Intensive Case Management for Patients with Substance Use Disorders and Complex Psychosocial Needs: A Randomized Controlled Trial

---

Study Type:	Other Clinical Trial according to ClinO, Chapter 4
Risk Categorisation:	A
Study Registration:	BASEC 2026-01365
Sponsor Investigator:	PD Dr. Med. Eva-Maria Pichler Zentrum für Abhängigkeitserkrankungen Psychiatrische Dienste Aargau AG Königsfelderstrasse 1 5210 Windisch
Co-Investigator	Johannes Senesi Zentrum für Abhängigkeitserkrankungen Psychiatrische Dienste Aargau AG Königsfelderstrasse 1 5210 Windisch
Investigated Intervention:	Intensive Case Management (ICM)
Protocol ID	n.a. (yet)
Version and Date:	Version 1.01 (dated 14/07/2026)

CONFIDENTIALITY STATEMENT
The information contained in this document is confidential and the property of the sponsor. The information may not be passed on, reproduced, published, or disclosed, in whole or in part, to any third party other than the relevant ethics committees and regulatory authorities without the prior written consent of the sponsor, except to the extent necessary to obtain informed consent from the participants in the study.

PROTOCOL SIGNATURE FORM

Study Title	Intensive Case Management for Patients with Substance Use Disorders and Complex Psychosocial Needs: A Randomized Controlled Trial
Study ID	ICM Aargau

The Sponsor-Investigator and the Co-Investigators have approved the protocol version 1.01 (dated 14.07.26) and confirm hereby to conduct the study according to the protocol, current version of the World Medical Association Declaration of Helsinki, and ICH-GCP guidelines as well as the local legally applicable requirements.

Sponsor-Investigator:

Name: PD Dr. med Eva-Maria Pichler

Date: 14.07.2026 Signature: _____

Co-Investigator and Study Coordinator:

Name: Johannes Senesi

Date: 14.07.2026 Signature: _____

TABLE OF CONTENTS

TABLE OF CONTENTS 2
GLOSSARY OF ABBREVIATIONS 3
1 STUDY SYNOPSIS 4
2 BACKGROUND AND RATIONALE 6
3 STUDY OBJECTIVES AND DESIGN 10
3.1 Hypothesis and primary objective 10
3.2 Primary and secondary endpoints 11
3.3 Study design 14
3.4. Study intervention 15
3.5. Patient and public involvement 16
4 STUDY POPULATION AND STUDY PROCEDURES 16
4.1 Inclusion and exclusion criteria, justification of study population 16
4.2 Recruitment, screening and informed consent procedure 17
4.3 Study procedures 19
4.4 Withdrawal and discontinuation 20
5 STATISTICS AND METHODOLOGY 20
5.1. Statistical analysis plan and sample size calculation 20
5.2. Handling of missing data and drop-outs 23
6 REGULATORY ASPECTS AND SAFETY 23
6.1 Local regulations / Declaration of Helsinki 23
6.2 (Serious) Adverse Events and notification of safety and protective measures 24
6.3 Periodic reporting of safety and general progress of the clinical trial. 25
6.4 Amendments 25
6.5 Notification and reporting upon completion, discontinuation or interruption and resumption of the study 25
6.6 Insurance 26
7 FURTHER ASPECTS 26
7.1 Overall ethical considerations 26
7.2 Risk-benefit assessment 27
8 QUALITY CONTROL AND DATA PROTECTION 27
8.1 Quality measures 27
8.2 Data recording and source data 28
8.3 Confidentiality and coding 28
8.4 Retention and destruction of study data 29
9 MONITORING AND REGISTRATION 29
10. FUNDING / PUBLICATION / DECLARATION OF INTEREST 29
11. REFERENCES 30
Appendix 1: Schedule of assessments 34

GLOSSARY OF ABBREVIATIONS

ACT	*Assertive Community Treatment*
AE	*Adverse Event*
ASSIST	*Alcohol, Smoking and Substance Involvement Screening Test*
AUD	*Alcohol Use Disorder*
BASEC	*Business Administration System for Ethical Committees*
BFS	*Bundesamt für Statistik, Federal Statistical Office of Switzerland*
BSCL	*Brief Symptom Checklist*
ClinO	*Ordinance on Clinical Trials in Human Research (in German: KlinV)*
CM	*Case Management*
CoC	*Continuity of Care*
CRF	*Case Report Form*
CSSRI	*Client Sociodemographic and Service Receipt Inventory*
CTCAE	*Common Terminology Criteria for Adverse Events*
DACTS	*Dartmouth Assertive Community Treatment Scale*
eCRF	*electronic Case Report Form*
EQ-5D-5L	*EuroQol Group 5-Dimensional, 5-Likert Scale Health Questionnaire*
FADP	*Federal Act on Data Protection (in German: DSG)*
FHNW	*School for Applied Sciences Northwestern Switzerland (Fachhochschule Nordwestschweiz)*
FOPH	*Federal Office of Public Health*
GCP	*Good Clinical Practice*
HRA	*Human Research Act (in German: HFG)*
ICER	*Incremental Cost-Effectiveness Ratio*
ICF	*Informed Consent Form*
ICH	*International Conference on Harmonization*
ICM	*Intensive Case Management*
IRR	*Incidence Rate Ratio*
NICE	*National Institute for Health and Care Excellence (UK)*
NOIA	*Number of Inpatient Admissions*
NOID	*Number of inpatient days*
PDAG	*Psychiatrische Dienste Aargau (Psychiatric services of the canton of Aargau)*
PSQ-8	*Patient Satisfaction Questionnaire*
QALYs	*Quality-adjusted Life Years*
RICID	*Reduction in cumulative inpatient days*
SAE	*Serious Adverse Event*
SFQ	*Social Functioning Questionnaire*
SUD	*Substance use disorder*
TAU	*Treatment as usual*
WHOQoL-BREF	*World Health Organisation Quality of Life Brief Questionnaire*
ZAE	*Zentrum für Abhängigkeitserkrankungen (Center for Addiction Disorders)*
ZUF-8	*Fragebogen zur Messung der Patientenzufriedenheit, see PSQ-8*

1 STUDY SYNOPSIS

Sponsor	Eva-Maria Pichler, Chefärztin, Psychiatrische Dienste Aargau AG (PDAG), Postfach 432, Windisch
Study Title	Intensive Case Management for Patients with Substance Use Disorders and Complex Psychosocial Needs: A Randomized Controlled Trial
Short Title / Study ID	ICM Aargau
Protocol Version and Date	Version 1.01 (dated 14/07/2026)
Study Registration	BASEC 2026-01365
Study Category and Rationale	A, Research with minimal Risks and burdens for participants, since both treatments in this study, Intensive Case Management (ICM) and Treatment as Usual (TAU), are non-invasive, not new and non-experimental interventions and are standard clinical practice. The standardized questionnaires and psychometric tests are minimally invasive and do not represent significant risks or burdens for the participants. Furthermore, all data is encrypted and processed in accordance with applicable data protection guidelines. Therefore, the study is classified as research with minimal risks and burdens.
Background and Rationale	In the light of treatment gaps, ICM could address substance use disorders (SUD) with additional complex psychosocial problems. These patients repeatedly make use of (partly) inpatient treatments or other forms of hospitalizations, since a substantial proportion of patients with SUDs tend to have a chronic and relapsing clinical picture (Hesse et al., 2007; Blodgett et al., 2014; McLellan 2002). In Switzerland, 10.3 hospital admissions per 1000 inhabitants in 2023 had a main or secondary diagnosis of SUD, with alcohol use disorder (AUD) being the most frequent, and approximately 22% of all mental and behavioral disorder admissions are linked to substance use, with SUDs contributing about 25% of psychiatric first admissions (Bundesamt für Statistik [BFS], 2024). In 2022, about 40 000 individuals in Switzerland entered treatment for SUDs, of whom roughly 36% initiated inpatient treatment (BFS, 2023). This illustrates the substantial clinical burden and demand for services relevant to this study. Case Management, especially for people with multiple and complex needs, is an intervention designed to enhance coordination and continuity of support and care (Vanderplasschen et al. 2019). Also, for people with high levels of disability due to mental illness, ICM is widely claimed to be an evidence-based and cost-effective program (King, 2006). Furthermore, key ICM components, linkage and retention, seem to show the largest effect sizes (SMD = 0.33, 95% CI 0.18–0.48) in ICM. Linkage and retention are necessary prerequisites that keep patients with SUDs in contact with health services (Vanderplasschen et al., 2019). Although evidence across all outcome measures, according to the same author, is significant and positive, but small (SMD = 0.18, 95% CI [0.07–0.28]). There is mixed evidence in outcomes such as health outcomes (SMD = −0.16, 95%CI [−0.40, 0.08]), social functioning (SMD = 0.14, 95% CI [−0.01, 0.28]) or reduced substance use (SMD = 0.10, 95% CI [−0.02, 0.21]). Moreover, ICM and closely related models (i.e., Assertive Community Treatment, ACT) show a Reduction in Cumulative Inpatient Days (RICID) and a reduction in inpatient admissions (Dietrich et al., 2017; Burns et al., 2007). This is a common outcome in ICM literature and is also a measure for reductions in healthcare costs, since inpatient treatments are bound to high costs. In this study, there are mainly four groups of patients with SUDs that, despite previous or present linkages to health services, do need further or a different kind of treatment. Those patients are: - People with low treatment satisfaction and high usage of health and social services: These patients, despite their previous treatments and social connections, do not improve sufficiently and continue to utilize healthcare services. - people that already are in complex helping systems and make use of a high number of treatments but show a high need for coordination to be effective - patients with dual diagnosis, with SUD being one of those in combination with, e.g., schizophrenia, personality disorders and anxiety disorders and would need intense and continuous care. - people that, due to their clinical picture or other difficulties in life, do not have access to existing treatments (anymore) and fall through the social network. It includes people without permanent addresses, people with precarious housing conditions or socially isolated people, independent of their employment status. Sex and gender will be treated as potential covariates and will be considered in the analysis.

