Review and a thematic synthesis of GPs perspectives on deprescribing of long-term antipsychotic drugs

Alenus Ulysse, Universiteit Gent

Promotor: Van Leeuwen Ellen, Universiteit Gent

Co-promotoren: Christiaens Thierry, Universiteit Gent

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Nederlandse samenvatting

Dementie is een frequent voorkomende progressieve aandoening in de hedendaagse maatschappij. Naar schatting zouden 47 miljoen mensen wereldwijd hieraan lijden. In België heeft 1,7% van de totale bevolking, een neurocognitieve aandoening. Vermoedelijk zal dit cijfer enkel nog toenemen in de toekomst en speculeert men dat in 2050 het aantal patiënten zal verdriedubbelen. Hieruit kunnen we besluiten dat dementie één van de voornaamste uitdagingen zal worden van de toekomst op vlak van gezondheidszorg.

Neurocognitieve aandoeningen zijn een complex probleem en vertonen vaak verschillende symptomen over het verloop van deze chronische ziekte. Probleemgedrag, is een symptoom dat vaak aanwezig is. In de literatuur wordt het beschreven als “behavioral and psychological symptoms of dementia” (BPSD). Probleemgedrag bij mensen met dementie manifesteert zich bijvoorbeeld onder de vorm van roepen, onrustigheid, agitatie en agressie.

Dit probleemgedrag wordt vaak behandeld met antipsychotica. Uit onderzoeken van de afgelopen jaren is gebleken dat deze medicatie potentieel gevaarlijke bijwerkingen heeft en dat de werkzaamheid voor het behandelen van BPSD eerder beperkt lijkt te zijn. Bovendien houdt het gebruik van antipsychotica verband met een verhoogde mortaliteit. Uit een studie gepubliceerd in 2011 door Azermai et al., blijkt dat 30% van de bewoners in Belgische woonzorgcentra, antipsychotica nemen. Van Leeuwen et al., publiceerde een systematische review waaruit we kunnen concluderen dat afbouwen van antipsychotica bij mensen met dementie op een veilige manier kan gebeuren, zonder significant risico op herval van probleemgedrag.

De risico-batenverhouding van antipsychotica voor patiënten die BPSD vertonen is ongunstig. Afbouwen van deze medicatie wordt aanbevolen en kan op een veilige manier gebeuren. In realiteit is het stopzetten van deze geneesmiddelen vaal complexer. Gezien patiënten met een neurocognitieve aandoeningen vaak hulpbehoevend zijn en in woonzorgcentra verblijven valt hun zorg grotendeels op de schouders van het verzorgend personeel. Tevens kunnen deze patiënten omwille van cognitieve achteruitgang geen beslissingen meer maken waardoor deze verantwoordelijkheid bij de familie valt. Meerdere actoren spelen in een rol in deze beslissing.

De huisarts speelt een centrale rol in het medicatiebeleid van zijn patiënt en draagt de eindverantwoordelijkheid. Het doel van deze studie is, de ervaringen die artsen ondervinden bij het stopzetten van antipsychotica bij patiënten met BPSD, te gaan exploreren. Via systematisch literatuur onderzoek werden kwalitatieve studies gezocht die over dit onderwerp rapporteerden. Uiteindelijk

werden 8 onderzoeken weerhouden die voldeden aan de vooropgestelde inclusiecriteria. Nadien werden 5 categorieën gekozen waarin de verschillende ervaringen van artsen konden worden ingedeeld. De categorieën zijn: denkkader van de arts, professionele samenwerking, patiënt gerelateerde factoren, familie gerelateerde factoren en omgevingsfactoren.

We kunnen besluiten dat afbouw van antipsychotica complex is en wordt beïnvloedt door meerdere factoren. Barrières in het stopzetten die werden weerhouden zijn: beperkte kennis van huisartsen over niet-medicamenteuze opties omtrent BPSD, angst voor toenemende zorg van ouderenzorgpersoneel, angst voor hogere werkdruk van verpleegkundigen, angst voor herval symptomen en verlies in levenskwaliteit, tijdsdruk, en geloof in de werkzaamheid van antipsychotica. Argumenten die het stopzetten faciliteren: huidige richtlijnen met negatieve risico-baten verhouding, professionele samenwerking, positieve ervaringen bij stopzetten medicatie en goede communicatie met familie.

Door het exploreren van deze kwalitatieve data en het opstellen van barrières en facilitatoren die huisartsen ervaren tijdens het stopzetten van psychofarmaca, krijgen we een beter beeld op dit complex probleem. Educatieve stappen voor huisartsen kunnen worden ondernomen om hun niet-medicamenteus beleid te verrijken. Meer initiatieven tot professionele samenwerking kunnen ondernomen worden. De huidige druk en personeelstekort in de ouderenzorg wordt nogmaals bevestigd en kan helpen voor maatregelen op beleidsniveau. Door moeilijkheden te beschrijven geven we enerzijds een aanzet om probleemoplossend te denken en anderzijds een springplank voor verder specifiek onderzoek.

Table of Contents

1. Abstract 2
2. Introduction 3
   - 2.1 BPSD 3
   - 2.2 Management of BPSD 4
   - 2.3 Antipsychotic drugs 5
   - 2.4 Deprescribing 6
3. Methods 7
   - 3.1 Search Strategy 7
   - 3.2 Inclusion criteria 8
   - 3.3 Study Selection 9
   - 3.4 Quality Assessment 10
   - 3.5 Data extraction 10
4. Results 12
   - 4.1 Quality Assessment 12
   - 3.2 Synthesis of the results 12
5. Discussion 17
   - 5.1 Summary 17
   - 5.2 Strengths and Limitations 19
   - 5.3 Comparison with existing literature 20
   - 5.4 Future implications 21
6. Conclusion 22
7. References 23
8. Appendix 27
   - 8.1COREQ- Checklist 27
   - 8.2 Search Hits 28

1. Abstract

Background Dementia is a significant challenge for current healthcare and will exponentially increase in the following decades. Behavioral and psychological symptoms are a manifestation of this disease and, consequently, are a burden for healthcare workers. This problem occurs mainly in nursing homes. Despite guidelines advocating for non-pharmacological approaches, antipsychotics are still prescribed frequently in this population. Literature shows concerns about these medications' efficacy and safety for treating this problem. Once prescribed, they often are used longer than needed. Deprescribing these drugs imposes itself and can be done without losing quality of life and without reoccurrence of the symptoms. General practitioners play a central role in the medication management of their patients, which makes it interesting to explore their experience when undertaking discontinuation of psychotropic drugs. Many factors influence these complex decisions, but they remain poorly understood.

Objective This systematic review aims to investigate the barriers and facilitators general practitioners experience when deprescribing antipsychotic drugs to patients who suffer from behavioral and psychological symptoms of dementia.

