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Testing an integrated model of population mental health: study protocol for the Mannheim incidence and inception cohort study (MAKO)

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Abstract

Background: Monitoring of population mental health is now considered to play a vital role in health, risk factor and demographic surveillance systems across the globe. Adopting a public mental health perspective on monitoring and surveillance requires us to consider the entire spectrum of mental health, which broadly ranges from positive mental health and well-being to severe mental disorders via at-risk populations. This population mental health approach has become the mainstay of public mental health provision in many European countries, but there is a dearth of research on this issue in Germany in the past 20 years, and fundamental conceptual and methodological issues remain to be addressed at both the national and international level.

Methods: The Mannheim incidence and inception cohort study (MAKO) is a recently established two-arm population-based incidence (arm 1) and inception cohort (arm 2) study in the catchment area of Mannheim, Germany. In the incidence-arm, case ascertainment of incident cases is carried out for the years of 2024 and 2025 based on clinical assessment via structured clinical interviews and retrospective case record evaluation. In the inception cohort arm, we recruit and follow an epidemiologically characterized, population-based cohort of individuals a) without symptoms (i.e., stage 0), b) with criteria for non-specific psychological distress (i.e., stage 1a), or c) a clinical high at-risk mental state for severe mental disorder (i.e., stage 1b) at baseline and up to four follow-up assessments every six months. Assessments include clinical interviews, self-report measures, and ecological momentary assessment.

Results: Enrolment started in January 2024. Data collection is expected to be completed in 2027.

Conclusion: A combined, two-arm incidence and inception cohort study reflects the optimal design in terms of both efficiency and capacity for delineating the basic epidemiology of population mental health for the first time in over 20 years in Germany. Given the heterogeneity in neighbourhood characteristics and migrant and ethnic minority populations in the city of Mannheim, our methodology will offer a unique population laboratory to study variation in incidence and clinical stage transitions in terms of place and ethnicity with high external validity.

Background

Monitoring population mental health is now considered to play a vital role in health, risk factor and demographic surveillance systems across the globe. It can serve as a basis for assessing the mental health consequences of societal developments (e.g., social, economic and/or pandemic crises (1–5)), evidence-based service planning (6), and determining the impact of public mental health services at the population level (2,6,7). The shift in focus to early intervention for severe mental disorders (2,8,9), prevention as a tangible goal (2), and the emphasis on promoting the positive dimensions of mental health (10) all imply that adopting a public mental health perspective on monitoring and surveillance requires us to consider the entire spectrum of mental health. This spectrum broadly ranges from positive mental health to severe mental disorders such as psychotic, bipolar, severe depressive and borderline personality disorder (2,7). These approaches now form part of public mental health surveillance in some countries (e.g., Canada) but have not been sufficiently adopted in others (11). For the first time in over two decades, the protocol for the current study described in this paper seeks to address this gap, which will allow the precise and robust estimation of the incidence of severe mental disorders in Germany based on primary data (12–15). We also seek to address fundamental conceptual and methodological issues in the epidemiology of population mental health that are essential for the public mental health field to progress at both the national and international level. For example, in recent years there has been an upsurge of interest in public mental health provision, including mental health promotion, mental health prevention, and delivery of treatment and services for severe mental disorders (16,17), as well as renewed interest in the social determinants of mental health(18). These efforts are ultimately geared toward targeting mental health at the population level and centrally build on the seminal 'population strategy' advocated by Geoffrey Rose (19). At its core, Rose's population strategy posits that for continuously distributed traits, the population mean is closely linked to the prevalence of the corresponding disorder. Consequently, small change in the trait distribution ("shifting the curve") will be associated with a substantial change in prevalence of the disorder.

In mental health, there is evidence that, first, most mental health problems are continuously distributed (20), second, the population mean is associated with the prevalence of mental disorders in that population, and, third, a change in population mean is closely related to a marked change in prevalence in that population (19,21–23). However, there are at least three fundamental conceptual and methodological issues in relation to population-based strategies that remain to be addressed for this approach to realise its full potential.

First, this approach, so far, has primarily focused on the association of the population mean with prevalence but not *incidence* (i.e., the occurrence of new cases in a population over a specified time period) of disorder. If, in an extrapolation of Rose's approach (19), the effect of mental health promotion and primary prevention produces a leftward shift in the curve, then this could become evident, first and foremost, in the form of a reduction in incidence (rather than prevalence) of disorder. Focusing on incidence will provide an approach that will allow us to understand more fully the link and timing between potential shifts in population mean and subsequent occurrence of new cases of disorder and, hence, make the impact of public mental health services at the population level more readily accessible and measurable.

Meta-analytic evidence suggests that incidence rates of psychosis as one of the most prominent severe mental disorders vary by place and are particularly high in urban areas as well as in many, but not all, migrant and ethnic minority groups (12–14,24). Further, for migrant and ethnic minority groups, rates of psychosis are highest in areas where they constitute a small proportion of the local population (i.e., areas with low ethnic density) (13). The latest and largest international incidence study (25) from the EU-GEI consortium thoroughly documented marked variation in incidence of psychosis across 17 catchment areas and six countries, which emphasizes the need to determine rates at the local level standardized according to important demographic characteristics. However, while variation in incidence rates in terms of place and ethnicity has been reported in many countries, there has been a dearth of research on this issue in Germany (12–14,24), with the last studies to investigate incidence of severe mental disorders based on primary data having been conducted in the 1990s (26–28). Given the well-documented variation in terms of place and, hence, context-dependent nature, incidence rates

from international studies do not readily generalize to local contexts and populations in Germany and, thus, remain largely unknown in this country. In fact, only one study to date has reported treated incidence rates by German population and population with migrant minority status, respectively, in Germany (29). The study is based on data from 1974 – 1980, therefore, incidence, and especially, treated incidence for individuals with migrant and ethnic minority status might have changed dramatically within the past 45 years due to changes in society and the mental health care system. It is therefore not surprising that planning services in Germany is largely operated in the absence of evidence on basic epidemiological data on incidence and other important metrics of population mental health, which may lead to population-level strategies that are not equally accessible across diverse groups. Further, evidence on variation in incidence in terms of place and ethnicity for severe mental disorders other than psychosis, such as severe affective disorders, is much more limited not only in national but also international studies (30). It has recently been shown how this can be used to predict needs for care and inform planning services in defined catchment areas in the UK (6). Overall, the limited evidence on (and variation in) the incidence of severe mental disorders reflects a pressing public health issue, particularly in an increasingly diverse society (31). A key next step is to more precisely delineate their link to the population mean, such that more comprehensive monitoring of mental health can be developed and implemented.

The second issue that remains to be addressed is that the 'population strategy' by Rose (32) has been taken to suggest that a leftward shift in the distribution of mental health is associated with a substantial decrease in prevalence of not only disorder but also, and even more markedly, in those at *moderate* risk or with *subthreshold* disorder (16). This proposition builds on an earlier observation by Rose that, for continuously distributed health problems, the largest proportion of disorder may occur in those just below the upper tail of the distribution, given more individuals are located within that range. It assumes, however, that mental health promotion and prevention shift mental health in a uniform way across the population (i.e., without impact on the shape of the population curve), disregarding the individuals' position on the risk distribution; an assumption challenged by evidence demonstrating that public health

campaigns have been more successful in benefitting individuals with higher socioeconomic status (33,34). The 'prevention paradox' implies that universal interventions that may confer little individual benefit to a large number of people at low or moderate risk may have a greater impact at the population level than selective interventions that may confer considerable individual benefit to a smaller number of individuals at high risk.

A third concern has been raised about population strategies to yield the unintended effect of augmenting social inequalities in health in vulnerable populations such as ethnic minority groups or those living in poverty, who are at higher risk of risk exposure due to shared social characteristics (e.g., language barriers, experiences of discrimination, social exclusion), and, hence, reflect a driving factor for mental health inequalities. This becomes the case if population strategies are less effective or less accessible for those at higher risk, compared to those at lower risk. This phenomenon is widely referred to as 'inequality paradox' (16). However, before this putative paradox can be empirically tested and inform strategies for prevention and intervention, population-based approaches need to be considered and investigated in relation to, and jointly with clinical staging models. These models distinguish and operationalize various levels of low, moderate and high risk groups, as well as those who ultimately meet clinical thresholds for disorder across the continuum of mental health. Thus, their integration would allow us to increase precision of testing population-level approaches by determining the stages most sensitive to specific strategies, and ultimately, tailoring of interventions. Clinical staging models in psychiatry have primarily been developed within clinical early intervention services (9) and have largely emerged separately from approaches to population mental health. Early versions of clinical staging models have focused on a clinical high-risk state for psychosis (CHR-P) for a long time. More recently, evidence on a putative pluripotent risk state (35) or extended transdiagnostic phenotype (36), with various exit syndromes (incl. psychotic, bipolar, severe depressive and borderline personality disorder), have led to an extension of clinical staging to a broad range of severe mental disorders (37–40). This extension is further informed by evidence that symptom severity, functional impairment, and complexity of course and outcome play an important role as much in the so-

