

Evidence Table 1. Summary of Rejected Studies

Rejected	Reason for Rejection ¹
96	Studies published prior to 1990
81	Studies with less than 24 weeks of follow-up (other than diagnosis)
72	Studies that are not RCTs (pharmacological treatment only)
52	Abstracts, letters, comments, reviews, editorials, case reports, or meta-analyses
49	Studies not including tests to establish or support diagnosis of PD
29	Studies with less than 10 patients
17	Outcomes not extractable
24	Studies not including treatment or diagnosis
13	No outcome of interest
6	Cross-over studies
6	Mixed populations where results for PD patients cannot be separately extracted
10	Studies not including an objective clinical outcome measure of PD activity
2	Duplicate studies
2	In vitro studies
2	Languages other than English
2	Pharmacodynamic or pharmacokinetic study
2	Study populations not including Parkinson's Disease
465	TOTAL

¹ Based on

Evidence Table 2. Study Level Characteristics

	Total			Diagnosis			Pharmacological			Surgical			Psychiatric			Ancillary		
	k	t	n	k	t	n	k	t	n	k	t	n	k	t	n	k	t	n
Totals	180	353	16,158	59	141	3,369	49	111	9,968	42	52	1,380	10	12	392	20	37	1,049
Location																		
Europe	90	186	6,327	40	94	1,948	25	52	3,478	14	20	393	2	3	73	9	17	435
North America	66	118	6,819	12	27	1,226	14	38	3,902	25	29	831	7	8	292	8	16	568
Other	15	29	888	5	13	94	5	10	708	1	1	13	1	1	27	3	4	46
Multi-National	9	20	2,124	2	7	101	5	11	1,880	2	2	143	0	0	0	0	0	0
Study Design																		
RCT	68	151	10,996	0	0	0	49	111	9,968	4	8	105	2	4	57	13	28	866
nRCT	6	16	273	2	5	83	-	-	-	2	7	117	0	0	0	2	4	73
UCS	49	49	1,627	5	5	278	-	-	-	35	35	1,145	6	6	114	3	3	90
XS	48	119	2,075	46	117	2,055	-	-	-	0	0	0	0	0	0	2	2	20
Other	9	18	1,187	6	14	953	-	-	-	1	2	13	2	2	221	0	0	0
Level of Evidence																		
I	28	70	8,945	0	0	0	26	65	8,454	0	0	0	0	0	0	2	5	491
II	40	79	2,051	0	0	0	23	46	1,514	4	8	105	2	2	57	11	23	375
III	112	204	5,162	59	141	3,369	0	0	0	38	44	1,275	8	10	335	7	9	183
Quality Score																		
1	7	15	180	0	0	0	1	2	20	0	0	0	0	0	0	6	13	160
2	17	35	2,241	0	0	0	8	16	1,502	1	2	13	1	2	20	7	15	706
3	13	28	2,014	0	0	0	11	24	1,959	2	4	55	0	0	0	0	0	0
4	22	51	4,147	0	0	0	20	47	4,073	1	2	37	1	2	37	0	0	0
5	9	22	2,414	0	0	0	9	22	2,414	0	0	0	0	0	0	0	0	0
Industry Sponsorship	42	90	7,355	1	1	30	29	72	6,612	4	4	134	4	5	116	4	8	463