Methods A literature review was conducted using databases such as PubMed, Embase, and Google Scholar. The search was conducted in January 2023. Before the search was performed, inclusion criteria based on the research question were made. Thematic analysis was used to analyze the qualitative data of the included articles. Five themes were developed using a deductive method. Quantitative data was used to confirm or contradict the statements from the qualitative data.

Results 6567 records were identified through searching the database. Eight articles met the eligibility criteria and were used for a thematic analysis. Five themes were made: physician mindset, professional collaboration, patient-related factors, family-related factors, and environmental factors. The barriers and facilitators retrieved from the articles were then divided into the categories they belonged to. Physician mindset, professional collaboration, and family-related factors contained both barriers and facilitators, whereas patient-related factors only had barriers and environmental factors only contained facilitators.

Conclusion Deprescribing antipsychotic drugs that are used for treating behavioral and psychological symptoms of dementia presents a complex challenge influenced by multiple factors. Despite guidelines advising non-drug interventions, psychotropic medications continue to be prescribed frequently. Barriers to deprescribing identified: limited knowledge about non-pharmacological interventions by GPs, fear for increased workload of nursing staff, over expected efficacy of antipsychotics used for treating BPSD, fear for relapse of neuropsychiatric symptoms and a loss in quality of life, and limited time. Facilitators identified while deprescribing: current guidelines, negative risk-harm balance for antipsychotics, professional collaboration, positive experience with deprescribing, and communication with family. Addressing barriers and facilitators encountered by general practitioners is necessary for a deeper understanding of the problem and can inspire further focused work.

2. Introduction

Dementia, a neurodegenerative disorder defined as the loss of cognitive functioning to such an extent that it interferes with a person's daily life and activities, is an omnipresent health issue today. Although nowadays the term Dementia is replaced by the term major neurocognitive disorder, it is still used a lot in medical literature and daily practice.

According to the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), major neurocognitive disorder or dementia is defined as a significant cognitive decline in at least one of the cognitive domains (e.g., executive function, complex attention, language, learning, memory, perceptual-motor, or social cognition) and the cognitive deficits interfere with independence in everyday activities of the patient and the cognitive deficits are not in the context of delirium or not better explained by another mental disorder(1).

The symptoms are often persistent and progressive. Until this day, no cure exists for the causes of dementia. The DSM-5 classifies the mild and major neurocognitive disorders based on etiology. There are thirteen etiological subtypes. Alzheimer's dementia is the most common and represents 70% of the cases. Other common causes are vascular dementia, dementia with Lewy bodies, frontotemporal dementia, and Parkinson's disease dementia(2).

Currently, major neurocognitive disorder affects 47 million people worldwide. In Europe, 8% of the population older than 75 years suffers from dementia(3, 4). In Belgium's population, the overall prevalence was 1,7% in 2020(5). As our global population ages, the prevalence and incidence of this condition exponentially increases. It is expected that in 2050, the prevalence number will triple and, therefore will bring a huge burden to caregivers, healthcare systems, the economy and society at large. In other words, this condition has emerged as one of the biggest challenges in contemporary healthcare and future.

2.1 BPSD

Besides the impact on cognitive functions, there are alterations in patients' personality and behaviors. One of the first manifestations of this disease are the behavioral and psychological symptoms of dementia (BPSD). It is also known as the neuropsychiatric symptoms of dementia (NPS). BSPD is defined as the symptoms of disturbed perception, thought content, mood, and behavior frequently occurring in patients with dementia(6). It manifests itself in a heterogeneous group of symptoms such as anxiety, apathy, aggression, wandering, care refusal, hallucinations, etc. The symptoms are often divided into different

clusters such apathy, psychosis, aggression/agitation, hyperactivity and affective. BPSD tends to fluctuate in episodes that can take up to six months making it a complex health issue in prevention and management.

BPSD affects 90% of patients with a major neurocognitive disorder. The five-year prevalence of BPSD of dementia is 97%(7). The etiology is somewhat complex and is often a combination of multiple factors, such as biological, psychological, and social. These symptoms manifest themselves in all different types of dementia.

Consequently, BSPD significantly impacts this patient population, their informal caregivers and healthcare workers. Patients suffering from neuropsychiatric symptoms have more emotional stress, a lesser quality of life, higher hospitalizations, and overall, a lower life expectancy. In the beginning stages of this progressive condition, informal caregivers often bear the weight of emotional, physical, and financial burdens while caring for the patients. Giving round-the-clock support can cause exhaustion, stress, and feelings of isolation. Coping with the unpredictable nature of dementia makes it even harder. In reality, it is seen that after a significant period, admission to a nursing home is inevitable. A shortage in staff, limited resources, and an overwhelming number of patients put an immense burden on the medical personnel of these care facilities, resulting in stress, burnout, and work absence.

2.2 Management of BPSD

There are different neuropsychiatric scales to assess the behaviors and symptoms resulting from BPSD. There is for instance the "Neuropsychiatric Inventory" (NPI) or the "Cohen Mansfield Agitation Inventory" (CMAI). Using these scales in daily practice can help measure NP and the follow-up on specific treatments.
The management of BPSD consists of a pharmacological and a non-pharmacological approach. The guidelines suggest following a flowchart consisting of different steps. The first approach involves recognizing BPSD, describing the behavior, and analyzing the situation. Second, the caregiver must ensure that the patient's basic needs are met. After that, it is necessary to rule out if there is no pain or other explanatory physical conditions. The last step in the non-medical approach is to investigate the psychosocial and personal needs of the patient. In each step, if a potential causative factor is discovered, an intervention is indicated.
Interventions supported in the literature are exercise, cognitive training, stimulation and training of caregivers(8). These interventions reduce BPSD and could limit the usage of antipsychotics(9).

If the non-pharmacological approach does not work, guidelines advice the use of medications. The next step in the flow chart is a test with pain medication. A randomized clinical trial by Husebo et al. states that effective pain management in patients with dementia can significantly reduce agitation(10). Therefore, it is an important step to consider before passing on to psychotropic drugs. The last step in the chain is the use of antipsychotic agents for BPSD. Using these medications should be considered when there is no reversible cause for the patient's behavior, a non-pharmacological approach is ineffective and the behavioral pattern is dangerous for the patient, the caregivers, and their surroundings(8).

2.3 Antipsychotic drugs

Antipsychotic drugs are divided into two big categories: typical and atypical. De typical antipsychotics have a high affinity for dopamine receptors. Therefore, the well-known side effects are extrapyramidal syndrome and tardive dyskinesia. The atypical antipsychotic drugs bind to dopamine receptors and serotonin receptors resulting in lesser extrapyramidal side effects. However, these newer agents also have serious side effects(11). Nowadays, antipsychotic drugs can be used for psychosis, hallucinations, delirium, and psychomotor agitation. It is also indicated for symptoms such as aggression, manic episodes, and agitation, as observed in patients with BPSD. An important note is that, if possible, these medications should be avoided. If used in severe situations, the duration of the treatment should be kept as short as possible and the dose as low as possible. The need for continuation should be evaluated regularly, and a discontinuation date should be provided within three months(12).

