QUALITATIVE PAPER

Psychotropic drug treatment for agitated behaviour in dementia: what if the guideline prescribing recommendations are not sufficient? A qualitative study

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Abstract

Background: Agitation is a common challenging behaviour in dementia with a negative influence on patient’s quality of life and a high caregiver burden. Treatment is often difficult. Current guidelines recommend restrictive use of psychotropic drug treatment, but guideline recommendations do not always suffice.

Objective: To explore how physicians decide on psychotropic drug treatment for agitated behaviour in dementia when the guideline prescribing recommendations are not sufficient.

Methods: We conducted five online focus groups with a total of 22 elderly care physicians, five geriatricians and four old-age psychiatrists, in The Netherlands. The focus groups were thematically analysed.

Results: We identified five main themes. Transcending these themes, in each of the focus groups physicians stated that there is ‘not one size that fits all’. The five themes reflect physicians’ considerations when deciding on psychotropic drug treatment outside the guideline prescribing recommendations for agitated behaviour in dementia: (1) ‘reanalysis of problem and cause’, (2) ‘hypothesis of underlying cause and treatment goal’, (3) ‘considerations regarding drug choice’, (4) ‘trial and error’ and (5) ‘last resort: sedation’.

Conclusion: When guideline prescribing recommendations do not suffice, physicians start with reanalysing potential underlying causes. They try to substantiate and justify medication choices as best as they can with a hypothesis of underlying causes or treatment goal, using other guidelines, and applying personalised psychotropic drug treatment.

Keywords: psychotropic drugs, agitated behaviour in dementia, non-guideline treatment, decision making, focus group, qualitative, older people

Key Points

• Agitated behaviour in dementia is a symptom of underlying causes and not a diagnosis itself.
• Hypotheses of underlying causes of agitation in dementia and treatment goals can guide psychotropic drug treatment.
• By using less strict diagnostic criteria for underlying psychiatric disorders, other guidelines may support drug choices.
Introduction

Neuropsychiatric symptoms (NPS) are a common manifestation in people with dementia, with a 4-week prevalence rate of 65% in primary care patients and a 2-week prevalence rate of 80% in nursing home (NH) residents [1–3]. NPS, and especially agitated behaviour, negatively affect the patient’s quality of life and cause a high caregiver burden [4]. Agitated behaviour includes various types of restlessness or irritability, like wandering, aggression, vocal agitation and nocturnal agitation [5] and is one of the most common NPS [1, 3, 6, 7]. Prevalence rates of clinically relevant agitation assessed by the Neuropsychiatric Inventory (NPI) are 23% in primary care patients [3] and 30% in NH residents [1, 7]. In addition, agitation and aggression are main reasons to start drug interventions [8]. Therefore, knowledge regarding the best treatment approach to agitated behaviour in dementia is essential.

Treatment of agitated behaviour in dementia is often challenging. Non-pharmacological interventions for agitation in dementia are recommended as first-line approach, although the evidence for efficacy is moderate [5, 9–13]. Additional drug treatment may be warranted in case of acute or dangerous situations or high levels of suffering [5, 12–14]. Drug treatment may consist of various psychotropic drugs (PDs), such as antipsychotics, hypnotics, anxiolytics, antidepressants, antiepileptics and anti-dementia drugs [12, 15–17]. Although almost none of these PDs are registered for treating agitation in dementia [15, 18], and evidence for their efficacy is limited [16], literature shows high prevalence rates of PD use [3, 19–22]. Also, PD treatment may cause serious harm due to side effects [15, 17, 23]. Therefore, the place for PD treatment in the management of agitated behaviour is limited and prescription requires careful consideration.

The Multidisciplinary Guideline of the Dutch Association of Elderly Care Physicians provides recommendations for the approach and treatment of challenging behaviour in dementia. The core recommendation of this guideline is to start with a multidisciplinary problem analysis and treat underlying problems if possible. Next to non-pharmacological interventions, only a few PDs are recommended (Appendix 1) (hereafter referred to as the ‘guideline prescribing recommendations’) [5]. International guidelines of the National Institute for Health and Care Excellence (NICE) and the American Psychiatric Association (APA) hold similar recommendations [13, 14]. Some guidelines recommend (based on low levels of evidence) for specific groups of dementia patients with agitated behaviour in addition the use of antidepressants or antiepileptics [24–26].

When treatment of agitated behaviour in dementia according to the guideline prescribing recommendations is not sufficient, other PDs are prescribed, generally based on expert opinion [18, 27]. A Dutch study showed that only 36% of PD use in NH residents was appropriate for indication [21]. This also holds true for other countries, for example in the USA, where 43–58% of treated NH residents received antipsychotic treatment outside the prescribing guidelines [28, 29]. These examples of PD use outside prescribing guidelines raises the question what substantiates the individual PD prescription, as it is not clear how and why physicians deviate from the guideline prescribing recommendations.