k - number of studies

t - number of treatment arms

n - number of patients

Multi-National - on more than one continent

RCT - randomized controlled trial

nRCT - non-randomized controlled trial

UCS - uncontrolled case series

XS - cross-sectional

Evidence Table 3. Overall Treatment Level Characteristics

	Total		Pharmacological		Surgical		Psychiatric		Ancillary	
	t	n	t	n	t	n	t	n	t	n
Patients Randomized/Enrolled	212	12,789	111	9,968	52	1,380	12	392	37	1,049
Male (n = %)	164	60%	82	60%	40	64%	10	59%	32	62%
Female (n = %)	164	40%	82	40%	40	36%	10	41%	32	38%
Mean Age > 65	64	2,743	17	1,225	10	270	11	373	26	875
Mean Age < 65	130	8,613	80	7,380	41	1,066	1	19	8	148
Disease Stage										
Early*	80	7,505	74	7,405	2	28	NR	NR	4	72
Advanced**	114	4,758	37	2,563	41	1,030	9	344	27	821
Mean Age of Onset > 50	22	1,118	15	928	3	102	1	49	3	39
Mean Age of Onset < 50	3	49	NR	NR	3	49	NR	NR	NR	NR
Race	11	567	8	506	NR	NR	1	11	2	50
Socioeconomic status	10	890	6	820	NR	NR	2	20	2	50

*Early = author defined as "early" or "de novo" or disease duration < 5 years

**Advanced = author defined as "advanced" or disease duration > 5 years

t - number of treatment arms

n - number of patients

NR - not reported

Evidence Table 4. Treatment Level Characteristics of Diagnostic Studies

Test Category	Diagnosis Studies		
	k	t	n
Apomorphine challenge	5	6	229
Autopsy	6	15	253
Clinical or laboratory	10	26	1,412
Color vision test	2	3	35
MRI	3	8	140
Olfactory testing	7	21	355
PD Test battery	3	7	180
PET scans	8	21	185
SPECT scans*	13	29	460
Other scans	2	5	120
Total	59	141	3,369

SPECT - single photon emission computed tomography

PET - positron emission tomography

MRI - magnetic resonance imaging

k - number of studies

t - number of treatment arms

n - number of patients

* includes 5 studies that reported SPECT results before and after administration of apomorphine and one study that compared SPECT and PET results

Evidence Table 5. Treatment Level Characteristics of Pharmacological Studies

Treatment class	Total		Early		Advanced	
	t	n	t	n	t	n
Monotherapy						
LD	41	3,927	25	2,835	16	1,092
Dopamine Agonist	6	508	6	508	0	0
MAO-B inhibitor	5	336	5	336	0	0
Combination therapy						
LD/DA	33	2,935	18	1,907	15	1,028
LD/COMT inhibitor	8	639	2	196	6	443
LD/DA/MAO-B inhibitor	2	68	2	68	0	0
LD/MAO-B inhibitor	7	700	7	700	0	0
DA/MAO-B inhibitor	1	10	1	10	0	0
Other Combinations	4	471	4	471	0	0
Placebo	4	374	4	374	0	0
Total	111	9,968	74	7,405	37	2,563

LD - levodopa (always given with peripheral decarboxylase inhibitor)

DA - dopamine agonist

MAO-B - monoamine oxidase-B

COMT - catechol O-methyl transferase

Other Combinations included 2 studies with LD/Selegiline/Tocopherol and LD/ Tocopherol

k - number of studies

t - number of treatment arms

n - number of patients

Evidence Table 6. Statistical Analysis: Dopamine Agonists with L-Dopa vs. L-Dopa alone

First Author	Year	Dopamine Agonist Tested	Patients on L-dopa	Patients on DA and L-Dopa	Disease Stage	Time of Evaluation (months)	Mean Age (years)	Change-score Effect Sizes
Alarcon	1998	Bromocriptine	38	40	Early	36	63.8	0.137
Allain	2000	Lisuride	41	41	Early	12	59.0	0.411
Gimenez-Roldan	1997	Bromocriptine	23	27	Early	8	60.3	1.463
Hutton	1996	Cabergoline	65	123	Advanced	6	63.1	0.299
Kulisevsky	2000	Pergolide	10	10	Early	24	65.5	-0.057
Lieberman	1997	Pramipexole	172	179	Advanced	8	63.4	0.264
Nakanishi	1992	Bromocriptine	124	117	Early	60	61.4	0.257
Olanow	1994	Pergolide	187	189	Advanced	6	63.0	0.203
Olanow	1995	Bromocriptine	21	19	Early	14	66.2	-0.239
Olsson	1990	Bromocriptine	140	137	Early	12	58.5	0.230
Parkinson Study Group	2000	Pramipexole	150	151	Early	24	61.2	-0.398
Przuntek	1996	Bromocriptine	302	285	Early	48	65.0	0.240
Rabey	1990	Lisuride	13	15	Advanced	48	65.4	0.329
Rascol	2000	Ropinirole	89	179	Early	60	63.0	-0.418
Rinne	1998	Cabergoline	205	208	Early	18	61.6	-0.288
Sethi	1998	Ropinirole	77	70	Early	12	61.9	0.521
Steiger	1996	Cabergoline	11	6	Advanced	6	62.1	-0.102
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Inzelberg*	1996	Cabergoline vs. Bromocriptine	22 (Caber.)	22 (Bromo.)	Advanced	12	-	0.167
Korczyn*	1999	Ropinirole vs. Bromocriptine	102 (Ropin.)	112(Bromo.)	Early	36	62.9	-0.164