Risk / Benefit Assessment	The potential benefits likely outperform the potential risks of the aforementioned population and intervention, since ICM with its outreach characteristics evidently keeps patients connected to health services when inpatient settings may fail.
Objective(s)	This study aims to assess the effectiveness of ICM compared to TAU. Economically, this study could contribute to more cost-effective treatments, since relatively expensive inpatient care could be relieved of patients not benefiting from inpatient care, and those patients would receive a more adequate and effective treatment. Our first goal is to evaluate the effectiveness of ICM as a treatment for people with SUDs in the canton of Aargau compared to TAU. To assess the effectiveness, the outcome measured will be the RICID and the NOIA. Furthermore, the increase in Quality of Life and Social Integration with appropriate Questionnaires (mentioned below) of Patients in ICM is compared to Patients in TAU. The second goal of this study is to evaluate the cost-effectiveness of ICM for the aforementioned patients compared to TAU.
Endpoint(s)	**The primary endpoint** is the RICID in the ICM group compared to TAU after the 6-month period following randomization. NOIA, Linkage, Retention, and Continuity of Care (CoC) indices will be assessed with a combination of routine patient data and the Client Sociodemographic and Service Receipt Inventory (CSSRI) to fortify the RICID results and are not confirmatory endpoints on their own. **The second endpoint** is the comparison of the mean of ICM and TAU in social integration (social functioning questionnaire, SFQ) and in quality of life (World Health Organization Quality Of Life - Brief, WHOQOL-BREF). **Regarding the third endpoint**, the Incremental Cost-Effectiveness Ratio (ICER) will be used and is calculated by the difference in treatment effects (EQ-5D-5L) divided by the difference in treatment cost (assessed by the CSSRI). Additionally, the Alcohol, Smoking and Substance Involvement Screening Test (ASSIST) and Brief Symptoms Checklist (BSCL) scores will also be assessed to exploratively compare scores between groups and over time. Furthermore, the BSCL scores are treated as potential covariates for the first and second endpoint. The German Version of the Patient Satisfaction Questionnaire-8 (PSQ-8, ZUF-8 in German) will be assessed at the end of treatment. For descriptive analyses only, adherence to ICM protocol will be assessed with a modified version of Dartmouth Assertive Community Treatment Scale (DACTS), without ACT-specific items and components.
Study Design	Two arm, randomized controlled trial in a waiting list design (6 months), ICM vs. TAU. Patients in TAU will receive ICM after 6 Months and serve as a control group during that timeframe, where the experimental group will receive ICM immediately. For analyzing effects from when TAU received ICM onwards, LMMs will be used for dose-dependent within-subject comparison of ICM. For each patient, the study will last until graduation of ICM or a maximum of 24 months.
Inclusion- / Exclusion Criteria	Inclusion criteria - Age over 18 - A diagnosed SUD (ICD-10: F1x) - patients with four or more past inpatient treatments two years before the current admission - voluntary participation by written informed consent - residence (or a place with reliable access for the ICM team for treatment) in the Canton of Aargau Exclusion criteria: - acute risk to self or others - heavy cognitive impairment - insufficient German fluency Sex and gender will be treated as potential covariates and will be considered in the analysis.
Number of Participants with Rationale	With a pooled reduction of inpatient days per subject and month of -0.44 (Burns et al., 2007) and a Power of 0.8, the sample size needed to detect the effect before dropout (20%) is 180 in total. Therefore, we aim to recruit 180 Participants with an allocation ratio of 1:1 between study arms.
Study Intervention	ICM
Control Intervention	Inpatient TAU in a waiting list design, that receives ICM after 6 months.
Study procedures	Recruiting takes place at the PDAG in the Center for Substance Use Treatment (ZAE), where patients will be screened for eligibility for the study. If patients are eligible and voluntarily agree in participating in the study, staff will meet the patient in person to clarify

	study procedures, and the informed consent form will be handed to them. After signing the informed consent form, patients will be randomized between the two study arms (ICM or TAU). In the ICM group, questionnaires (see endpoints) will be handed to participants at the above-mentioned timepoints. TAU will enter a 6 month long waiting list. For every patient, 6 months after entering the study, patients in TAU will be transferred to regular ICM, identical in treatment as the experimental group, only 6 months later. Assessment timepoints of questionnaires (ASSIST, BSCL, CSSRI, SFQ, WHOQOL-BREF, EQ-5D-5L, ZUF-8 at t4 only): - t0, baseline, right before the start of ICM, - t1, 6 months, - t2, 12 months, - t3, 18 months, - t4, 24 months after the start of ICM
Study Duration and Schedule	**RCT**: Planned 07/2026 of First-Participant-In, planned 07/2029 of Last-Participant-Out
Investigator(s)	Johannes Senesi, MSc Psychologe und Studienkoordinator Psychiatrische Dienste Aargau AG Klinik für Psychiatrie und Psychotherapie ZAE Königsfelderstrasse 1 5210 Windisch
Study Center(s)	Psychiatrische Dienste Aargau AG Klinik für Psychiatrie und Psychotherapie ZAE Königsfelderstrasse 1 5210 Windisch
Statistical Considerations:	The study uses descriptive statistics to characterize the study population. Differences between the experimental and control groups are analyzed using appropriate statistical tests (e.g., t-test, chi-square test, multiple regression analyses). Mixed linear Models are used to assess outcome changes over time and between groups. For the analysis of the primary endpoint (RICID), a negative binomial regression (GLM with log link, see Section 5.1) will be used, likewise for NOIA. All analyses are performed according to the intention-to-treat principle. For missing data, multiple imputation will be used and controlled with sensitivity analyses. A significance level of $p < 0.05$ is set for all tests. Effect sizes are calculated to assess the clinical relevance of the results. Sex and gender will be treated as potential covariates and will be considered in the analysis.
Data privacy	All data will be encrypted and used and stored exclusively within the scope of this study.
Ethical consideration	The study does not use experimental interventions or placebo controls. All collected data are encrypted, and participation is voluntary. Participants are fully informed about the purpose, risks, and benefits of the study and have the right to withdraw at any time without negative consequences.
GCP Statement	This study will be conducted in compliance with the protocol, the current version of the Declaration of Helsinki, the ICH-GCP, the HRA as well as other locally relevant legal and regulatory requirements.

2 BACKGROUND AND RATIONALE

Introduction

In Switzerland, 10.3 hospital admissions per 1000 inhabitants in 2023 had a main or secondary diagnosis of a substance-related disorder, with alcohol use disorder being the most frequent, and approximately 22% of all mental and behavioral disorder admissions are linked to substance use, with substance use disorders (SUDs) contributing about 25% of psychiatric first admissions (Bundesamt für Statistik [BFS], 2024). In 2022, about 40 000 individuals in Switzerland entered treatment for SUD, of whom roughly 36% initiated inpatient treatment (Bundesamt für Statistik [BFS], 2023). Furthermore, patients suffering from SUDs in Switzerland often show additional psychological and social problems (Maffli & Astudillo, 2018; Lay et al., 2006).

Substance use disorders (SUDs) are complex and chronic conditions characterized by relapsing courses and substantial clinical heterogeneity (Blodgett et al., 2014; Hesse et al., 2007; McLellan 2002). Treatment is further complicated by fluctuating motivation, ambivalence toward change, and difficulties in establishing and maintaining a stable therapeutic alliance (Clarkin & Levy, 2004; Meier et al., 2005; Opsal et al., 2019; Sharf, 2008). In addition, individuals with SUDs frequently experience psychiatric and somatic comorbidities, as well as public stigma and self-stigmatization (Livingston et al., 2011). Beyond individual and clinical factors, structural and systemic barriers, such as limited access to harm reduction services, e.g., supervised consumption facilities, drug checking, and stable housing interventions, further constrain effective care (Austin et al., 2021; Farhoudian et al., 2022; Levengood et al., 2021).

As a result of these interacting challenges, treatment trajectories are often fragmented, with high rates of premature discharge and discontinuity of care in inpatient settings (Simon et al., 2020; Stanojlović & Davidson, 2020; Rowell-Cunsolo et al., 2020). These patterns undermine sustained therapeutic engagement and contribute to a mismatch between patient needs and available services.

A subgroup of such patients repeatedly make use of (partly) inpatient treatments or other forms of hospitalizations, with early discharge (also initiated by patients), leading to the so-called "Revolving Door Phenomenon" (di Lorenzo et al., 2016, Menzies et al., 2023). One study reported that self-discharged AUD patients were shown to be three times as likely to relapse (Geniş et al., 2020). Short treatment duration, comorbidities, missing aftercare and missing harm reduction services are additional potential risk factors for re-hospitalization. (Levengood et al., 2021; Ssentongo et al., 2025). Therefore, treatment response in inpatient treatments with early discharge could indicate suboptimal treatment satisfaction. Despite that, frequent readmissions indicate that inpatient treatment is among the most viable treatment options available for this subgroup, possibly due to it being low threshold among the available interventions.

Recommendations in SUDs treatments encompass long-term stabilization, outpatient treatment or aftercare, and medically supported care if needed, at least for opioids and high-risk alcohol consumption (NICE, 2007; NICE, 2011). This contrasts with the treatment characteristics of the aforementioned population. Consequently, a treatment gap potentially persists among individuals with complex SUDs that cannot necessarily be solved with inpatient care (Stanojlović & Davidson, 2020).

Intensive Case Management

In the light of treatment gaps, Intensive Case Management (ICM) could address SUDs with additional complex psychosocial problems. ICM is claimed to be cost-effective and evidence-based intervention for mental illnesses with high levels of disability following the mental illness (King, 2006). Case Management (CM) Models such as ICM have successfully been applied for severely affected SUD patients, including dual diagnoses (Vanderplasschen et al. 2007). For

people with multiple and complex needs especially, CM interventions are designed enhance coordination and continuity of care and support (Vanderplasschen et al. 2019). Furthermore, the study shows that key ICM components, linkage and retention, are measures with larger effect sizes (SMD = 0.33, 95% CI 0.18–0.48) in ICM when compared to treatment as usual (TAU), although the effect itself is of medium strength. Linkage and retention are necessary prerequisites that keep patients with SUDs in contact with health services. Retention to substance abuse treatment specifically shows the largest effects in ICM (SMD = 0.47, 95% CI [0.13, 0.81]). Considering that patients dropping out of inpatient treatment have little to no treatment options left, linkage and retention are necessary prerequisites that keep patients with SUDs in contact with health services. Evidence across all outcome measures, according to the same study, is significant and positive, but small (SMD = 0.18, 95% CI [0.07–0.28]). There is mixed evidence in outcomes such as health (SMD = −0.16, 95%CI [−0.40, 0.08]), social functioning (SMD = 0.14, 95% CI [−0.01, 0.28]) or reduced substance use (SMD = 0.10, 95% CI [−0.02, 0.21]). Other outcomes, like symptoms, substance use and quality of life have also been reported, albeit with moderate or no improvements (Mueser, 1998; Bond et al., 2001; Vanderplasschen et al., 2019).

