THE OTHER SUICIDE PILL?
Investigating the potential association between SSRI intake and increased risk of suicide
Carlos Escudero and Stephanie Leduc
Interdisciplinary School Of Health Sciences

Background
Antidepressants are prescribed as the main treatment of depression for severe depressive episodes and will often be used in conjunction with therapy for mild or moderate depression. While the prescription of antidepressants aims to reduce the severity of affective disorders, their use has been associated with adverse effects, including aggression, agitation, insomnia, and suicide. In 2003, the FDA released a study reporting results of a two-fold increase in suicidal behaviours for children and adolescents, and consequently, it has issued a warning detailing suicidal ideation as an adverse effect of SSRI use in youth with major affective disorders. The FDA had also emphasized the continued uncertainty surrounding this association and has called for additional research on the topic.

Abstract
Selective Serotonin Reuptake Inhibitors (SSRIs) are the most frequently prescribed antidepressant in the world (Bridge et al., 2007), and though they are meant to reduce depressive symptoms such as suicidal thoughts, some studies have associated their use with an increase in suicidal ideation, particularly in youth (defined as those under 19 years old).

This study investigates the association between SSRI intake and increased risk of suicide as a consequent adverse effect. This was done by conducting a structured literature review. Two independent reviewers analyzed and compared relevant research from peer-reviewed journals obtained from online databases including PubMed, JAMA Network, and the University of Ottawa online databases. A combination of observational studies, RCTs, and meta-analyses were reviewed. These studies analyzed the association between suicide rate and self-reported suicidal ideation in relation with different durations of SSRI intake and severities of disease, and had to include a comparison between randomly selected treatment groups and placebo control groups.

After reviewing 10 peer-reviewed articles, the results appear to be mixed from one study to another. Some studies report slight increases in suicidality, while others report a decrease associated with SSRI intake. Overall, the evidence is inconclusive as to an association with suicidal ideation and SSRI intake. However, as Antonuccio & Healy (2012) observed, a drug that is prescribed with the promise of treating depression should have a distinguished effect in reducing conditions such as suicidal ideation compared to placebo. The lack of conclusive evidence is thus a problem in itself, and further investigation is required as well as consideration regarding SSRI prescription.

Research Question
Does the use of prescription SSRIs to treat Major Depressive Disorder, OCD, or General Anxiety disorder increase risk of suicidal ideation and suicide attempts in children and adolescents (aged under 19)?

Methods
PubMed, JAMA Network and the University of Ottawa online databases were systematically searched using the keywords ‘SSRIs’, ‘Depression’, ‘Association’, ‘Suicide Risk’ and ‘Literature Review’. Meta-analyses, Observational studies and Randomized control trials were reviewed. The inclusion and exclusion criteria represented in the table below were used to determine which articles to include and which to exclude for the study. The articles obtained from the searches were then assessed by appraisal of the abstract for relevance to the research topic after a screening of the titles. Two independent reviewers then analyzed and compared relevant research.

Table 1. Inclusion/Exclusion Criteria

<table>
<thead>
<tr>
<th>Population</th>
<th>Drug</th>
<th>Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>SSRI</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Results
Based on inclusion and exclusion criteria, 10 articles were included in our study. The association between SSRI intake and increased suicide showed conflicting results. For this reason, the findings of each study were summarized into the following table.

Table 2. Results of 10 included articles

<table>
<thead>
<tr>
<th>Study</th>
<th>Population</th>
<th>Drug</th>
<th>Information</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bridge, J., K., &amp; Mann, J. (2006). Do SSRIs Increase Risk of Suicide in Children?</td>
<td>SSRI</td>
<td>No</td>
<td>Yes</td>
<td>Decrease</td>
</tr>
<tr>
<td>Wahlbeck, K., T., &amp; Haukka, J. (2013). The Relationship Between SSRIs and Suicide in Children</td>
<td>SSRI</td>
<td>Yes</td>
<td>Yes</td>
<td>Increase</td>
</tr>
<tr>
<td>Antonuccio, D., &amp; Mann, J. (2006). The Relationship Between Antidepressants and Suicide</td>
<td>SSRI</td>
<td>Yes</td>
<td>Yes</td>
<td>Increase</td>
</tr>
</tbody>
</table>

Discussion
While the majority of studies (6/10) selected did show a statistical increase in suicidal ideation during SSRI use, only one determined this increase to be significant enough for a positive association to be drawn between two factors. 10 years of mixed results without a trend developing is disconcerting and suggests there may be confounding variables that are not accounted for. Botvinick (2008) suggests that psychiatric comorbidity and certain demographic factors, rather than medication, may be the actual cause for an increase in the risk of suicide attempts in certain cases. Regardless, a noticeable trend that has arisen from these studies is that few of them have been able to show a marked difference between treatment and placebo groups with regard to consequent suicidal attempts or behaviour. Thus, while no research study has been able to demonstrate that SSRIs increase risk of suicide in youth, they have not been shown to decrease it either, which is one of their purposes. Future considerations must therefore be taken by practitioners when prescribing SSRIs to children since the literature provides mixed results regarding their efficacy and adverse effects.

Limitations
• Subjects with previous suicide attempts excluded from these studies due to ethical concerns. Thus, the strength of association between SSRI use and suicidal ideation is not fully represented or generalizable to real world circumstances.
• ‘Suicidal Ideation’ is a subjectively defined concept that cannot be quantitatively measured.
• Not all included studies adjusted for confounders, particularly long-term studies such as cohort and case-control studies.
• Studies measured different age ranges, all categorized as ‘youth’ under each study’s subjective definition (all fell under 19 years of age).

Conclusion
From the literature reviewed, mixed results regarding SSRI influence on suicidal ideation and attempts means there is no conclusive evidence to ascertain an association between the two. Further investigation must therefore be conducted regarding the association between SSRI intake and suicidal ideation in youth with major affective disorders, with a particular emphasis on identifying possible confounding variables.

References