L-dopa = Levodopa

DA = Dopamine Agonist

Caber = Cabergoline

Bromo = Bromocriptine

Ropin = Ropinirole

*Both groups were on both DA and L-dopa. The names in parentheses indicate which DA was used to treat a particular group.

Evidence Table 7. Statistical Analysis: Selegiline with L-Dopa vs. L-Dopa alone

First Author	Year	Patients on L-dopa	Patients on Selegiline and L-Dopa	Disease Duration (years)	Time of Evaluation (months)	Mean Age (years)	Change-score Effect Sizes
Larsen	1999	81	73	Early	60	64.3	0.593
Lees	1995	213	233	Early	12	63.2	0.810
Myllyla	1992	25	27	Early	12	61.1	-0.277
Olanow	1995	21	20	Early	14	NR	0.931
Palhagen	1998	81	76	Early	12	63.8	-0.343

L-dopa = Levodopa

Evidence Table 8. Statistical Analysis: COMT Inhibitors with L-Dopa vs. L-Dopa alone

First Author	Year	COMT Inhibitor Tested	Patients on L-dopa	Patients on COMT Inhibitors and L-Dopa	Disease Duration (years)	Time of Evaluation (months)	Mean Age (years)	Change-score Effect Sizes
Baas*	1997	Tolcapone	58	60	9.75	3	63.0	0.263
Baas*	1997	Tolcapone	58	59	10.25	3	63.5	0.553
Parkinson Study Group	1997	Entacapone	102	103	11.05	7	63.3	0.278
Rajput*	1997	Tolcapone	66	69	10.75	3	64.0	0.180
Rajput*	1997	Tolcapone	66	67	10.80	3	64.5	0.103
Rinne	1998	Entacapone	86	85	10.75	6	62.7	0.310
Waters*	1997	Tolcapone	102	98	4.15	6	67.0	0.397
Waters*	1997	Tolcapone	102	98	3.75	6	65.0	0.471