Effectiveness of ICM and covarying measures

Regarding the overall effectiveness and mixed results of ICM in the literature, there are suspected moderating effects possibly masking the real effect of CM interventions, such as the specific CM model or characteristics of the treated population (Vanderplasschen et al., 2019). It is important to mention that there are descriptions on how CM models differ conceptually from each other (Mueser et al., 1998; Ziguras et al., 2002; Lukersmith et al., 2016), only that those model descriptions also deviate from each other. Amongst others, Bond & Drake (2015) tried explaining treatment differences due to the different "ingredients" regarding the ACT model, namely, which critical components of the model bear more weight in outcome, for example, a small case load per case worker. Contemporary evidence (Lukersmith et al., 2016; Vanderplasschen et al., 2019) further notes that while models such as ACT and ICM are conceptually differentiated, empirical separation of outcomes across models remains inconsistent, largely due to overlapping components, variability in fidelity to the CM model, and contextual adaptation in routine practice. For example, ICM and ACT are both designated as intensive comprehensive care (Mueser et al., 1998), while in the meta-analysis of Vanderplasschen et al. (2019), the authors consider ACT to be a conceptual form of ICM, and no difference between CM models was found regarding outcome effect strength ($Q = 2.57$, $df = 4$, $p = 0.63$). Rapp et al. (2014) confirm this with $F(3, 15.7) = 0.23$, $p = 0.88$, but also when only considering personal functioning outcomes ($F[3, 12.4] = 0.73$, $p = 0.57$).

Another suspected moderator is the adherence to the CM-specific protocol, also known as fidelity (Clarke et al., 2000). Despite ICM being widely implemented in the USA, there is no (single) standard conceptualization or definition for ICM, even consensus about its operationalization is

moderate (Schaedle & Epstein, 2000). According to that study and our knowledge, there is neither a valid program theory nor reliable fidelity measure for ICM. In contrast, Assertive Community Treatment (ACT) has proliferated as the most standardized (Allness & Knoedler, 2003; Salyers et al., 2003). Even a validated fidelity measure for ACT has been developed, called DACTS (Teague et al., 1998). Due to the lack of reliable fidelity measures for ICM and the high relation to ACT, a modified version of the DACTS without ACT-specific elements (i.e., items) will be used in this study for exclusively descriptive measuring of the adherence to ICM protocol. Specifics of the DACTS used in this study are described in section 3.3.

As mentioned above, reduced substance use as an outcome has also yielded mixed results. However, one meta-analysis (Rapp et al., 2014) found a small, but positive effect of substance use as a moderator on outcomes over studies ($\hat{\delta}$ = 0.08, p = 0.01), but only when analyzing data regarding personal functioning separately from treatment tasks (i.e., linkage and retention). Another meta-analysis (Vanderplasschen et al., 2019) found that, while different kinds of substance use did not show moderating effects (Q = 1.29, df = 2, p = 0.52), it did find a main effect of substances used by SUD patients on outcomes (SMD = 0.33 for injecting substances vs. 0.18 for polysubstance users, and 0.03 for alcohol). Therefore, measuring substance use is sensible, not necessarily to show a reduction, but to treat it as a possible moderator of outcomes.

As mentioned earlier, personal functioning outcomes like quality of life and social functioning has been reported (SMD = 0.14, 95% CI [−0.01, 0.28], Vanderplasschen et al., 2019), as well as social inclusion as a moderator on personal functioning outcome ($\hat{\delta}$ = 0.09, p = 0.02, Rapp et al., 2014). For this reason, social functioning will also be assessed in this study as a potential moderator. In contrast, quality of life measures have been assessed rather rarely (Vanderplasschen et al., 2019), an improvement in quality of life is shown in some studies (Drake et al., 1998; Karow et al., 2010), also for ACT (Bond et al., 2001). Nonetheless, not knowing if it will increase as a result of ICM or having explanative power in outcomes (e.g., as a moderator), quality of life will be assessed in this study.

Main effect of ICM

Most importantly, ICM and closely related models show a Reduction in Cumulative Inpatient Days (RICID) and a reduction in inpatient admissions (Dietrich et al., 2017; Burns et al., 2007), reflecting the capacity of such interventions to prevent recurrent hospitalizations rather than to directly modify symptoms. It is important to note that, within the CM literature, the prevention of recurrent or inadequate inpatient hospitalizations among high-need individuals with complex SUDs constitutes a central outcome of interest and reflects the core mechanism by which case management models are intended to operate (Vanderplasschen et al., 2019; Burns et al., 2007). Furthermore, it is also a measure for assessing healthcare costs, which tend to be higher in inpatient treatments (Bachmann et al., 2022; Gehrig et al., 2012; Peterson et al., 2021; Stocker et al., 2018).

At first glance, RICID or reduced number of inpatient admissions (NOIA) may appear agnostic to patient well-being or adequacy of care, seemingly questionable for an outcome measure. However, because inpatient treatment is neither restricted nor discouraged within the study context, fewer admissions among patients receiving ICM indicate that clinical crises requiring hospitalization occur less frequently despite continued access to inpatient care. In this setting, reduced inpatient utilization therefore reflects improved stability and more effective management of care needs in the community rather than unmet treatment need or care avoidance. To ensure that RICID and reduced NOIA do not reflect service disengagement or displacement of care, indicators of care processes, namely linkage, retention and Continuity of Care (CoC) are assessed to support the interpretation of RICID and reduced NOIA of this study. The Bice-Boxerman index has been chosen to quantify CoC in this study. This index is feasible regarding assessment of longitudinal continuity of care and is shown to correlate highly to other indexes, like the Usual provider of Care (UPC) score (r = 0.99, Hull et al., 2022).

ICM orients itself on a structured and standardized model and uses specific working tools to assess complex tasks in health- and social services. The whole process follows clearly defined phases to ensure goal-oriented and effective care and is described in section 3.4

In sum, there is a treatment gap for a subset of patients with SUDs in inpatient care. ICM could close this treatment gap by reducing NOIA and NOID, thereby moderately increasing Quality of Life and social integration, and possibly lowering symptom severity and substance use. Sex and gender will be considered as potential covariates in all analyses.

3 STUDY OBJECTIVES AND DESIGN

3.1 Hypothesis and primary objective

The time window for the primary analyses (including the hypotheses described below) will be the first 6 months during the RCT phase for comparison of ICM vs. waiting list. The confirmatory analysis consists of the first hypothesis (H1a) only during the RCT phase. H2 and H3 are considered secondary, exploratory hypotheses during the RCT phase. All longitudinal analyses over the whole study duration (i.e., after the crossover), are explorative only. The primary objective of this study is to assess whether ICM can be implemented for patients with SUDs that do not benefit enough from inpatient care. Regarding this assessment, multiple aspects are considered. Namely, (1) if usage of ICM translates into less usage of emergency admissions and inpatient treatment, (2) if ICM strengthens patients' social network and increases quality of life, and (3) if ICM is more cost effective than the treatment as usual for the target population.

The following research questions have been proposed:

- Does ICM reduce usage of emergency and inpatient services?
- Does ICM increase social integration and life quality?

- Is ICM more cost effective than TAU?

From these questions, the following hypotheses have been formulated to detect effects during the 6-month RCT time window:

- H1a: Inpatient admissions are less in duration in ICM compared to TAU.
- H1b: The number of inpatient admissions is less in ICM compared to TAU.
- H2: Patients in ICM show a higher average WHOQOL-BREF score than patients in TAU.
- H3: Patients in ICM show a lower average SFQ score than patients in TAU.

3.2 Primary and secondary endpoints

For assessing the primary endpoint, a combination of the CSSRI and routine data will be used. When available, routine data will be preferred over questionnaire data due to higher objectivity (e.g., past inpatient treatments). Here, the CSSRI serves as a backup. To fortify the result of RICID, the CoC-Index, Retention and Linkage will be assessed. These also represent control variables and will be calculated from:

Measure	**Variable**	**Purpose**	**Source**
Intake completed (yes/no, date)	Linking	Entry into care	Routine
Needs assessment completed (yes/no, date)	Linking	Structured care planning	Routine
Number of distinct service domains addressed	Linking	Breadth of care linkage	Routine + CSSRI
Number of successful referrals	Linking	Effective service connection	CSSRI only
Referral-to-contact latency (days)	Linking	Speed of care access	Routine + CSSRI
Inter-agency contacts per case	Linking / CoC	Coordination intensity / Cross system integration	Routine + CSSRI
Time to dropout (survival analysis)	Retention	Durability of engagement	Routine
Still engaged at X months (binary)	Retention	Sustained participation	Routine
Gap-based retention (>30 days no contact)	Retention	Continuous care engagement	Routine
Case reviews conducted (count)	CoC	Team-based coordination	Routine
Re-assessments performed (yes/no, count)	CoC	Ongoing clinical monitoring	Routine
CoC Index (Bice–Boxerman)	CoC	Formal continuity metric	CSSRI + Routine

Service use intensity (outpatient, social, legal, housing etc.)	ICER	Cost quantification	CSSRI only
Inpatient costs	ICER	Major cost driver	Routine
Case management time	ICER	Intervention cost	Routine
Travel, legal, welfare services	ICER	Societal costs	CSSRI only

Those measures can be calculated from raw data regarding: date of first contact between CM and client, date of first referral to each service provider, and provider ID, including type and location of services. These additional measures are taken because RICID and reduced NOIA alone do not reflect the well-being of patients directly; in other words: Just because a patient is not in inpatient treatment, doesn't mean that treatment is not necessary. Only if we use Linkage (Patients are concurrently in ICM) and CoC (patients engage continuously in treatment) as control measures and still allow the option of inpatient admission during ICM, is RICID a viable outcome measure. Furthermore, age, gender, baseline inpatient utilization and prior service use intensity, as well as ASSIST and BSCL scores are treated as potential covariates for the primary endpoint. Assessment timepoints (t1–t5) have a pre-specified tolerance window (e.g., ±8 weeks) to accommodate this hard-to-reach population; assessments that fall outside the window or are missed are handled under the intention-to-treat principle with multiple imputation (Section 5.2) and do not constitute study withdrawal. The primary endpoint (inpatient days and admissions) is derived from routine data over a fixed 6-month window defined per arm – for the ICM group the first 6 months from ICM start, and for the waiting-list group the 6-month waiting period from randomization to ICM start – and is therefore independent of assessment attendance.
The Bice-Boxmerman CoC-Index will be used in this study, where p is the total number of providers, n is the total number of attended visits, n_i is the number of attended visits to provider i.

$$CoC = \frac{(\sum_{i=1}^{p} n_i^2) - n}{n(n-1)}$$

Regarding the secondary endpoint, Quality of life will be assessed by the WHOQoL-BREF, as well as social functioning, assessed by the SFQ. It is important to note that the SFQ was not currently available in German, therefore, a translation from English into German has been carried out and reviewed by two psychologists, and two native English-speaking co-workers were presented the translated version into German to translate it backwards into English. For this, the process laid out in Beaton et al. (2000) was used to document and implement a forwards-backwards translation, namely Stages I to III. Stages IV to VI (involving an expert committee,

testing a prefinal version, and Submission of Documentation to the Developers) were left out of the procedure as it was not in the scope of the study.
Concerning the third objective, the ICER will be determined to assess cost-effectiveness. The slope of the ICER and the position of the difference in costs and outcome of ICM in relation to TAU determines the overall cost-effectiveness. Uncertainty around ICER estimates will be assessed using non-parametric bootstrapping, and results will be presented using cost-effectiveness planes and acceptability curves.