called ‘common mental disorders’ as they do in psychotic and bipolar disorders (16). Latest transdiagnostic clinical staging models seem to converge on distinguishing three symptomatic stages: current non-specific psychological distress with mild to moderate impact on functioning (stage 1a), a broad Clinical High At-Risk Mental State (CHARMS) including attenuated symptoms, trait vulnerability and functional decline (stage 1b), and a first episode of severe mental disorder (stage 2), with psychotic, bipolar, severe depressive, and borderline personality disorders as exit syndromes that contribute substantially to disease burden and involve significant impairment (37–40). Asymptomatic individuals are commonly classified as stage 0. While there is meta-analytic evidence on the predictive validity of a CHR-P (41), only a small number of studies have investigated this in relation to a broad CHARMS for severe mental disorders (37–40,42). These studies, in part, used crude operationalizations of clinical stages, included no or very small samples for earlier stages (i.e., stage 0, 1a) (37,40), and evidence on transition rates in CHARMS remains very limited. Furthermore, the structural validity of categorical clinical stages still requires further empirical testing by latent categorical variable models and through a dimensional lens, as proposed by the Hierarchical Taxonomy of Psychopathology (HiTOP) (43–45). Categories generated based on dimensional approaches to psychopathology need to be empirically derived and demonstrate clinical utility (e.g., for clinical and preventative decision making). This evidence is urgently needed for clinical staging models to be considered and understood more fully in the context of population-based and vulnerable population approaches. Methodologically, sampling by clinical stages enables us to generate variance across the continuum of mental health required to test clinical staging and dimensional models empirically based on established measures of these approaches (e.g., CAARMS, HITOP-SR).

The fourth issue that needs to be addressed in relation to the population mental health approach is that contemporary models of mental health, including clinical staging and dimensional models, have primarily focused on psychopathology, with absence of symptoms being used synonymously with a state of well-being or positive mental health. However, there is widespread consensus that mental health is much more than just the absence of

196 psychopathology (10). Thus, some governments have started to explore and implement
197 strategies for assessing and monitoring positive mental health at the population level to inform
198 measures for mental health promotion and evaluate policy (7). However, psychometric
199 evidence on measuring positive mental health has rarely been integrated with categorical or
200 dimensional models of psychopathology. For example, HiTOP (43), which quantifies disorders
201 according to several hierarchical levels, and characterize them dimensionally, have, to date,
202 primarily focused on dimensions of mental disorder rather than positive mental health. Also,
203 clinical staging models commonly include a stage of no symptoms (stage 0) without explicitly
204 covering the measurement range of positive mental health.
205 Similarly, there is an urgent need to not only consider risk factors (e.g., urbanicity (13), ethnic
206 minority status (12,25,46,47), area-level ethnic density (13)) but also resilience (i.e., the ability
207 to recover from and overcome the effects of adversity (48)) and protective factors, such as
208 social support (49) and self-efficacy (50), in relation to clinical stages and dimensions of mental
209 health. This includes digital momentary phenotypes (such as stress reactivity, mood and
210 activity patterns) as investigated in our work based on innovative multimodal ecological
211 momentary assessment (EMA) (51–54), which can provide the basis for digital monitoring of
212 population mental health. Monitoring of positive mental health, resilience and protective factors
213 alongside risk factors and levels of mental disorder at the population level is considered a vital
214 task of public mental health (7) and should embrace novel EMA-based approaches to real-
215 world monitoring of digital momentary phenotypes in daily life.
216 Therefore, it is important to extend investigations of dimensional and clinical staging models
217 to the full range of mental health in order to clarify and calibrate the nature of the common
218 ground between positive mental health and mental disorder. This study is agnostic regarding
219 the value which dimensional and clinical staging models each present and seeks provide a
220 basis for formally validating both approaches. Taken together, integrating the entire continuum
221 of mental health is of considerable importance, but high-quality research is needed first, which
222 allows us to address the fundamental conceptual and methodological issues outlined above.

So far, these issues have been investigated by various fields – including psychiatric epidemiology, early intervention in psychiatry, prevention, mental health promotion, mental health services research, psychometrics, and public health – that largely operate in separate silos. Public mental health is geared towards bringing these fields together in interdisciplinary investigations that allow us to understand more fully how the different approaches overlap and relate to each other and, thereby, establish the basic epidemiology of population mental health (incl. epidemiology of vulnerable and marginalized populations). This is what the current study is designed to achieve. In reviewing and synthesising the state of the art, we propose here an integrated transdiagnostic model of population mental health that encompasses the entire continuum of mental health. It spans and calibrates positive mental health and well-being all the way through to incidence of severe mental disorders and seeks to empirically integrate, for the first time, transdiagnostic clinical stages and dimensions of psychopathology and positive mental health, including how they relate to each other (see Figure 1). This will allow us to jointly examine the central link between population mean (and other relevant distributional measures), various levels of risk, access to public mental health services, and incidence of full-threshold disorder.

Aim and objectives

The overarching aim of the proposed programme is to establish and delineate the basic epidemiology of population mental health by testing key aspects (i.e., incidence, clinical stage transitions) of an integrated transdiagnostic model encompassing the entire continuum of mental health. To this end, we will implement a highly innovative, two-arm population-based incidence and inception cohort study, in a defined catchment area (Mannheim, Germany) using robust statistical methods and digital technology. This two-arm design will allow us to examine conceptual and methodological questions central to population mental health research and provides the basis for evaluating the feasibility of comprehensive monitoring of population mental health.

To achieve our overall aim, this programme has four objectives with corresponding hypotheses:

Objective 1 (Incidence): To estimate the incidence of severe mental disorder (i.e., psychotic, bipolar, severe depressive, and borderline personality disorder) in Germany in the population at-risk, including by demographic and environmental characteristics.

We will meet this objective in the incidence arm of the study by: a) estimating the treated incidence of severe mental disorders in the defined catchment area of Mannheim, Germany, with a population at-risk of 225,700 between ages 14-64 (55); b) investigating variation in incidence rates of these disorders by age, sex, neighbourhoods, and migrant/ethnic minority group status; and by c) investigating which demographic/risk factors are associated with access to, and help-seeking from, public mental health services. We will test the following hypotheses:

- H1.1 Primary hypothesis: The incidence of severe mental disorders during 451,400 person-years at risk will vary by age, neighbourhood and migrant/ethnic minority status, such that rates will be higher in younger age groups, urban areas, and migrant/ethnic minority groups.
- H1.2 a. Psychotic disorders will exhibit greater variation by place than other severe mental disorders, while b. psychotic and bipolar disorders will exhibit greater variation by ethnic/migrant group status than depressive disorders and borderline personality disorder.
- H1.3 Variation in incidence by sex will occur at the level of specific diagnoses of severe mental disorders and will interact with age (e.g., higher rates of psychosis in younger men).
- H1.4 For migrant/ethnic minority groups, rates of psychosis will be highest in areas where they constitute a small proportion of the local population (i.e., an migrant/ethnic density effect).

***Objective 2 (Clinical stage transitions)*:** To determine rates of transition from earlier to later stages of severe mental disorders, in the population at-risk, including by important demographic, risk and protective factors in order to test the predictive value and clinical utility of earlier clinical stages. We will meet this objective in the inception cohort arm of the study by: a) estimating transition rates from earlier (stage 0, 1a, 1b) to later (stage 1a, 1b, 2) clinical stages of severe mental disorder at 12-month follow-up; b) examining whether transition rates are greater in individuals with non-specific psychological distress (stage 1a) and CHARMS (stage 1b) than in individuals without symptoms (stage 0); c) examining whether transition rates vary by demographic, risk and protective factors; and by d) investigating which demographic/risk factors are associated with access to, and help-seeking from, public mental health services. Specifically, we will test the following hypotheses:

- H2.1 Transition rates from earlier to later clinical stages will be greater in individuals with nonspecific psychological distress (stage 1a) than in individuals with no symptoms (stage 0).
- H2.2 Transition rates from earlier to later clinical stages will vary by demographic characteristics (e.g., age, sex), risk factors (i.e., neighbourhood, migrant/ethnic minority group status, socio-economic status), protective factors (i.e., social support, resilience, self-efficacy), with, e.g., higher transition rates in migrant/ethnic minority than in ethnic majority groups, more urban neighbourhoods, and those with lower socioeconomic status, and lower transition rates in those with higher social support, resilience, and self-efficacy.

