Loss to Outcomes Stakeholder Survey: The LOSS Study

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Background
There is variable attrition from randomized controlled trials (RCTs) evaluating treatments for the people with schizophrenia.

Though most of these studies mention high attrition rates as a weakness, it is unclear at what degree of loss from such studies clinicians, researchers and service users or their carers begin to consider the results meaningless.

Those undertaking systematic reviews do not have empirical data upon which to make decisions regarding the utility of such data as perceived by important stakeholders.

Objectives
To derive estimates for subjectively acceptable attrition rates in schizophrenia drug trials as viewed by three different groups of stakeholders.

Methods
Design - Postal/email survey
Questionnaire - designed with the assistance of all three stakeholders, piloted within these groups, in order to ensure brevity, clarity and relevance.

Sampling frames
- 100 senior psychiatrists (Yorkshire)
- 100 researchers
- 100 service user/carers

The questionnaire was sent by email/post to all the participants. Where there was no response in 5 weeks, reminders were sent.

The questionnaire
Research plays a valuable role in the testing and development of new treatments for mental illness. It is important that we are confident that research results are reliable.

A randomised control trial (RCT) is one of the most common research methods of testing treatments for effectiveness.

Example: 100 people take part in a randomised control trial comparing two drugs for schizophrenia, drug A and drug B. Each participant has a fair chance of being given either drug A or B. The effectiveness of both treatments is compared after a period of time (in this example, 12 weeks).

For a variety of reasons, a number of participants may leave this trial before it is finished. This creates a challenge because there is not a complete set of results to consider when making conclusions and recommendations.

It is important when we look at results from research testing new drug treatments or services for people with mental illness that we can trust that the findings are accurate.

We would like you to consider the following question—there is no right or wrong answer, we would simply like to know your opinion:

How many of the hundred people who started a study would need to finish for you to really trust the results?

0 10 20 30 40 50 60 70 80 90 100

(Please mark a ‘X’ on the line to indicate your opinion)

Results

<table>
<thead>
<tr>
<th></th>
<th>Responses</th>
<th>Follow up necessary for credibility</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinicians</td>
<td>55/128 (43)</td>
<td>75.3 (CI 72-78)</td>
</tr>
<tr>
<td>Researchers</td>
<td>32/100 (32)</td>
<td>76.4 (CI 73-80)</td>
</tr>
<tr>
<td>Carers</td>
<td>81/104 (78)</td>
<td>70.6 (CI 67-74)</td>
</tr>
</tbody>
</table>

Discussion
Many statistical techniques have evolved to attempt to compensate for loss to follow up.

Table 1. Loss from atypicals vs typicals trials

<table>
<thead>
<tr>
<th>RCTs</th>
<th>Lost</th>
<th>Total</th>
<th>% Loss</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clozapine</td>
<td>23</td>
<td>251</td>
<td>15</td>
<td>15-19</td>
</tr>
<tr>
<td>Amisulpride</td>
<td>11</td>
<td>213</td>
<td>28</td>
<td>27-34</td>
</tr>
<tr>
<td>Risperidone</td>
<td>18</td>
<td>901</td>
<td>21</td>
<td>29-31</td>
</tr>
<tr>
<td>Sertrindole</td>
<td>2</td>
<td>164</td>
<td>31</td>
<td>27-35</td>
</tr>
<tr>
<td>Zotepine</td>
<td>7</td>
<td>170</td>
<td>31</td>
<td>31-40</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>6</td>
<td>589</td>
<td>36</td>
<td>34-39</td>
</tr>
<tr>
<td>Olanzapine</td>
<td>14</td>
<td>1264</td>
<td>36</td>
<td>36-39</td>
</tr>
<tr>
<td>Aripiprazole</td>
<td>7</td>
<td>1138</td>
<td>40</td>
<td>38-41</td>
</tr>
<tr>
<td>Ziprasidone</td>
<td>1</td>
<td>46</td>
<td>51</td>
<td>41-61</td>
</tr>
</tbody>
</table>

All such techniques have to fabricate data based on differing assumptions.

The techniques evolve and go in and out of fashion.

This limited but unique survey suggests that clinicians, consumers of care and even researchers may feel that the data to which these techniques are applied are not credible because of loss to follow up.

Conclusion
- Data with more than 25% loss to follow up within 12 weeks are weak.
- Such data are not credible to important stakeholders.
- Something is wrong with trial design if attrition greatly exceeds what would be expected in routine care.
- All stakeholders, including those in medicines control agencies, should require trial data with attrition more reflective of everyday care.

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