

Ekbom syndrome, an evidence based review of literature

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ABSTRACT

Delusional Parasitosis (DP) is a Psychocutaneous disorder that was 1st described in the late 17th century in France. The etiology is neuro-chemical. The classic "matchbox" and "specimen" signs are characteristic. Management is via a multidisciplinary approach. This review paper is based on detailed systematic review of literature via an up-to-date evidence based approach. This paper reviews: Historical facts, epidemiology, pathogenesis, clinical features, subtypes, associated diseases, psychosocial impact, economic considerations and management. An exhaustive search strategy was utilized across five medical literature databases led by 62 pre-specified keywords, followed by database-specific filters' application to scrutinize the hierarchy of literature, from systematic reviews and randomized controlled trials to medical papers with weak evidence. Forty references were utilized to extract the most relevant data. This review article is level II-3 (level of evidence); it will enable the researcher to obtain a perspective of DP, upon which an original research can be developed.

Key words: Delusional parasitosis, Ekbom, Morgellons, Matchbox sign, Specimen sign

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INTRODUCTION

Patients with Delusional Parasitosis (DP), also known as *Ekbom syndrome* (ES), have the false and unshakeable belief that organisms or bugs are living in the skin and sometimes in other parts of the body. In young patients, DP can be the earliest sign of a major psychotic illness. It was first described by Thiebierge & Perrin. Alistair Munro considered it a type of monosymptomatic hypochondriacal psychosis. Karl Ekbom described its principal manifestations in 1937–1938. In 1978, a pivotal monograph (by Annika Skott) with the term *Dermatozoenwahn* (coined by Ekbom) was published. Regarding a similar non-synonymous condition (but within the same delusional complex) called *Morgellons disease*, first described by Thomas Browne in 1690. Mary Leitao in 2002, a frustrated mother by her two years old son, named it "*Morgellons disease*", which refers to a local area in France, in which delusional skin infestation is related to inanimate materials rather than bugs. Somatic delusions are among

the most difficult conditions to treat in dermatology, and dermatologists must be sufficiently prepared to treat them; classical treatment is with anti-psychotics.¹⁻⁸

This study will aim to find the highest and the most up-to-date evidence, to create a literature review of a competitive quality to the superior evidence-based systematic reviews.

MATERIALS AND METHODS

A detailed search strategy was utilized across five databases: PubMed, The Cochrane Library, Scopus, metaRegister of Controlled Trials, and Open Gray. The search was conducted from June 15 to August 1, 2015.

The search was led by an exhaustive list of pre-specified keywords of free text, Medical Subject Headings (MeSH), and their combination. The total of number of keywords reached 62, and they were categorized into five main

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groups: delusional parasitosis (DP) disease nomenclature and related terminology, gender categorization, age groups, terminology of investigative modalities, and therapeutics' terminology. Boolean operators and truncation were used to narrow and expand the search, respectively.

This was followed by the application of database-specific filters (Table 2-1). However, some restrictions (filters) were not applicable (N/A) due to the nature of some databases. Additionally, inclusion and exclusion criteria (Table 2-2) were created to scrutinize the hierarchy of available medical literature, from guidelines, systematic reviews, and randomized controlled trials (RCTs) to medical papers with weak evidence. Guidelines databases were also searched, but no well-structured guidelines were found.

Table 2-1: The filters (limits) that were applied across the searched databases	
Database	Applied filters
PubMed	English language Full text search Priority to publication date in the last 5 years Human studies only Priority to systematic reviews, RCTs, multicenter studies
The cochrane library	English language Publication date 2010 to 2015, were a priority Human studies only Full text search Priority to papers of higher level of evidence
Scopus	English language Articles and reviews under the topic of "Medicine" Literatures from all countries Humans only
Open gray	N/A
Meta register of controlled trials	N/A

Table 2-2: Inclusion and exclusion criteria, used to filter the searched papers	
Inclusion criteria	Exclusion criteria
Primary DP*, Secondary functional DP, Secondary organic DP, orificial DP, Delusory cleptoparasitosis, Delusional Infestation (DI), and Morgellons disease Females and males (all age groups)	Conditions related to the DP, including: Formication, and Illusions of parasitosis
Literature of high level of evidence Literature from: Dermatology, Psychiatry, Neurology, Psychology and Entomology	Literature of low quality level of evidence was conditionally excluded. Exclusion was based on low scoring on CASP critical appraisal tool