Objective 3 (Transdiagnostic stages, dimensions, momentary phenotypes, population mean): To establish the structural, convergent and predictive validity and clinical utility of empirically derived transdiagnostic stages, HiTOP dimensions, digital momentary phenotypes, and population mean of mental health (incl. symptoms, well-being and positive mental health). We will meet this objective in the combined sample of incidence and inception cohort arms by: a) identifying empirically-based clinical stages (latent classes) of mental health at baseline; b)

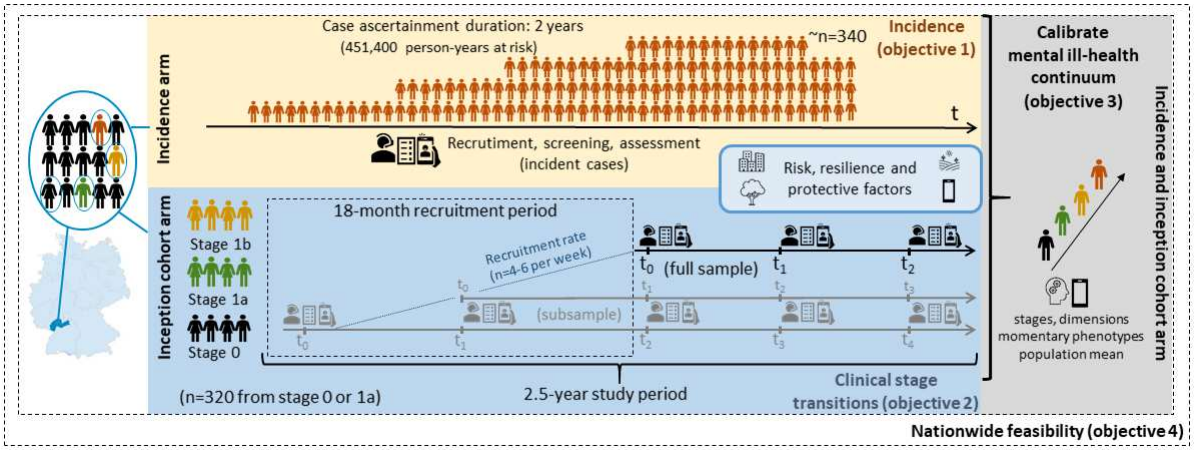
determining the convergent validity of empirically-derived clinical stages with contemporary staging models (i.e., stage 0, 1a, 1b, 2) at baseline; c) examining whether transdiagnostic dimensions and digital momentary phenotypes of mental health (identified based on measures of symptoms, well-being and positive mental health, building on and extending previous work (36,43,46,47)) converge with (empirically derived) clinical stages at baseline; d) examining whether the population mean and distribution (and other measures of central tendency, as appropriate) of transdiagnostic dimensions, digital momentary phenotypes and established measures of mental health are associated with incidence of severe mental disorder; e) investigating whether a shift in the population mean and f) a shift in the distribution predict an increased risk for transition from earlier (stage 1a, 1b) to later clinical stages (stage 1b, 2). We will test the following hypotheses:

- H3.1 There will be at least four latent classes of mental health, including i) no symptoms, ii) nonspecific psychological distress, iii) clinical high-risk state, and iv) severe mental disorder (consistent with contemporary models of clinical staging).
- H3.2 The identified latent classes (i.e., identified in H3.1) will converge with clinical stages of contemporary clinical staging models (i.e., stage 0, 1a, 1b, 2).
- H3.3 Transdiagnostic dimensions and digital momentary phenotypes of mental health will allow for accurate classification into clinical stages.
- H3.4 The population mean and distribution of both transdiagnostic dimensions, digital momentary phenotypes and established measures of mental health will be associated with incidence of severe mental disorder.
- H3.5 Changes in the population mean and distribution (in transdiagnostic dimensions, digital momentary phenotypes and established measures) predict changes in risk for transition from earlier to later clinical stages (inception cohort arm only).

Objective 4 (Nationwide feasibility): To determine the feasibility of expanding the design and methods (i.e., incidence and inception cohort design, recruitment, case ascertainment, denominator population, measures, psychometric models) to large-scale investigations of

population mental health throughout Germany. This may serve as a basis for establishing a more comprehensive mental health surveillance, evidence-based service planning and making the impact of public mental health services in Germany accessible and measurable.

Figure 1. *Study design of the two arm incidence and cohort study.*



Method

Study design and setting

A two-arm population-based incidence and inception cohort study will be conducted in a tightly defined catchment area (Mannheim) in Germany. In the *incidence arm*, we aim to identify all cases between ages 14 to 64 with a first (treated) episode of a severe mental disorder meeting inclusion criteria (see Participants section). Case ascertainment will take place over a two-year period between 1 January 2024 and 31 December 2025, and involve the research team making weekly contact with mental health services in Mannheim to identify cases with a suspected first episode or treatment based on clinical guidelines for severe mental disorder. Clinical teams will be contacted weekly by the research team to optimize identification of potential cases by clinicians. For all individuals with a suspected first episode of severe mental disorder, we will conduct clinical assessments to determine presence of a research-based ICD-10 diagnosis of an untreated first episode of severe mental disorder using the Structured Interview for DSM-5 (SCID-5-CV, SCID-5-PD, First et al., 2015; 2016) and a version of the Nottingham Onset Schedule (NOS; Yung et al., 2005) modified to apply to all severe mental disorders of

interest in this study. Using the NOS, we will carefully trace onset of symptoms, first contact with mental health services, and beginning of treatment based on clinical guidelines for severe mental disorder to confirm incident status. Case ascertainment will also include retrospective case note evaluation of patients treated at the Central Institute of Mental Health (see section on 'Data collection' for further details) and will be further optimized through the population-based inception cohort arm of the study, which will identify individuals who transition to a first episode of severe mental disorder (stage 2) over the case ascertainment period.

The population at-risk, 14 to 64 years old, in this catchment area is estimated to be 225,700 (55). Based on a conservative estimate of 75 incident cases per 100,000 person-years of psychotic an severe affective disorders (25,56,57), and a case ascertainment duration of two years, we would expect the incidence arm of the study to yield a sample of approximately n=340 incident cases. Our estimate of incident cases is conservative as these are well within previously reported rates for psychotic and affective disorder only (25,56,57). We will use census data from 2022 to estimate the denominator population and person-years at-risk in the catchment area, stratified by neighbourhood, age group, sex, and migrant/ethnic minority group status.

The *inception cohort arm* of the study entails a prospective, epidemiologically characterized, population-based cohort in which we recruit a quota sample stratified by age, sex, neighbourhood, and migrant/ethnic minority group status. Participants will be classified into those, who 1) meet criteria for a) non-specific psychological distress (i.e., stage 1a), b) a clinical high-risk state for severe mental disorder (CHARMS, i.e., stage 1b), or 2) do not meet criteria for stage 1a, 1b and 2 (with the latter including those with severe mental disorder before 2024) (i.e., stage 0) drawn from the same catchment area as incident cases (Mannheim, Germany; aged 14-35 years). At baseline (t_0), we aim to recruit n=320 individuals with a) non-specific psychological distress (stage 1a) and b) asymptomatic individuals (stage 0), with at least N=160 individuals from stage 1a. Moreover, we will recruit at baseline a convenience sample of individuals with CHARMS (stage 1b). This cohort will be recruited at a constant rate over a period of 18 months and followed every 6 months from baseline, with a minimum follow-up

time of 12 months for all participants, corresponding to a total duration for recruitment and assessment of 2.5 years. This will ensure that all participants from the inception cohort arm will be followed at 6-months (t_1) and 12-month (t_2) follow-up, whilst allowing to collect data, where possible, at 18-month (t_3) and 24-month (t_4) follow-up, thereby making optimal use of time-to-event (survival) data. For a visual depiction of the study design, see Figure 1.

Participants

Incidence arm

Eligibility criteria

Incident cases will be all individuals with a first episode or start of first ever treatment for a severe mental disorder according to clinical guidelines (as defined in Supplement Table S2) in public mental health services, meeting the following eligibility criteria: diagnosis of severe mental disorder (psychotic disorders: F20, F22-29, F1x.5; mania: F30, bipolar disorder: F31; severe depression: F32.2, F32.3, F33.2, F33.3; borderline personality disorder: F60.3 in ICD-10 (58)); aged 14-64 years; living in the catchment area of Mannheim, Germany (registered in Mannheim and/or regularly living in Mannheim). Eligibility is assessed based on clinical assessment via structured clinical interviews and retrospective case record evaluation. For clinical assessment via structured clinical interviews, additional inclusion criteria are: willingness to participate, ability to provide informed written consent, and consent by legal guardians in case of minors. Exclusion criteria for both clinical assessment via structured clinical interviews and retrospective case record evaluation are as follows: guideline-based treatment by mental health services for the same severe mental disorder before 2024, presence of an organic medical cause, transient symptoms due to acute intoxication (ICD-10, codes F1X.0), insufficient knowledge of German, English, Turkish, or Russian. An additional exclusion criterion for clinical assessment via structured clinical interviews in study assessments is a documented history of intellectual disability. Patients will still be eligible if they received prior diagnosis of or treatment for a *different* severe mental disorder (as defined

in the inclusion criteria) or had prior contact to mental health services for a disorder not included in the severe mental disorders (e.g. mild depression).

