

Diagnosis and Treatment of Parkinson's Disease: A Systematic Review of the Literature

Prepared for:

Agency for Healthcare Research and Quality
U.S. Department of Health and Human Services
540 Gaither Road
Rockville, MD 20850
www.ahrq.gov

Contract No: 290-97-0016

Prepared by:

MetaWorks, Inc., Evidence-based Practice Center
Medford, MA

Investigators

Cindy B. Levine, MD
Kyle R. Fährbach, PhD
Andrew D. Siderowf, MD
Rhonda P. Estok, RN, BSN
Veronica M. Ludensky, BA
Susan D. Ross, MD, FRCPC

This report may be used, in whole or in part, as the basis for development of clinical practice guidelines and other quality enhancement tools, or a basis for reimbursement and coverage policies. AHRQ or U.S. Department of Health and Human Services endorsement of such derivative products may not be stated or implied.

AHRQ is the lead Federal agency charged with supporting research designed to improve the quality of health care, reduce its cost, address patient safety and medical errors, and broaden access to essential services. AHRQ sponsors and conducts research that provides evidence-based information on health care outcomes; quality; and cost, use, and access. The information helps health care decisionmakers—patients and clinicians, health system leaders, and policymakers—make more informed decisions and improve the quality of health care services.

This document is in the public domain and may be used and reprinted without permission except those copyrighted materials noted for which further reproduction is prohibited without the specific permission of copyright holders.

Suggested Citation:

Levine CB, Fährbach KR, Siderowf AD, et al. Diagnosis and Treatment of Parkinson's Disease: A Systematic Review of the Literature. Evidence Report/Technology Assessment Number 57. (Prepared by Metaworks, Inc., under Contract No. 290-97-0016.) AHRQ Publication No. 03-E040. Rockville, MD: Agency for Healthcare Research and Quality. June 2003.

Preface

The Agency for Healthcare Research and Quality (AHRQ), through its Evidence-based Practice Centers (EPCs), sponsors the development of evidence reports and technology assessments to assist public- and private-sector organizations in their efforts to improve the quality of health care in the United States. The reports and assessments provide organizations with comprehensive, science-based information on common, costly medical conditions and new health care technologies. The EPCs systematically review the relevant scientific literature on topics assigned to them by AHRQ and conduct additional analyses when appropriate prior to developing their reports and assessments.

To bring the broadest range of experts into the development of evidence reports and health technology assessments, AHRQ encourages the EPCs to form partnerships and enter into collaborations with other medical and research organizations. The EPCs work with these partner organizations to ensure that the evidence reports and technology assessments they produce will become building blocks for health care quality improvement projects throughout the Nation. The reports undergo peer review prior to their release.

AHRQ expects that the EPC evidence reports and technology assessments will inform individual health plans, providers, and purchasers as well as the health care system as a whole by providing important information to help improve health care quality.

We welcome written comments on this evidence report. They may be sent to: Director, Center for Practice and Technology Assessment, Agency for Healthcare Research and Quality, 540 Gaither Road, Rockville, MD 20850.

Carolyn Clancy, M.D.
Director
Agency for Healthcare Research and Quality

Jean Slutsky, P.A., M.S.P.H.
Acting Director, Center for Practice and
Technology Assessment
Agency for Healthcare Research and Quality

The authors of this report are responsible for its content. Statements in the report should not be construed as endorsement by the Agency for Healthcare Research and Quality or the U.S. Department of Health and Human Services of a particular drug, device, test, treatment, or other clinical service.

Structured Abstract

Objectives. Parkinson's Disease (PD) is estimated to affect over 1 percent of the population over age 65. The objective of this systematic review is to assess the quantity and quality of published evidence regarding diagnosis and treatment of patients with PD.

Search Strategy. English-language literature published from 1990 to 2000 was searched using electronic databases. Searches were supplemented by manually reviewing bibliographies of all accepted studies and selected review articles.

Selection Criteria. Studies were required to evaluate at least 10 human patients and address pre-defined areas of interest. Only randomized controlled trials (RCTs) were accepted for studies regarding pharmacological treatment.

Data Collection and Analysis. Pertinent data were evaluated for quality and level of evidence, extracted from accepted studies by one researcher, and reviewed by a second. Data were summarized and synthesized qualitatively. Meta-analyses were performed, comparing standardized mean changes from baseline to outcome in PD severity rating scales.

Main Results. The database includes 59 studies (3,369 patients) regarding diagnosis, 49 studies (9,968 patients) on pharmacological treatment, 42 studies (1,380 patients) on surgery, 10 studies (392 patients) on psychiatric treatment, and 20 studies (1,049 patients) on ancillary treatment of PD.

PD is diagnosed clinically; evidence does not show that specific tests improve diagnostic accuracy. There is no evidence that different dopamine agonists (DAs) vary in treatment effects. Meta-analysis suggests that in early PD, treatment with DAs plus levodopa (L-dopa) may control PD symptoms better than treatment with L-dopa alone, but this was not a consistent finding. Similarly, no consistent difference in symptom control was found between L-dopa alone and the combination therapy of L-dopa plus selegiline. In patients with advanced disease, treatment with catechol O-methyl transferase (COMT) inhibitors combined with L-dopa provides significantly greater PD symptom control than treatment with L-dopa alone and is associated with lower L-dopa doses; however, long-term (greater than 7 months) results are lacking, and hepatotoxicity is a rare but potentially lethal side effect associated with tolcapone.

For pallidotomy and deep brain stimulation (DBS), endpoint PD scale scores are significantly better than baseline scores. DBS of the subthalamic nucleus (STN) and globus pallidus (GPi) result in significant improvement in PD symptoms, but only STN DBS is associated with decreased L-dopa doses. There are insufficient studies of thalamotomy and tissue transplantation to draw any conclusions regarding their efficacy and safety.