LD - Levodopa

COMT - Catechol O-Methyl Transferase

* Separate treatment groups (different doses) of the same study

Evidence Table 9. Pharmacological Studies: Adverse Events

Adverse Events	Total		LD		DAs		MAO-B		LD/DA		LD/COMT		LD/DA/MAO-B		LD/MAO-B		Other		Placebo	
	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n
Deaths	4.8	5,635	5.0	2,342	14.0	64	0.9	336	3.3	1,708	-	0	-	0	13.1	634	0.0	409	0.7	142
Treatment Related Deaths	0.0	1,232	0.0	317	-	0	0.0	255	0.0	557	-	0	-	0	0.0	27	0.0	10	0.0	66
Withdrawals	29.2	8,961	30.4	3,605	48.4	508	12.8	336	28.8	2,505	39.1	384	32.4	68	32.6	700	9.8	481	17.4	374
Efficacy Withdrawals	5.1	5,840	6.1	2,597	10.0	468	-	0	3.4	2,077	1.9	103	0.0	41	3.8	373	0.0	10	4.1	171
Safety Withdrawals	11.2	7,444	8.3	3,268	20.6	490	-	0	12.8	2,256	15.5	639	9.8	41	13.0	446	5.6	72	4.7	232
Adverse Events																				
Cardiac	12.2	4,332	10.8	1,637	9.6	228	0.4	255	16.9	1,712	4.2	119	-	0	3.7	134	0.0	10	4.6	237
Cerebrovascular	0.6	345	1.2	81	-	0	0.5	191	-	0	-	0	-	0	0.0	73	-	0	-	0
GI	23.8	6,019	22.0	2,326	30.3	228	0.8	255	28.2	2,067	29.3	639	-	0	22.4	134	16.7	72	13.4	298
Infections	9.8	1,641	8.2	451	-	0	-	0	11.4	797	9.9	332	-	0	0.0	61	-	0	-	0
Musculoskeletal	8.2	1,796	5.5	990	-	0	-	0	10.9	614	19.3	119	-	0	5.5	73	-	0	-	0
Pulmonary	2.8	689	1.6	255	-	0	-	0	3.5	315	3.4	119	-	0	-	0	-	0	-	0
Urinary system	7.8	903	0.5	366	-	0	-	0	5.9	17	12.9	520	-	0	-	0	-	0	-	0
Other*	8.6	3,308	5.3	1,524	14.6	164	-	0	11.4	1,376	-	0	-	0	8.2	73	-	0	8.8	171

n - number of patients

LD - levodopa

DA - dopamine agonist

MAO-B - monoamine oxidase-B

COMT - catechol O-methyl transferase

GI - gastro-intestinal

*Other includes: asthenia, fatigue, pain, peripheral edema, pruritis, sweating increased, syncope, weight increased.

Evidence Table 10. Pharmacological Studies: Neurological and Psychiatric Adverse Events

Adverse Events	Total		LD		DAs		LD/DA		LD/COMT		LD/DA/MAO-B		LD/MAO-B		Other		Placebo	
	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n
Neurological																		
Akinesia	20.6	413	23.9	205	-	0	17.3	208	-	0	-	0	-	0	-	0	-	0
Ataxia	10.8	622	6.5	245	-	0	16.1	274	6.8	103	-	0	-	0	-	0	-	0
Dizziness	18.9	4,076	15.5	1,975	-	0	26.3	1,511	14.6	384	-	0	9.6	73	2.8	72	1.6	61
Dyskinesias	23.1	5,828	20.2	2,522	1.9	262	24.7	2,052	35.8	639	4.9	41	30.1	312	-	0	-	0
Dystonia	12.0	2,640	11.4	1,303	7.4	270	10.2	714	-	0	12.2	41	22.4	312	-	0	-	0
Headache	9.9	3,297	7.6	1,657	-	0	13.8	1,192	8.9	315	-	0	-	0	8.3	72	0.0	61
PD Aggravated	24.5	1,203	31.4	328	-	0	20.2	772	35.0	103	-	0	-	0	-	0	-	0
Tremor	11.1	934	10.7	476	-	0	11.6	458	-	0	-	0	-	0	-	0	-	0
Other	5.7	724	4.1	539	62.5	8	13.0	92	2.4	85	-	0	-	0	-	0	-	0
Psychiatric																		
Confusion	6.5	1,548	3.7	804	4.7	64	10.0	680	-	0	-	0	-	0	-	0	-	0
Depression	9.6	2,576	7.8	1,351	-	0	12.0	1,152	-	0	-	0	5.4	73	-	0	-	0
Hallucinations	7.6	4,052	5.1	1,790	9.9	172	10.2	1,595	10.2	324	-	0	-	0	-	0	2.3	171
Sleeping Disorders	25.4	5,009	19.2	2,238	43.9	164	30.4	1,697	31.6	639	-	0	15.0	100	-	0	21.6	171
Other	12.2	2,048	9.9	817	-	0	10.4	769	20.2	435	-	0	3.7	27	-	0	-	0

