Table S1: Criteria for risk of bias assessment of case-control studies

1. Can we be con	fident about the exposure assessment?
Definitely yes	There is no situation to be considered as "definitely yes" because case- control studies are retrospective and exposures might have happened long time before recruitment of participants. Thus, the analysis of fluids (blood/urine) to assess paraquat internal dose probably wouldn't reveal the
	past exposures.
Probably yes	Exposures were assessed by occupational exposure matrix, occupational exposure assessment by a certified industrial hygienist/agronomist/epidemiologist or georeferencing coding systems, AND Assessors and subjects were blinded to the study hypothesis or to the case status of participants, OR Exposures were reported by the participants in structured interviews/questionnaires, AND
	Assessors and subjects were blinded to the study hypothesis or to the case status of participants, AND If the authors reported details, such as frequency (days/year), duration (hours/year), method (portable, tractor), and years (beginning/end) of paraquat use.
Probably not	 Exposures were assessed by occupational exposure matrix, occupational exposure assessment by a certified industrial hygienist/agronomist/epidemiologist or georeferencing coding systems, AND Assessors and subjects were clearly not blinded to the study hypothesis or to the case status of participants, CR Exposures were reported by the participants in structured interviews/questionnaires, AND Assessors and subjects were blinded to the study hypothesis or to the case status of participants,

	AND	
	Authors did not inform if interviews/questionnaires covered details,	
	such as frequency (days/year), duration (hours/year), method (portable,	
	tractor), and years (beginning/end) of paraquat use.	
	Exposures were reported by the participants in structured	
	interviews/questionnaires,	
Definitely not	AND	
	Assessors and subjects were clearly not blinded to the study hypothesis or to	
	the case status of participants,	
	AND	
	Authors did not inform if interviews/questionnaires covered details, such as	
	frequency (days/year), duration (hours/year), method (portable, tractor), and	
	years (beginning/end) of paraquat use.	
2. Can we be confident about PD diagnosis?		
	An accurate PD diagnosis should correlate data from autopsy findings and	
	clinical symptoms (Hughes et al. 1992a). Since it is not possible to account	
	for histopathological analyses, a "definitely yes" was considered when PD	
Definitely yes	was based on clinical features, diagnosed by a neurologist who examined	
	each case at recruitment, according to the criteria adapted from the UK PDS	
	Brain Bank ^a (Hughes et al. 1992b).	
	Cases were evaluated by neurologists or trained health professionals at least	
	once, not necessarily at recruitment (e.g., recruited from movement disorder	
	clinics or hospitals),	
	AND	
	At least the following criteria were specified: (I) at least two of the four	
	cardinal signs of PD (bradykinesia, resting tremor, postural instability	
Probably yes	and rigidity), (II) without early atypical features that might support	
	differential diagnoses, and (III) no evidence of other possible causes of	
	parkinsonism that may explain the patient's symptoms (e.g., drug-	
	induced, head trauma, brain tumor, infections),	
	OR	
	Diagnostic criteria were not described in detail, but it points to PD.	
Probably not	Cases assessed by neurologists/trained health professionals or recruited from	
	neurological clinics,	
	AND	
	Diagnostic criteria were not mentioned.	

Definitely not	Cases randomly recruited from telephone lists or electoral zones, and the PD	
	diagnoses were reported by the participants in questionnaires or interviews,	
	OR	
	When clearly only parkinsonism was investigated.	
3. Were the case	s properly selected?	
Definitely yes	Cases selected from a specific catchment area,	
	AND	
	Cases were selected in a given time frame,	
	AND	
	The criteria used for PD diagnosis did not change from the study period up	
	to the moment of this review.	
	The criteria used for PD diagnosis did not change to up to the moment of	
	this review,	
Probably yes	AND	
1 tobably yes	Cases were selected from a specific catchment area,	
	AND	
	The time frame was not clearly stated.	
	Criteria used for PD diagnosis did not change up to the moment of this	
	review,	
	AND	
Probably not	There was clear evidence that cases were not selected from a defined	
	catchment area,	
	OR	
	Cases were clearly selected from very different time frames.	
	Criteria used for PD diagnosis changed from the study period up to the	
Definitely not	moment of this review,	
	OR	
	There was clear evidence that the cases were from different populations	
	(urban vs. rural).	
4. Can we be confident that controls did not have PD?		
	Controls evaluated by a neurologist who confirmed that there was no PD or	
Definitely yes	any neurodegenerative disease at recruitment.	
	Controls were selected from pharmacy databases, neurological clinics or	
Probably yes	hospitals for the treatment of non-neurodegenerative diseases,	
	OR	

	Controls randomly recruited from telephone lists or others, and participants	
	with any type of neurodegenerative disease were excluded.	
	Controls were recruited from neurological clinics/health insurance	
	databases,	
Probably not	AND	
	It was not clear whether they had any type of other neurodegenerative	
Definitely not	diseases.	
	Controls randomly recruited from telephone lists or others,	
	AND	
	It was not clear whether they had any type of other neurodegenerative	
	diseases.	
5. Were the controls properly selected?		
	Controls selected from the same population as the cases (same time frame	
	and same location/practice),	
Definitely yes	AND	
	They were equally at risk of exposure to paraquat (environmentally and	
	occupationally) as the cases.	
	Controls selected from the same location/practice as the cases,	
	AND/OR	
Probably yes	The time frame information was not clearly stated,	
	AND/OR	
	They were not equally at risk of exposure to paraquat as the cases.	
	There was clear evidence that they were not selected from the same location	
Probably not	as the cases,	
	OR	
	There is clear evidence that they were not selected from the same time	
	frame as the cases.	
	Controls were clearly recruited within very different geographic regions as	
Definitely not	the cases,	
	AND	
	Controls were clearly recruited within very different time frames.	
6. Were cases and controls matched according to important prognostic variables or was		
statistical adjust	ment carried out for those variables?	

Definitely yes	When the authors adjusted for all the following variables: age, sex, duration of exposure, rural life, well water consumption, smoking, use of personal protective equipment (PPE), and family history of PD.
Probably yes	When the authors considered at least the variables "age", "sex", "duration of exposure", and "smoking" in the adjustments.
Probably not	When the authors considered only the variables "age", and "sex" and "smoking" in the adjustments.
Definitely not	When the above variables were not considered.

^a First step, diagnosis of a parkinsonian syndrome characterized by: bradykinesia and at least one of the following: muscular rigidity, resting tremor (4–6 Hz) or postural instability unrelated to primary visual, cerebellar, vestibular or proprioceptive dysfunction. Second step (exclusion criteria for PD): repeated strokes with stepwise progression, repeated head injury, use of antipsychotic or dopamine-depleting drugs, definite encephalitis and/or oculogyric crises on no drug treatment, sustained remission, negative response to large doses of levodopa (if malabsorption excluded), strictly unilateral features after 3 years, other neurological features, such as supranuclear gaze palsy, cerebellar signs, Babinski sign (plantar reflex), early severe dementia with disturbances of language, memory or praxis, presence of a tumor and exposure to a known neurotoxin. Third step (supportive criteria for PD): when there are three or more fulfilled items - unilateral onset, resting tremor, progressive disorder, persistent asymmetry affecting mostly the side of onset (if patients were not submitted to surgery and to the use of neurostimulator devices), and excellent response to levodopa (Hughes et al. 1992b).