of SCNR outcome for inpatient (n=2,475) and residential rehabilitation (n=1,054) samples

Covariate	IW (n=2,475)	RR/Combined (n=1,054)
Socio-demographic [a]		
Male	0.93 (0.77, 1.13), p=0.484	0.84 (0.62, 1.15), p=0.277
Age	1.01 (1.01, 1.02), p=0.002	1.00 (0.99, 1.01), p=0.989
Black or minority ethnic group	0.90 (0.67, 1.21), p=0.486	1.51 (0.92, 2.49), p=0.103
Deprivation quintile: [b]		
2	1.11 (0.81, 1.51), p=0.512	1.16 (0.76, 1.78), p=0.491
3	0.99 (0.73, 1.34), p=0.929	1.02 (0.64, 1.64), p=0.928
4	0.96 (0.71, 1.30), p=0.785	0.78 (0.49, 1.24), p=0.293
5 (most deprived)	1.03 (0.76, 1.41), p=0.830	0.87 (0.54, 1.40), p=0.555
Housing problems	0.67 (0.51, 0.88), p=0.004	0.95 (0.65, 1.37), p=0.771
Paid employment	1.32 (1.03, 1.70), p=0.028	1.52 (1.02, 2.26), p=0.038
Clinical [a]		
DDD group: [c]		
Abstinent	1.29 (0.78, 2.16), p=0.324	0.69 (0.42, 1.13), p=0.139
Low-High	1.07 (0.82, 1.40), p=0.615	1.10 (0.69, 1.74), p=0.700
Extreme	0.90 (0.73, 1.10), p=0.301	0.95 (0.67, 1.34), p=0.749
Previous treatment for AUD	0.90 (0.75, 1.08), p=0.253	0.82 (0.61, 1.10), p=0.177
Referral source: [d]		
Self/family member/friend	1.22 (0.97, 1.54), p=0.090	1.89 (1.37, 2.60), p<0.001
Criminal justice	1.23 (0.52, 2.89), p=0.636	0.76 (0.26, 2.24), p=0.616
Treatment exposure		
Days IW exposure	1.00 (1.00, 1.00), p=0.290	-
Weeks RR exposure	-	1.09 (1.07, 1.11), p<0.001
Received IW	-	0.60 (0.38, 0.94), p=0.026
Any prescribing in RR	-	1.18 (0.80, 1.73), p=0.405
Prior structured community-based treatment	1.59 (1.17, 2.17), p=0.003	0.67 (0.45, 0.99), p=0.047
Subsequent structured community-based treatment	1.47 (1.11, 1.96), p=0.008	1.69 (1.10, 2.60), p=0.016
Recovery support	1.06 (0.82, 1.37), p=0.681	0.69 (0.48, 1.00), p=0.047
Model parameters		
Treatment clinic (ICC) [e]	0.17, 0.18	0.09, 0.10
Constant	0.41 (0.23, 0.74)	0.76 (0.32, 1.78)
Wald [e]	104.34, 106.42	99.61, 104.26
LR [e]	171.69, 176.13	13.38, 15.33

SCNR, successful completion of treatment and no representation within 6 months; IW, inpatient withdrawal; RR, residential rehabilitation; IW + RR, inpatient withdrawal and residential rehabilitation; DDD, drinks per drinking day; AUD, alcohol use disorder; ICC, intra-class correlation; LR, Likelihood-Ratio Test.

Numbers in table are adjusted odds ratios (95% confidence intervals) with p-values. These outputs are based on multiple imputation.

[a] Recorded at triage assessment with reference to the preceding 28 days as appropriate; [b] Referent category: Deprivation first quartile; [c] Referent category: High-Extreme, recoded at treatment commencement with reference to the preceding 28 days were appropriate; [d] Referent category: Health service; [e] Range for imputed models reported here

Table S1
Multi-level, mixed effects, multivariable logistic model SCNR outcome for inpatient (n=2,324) and residential rehabilitation (n=963) samples (complete-case analysis)