$$ICER = \frac{Costs_{ICM} - Costs_{TAU}}{Outcome_{ICM} - Outcome_{TAU}} = \frac{\Delta Costs}{\Delta Outcome}$$

Costs will be the product of health service utilization and unit costs. As unit costs, TARPSY 5.0 will be used for inpatient services and TARDOC for outpatient tariffs. Additionally, usage of linked health services to patients will also be assessed, since linking is such a crucial part of ICM, despite the likely scenario that linked services will be outweighed by inpatient and emergency service costs. Linked services will be categorized by type, e.g., substance use counseling.
Health-related quality of life will be assessed using the EQ-5D-5L. Utility values will be derived using the German value set (Ludwig et al., 2018) and used to calculate QALYs over the randomized-control period (6 Months) using the area-under-the-curve method. Costs will include health service utilizations and ICM costs (ICM staff wages, utilizations of categorized linked services). Although "classic" health service utilization is likely to outweigh linked services in ICM, measuring utilization of linked services is necessary because ICM acts on a system-level. Categories will be comprised of: Addiction counseling services, guardianships, social (welfare) services, opioid agonist treatment programs, housing support services, debt and financial counseling, employment and vocational services, legal and probation services, emergency housing / homeless services, and "other" services. These categories may be subject to change during treatment and will be adapted to better reflect utilization of linked services in case of discrepancies between pre-stated categories and actual utilization. Health service utilization will be collected using the CSSRI and routine data from a healthcare system perspective (psychiatric acute inpatient treatments, inpatient psychotherapy treatment, rehabilitation treatment, psychiatric long-term inpatient treatments, emergency and crisis intervention stays, hospital stays, and other inpatient treatments which do not fall into one of the categories above, as well as outpatient treatments in clinics and private practitioners). The range of willingness-to-pay thresholds (λ) will be from CHF 20'000.- to 100'000.- per QALY, and cost-efficiency acceptability curves will be analyzed with a low (CHF 20'000.-), medium (CHF 50'000.-) and high λ (CHF 100'000.-). The time horizon will be 6 months to fit the RCT time window. The ICER will be calculated as the difference in mean costs between groups divided by the difference in mean

QALYs. Unlike the other measures, the EQ-5D-5L will only be used to calculate ICER and not as an outcome in any way.
Income brackets of the CSSRI have been replaced with asking for the monthly income to avoid floor effects, since a large part of the sample might end up in the lowest bracket (CHF 0 to 2500.-) and have little descriptive value and poor discriminatory ability.
Concerning the explorative, descriptive measure of adherence to CM protocol, the DACTS will be used to see how well a traditionally ACT-oriented fidelity instrument meaningfully characterizes ICM services. In other words, the mapping of DACTS onto ICM as a fidelity measure will rate DACTS items if they are scorable (e.g. floor and ceiling effects), relevant for ICM, including a narrative description of problematic items. Although the DACTS is not to be used as a fidelity measure for ICM, fidelity to treatment protocol measured this way can yield insights into the relation between fidelity to treatment and outcomes of ICM.

3.3 Study design

The study design will be a monocentric, cantonal, open, two-arm RCT (Treatment vs. TAU) in a simple waiting list design. The time delay for enrolment into ICM of the TAU group respective to the experimental group will be 6 months. Due to the nature of the intervention, participants and treating personnel cannot be blinded. Personnel evaluating outcomes will be blinded to treatment allocation whenever feasible. However, unblinding may occur during participant interactions. This sample will not be stratified because we have insufficient information about relevant factors needed for stratification (e.g., sex and gender ratios, NOIA, NOID).

Randomization

Randomization of study arm allocation was performed using an online tool on the website of the U.S. National Cancer Institute (https://ctrandomization.cancer.gov/tool/). The output was an Excel spreadsheet containing all the data. The following inputs were selected:
- Participant Count: 200, assign the final few participants randomly (Default).
- Number of Trial Arms: 2, Arm 1 Allocation Ratio: 1, Arm 2 Allocation Ratio: 1.
- Stratify Trial: no, randomization method: asymptotic maximal, maximum tolerated imbalance: 5.

The generated Excel spreadsheet contains one sheet. The rows represent the participants, while the columns represent variables (Group, Subject No., Assignment, Assigned Arm Index, Arm 1 Posterior Totals, Arm 2 Posterior Totals). The "Assignment" column contains the participant's assigned study arm. Another online tool was used for randomizing the participant IDs (https://www.random.org/sequences/) and the following inputs were used: Smallest Value: 1, Largest Value: 200, Format in 1 column(s). The output containing the randomized participant IDs was then inserted into the aforementioned Excel spreadsheet. Furthermore, the columns containing treatment information (Assignment, Assigned Arm Index, Arm 2 Posterior Totals, Arm 2 Posterior Totals) in the Excel spreadsheet were colored black. The purpose of this is that the

cells are only destained (thus revealing the assignment of participants to the randomized study arms) when a new patient joins the study. This Excel spreadsheet is password-protected and stored in a secure, password-protected folder (with a different password). This folder was then stored on secure, internal servers of HINT AG, which manages the IT infrastructure of PDAG.
With exception of the DACTS, all questionnaires used in this study are validated. There will be outcome measurements of the questionnaires ASSIST, BSCL, CSSRI, SFQ, WHOQOL-BREF and EQ-5D-5L at the following timepoints (ZUF-8 is measured at t4 only):

- t0, baseline, right before the start of ICM,
- t1, 6 months,
- t2, 12 months,
- t3, 18 months,
- t4, 24 months after the start of ICM

Since the recruitment will take place at the center for substance use treatment (ZAE) at the psychiatric hospital of Aargau (PDAG), only study participants will be recruited with a place of residence in the canton of Aargau. The place of residence or temporary location of patients must be accessible to the CM team.

3.4. Study intervention

The ICM intervention involves regular, proactive contacts between case managers and participants. Contacts may take place in outpatient settings, in the participant's living environment, or via telephone, depending on individual needs. The frequency and duration of contacts are not fixed but are adapted flexibly according to the participant's situation and phase of support. Case managers are responsible for coordination, needs assessment, care planning, and monitoring. The functionally separate addiction counselor provides addiction-specific counseling and supports treatment engagement. Both roles collaborate closely while maintaining distinct responsibilities. Participation in ICM does not require compliance with specific treatment goals, and no services are mandatory. Participants retain autonomy over treatment decisions at all times. ICM does not replace existing medical, psychiatric, or psychotherapeutic treatments, but aims to coordinate and facilitate access to appropriate services within the existing care system. The implementation of this ICM intervention is based on the seven following steps:

1. **Intake**: Initial assessment and evaluation of each client's individual situation, including a preliminary needs analysis.
2. **Case allocation**: Assignment of a case manager and an functionally separate addiction counsellor that addresses the specific needs of each case.
3. **Clearing**: Clarification of relevant issues, resources, and existing networks to fully understand the initial situation and available courses of action.
4. **(Re)Assessment**: Ongoing needs analysis, regular review and adjustment of measures

to reflect changes in the client's situation.

5. **Care planning/Linking**: Development and implementation of a tailored care plan, including referral to and connection with other support services and relevant institutions.
6. **Monitoring**: Continuous progress monitoring and regular evaluation of measures to ensure goal achievement and to make adjustments as needed.
7. **Conclusion / Evaluation:** Conclusion of the support with a final assessment of goal achievement and recommendations for future support or care.

A central mechanism of the above described ICM is the "cycling" between step 4, 5 and 6 when necessary or appropriate, e.g., new relevant issues coming up during ICM treatment. This iterative process ensures ongoing coordination and adaptation of care in response to changing needs. Additionally, two focus points are implemented to increase adherence and engagement:

Intensive crisis intervention: Offering immediate, flexible support in acute crises, preventing escalations early and strengthening the stability of patients.

Relationship continuity: Establishing an empathetic & constant presence, breaking down barriers, creating a trustful, stable relationship.

3.5. Patient and public involvement

Patients or members of the public (PPI-contributors) have not been involved in the design of the protocol and study-related procedures.

4 STUDY POPULATION AND STUDY PROCEDURES

4.1 Inclusion and exclusion criteria, justification of study population

Description of the target population

The target population of our project consists of individuals with severe SUDs who also suffer from complex psychosocial problems and frequently require multiple and recurring inpatient or partial inpatient treatment. Many of these individuals have a history of multiple hospitalizations or repeated failed placements. ICM offers integrated care by proactively supporting those affected, and if necessary and desired, their social network, after discharge from the hospital, providing needs-based and resource-oriented assistance. The project is particularly aimed at:

1. Individuals with limited treatment benefits and high utilization of health and social services: People who, despite previous treatment approaches and social support, do not experience sufficient improvement and must regularly utilize the healthcare system.

2. Individuals within a complex support system requiring significant coordination: Individuals who utilize a multitude of institutions and support services and signal feelings of being overwhelmed, thus necessitating extensive coordination of their care.

3. Hard-to-reach individuals: People who, due to their illness or difficult life circumstances, no

longer have access to existing support services and often fall through the cracks of the social safety net. This includes people without a fixed address, people in precarious housing situations, or socially isolated individuals, regardless of their employment status.

4. Individuals with a dual diagnosis: Individuals who, in addition to their SUD, suffer from a mental illness (e.g., schizophrenia, other psychotic disorders, depression, anxiety disorders, or personality disorders) and therefore require intensive and continuous support.

Characteristics of the target group:

• Social isolation: Lack of social networks and support systems.

• Health problems: In addition to SUDs, there are often other physical or mental health problems.

• Lack of ability or motivation to seek help: Due to their life circumstances or illness, those affected are often unable or unmotivated to access existing services.

Inclusion criteria for participation in the ICM

• 4 or more inpatient stays in the last 24 months: Due to the endpoint to be measured and the description of the target groups, a high utilization of inpatient facilities is a prerequisite.

• Diagnosed substance use disorder (ICD-10: F.1x): The intervention is generally aimed at patients with a substance use disorder, including dual diagnoses, one of which is a SUD.

• Over 18 years of age - The intervention is exclusively for adults.

• Residence or place of stay in the Canton of Aargau: Participants must be staying in the Canton of Aargau in an accessible location (such as their own apartment, emergency shelters, or with relatives) to ensure continuous support from the ICM.**Exclusion criteria:**

• Acute, unstable psychotic symptoms: Acute psychotic symptoms that prevent cooperation and participation in the ICM will lead to exclusion.

• Acute risk of harm to self or others: Participation is only possible if there is no immediate danger to others or acute risk of suicide, as specialized and close monitoring is necessary in these cases.

