Diverse definitions of the early course of schizophrenia: results of a pragmatic literature review

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BACKGROUND

- Schizophrenia is a chronic, disabling and progressive mental health disorder with symptoms and disease course that vary between patients.1
- Research has suggested that treating patients during the earlier stages of schizophrenia increases the chance of recovery and therefore provides patients with more favourable long-term outcomes.4
- There is therefore an increasing need for consensus regarding definitions of early stage disease.

OBJECTIVES

- This pragmatic literature review aimed to map definitions currently used to describe patients with a recent diagnosis of schizophrenia who are early in the disease course (‘early schizophrenia’), as reported in clinical guidelines and as used in study inclusion criteria.
- Discrepancies in the use of these definitions, potential overlap in their use and the extent to which they can be used interchangeably were also evaluated.

METHODS

- Searches for published studies, clinical trial entries and guidelines were conducted between 1/4/2015 and 21/10/2015 using MEDLINE and EMBASE In-Process (via PubMed), the Australian New Zealand Clinical Trials Registry, ClinicalTrials.gov, the EU Clinical Trials Register, the International Standardised Randomised Controlled Trial Number database, and Google.
- Articles were excluded for inclusion if they included a distinct population of patients with early schizophrenia or discussed definitions of early schizophrenia, and if they had abstracts or full-text articles written in the English language. Case studies were excluded, but there was no other restriction on study design. No limits were applied regarding interventions, comparators or outcomes. So as to focus on recent literature, searches in PubMed were limited to publication on or after 01/01/2005.
- Articles were reviewed against the eligibility criteria by a single reviewer. Where the applicability of the eligibility criteria was unclear, the article was assessed by a second reviewer.
- Information extracted from relevant studies relating to the search objectives was inputted into pre-specified Excel workbooks. Data extraction was performed by a single individual for each included study and any uncertainties were reviewed by a second individual.

RESULTS

- 1,845 articles from MEDLINE/EMBASE In-Process and 656 records from the clinical trial registries were identified and reviewed for relevance. From these records, 470 primary studies used some form of early schizophrenia definition (Table 1).
- A summary of the early schizophrenia terminology used in these studies is provided in Figure 1.

Table 1. Summary of primary studies identified in the review

<table>
<thead>
<tr>
<th>Region</th>
<th>Number of studies</th>
<th>Total number of participants</th>
<th>Publication years</th>
</tr>
</thead>
<tbody>
<tr>
<td>North America</td>
<td>46</td>
<td>4,723</td>
<td>2000-2015</td>
</tr>
<tr>
<td>Europe</td>
<td>177</td>
<td>37,180</td>
<td>2005-2015</td>
</tr>
<tr>
<td>Australia</td>
<td>19</td>
<td>1,484</td>
<td>2005-2015</td>
</tr>
<tr>
<td>Other</td>
<td>106</td>
<td>31,131</td>
<td>2005-2015</td>
</tr>
</tbody>
</table>

CONCLUSIONS

- A wide variety of definitions have been used to identify patients with early schizophrenia, with no apparent consensus.
- First-episode schizophrenia is the most frequently reported terminology in studies of patients with early schizophrenia, in line with the clinical guidelines. When not referring specifically to first-episode patients, ‘recent-onset’ was the next most frequently used term.
- Duration-based definitions most frequently used duration less than 1, 2 or 5 years.
- Better agreement on the definition of early schizophrenia could aid interpretation and comparison of studies in this patient population.

Figure 2. Summary of definition types used in primary studies identified in the literature review

Figure 3. Proportion of studies using single vs. overlapping early schizophrenia definitions, stratified by (A) study location and (B) design (%)

Figure 4. Early schizophrenia definitions used in 10 studies utilizing multi-episode definitions

Figure 5. Disease onset definitions used with duration-based criteria (%)

Figure 6. Distribution of cut-offs used with duration-based criteria, stratified by disease onset definition (%)

REFERENCES

A bibliography of articles included in the review is available on request to the corresponding author.

Disclosures

All and both employees of Lundbeck SAS and H. Lundbeck A/S respectively, JLS and FS are employees of Otsuka Europe and Otsuka Pharmaceutical Development & Commercialization, Inc; respectively. SS is an employee of Costello Medical Consulting Ltd, who was contracted by Lundbeck SAS to support the review.

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