Inception cohort arm

Eligibility criteria

Inclusion criteria for the inception cohort arm comprise being resident of Mannheim (registered in Mannheim and/or regularly living in Mannheim), age of 14-35 years, mental health state: stage 0, 1a, or 1b (see Table 1), willingness to participate, ability to give written informed consent, and parental consent for minors. Exclusion criteria comprise a current or past diagnosis or treatment for a severe mental disorder (stage 2 and up) (based on self- or clinician-report), a lifetime or current severe mental disorder detected in the study assessments using SCID-5, a documented history of intellectual disability, and insufficient knowledge of German, English, Turkish, or Russian.

At 6 months (t_1) and 12 months (t_2), we will seek to follow-up all those who participate at baseline, with transition to later clinical stage (i.e., stage 1b, stage 2) as outcome of primary interest (with stage 2 transition resulting in end of study participation). For each participant, we will carefully document the time to transition to a later stage. We anticipate an attrition rate (i.e., attrition for other reasons than 'administrative censoring' due to study termination at a fixed point in calendar time) of 10% in each of the two pre-scheduled follow-up intervals (t_0, t_1) and (t_1, t_2). On this basis, we anticipate following, of the original cohort, 90% at 6-month follow-up (t_1) and 80% at 12-month follow-up (t_2). We will also follow participants, where possible, at 18-month (t_3) and 24-month (t_4) follow-up, respectively.

Recruitment and quota sampling

In the inception cohort arm, a quota sample stratified by age, sex, neighbourhood, and migrant/ethnic minority group status will be drawn from the same geographical area as incident cases. Participants will be recruited to fill quota, where possible, through random sampling (i.e., via postal address file from the registry office). Where required, quota sampling will be complemented by non-random sampling, among others, via schools, youth centres, public

information stands, sports clubs, religious institutions (e.g., mosques), Muslim pastoral care and counselling, food banks, social services, self-help groups, migrant/ethnic minority group associations and services, and (social) media, applying recommended strategies to reach and include vulnerable and marginalized groups (59). Table 1 shows the clinical staging criteria which will be applied throughout the incidence and inception cohort arm.

Table 1. *Clinical staging criteria*

Stage 0: Asymptomatic	
	Do not meet criteria for stages 1a, 1b, or 2, and no past severe mental disorder part of stage 2 criteria.
Stage 1a: Non-specific distress	
Reduction in functioning	At least mild to moderate reduction of social functioning: SOFAS < 75 (last month)
Help seeking	Help-seeking or referral to professional help
Psychological distress	Current non-specific psychological distress: K10 ≥ 20
Stage 1b: Clinical high-risk state for severe mental disorder (CHARMS)	
Psychosis trait vulnerability	(1) SCID-5-PD schizotypal personality disorder OR FRQ: 1st degree relative is/was treated/diagnosis for psychosis (2) AND SOFAS ≤ 50 in the last 12 months OR SOFAS at least 30% below previous level
Attenuated psychotic symptoms (APS)	(1) Subthreshold intensity: i. CAARMS: at least one of the following: 1. Global rating of 3-5 on the unusual thought content subscale 2. Global rating of 3-5 on the non-bizarre ideas subscale 3. Global rating of 3-4 on the perceptual abnormalities subscale 4. Global rating of 4-5 on the disorganized speech subscale ii. AND CAARMS: frequency score of 3-6 for the respective subscale iii. AND SOFAS ≤ 50 in the last 12 months OR SOFAS at least 30% below previous level for at least one month OR:

	(2) Subthreshold frequency: i. CAARMS: at least one of the following: 1. Global rating of 6 on the unusual thought content subscale 2. Global rating of 6 on the non-bizarre ideas subscale 3. Global rating of 5-6 on the perceptual abnormalities subscale 4. Global rating of 6 on the disorganized speech subscale ii. AND CAARMS: frequency score of 3 on the respective subscale AND AND SOFAS ≤ 50 in the last 12 months OR SOFAS at least 30% below previous level for at least one month
Brief limited intermitted psychotic symptoms (BLIPS)	(1) CAARMS: at least one of the following: i. Global rating of 6 on the unusual thought content subscale ii. Global rating of 6 on the non-bizarre ideas subscale iii. Global rating of 5-6 on the perceptual abnormalities subscale iv. Global rating of 6 on the disorganized speech subscale (2) AND CAARMS: Frequency scale score of 4-7 on the respective subscale (3) AND SOFAS ≤ 50 in the last 12 months OR SOFAS at least 30% below previous level for at least one month AND each episode of symptoms preset for < 7 days with spontaneous remission each time
Bipolar trait vulnerability	(1) SCID-5 (current) for at least 1 week: depressed mood (QIDS-C 1 ≥ 2) or loss of interest or pleasure (QIDS-C 8 ≥ 2) (2) AND at least 2 criteria: i. significant weight loss (QIDS-C 12 or 13 ≥ 2) ii. insomnia or hypersomnia nearly every day (QIDS-C 4, 5, 6, or 7 ≥ 2) iii. psychomotor retardation or agitation (QIDS-C 15 or 16 ≥ 2) iv. fatigue or loss of energy (QIDS-C 14 ≥ 2) v. feelings of worthlessness or excessive or inappropriate guilt (QIDS-C 2 ≥ 2)

	vi. diminished ability to think or concentrate (QIDS-C 9 ≥ 2) vii. recurrent thoughts of death, recurrent suicidal ideation (QIDS-C 3 ≥ 2) AND at least one of (3) or (4) (3) FRQ: 1st degree relative is/was treated/diagnosis for bipolar disorder AND/OR (4) For a minimum of 6 months (lifetime) high and low mood (no more than 2 consecutive months without symptoms) and at least 3 criteria (assessed with the Affective Disorders Evaluation (ADE)): i. decreased need for sleep (e.g., feels rested after only 3 hours sleep) ii. increased energy iii. inflated self-esteem or grandiosity iv. increased goal directed activity, v. restlessness vi. more talkative than usual or pressure to keep talking vii. unusual ideas, clear thinking viii. troublesome behavior ix. inappropriate sense of humor (does not need to cause a clinically significant drop in functioning)
Subthreshold manic symptoms (as used by Ratheesh et al. (2023) and in accordance with the Bipolar at Risk (BAR) Criteria – extended to	(1) no lifetime episodes of depression and mania AND full criteria for current/past hypomanic episode OR (1) Current SCID-5: at least 2 consecutive days of abnormally and persistently elevated, expansive, or irritable mood (2) AND SCID-5: at least 2 additional criteria i. inflated self-esteem or grandiosity ii. decreased need for sleep iii. more talkative than usual or pressure to keep talking

include all possible symptom combinations)	iv. flight of ideas or subjective experience that thoughts are racing v. distractibility vi. increased goal-directed activity (socially, at work, or sexually) or psychomotor agitation (1) if 4 or more days of abnormally and persistently elevated, expansive, or irritable mood with at least 2 criteria: i. no functional decline ii. no atypical change in functioning compared to symptom-free periods OR mood changes or functional decline is not noted by others
Moderate depressive symptoms	(2) SCID-5: current or past episode of depression (with at least 1 cardinal symptom, 5 additional symptoms) (2) AND current QIDS-C: 11-20
Subthreshold borderline	(1) SCID-5-PD: 2-4 criteria (scored with "2") for at least the past 12 months: i. frantic efforts to avoid real or imagined abandonment ii. a pattern of unstable and intense interpersonal relationships characterised by alternating between extremes of idealisation and devaluation iii. identity disturbance: markedly and persistently unstable self-image or sense of self iv. impulsivity in at least 2 areas that are potentially self-damaging (not suicidal or self-harming behavior) v. recurrent suicidal behaviour, gestures, or threats, or self-mutilating behaviour vi. affective instability due to a marked reactivity of mood—intense feelings that can last from a few hours to a few days vii. chronic feelings of emptiness viii. inappropriate intense anger or difficulty controlling anger

	ix. transient, stress-related paranoid ideas or severe dissociative symptoms
Stage 2: Severe mental disorder	
	(1) Psychosis (ICD10: F20, F22-29) (2) Substance induced psychosis (ICD10: F1X.5) (3) Mania (ICD10: F30) (4) Bipolar disorder (ICD10: F31) (5) Severe/psychotic depression (ICD10: F32.2, F32.3, F33.2, F33.3) (6) Borderline personality disorder (ICD10: F60.31)

Data collection

Clinical assessment (incl. structured clinical interviews)

Data collection and management is carried out via REDCap (Research Electronic Data Capture) (60,61). EMA data are collected via the movisensXS app using study smartphones or personal smartphones (movisens GmbH). Potentially eligible individuals first undergo a phone call or in-person conversation for pre-screening. Based on available and self-reported information on the mental health status and history, individuals complete informed consent procedures (incl. written informed consent) for the incidence arm (i.e., for clinical interviews, not for retrospective case record evaluation) or the inception cohort arm. All participants who provide written informed consent complete a set of screening measures determining whether CAARMS and SCID-5-CV sections on *current* symptoms are required, and thus the length of the subsequent interview session. The *full* interview, including lifetime *and current* symptoms, is conducted if participants meet one of the following criteria: a) presence of psychotic symptoms on the Prodromal Questionnaire (PQ-16 (62) indicated by a total number of symptoms of ≥ 5 or a distress score of ≥ 8 (63); b) current difficulties in emotion regulation (at least one of the subscale cut-offs on the Difficulties in Emotion Dysregulation – Short Form (DERS-SF (64)), indicated by a Strategies subscale score of ≥ 3; Non-Acceptance subscale score of ≥ 3; Impulse subscale score of ≥ 2.5; Goals subscale score of ≥ 3.5; Awareness subscale score of ≥ 3.5; or Clarity subscale score of ≥ 3 c) presence of hypomanic symptoms:

Hypomania Checklist-32 (HCL-32 (65)) score of ≥ 14 (66) ; d) reduced functioning: Work an Social Adjustment Scale (WSAS (67)) score of ≥ 10 (68); e) elevated psychological distress: K10 (69) score of ≥20 (70) ; f) currently help-seeking (intentions): seeking or in contact with or referral for professional mental health support.