*Delusional parasitosis

The Critical Appraisal Skills Programme (CASP) appraisal tool was used to evaluate the papers from the filtered search results. This tool was practical and convenient due to a number of reasons. Many articles failed or scored low during the analysis via the CASP tool. Among the appraised papers that were used to create this review article; five papers scored the highest. These five papers were thoroughly used in the citation of this literature review paper. It's worthy to mention that only one well-structured systematic reviews were found in the searched literature (across five different databases). No well-structured Randomized Controlled Trials (RCTs) or other systematic reviews were found, possibly due to disease rarity.

RESULTS

An in-depth analysis of the papers extracted via database search engines (Figure 1-1 and 1-2), revealed:

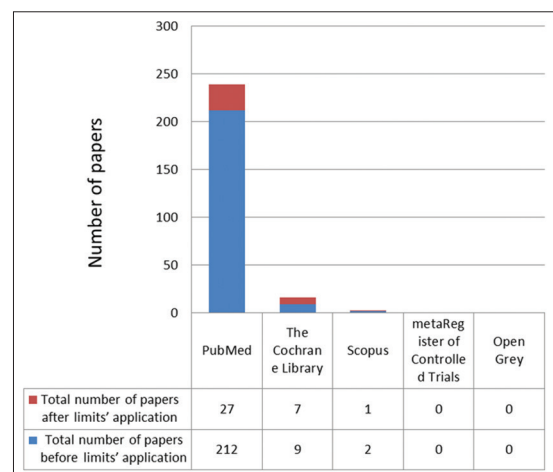


Figure 1-1: Component bar chart, for numerical analysis of the searched papers, across five medical literature databases.

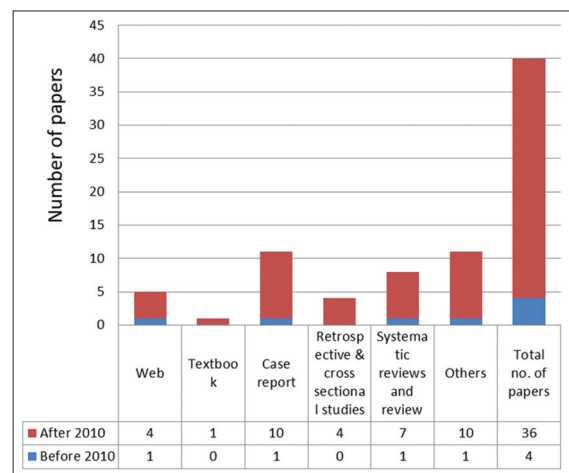


Figure 1-2: A component bar chart for numerical analysis of appraised papers, based on the source and its chronology

- Out of 223 papers (prior to the application of filters and limits), only 40 papers (filters applied) were utilized for the citation and referencing of this literature review paper. Out of the 40 cited references, only five papers (Table 3) scored with the highest available level of evidence. These papers were thoroughly used in the citation of this paper.
- In the references, there were 7 types of papers: websites, textbooks, case reports, retrospective and cross-sectional studies, reviews and systematic reviews and others (where categorization of type of study/paper was not applicable).
- The five papers (of the highest evidence) were: one systematic review, two review articles, and two retrospective studies. Lepping et al.,¹ in his systematic review, studied the Antipsychotic treatment of primary of DP. This paper scored with highest level of evidence despite it dates back to 2007.
- The overall level of evidence, based on the searched papers' analysis via CASP appraisal tool, was of level II-3. This corresponds to evidence extracted from papers of multiple time series with or without the intervention. Dramatic results in uncontrolled trials might also be regarded as this type of evidence.