Antipsychotic drugs have a negative risk-benefit balance as a treatment for BPSD. The side effects of these medications are dangerous and should always be taken into account when prescribed. An increased risk of cerebrovascular events, cardiac effects, cognitive decline, extrapyramidal symptoms, sedation, infections, and an increased mortality rate can occur with this type of medication. These risks apply to all different kinds of antipsychotic medications. An RCT conducted by Ballard et al. states that there is an increased long-term risk of mortality in patients with Alzheimer’s disease who were prescribed antipsychotic agents in comparison to the placebo group(18, 19). In addition, the elderly population is more susceptible to the side effects of medications due to their physiology. Moreover, it is seen in literature that the efficacy of psychotropic drugs used for treating BPSD is overrated and that the effect is rather modest(20, 21). This kind of medication has a lot of interactions with other drugs; therefore, it is another potential risk for patient’s health, definitely in older patients with polypharmacy. A considerable amount of people with dementia are currently prescribed antipsychotic medications(13-15). Azermai et al

conducted a cross-sectional study in 2013, investigating drug use in nursing homes in Belgium. It is showed that the overall prevalence of antipsychotic drug use was 33% and that 93% from this group used it chronically. The main reason for prescribing was aggression as a manifestation of BPSD(16). In a rapport conducted by De Bleser et al. about antipsychotic usage in nursing homes in Belgium, it is seen that 31,37% of the residents older than 75 years and , were using psychotropic drugs in 2020(17).

We can conclude that antipsychotic medications are a short-term solution for BPSD. Prescription of these medications without considering different options is not recommended. Because of the negative harm-benefit ratio, it is essential to evaluate the pros and contras of this pharmacological treatment. Non-pharmacological interventions are definitely a safer option for the treatment of neuropsychiatric symptoms.

2.4 Deprescribing

Inappropriate prescribing and polypharmacy in older patients are often associated with increased risks. Antipsychotics, despite their adverse effects and limited efficacy, are often prescribed to manage BPSD. More than one-third of people with dementia in nursing homes are prescribed psychotropic agents, and they are often used much longer than the recommended duration(22, 23).

Deprescribing is defined as the process of stopping, tapering, discontinuing, or withdrawing drugs to manage polypharmacy and improve outcomes for patients. In 2014, Pan et al. and in 2018, Van Leeuwen et al. published reviews summarizing trials about the discontinuation of antipsychotic medication in patients with dementia. They concluded that deprescribing these drugs did not significantly differ in BPSD severity and mortality. However, it is suggested that discontinuation may have a negative impact on the symptoms in severe forms of BPSD. Though this was based on a subgroup analysis and further research is necessary. In patients suffering from less severe BPSD it was seen that deprescribing had a positive impact. Eventually both studies suggest that more evidence is needed to explore the effect of deprescribing(24, 25).

Deprescribing antipsychotic medicines is not apparent. Patients with mild or major neurocognitive diseases often live in nursing homes because they cannot take care of themselves anymore, making them rely on other people, such as healthcare workers and family members. Because of neurocognitive deficits, the decisions around medical treatments are made by others than themselves. The treating doctor has the

final responsibility when it comes to medication management, but numerous factors must be considered when undertaking a discontinuation of psychotropic drugs.

Different qualitative studies have been conducted to explore the experience of healthcare workers when deprescribing antipsychotics used for treating BPSD. This review aims to investigate and collect barriers and facilitators identified in different studies that general practitioners encounter during deprescribing endeavors.

3. Methods

This review aims to answer our research question: "Which barriers/facilitators do general practitioners (GPs) experience when deprescribing antipsychotic drugs in patients with dementia?". We intend to find the experiences and opinions of different GPs in qualitative studies such as interviews and quantitative studies such as questionnaires or a combination of both. We created a search strategy to select valuable articles that may contribute to answering this question. First, an exploratory search was done to examine the contemporary literature. The PICO criteria were used to outline a clear vision of which key concepts were needed. In consultation with researchers from the knowledge center at Ghent University (KCGG), a framework different from PICO was used because it didn't address all the topics from our research question. Therefore, the SPIDER criteria (Subject, Phenomenon of Interest, Design, Evaluation, and Research type) were used.

3.1 Search Strategy

Using the SPIDER criteria, five key concepts were identified for the search: "general practitioners," "deprescribing antipsychotic drugs with patients who have dementia," "interviews," "experiences," and "qualitative studies." Some trial searches were performed with the key concepts to evaluate the hits we got in the databases. These five concepts are a part of the inclusion criteria we used for selecting the articles.

For the key concepts "general practitioners," "antipsychotics," "deprescribing," and "dementia," we search for synonyms in abstract and titles, thesaurus, mesh terms, and previously generated search strategies to create a sensitive search in the literature. In collaboration with the specialists of the knowledge centrum, the last search was conducted. The key concepts "experience," "interviews," and

“qualitative studies were not included in the search because the results were too narrow. We chose to use “neurocognitive disorders,” “deprescribing,” and “antipsychotics” and all their synonyms as Mesh terms and Title/Abstract to conduct our search. The exploring research was performed in March 2022. The final search was performed in January 2023. Scanning articles on title and abstract was done between February and May in 2023. PubMed, Google Scholar, and Embase were used.

3.2 Inclusion criteria

Sample: General practitioners

In this study, we are only interested in the opinions of doctors, particularly general practitioners. The aim of this review is to explore the experience of physicians, who have the main responsibility in the deprescribing process. Some studies are examining the same research question but focus on the opinions of nurses and other healthcare workers. These articles will be excluded from the review. If several health professions are combined, then the specific data of GPs will be extracted.

The phenomenon of interest: Deprescribing antipsychotics in a population with BPSD

A contemporary health issue nowadays is that patients with BPSD often get antipsychotics prescribed to treat their symptoms. However, it is known that these medications have considerable side effects.

The phenomenon of interest in our review is deprescribing these antipsychotics. Deprescribing is defined in the literature as the planned and supervised process of dose reduction or stopping medication that might be causing harm or no longer be of benefit to patients. Articles reporting on prescribing were excluded.

In summary, the selected studies had to report on deprescribing psychoactive drugs in a population suffering from behavioral and psychological symptoms of dementia.

Design

The design of studies included in the review is a collection of qualitative studies, such as interviews, focus group studies, or surveys. Open-ended questions and close-ended questions are used. Studies combining qualitative data and quantitative data will be included. There were no restrictions on the publication date.

Evaluation

The review compares the facilitators and barriers identified in the included articles. Various themes of facilitating factors and barriers will be created. Quantitative data extracted from the questionnaire will be used to confirm or deny statements subtracted from open questions.

Research type

Qualitative studies are included. Mixed methods studies with qualitative and quantitative data will also be selected to use information of our interest.