• Severe cognitive impairment: Severe cognitive impairment (e.g., dementia, severe organic brain damage) that prevents informed consent or cooperation in the ICM will lead to exclusion.

• Insufficient German language skills: German language skills must be sufficient for ICM treatment and completing the questionnaires**.**

No pilot data is available for estimating age distribution or gender ratio. This distribution and ratio will be documented and considered analytically.

4.2 Recruitment, screening and informed consent procedure

Place of Recruitment

The recruitment and informing of potential participants take place at the PDAG. After being deemed suitable for the study, they are randomly assigned to one of the two study groups.

Recruitment Method

Participants are identified during the triage process upon admission. Their capacity to consent is assessed by qualified personnel prior to the informed consent discussion. A diagnosed SUD does not preclude participation. However, individuals who are temporarily incapable of giving informed consent due to acute intoxication, severe withdrawal symptoms, or any other temporary condition that impairs their capacity, will only be invited to the informed consent discussion once they have regained their capacity to consent. Participant selection is based on predefined inclusion and exclusion criteria, ensuring that only individuals for whom ICM is indicated and feasible are included. No recruitment tools such as flyers or promotional materials are used in this process. The randomization mechanism for assigning participants to either the experimental or control group is described in section 3.3. The first participant will be enrolled in the study within the first two years after approval by the ethics committee. An extension request is mandatory if this period is exceeded; otherwise, the study is considered paused. The sponsor notifies the ethics committee of the first visit of the first study participant in accordance with art 62 lit. c ClinO, resp. art 38 ClinO. If the first participating person is not included in the trial within two years following the issuance of the authorization, the trial is considered interrupted (art. 23a ClinO). The clinical trial may not be commenced until an application for an extension of the time limit has been approved. The application for the extension is submitted to the CEC as a substantial amendment..

Informed consent

The process for obtaining informed consent begins as soon as a potential participant has been identified. The study information is given orally and in writing, with enough time available for participants to understand the information material and ask questions, as well as time to consider participation in the study. Consent is only given after detailed explanation and secure confirmation of understanding of the study goals, processes and rights. The participant will be informed that his or her medical records may be examined by authorized individuals other than their treating physician. It is explicitly stated that participation in the study is voluntary, and that participants are allowed to withdraw from the study at any time. Stopping the study prematurely has no influence on subsequent care and treatment. No study-specific examinations will take place before the written, informed consent form is signed by the patient. The informed consent is signed by the study doctor or the study coordinator/investigator at the same time as the patient. A dated copy of the fully signed consent form is then given to the patient. The signed informed consent will be retained as part of the study records. Consent is documented in the presence of a clinically trained employee, without any financial compensation being provided. Participation in the ICM takes place as part of the study; However, the participants are not persuaded to stay in the study. A missed or postponed survey - for example due to temporary unavailability - is expressly not considered a withdrawal from the study: the person concerned remains in the project, their place in the ICM is retained and the ICM treatment is continued if they can be reached again; Missing values are treated within the framework of the intention-to-treat principle (Section 5.2).

Discontinuation of the study is possible at any time, without giving reasons and without disadvantage for further treatment. If a person in the waiting list/control group withdraws from the study before the start of ICM (month 6), standard care will continue without restriction; In this case, the ICM cannot be provided within the scope of the study, but re-registration is possible if the indication continues. The usual standard treatment will be offered regardless of the study. Since ICM is currently not available as an established care offer outside of the study, the obligation to participate in the study will be explained transparently to the test subjects; It is expressly emphasized that the decision to participate has no influence on access to standard care and can be revoked at any time without giving reasons.

Screening

Following the patient's initial contact via PDAG, a screening process is conducted to confirm the diagnosis of mental illness according to ICD-10 criteria and to verify whether the study's inclusion and exclusion criteria are met. This screening includes an assessment of the patient's current mental health, treatment history, and other relevant information from their clinical documentation.

Monetary compensation

A cash payment of CHF 15.- per completed questionnaire per person is offered, totaling CHF 75.- per person across all measurement points. These amounts will be reimbursed directly to the participants by the case managers upon receipt of the completed questionnaires. Offering a cash payment option significantly increases the response rate, even among patients with severe SUDs, and has no impact on consumption patterns, increased substance use, or obsessive-compulsive disorder (Festinger et al., 2008; Kubica et al., 2026; Pieper et al., 2018). Participants will receive a receipt for each cash payment, which will be signed by both the case manager and the patient.

The investigator or the sponsor notifies the Ethics Committee of the first study participant, in accordance with art 62 lit. c ClinO, resp. art 38 ClinO. If the first participating person is not included in the trial within two years following the issuance of the authorization, the trial is considered interrupted (art. 23a ClinO). The clinical trial may not be commenced until an application for an extension of the time limit has been approved. The application for the extension is submitted to the CEC as a substantial amendment.

4.3 Study procedures

1) Identifying potential participants on the wards of the ZAE

2) Screening by a Case Manager (CM): if interested, referral to an introductory interview with the ICF

3) Introductory interview with participants: Immediately after signing the ICF form, participants are informed which study arm they are in.

a) Experimental group: Participants are referred back to the CM and complete the first questionnaire (t0). The intervention then begins.

b) Waiting list: Participants are enrolled in standard, recognized treatment (TAU) and complete the first questionnaire (t0). TAU includes regular inpatient and outpatient SUD treatment at the PDAG (Psychiatric Services Agencies) including standard aftercare, but without ICM-specific components (no dedicated case management, no proactive contact). After six months, the second questionnaire (t1) is completed, and the intervention begins.

4) Due to the intention-to-treat (ITT) approach, the study and data collection run for 24 months (30 Months in the waiting list group) per patient. Treatment by the ICM will be terminated regardless of the study duration, either due to a regular completion of treatment or due to early termination.

4.4 Withdrawal and discontinuation

Voluntary Participation

Participation in the study is voluntary, and participants may discontinue the intervention at any time without giving a reason.

Reasons for Discontinuation of the Intervention: There are various reasons that may lead to discontinuation of the intervention, both as part of a regular case closure and due to unforeseen events. However, discontinuation or interruption of the intervention should not be equated with study termination, as the study duration is fixed at 24 months (30 months in the waiting list group). Discontinuation or interruption of the intervention, as well as study termination, is possible at any time, without giving reasons and without negatively impacting further treatment. A missed or postponed data collection is not considered study termination; in this case, the ICM treatment is not terminated but resumed when the data collection becomes available again.

Discontinuation procedure - Documentation: All discontinuations are carefully documented, including the known reasons. Analyzing these reasons allows for conclusions to be drawn regarding potential improvements in indication and funding security.

Final Interview (if possible): In cases of voluntary withdrawal, a final interview will be offered to assess satisfaction with the care received so far and to gather valuable feedback.

Measures to Reduce Dropouts

- Regular Communication and Support: Close support and clear information about the study's progress are intended to promote patient satisfaction and understanding.

- Flexibility in Scheduling: Flexible scheduling of data collection appointments minimizes the risk of withdrawals due to scheduling conflicts or organizational obstacles. Additionally, the two key areas described in section 3.4 are intended to reduce the withdrawal rate**.**

5 STATISTICS AND METHODOLOGY

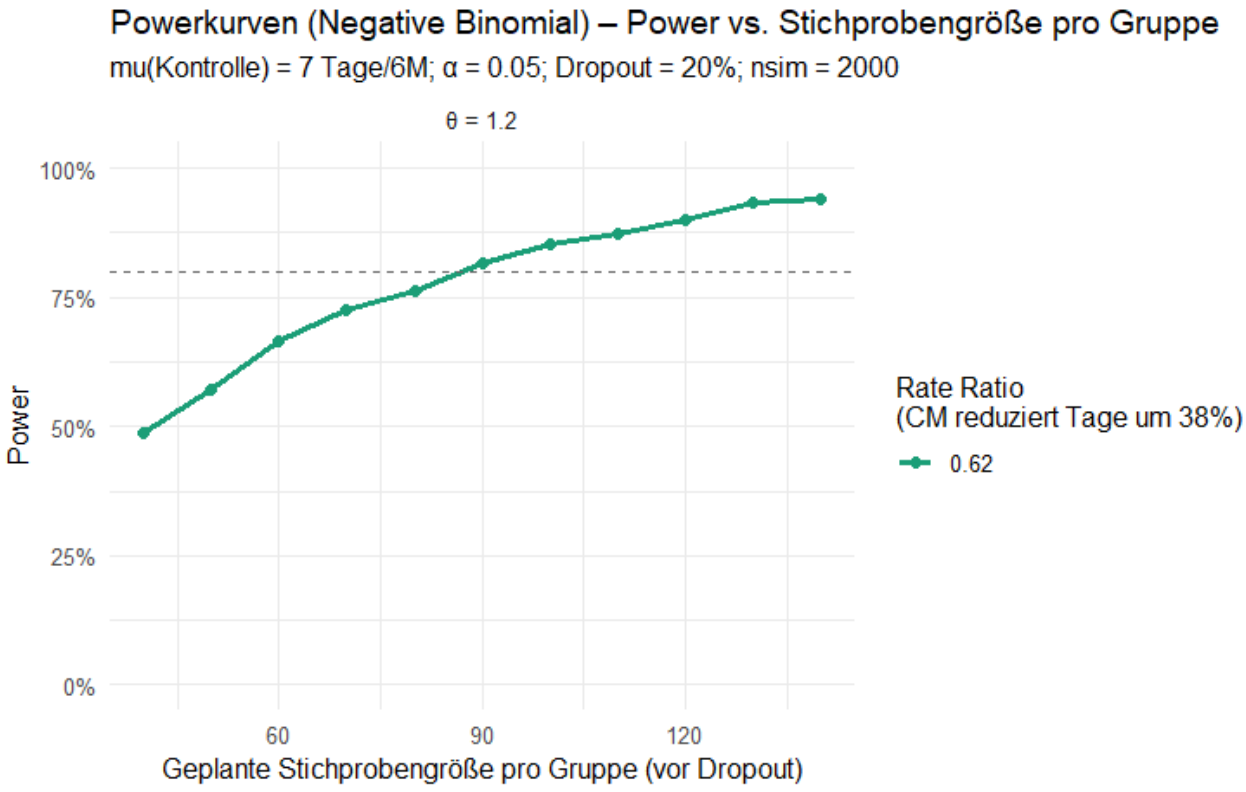
5.1. Statistical analysis plan and sample size calculation

Statistical Software

The analysis is carried out with R. On one hand, this application offers various tools to implement planned models and adjust for multiple testing, on the other hand, it allows for detailed tracking of programmed analyses (scripts) of how the statistics are carried out, and thus ensuring the traceability of analyses. A simulation-based power analysis was conducted using R Version 2025.05.1. The expected intervention effect was derived from Burns et al. (2007), who reported a reduction of 0.44 inpatient days per month (i.e., 2.64 days over 6 months) associated with Intensive Case Management.

$$\frac{Possible\ RICID_{6m}}{Baseline\ Inpatient\ Days_{6m}} = \frac{6 \times \frac{0.44\ days}{month}}{\frac{7\ days}{6\ months}} = \frac{2.64}{7} \approx 0.38$$

Assuming an average of 7 inpatient days over a 6-month period in the control group (based on internal routine data), this corresponds to an expected relative reduction of approximately 38% in cumulative inpatient days. Sample size estimation was performed using a negative-binomial model with a dispersion parameter (θ) of 1.2 and 2,000 simulation runs. Assuming a two-sided significance level of α = 0.05, a statistical power of 80%, and an anticipated dropout rate of 20%, a total sample size of 180 recruited participants (90 per study arm) was estimated to be sufficient to detect the expected effect on the primary endpoint. A graphical representation of statistical power vs. needed sample size is provided below.



