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**Early intervention services in psychosis:  
from evidence to wide implementation**

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## Title page

# Early Intervention services in psychosis: from evidence to wide implementation

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Running title:

From evidence to wide implementation

## **Abstract and keywords**

### **Abstract**

#### Aim

Early intervention (EI) in psychosis is a comprehensive and evidence-based approach aimed at detection and treatment of psychotic symptoms in their early stages. This paper presents core features and noteworthy aspects of the evidence basis and limitations of EI, the importance of program fidelity, challenges for its widespread dissemination, and economic perspectives related to it.

#### Methods

This paper is a narrative review about the evidence supporting EI and the challenges to its widespread dissemination.

#### Results

In spite of evidence of a wide range of benefits, widespread dissemination has been slow, and even currently implemented programmes might be threatened. This reflects in part the shortcomings of mental healthcare in general, such as low priority for funding, stigma and structural problems. Successful examples of advocacy, mobilisation and destigmatisation campaigns have overcome these difficulties.

#### Conclusions

Funding for mental health in general and for EI services appears low relative to need. One key argument for better funding for EI can be found in its favourable cost-effectiveness, but not all stakeholders beyond mental health administrators are aware of this. Positive impacts of EI programmes on excess unemployment and tax forgone suggest that social affairs and labour ministries – and not only health ministries – could be more involved in governance of mental health issues; ministries of justice and education are other sector stakeholders than can benefit. Wider dissemination of EI services will probably benefit from better integration of potential funders, promotion of joint targets and shared financial or budgetary incentives.

#### Key words:

Early intervention in psychosis; evidence-based medicine; health planning; implementation; psychiatric services

## Introduction

Early intervention (EI) in psychosis is a comprehensive and evidence-based approach aimed at detection and treatment of psychotic symptoms in their early stages, in order to reduce the long-term adverse impact of psychosis and prevent relapses. It focuses on people with ultra-high risk for psychosis and those with initial psychotic symptoms; it relies on the concept of clinical staging of psychosis – which states that early and milder clinical phenomena differ from those that accompany illness extension, progression and chronicity <sup>1</sup>.

EI programmes have originated out of research showing convincing evidence of association between shorter duration of untreated psychosis (DUP) and benefit on relevant outcomes at 12 months, including positive and negative symptoms, depression, anxiety, overall functioning, and social functioning <sup>2</sup>.

At the core of EI services is the concept of specialized assertive teams, in which staff members have a reduced caseload compared to conventional mental health services <sup>3</sup>. These teams are usually multidisciplinary and can include psychiatrists, psychiatric nurses, psychologists, social workers, occupational therapists and employment support specialists, among others. Clinical management is not restricted to pharmacological intervention, and other areas are likewise prioritised, including interpersonal problems, social skills, vocational and educational issues, functional recovery, substance abuse, suicidal ideation, and financial problems. Family relatives and people close to the patients are generally encouraged to be involved in programmes. Teams exert assertive outreach by promoting contact with the patient not only at the team offices but also in community settings and patients' homes, and often outside working hours.

Besides this set of characteristic elements, EI services relate to external factors in specific ways. They usually have limited catchment areas, where different local agencies such as primary and secondary health care professionals, schools and the police are encouraged to make direct referrals <sup>4</sup>. Community awareness and education of local stakeholders in the health care system and other services relevant to the mental health of young people are often other core elements of EI services <sup>5</sup>.

Clinically, EI services have shown that it is possible to shorten untreated psychosis, and that some positive effects, for instance on employment participation, have persisted for at least 10 years <sup>6</sup>. Some of the earliest results have shown that EI services are superior to standard care. The Lambeth Early Onset trial, for example, reduced the number of readmissions in psychiatric wards as well as dropout rates significantly <sup>7</sup>. Besides reducing hospitalisation, including bed days, and increasing retention in care, EI services have also been shown to improve social functioning <sup>8</sup> and user satisfaction <sup>3</sup>.

These robust results were also seen in OPUS, a Danish trial identified as the largest and highest quality randomised study by the authors of a systematic review of the scientific

literature, published in 2011 in the Cochrane Library<sup>9</sup>. OPUS compared EI with standard care and showed positive effects not only on psychotic symptoms, but also on incapacitating negative symptoms, such as emotional blunting, lack of drive, inability to experience pleasure, and social withdrawal, among others<sup>10,11</sup>. Significant effects were also seen regarding substance abuse and reduced burden of illness experienced by family members<sup>12</sup>.