Covariate	IW (n=2,324)	RR/Combined (n=963)
Socio-demographic [a]		
Male	0.89 (0.73, 1.09), p=0.274	0.88 (0.64, 1.21), p=0.444
Age	1.01 (1.00, 1.02), p=0.007	1.00 (0.98, 1.01), p=0.611
Black or minority ethnic group	0.93 (0.69, 1.25), p=0.632	1.56 (0.92, 2.64), p=0.097
Deprivation quintile: [b]		
2	1.13 (0.82, 1.55), p=0.464	1.20 (0.77, 1.88), p=0.414
3	0.99 (0.73, 1.35), p=0.952	1.13 (0.69, 1.85), p=0.618
4	0.92 (0.68, 1.26), p=0.619	0.84 (0.52, 1.36), p=0.474
5 (most deprived)	1.03 (0.75, 1.42), p=0.850	0.83 (0.50, 1.38), p=0.463
Housing problems	0.65 (0.49, 0.85), p=0.002	0.94 (0.64, 1.39), p=0.757
Paid employment	1.29 (1.00, 1.67), p=0.048	1.62 (1.07, 2.46), p=0.023
Clinical [a]		
DDD group: [c]		
Abstinent	1.27 (0.75, 2.14), p=0.370	0.63 (0.37, 1.06), p=0.079
Low-Extreme	1.09 (0.83, 1.44), p=0.519	1.13 (0.70, 1.82), p=0.624
Extreme	0.87 (0.70, 1.08), p=0.198	0.88 (0.61, 1.26), p=0.489
Previous treatment for AUD	0.89 (0.74, 1.08), p=0.243	0.82 (0.60, 1.12), p=0.221
Referral source: [d]		
Self/family member/friend	1.18 (0.93, 1.50), p=0.162	1.97 (1.40, 2.76), p<0.001
Criminal justice	1.22 (0.52, 2.87), p=0.645	0.71 (0.23, 2.19), p=0.548
Treatment exposure		
Days IW exposure	1.00 (1.00, 1.00), p=0.239	-
Weeks RR exposure	-	1.09 (1.07, 1.11), p<0.001
Received IW	-	0.54 (0.34, 0.85), p=0.009
Any prescribing in RR	-	1.08 (0.72, 1.60), p=0.719
Prior community-based treatment	1.49 (1.09, 2.06), p=0.013	0.59 (0.39, 0.89), p=0.012
Subsequent community-based treatment	1.38 (1.03, 1.84), p=0.030	1.64 (1.06, 2.56), p=0.028
Recovery support	1.02 (0.79, 1.33), p=0.862	0.77 (0.52, 1.13), p=0.181
Model parameters		
Treatment clinic (ICC)	0.17	0.08
Constant	0.55 (0.30, 0.99)	0.87 (0.36, 2.15)
Wald	82.33	102.97
LR	142.31	10.01

IW, inpatient withdrawal; RR, residential rehabilitation; IW + RR, inpatient withdrawal and residential rehabilitation; DDD, drinks per drinking day; AUD, alcohol use disorder; ICC, intra-class correlation; LR, Likelihood-Ratio Test.

Numbers in table are adjusted odds ratios (95% confidence intervals) and p-values. These outputs are based on complete-case analysis.

[a] Recorded at triage assessment with reference to the preceding 28 days as appropriate; [b] Referent category: Deprivation first quartile; [c] Referent category: High-Extreme, recoded at treatment commencement with reference to the preceding 28 days were appropriate; [d] Referent category: Health service.

Supporting Information – not for publication
RECORD statement

	Item No.	STROBE items	Location in manuscript where items are reported	RECORD items	Location in manuscript where items are reported
Title and abstract					
	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found	Title (page 1) Abstract (page 3)	RECORD 1.1: The type of data used should be specified in the title or abstract. When possible, the name of the databases used should be included. RECORD 1.2: If applicable, the geographic region and timeframe within which the study took place should be reported in the title or abstract. RECORD 1.3: If linkage between databases was conducted for the study, this should be clearly stated in the title or abstract.	Title (page 1) Abstract (page 3)
Introduction					
Background rationale	2	Explain the scientific background and rationale for the investigation being reported	Background (page 4-7)		Background (page 4-7)
Objectives	3	State specific objectives, including any prespecified hypotheses	Background (page 6-7)		Background (page 6-7)
Methods					
Study Design	4	Present key elements of study design early in the paper	Design (page 8)		Design (page 8)
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Design, Patient and Treatment Information, Study		Design, Patient and Treatment Information, Study Cohort, Outcome

			Cohort, Outcome Measure (page 8-10)		Measure (page 8-10)
Participants	6	*(a) Cohort study* - Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study* - Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study* - Give the eligibility criteria, and the sources and methods of selection of participants *(b) Cohort study* - For matched studies, give matching criteria and number of exposed and unexposed *Case-control study* - For matched studies, give matching criteria and the number of controls per case	Study Cohort and Outcome Measure (page 8-10)	RECORD 6.1: The methods of study population selection (such as codes or algorithms used to identify subjects) should be listed in detail. If this is not possible, an explanation should be provided. RECORD 6.2: Any validation studies of the codes or algorithms used to select the population should be referenced. If validation was conducted for this study and not published elsewhere, detailed methods and results should be provided. RECORD 6.3: If the study involved linkage of databases, consider use of a flow diagram or other graphical display to demonstrate the data linkage process, including the number of individuals with linked data at each stage.	Study Cohort and Outcome Measure (page 8-10)
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable.	Outcome Measure and Covariates (page 9-11)	RECORD 7.1: A complete list of codes and algorithms used to classify exposures, outcomes, confounders, and effect modifiers should be provided. If these cannot be reported, an explanation should be provided.	Outcome Measure and Covariates (page 9-11)
Data sources/ measurement	8	For each variable of interest, give sources of data and details of methods of assessment (measurement).	Outcome Measure and Covariates (page 9-11)		Outcome Measure and Covariates (page 9-11)