3.3 Study Selection

A preliminary search was done on the different databases that were used. All articles were screened based on title and abstract. They were stored in our citation manager if they met the eligible criteria. With this tool, we could identify and eliminate duplicate records.

Articles had to address topics of deprescribing antipsychotic drugs in people with dementia. Studies that didn't meet the review's aim were excluded (e.g., wrong medication, wrong psychiatric disease, wrong population). Studies in English or Dutch were included. There were no restrictions on years of publication.

By combining the different mesh terms "neurocognitive disorders," "deprescribing," and "antipsychotics" and all their synonyms as Mesh terms and Title/Abstract, we conducted our first search. PubMed, Google Scholar, and Embase were used. A detailed view of the search strategy can be found in the appendix. There were no restrictions on years of publication. To ensure literature saturation, we scanned the reference lists of included studies identified via the electronic database search and relevant reviews published in peer-reviewed journals.

A flow chart of the study selection is shown in Fig. 1. 6567 records were identified through the different databases. After removing 105 duplicates via endnote, 6462 studies remained. They were all screened based on title and abstract. One hundred five were withheld for full-text assessment. Sixteen were not

focused on antipsychotic drugs, 27 concentrated on deprescribing polypharmacy, 17 focused on prescribing, 14 weren't the correct type of study, 22 didn't focus on general practitioners, and one full text wasn’t available. In the end, eight articles met our eligibility criteria.

3.4 Quality Assessment

The included qualitative studies underwent a quality assessment via the COREQ checklist. This tool is designed to improve the reporting of qualitative research studies. It is a comprehensive checklist that consists of criteria that researchers can use to ensure they have essential aspects for their qualitative study. It consists of three domains: research team and reflexivity, study design, and analysis and findings(27). It is scored on 32 points. No articles were excluded after the assessment was performed. (See table in the appendix).

3.5 Data extraction

Thematic analysis was used to analyze the qualitative data of the included articles. The data originated from the questionnaire with open-ended questions. Via an inductive approach, five potential themes were developed that contained barriers and facilitators experienced by general practitioners when trying to stop antipsychotic medication in people with dementia. Topics that reoccurred consistently in different studies were used as a theme. Then, the qualitative data was analyzed and divided into the theme it belonged to. The additional quantitative findings were used to confirm or contradict the statements from the qualitative data.

