Statistical analysis plan

The CORE study: A stepped wedge cluster randomised controlled trial to test a co-design technique to optimise psychosocial recovery outcomes for people affected by mental illness in the community mental health setting.

Funding Acknowledgement: The CORE study is funded by the Mental Illness Research Fund and the Psychiatric Illness and Intellectual Disability Donations Trust Fund (MIRF 28). The Mental Illness Research Fund aims to support collaborative research into mental illness that may lead to better treatment and recovery outcomes for Victorians with mental illness and their families and carers.

Date: 1 June 2017

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Background

The CORE study is a stepped wedge cluster randomised controlled trial (SWCRCT) with a nested process evaluation that will be conducted over nearly four years in Victoria, Australia. The CORE study tests whether the Experience Based Co-Design (EBCD) intervention designed to change recovery orientation of services improves psychosocial recovery outcomes in people with severe mental illness. The EBCD intervention is a modified version of the Mental Health Experience Co-Design (MH ECO) method, a structured process for service users (consumers), carers and mental health staff to come together to identify improvements to service planning and delivery and co-design the solutions to these improvements developed by the Victorian Mental Illness Awareness Council and Tandem representing Victorian mental health carers. The intervention will be delivered in four non-government organisations and teams who deliver mental health community support services (MHCSS) in Victoria. Mental health community support services are provided largely by non-government organisations and community health centres in Victoria. They are funded to provide people with daily living skills assistance, social and recovery oriented support for their mental health conditions and deliver case management with recovery planning at the centre, this case management can include providing links and referring people to activities and suitable groups within the community to work on goals and facilitating access to health care services where possible. Eligibility criteria to receive services are set out by the Victorian government and include people being between ages 18-65 years and having a persistent and enduring mental illness. Details of the setting, eligibility criteria and context for the intervention can be found in the published study protocol [1]: http://bmjopen.bmj.com/content/5/3/e006688.

Figure 1 shows the schematic of the SWCRCT for the CORE study. Nine clusters (teams that

deliver mental health community support services) will be randomly allocated the three arms, three clusters to each arm. Data collection will occur at baseline (October 2014 to July 2015) prior to randomisation (Time 1) and subsequently at 9, 18 and 27 months post randomisation. All clusters will be followed up longitudinally. The study utilises an open cohort [2], where individuals may enter/leave the study at each time collection point and may contribute varying data points over the period of the study. Thus, the stepped wedge design consists of a combination of individuals that are recruited at baseline and followed up longitudinally and new individuals that are recruited at a later stage of the study who may contribute one or more data observations. Details of the rationale for the open cohort study design (referred to as a mixed cohort and cross sectional design in the study protocol) can be found in the published study protocol [1]. The aim of this document is to describe in greater detail the statistical analysis plan for the CORE study. A nested process evaluation is also planned; this is detailed in the published nested process evaluation protocol [3].

Figure 1: Schematic of SWCRT for the CORE study

	Follow-up time (t_j)			
Arms	Baseline	9 months	18 months	27 months
1	0	**9 months**	**18 months**	**27 months**
2	0	0	**9 months**	**18 months**
3	0	0	0	**9 months**

0=Control phase; **9, 18, 27 months**=Intervention phases (indicates length of time since start of the intervention)
Arm is the allocation of group of clusters/individuals
j=1, 2, 3, 4 (four time points)
Note: Three clusters will be randomised to each arm

Primary hypothesis

An EBCD intervention aimed to make mental health community support services recovery-orientated will improve mean psychosocial recovery measured at 9 monthly intervals by a standardised effect size of 0.35 compared to the control phases for people affected by mental illness.

Secondary hypotheses

In addition, it is hypothesised that the intervention will improve service users' and carers' mental health and well-being, and change staff attitudes to recovery and the recovery orientation of services.

Outcomes

Outcome data will be collected during a baseline period and every 9 months at the end of each intervention phase.