The OPUS trial showed not only the benefit of EI and its core elements – it demonstrated also an incremental improvement in a health system that already had a good standard of care. The existing literature is in line with this. Thus, a Cochrane review that showed the superiority of intensive case management for severe mental illness as compared to standard care included 38 studies – all from developed countries<sup>8</sup>. Another systematic review that showed the benefit of a reduced DUP included 26 studies with a total of 5000 patients – only 3 (with around 200 patients) were from developing countries<sup>2</sup>.

All identified core elements of EI seem to contribute to these positive effects. In Hong Kong, enormous efforts to enhance public awareness were undertaken in combination with implementation of EI services. During the period from 2000 to 2010, EI was associated with decreases of up to two thirds in the duration of untreated psychosis, particularly among patients who were expected to benefit from a higher level of awareness in the general population (and thus better early detection and referral): patients with gradual onset of symptoms, patients without family experience of psychosis, and adult patients, suggesting that public awareness actions reduced the duration of untreated psychosis in groups previously suffering from the longest delay<sup>13,14</sup>.

Not only people who already have symptoms benefit from EI programs. Focus on people at ultra-high risk has been associated with fewer admissions to hospital, less compulsory treatment<sup>15</sup>, and a reduction of the period of untreated psychosis to 11 days<sup>16</sup>.

But evidence of the benefit of EI services is not yet conclusive. Beneficial effects on symptoms and function seen after two years of specialized and intensive services in the OPUS trial, for example, were not sustained after five years (i.e. after three years of standard treatment)<sup>17</sup>. It is unknown whether the desired effects on symptoms and function require on-going EI services; or whether a two-year EI program, as it was offered in that particular program, was too short. On the other hand, an EI program from Canada suggests that a five-year program might have long-lasting effects<sup>18</sup>. Researchers are actively investigating this question, and results from on-going trials are expected to help determine optimal duration of services<sup>19,20</sup>. It is necessary not only to understand the impact of the ingredients of early intervention, but also to reappraise the elements of the standard care to which patients are transferred to after EI<sup>21</sup>. This is especially important in developing countries, where constraints in manpower, funding and even basic supplies affect standard care<sup>22</sup>.

Besides, it is important to adequately evaluate standard care in general – both in rich and developing countries – and to identify the elements of standard care; otherwise there is a

danger that EI programmes will appear more effective than they would otherwise, where standard care is poorer than should be the case.

The long-term impact on physical health and mortality due to somatic diseases is also unknown. Increased mortality and avoidable ill-health are well known and costly problems among people with psychotic disorders<sup>23,24</sup>, and the impact of EI programmes on these outcomes will take years to be clearly measurable.

Another challenge regards EI services for people at ultra-high risk for psychosis. The risk of conversion to psychosis versus benefit of preventive approaches and the ratio and acceptability of intervention (e.g. antipsychotic vs. psychotherapy as primary intervention) are two issues that show how ethically complex EI can be in such a population<sup>25,26</sup>.

### **Fidelity to EI programmes**

An EI programme will only deliver the expected results if it is actually implemented and conducted as originally designed. To ensure this, EI programmes prioritize what are called fidelity measures: instruments to assess how strictly the delivered program adheres to the proposed model. Adherence to the protocol or programme originally developed means more than only including features that are critical to achieving the intended outcomes; it should also exclude those that would interfere<sup>27</sup>.

Fidelity measures are supported by research evidence showing that best results are actually achieved with the highest levels of fidelity to models<sup>28</sup>.

In Australia, researchers identified core components from the Early Psychosis Prevention and Intervention Centre (EPPIC), which is among the first EI programmes ever implemented, and are using them to form a fidelity measure instrument<sup>29</sup>. This instrument will be applied throughout the country, as the EPPIC model expands.

To ensure best and sustained effect of EI programmes, fidelity measures are not restricted to therapeutic interventions. Essential elements in the Australian model include aspects such as community awareness and ease of access to service – without which patient enrolment would risk being compromised – and continued staff development and training; clinical parameters include case management, medical and psychological treatments, and functional recovery, among others.

The ambitious Recovery After an Initial Schizophrenia Episode: Early Treatment Program (RAISE-ETP), launched in the United States by the National Institute of Mental Health (NIMH), had fidelity measures incorporated in its design from its inception. Fidelity measures in RAISE-ETP include demanding parameters such as “time to first self-reported meeting with a person who helped you get a job in the community or further your education” and “Were you asked to record your symptoms and side effects before you met with your psychiatrist or nurse

practitioner?” Such precisely formulated measures are also intended to ensure another key request from the NIMH: that the program would be capable of being delivered in US settings utilizing current funding mechanisms <sup>30</sup>.