DISCUSSION

Epidemiology and demographics

Psycho-cutaneous disorders are more common in females; however, DP affects both sexes equally below 50 years of age, and the male-to-female ratio of having the disease is 1:3. DP is considered rare; however, Ekblom stated that it is common for mentally ill people to believe they have creatures in and/or on the body. DP affects 2.37–17 per million per year. The age of onset ranges from 55–68 years; however, primary DP may occur in adolescents, and those in the age group of 20–40 years must be dealt with the utmost concern due to recreational drugs that may trigger or cause DP. The average duration of the disease is 3 years, but it may last decades. There are no socio-economic, racial or peculiar predilections; however, social demographics can be a factor. Many ES-sufferers are intelligent, high-functioning, professionals, medical professionals and even psychologists.^{3,6–10}

Pathogenesis

DP may evolve as sensory misinterpretation that transforms into a tactile hallucination and consolidates into delusions, or it may start as a hallucination that progresses to somatic delusion. To understand the pathogenesis, it is essential to know the DP subtypes, these are: primary, secondary organic, and secondary functional.^{3,6,11}

DP's exact etiology is multifactorial. It is of a neuro-chemical base, and this is confirmed by DP-triggering by psychoactive agents, such as cocaine and amphetamine, its association with neuro-hormonal disorders and the aging process.^{3,12}

Huber et al.¹³ proposed that decreased striatal dopamine transportation (DAT) leading to increased extracellular dopamine underlies DP pathogenesis, and this was confirmed by Millard and Millard:³

- Primary DAT inhibitors (cocaine, pemoline, bupropion, amphetamines & others).
- Secondary DAT dysfunction (Parkinson's disease, brain injury and others) Roland W.

Huber et al.¹³ made the first structural MRI study showing the relevance of structural lesions in the corpus striatum (mainly the putamen) in secondary organic DP. This caused disturbed functioning of the putamen (which mediates motor & visual-tactile perception) and associated brain areas of the somatic dorsal striato-thalamo-cortical loop. Moreover, the involvement of the striatum and the efficacy of antidopaminergic-antipsychotics in treating DP indicate dopaminergic dysfunction in DP. The role of postsynaptic-D2 receptors (in mediating the anti-psychotics' effect) and the role of fronto-striato-thalamo-parietal brain circuits in mediating Delusional Infestation (DI), which is in the same spectrum as DP, was confirmed.^{2,6,11–16}

Clinical features

Presentation can be diverse, and patients are regular visitors to hospitals, persisting in their need for a cure. More advanced/established cases involve repeated consultations to specialist services (emergency physicians, family physicians, entomologists, veterinary services and even esteemed scientists) to eradicate the imagined infestation. Patients may present with ill-defined, persistent itching

Table 3: Papers that scored with the highest level of evidence

Title	Author	Type	Level of evidence
Antipsychotic treatment of primary delusional parasitosis	Lepping et al. ¹	Systematic review	Level II-3
Morgellons disease and delusions of parasitosis	Robles et al. ²	Review article	Level II-3
Les délires d'infestation cutanée parasitaire. Syndrome d'Ekblom	Bourgeois ⁴	Review article	Level II-3
Delusional infestation is typically comorbid with other psychiatric diagnoses: Review of 54 patients receiving psychiatric evaluation at Mayo clinic.	Hylwa et al. ¹⁸	Retrospective	Level II-3
Treatment options of delusional parasitosis: Case series of 14 patients	Coşar et al. ³⁵	Retrospective	Level III

without evident delusions.³ This is sometimes accompanied by the cutaneous sensation of bugs (formication), or even visual confirmation of bugs, involvement of the genital, oral or ocular areas (orificial DP).^{3,11} Pruritus is reported in more than 80% of sufferers, and others describe crawling, burrowing and biting. Attempts to extract the bugs produce extensive skin excoriations, which can also present with bruising, traumatic alopecia, contact dermatitis and scarring.^{3,6,8}

To relieve symptoms, the patient uses: Scissors, files, needles, penknives and tweezers, and the most disturbed patients use surgical instruments, chemicals, corrosives and pesticides. Old self-mutilated lesions appear: Lichenified, excoriated, ecthymatous or crusted.^{3,6,8} Patients usually provide a small container (matchbox, pill container or a sealed plastic bag), classically known as a “matchbox sign”, or better called a “specimen sign”, enclosing the assumed/imagined organisms. On microscopy, samples appear to be hair, skin, fabric, dust, dirt, serum, ants and fleas, but devoid of real pathogenic organisms.³

The patient may even provide detailed description(s) and/or drawing(s) of the organisms’ movement/life cycle. A scientist claimed he had discovered a new insect that infested his skin, and he made detailed sketches of the insect and its copulation as seen by him under microscopy.^{3,8}