For the first endpoint, a GLM with a negative binomial distribution (log link and expressed as incident rate ratios, IRR) will be used. The study group is the categorical predictor and is corrected by for baseline, while RICID represents the outcome.

- H1a: Inpatient admissions are less in duration in ICM compared to TAU.

GLM (negative binomial): Inpatient days ~ group + baseline inpatient days

For the NOIA at t1, a negative binomial regression (GLM) will be used with a log link to express the coefficients into IRRs. NOIA represents the outcome, while the study group is the predictor, corrected by baseline NOIA.

- H1b: The NOIA is less in ICM compared to TAU.

GLM (negative binomial): inpatient admissions ~ group + baseline inpatient admissions

The primary analysis follows a treatment-policy estimand (ICH E9(R1)): it estimates the effect of randomization to ICM irrespective of treatment interruptions or temporary disengagement, which are regarded as intercurrent events under the treatment-policy strategy. Both count models (H1a, H1b) include an offset for log person-time at risk to account for differential follow-up; death, permanent relocation out of the canton, or incarceration are handled as censoring events. In addition to the intention-to-treat analysis, a pre-specified per-protocol / dose sensitivity analysis (e.g., a minimum ICM-contact threshold) will estimate the effect when the intervention is actually delivered.

Regarding the secondary endpoints, ANCOVAs will be used to quantify the effects. Group is the predictor, corrected for baseline scores.

- H2: Patients in ICM show a higher average WHOQOL-BREF score than patients in TAU.

ANCOVA: WHOQoL-BREF ~ group + baseline WHOQoL-BREF

- H3: Patients in ICM show a lower average SFQ score than patients in TAU.

ANCOVA: SFQ ~ group + baseline SFQ

For the within-subject analyses following the 6-month waiting period, when all participants receive ICM, no between-group comparisons will be conducted in this phase; analyses are descriptive and exploratory in nature. LMMs will be used to track intraindividual changes.

Regarding measurements of the first endpoint after the 6-month waiting period, the RICID is again the outcome, while group and timepoint represent the categorical factors and are its predictors. It is important to note that we do not expect an effect of group on RICID, since both groups will have received ICM treatment and therefore should be dependent on duration rather than the study group. If random intercept models will have a better model fit than random slopes models, it will be reported accordingly, and the comparison of models will be described.

- GLMM (negative binomial): inpatient days ~ group * timepoint + (1 + timepoint | Subject)
- GLMM (negative binomial): inpatient admissions ~ group * timepoint + (1 + timepoint | Subject)
- LMM: WHOQoL-BREF-Scores ~ group * timepoint + (1 + timepoint | Subject)
- LMM: SFQ-Scores ~ group * timepoint + (1 + timepoint | Subject)

Gender and age may influence treatment outcomes. For statistical handling, gender and age will be recorded at baseline and included as a covariate in outcome analyses. The study is not powered to detect subgroup effects, therefore analyses stratified by gender or age will be considered exploratory for all analyses.

5.2. Handling of missing data and drop-outs

Intention-to-Treat (ITT):

All randomized participants are included in the final analysis, regardless of whether they completed the intervention or not. This approach ensures that the results reflect the overall population and allows for a robust estimation of the intervention effects. **Missing Values:** For missing values during the randomized controlled trial, multiple imputation (prerequisite: missing at random) is used to replace values estimated based on available values and response patterns, as well as the interdependencies of the responses, plus a random error to account for uncertainty. This reduces bias and improves efficiency compared to simple imputation, which involves analyzing each dataset separately and then merging the results. Missing values are addressed using multiple imputation by chained equations and predictive mean matching as the imputation method. The imputation model includes study arm, baseline for hospital stays and days, WHOQoL-BREF, SFQ, and ASSIST scores, as well as age, sex, and follow-up data. The number of imputations is determined based on the extent of the missing data. At least one imputation is performed for each percentage point of missing data, generating a minimum of 20 imputations. This ensures the robustness of the results. For the period after the randomized controlled phase, multiple imputation is not required, as LMMs are flexible in dealing with missing values (prerequisite: Missing at random); therefore, a complete-case analysis is performed as an additional sensitivity analysis during this timeframe.

6 REGULATORY ASPECTS AND SAFETY

6.1 Local regulations / Declaration of Helsinki

This study is conducted in compliance with the protocol, the current version of the Declaration of Helsinki, the ICH-GCP, the HRA as well as other locally relevant legal and regulatory requirements.

6.2 (Serious) Adverse Events and notification of safety and protective measures

An Adverse Event (AE) is any untoward medical occurrence in a patient or a clinical investigation participant which does not necessarily have a causal relationship with the trial procedure. An AE can therefore be any unfavourable or unintended finding, symptom, or disease temporally associated with a trial procedure, whether or not related to it.

A Serious Adverse Event (SAE) (ClinO, Art. 63) is any untoward medical occurrence that Results in death or is life-threatening, Requires in-patient hospitalisation or prolongation of existing hospitalisation, Results in persistent or significant disability or incapacity, or Causes a congenital anomaly or birth defect.

Both Investigator and Sponsor make a causality assessment of the event to the trial intervention, (see table below based on the terms given in ICH E2A guidelines). Any event assessed as possibly, probably or definitely related is classified as related to the trial intervention.

Relationship	Description
Definitely	Temporal relationship Improvement after dechallenge* Recurrence after rechallenge (or other proof of drug cause)
Probably	Temporal relationship Improvement after dechallenge No other cause evident
Possibly	Temporal relationship Other cause possible
Unlikely	Any assessable reaction that does not fulfil the above conditions
Not related	Causal relationship can be ruled out
*Improvement after dechallenge only taken into consideration, if applicable to reaction	

Both Investigator and Sponsor make a severity assessment of the event as mild, moderate or severe. Mild means the complication is tolerable, moderate means it interferes with daily activities and severe means it renders daily activities impossible.

Reporting of SAEs (see ClinO, Art. 63)

All SAEs are documented and reported immediately (within a maximum of 24 hours) to the Sponsor of the study.

If it cannot be excluded that the SAE occurring in Switzerland is attributable to the intervention under investigation (i.e., the SAE is definitely, probably, or possibly related to the intervention), the Investigator reports it to the Ethics Committee via BASEC within 15 days.

Follow up of (Serious) Adverse Events

Adverse events (AEs) and serious adverse events (SAEs) occurring during the study period will be documented by the study team. Participants experiencing acute medical or psychiatric emergencies will receive appropriate care according to standard clinical procedures, including referral to emergency medical services if required.

Participants who terminate the study while experiencing an ongoing AE or SAE will be followed up until the event has resolved or stabilized, or until appropriate medical care has been ensured. Information on the course and outcome of the event will be documented where available.

Notification of safety and protective measures (see ClinO, Art 62, b)

If immediate safety and protective measures have to be taken during the conduct of the study, the investigator notifies the Ethics committee of these measures, and of the circumstances necessitating them, within 7 days.

6.3 Periodic reporting of safety and general progress of the clinical trial.

Once a year, the investigator submits to the Ethics Committee a list of the safety events including the severity of the events, their causality to the intervention and the safety of the study participants. The investigator also informs the Ethics Committee about the general progress of the clinical trial (ClinO, Art. 43). The Sponsor-Investigator distributes both the safety reports and the general progress report to all the participating Investigators.

6.4 Amendments

Substantial changes to the study setup and study organization, the protocol and relevant study documents are submitted to the Ethics Committee for approval before implementation. Under emergency circumstances, deviations from the protocol to protect the rights, safety and well-being of participants may proceed without prior approval of the Ethics Committee. Such deviations shall be documented and reported to the Ethics Committee as soon as possible.

Substantial amendments are changes that affect the safety, health, rights and obligations of participants, changes in the protocol that affect study objective(s) or central research topic, changes of study site(s) or of investigator and sponsor (ClinO, Art. 29).

A list of substantial changes is also available on www.swissethics.ch.

A list of all non-substantial amendments will be submitted once a year to the competent EC together with the safety report / general study progress report.

6.5 Notification and reporting upon completion, discontinuation or interruption and resumption of the study

Upon regular study completion, the Ethics Committee is notified via BASEC within 30 days

(ClinO, Art. 38).

The Sponsor may terminate the study prematurely according to certain circumstances, e.g.

- Ethical concerns,
- Insufficient participant recruitment,
- When the safety of the participants is doubtful or at risk (e.g. when the benefit-risk assessment is no longer positive),
- Alterations in accepted clinical practice that make the continuation of the study unwise.

The investigator reports the premature termination, interruption or resumption of the study, including reasons thereof, to the Ethics Committee within 15 days. An interruption lasting more than two years is considered a premature termination (Article 38 ClinO). A final report is submitted to the Ethics Committee via BASEC within a year after completion or discontinuation of the study, unless a longer period is specified in the protocol (ClinO, Art. 38).

6.6 Insurance

In the event of damages or injuries that may occur as a result of the study, the PDAG's liability insurance provides compensation. Separate participant insurance is not required for risk category A according to Art. 15 KlinV, as the study does not involve any hazards exceeding the standard risk.

7 FURTHER ASPECTS

7.1 Overall ethical considerations

The target group for this study may be considered vulnerable. The inclusion of these groups is based on the principle of subsidiarity, which states that equivalent findings cannot be obtained through other means. The results of this study and its implications could significantly contribute to current SUD treatment, particularly for patients with high demands on the healthcare system. An RCT waitlist design maintains high methodological standards, while the waitlist ultimately ensures that treatment is accessible to all participants.

Handling of incidental findings

As the study consists primarily of questionnaires and case management procedures, clinically relevant incidental findings are not expected. If responses or interactions during study procedures indicate acute distress or risk to the participant, appropriate clinical support or referral to treating services will be ensured according to standard care procedures. Should acute suicidality emerge during study participation, an immediate clinical risk assessment will be initiated. Depending on the assessed level of risk, appropriate measures will be taken in accordance with institutional standards, including involvement of the responsible treatment team, emergency psychiatric

evaluation, or referral to inpatient care. Any necessary clinical intervention will take precedence over study-related procedures.