Primary outcome will be the recovery score of service users measured using the 24-item Revised Recovery Assessment Scale (RAS) [4]. The RAS was developed as an evaluation measure, and was designed to assess various aspects of recovery from the perspective of the service user, with a particular emphasis on hope and self-determination. RAS-R uses a 5 point Likert rating scale from 1="Strongly Disagree" to 5="Strongly Agree". Responses to the 24 items are summed to calculate a total score ranging from 24 to 120, with higher scores indicating greater recovery. The RAS-R covers **five domains** related to recovery: (i) personal confidence and hope (9 items; range 9 to 45), (ii) willingness to ask for help (5 items; range 5 to 25), (iii) goal and success orientation (3 items; 3 to 15), (iv) reliance on others (4 items; range 4 to 20) and, (v) no domination by symptoms (3 items; range 3 to 15). A higher rating

within each domain indicates recovery progress [4].

Secondary outcomes will include**:**

1) Mental health and well-being of service users and carers measured using shortened 8-item version of the WHOQOL Quality of Life scale (EUROHIS-QoL 8-item index) [5]. The EUROHIS-QOL 8-item index is composed of eight items empirically derived from the WHOQOL-Bref using structural equation and Rasch modelling. The EUROHIS-QOL questions are primarily about personal satisfaction with different life aspects items (overall quality of life, general health, energy, daily life activities, self-esteem, relationships, finances, and home). The eight items are scored on a 5 point Likert scale, ranging for example from 1= “Not at all” to 5=”Completely”. The 8 items are summed to generate a total score, ranging between 8 and 40 with higher scores indicating to a better quality of life.

2) Staff attitudes measured using the 19-item Staff Attitudes to Recovery Scale (STARS) [6]. STARS was developed as an evaluation tool to assess the impact of a recovery-based training program on staff attitudes towards recovery. It measures staff attitudes and hopefulness related to service users’ goal striving and recovery possibilities. It consists of 19 items, rated on a 5 points Likert scale ranging from 1=Strongly disagree, 2=Somewhat disagree, 3=Neither agree nor disagree, 4=Somewhat agree, 5=Strongly agree. Items are averaged to generate an overall score, with higher scores corresponding to positive and hopeful attitude towards recovery and goal striving of the service users.

3) Recovery orientation of services measured using the 36-item service provider version of the Recovery Self-Assessment Scale (RSA) [7]. The RSA is designed to measure the extent to which recovery-supporting practices are evident in mental health services. It

consists of 36 items, with responses on a 5 point Likert scale that range from 1= "Strongly disagree" to 5="Strongly agree" response; or a "not applicable" response which is coded as missing. The 36 items are averaged to generate an overall summary score, with higher scores corresponding to positive attitude towards recovery. A mean score is also calculated for each of the five sub-domains: Life Goals (11 items), Involvement (8 items), Diversity of treatment options (6 items), Choice (6 items) and Individually tailored services (5 items).

4) Health services use and prescribed medications using routinely de-identified Australian government data. Specifically:
    1. Number of visits to health professionals (including general practitioners, specialist, allied health etc.) and treatment plans using the Medicare Benefits Schedule data (Website: www.mbsonline.gov.au/)
    2. Number and types of medications prescribed using the Pharmaceutical Benefits Scheme data (Website:www.pbs.gov.au/)
    3. Number and type of hospitalisations using the Victorian Admitted Episodes Dataset (Website: https://www2.health.vic.gov.au/hospitals-and-health-services/data-reporting/health-data-standards-systems/data-collections/vaed/).

Participant characteristics

Participants affected by mental illness (Service users)

Demographic data will be collected on participant's age, sex, postcode, English as the first language, level of education, employment status, and whether they received a pension, and if yes was a pension their main source of income. In addition, service users are asked to provide names given for their mental health conditions and the onset for each of the conditions.

Carers of participants affected by mental illness

Demographic data will be collected on carer's age, sex, postcode, English as the first language, level of education, employment status, and whether they received a pension, and if yes was a pension their main source of income. They will also be asked questions about the person they care for, including the length of time they have been a carer, their relationship to the person affected by mental illness, as well as the duration and type of condition(s) of the person they care for.

Mental Health Community Support Services (MHCSS)

Data will be collected by the research study coordinator on the:

- Number of staff delivering mental health community support services;
- Number of staff who completed the staff surveys within each of the four non-government organisations;
- Geographical location of the MHCSS
- Estimates of service users registered at MHCSS.