Shared delusion

About 5–15 % of patients have associated delusion with a close relative; these are mostly female family members or sympathetic/submissive/socially and culturally-isolated individuals. Such delusions are called “folie à deux”, “folie à trois” and “folie à famille” (folie is the French word for “madness”). Recently, the role of the media and internet has been observed in shared delusions (referred to as “folie à Internet” or “cyberchondria”). The quality of life of the patient and their family members is severely jeopardized.^{3,8,11,17}

Variants, subtypes and related conditions

Many variants, subtypes and related conditions of DP exist (Table 4-1). Similarly, there are numerous conditions that may coexist with DP.^{3,4,6,11,18–20}

Associated diseases

DP can occur in disease, affecting the non-dominant hemisphere, as in Cerebro-Vascular Accidents (CVA). Structural brain abnormalities that have been reported include subcortical vascular encephalopathy and right hemisphere stroke in the temporo-parietal cortex. Similarly, DP can be a part of senile dementia. It has also been described in pellagra, B12-deficiency, after coronary bypass surgery, as a side-effect of phenelzine, severe renal disease

and others (Table 4-2). In a young adult, recreational drug abuse must be considered.^{3,13,15,21–24}

Histopathology

Skin histology is completely normal without specific findings; however, secondary lesions due to rubbing, scratching and picking. While other patients, may attempt to persecute the invisible organism or the inanimate subject can lead to lichenification, excoriations, ecthymatous changes, bruising, traumatic alopecia, contact dermatitis and scarring.^{3,6,8,12}

Psychological, social, and economic impact

As in any psychological or physical disfiguring skin disorder, there is a negative impact on body image and self-esteem. Depression, frustration, anxiety and social phobia may develop. Even the management of DP is always challenging and frustrating. To quote a patient’s frustration: “My creepy crawl lies definitely caused anxiety and agitation. I remember fantasizing about cutting my own skin open and ripping my leg muscles to shreds”. Moreover, shared delusions will jeopardize the quality of life of both the patient and their family and make treatment more challenging.^{3,25,26}

Suicide is a risk in such patients, and they should be admitted to hospital and to be carefully monitored. In severe DP, the physician may persuade the patient that treatment is necessary because of the psychological impact, telling them that the organism can be virulent in psychologically and physically-fragile individuals. DP can revolve on a bio-psycho-social management model in collaboration with psycho-dermatologists, where stress reduction is pivotal.^{3,27,28} Chronic DP will eventually result in skin scarring. In all chronic scarring dermatoses, psychosocial and economic impacts are evident. High economic impact arises from: Specialist referrals, doctor shopping-physician odyssey, utilization of many laboratory/diagnostic resources, thorough initial work-up, self-financed diagnostic evaluations, absences from work and consequences of unemployment, self-imposed limitations on social interaction, family disruption, utilization of toxic and caustic chemicals/drugs/remedies, substance abuse, and fear(s) of contagion & social phobia.^{3,29–33}

Treatment

The dilemma in DP (especially the primary type) is convincing the patient that their condition is psychiatric. Therefore, solid doctor-patient trust is essential (Table 4-3). If left untreated, DP becomes fortified against further measures. Delusion almost never resolves itself naturally, but there is a 50% chance of remission if a psychotropic drug is administered early after the onset of symptoms.

Table 4-1: Variants, subtypes and conditions related to DP^{3,4,6,11,18-20}

Condition	Description/notes
Primary DP	No organic or psychiatric causes
Secondary functional DP	Associated with other psychiatric conditions
Secondary organic DP	Caused by medical illness or substance abuse
Orificial DP	A variant of DP involving body orifices
Delusory cleptoparasitosis	Patients think the organism is in their dwelling
Delusional infestation (DI)	Includes both DP & delusion of infestation with inanimate objects. Patients usually have other psychiatric disorders. ^{18,19}
Morgellons disease	Combination of delusional infestation with cognitive defects, behavioral changes, tiredness & others. ^{3,11,20}
Formication	Similar to DP, but patients are not delusional (i.e. they can be convinced with evidence that they do not have a real infestation)
Illusions of parasitosis	Produced by actual physical causes. As insulation/static electricity/fragments that feel like stings & various allergens/materials, such as formalin, produce dermatitis, such individuals are not delusional and are convinced when the condition is explained. ^{3,6}

