

Re: Cost effectiveness of rasagiline and pramipexole as treatment strategies  
in early Parkinson's disease in the UK setting:  
an economic Markov model evaluation

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**Abbreviations:** CNS =central nervous system; STN = subthalamic nucleus; SVV = subjective visual vertical

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**[http://adisonline.com/aging/Citation/2011/28020/Cost Effectiveness of Rasagiline and Pramipexole.8.aspx](http://adisonline.com/aging/Citation/2011/28020/Cost_Effectiveness_of_Rasagiline_and_Pramipexole.8.aspx)**

**Dear Editor,**

We have read the article of Alan Haycox and his coworkers' on the cost-effectiveness of rasagiline use in early Parkinson's disease (PD)<sup>[1]</sup> with a great interest. Because the symptoms of PD can interfere with the patients' working capabilities and the sociocultural relations, the indirect costs of lost productivity and nursing along with the direct medical costs has a great impact on the reimbursement and welfare systems. Therefore, establishing the cost-effectiveness of different antiparkinsonian medications may be helpful in the development of treatment strategies from healthcare payers' perspective.

Haycox et al. contrasted the cost-effectiveness of rasagiline, a second-generation monoamine oxidase B inhibitor (MAOB-I), with that of pramipexole, a non-ergot dopamine-agonist (DA), in the treatment of uncomplicated (early) PD. This comparison is of cardinal importance, because according to the current treatment guidelines of the European Federation of Neurological Societies<sup>[2]</sup> both MAOB-I or DA monotherapy may be initiated.

As no direct head-to-head data between rasagiline and non-ergoline dopamine receptor agonists were available, the authors implemented an economic Markov model with a Monte Carlo simulation technique to estimate cost utility of the two treatment strategies over a period of 5-years<sup>[1]</sup>. This model was based on the results from the pivotal Parkinson Study Group TEMPO (TVP-1012 in Early Monotherapy for PD Outpatients)<sup>[3, 4]</sup> and the long-term pramipexole vs. levodopa comparative studies<sup>[5, 6]</sup>.

From clinical perspectives, we have several concerns about the study and the applied modeling techniques:

1. As mentioned in the methods section, the cost-efficiency estimation of rasagiline was based on two studies<sup>[3, 4]</sup> where the follow up varied from 26 weeks<sup>[3]</sup> to 12 months<sup>[4]</sup>. However, the utilized studies about pramipexole were conducted from 23 months<sup>[5]</sup> to 4 years<sup>[6]</sup>. Because PD has a progressive course with an individually variable speed, the comparison of pharmacological studies with entirely different follow-up periods (1 year vs. 4 years) is unfortunate.

2. Despite that the age, sex ratio and Hoehn-Yahr Stages were similar in both groups, the severity of baseline motor symptoms were certainly not equal. As the authors state in Table 1, the pramipexole group had longer disease duration (18 vs. 12 months), worse activities of daily living (Unified Parkinson Disease Rating Scale, UPDRS part II) and motor examination (UPDRS-III) scores (9 vs. 6 points and 22 vs. 18 points, respectively). Therefore, the total score of UPDRS probably differed by at least 7 points (3 points difference on UPDRS-II with an additional 4 points on UPDRS-III). Because these discrepancies exceeded the size of minimal clinically important difference (2.5 points on UPDRS-III and 4.3 points on total UPDRS scores)<sup>[7]</sup>, we can assume that the two groups clinically differed from each other in the respect of baseline motor symptoms of PD.
3. Based on the data available in the TEMPO study<sup>[3]</sup>, the motor symptoms measured by UPDRS-III improved by 2.71 points (at 1 mg/day dosage) compared to placebo, which hardly exceeds the size of minimal clinically important change<sup>[7]</sup>. Therefore, the 4-points difference on UPDRS-III between the baseline characteristics of rasagiline and pramipexole group is larger than the size of estimated short-term effect of rasagiline on motor symptoms of PD.
4. In their model, the authors estimated the treatment strategies over a 5-year follow-up period. Patients entered the model in either rasagiline monotherapy state or pramipexole monotherapy state. According to the model, when the efficacy of rasagiline monotherapy became insufficient for controlling PD symptoms, patients switched to either pramipexole or levodopa monotherapy. Haycox et al. assumed that only 20% of patient switched from rasagiline monotherapy to either DA or levodopa monotherapy at the end of the first year (Table 2)<sup>[1]</sup>. However, the 6-years follow up study of rasagiline<sup>[8]</sup> contradicts these estimations: According to this open-label extension study<sup>[8]</sup>, 65.8-70.3% of the patients received dopamine agonist or levodopa add-on therapy to rasagiline at entering the open-label phase (12 months after TAMPO baseline)<sup>[8]</sup>. This phenomenon might be due to the fact that MAOB-Is have weaker therapeutic effects than dopamine agonists or levodopa, as a recent Cochrane review states<sup>[9]</sup>. Because the applied Markov model underestimated the need for dopaminergic therapy (20% vs. 65.8-70.3%) and the option of pramipexole or levodopa add-on therapy was not considered, the therapeutic strategies in the applied Markov model were not realistic.

5. One of the largest indirect costs of PD in young patients arises from losing their working-capabilities and getting a pension due to illness. This approach represents a major burden on the welfare systems; therefore, this clinical setup also should be incorporated in any cost-effectiveness studies.

Based on their results, Haycox et al. stated a clear superiority of rasagiline over pramipexole in the respect of cost-effectiveness. However, we believe that to assess the cost-efficacy of rasagiline over pramipexole in early PD, a new study should be performed incorporating the above mentioned concerns.

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