Utility of feasibility measures exceeds ensuring adherence to the proposed EI model and enabling its replication. Since best outcomes are achieved with the highest levels of adherence to models, they can be used as proxy markers of success, and this is particularly useful in programmes aimed at psychosocial and social outcomes, because these typically take a long time to demonstrate effect <sup>27</sup>.

Considerable effort is dedicated to the development of fidelity measures. Instruments are aimed at assessing not only general programme parameters, but also adherence at staff team level and even at individual staff member’s level. Some instruments are formed as a scale, which yields a total score that can be translated into a quantified level of fidelity, such as the OPUS fidelity-scale, from Denmark, and the Calgary Fidelity Scale for First Episode Psychosis Services, from Canada <sup>31</sup>.

### **Dissemination of EI services**

Convincing evidence of effectiveness and methods to ensure fidelity has contributed to the dissemination of EI programmes throughout the world.

Several convergent lines of evidence and theoretical models promoted stakeholders’ synergistic efforts. Ideas of kindling and neural networks were valued by biological psychiatrists; clinical psychologists were interested in theories that trauma might be at the root of psychotic phenomena and that the experience of positive psychotic phenomena is in itself traumatizing; social workers and social scientists were attracted by the model that links longer duration of untreated psychosis to loss of social capital, opportunities and friends, disintegration of families, and social breakdown. Furthermore, concepts of age-appropriate services, recovery and – last but not least – health economics also converged. These stakeholders were agreeing with patients, families, advocacy groups, carers, and policy makers about the importance of early intervention.

In spite of persuasive high-quality evidence, there are still threats to wider dissemination and even continuity of EI programmes. For example, in Japan there are several leading centres of EI research and practice, but most of them are driven by university departments <sup>32</sup>, and this is the reality in most of the world, including most of Europe.

To understand why effective and well-accepted services with a favourable cost-benefit balance are not yet widely implemented throughout the world, it is necessary to acknowledge that EI shares some of the same obstacles that mental health care in general faces. These include low prioritization, stigmatisation, and structural problems, within a context of constrained health system budgets, to name a few.

Expenditure on mental disorders is one of the highest areas of health expenditure, representing between 5% and 18% of all health expenditures for a selection of countries<sup>33</sup>. At first sight these figures might seem adequate, but when the burden of ill mental health care on society is taken into account, the proportion of public expenditure to healthcare is often small. For instance, mental illness is responsible for 23% of England's total burden of disease, but receives 13% of the National Health System health expenditures<sup>33</sup>. Moreover these costs are highly conservative, as they exclude the impacts of avoidable somatic comorbidities.<sup>34</sup>

The problem is exacerbated by the effect of stigmatisation of mental illness. Suppressing stigmatisation requires additional specific resources and well-orchestrated initiatives. For instance, about 15 years ago, the general public in Hong Kong could not differentiate between symptoms of psychosis and symptoms of stress. Efforts to raise awareness about psychosis and facilitate EI led to a series of comprehensive, long-term and focused campaigns that changed the general perception about psychosis; this included changing the Chinese term for psychosis from "serious mental illness" to something that means "thought and perception dysregulation"<sup>35</sup>.

Insufficient recognition of specific needs of patients with early psychosis can be detected even where it is less expected. A survey of 160 psychiatrists in Tokyo suggested that the concept of at-risk mental state and prodromal state might not be widely recognized among Japanese psychiatrists<sup>32</sup>. In line with this, criticism has been made of university training curricula, which rarely include the topic of prevention and early detection of mental disorders<sup>36</sup>.

Structural problems can also represent a big obstacle, as is the case of a mental healthcare system largely based on institutionalised patients. In Japan, for example, where institutionalisation and social isolation of patients with severe mental illness is common, the task of deinstitutionalisation is considered a priority<sup>32</sup>. But deinstitutionalisation might prove challenging in a country with a high reliance on hospital-based psychiatry, and where 90% of psychiatric beds are operated by the private sector<sup>37</sup>. Experience from countries where deinstitutionalisation and implementation of EI services started earlier, as in Denmark, might thus be usefully shared with countries at earlier stages in the deinstitutionalisation process<sup>33</sup>.

The successful case of dissemination of EI in Australia illustrates how early and isolated programmes, with no consistent policy or funding support and led by champions in local areas, can be transformed and expanded by lobbying, national mobilisation, destigmatisation campaigns, and good integration with other sectors. These efforts resulted in the creation of cabinet-level political administration for mental issues and enormous popular support for mental health issues<sup>38</sup>.