7.2 Risk-benefit assessment

The study does not include any invasive or medically burdensome procedures. Data is collected using validated questionnaires established in clinical research with comparable populations. Since individual items may touch upon personal or sensitive topics, case managers are available as low-threshold points of contact; if needed, further support from the clinical team will be arranged. The risk of unauthorized data access or unintentional identification of study participants is minimized through strict data protection measures and security protocols.

8 QUALITY CONTROL AND DATA PROTECTION

8.1 Quality measures

To ensure the highest standards in project execution, comprehensive quality assurance and quality control measures are implemented:

• **Data entry validation:** All data collected within the project will be validated and checked for consistency by another member of the study team to prevent errors.

• **Quality checks:** Regular internal quality controls and audits are planned to monitor compliance with the study protocols and ensure data integrity. This includes scheduled quality visits and independent data reviews.

• **Access to source data**: Direct access to the source data and all project-related files and documents will be granted for quality reviews by the ethics committee or other regulatory bodies. This will allow the data to be checked for accuracy and completeness.

• **Documentation and archiving:** All project-related documents, including ICF, protocol amendments, and correspondence with the ethics committee, will be archived in accordance with legal requirements and regulations.

• **Continuous monitoring:** Throughout the entire project, ongoing monitoring is conducted to identify any deviations from the study protocols early on and to initiate corrective measures. These quality assurance measures are crucial to maintaining the integrity of the project and ensuring that the collected data are reliable and valid. They contribute to ensuring that the project results meet the highest scientific standards and that the rights, safety, and well-being of the participants are protected.

For quality assurance the sponsor, the Ethics Committee or an independent trial monitor may visit the research sites. Direct access to the source data and all study related files is granted on such occasions. All involved parties keep the participant data strictly confidential.

8.2 Data recording and source data

Within the framework of this study project, all project data will be treated with the utmost discretion and are accessible only to authorized study personnel who require the data to fulfill their tasks within the research project. Participants are identified on the CRFs and other project-specific documents solely by a unique participant number.

The project will exclusively use coded, non-genetic, and non-biological data. The list of participant identifications will be securely stored in a protected location accessible only to the project leader and authorized personnel. To ensure the protection of the data against unauthorized or accidental access, alteration, deletion, copying, and theft, multi-layered security measures are employed. These include encrypted databases, regular backups, and secure, password-protected storage media.

All study data will be securely stored in REDCap on encrypted servers of the DAUnit at the University of Applied Sciences and Arts Valais (HES-SO Valais), in compliance with data protection regulations. Access to this data is restricted to role-based, authorized personnel (e.g., the study physician, the sponsor). Data transmission is encrypted via SSL. Regular backups are planned to ensure data security.

Processes have been established to guarantee complete traceability (audit trail). The REDCap database includes an automatic audit trail function that records all data entries with a timestamp and identification of the respective user. This ensures transparency and accountability for data modifications during the study.

8.3 Confidentiality and coding

All data access is logged, and passwords are used for accessing electronic systems. To prevent misuse, all storage media are regularly backed up, and data recovery strategies are in place in the event of a technical failure. The investigator possesses the necessary knowledge and skills in the areas of data protection and security or can ensure compliance by involving appropriate specialists (in accordance with Art. 6, ClinO).

The medical and personal information of individual participants collected within the scope of this study is confidential and may not be disclosed to third parties. Study and participant data are treated with strict confidentiality and are accessible only to authorized personnel who require the data to fulfill their tasks within the study.

The investigator affirms and upholds the principle of the participant's right to privacy and that they shall comply with applicable privacy laws. Especially, anonymity of the participants shall be guaranteed when presenting the data at scientific meetings or publishing them in scientific journals.

The investigator has appropriate knowledge and skills in the areas of data security and data protection or is able to ensure compliance by calling in appropriate expertise (Art. 6, ClinO).

Individual subject medical information obtained as a result of this study is considered confidential and disclosure to third parties is prohibited.
Trial and participant data will be handled with the utmost discretion and is only accessible to authorized personnel who require the data to fulfil their duties within the scope of the study. On the CRFs and other study specific documents, participants are only identified by a unique participant number.

8.4 Retention and destruction of study data

For this project, all health-related data will be archived in accordance with legal regulations and the PDAG's institutional guidelines and will continue to be stored even after the project leader leaves the organization. The project data will be stored securely for at least 20 years after the publication of the research project. This ensures the traceability of the research results and allows for responses to any inquiries even after the project's completion. No biological materials will be collected as part of the project; therefore, no policy for the destruction of such materials is necessary.

The investigator retains all documents necessary for the identification and follow-up of the trial participants and all other original data for at least twenty years after completion or discontinuation of the clinical trial.

9 MONITORING AND REGISTRATION

Monitoring will be conducted using a risk-adapted internal monitoring procedure. A member of the study team who is not responsible for primary data entry will periodically (every 6 months) review study documentation to ensure protocol adherence and data quality. Monitoring activities include verification of informed consent forms, eligibility criteria, completeness and plausibility of case report forms, completeness of questionnaire data, and documentation of protocol deviations. Questions resulting from monitoring activities are answered during monitoring. These documents will be made accessible to the monitor. Monitoring will be performed before the start of the trial, after the inclusion of the first participant, and subsequently at regular intervals during the study. All monitoring activities will be documented and any identified issues will be addressed to the study team. The study will be registered in the Swiss Human Research Portal (HumRes) via BASEC in German.

10. FUNDING / PUBLICATION / DECLARATION OF INTEREST

The results of the study project are published to promote transparency and in accordance with the project funding requirements. The project received a total of CHF 2,237,750.- in funding. The Canton of Aargau is contributing CHF 1,989,750 to the service providers (PDAG: CHF 757,750.-,

BZBplus: CHF 308,000.-, ags: CHF 924,000.-). The remaining CHF 248,000.- is being financed by the project sponsor and relates to their own contribution of at least 10% (in this case, 11.1%). The funding institutions had no influence on the study design and will have no influence on the conduct of the study, data collection, data management, statistical analyses, interpretation of results, or the decision to publish. The researchers declare that there are no financial or personal conflicts of interest related to this study. All participants commit to upholding the highest standards of scientific integrity and impartiality. The publication policy adheres to the ethical standards of research and the guidelines for publication in scientific journals. If age or gender effects are observed, these will be included in the analysis and its publication. If no such effects are observed, this will also be reported.

One year after the study's completion, a lay-friendly summary of the study results will be submitted to the relevant ethics committee. This summary will be published in a public register.

11. REFERENCES

1. Allness, D., & Knoedler, W. (2003). National program standards for ACT teams.
2. Austin, A. E., Shiue, K. Y., Naumann, R. B., Figgatt, M. C., Gest, C., & Shanahan, M. E. (2021). Associations of housing stress with later substance use outcomes: a systematic review. *Addictive behaviors*, *123*, 107076.
3. Bachmann, R., Schutz, K., & Zehnder, S. (2022). Les soins psychiatriques ambulatoires durant la pandémie. *Bulletin des médecins suisses*, *103*(35), 1078-1080.
4. Beaton, D. E., Bombardier, C., Guillemin, F., & Ferraz, M. B. (2000). Guidelines for the process of cross-cultural adaptation of self-report measures. *Spine*, *25*(24), 3186-3191.
5. Blodgett JC, Maisel NC, Fuh IL, Wilbourne PL, Finney JW. How effective is continuing care for substance use disorders? A meta-analytic review. J Subst Abuse Treat. (2014) 46:87–97. doi: 10.1016/j.jsat.2013.08.022
6. Bond, G. R., Drake, R. E., Mueser, K. T., & Latimer, E. (2001). Assertive community treatment for people with severe mental illness: Critical ingredients and impact on patients. *Disease management and health outcomes*, *9*(3), 141-159.
7. Bond, G. R., & Drake, R. E. (2015). The critical ingredients of assertive community treatment. *World Psychiatry*, *14*(2), 240.
8. Bundesamt für Statistik. (2023). *Sucht: Entwicklung der Eintritte in Behandlung*. Schweizerisches Gesundheitsobservatorium (OBSAN). https://ind.obsan.admin.ch/de/indicator/monam/sucht-entwicklung-der-eintritte-in-behandlung
9. Bundesamt für Statistik. (2024). *Psychische und Verhaltensstörungen: Hospitalisierungen nach Diagnosegruppen*. Swiss Statistics. https://www.swissstats.bfs.admin.ch
10. Burns, T., Catty, J., Dash, M., Roberts, C., Lockwood, A., & Marshall, M. (2007). Use of intensive case management to reduce time in hospital in people with severe mental illness: systematic review and meta-regression. *Bmj*, *335*(7615), 336.
11. Clarke, G. N., Herinckx, H. A., Kinney, R. F., Paulson, R. I., Cutler, D. L., Lewis, K., & Oxman, E. (2000). Psychiatric hospitalizations, arrests, emergency room visits, and homelessness of clients with serious and persistent mental illness: findings from a randomized trial of two ACT programs vs. usual care. *Mental health services research*, *2*(3), 155-164.

12. Clarkin, J. F., & Levy, K. N. (2004). The influence of client variables on psychotherapy. *Bergin and Garfield's handbook of psychotherapy and behavior change*, *5*, 194-226.

13. Common Terminology Criteria for Adverse Events (CTCAE): https://evs.nci.nih.gov/ftp1/CTCAE/

14. Declaration of Helsinki: https://www.wma.net

15. Dieterich, M., Irving, C. B., Bergman, H., Khokhar, M. A., Park, B., & Marshall, M. (2017). Intensive case management for severe mental illness. *Cochrane database of systematic reviews*, (1).

16. Di Lorenzo, R., Sagona, M., Landi, G., Martire, L., Piemonte, C., & Del Giovane, C. (2016). The revolving door phenomenon in an Italian acute psychiatric ward: a 5-year retrospective analysis of the potential risk factors. *The Journal of nervous and mental disease*, *204*(9), 686-692.

17. Drake, R. E., McHugo, G. J., Clark, R. E., Teague, G. B., Xie, H., Miles, K., & Ackerson, T. H. (1998). Assertive community treatment for patients with co-occurring severe mental illness and substance use disorder: a clinical trial. *American journal of orthopsychiatry*, *68*(2), 201-215.

18. Farhoudian, A., Razaghi, E., Hooshyari, Z., Noroozi, A., Pilevari, A., Mokri, A., ... & Malekinejad, M. (2022). Barriers and facilitators to substance use disorder treatment: An overview of systematic reviews. *Substance abuse: research and treatment*, *16*, 11782218221118462.

