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Levodopa Dose  
Equivalency

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A Systematic Review

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# Background

- **Complex medication regimens**
  - Levodopa
  - Dopamine agonists
  - MAOB inhibitors
  - COMT inhibitors
  
- **Difficult interpreting clinical trials comparing different drugs**
  
- **Levodopa equivalent dose (LED)**
  - Same anti-parkinsonian effect as 100mg levodopa
  
- **LED for each drug calculated then added together = Total LED**

# Background

- **Calculate LED:**
  - Many different formulae
  - No standard scheme
  
- **Based on:**
  - previous clinical trials
  - drug manufacturers advice
  - summaries of product characteristics
  - clinical experience

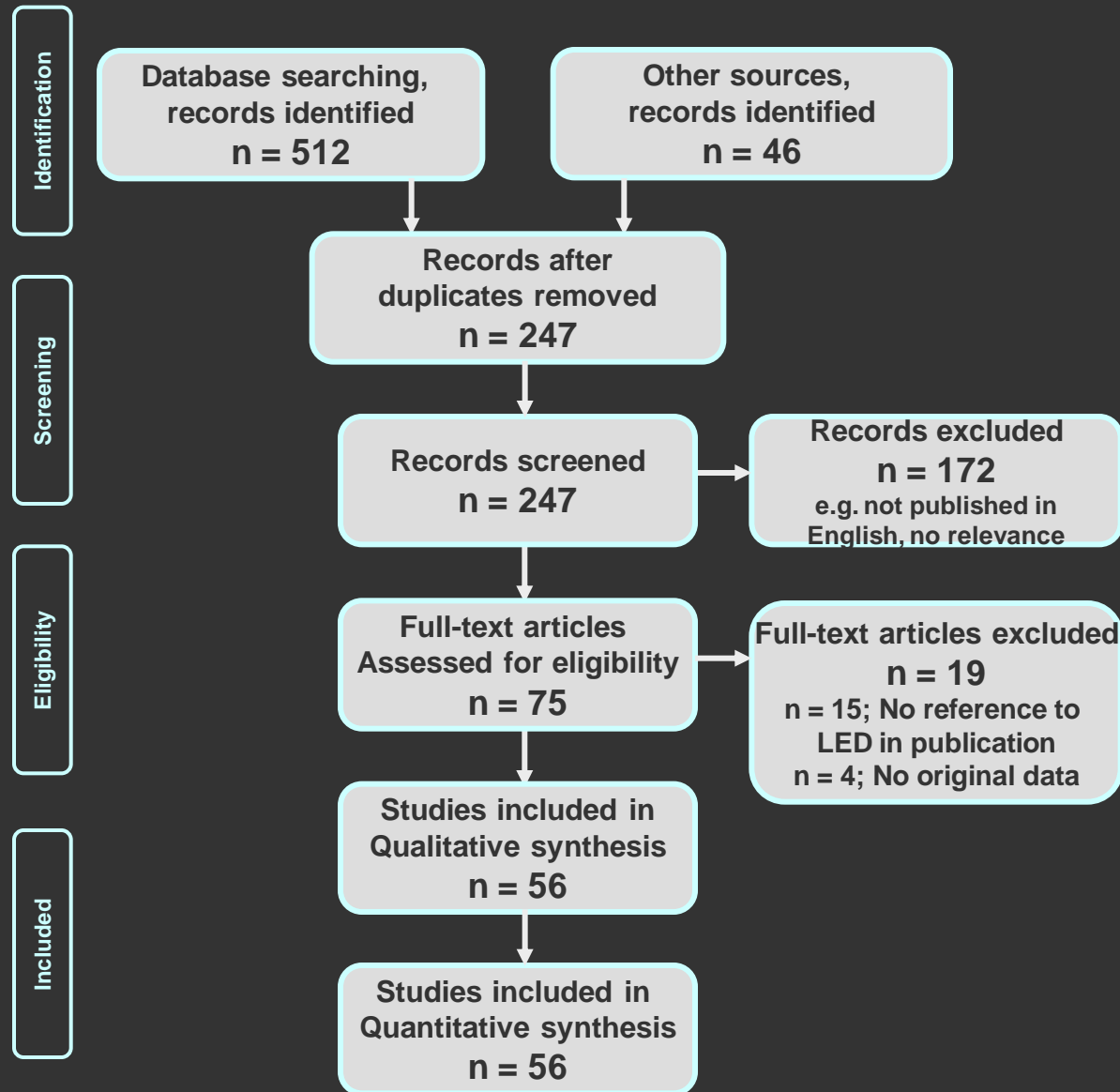
# Aim

- Search for publications reporting LED conversion formula
- Combine data
- Provide a standard formula
- Used to compare dose intensity of different PD treatment regimens