Staff

Sex, age, level of education, and equivalence full-time status will be collected on staff who complete the surveys. In addition, they will be asked about their involvement in other research projects at the service, their stress related to their work environment (MABEL) [8] and staff engagement measured using the Staff Friends and Family Test (FFT) [9].

Statistical analysis

Flow charts will be created to show the number and percentage of participants (service users, carers and staff) by each allocation group (arm) at each follow up time. Figure 1 provides an example of a flow chart for service users. The flow charts will show the recruitment rate (including the number of individuals approached to participate in the study, ineligible, declined and agreed to participate), new participants recruited at each step (replenishment sample), attrition rate (withdrawal and loss to follow-up) and the number of participants that completed the surveys and were analysed at each time point. The number of participants recruited (service users, carers and staff) within each arm at each time point will be summarised as an average and range (minimum and maximum) at each follow-up time point.

Descriptive statistics will be used to summarise the characteristics of service users and carers when they first entered the open cohort (baseline, 9 months, 18 months and 27 months) by each arm and in total (see Table 1). As staff respond anonymously at each time point, characteristics of staff will be summarised by each arm at each follow-up time.

An intention-to-treat (ITT) analysis strategy will be used, where all participants will be analysed in the arm that the site was assigned to at each time point [10]. Linear mixed effects model will be used to compare the intervention and usual care phases for continuous outcomes and generalised linear mixed effects model for binary outcomes. In using mixed effects model analyses, participants who have provided some data, but have missing responses at one or more data collection time points will be included in the analysis. Under these models, data are implicitly assumed to be missing at random (MAR) [10].

The outcome(s) measured at each follow-up time will be arranged into a single variable, and a second variable will identify the time point that the data were collected. The models will include indicator variables for **study arm** (0=Control phase, 1=Intervention phase) and **time** (1=Baseline, 2=9 months, 3=18 months, 4=27 months) as fixed effects. The intercept will be constrained to be equal during the control phases because we expect no intervention effect. Study arm is time-dependant, and thus we will need to adjust for **time** in the model because it may be a potential confounder if patients recover or deteriorate with time regardless of the intervention phase [11]. **Cluster** and **individuals** will be treated as random effects to account for the correlation of outcomes of individuals that belong to the same site(within-cluster correlation) and repeated measures on the same individual over time (within-individual correlation) [11]. The intra-cluster correlation coefficient will also be reported for the clusters and individuals.

The estimated intervention effect will be reported as mean outcome difference for continuous outcomes and odds ratio for binary outcomes between intervention and control phases. For these analyses, the underlying assumption is that treatment effect is constant across the different individuals (both cross-sectionally and longitudinally) and at the different time points, regardless of length and intensity of exposure to the intervention phase. The estimated intervention effects will be reported with 95% confidence intervals and p-values. All analysis will be conducted using Stata statistical software 13.1 [12].

Secondary analysis

Where appropriate, organisational and individual factors strongly correlated with the outcome may also be included as fixed effects in the model. Specifically for the primary outcome, we will consider adjusting estimates of the intervention effect for education level, employment

status and quality of life of service users [5]. Previous studies showed that age and sex were not correlated with psycho-social recovery [13] and thus will not be considered for adjustment in the regression models.

We also plan to extend the regression analyses described above to estimate the direct effects of the length of exposure to the intervention. This analysis will account for the length of time that individuals spend in the intervention phase, and thus we will be able to determine whether the intervention effect changes the longer participants are exposed to the intervention. For instance, if the intervention effect is immediate it may taper off or increase over time; or there is a delay in the intervention effect. For this analysis **study arm** will be re-coded to indicate the length of time an individual has been exposed to the intervention phase (namely, 0, 9, 18 and 27 months) at each data collection time point. As before, we will use linear mixed effects model, where study arm will be treated as a fixed effect and adjusted for follow-up time points. Estimates will be reported as mean outcome difference at 9, 18 and 27 months compared to “0 months”, the time when individuals were in the control phase. We will also use the log-likelihood ratio test to assess whether to treat the study arm status variable as continuous rather than categorical variable in the mixed effects model. Treating study arm as continuous assumes that the increase in the intervention effect is linear with the length of exposure to the intervention.