19. Federal Act on Data Protection (FADP): https://www.fedlex.admin.ch/eli/cc/2022/491/en

20. Festinger, D. S., Marlowe, D. B., Dugosh, K. L., Croft, J. R., & Arabia, P. L. (2008). Higher magnitude cash payments improve research follow-up rates without increasing drug use or perceived coercion. *Drug and alcohol dependence*, *96*(1-2), 128-135.

21. Gehrig, M., Künzi, K., & Stettler, P. (2012). Finanzierung der stationären Suchthilfe. *Situation, Handlungsbedarf und Handlungsoptionen. Bern: Büro BASS*.

22. Geniş, B., Coşar, B., & Arikan, Z. (2020). Readmission rates and causes within the first six months after discharge in patients with alcohol addiction. *Archives of Neuropsychiatry*, *58*(1), 57.

23. Hesse M, Vanderplasschen W, Rapp RC, Broekaert E, Fridell M. Case management for persons with substance use disorders. Cochrane Database Syst Rev. (2007) 4:CD006265. doi: 10.1002/14651858.CD006265.pub2

24. Hull, S., Williams, C., Schofield, P., Boomla, K., & Ashworth, M. (2022). Measuring continuity of care in general practice: a comparison of two methods using routinely collected data. *British Journal of General Practice*.

25. Human Research Act (HRA) https://www.fedlex.admin.ch/eli/cc/2013/617/en

26. International Conference on Harmonization (ICH) E6 Guideline for Good Clinical Practice (GCP): https://www.ich.org

27. International Conference on Harmonization (ICH) E2A Clinical Safety Data Management: Definitions and Standards for Expedited Reporting: https://www.ich.org

28. Karow, A., Reimer, J., Schafer, I., Krausz, M., Haasen, C., & Verthein, U. (2010). Quality of life under maintenance treatment with heroin versus methadone in patients with opioid dependence. *Drug and Alcohol Dependence, 112,* 209–215. doi:10.1016/j.drugalcdep.2010.06.009

29. Kelle, U., & Kluge, S. (2010). Vom Einzelfall zum Typus: Fallvergleich und Fallkontrastierung in der qualitativen Sozialforschung. 2., überarb. *Aufl. Wiesbaden*.

30. King, R. Intensive Case Management: A Critical Re-Appraisal of the Scientific Evidence for Effectiveness. Adm Policy Ment Health 33, 529–535 (2006). https://doi.org/10.1007/s10488-006-0051-5

31. Kubica, A., Evans-Durán, B., Buchman, D.Z. *et al.* Advocating for cash incentives instead of gift cards in public health research: Dollars over donuts. *Can J Public Health* **117**, 40–43 (2026). https://doi.org/10.17269/s41997-025-01039-z

32. Kuckartz, U., & Rädiker, S. (2022). *Qualitative inhaltsanalyse: Methoden, praxis, computerunterstützung: Grundlagentexte methoden*. Beltz Juventa.

33. Lay, B., Lauber, C., Stohler, R., & Rössler, W. (2006). Utilisation of inpatient psychiatric services by people with illicit substance abuse in Switzerland. Swiss medical weekly, 136(2122), 338-338.

34. Levengood, T. W., Yoon, G. H., Davoust, M. J., Ogden, S. N., Marshall, B. D., Cahill, S. R., & Bazzi, A. R. (2021). Supervised injection facilities as harm reduction: a systematic review. *American journal of preventive medicine*, *61*(5), 738-749.

35. Livingston, J. D., Milne, T., Fang, M. L., & Amari, E. (2012). The effectiveness of interventions for reducing stigma related to substance use disorders: a systematic review. *Addiction*, *107*(1), 39-50.

36. Ludwig K, Graf von der Schulenburg JM, Greiner W. German Value Set for the EQ-5D-5L. Pharmacoeconomics. 2018 Jun;36(6):663-674.

37. Lukersmith, M. S., Millington, M., & Salvador-Carulla, L. (2016). What is case management? A scoping and mapping review. *International journal of integrated care*, *16*(4), 2.

38. Maffli, E., & Astudillo, M. (2018). Multiple substance use among patients attending treatment for substance-related problems in Switzerland. Drugs and alcohol today, 18(3), 178-187.

39. Mayring, P. (2010). Qualitative Inhaltsanalyse, Grundlagen und Techniken, vol. 11. *Auflage Belzverlag Weinheim und Basel, Berlin, Germany*.

40. McLellan AT. Have we evaluated addiction treatment correctly? Implications from a chronic care perspective. Addiction. (2002) 97:249–52. doi: 10.1046/j.1360-0443.2002.00127.x

41. Meier, P. S., Barrowclough, C., & Donmall, M. C. (2005). The role of the therapeutic alliance in the treatment of substance misuse: a critical review of the literature. *Addiction*, *100*(3), 304-316.

42. Menzies, R. E., Richmond, B., Sharpe, L., Skeggs, A., Liu, J., & Coutts-Bain, D. (2024). The 'revolving door'of mental illness: A meta-analysis and systematic review of current versus lifetime rates of psychological disorders. *British Journal of Clinical Psychology*, *63*(2), 178-196.

43. Mueser, K. T., Bond, G. R., Drake, R. E., & Resnick, S. G. (1998). Models of community care for severe mental illness: a review of research on case management. *Schizophrenia bulletin*, *24*(1), 37-74.

44. National Institute for Health and Care Excellence. (2007). *Drug misuse in over 16s: psychosocial interventions* [Clinical guideline CG51]. https://www.nice.org.uk/guidance/cg51

45. National Institute for Health and Care Excellence. (2011). *Alcohol-use disorders: diagnosis and management* [Clinical guideline QS11] https://www.nice.org.uk/guidance/qs11

46. Opsal, A., Kristensen, Ø., & Clausen, T. (2019). Readiness to change among involuntarily and voluntarily admitted patients with substance use disorders. *Substance Abuse Treatment, Prevention, and Policy*, *14*(1), 47.

47. Ordinance on Clinical Trials in Human Research (ClinO): https://www.fedlex.admin.ch/eli/cc/2013/643/en

48. Peterson, C., Li, M., Xu, L., Mikosz, C. A., & Luo, F. (2021). Assessment of annual cost of substance use disorder in US hospitals. *JAMA network open*, *4*(3), e210242.

49. Pieper, D., Kotte, N., & Ober, P. (2018). The effect of a voucher incentive on a survey response rate in the clinical setting: a quasi-randomized controlled trial. *BMC medical research methodology*, *18*(1), 86. https://doi.org/10.1186/s12874-018-0544-4

50. Rapp, R. C., Van Den Noortgate, W., Broekaert, E., & Vanderplasschen, W. (2014). The efficacy of case management with persons who have substance abuse problems: a three-level meta-analysis of outcomes. *Journal of consulting and clinical psychology*, *82*(4), 605.

51. Rosen, A. D., Takada, S., Juillard, C., Fernandez Montero, Y. L., Richards, A. M., Ngekeng, S., ... & Bholat, M. A. (2025). Unpacking the link between substance use disorders and 30-day unplanned readmission. *Addiction*, *120*(12), 2538-2546.

52. Rowell-Cunsolo, T. L., Liu, J., Hu, G., & Larson, E. (2020). Length of hospitalization and hospital readmissions among patients with substance use disorders in New York City, NY USA. *Drug and alcohol dependence*, *212*, 107987.

53. Salyers, M. P., Bond, G. R., Teague, G. B., Cox, J. F., Smith, M. E., Hicks, M. L., & Koop, J. I. (2003). Is it ACT yet? Real-world examples of evaluating the degree of implementation for assertive community treatment. *Journal of Behavioral Health Services Research, 30*, 304–320.

54. Schaedle, R. W., & Epstein, I. (2000). Specifying intensive case management: A multiple perspective approach. *Mental Health Services Research*, *2*(2), 95-105.

55. Sharf, J. (2008). *Psychotherapy dropout: A meta-analytic review of premature termination* (Doctoral dissertation, ProQuest Information & Learning).

56. Simon, R., Snow, R., & Wakeman, S. (2020). Understanding why patients with substance use disorders leave the hospital against medical advice: a qualitative study. *Substance abuse*, *41*(4), 519-525.

57. Ssentongo, P., Nunez, J., Dissinger, D., & Bali, B. (2025). Rates and factors for 30-day readmission in patients with substance use disorders during the COVID-19 pandemic. *Frontiers in Psychiatry*, *16*, 1654157.

58. Stanojlović, M., & Davidson, L. (2021). Targeting the barriers in the substance use disorder continuum of care with peer recovery support. *Substance abuse: research and treatment*, *15*, 1178221820976988.

59. Vanderplasschen, W., Wolf, J., Rapp, R. C., & Broekaert, E. (2007). Effectiveness of different models of case management for substance-abusing populations. *Journal of psychoactive drugs*, *39*(1), 81-95.

60. Vanderplasschen, W.; Rapp, R. C.; De Maeyer, J.; Van Den Noortgate, W. (2019): A Meta-Analysis of the Efficacy of Case Management for Substance Use Disorders: A Recovery Perspective. Front. Psychiatry 10:186

61. Witzel, A. (2000). The Problem-centered Interview. *Forum Qualitative Sozialforschung Forum: Qualitative Social Research*, *1*(1). https://doi.org/10.17169/fqs-1.1.1132

62. Ziguras, S. J., Stuart, G. W., & Jackson, A. C. (2002). Assessing the evidence on case management. *The British Journal of Psychiatry*, *181*(1), 17-21.

Appendix 1: Schedule of assessments

Time (hour, day, week)	**Intake / Screening**	**t0**	**t1 (6 months)**	**t2 (12 months**	**t3 (18 months**	**t4 (24 months**	**t5 (30 months, for waiting list only)**
Visit	Intake & screening	Informed Consent	1st visit	2nd visit	3rd visit	4th visit	5th visit
Oral and written patient information	+	+					
Written consent		+					
Inclusion-/ exclusion criteria	+	+	+	+	+	+	+
Medical history	+	+					
Physical examination							
Participant characteristics	+	+					
Intervention		+(Experimental group only)	+	+	+	+	+ (Waiting list only)
Questionnaire		ASSIST, BSCL, CSSRI, SFQ, WHOQOL-BREF, EQ-5D-5L	ASSIST, BSCL, CSSRI, SFQ, WHOQOL-BREF, EQ-5D-5L	ASSIST, BSCL, CSSRI, SFQ, WHOQOL-BREF, EQ-5D-5L	ASSIST, BSCL, CSSRI, SFQ, WHOQOL-BREF, EQ-5D-5L	ASSIST, BSCL, CSSRI, SFQ, WHOQOL-BREF, EQ-5D-5L, ZUF-8 (Experimental group only)	ASSIST, BSCL, CSSRI, SFQ, WHOQOL-BREF, EQ-5D-5L, ZUF-8 (Waiting list only)
Sampling			+	+	+	+	+
Safety		+	+	+	+	+	+