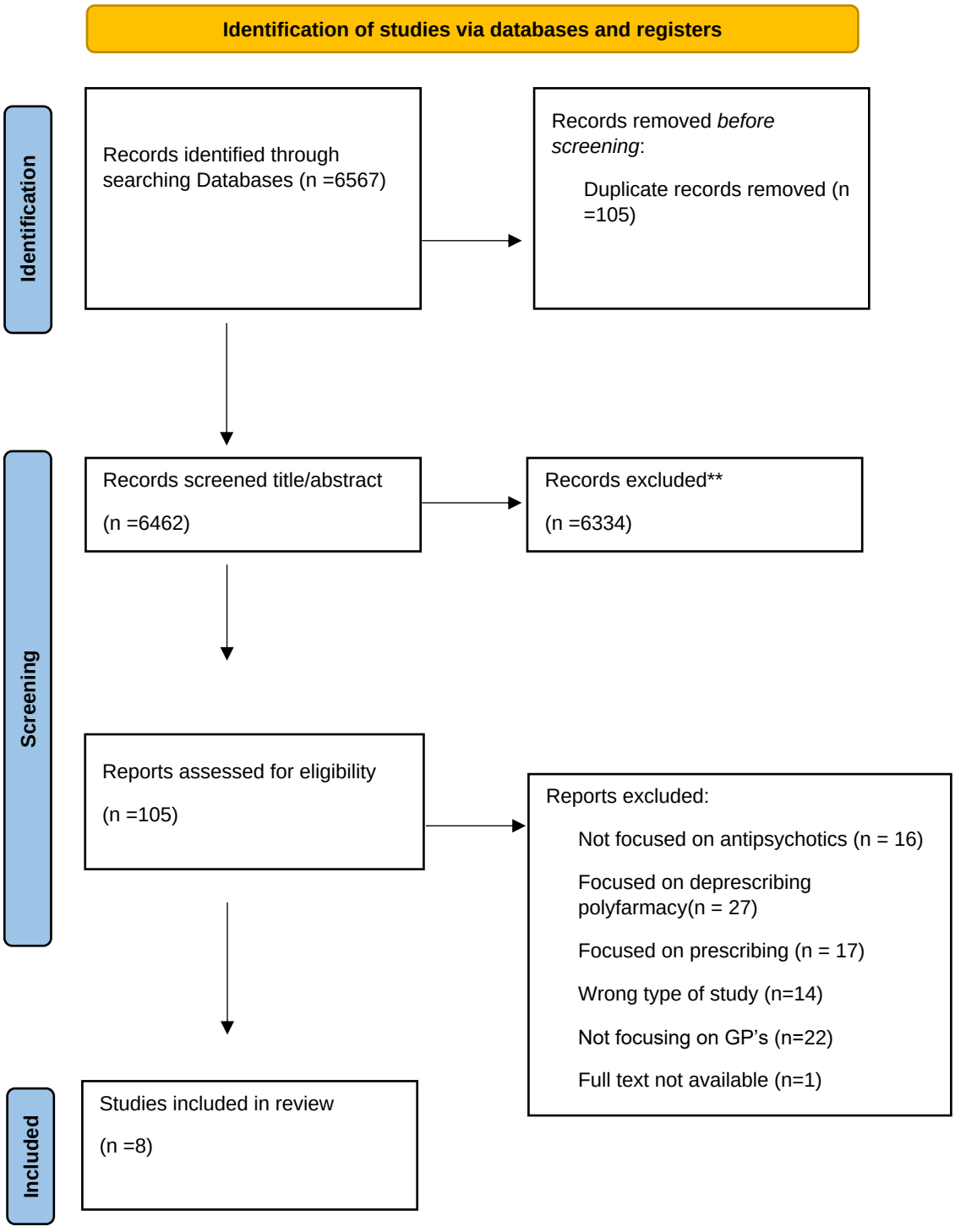


Fig 1: Flow chart study selection

Source	Publication Year	Country	Study objective	Inclusion criteria	Total participants	Participants(GP /physicians)	Methodology
Aerts et al.(22)	2019	Australia	Investigate the reasons for represcription of antipsychotic medication in health care workers	Deprescribing antipsychotics GP's Qualitative study	6	2 GP's	Questionnaire: open-ended questions / Likert-scale questions
Almutairi et al.(28)	2018	UK	Develop an in-depth explanatory model about inappropriate prescribing of antipsychotics in dementia.	Barriers for GP's to deprescribe	28	5 GP's (28 participants, 5 psychiatrists, 2 geriatricians)	Semi-structured interview.
Azermai et al.(23)	2014	Belgium	Documenting barriers experienced to antipsychotic discontinuation	Barriers for GP Antipsychotic discontinuation	41	28 GP's	Mixed method study: expert meeting + structured questionnaire survey
Cousins et al.(29)	2017	Australia/Tasmania	Identify factors influencing prescribing of psychotropic medication	GP experience Barriers deprescribing antipsychotics Nursing homes	244	244 GP's	26-question survey
Dhuny et al.(30)	2020	Ireland	Explore knowledge and opinions of GP's in prescribing psychoactive drugs for BSPD	GP BSPD	168	168 GP's	Close-ended questions + open ended questions Survey
Sawan et al.(31)	2016	Australia	Identify key visible components related to the use of psychotropic medicines in nursing homes	GP Psychotropic medicines	40	3 GP's	Semi-structured interviews
Sawan et al.(32)	2017	Australia	Explore the key dimensions of organizational climate and the subsequent influence on the use of psychotropic medicines	GP Barriers in deprescribing	40	6 GP's	Semi-structured interview
Smeets et al.(33)	2014	Netherlands	Explore factors that elucidate reasons for psychotropic drug prescription	GP Psychotropic drugs for neuropsychiatric symptoms	15	15 physicians	Semi-structured interviews

Tabel 1: Study characteristics

4. Results

4.1 Quality Assessment

The eight articles were assessed using the COREQ-checklist. The score varied between 17 and 26 with an average score of 21. Research team was the domain with the lowest score concerning transparency. Occupation of the research team wasn't present in any of the studies.

3.2 Synthesis of the results

Eight articles were included to use in this review. Four studies were conducted in Australia. One in the Netherlands, one in Ireland, one in Belgium, and one in the United Kingdom. Four studies were semi-structured interviews. Three of the eight were survey studies using a combination of closed- and open-ended questions(22, 23, 30). One study used a closed-ended survey(29). One study used a nominal group technique as a qualitative research method. Via a group of experts, they tend to provide information on the given issue. In total, 471 general practitioners' opinions were investigated on the matter of deprescribing psychotropic medications. The aims of the studies included were diverse. One article described facilitators and barriers to deprescribing antipsychotics(23). The other seven articles investigated prescribing psychotropic drugs for people with BPSD, where deprescribing was a part of the study. Articles were published between 2014 and 2020.

In the selected eight articles, barriers and facilitators were identified that general practitioners experience in deprescribing antipsychotic medicines to people with cognitive deficits showing BPSD. Five overreaching themes were used to classify the different barriers and facilitators: physician mindset, professional collaboration, patient-related factors, family-related factors, and environmental factors.

Physician mindset

The personal thinking framework of the general practitioner is a significant theme concerning whether or not to continue the usage of psychotropic drugs in people with dementia. This theme occurred in six of the eight articles. The general knowledge of the GP on the matter served as a facilitator or a barrier in deprescribing these medications. Knowledge about the effectiveness, side effects, and current guidelines is a facilitator to discontinue antipsychotic drugs(29, 33). On the other hand, a general practitioner and a psychiatrist state that antipsychotics are considered to be the best option available because the benefits outweigh the harms(28). 63% of GPs in the study conducted by Cousins et al. overestimated the benefits of antipsychotic medication(29). Azermai et al. describes that GPs do not believe in non-pharmacological treatment and should be educated more about it. 13,8% of the GPs showed a willingness to undertake discontinuation(23). On the other hand, Cousins et al. and Dhuny et al. reported that 81% and 69% of the interviewed doctors consider a non-pharmacological option before choosing medications(29, 30).

"And yeah, I feel the benefits sometimes do outweigh the risks."(28)

Another critical factor is the personal experience a physician has. Positive effects experienced in individual cases might encourage deprescribing and is sometimes even stronger than evidence-based medicine guidelines (22, 23, 33). Depending on a negative or positive experience, it can serve both as a barrier or

facilitator. Cousins et al. reported that the confidence in GPs, after a first failed attempt, was variable. 35% felt not comfortable and 42% did(29).

A barrier that GPs experience in their process of discontinuation, is that psychotropic drugs that are initiated by other prescribers, are easily continued, especially when they were started in the hospital(28). Physicians with limited work experience appear to be reluctant to stop previously prescribed psychotropic agents(33). Although Dhuny et al state that here was no relation found between experience of GP and the confidence to stop these medications. 54% felt reasonably confident to stop psychotropic medication in a stable patient with dementia that was initiated in secondary care(30, 33).

Time is also described as a barrier in certain articles. The non-pharmacological interventions demand time and energy and therefore can be frustrating for clinicians(30).

"Dementia is very challenging to deal with, needs a huge amount of time and the reality is that we just don't have it and the patients suffer as a result.(30)"

Professional collaboration

Professional collaboration is an essential theme regarding the management of BPSD. Collaboration has a significant impact on the deprescribing process in multidisciplinary care for patients with dementia. Different healthcare workers influence each other through their own experiences and work situations. When they collaborate, each health professional is capable of contributing to or hindering deprescribing efforts. All eight articles reported about this theme.

GPs experienced pressure and resistance from the nursing staff, resulting in a barrier to deprescribing medications(22, 23, 28-33). BPSD often becomes problematic for the care home, and antipsychotics can return a sense of balance to the workplace. Deprescribing could lead to a higher workload and a more intensive observation of residents. Nurses are often reluctant to deprescribing when a considerable effort is made to stabilize the symptoms and are scared to return to previous situations(33). In the HALT study conducted by Aerts et al., nursing staff was in 65% of the cases the primary influencer for incomplete deprescribing(22). In Cousins et al. 91% of the GPs indicated that their prescribing was influenced by nurses and Dhuny et al. reported a percentage of 80%.

Increased staff levels are necessary to implement non-pharmacological techniques when deprescribing. A lack of resources and nursing staff is a barrier. There is also more reluctance to deprescribing when the

nursing staff has limited knowledge about the BPSD and non-pharmacological techniques. Additionally, the expectations regarding the effectiveness of the drugs are too high(23, 28, 29, 33).

"I think there is a very hesitant reaction to problem behavior by the nursing staff. That in general there is little knowledge and few skills related to dementia and types dementia"(33).

On the other hand, GPs experienced that effective communication and cooperation between professionals may prevent the escalation of symptoms or side effects. Clear reporting on the occurrence and severity of neuropsychiatric symptoms facilitated the process of deprescribing. Additionally, easy access and communication with geriatricians and psychiatrists in secondary care were facilitators of discontinuing medications(28-30, 32). 58% of the GPs in the study conducted by Dhuny et al reported that they could consult geriatricians easily(30).

"At a certain moment, we started to have some kind of meeting purely to discuss the residents. By joint looking at the problems and by learning from each other we gained more clarity. And also had a significant decrease in prescribed medication"(33).