# Methods

- **Systematic search:**
  - **'levodopa', 'equivalent', 'equivalency'**
  - **Electronic databases, general & hand searching**
  - **1980 - end 2009**
  
- **Included all types of studies published in English**
  
- **LED of a drug as that which produces same anti-parkinsonian effect as 100mg of immediate release levodopa.**
  
- **Mean & mode calculated.**

# Results – PRISMA flowchart



# Results – CR L-dopa, Duodopa

Drug Class	Drug	No. Studies reporting LED	Total levodopa Equivalent dose (LED)
Levodopa	Levodopa	-	100
	CR Levodopa	29	133
	Duodopa®	0	90

- **CR levodopa:**
  - Mean = 129mg
  - Mode = 133mg
- **Duodopa®:**
  - Manufacturers info

# Results – COMT Inhibitors

Drug Class	Drug	No. Studies reporting LED	Total levodopa Equivalent dose (LED)
COMT Inhibitors	Entacapone	8	LD x 0.33
	Tolcapone	2	LD x 0.5
	COMT Inhibitor	5	-

- **COMT Inhibitors:**
  - Conversion ratio

**Total levodopa dose + [total levodopa dose x COMT inhibitor value]**



# Results – Dopamine agonists

- **Bromocriptine:**
  - Most consistently reported

- **Pramipexole:**
  - LED 0.25 – 1.67mg
  - Mean = 1.1mg
  - Mode = 1.0mg

- **Ropinirole:**
  - LED 2.5 – 6mg
  - Mean 4.9mg
  - Mode 5.0mg

Drug Class	Drug	No. Studies reporting LED	Total levodopa Equivalent dose (LED)
Non-ergot derived dopamine receptor agonists	Pramipexole	24	1mg salt
	Ropinirole	34	5
	Rotigotine	1	3.3
	Piribedil	7	100
Ergot-derived dopamine receptor agonists	Lisuride	9	1
	Bromocriptine	30	10
	Pergolide	28	1
	Cabergoline	14	1.5
	DHEC	6	20

# Results – MAOBIs, Other

- Few reports for MAOBIs

- Oral Selegiline:

- Mean 10mg
- Mode 10mg

- Sublingual Selegiline:

- No data
- BNF: 1.25mg=10mg

- Apomorphine:

- LED 1 – 20mg
- Mean 9.1mg
- Mode 10mg

Drug Class	Drug	No. Studies reporting LED	Total levodopa Equivalent dose (LED)
MAOB Inhibitors	Selegiline 10mg (Oral)	2	10
	Selegiline 1.25mg (Sublingual)	0	1.25
	Rasagiline	0	1
Other	Amantadine	1	100
	Apomorphine (Infusion or Intermittent injections)	14	10

# Conversion Factors

Drug	Conversion factor
Immediate release L-dopa	X 1
Controlled release L-dopa	X 0.75
Entacapone (or Stalevo®)	LD x 0.33
Tolcapone	LD x 0.5
Duodopa®	X 1.11
Pramipexole (as salt)	X 100
Ropinirole	X 20
Rotigotine	X 30
Selegiline-Oral	X 10
Selegiline – sublingual	X 80
Rasagiline	X 100
Amantadine	X 1
Apomorphine	X 10

# Calculating Total LED

	Actual total daily dose (mg)	Conversion factor	Subtotal LED (mg)
Immediate release L-dopa	400	X 1	400
Controlled release L-dopa	100	X 0.75	75
Entacapone (or Stalevo®)	800	LD x 0.33	132
Ropinirole	20	X 20	400
Rasagiline	1	X 100	100
Amantadine	200	X 1	200
<b>Total levodopa equivalent dose</b>			<b>1307 mg/d</b>

# Discussion

- **1<sup>st</sup> systematic review of LED studies in PD**
- **Requires assumptions, prone to limitations**
- **Standardised formula:**
  - **Allow straight forward comparisons**
  - **Appropriate in context of clinical trials**

# Summary

- Express different doses of anti-parkinsonian medications on a single scale
- Eliminate inconsistencies
- Use conversion formulae to report LEDs in PD MED and PD SURG

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