		Describe comparability of assessment methods if there is more than one group			
Bias	9	Describe any efforts to address potential sources of bias	Statistical Analysis (page 11-13)		Statistical Analysis (page 11-13)
Study size	10	Explain how the study size was arrived at	Study Cohort (page 8-9)		Study Cohort (page 8-9)
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	Outcome Measure, Covariates and Statistical Analysis (page 9-13)		Outcome Measure, Covariates and Statistical Analysis (page 9-13)
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) *Cohort study* - If applicable, explain how loss to follow-up was addressed *Case-control study* - If applicable, explain how matching of cases and controls was addressed *Cross-sectional study* - If applicable, describe analytical methods taking account of sampling strategy (e) Describe any sensitivity analyses	Statistical Analysis (page 9-13)		Statistical Analysis (page 9-13)
Data access and cleaning methods		..		RECORD 12.1: Authors should describe the extent to which the investigators had access to the database population used to create the study population.	Design (page 8) and Statistical Analysis (page 9-13)

				RECORD 12.2: Authors should provide information on the data cleaning methods used in the study.	
Linkage		..		RECORD 12.3: State whether the study included person-level, institutional-level, or other data linkage across two or more databases. The methods of linkage and methods of linkage quality evaluation should be provided.	Design (page 8)
Results					
Participants	13	(a) Report the numbers of individuals at each stage of the study (*e.g.*, numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed) (b) Give reasons for non-participation at each stage. (c) Consider use of a flow diagram	Study Cohort (page 8-9), Statistical Analysis (page 9-13), Results (page 15), Supplementary Table 1	RECORD 13.1: Describe in detail the selection of the persons included in the study (*i.e.,* study population selection) including filtering based on data quality, data availability and linkage. The selection of included persons can be described in the text and/or by means of the study flow diagram.	Study Cohort (page 8-9), Statistical Analysis (page 9-13), Results (page 15), Supplementary Table 1
Descriptive data	14	(a) Give characteristics of study participants (*e.g.*, demographic, clinical, social) and information on exposures and potential confounders (b) Indicate the number of participants with missing data for each variable of interest (c) *Cohort study* - summarise follow-up time (*e.g.*, average and total amount)	Socio-Demographic and Clinical Characteristics (page 14); Treatment Exposure and Status (page 14); Table 1		Socio-Demographic and Clinical Characteristics (page 14); Treatment Exposure and Status (page 14); Table 1
Outcome data	15	*Cohort study* - Report numbers of outcome events or summary measures over time	Treatment Exposure and Status (page 14), Table 3		Treatment Exposure and

		Case-control study - Report numbers in each exposure category, or summary measures of exposure *Cross-sectional study* - Report numbers of outcome events or summary measures			Status (page 14), Table 3
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Outcome Measure, Covariates and Statistical Analysis (page 9-13)		Outcome Measure, Covariates and Statistical Analysis (page 9-13)
Other analyses	17	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses	Statistical Analysis (page 11-13), Supplementary Table 1		Statistical Analysis (page 11-13), Supplementary Table 1
Discussion					
Key results	18	Summarise key results with reference to study objectives	Discussion (page 17-19)		Discussion (page 17-19)
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	Strengths and Limitations (page 19-20)	RECORD 19.1: Discuss the implications of using data that were not created or collected to answer the specific research question(s). Include discussion of misclassification bias, unmeasured confounding, missing data, and changing	Strengths and Limitations (page 19-20)

				eligibility over time, as they pertain to the study being reported.	
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Conclusion (page 20)		Conclusion (page 20)
Generalisability	21	Discuss the generalisability (external validity) of the study results	Strengths and Limitations (page 19-20)		Strengths and Limitations (page 19-20)
Other Information					
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Role of Funding Source (page 2)		Role of Funding Source (page 2)
Accessibility of protocol, raw data, and programming code		..	Supplementary Material (page 22)	RECORD 22.1: Authors should provide information on how to access any supplemental information such as the study protocol, raw data, or programming code.	Supplementary Material (page 22)