There are circumstances where, once prescribed, medication needs to be reviewed, but there are barriers to this; for example, when GPs lack time, and do not prioritize care homes(28). In Azermai et al. a medication review by doctors had occurred in 74,1% of the cases in the last three months where an actual discontinuation attempt was performed in 9,8%(23).

A Medication advisory committee that reviewed patients' medications and initiated a deprescribing process raised physicians' awareness and is, therefore, a facilitator. Pharmacist medical reviews were done and sent to the GP. This was used as a safety net for medications that were overlooked by nursing staff and GPs(32). Some doctors ignored the pharmacists' recommendations and did not use the tool (28, 29, 32). In line with this, Cousins et al shows that pharmacists were cited by more than half of GPs as the most likely health profession to request dose reduction. Although only 28% of doctors actually felt influenced by them.

"I think the problem with dementia is that, I would have say, I don't think that they do a lot of reviews of this type on patients with dementia"(28).

Patient related factors

Factors influencing the patient's health is another theme retained from the selected qualitative studies and was found in five articles. The concerns about the quality of life of patients after stopping antipsychotic agents were experienced as a barrier to deprescribe(23, 28, 30, 33). A majority of the GPs were concerned that withdrawing medication would negatively impact a person's behavior, leading to a return of challenging behaviors of BPSD(30). Physicians were also concerned about the hindrance to others and the risk of harm to themselves and staff(23). The medication brings symptomatic and personal relief and allows the patient to be treated in a nursing home. In the study conducted by Azermai et al., negative impact on the quality of life, had the highest score on a barrier scale from 1 to 10, scoring a mean of 7,5. Dhuny et al. and Cousins et al. reported that 63% and 42% of GPs were concerned about withdrawing and losing quality of life(23, 29, 30).

"Because you simply are afraid that the same behavior will come back. Moreover, at that moment, you are actually glad someone is doing well. And then you think, gosh, should you take the risk to say- stop and see the problems return?"(34)

"The antipsychotics certainly have a calming effect and really allow that the individual stays in the nursing home rather than them become unmanageable and moved back to the hospital"(28)

Family related

The care for people in nursing homes is often influenced by the opinion of the family, definitely in patients who have dementia. This theme was less present then the above, making it appear in 4 included studies. The family's opinion is a significant factor in the process of deprescribing antipsychotics. Family can be experienced as a barrier for deprescription because of the fear of recurrence of BPSD(22, 23, 29, 33).

"(…) once residents are using PD's and the NPS are (…) no longer perceived as too troublesome, there is a preference to continue. There can even be resistance from nurses and family to withdraw PD's, especially when considerable effort was put into stabilizing the NPS."(33)

The family was also a facilitator when communication between them and the physician was clear. Involving family members in a shared decision and explaining the interventions made them tend to follow the advice of the GP(33).

Environmental factors

The last major theme identified is the environmental factors impacting deprescribing. GPs thought the public tends towards critical scrutiny and assumed that the zeitgeist favors limiting the prescription of psychotropic drugs and, therefore, facilitates deprescribing(33). Better understanding from society and patients on the matter is also a facilitator.

Physicians stated that increased funding for aged care services would facilitate the deprescription. Having more nursing home staff and resources to implement non-pharmacological techniques could support the deprescribing of psychotropic drugs(29).

5. Discussion

5.1 Summary

Five major themes, that influence decisions to discontinue or continue psychotropics drugs were developed: physician mindset, professional collaboration, patient-related factors, family-related factors and environmental factors. Barriers and facilitators to deprescribe as experienced by GPs were grouped in the category where they belonged.

Different studies show that physicians' thinking framework, knowledge and experience, can be either a barrier or facilitator and are crucial in the decision process. The articles also show that the opinion of the GPs concerning deprescribing are contradictory. Some doctors don't believe in non-pharmacological interventions and tend more to use medications(23, 28, 29, 33). Moreover, they overestimated the benefits of symptom relief of antipsychotics(23, 28). Others, as stated by Dhuny et al. routinely recommend interventions without psychotropic medicines. Although an important note made in this study, is the theory/practice gap. Meaning GPs have knowledge about the limited efficacy of antipsychotics but would prescribe them anyway because other factors are more determinant.

Individual experience of a physician also serves as a facilitator or a barrier in deprescribing. Previous positive and negative experiences influence decision-making and sometimes go against evidence-based guidelines (23, 33). While psychotropic drugs started by another prescriber could be a barrier to deprescribing, it's seen that an acceptable number of physicians feel comfortable initiating a stop nonetheless(30).

Professional collaboration between nursing staff, colleagues and pharmacists plays a crucial role in the complex problem of deprescribing. One main barrier and two facilitators were found concerning

interprofessional collaboration in the articles used for this review. Resistance and pressure from nursing staff against deprescribing is a major barrier described by all eight selected articles. In three articles, it was identified as the main factor against the deprescribing process(22, 29, 30). Quantitative data from surveys showed that more than 65% of interviewed GPs felt influenced by nurses. Reasons for this reluctant behavior are: first, non-pharmacological interventions need more staff and resources, which often aren't available (23, 29, 31, 32). Second, confidence regarding the efficacy of psychotropic drugs in addressing BPSD is high, coupled with a limited knowledge of their side effects (28, 33). Third, the staff is worried about the setback in the quality of life of the residents following deprescribing (23, 28, 30, 33).

Cooperation between different healthcare workers could on the other hand serve as a facilitator. GPs find effective communication with secondary care colleagues helpful and are then more confident in deprescribing. Additionally, working co-operatively with the nurses and maintaining clear communication, benefits the patients. Involving pharmacists in the medication management of patients, where they inspect the usage of medicines and make recommendations, could also help with deprescribing. A few articles showed that some GPs are reluctant towards these recommendations and don't follow them. Although in Cousins et al., half of the doctors were confident that pharmacist-conducted medication reviews would be beneficial in managing BPSD(29, 32).

Considering the management of BPSD as a complex problem with influences from different angles, the patient's health and quality of life are still a decisive factor. Deprescribing psychotropic agents can negatively affect the quality of life of a patient and induce more suffering. This is considered by GPs as a barrier(23, 28, 30, 33). However, this contradicts the current guidelines with the evidence of limited efficacy and adverse effects of psychotropic drugs(35). Azermai et al. also state that doctors have concerns about recurring BPSD and withdrawal symptoms following a medication stop. Several studies showed that discontinuation can be done with limited relapse of BPSD(18, 23, 35).

Patients suffering from dementia can't express their will anymore, often resulting in a shift of responsibility towards the family. Therefore, the family can be a facilitator or barrier to discontinue medication. GPs find that communication with them is crucial and influences their perception and judgement about psychotropic agents.

It's seen that the deprescribing of polypharmacy in elderly patients has become an important topic in the last decade. Recent guidelines are in line with this, promoting non-pharmacological options before considering psychotropic agents. These recommendations are a facilitator to deprescribing.