The routinely de-identified data will be linked to participant characteristics and study arm allocation. Descriptive statistics will used to summarise health services use, medications and hospitalisations for participants for each study arm.

Missing data

Every effort will be made to minimise missing outcome data at each wave and reasons individuals are lost to follow-up will be recorded. If a participant withdraws or refuses/unable to complete the Computer Assisted Telephone Interview, we will ask participants, where appropriate, if they can complete the primary outcome measure. Where available, reasons for withdrawal will be assessed to determine if loss to follow up differed between study arms. Characteristics of the completers will also be compared to the participants that were lost follow-up. At the time of publishing this data analysis plan, there were no readily accessible approaches to conduct sensitivity analyses for the stepped wedge design to explore the impact of departures from the MAR assumption for the primary analysis [10]. We will consider using multiple imputation approach to assess whether it will impact the estimated intervention effect of the primary outcome.

Exploratory analysis

We will also investigate whether long-term intervention effects are sustained over a period of time using the **inception** cohort only, that is, participants that entered at the study at Time 1 only. We will repeat the secondary analysis described earlier to estimate the direct effects of the length of exposure to the intervention on the **inception** cohort only, using linear mixed effects model, where **study arm** (fixed effect) is the months in intervention phase (0, 9, 18 and 27 months) at each follow-up time point.

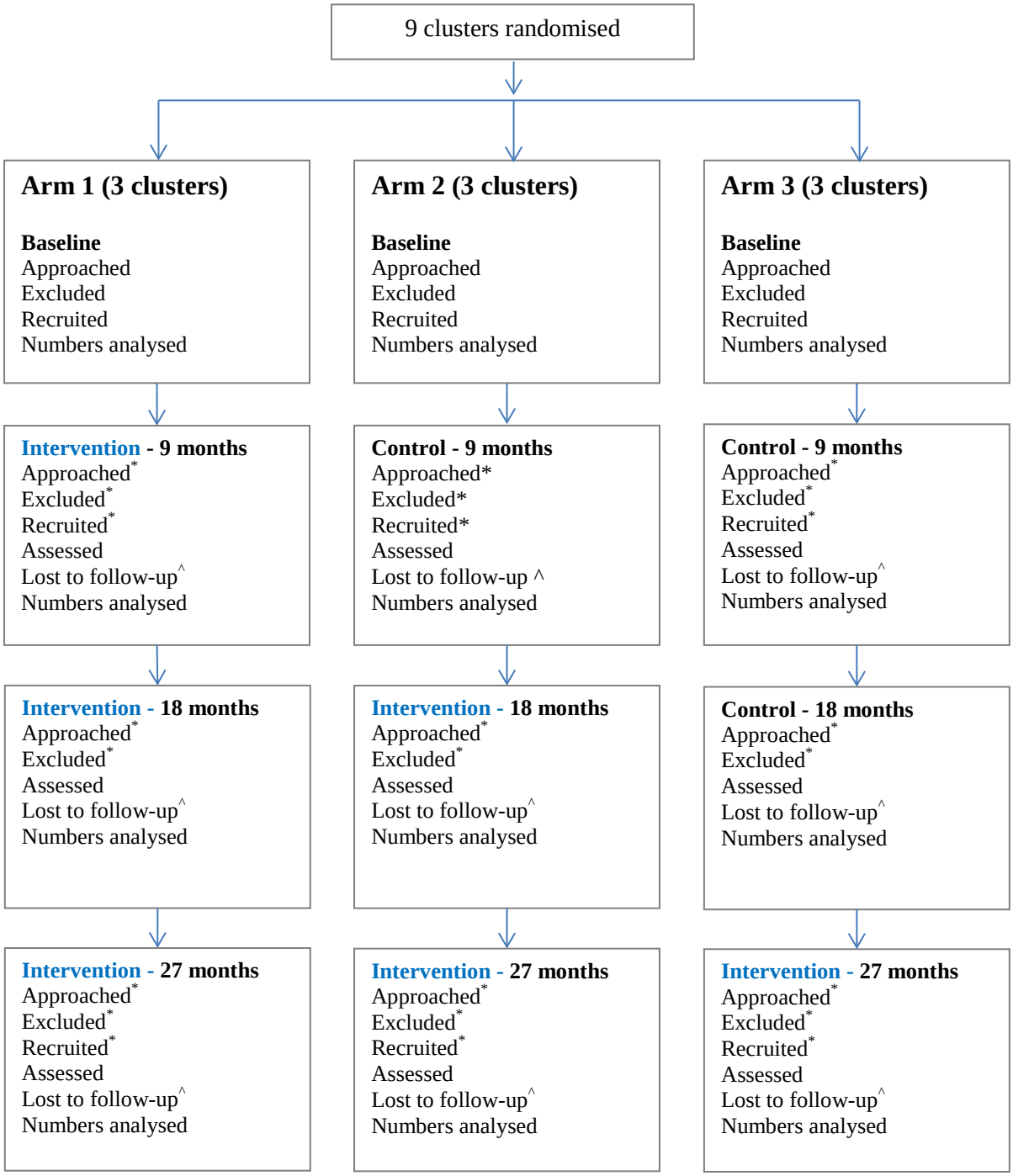
We will also examine the intervention effects in the period immediately after the intervention is completed (immediate effect) using three pre-post comparisons with no adjustment for time.