The duration of the diagnostic interview addressing affective symptoms, psychotic symptoms, schizotypal personality disorder symptoms, borderline personality disorder symptoms, severe mental disorder onset and treatment, and psychosocial functioning is expected to take between 1-2 hours to administer in the inception cohort arm and between 1-3 hours in the incidence arm. Interviews can take place on site or online via an encrypted video conferencing system. Following the interview, participants receive a link to complete a set of self-report measures (approximate duration: 90-120 minutes). For a comprehensive list of measures used, see Table 2. All participants eligible for the inception cohort arm will be invited to complete assessments at 6-month, and 12-month follow-up, and some participants, who are included in the study in the first years of the study period at 18-month and 24-month follow-up. Methods to reduce attrition include reminders, update and thank-you emails, and additional compensation for participation in 18- and 24 month follow-ups. See Figure 2 for the participant flow chart.

Table 2. *Measures*

	Instrument	**Construct**	**Timepoint**	
			t_0	t_1 - t_4
Sociodemographic				
self-report				
	Client Service Receipt Inventory (CSRI) – modified (71), including Maudsley Environmental Risk Score (72)	- age - sex - gender - city district of Mannheim	x	x (only changeable characteristics at follow-ups)

		- height - weight - ethnicity - citizenship - migration history (up to the 3rd generation, country of birth, country of birth of migrated parents, age at migration) - birth weight - paternal age (at birth) - urbanicity - mother tongue - religion - education (years, highest, current) - living situation - children - employment - financial situation - income - recent serious physical illness - physical disability - political orientation - sexual orientation		

	McArthur Scale (73)	- subjective social status	x	x
	Familial risk, adapted from (74)	mental disorder, drug use problem or suicide type of disorder and certainty with diagnosis (for first-degree relatives)	x	x
Mental health, cognition and behavior				
interview				
	SCID-5-CV (75)	section A-D: affective and psychotic disorders, differential diagnosis	x	x
	SCID-5-PD (76)	Schizotypal personality disorder, borderline personality disorder	x	x
	OPCRIT-4 checklist (77), adapted for DSM-5 (incidence arm)*	appearance and behavior, speech and form of thought, affect and associated features, abnormal beliefs and ideas, abnormal perceptions	x	x
	Comprehensive Assessment of At-Risk	dimensional assessment of at-risk mental state: unusual	x	x

	Mental States (CAARMS) (78)	thought content, non-bizarre ideas, perceptual abnormalities, disorganized speech		
	Quick Inventory of Depressive Symptomatology – Clinician Rated QIDS-C (79)	depressive symptom severity	x	x
	Affective Disorders Evaluation (ADE) (80,81)	cyclothymia	x	x (for past 6 months)
	Social and occupational functioning assessment scale (SOFAS) (82)	social and occupational functioning	x	x
self-report				
	Hierarchical taxonomy of psychopathology (HiTOP) (83)	multidimensional assessment of mental health problems (excl. questions on sexual dysfunctions, risky sex, sexual drug use for participants < age 18)	x	x
	Psychiatric medication (71)	type, name	x	x
	Kessler Distress Scale (69)	anxious and depressive symptoms	x	x
	Prodromal Questionnaire (PQ-16) (62)	psychotic-like experiences	x	x

	Hypomania Checklist 32 (HCL-32) (65)	history of hypomanic symptoms	x	x
	Difficulties in Emotion Regulation Scale - Short Form (DERS-SF) (64)	emotion dysregulation	x	x
	Cognitive Emotional Regulation Questionnaire (CERQ) (84)	adaptive and maladaptive emotion regulation strategies	x	x
	Personality Inventory for DSM-5- Brief Form Plus (PID-5-BF+) (85)	maladaptive traits / AMPD Criterion B	x	x
	Level of Personality Functioning Scale-Brief Form 2.0 (LPFS-BF 2.0) (86)	personality dysfunction / AMPD Criterion A	x	x
	Climate Change Distress and Impairment Scale (CC-DIS) (87)	climate change-related distress and impairment	x	x
	Work and Social Adjustment Scale (WSAS) (68)	functional impairment	x	x
	Three-Item Loneliness Scale (88)	loneliness	x	x
	Pro-Environmental Behaviours (PEB) Measure; based on (89)	personal and collective pro-environmental behavior	x	x
	Multidimensional Scale of Perceived Social Support (F-sozU) (90)	perceived social support	x	x

	General Self Efficacy Scale (GSE) (50)	self-efficacy	x	x
	Warwick-Edinburgh Mental Well-being Scale (WEMWBS) (91)	mental well-being	x	x
	MyLifeTracker (92)	quality of life	x	x
	World Health Organization Quality of Life (WHO-QoLBref) (93)	quality of life	x	x
	Subjective Happiness Scale (SHS) (94)	happiness	x	x
	Connor-Davidson Resilience Scale (CD-RISC) (48)	resilience	x	x
Help-seeking and service use				
interview				
	Nottingham Onset Schedule (NOS) – modified; adapted from (95)	onset of symptoms and treatment	x	x
self-report				
	Pathways to Care; based on (96)	sequence and points of professional contact during help-seeking	x	x
	Current help-seeking (self-created)	current help-seeking status (current use, currently seeking, received	x	x

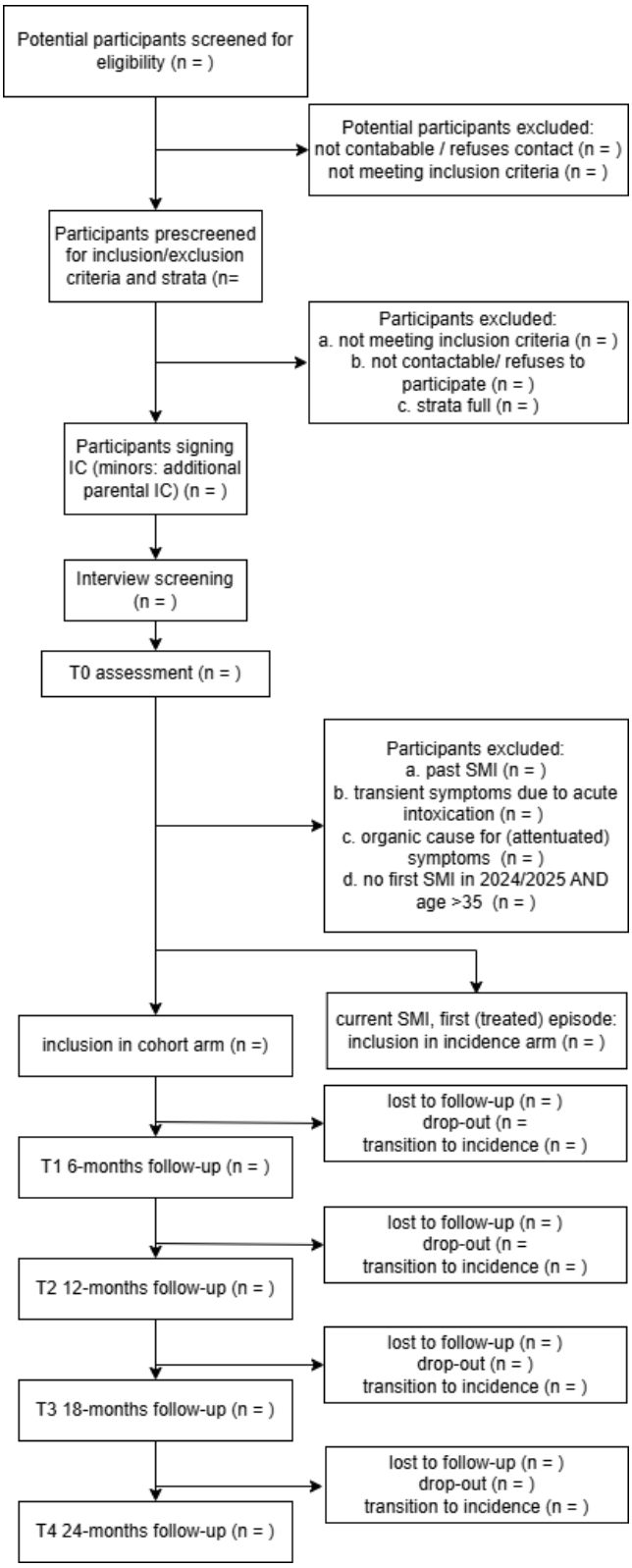
		recommendation, no use)		
	Trust in mental health professionals and science (97)	trust in (mental) health professionals, confidence in importance of science in treatment of mental health problems	x	x
	Client Service Receipt Inventory (CSRI) – modified (71)	health insurance psychological treatment service usage of outpatient, inpatient, partly inpatient and complementary health services	x	x
	Barriers to Access to Care Evaluation (BACE) (98)	barriers to access to mental health care	x	x
	General Help Seeking Questionnaire (GHSQ) (99)	help-seeking intentions	x	x
	Attitudes Toward Seeking Professional Psychological Help - Revised (ATSPPH-SF) (100)	openness to seeking professional help subscale	x	x
Environmental exposures				
	Childhood trauma questionnaire (CTQ) (101)	childhood experiences of abuse and neglect	x	x (for participants < age 18)