*Delusional parasitosis

Table 4-2: Disorders associated with secondary delusional parasitosis³

Systems	Disease/disorder	
Neurological	Dementia and neurodegenerative diseases	
	Parkinson's disease	
	Huntington's disease	
	CNS tumors	
	Head injuries	
	Encephalitis	
	Meningitis	
	Multiple sclerosis	
	Learning disability	
	Cardiovascular disorders	Arrhythmias
		Heart failure
Coronary artery bypass		
Renal diseases	Chronic renal failure	
	Dialysis	
Liver disease	Hepatitis	
Endocrine disease	Diabetes mellitus	
	Hyperthyroidism	
	Hypothyroidism	
	Panhypopituitarism	
	Hyperparathyroidism	
Nutritional disorders	Acromegaly	
	Pellagra	
	Folate deficiency	
	Vitamin B12 deficiency	
Infectious diseases	Anorexia nervosa	
	Syphilis	
	AIDS	
	Tuberculosis	
Malignancy	Leprosy	
	Breast cancer	
	Colon cancer	
	Lung cancer	
	Lymphoma	
Substance abuse	Chronic lymphatic leukaemia	
	Amphetamines	
	Cannabis	
	Cocaine	
	Ecstasy	
Medicines	Opiates	
	Corticosteroids	
	Ciprofloxacin	
	Mefloquine	
	Pemoline	
	Phenelzine	
Pargyline		

Table 4-3: Step-by-step approach to gain solid rapport with patients of delusional parasitosis^{3,4,6,8}

First consultation/encounter is crucial
 It is important to look, listen & be empathetic
 Comfort patient by saying that this condition has been seen/ treated before
 Reduce patient's agitation/preoccupation
 Conduct a thorough skin examination
 Microbiological/parasitological testing to be conducted of the patient's "specimens"
 Examine more "specimens" in the consulting room & laboratories
 Pay attention to recreational drug abuse
 Avoid being misunderstood by patient as supporting their delusions
 Acknowledge that the patient's symptoms are real (though delusional)
 Avoid premature confrontation with patient
 Delusional patients who perceive agreement or confrontation are difficult to treat
 Within 2–3 visits, it is possible to start to explore/discuss the whole illness to patient
 Shake ability of delusion can be estimated at this point of time
 Start with non-irritating local therapy for self-induced lesions
 For patients with anxiety/depression, anti-depressants can be offered
 Psychotherapeutics should only be suggested when you gain patient's trust
 If offered, very few delusional patients would accept an antipsychotic agent
 Psychiatrist help can be utilized in immediate future
 Psychiatric colleague can see the patient in the dermatology ward
 When starting anti-psychotics, initially it is better to hospitalize patient
 Family members must ensure/monitor patient's compliance with therapy
 Be cautious if shared delusion exists among family members
 Further management is joint consultation with psychiatry department

A multi-disciplinary approach between physicians, laboratory workers, entomologists and pest control organizations is essential. The physician must struggle until the patient is motivated to use a specific therapy, usually a combination psychiatric and psychosomatic therapy. It is vital to watch for secondary and self-induced skin lesions,