Ultimately, it is unavoidable to deny that resources and funding are major topics. Financing for aged care services and staffing levels in nursing homes is highlighted as crucial in supporting non-pharmacological interventions and facilitating deprescribing efforts. GPs find that a lack of these is a huge barrier(29). This is a challenge for the future, where the number of patients with dementia in dire need of care will only increase.

5.2 Strengths and Limitations

A strength of this review is the systematic approach that was used. The KCGG (Kenniscentrum gezondheidszorg Gent) was appealed to conduct a research question. Three different databases were consulted. An experienced researcher followed the search and the course of the review. Although this is a qualitative review reporting on qualitative data, quantitative data was also used. In the results, the quantitative data confirmed, or contradicted opinions made by GPs. Combining these two types of data is a strength of this review. As the results show, some statements gain more power by supporting them with numbers.

The quality of reporting between the studies, assessed by the COREQ-checklist, was considerable. Information regarding the research team was the least reported domain. An acceptable level of transparency was present in the selected articles and could be considered as a strength.

A limitation of this review is the narrow research question followed by severe inclusion criteria. Therefore, only eight articles were withheld. Despite the significant usage of antipsychotics in nursing homes and the future trend that older people will live longer at home, makes the experience of GPs essential. This still remains an under-researched topic with limited qualitative data available. Doctors were the targeted audience and had the final responsibility when it came to deprescribing. However, we can conclude that the opinions of other healthcare workers, such as nurses and pharmacists, as they are also included in the medication process, play a significant role. Including studies with their opinions could explore more barriers and facilitators. Also, we only included papers focusing on the deprescribing process. Even if we are convinced that deprescribing is different from prescribing and continuation of medication, it can give us a broader view of the current situation and maybe show other insights for discontinuation of antipsychotics.

There is limited qualitative data available in the literature concerning the experience of general practitioners deprescribing antipsychotics. Only eight articles with a total of 471 GPs were used. Making it

realistic that not all barriers and facilitators experienced by GPs were identified. Poor response rates from questionnaires and surveys were seen in a few articles. Making conclusions and patterns, made from that qualitative data, less realistic.

The qualitative data analyzed in this review originates from different countries and healthcare systems, introducing heterogeneity in terms of cultural contexts, healthcare practices, and organizational structures. This variability makes it challenging to compare and synthesize findings across studies and may limit the applicability of the results to specific settings. On the other hand, the aim of a qualitative review is not to provide definitive answers to complex questions but to collect as much data as possible for a better understanding of a complex problem(36).

5.3 Comparison with existing literature

It is clear that current literature and guidelines about managing BPSD in patients with dementia don't recommend antipsychotics. Their effectiveness is questionable, adverse events are considerable, and have an increased mortality rate(8, 22, 24, 37, 38). Banerjee et al states in 2009 that the use of psychotropic drugs for people with dementia have substantial clinical risks, such as an increased mortality rate and serious adverse events(19). Non-pharmacological options are preferred. In some cases, psychotropic medications are necessary and should be used for a limited time and at the lowest dose possible. It is a fact that nowadays a lot of patients in care home facilities are still using a lot of antipsychotics(22, 23). The literature states that discontinuation of antipsychotic drug use in people with dementia can be done without making the behavior worse. In the qualitative data retrieved for this review, we can conclude that there are still a considerable number of GPs and other doctors who prefer pharmacological options to treat NPS. Roßmeier et al. state that in Germany, there are still no specific recommendations for the reduction and discontinuation of antipsychotics used to treat BPSD(38). Current guidelines state that the evidence is of low quality because of the small study population.

Discontinuation of psychotropic agents may make no difference to adverse events and quality of life(24). It is seen in our themes "patient-related factors" and "family-related factors" that doctors and families are concerned about the quality of life of the patient after withdrawing medications. There is still no high-quality evidence available about this topic, and further research is necessary.

Another systematic review reporting on this data was conducted by Moth et al. The Danish study originates from 2021 and reports on the same subject as this review(39). Our research question is narrower, focusing

only on the experience of GPs and deprescribing, whereas they also include studies with the experience of nurses and other healthcare workers. This article also included studies reporting on prescribing and not only deprescribing. Although there are differences in inclusion criteria, our conclusions are similar. We can conclude that the number of qualitative reviews is limited and that conducting more qualitative data to explore more barriers and facilitators is indicated.

In line with the existing literature, there are still more barriers than facilitators present to deprescribe. A lack of nurses, resources, funding, and more education and training are barriers that keep coming back in the consistent literature.

5.4 Future implications

The qualitative data on the experience of general practitioners undertaking deprescribing is limited. Moreover, the results are heterogeneous, making finding reliable patterns difficult. More qualitative data on GPs in more countries could help clear out those patterns. Although it may not provide definite answers to this complex problem, it can lead to better insights and inspire further focused work.

Of course, the first step in prevention is not prescribing these drugs in the first place. However, because of the danger of antipsychotics, non-pharmacological interventions are essential and should be further explored. Many approaches, such as music therapy and reminiscence therapy, are known. Nevertheless, there is still much to delve into regarding effectiveness, optimal delivery methods, and long-term impact. Psychotherapists are healthcare workers who could contribute to the non-pharmacological options. Their expertise in addressing psychological and emotional challenges can contribute significantly to the holistic care approach for BPSD, which is not often used currently.

A standardized questionnaire based on this review could quantify barriers and facilitators and, therefore, show us which barriers and facilitators are more frequent and where interventions should be built on. . However, following the heterogeneity of experience and environmental factors between GPs internationally, it could also be interesting to add some open questions to identify yet unknown facilitators and barriers. Qualitative research by itself can help generate and refine hypotheses. Followed by quantitative research with more power and high-quality evidence.

The importance of expanding healthcare professionals' knowledge about deprescribing and non-pharmacological options cannot be underestimated. Educational initiatives, particularly those tailored for

doctors and nurses, can be a potent tool in achieving this. By emphasizing the potential for mindset change, we can empower healthcare professionals not only to acquire knowledge but also to question and challenge their existing beliefs. This shift in mindset can lead to more informed and patient-centric care.

The role of nurses in care home facilities in managing BPSD is pivotal and often underappreciated. Research is needed to determine the most cost-effective manner to utilize the best combination of nursing skill levels. Moreover, it is essential that nurses receive more support regarding non-pharmacological interventions. By highlighting the importance of nurses and advocating for their support, we can potentially improve patients' outcomes and recognize the valuable contribution of nurses in this field.

Another area for future focus is enhancing professional collaboration. A better understanding and confidence between different healthcare workers could significantly contribute to limiting the overuse of psychotropic drugs. Some professional relationships, like between pharmacists and GPs, have room for improvement. Involving pharmacists in the deprescribing process via medication management reviews and better ways of communicating with GPs could serve as a facilitator in the discontinuation of antipsychotics. By emphasizing the potential benefits of improved collaboration, we can encourage stakeholders to invest in such initiatives. Providing incentives, such as financial supplements when attending a multidisciplinary meeting, can motivate different healthcare workers to function more as a team. This will ultimately lead to better patient care.