Economic evaluation

Costs of the delivery of the intervention will be recorded but no economic evaluation will be undertaken.

Table shells and figures

Figure 1: Flow chart of service users at each follow up time



*New participants at each measurement time point / Replenishment sample

^Record the reasons for withdrawal / loss to follow-up at each stage

Reference: [14]

Table 1: Characteristics of service users when they first entered the cohort by arm

Characteristics	Entry into Cohort*	Total (n)	By allocation arm		
			Arm 1	Arm 2	Arm 3
Sex - % female	Baseline				
	9 months				
	18 months				
	27 months				
Age – mean (SD)	Baseline				
	9 months				
	18 months				
	27 months				
Educational level – n (%)	Baseline				
	9 months				
	18 months				
	27 months				
Employment status – n (%)	Baseline				
	9 months				
	18 months				
	27 months				
etc.					

SD - Standard deviation
*New participants at each measurement time point

Table 2: Mean (standard deviation) of the primary and secondary outcomes for the allocation arms at each follow-up time point (*t*)

	Follow-up time point (*t*)			
	Baseline	**9 months**	**18 months**	**27 months**
Intervention phase compared to control phase at each follow-up time point*				
Intervention		mean (SD)	mean (SD)	mean (SD)
Control	mean (SD)	mean (SD)	mean (SD)	
Length of time in the intervention phase at each follow-up time point^				
0 months	mean (SD)	mean (SD)	mean (SD)	
9 months		mean (SD)	mean (SD)	mean (SD)
18 months			mean (SD)	mean (SD)
27 months				mean (SD)
ICC for individual level				
ICC for cluster level				

ICC - Intra-cluster correlation coefficient; SD - Standard deviation
* Primary analysis: 0=Control phase; 1=Intervention phase (Method 1 in paper by Twisk *et al* (2016) [11])
^ Secondary analysis (Method 3 in paper by Twisk *et al* (2016) [11])

Note: Table will be expanded to include the primary (RAS) and secondary outcome measures

Table 3: Estimates of the intervention effects

		Intervention vs control phases	Time-specific intervention effect^		
Outcome measures	**n**	**Coefficient (95% CI)***	**9 months Coefficient (95% CI)***	**18 months Coefficient (95% CI)***	**27 months Coefficient (95% CI)***
Service users					
RAS (Primary outcome)[4]					
EUROHIS_QoL[5]					
Carers					
EUROHIS_QoL[5]					
Staff					
STARS[6]					
RSA[7]					

CI = Confidence Interval

* Differences in mean outcome estimated using linear mixed effects regression; Primary analysis: 0=Control phase; 1=Intervention phase [11]. If appropriate, may also present coefficients adjusted for confounders [11].

^Secondary analysis: Reference group is "0 months" [11]

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