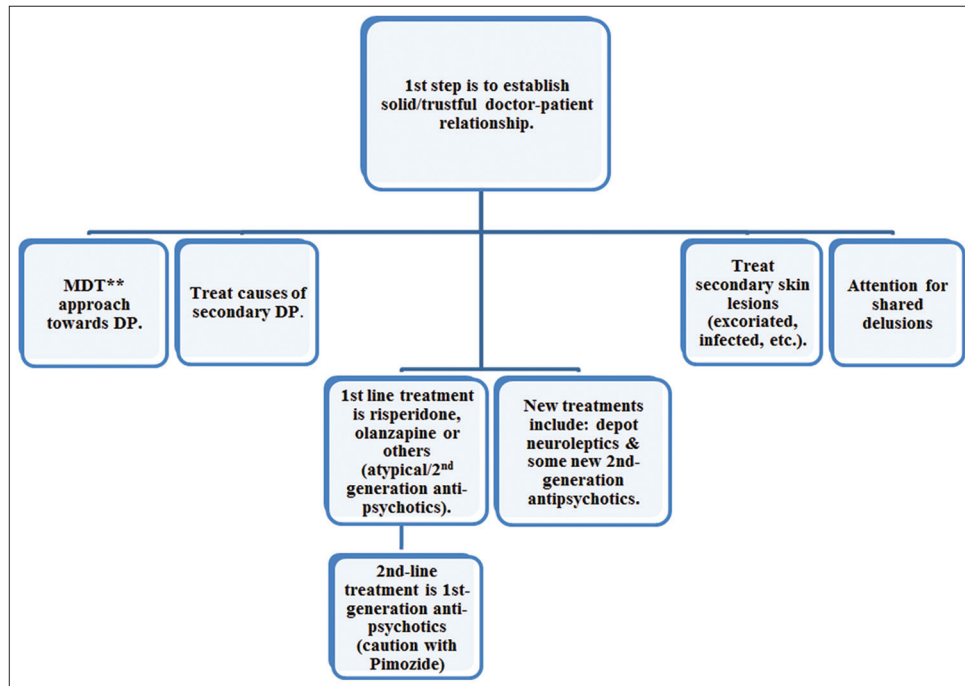


Figure 2: Treatment algorithm for DP^{3,4,6,8,34}, *Delusional parasitosis, **Multidisciplinary approach

such as cellulites, bruising, traumatic-alopecia, contact dermatitis and scarring. The underlying cause in secondary DP should never be forgotten.^{3,4,6,8,34}

The current first-line treatment is risperidone and olanzapine (atypical or second-generation anti-psychotics), and the classical treatment was Pimozide (first-generation anti-psychotics). Pimozide showed recovery in 90% of cases; however, due to its risk profile (extrapyramidal and cardiac toxicity), Pimozide is now the second-line treatment. However, safer first-generation treatment includes: Haloperidol, perphenazine and sulpiride (Figure 2).^{3,8,12}

Atypical (second-generation) anti-psychotics have a safer profile and are better tolerated (than Pimozide); however, major risks include metabolic dysfunction. Risperidone (dopamine blocker and serotonin antagonist) treat DP effectively at 1–8 mg/day. Olanzapine (a higher affinity serotonin blocker than dopamine antagonist) is effective at 5–10 mg/day. Full remission with second-generation antipsychotics is accomplished in 75% of cases within 3 months of therapy. Safe first-generation treatment is used as a second-line treatment, with sulpiride (selective dopamine antagonists) at 200–400 mg/day. Huang et al.²¹ reported an unusual association of an ocular disorder with DP, which was treated with Aripiprazole.^{3,8,11,12,14,21,35}

Pimozide (as the second-line option): The initial dose is 2 mg/day, increased by 2 mg/week, up to 12 mg/day; however, Pimozide can be effective at 2–4 mg/day. If the patient's improvement persists, Pimozide is decreased

gradually by 1 mg every 1–2 weeks to reach the maintenance dose or total weaning; however, if the patient deteriorates later, Pimozide can be restarted in a time-limited fashion to control an episode rather than continuous treatment. Similar recurrence may occur with atypical antipsychotics in DP, DI and Morgellons disease.^{3–6}

New treatments

Freudenmann et al.¹⁴ reported the first effective use of aripiprazole (atypical antipsychotic) in drug-induced DI and ziprasidone in organic DI. Contreras et al.³⁶ reported a good response to Pimozide combined with ziprasidone, an atypical antipsychotic (with a lower risk of extrapyramidal manifestation); thus, ziprasidone might be a good first treatment option.

Depot anti-psychotics can be considered in the case of a patient's poor compliance with oral medications. To convince the patient of such an approach (depots), the "hyposensitization" motivational strategy is used by explaining to the patient that their condition is analogous to extreme hypersensitivity of the most peripheral skin nerves.^{3,14,35–40}

CONCLUSION

DP is a rare unique psychosomatic disorder that is challenging to both the patient and physician. Delusional infestation and Morgellons disease are within the same delusional complex. Mean age of onset from the sixth to seventh decades; however, it may occur from the second

to fourth decades, where recreational substance abuse should be considered. DP pathogenesis is related to neuro-hormonal mechanisms. Management is via a multi-disciplinary approach, building a solid patient-physician rapport, and psychotherapy using second-generation antipsychotics as the first line of treatment.

Conflict of Interest

None.

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Authors Contribution:

AA - Study concept and design, Acquisition of data, Analysis and interpretation of data, Drafting of the manuscript, and Critical revision of the manuscript for important intellectual content

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