Last, a few articles describe the need for more funding and resources to support healthcare workers. These improvements can be made on a national level. Creating awareness programs for the public could also contribute to a better understanding of managing BPSD.

6. Conclusion

We can conclude that deprescribing psychotropic agents in patients with neurocognitive disease showing BPSD is a complex problem because many factors must be taken into account. The current guidelines tell us that the medications used for this problem have a negative risk-benefit balance as a treatment for BPSD. Many patients still get pharmacological treatment for this issue, making deprescribing those medications a vital topic. This review identified barriers and facilitators that general practitioners experience while considering discontinuation of these drugs.

In conclusion, more barriers than facilitators were identified. Some barriers were present in different articles and, therefore, could have more impact on the decision of clinicians. Identifying these factors can be useful for generating hypothesis and provide grounds for further research.

First, the knowledge and beliefs towards the deprescribing itself and the reliance on non-pharmacological options will be a challenge in the future. Via education, this could be the first step towards less usage of medications. Second, and maybe one of the most significant barriers, is the lack of resources and nursing staff, therefore making it challenging to provide good care without antipsychotic agents. Still, it is a fact that the number of patients suffering from BPSD will increase and have a massive impact on the healthcare systems in the future. Third, professional collaboration could improve, giving the deprescribing a higher chance of success. By exploring and exposing the positive and negative influencing factors on the management of BPSD, we set up an incentive towards further research and implementation in the daily practice of GPs.

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8. Appendix

8.1COREQ- Checklist

	Aerts et al.	Almutairi et al.	Azermai et al.	Cousins et al.	Dhuny et al.	Sawan 2016	Sawan 2017	Smeets et al.
Research team								
Interviewer	1	1	1	1	1	1	1	1
Crendetials interviewer	0	1	0	0	0	0	1	1
Occupation	0	0	0	0	0	0	0	0
Gender	0	1	0	0	0	0	0	0
Experience and training	0	1	0	0	0	0	0	0
Relationship	0	0	0	1	0	1	1	1
Participants knowledge	1	1	1	1	1	1	1	1
Interviewer characteristics	0	1	0	0	0	0	0	0
Study design								
Methodological orientation	1	1	1	1	1	1	1	1
Sampling	1	1	1	1	1	1	1	1
Method of approach	1	1	1	1	1	1	1	1
Sample size	1	1	1	1	1	1	1	1
Non-participation	1	0	0	1	1	0	0	0
Setting of data collection	1	1	1	1	1	1	1	1
Description of sample	1	0	1	1	1	1	1	1
Interview guide	1	0	0	1	1	1	1	1
Repeat interviews	1	1	1	1	1	1	1	1
Audio/visual recording	0	1	0	0	0	1	0	1
Field notes	0	1	0	0	1	1	1	1
Duration	0	1	1	1	0	0	1	0
Data saturation	0	1	0	1	0	0	1	0
Transcripts returned	1	1	1	1	1	1	0	1
Analysis and findings								
Number of data coders	0	1	0	0	0	0	0	1
Description of the coding tree	1	1	1	1	1	1	1	1
Derivation of themes	1	1	1	1	1	1	1	1
Software	1	1	1	1	1	1	1	1
Participant checking	0	1	0	0	0	0	0	0
Quotations presented	1	1	0	0	1	1	1	1
Data and findings consistent	1	1	1	1	1	1	1	1
Clarity of major themes	1	1	1	1	1	1	1	1
Clarity of minor themes	1	1	1	1	1	1	1	1
	19	26	17	21	20	21	22	23

8.2 Search Hits

BRON	ZOEKTERMEN	HITS	Titel en abstract
Pubmed	("Neurocognitive Disorders"[MeSH Terms] OR "Dementia"[MeSH Terms] OR "alzheimer*"[Title/Abstract] OR "dementi*"[Title/Abstract] OR "amenti*"[Title/Abstract] OR "mental illness"[Title/Abstract] OR "mental deterioration"[Title/Abstract] OR "senile"[Title/Abstract] OR "amentia"[Title/Abstract] OR "neurocognitive disease"[Title/Abstract] OR "cogniti*"[All Fields]) AND ("Drug Therapy"[MeSH Terms] OR "Deprescriptions"[MeSH Terms] OR "Drug Prescriptions"[MeSH Terms] OR "Inappropriate Prescribing"[MeSH Terms] OR "medication discontinuation"[Text Word] OR "deprescribing intervention"[Text Word]) AND ("Psychotropic Drugs"[MeSH Terms] OR "Antipsychotic Agents"[MeSH Terms] OR "Central Nervous System Agents"[MeSH Terms] OR "antipsychotic*"[Title/Abstract] OR "psychoactive drug*"[Title/Abstract])	6413	103
	("Neurocognitive Disorders"[MeSH Terms] OR "Dementia"[MeSH Terms] OR "alzheimer*"[Title/Abstract] OR "dementi*"[Title/Abstract] OR "amenti*"[Title/Abstract] OR "mental illness"[Title/Abstract] OR "mental deterioration"[Title/Abstract]	236	/

	OR "senile"[Title/Abstract] OR "amentia"[Title/Abstract] OR "neurocognitive disease"[Title/Abstract] OR "cogniti*"[All Fields]) AND ("Drug Therapy"[MeSH Terms] OR "Deprescriptions"[MeSH Terms] OR "Drug Prescriptions"[MeSH Terms] OR "Inappropriate Prescribing"[MeSH Terms] OR "medication discontinuation"[Text Word] OR "deprescribing intervention"[Text Word]) AND ("Psychotropic Drugs"[MeSH Terms] OR "Antipsychotic Agents"[MeSH Terms] OR "Central Nervous System Agents"[MeSH Terms] OR "antipsychotic*"[Title/Abstract] OR "psychoactive drug*"[Title/Abstract]) AND "residential facilities"[MeSH Terms AND "residential facilities"[MeSH Terms]		
EMBASE	((('psychoactive agent' OR 'psychoactive drug' OR 'psychodynamic agent' OR 'psychopharmaceutic agent' OR 'psychopharmacon' OR 'psychotropic' OR 'psychotropic drug' OR 'psychotropic drugs' OR 'psychotropic treatment' OR 'psychotropics') AND 'amentia' OR 'demention') AND 'de-prescribing' OR 'de-prescription' OR 'deprescribing' OR 'deprescriptions') AND ('family doctor' OR 'family physician' OR 'family physicians' OR 'family practitioner' OR 'general physician' OR 'general practice physician' OR 'general practitioners' OR 'gp (general practitioner)' OR 'physicians, family' OR 'physicians, primary	245	33

	care' OR 'practitioner, general' OR 'primary care doctor' OR 'primary care physician' OR 'primary care physicians').		
Google Scholar	antipsychotics dementia deprescribing qualitative review general practitioner.	1010	/