Ancillary treatments, such as physical therapy, improve some symptoms on a short-term basis, but long-term data are lacking. Intensive speech therapy has been shown to improve vocal intensity up to 12 months after treatment; however, long-term results are from only one study of 22 patients.

Conclusions. PD is diagnosed clinically; there is currently no gold standard premorbid diagnostic test for PD. Meta-analyses of different pharmacological treatments showed that the only medication that consistently controlled PD symptoms better than L-dopa alone was the

combination of L-dopa plus COMT inhibitors in patients with advanced PD. Meta-analyses suggest that pallidotomy and DBS result in improvement of PD rating scores. The published literature regarding PD suffers from lack of reporting standardized outcomes.

Contents

Summary	1
---------------	---

Evidence Report

Chapter 1. Introduction	11
Etiology	11
Clinical Features	12
Diagnosis	12
Assessment of PD Severity	14
Treatment.....	15
Pharmacological Treatment	15
Surgical Treatment.....	18
Ancillary Treatment	20
Objectives	20
Original Key Questions	20
Revised Key Questions	22
 Chapter 2. Methodology	23
Literature Search	23
Exclusion Criteria	24
Inclusion Criteria	25
Linked Studies.....	28
Rating the Evidence.....	28
Data Extraction	29
Database Development.....	29
Statistical Methods	29
Summary Statistics.....	29
Diagnosis.....	29
Pharmacologic Treatment	30
Surgery	30
Ancillary Treatments	30
Meta-Analyses	31
Role of Consultants	33
Peer Review.....	33
 Chapter 3. Results	35
Searches.....	35
Studies.....	35
Diagnosis	36
Apomorphine and L-Dopa Challenge Tests	36
SPECT Scans	37
PET Scans.....	38
Other Scans	38
Clinical Diagnosis.....	39

Blood and CSF Tests	40
Olfactory Tests	40
PD Test Battery	41
Autopsy	42
Pharmacological Treatment of PD	43
Early PD	44
Advanced PD	46
Meta-Analyses	46
On-Off Time	50
L-Dopa Doses	50
Dyskinesia Scores	51
Safety	51
Surgical Treatment of PD	51
Pallidotomy	52
Thalamotomy	53
Deep Brain Stimulation	53
Tissue Transplants	53
Meta-Analyses	54
Safety	57
Psychiatric Treatment	57
Ancillary Treatment	58
Physical Therapy	58
Speech/Swallowing Therapy	60
Other Therapies	61
Genetics	63
Chapter 4. Answers to Revised Key Questions	75
Chapter 5. Strengths and Limitations of the Evidence Base	79
Chapter 6. Recommendations for Future Research	81
Chapter 7. Harnessing the Available Evidence	85
References	87
Evidence Tables	103
Evidence Table 1. Summary of Rejected Studies	105
Evidence Table 2. Study Level Characteristics	106
Evidence Table 3. Overall Treatment Level Characteristics	107
Evidence Table 4. Treatment Level Characteristics of Diagnostic Studies	108
Evidence Table 5. Treatment Level Characteristics of Pharmacological Studies	109
Evidence Table 6. Statistical Analysis: Dopamine Agonists with L-Dopa vs. L-Dopa Alone	110
Evidence Table 7. Statistical Analysis: Selegiline with L-Dopa vs. L-Dopa Alone	111

Evidence Table 8. Statistical Analysis: COMT Inhibitors with L-Dopa vs. L-Dopa Alone .	112
Evidence Table 9. Pharmacological Studies: Adverse Events	113
Evidence Table 10. Pharmacological Studies: Neurological and Psychiatric Adverse Events.....	114
Evidence Table 11. Treatment Level Characteristics of Surgical Studies	115
Evidence Table 12. Statistical Analysis: Pallidotomy	116
Evidence Table 13. Statistical Analysis: Deep Brain Stimulation.....	117
Evidence Table 14. Statistical Analysis: Tissue Transplantation.....	118
Evidence Table 15. Surgical Studies: Adverse Events.....	119
Evidence Table 16. Treatment Level Characteristics of Ancillary Studies	120
Bibliography	121

Appendixes

Appendix A. Major Parkinson's Disease Rating Scales	139
Appendix B. Work Plan.....	181
Appendix C. Topic Assessment and Refinement	205
Appendix D. Causal Pathways: Diagnosis and Treatment of Parkinson's Disease	207
Appendix E. Screening Sheets and Data Extraction Forms.....	213
Appendix F. Statistical Reference.....	239
Appendix G. Technical Experts and Peer Reviewers	243
Appendix H. Accepted Studies Log.....	249
Appendix I. Rejected Studies Log	267
Appendix J. Studies of Interest Excluded from Database.....	297
Appendix K. Acronyms in This Report	303

Figures

Figure 1. MetaWorks Systematic Review Process Diagram	34
Figure 2. Study Attrition	65
Figure 3. Dopamine Agonist + L-Dopa vs. L-Dopa	66
Figure 4. Selegiline + L-Dopa vs. L-Dopa	67
Figure 5. COMT Inhibitor + L-Dopa vs. L-Dopa.....	68
Figure 6. Surgery: Pallidotomy (Off Scores).....	69
Figure 7. Surgery: Pallidotomy (On Scores).....	70
Figure 8. Surgery: Deep Brain Stimulation (Off Scores)	71
Figure 9. Surgery: Deep Brain Stimulation (On Scores)	72
Figure 10. Surgery: Fetal Cell Transplant (Off Scores).....	73
Figure 11. Surgery: Fetal Cell Transplant (On Scores)	74