	Retrospective Bullying Questionnaire; based on (102), modified in EU-GEI (103)	Childhood bullying experiences	x	x (for participants < age 18)
	Major Experiences of Discrimination (104)	Perceived unfair treatment in legal, public, and professional life areas based on demographic and identity factors	x	x
	Everyday Discrimination Scale (104)	Everyday discrimination experience	x	x
	Life Transitions (self-created)	Positive and negative life transitions	x	x
	Transitional Impact Scale (TIS-12) (105)	material and psychological impact of life transitions	x	x
	HITOP-SUD (substance use module) (106)	abuse of and substance use disorder symptoms involving alcohol, cannabis, nicotine, cocaine, prescription stimulants, methamphetamine, inhalants, tranquilizers,	x	x

		hallucinogetics, opioids, other drugs		
EMA				
		affect	x	x
		company	x	x
		activity	x	x
		positive and negative event intensity	x	x
		appraisal of interpersonal interaction, interpersonal theory, mentalizing**	x	x
	CC-DIS, short and adapted from (87)	climate change distress, pro-environmental behavior, climate-related events**	x	x
		national identity	x	x

Note. *OPCRIT checklist-based items are included in the interview as well as the case note evaluation of the incidence arm of the study. **Interpersonal EMA and climate change EMA elements are randomized to participants at a 50:50 ratio. Supplement Table S1 provides an overview and of the language versions used for German-, English-, Turkish-, Russian, and Ukrainian-speaking participants.

Figure 2. *Participant flowchart*



492

493

494 ***Retrospective case record evaluation***

495 Retrospective case record evaluation is conducted on clinical case notes from mental health

496 services. Specifically, clinical case notes are retrospectively screened on a regular basis for

patients admitted between 01/2024 and 02/2026 and evaluated for meeting criteria for (treated) incidence during the case ascertainment period (1 January 2024 to 31 December 2025) by trained research staff. The Operation CRITeria checklist (OPCRIT) (107) items will be used to complete a case note evaluation procedure to assess affective and psychotic symptoms (appearance and behavior, speech and form of thought, affect and associated features, abnormal beliefs and ideas, abnormal perceptions). Adapting the evaluation procedure to reflect DSM-5 diagnoses, items on the duration of symptoms and the link between symptom onset and substance use were added to the original OPCRIT item set and symptoms were rated on a yes (+) or no (-) scale to apply an algorithm extracting accurate DSM-5 diagnoses from case records. The nine SCID-5-PD items for BPD are entered to extract BPD diagnoses if five or more criteria were confirmed. Clinical diagnoses are entered and cross-checked with OPCRIT checklist-based/SCID-5-PD generated diagnoses. In case of discrepancies, the OPCRIT checklist-based/SCID-5-PD generated diagnoses will be used. In case OPCRIT checklist-based/SCID-5-PD applied algorithms do not supply a diagnosis, the clinical diagnosis is used, and this is flagged in the data set in order to enable sensitivity analyses. To evaluate whether the respective severe mental disorder was incident in 2024-2025, onset and prior guideline treatment of the diagnosis are evaluated using an adapted version the Nottingham Onset Schedule (95). Supplement Table S2 shows the definitions of guideline treatment for the diagnostic groups in this study. Based on available information in the case records, the trained researchers classify cases with one of the target severe mental disorders as “definitely not incident” (if prior contact for guideline-based treatment of the same diagnoses was documented), “unsure – insufficient information on treatment history”, “definitely incident” (if first manifestation or first contact for guideline-based treatment of the severe mental disorder was documented by clinicians), or “not to be classified – insufficient clinical and diagnostic information/data available”. Training of staff includes participation in a training session on OPCRIT items, DSM-5 criteria for respective diagnoses of severe mental disorder, an internal manual on conducting and documenting the case note evaluation, and regular consensus meetings.

EMA allocation and sampling

All participants are asked to complete EMA using our established and validated EMA protocol (52). Participants are asked to complete EMA at each time point (i.e., at baseline plus at least two follow-up time points). This study uses a hybrid time- and event-contingent EMA design. In the time-contingent design component with a blocked (semi-)random time schedule, the EMA includes eight assessments per day for six days, with EMA prompts being scheduled at semi-random time points within pre-defined blocks to ensure time is evenly sampled throughout the day. Participants can define the daily time frame within which they are willing to complete EMA prompts. Participants receive an alarm (sound and/or vibration) to complete the EMA. A window is scheduled between prompts, ensuring there are at least 30 minutes between consecutive EMA prompts. Participants have 20 minutes to respond to a prompt. Participants are block-randomized at a 1:1 ratio (using blocks of 10) to receive either the *climate change distress* (n=120) or *interpersonal experience* (n=120) EMA version. The *climate change distress* EMA includes 33-45 items and the *interpersonal experience* EMA includes 21-39 items (depending on response patterns in the branching of items). In each version, an event-contingent design component is included, with participants being able to self-initiate an EMA in case something in their life reminded them of climate change (*climate change distress* EMA) or they experienced an interpersonal interaction (*interpersonal experience* EMA). In the inception cohort arm, participants receive the same EMA version at follow-up as at baseline.

Leakage study

Quantitative: The inception cohort study arm will allow us to identify incident cases not identified in our case ascertainment procedures. Case records of potential incident cases classified during the first case record evaluation as “unsure – insufficient information on treatment history” or “not to be classified – insufficient information on diagnostic process” will be followed up at the end of the case ascertainment period to include potential new information from additional contacts with mental health services.

Qualitative: In order to identify sources of biases in recruitment and case ascertainment procedures, and ultimately, incident rates, a qualitative leakage study will be carried out. Specialised and non-specialized treating clinicians (GPs, psychiatrists, clinical psychologists and other mental health professionals from inpatient and outpatient services) as well as individuals with severe mental disorder will be interviewed to understand the social, economic and cultural contexts of individuals with an untreated severe mental disorder, barriers to accessing care, and factors associated with a long duration of untreated illness. Interviews will especially address social, economic, and cultural determinants.

