

## Research Project

# What Protects Patients at Risk for Psychosis? A Long-Term Follow-up Study

### Third-party funded project

**Project title** What Protects Patients at Risk for Psychosis? A Long-Term Follow-up Study

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Background: Previous research on early stages of psychosis has mainly focused on determining the risk of developing full-blown psychosis in at-risk mental state (ARMS) individuals and predicting the transition to psychosis. However, relatively few information is available on the disease trajectories in ARMS individuals not developing psychosis (so called false positives or ARMS-Non-Transition [ARMS-NT]) even though such individuals usually make up the largest part of ARMS samples. Furthermore, there have been very heated debates about potentially harming those who were falsely identified as having a risk, mainly by stigmatization. Objectives: The primary aim of the proposed study is to investigate the long-term outcome of ARMS individuals that were originally identified as being at risk for psychosis in the Früherkennung von Psychosen (FePsy) project and the Bruderholz study (BHS), but did not develop frank psychosis during the initial follow-up periods of these research projects. We are specifically interested in rates of remission from ARMS and in identifying resilience factors predicting remission from ARMS. Secondary aims of the proposed study are a) to investigate longitudinal changes in psychopathology, psychosocial functioning, brain structure, and neurocognition, including the interdependencies of these changes; b) to study the development of other psychiatric diseases over time; and c) to find out about individuals' experience of being informed of having a risk for psychosis and potential consequences, such as stigmatization. Hypotheses: Primary hypotheses: -ARMS individuals who did not develop frank psychosis during the first follow-up period of the above named projects can be divided into three outcome groups a) those that have remitted from their risk state (ARMS-R), b) those who suffer from a persisting at-risk mental state (ARMS-P), and c) those with a very late transition to psychosis (ARMS-T). Based on previous studies [2-4], we expect the latter group to be only small and the ARMS-R and ARMS-P groups about equal in size. -The likelihood of having a remission from an ARMS is predicted by demographic variables (such as age and gender), illness factors at baseline (such as less severe psychopathology, cognitive and functional impairment, and brain structural changes), but also by resilience and protective factors during follow-up (such as good coping and social support, adherence to treatment, and lack of drug abuse). Secondary hypotheses: -Remission from ARMS psychopathology is associated with improvements of neurocognition and social functioning. -Preservation of brain structure over time (i.e. no loss of grey matter volume) is associated with a better course regarding psychopathology, neurocognition and social functioning. -Some patients have developed other psychiatric disorders (apart from ARMS or psychosis) -Being educated about having a risk for psychosis and getting help is experienced by most ARMS individuals as more helpful than harmful. Design and Methods: Study

sample: In this long term follow-up study, we will examine individuals with an ARMS for psychosis, who have originally been identified within the FePsy project in Basel from March 2000 to February 2012 (n = 118) and within BHS study in the canton of Baselland from January 2003 to December 2006 (n = 99). During the first short follow-up periods, 30 and 10 of the ARMS individuals developed frank psychosis in the FePsy and BHS studies, respectively. All other ARMS individuals, i.e. those without transition to psychosis or those lost during the first follow-up periods, will be asked to take part (n = 177). They will be assessed regarding the following outcome measures: -Primary outcome: remission from ARMS, including time to remission -Secondary outcomes: a) neurocognition; b) structural MRI; c) general, social and occupational functioning; d) DSM-IV axis I diagnoses; e) patients' subjective experience of being informed to have a risk for psychosis and of potential stigmatization. Apart from self-report and observer ratings, patient records (case notes etc.) of the period concerned will be collected. Statistical analyses: The obtained data will be analyzed in cross-sectional analyses and in combination with existing data in longitudinal and time-to-event analyses. For prediction of time to remission/transition, we will use a proportional cause-specific hazards model, as well as automated pattern recognition methods, such as random survival forest. Expected value of the project: To the best of our knowledge, this is the first study on ARMS-individuals who do not make a transition to psychosis (ARMS-NT) within a short period with a) a follow up period of up to 14 years b) a multi-domain assessment and at the same time c) investigation about individuals' subjective experience of being informed about their risk and potential stigmatization.

**Keywords** schizophrenia, ultra-high risk (UHR), risk factors, resilience, neurocognition, long-term follow-up, psychosis, stigmatization, psychopathology, protective factors, neuroimaging, at-risk mental state (ARMS)

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