Neurological Other: Chorea, freezing, hemiparesis, hyperkinesia, paresthesia, vertigo
Psychiatric Other: Agitation, amnesia, anorexia, anxiety, appetite increase, dementia, psychosis

n - number of patients
LD - levodopa
DA - dopamine agonist
MAO-B - monoamine oxidase-B
COMT - catechol O-methyl transferase
GI - gastro-intestinal

Table 11. Treatment Level Characteristics of Surgical Studies

Type of Surgery	Surgical Studies	
	t	n
Pallidotomy	20	764
Thalamotomy	5	134
DBS	16	288
GPi	4*	22*
STN	8*	135*
thalamic	4*	131*
Tissue Transplant	9	165
Adrenal Medulla	3**	91**
Human fetal brain cells	5**	52**
Porcine fetal brain cells	1**	12**
No surgery	2	29
Total	52	1380

DBS - direct brain stimulation

Gpi- globus pallidus

STN- subthalamic nucleus

t- number of treatment arms

n- number of patients

* Subgroups of DBS

** Subgroups of Tissue Transplant

idence Table 12. Statistical Analysis: Pallidotomy

First Author	Year	Surgical Intervention	Number of Patients	Time of Evaluation (months)	Mean Age (years)	"Off" score Effect Sizes	"On" score Effect Sizes
Baron	2000	Unilateral	10	48	58.0	0.100	-0.200
Dalvi	1999	Medial	12	12	65.3	0.870	0.140
de Bie	1999	Unilateral	18	6	60.6	0.590	-0.130
Desaloms	1998	Unilateral	35	12	60.0	1.120	-
Dewey	2000	Unilateral	32	12	61.1	0.660	0.590
Dogali	1996	Unilateral	33	12	60.3	1.660	-
Eskandar	2000	Mixed	68	24	61.0	0.200	-0.100
Herrera	2000	Unilateral	13	16	60.0	0.930	-
Kondziolka	1999	Unilateral	58	9	67.0	0.750	0.280
Lang	1997	Unilateral	39	6	58.8	1.360	0.310
Masterman	1998	Unilateral	32	6	65.0	0.420	0.430
Melnick	1999	Medial	29	6	66.4	0.580	-
Samii	1999	Unilateral	20	12	61.0	1.430	-0.170
Samuel	1998	Unilateral	22	3	55.9	0.480	0.000
Shannon	1998	Unilateral	22	6	59.3	0.520	-0.200
Young	1998	Mixed	17	6	69.2	-	0.200

Evidence Table 13. Statistical Analysis: Deep Brain Stimulation

First Author	Year	Surgical Intervention	Number of Patients	Time of Evaluation (months)	Mean Age (years)	"Off" score Effect Sizes	"On" score Effect Sizes
Ardouin	1999	GPI	8	3	52.0	1.550	-
Ardouin	1999	GPI	5	6	55.0	0.990	-
Burchiel	1999	GPI	4	12	46.5	0.940	0.662
Krack	1998	GPI	5	6	51.0	1.665	-0.552
Ardouin	1999	STN	41	3	54.9	2.753	-
Ardouin	1999	STN	8	6	53.4	1.317	-
Bejjani	2000	STN	10	6	54.0	3.712	2.472
Burchiel	1999	STN	5	12	62.8	0.903	1.442
Houeto	2000	STN	23	6	53.0	1.644	0.795
Krack	1998	STN	8	6	51.0	3.243	0.335
Limousin	1998	STN	20	12	56.0	2.945	0.077
Molinuevo	2000	STN	15	6	60.9	-0.094	0.424
Kumar	1999	Thal	11	16	71.0	0.131	-
Limousin	1999	Thal	73	12	61.5	-0.108	-