In developing countries, challenges to the dissemination of EI are even greater. A recent study identified seven EI services in Latin America, four of which were based inside tertiary hospitals or universities; the authors point that lack of EI services in rural areas or in cities without

universities of tertiary hospitals can be problematic, and collaboration between clinical and research teams is warranted in order to expand EI services in the region<sup>39</sup>.

Even in countries where EI services are relatively well established, such as the UK, there are inequalities in access and referral to these services, as reflected by different pathways to care by different social-economic or ethnic populations<sup>40</sup>.

The path to widespread dissemination and implementation of EI might vary, but always depends on support from health authorities or politicians. In Denmark, robust evidence from the OPUS trial convinced politicians to support the dissemination of EI programmes, and special grants were created. Between 1998 and 2013 the country had a tenfold increase in the numbers of EI teams, though a further increase in 50% is still needed to meet the demand of incident cases<sup>41</sup>.

Finally, dissemination of EI programmes means not only proliferation of EI service locations or teams, but – just as important – continued high level of fidelity. This means not only adherence to the designed model, procedures, and staff training, but also continued funding of all these components.

## Discussion

As the figures from England and the NHS exemplified, there is a known and unquestionable funding gap for mental health services. Even while OECD health budgets are being squeezed, there is a strong case for ensuring adequate mental health service provision, and this may well mean increased funding. Efforts also need to be made to make sure that new, and existing resources, are spent as effectively as possible, delivering the best care and the best outcomes<sup>33</sup>.

There is clearly an economic case for investment in EI. For example, there is a high probability of OPUS being cost-effective, with lower costs and better outcomes, compared to standard treatment; and this analysis does not look into impact on employment or into issues such as education and housing needs<sup>42</sup>. In England, results show that EI costs less than standard care; services for early detection of high risk states cost more in the first 12 months, but by 24 months are already saving money, and cost-savings increase at 36 months, particularly when benefits beyond the health care system are considered<sup>15,43</sup>.

Therefore, arguments for more funding should not be restricted to the positive impact on the mental healthcare system, because this system alone does not benefit from all parts of EI programmes. It is necessary to identify all beneficiaries of the favourable outcomes of EI programmes and make them aware that they are in fact stakeholders. Positive impacts of EI programmes can be measured in terms of a reduction in excess unemployment and lost life opportunities, more people paying tax as a result of completing education and being in employment and potentially a reduction in the costs of managing avoidable physical health problems, to name a few.

Taken together, the effect on these areas represents a huge economic argument. In Japan, a conservative estimate that does not include impacts of poor physical health shows that 72% of costs of schizophrenia fall outside of the health system <sup>44</sup>.

Given the multi-sectorial nature of mental health issues, several ministries at national, regional and local level – including justice, labour, social affairs, housing and education – could be involved in governance for mental health, a healthcare sector that has moved away from the organisational and financial simplicity of a single setting for care delivery. Administrative responsibility for different areas of health and social care is often separate, with different governance and financial structures inhibiting meaningful integration of policies and approaches across fields.

EI is associated with significant net savings per person during a three-year period from improved employment and education outcomes <sup>45</sup>. The challenge here is that the health ministry does not benefit from these outcomes, it is the ministry of labour or of education. Different ways of incentivising sectors to work together to improve service delivery may be considered; these can include shared budgets for specific services or budgetary transfers by the ministry of finance between sectors. Lessons can be drawn from examples of effective approaches to partnership working across sectors in other areas of health policy <sup>46</sup>.

Research results about the impact of EI services on these different stakeholders are starting to accumulate, but more information is needed. Increased integration with other sectors might be part of the solution.

Innovative approaches are needed to assist healthcare planners and help integrate stakeholders. In England and Wales, a state-of-the-art free online tool generates accurate and reliable data on the expected incidence of new, clinically-relevant cases per year of psychotic disorder, thus allowing more effective planning with an appropriate allocation of resources <sup>47</sup>. Ultimately, the widespread implementation of optimised EI programmes is a matter of information transformed into action. Good and complete information – for instance on costs and outcomes – needs to be made available to governments and policy makers. Politicians and civil servants are obvious targets, but it is also about raising awareness more generally of the potential return on investment in services for people with psychosis.

To achieve this, professionals involved in EI should continue building and strengthening domestic and international networks. But, above all, researchers and practitioners have to keep pumping out evidence, and make a convincing story. Researchers have to answer the questions that clinicians and payers actually want to be answered - making the case by *matching what we know to what payers believe can be achieved*.

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