Sample size rationale

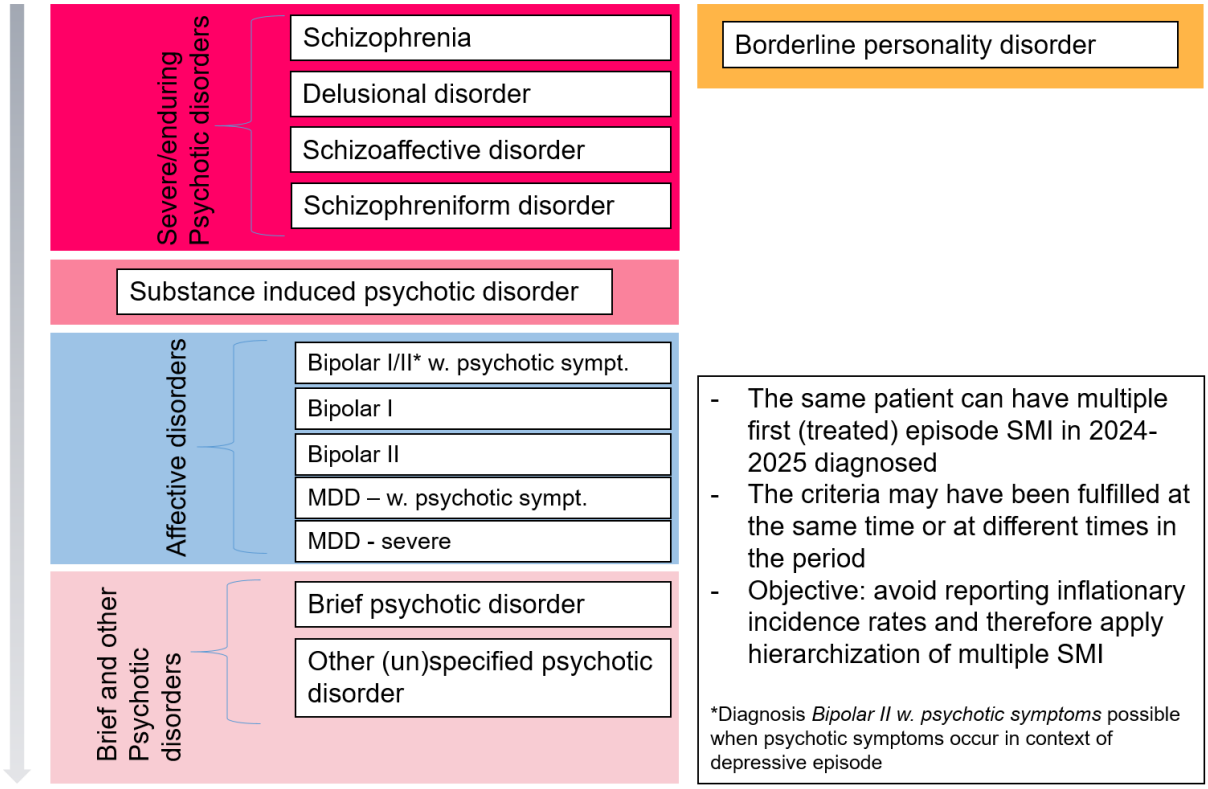
The incidence arm of this study is primarily powered to examine variation in the incidence of severe mental disorders by important demographic characteristics using Poisson regression (H1.1). Sample size calculation was conducted to examine the capacity of our sample size to detect a small effect size of an incidence rate ratio (IRR) of ~1.5 (i.e., an IRR previously reported for the elevated rates of psychosis in migrant/ethnic minority groups, an incidence rate under standard risk conditions of 21.4 per 100,000 person-years (108), and the proportion of participants with migrant/ethnic group minority status of 18.4%, which yielded a required sample size of n=152, with a power of 80% when testing at 1-sided level $\alpha = 0.05$. All else being equal, we found that, using the same statistical procedure, the anticipated sample size of 340 incident cases is sufficient for detecting an even smaller IRR of 1.30 with the same power (even though meta-analytic evidence suggests larger effect sizes for migrant/ethnic minority groups (IRRs of 2.1 to 5.6; (14,24) and urban areas (IRRs of 2.1; (72)).

Sample size calculation for the inception cohort arm was conducted to assess the capacity of our sample size to test our hypotheses on rates from earlier to later stages. Specifically, sample size calculation on the accuracy of the estimates to be obtained for transition rates from a given clinical stage at baseline, with transition from stage 1a to any later clinical stage (i.e., stage 1b, stage 2) as primary outcome (H2.1) showed that, assuming a probability of 0.355 for observing a transition event at 12-month follow-up (as previously reported for individuals transitioning

580 from stage 1a to stage 1b (40)) and allowing for an attrition rate of 20% at 12-month follow-up,
581 the ratio of confidence limits to λ, 1.6 as a fairly strict requirement can be met with the target
582 sample size of n = 160 individuals in stage 1a at baseline. Sample size calculation for
583 comparing a subpopulation with standard transition risk (∏ 0), and the subpopulation at
584 increased risk for transition due to exposure to a risk factor ∏1) further indicated that, based
585 on a transition probability of 0.355 during (t_0, t_2), and applying Schoenfeld's (109) sample size
586 formula, even a small effect of HR=1.60 (i.e., smaller than previously reported for, e.g.,
587 migrant/ethnic minority group status, for which a larger HR of around 2.6 can be assumed for
588 stage transitions (110)) can be detected with the target sample size of n=320 (as will be reached
589 jointly for stage 0 and stage 1a) with a power of 80% when testing at α = 0.05 (H2.2). This
590 holds a fortiori true for a log-rank test of the (alternative) hypothesis that transition rates from
591 stages 1a to any later (stage 1b or 2) is larger than that from stage 0 to any later stage (stage
592 1a, 1b, or 2) (H2.1).
593
594 **Statistical Analysis**
595 ***Treated incidence of severe mental disorder***
596 The primary diagnosis of severe mental disorder will be obtained via three routes for
597 participants to be included in the incidence analysis. For incident cases identified based on
598 clinical assessment via structured clinical interview, the primary diagnosis will be based on the
599 SCID-5-CV/PD interviews and, where required, validated further based on case records. For
600 incident cases identified via case record evaluation, the primary diagnosis will be based on the
601 case note evaluation using the OPCRIT checklist. If this procedure does not yield a diagnosis,
602 but the clinical diagnosis matches inclusion criteria, it will be entered as the primary diagnosis
603 for sensitivity analyses. While all psychotic disorders will be handled as mutually exclusive and
604 major depressive disorder and bipolar disorder are mutually exclusive, cases could be incident
605 for more than one severe mental disorder during the case ascertainment period. For primary
606 incidence analyses, we will apply a hierarchy of a primary incidence diagnosis of affective and
607 psychotic disorder (see Figure 3), and count each individual with multiple diagnoses only within

their primary incidence diagnosis in order to prevent inflated estimates of incidence rates due to errors and uncertainties in differential diagnosis. A primary incidence of borderline personality disorder will always be reported separately from this hierarchy.

Figure 3. *Hierarchy of DSM-5 diagnoses for incident cases of severe mental disorder.*



In the incidence arm, crude incidence rates and 95% confidence intervals (CIs) by age, sex, migrant/ethnic minority group status, and neighbourhood will be estimated and presented per 100,000 person-years. Direct standardization will then be used to compare incidence rates between neighbourhoods and compute age-, sex- and migrant/ethnic minority group-adjusted incidence rates. Rates in each neighbourhood will be standardized using the 2022 census data, stratified by age, sex and migrant/ethnic minority group status. Poisson regression will be conducted to quantify variation in incidence rates by age, sex, urbanicity, and migrant/ethnic minority group status, with random effects to account for the multilevel data structure (H1.1). We will inspect random effects for neighbourhood and their 95% CI of models for psychotic disorders compared to models of other disorders (H1.2a). A categorical variable for diagnostic

group and a diagnostic group × ethnic/migrant minority status will be added to address H1.2b. The commonly observed age × sex interaction will be tested to address H1.3. Further, a two-way interaction effect for individual-level migrant/ethnic minority group status × area-level migrant/ethnic minority density will be fitted to investigate whether, for migrant/ethnic minority groups, rates will be highest in areas where they constitute a small proportion of the local population (H1.4). We will test whether differences between directly observed incidence rates will be statistically significant.

Clinical stage transitions

In the inception cohort arm, we will perform maximum likelihood estimation of hazard rates of exponential distributions under noninformative right censorship (111) to estimate rates of transition from earlier stages to later stages. Post-stratification weights will be implemented to adjust for sample deviations from the Mannheim population on age, sex, and ethnic/migrant minority group status. We will further use Cox regression to test whether rates of transition from earlier to later clinical stages will be greater in individuals in stage 1a than in stage 0 (H2.1), and whether transition rates will be associated with demographic, risk and protective factors (H2.2), while controlling for potential confounders. Testing the regression coefficient for deviation from zero in a Cox model with single dummy covariate is asymptotically equivalent to a log-rank test for differences between two survival functions (with sample size calculations based on the formula by Schoenfeld (109)).

Transdiagnostic stages, dimensions, momentary phenotypes, population mean

Latent class analysis will be used to identify empirically-based clinical stages (i.e., subgroups/latent classes) that account for associations among the observed categorical variables for assessing mental health at baseline (H3.1). We will fit a series of models (in MPlus Version 8) to determine the classification that best represents associations among observed variables. Consistent with the number of hypothesized clinical stages of contemporary staging models, we expect to identify at least four latent classes (i.e., stage 0, 1a, 1b, 2), with the class of no symptoms/well-being separating into at least two additional distinct classes that improve model fit. Latent class membership will be used in subsequent analyses to establish

convergence with contemporary staging models (H3.2). Multidimensional item response modelling will be conducted on observer-rated, self-rated and EMA data on symptoms, well-being and positive mental health (in MPlus Version 8) to examine whether a bifactor model with general and specific factors of transdiagnostic and momentary phenotypes provides the best model fit compared with correlated multidimensional and other alternative item response models. We will use (multilevel) multinomial regression models to investigate whether factor scores for the identified dimensions and momentary phenotypes will be associated with clinical stages at baseline, while controlling for potential confounders (H3.3). Multinomial receiver operating characteristic analysis (112) will be used to investigate whether factor scores allow for accurate classification into clinical stages and establish optimal cut-off values based on sensitivity, specificity and area under the curve. Poisson regression will be conducted to test whether the population mean and distribution (and other measures of central tendency, as appropriate for the distribution) of transdiagnostic dimensions, digital momentary phenotypes, and established measures of mental health will be associated with incidence of severe mental disorder (H3.4). We will carefully examine and model the distribution of mental health data and, based on previous work (21,23), define populations by stratifying our incidence sample according to four a priori selected characteristics (i.e., age, sex, urbanicity, ethnicity) to examine the relationship between population mean and incidence in each of these populations. We will further use Cox regression to test, in our inception cohort sample, stratified according to the same a priori selected characteristics, whether changes in the population mean (in transdiagnostic dimensions, digital momentary phenotypes, and established measures) predict an increased risk for transition from earlier to later clinical stages in each population (H3.5).