GPI = globus pallidus

STN = subthalamic nucleus

Thal = thalamic

Table 14. Statistical Analysis: Tissue Transplantation

First Author	Year	Number of Patients	Time of Evaluation (months)	Mean Age (years)	"Off" score Effect Sizes	"On" score Effect Sizes
Fink	2000	12	12	61.0	0.740	-
Henderson	1991	9	12	56.0	0.480	-0.030
Kopyov	1996	22	24	55.0	0.830	0.830
Kopyov	1997	6	6	53.0	-	1.040
Kopyov	1997	7	6	60.0	-	2.380
Lopez-Lozano	1997	10	60	61.0	1.670	1.640

idence Table 15. Surgical Studies: Adverse Events*

	Total		Pallidotomy		Thalamotomy		DBS		Transplant	
	%	n	%	n	%	n	%	n	%	n
Deaths	5.4	672	3.0	398	1.5	65	4.8	84	15.2	125
Treatment Related Deaths	1.9	567	1.3	307	0	23	1.2	82	8.2**	73
Adverse Events										
Infections	7.4	122	3.6	56	-	NR	4.2	24	14.3	42
Cardiac	4.0	75	5.6	18	0	23	4.5	22	8.3	12
Neurological	6.7	668	5.3	488	15.3	59	8.1	111	10.0	10
Gastrointestinal	5.0	80	4.3	70	-	NR	-	NR	10.0	10
Musculoskeletal	6.3	96	6.3	96	-	NR	-	NR	-	NR
Neoplasm	4.1	48	4.1	48	-	NR	-	NR	-	NR
Psychiatric	6.9	404	6.0	250	8.7	23	8.3	60	8.5	71
Cerebrovascular	6.4	342	7.1	237	0	23	4.3	46	8.3	36

*Does not include studies in which adverse events were reported in terms of # of events, rather than # of patients

*Does not include short-term, transient, postoperative adverse events.

** All transplant-related deaths occurred in adrenal medulla transplant patients.

n - number of patients in treatment groups reporting event

% - % of patients with event in studies reporting the event

NR - Not Reported

0 - no events were reported and one or more studies reported 0 events

DBS - deep brain stimulation

Infections include pneumonia, sepsis, and nonspecific infections.

Cerebrovascular includes hemorrhage and stroke

Evidence Table 16. Treatment Level Characteristics of Ancillary Studies

Author	Year	Study design	Level of Evidence	Quality Score	n	Duration	Intervention
Adams	1992	XS	III	NA	10	NA	Speech Therapy
Comella	1996	XO-RCT	II	2	18	1 month	PT
Dam	1996	nRCT	III	NA	40	12 months	PT
DeAngelis	1997	UCS	III	NA	20	1 month	Speech Therapy
Formisano	1992	nRCT	III	NA	33	4 months	PT
Jahanshahi	1994	RCT	II	1	40	6 months	NP
Katsikitis	1996	RCT	II	1	16	1 month	OPT
Mally	1999	UCS	III	NA	10	10 days	TMS
Mercer	1996	RCT	II	2	50	12 months	PROPATH
Montgomery	1994	RCT	I	2	400	6 months	PROPATH
Nagaya	2000	XS	III	NA	10	NA	Swallowing Therapy
Pacchetti	2000	RCT	II	1	32	3 months	PT vs MT
Patti	1996	RCT	II	1	20	6 months	In-patient Rehab
Platz	1998	RCT	II	1	15	< 1 month	PT
Ramig	1995	RCT	II	2	45	1 month	LSVT
Ramig	1996	RCT	II	2	35	12 months	LSVT
Reynolds	2000	RCT	I	2	185	12 months	NP
Schenkman	1998	RCT	II	2	51	2.5 months	PT
Sitzia	1998	nRCT	III	NA	60	1-2 months	In-patient Rehab
Thaut	1996	RCT	II	1	37	< 1 month	PT (RAS)

Level of Evidence - I-V, I is best

Quality Score - 1-5, 5 is best

n = number of patients

PT = physical therapy

RAS = rhythmic auditory stimulation

LSVT = Lee Silverman Voice Treatment

NP = nurse practitioner

PROPATH = a patient education and health promotion program

OPT = orofacial physiotherapeutic treatment

TMS = transcranial magnetic stimulation

MT = music therapy