Published in final edited form as:

Mov Disord. 2017 July ; 32(7): 1111–1112. doi:10.1002/mds.27051.

Response to Letter by Friedman on “Incidence and Time Trends of Drug-Induced Parkinsonism: A 30-Year Population-Based Study”

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We appreciate the comments expressed by Dr. Friedman concerning our recent publication on time trends for drug-induced parkinsonism (DIP) in Olmsted County, Minnesota.¹ The first concern was that the time lag between symptom onset and the diagnosis of parkinsonism can be long. We clarify that a patient would only be missed by our criteria if the retro-dating of symptom onset was grossly misdocumented in the medical record. The second concern was that some patients may develop parkinsonism after many years of use of the offending drug. We clarify that a patient would only be missed by our criteria if after decades of treatment he/she discontinued treatment and developed parkinsonism more than 6 months after the discontinuation. A third concern was that some patients never discontinued treatment. This problem was addressed by our criteria that included DIP patients who never discontinued the offending drugs. If the patient discontinued the offending drug but continued to have symptoms for more than 6 months (arbitrary cut-off), we considered the patient to have Parkinson’s disease, unspecified parkinsonism, or another type of degenerative parkinsonism. We agree that some of these patients could have had a negative scan at functional imaging of the dopamine transporter (DAT-SPECT); however, a scan was not performed in routine medical care because DAT-SPECT was approved for clinical use only in 2011.² We do not foresee the feasibility of a population-based time trends study of DIP over a 30 year period that requires DAT-SPECT confirmation.

Another concern of Dr. Friedman was that the retrospective diagnostic review was based on non neurology records. To the contrary, because of the nature of our population (only one

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Author Contributions: Dr. Rocca drafted the letter and Dr. Savica and Mr. Grossardt made important clinical and methodological contribution to the final manuscript.

Financial Disclosure: Dr. Rocca receives research support from the NIH [AG034676 (Principal investigator), AG052425 (Principal investigator), AG006786 (Co-investigator), AG044170 (Co-director), and AG004875 (Co-investigator)]. Dr. Savica reports no disclosures. Mr. Grossardt reports no disclosures.

major neurology department in the county), the vast majority of our patients have been seen at least once by a neurologist, and most commonly by a movement disorders specialist.³

Dr. Friedman challenged our decision to exclude possible offending drugs without a recognized dopamine action (e.g., lithium and valproic acid). As discussed more extensively in our paper, we excluded drugs without a recognized dopamine action because the role of these drugs in causing parkinsonism remains uncertain; however, we agree that additional drugs can potentially cause parkinsonism.¹

The observation that the proportion of DIP among patients with parkinsonism was underestimated in our geographically-defined entire population compared to patients seen in a movement disorders clinic or to patients residing in a psychiatric ward, is not surprising and is caused by a selection bias.⁴ Patients with parkinsonism seen in a movement disorders clinic are younger than patients living in the general population, and we did observe a higher representation of DIP in the younger segment of the population (younger than age 40 years), but not in the older population. Patients residing in a psychiatric ward are a highly selected sample of people at increased risk of DIP. In summary, epidemiologic data can only be meaningfully compared with other epidemiologic data, and the experience of an individual specialist or the data from a selected clinical series may be systematically different.⁴

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