Research governance

The Central Institute of Mental Health is the sponsor of this incidence and inception cohort study. The study has received ethical approval from the local ethics committee (Medical Faculty Mannheim, Heidelberg University, 585-21). Amendments to the study protocol will be

submitted to the local ethics committee for approval and communicated to relevant parties (e.g., steering committee). The steering committee consists of clinicians in relevant services in Mannheim, a statistician, and representatives of local organisations for important and hard-to-reach subgroups of the Mannheim population, such as representatives of social services, food banks, or Muslim pastoral care and counselling. The role of the steering committee is to 1) advice on the science of the study, 2) advise on strategies for public and stakeholder engagement, dissemination and impact, 3) advise on ethical issues, 4) advise on practical issues of study conduct, 5) monitor progress of the study against the stated objectives and a specified timeline, 6) advice on addition of sub-studies, and 7) advise on any other matters raised by the study team, e.g. adverse events. Research data will be handled in compliance with the German and European Data Protection Regulation (GDPR). Data will be stored securely and pseudonymised, i.e., research data will be stored using a number code. Personal data will be kept separately from pseudonymized data. Participants who withdraw from the study can determine whether data collected up to the end of participation can be processed or should be destroyed. The principle investigator (PI) has overall responsibility for the trial. The study coordinator and research team are responsible for day-to-day management of the trial, monitoring trial progress (recruitment, assessment, training delivery), and preparation of reports to the steering committee and ethics committee.

Results

Study progress

Recruitment for the incident arm started on January 1st 2024. Active recruitment for the inception cohort arm started on February 1st 2024. The first assessments at 6-month follow up (t_1) were completed in August 2024 and the first assessments at 12-month follow-up (t_2) in February 2025.

Discussion

Monitoring of population mental health is a central aspect of health, risk and protective factor and demographic surveillance systems across the globe. Adopting a public mental health perspective on monitoring and surveillance requires us to consider the entire spectrum of mental health. While this population mental health approach has become an integral part of public mental health provision in many European countries, research on this issue in Germany remains very limited. Also, fundamental conceptual and methodological issues need to be addressed and evidence on validity (and ultimately, utility) of dimensional and clinical staging approaches generated to provide an integrated approach for monitoring population mental health optimally efficient way that can be adapted and applied elsewhere and tackle the pressing public mental health challenges of our times at both the national and international level.

The current two-arm incidence and inception cohort study will move beyond previous research by allowing us to examine fundamental conceptual and methodological issues in contemporary public mental health and establish the nationwide feasibility of design and methods for more comprehensive monitoring of population mental health. To achieve this, a combined, two-arm incidence and inception cohort study reflects the optimal design in terms of both efficiency and capacity for delineating the basic epidemiology of population mental health. Given the variation in neighbourhood characteristics and migrant and ethnic minority populations in the city of Mannheim, the methodology will offer a unique population laboratory to study variation in incidence and clinical stage transitions in terms of place and ethnicity with high external validity. This design will allow for re-establishing the basic epidemiology of severe mental disorders for the first time in over 20 years in Germany. Specifically, this study will generate evidence on the treated incidence of severe mental disorder by important sociodemographic characteristics based on primary data in Germany, while, at the same time, considering and investigating, in detail, the interface between incidence of severe mental disorder, contemporary transdiagnostic clinical staging models, dimensional representations of psychopathology (i.e., HiTOP) and positive mental health, across the entire spectrum of mental health and well-being.

While sampling by clinical stages initially adopts a categorical approach, all individuals along the continuum of mental health (from asymptomatic to severe mental disorder) are included in the current study and carefully characterized using established measures of clinical staging and dimensional approaches. Ultimately, empirically delineating clinical categories (such as stages) with clinical utility from transdiagnostic dimensional measures of mental (ill-)health will benefit clinical and preventative decision making as well as mental health surveillance in the public mental health field.

Social and ethnic inequities in mental health play an important role and have been delineated, for example, in the inequality paradox (16) for a long time; however, robust and appropriate evidence to empirically identify its driving factors remains limited. We are taking critical steps to capture the diversity of the population and to enable and increase participation of individuals and groups who may be vulnerable, marginalized and hard-to-reach due to structural and contextual factors, and who are often underrepresented in mental health research (113–115). First, given risk and protective factors, as well as access to and help-seeking from mental health services may differ for individuals with and without knowledge of German language, the present study implements multi-language assessment and relies on a multi-lingual and multicultural team. Second, we actively involve local stakeholders and relevant organisations in contact with residents in potentially vulnerable or marginalized positions due to structural and contextual factors that are still far too often not included in research despite forming a critical part of the population, such as migrant and ethnic minority groups or people currently living in poverty. To engage communities and create mutually beneficial collaborations, mental health professionals from our research team offer activities such as conversation groups or lectures about mental health topics relevant to the specific community. Including these organisations' representatives, we ultimately aim to conduct research jointly with, rather than only about, these populations and communities. In addition, the option to participate remotely in assessments via online video call and database systems reduces barriers for participation.

Taken together, by combining categorical, clinical staging, and dimensional approaches to mental health and well-being, promoting community engagement, and reducing barriers to participation, the current incidence and inception cohort study seeks to address several aspects crucial in putative pathways to social and ethnic inequities in mental health (17). Examining incidence of severe mental illness, along with barriers to access appropriate mental health care, we seek to provide an evidence base for planning of mental health services and reduction of barriers. We will carefully evaluate the feasibility of the proposed methodology and its potential to be extended to large-scale investigations including nation-wide monitoring of population mental health, as a basis for establishing comprehensive surveillance systems and, thereby, contribute to laying the ground for assessing the impact of novel public mental health interventions and services at the population level.

List of abbreviations

ADE: Affective disorders evaluation.

ATSPPH-SF: Attitudes toward seeking professional psychological help – short form.

BACE: Barriers to access to care evaluation.

CAARMS: Comprehensive assessment of at-risk mental states.

CC-DIS: Climate change distress and impairment scale.

CD-RISC: Connor-Davidson resilience scale.

CERQ: Cognitive emotion regulation questionnaire.

CHARMS: Clinical high at-risk mental state.

CHR-P: Clinical high-risk state for psychosis.

CSRI: Client service receipt inventory.

CTQ: Childhood trauma questionnaire.

DERS-SF: Difficulties in emotion regulation scale – short form.

DSM-5: Diagnostic and statistical manual of mental disorders, fifth edition.

EMA: Ecological momentary assessment.

F-sozU: Fragebogen zur sozialen Unterstützung / Social support questionnaire.

GDPR: General data protection regulation.

GHSQ: General help seeking questionnaire.

GSE: General self-efficacy scale.

HCL-32: Hypomania checklist 32.

HiTOP: Hierarchical taxonomy of psychopathology.

ICD-10: International statistical classification of diseases and related health problems.

IRR: Incidence rate ratio.

LPFS-BF 2.0: Level of personality functioning scale – brief form 2.0.

MAKO: Mannheim incidence and inception cohort study.

NOS: Nottingham onset schedule.

OPCRIT-4: Operational criteria checklist for psychotic and affective disorders.

PEB: Pro-environmental behaviours measure.

PID-5-BF+: Personality inventory for DSM-5 – brief form plus.

PQ-16: Prodromal questionnaire 16.

QIDS-C: Quick inventory of depressive symptomatology – clinician rated.

SCID-5-CV: Structured clinical interview for DSM-5 - clinician version.

SCID-5-PD: Structured clinical interview for DSM-5 - personality disorders.

SHS: Subjective happiness scale.

SOFAS: Social and occupational functioning assessment scale.

WEMWBS: Warwick-Edinburgh mental well-being scale.

WHOQOL-BREF: World Health Organization quality of life – brief version

WSAS: Work and social adjustment scale.

Declarations

Ethics approval and consent to participate: The study has received ethical approval from the local ethics committee (Medical Faculty Mannheim, Heidelberg University, 585-21) and is conducted in accordance with the Declaration of Helsinki. All participants (and in case of minors, their legal guardians) sign informed written consent.

Consent for publication: not applicable

Availability of data and materials: The datasets generated during the current study will be available from the corresponding author on reasonable request.

Competing interests: The authors declare that they have no competing interests

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