Several studies have revealed factors associated with the prescription of PDs. Relevant factors include patient factors such as type and severity of NPS and type of dementia; healthcare professional factors such as attitudes towards NPS and PDs, knowledge of and experience with NPS and PDs and communication and collaboration between different health care professionals and with family; and external factors like inadequate resources, staffing problems, limited time for patients and setting [8, 30–34]. To the best of our knowledge, the deliberations of physicians leading to prescription of PDs outside prescribing guidelines have not yet been investigated. Therefore, our aim was to explore how physicians specialised in dementia care decide on PD treatment for agitated behaviour in dementia when guideline prescribing recommendations are not sufficient.

Methods

Study design

We conducted an explorative focus group study using thematic analysis. This study is reported in line with the consolidated criteria for reporting qualitative research (COREQ) (Appendix 2).

Participants

In the Netherlands, several types of specialists provide care to people with dementia. Among specialists with the most expertise in the treatment of NPS in dementia are elderly care physicians (ECPs), geriatricians and old-age psychiatrists. Medical care for people with advanced dementia who reside in dementia special care units in NHs is mainly provided by ECPs. In addition, ECPs also do home consultations [35].

For our study, we approached physicians from the three aforementioned specialties, using the newsletter of their scientific societies. The inclusion of ECPs focused on ECPs who mainly practice in dementia care. Purposive sampling was used to compile the focus groups with a variety of physicians’ function (ECPs, geriatricians, old-age psychiatrists) and work setting (NH, hospital, psychiatry, extramural). After the first focus group, we noticed that most people worked in NHs, and it appeared that the considerations could be different in other work settings. Therefore, we specifically compiled the next focus groups based on specific work settings.

Data collection

The focus groups were conducted between April and June 2021. We used constant comparative analysis until no new
information was found. Due to COVID regulations the focus group meetings were online using a video conferencing platform. All focus groups were audio- and video-recorded. An initial topic list was developed (MD, ES, MS) and pilot tested. Each focus group consisted of five to seven participants, an experienced moderator (ES or CR) and one or two researchers (MD and ST). After the introduction the focus groups started with a general question: ‘Are you able to sufficiently treat agitated behaviour in dementia using the guideline prescribing recommendations? In which case not?’ After that the main question followed: ‘In case you cannot manage with haloperidol and risperidone, how do you decide on PD treatment outside the guideline prescribing recommendations?’ During the focus groups the different topics, containing questions about the reasons for possible use of different (groups of) PDs, were introduced, if not addressed spontaneously by the participants (Appendix 3). The focus group meetings lasted about 90 min each and were discussed directly afterwards by the moderator and researcher to identify standouts and possible new topics. The recordings were transcribed ad verbatim by one of the researchers and cross-checked by the other (ST and MD). In addition, they were anonymized by using a letter–number combination for each participant. After each of the focus group meetings, findings were discussed among a small research group (ST, MD, ES, MS). After four focus group meetings, preliminary results were discussed within the project group. Suggestions on more in-depth exploration of certain topics were taken into the last focus group meeting.

Data analysis
The data were analysed using inductive thematic analysis as described by Braun & Clarke [36] using Atlas.ti version 9. Data analysis was an iterative process involving several steps. First, we became familiar with the data by reading and re-reading the transcripts (MD, ST, ES, MS). Second, the transcripts were coded by two to three researchers independently and discussed until consensus was reached (MD, ST and partially by ES). Third, initial themes were formulated (MD, ST, ES, MS). Fourth, the themes were reviewed (MD, ST, ES, MS) and discussed with all authors and additional project group members. Fifth, the themes were determined (MD, ST, ES, MS). After the fourth focus group we suspected saturation, and since no new essential topics emerged in the fifth focus group we believe saturation was reached.

Ethical considerations
The study was rated by the Medical Ethics Review committee of Amsterdam UMC, location VU University Medical Centre (number 2021.0094), which stated that the study was not subject to the Medical Research involving Human Subjects Act. All participants gave their written- or video recorded consent.

Results
Participants
Five focus groups were conducted including 22 ECPs, five geriatricians and four old-age psychiatrists (Table 1). All the physicians were experienced in the care for people with dementia and NPS. The years of experience in the care for people with dementia ranged from 1.5 to 33 years.

Main themes
Analysis of the focus groups led to five interrelated main themes (Figure 1). These themes reflect physicians’ considerations when deciding on a PD treatment outside the guideline prescribing recommendations for agitated behaviour in dementia: (1) ‘reanalysis of problem and cause’, (2) ‘hypothesis of underlying cause and treatment goal’, (3) ‘considerations regarding drug choice’, (4) ‘trial and error’ and (5) ‘last resort: sedation’. Main themes and subthemes will be explained in the following paragraphs.

Not one size fits all
Transcending the themes, in each of the focus groups physicians indicated that there is not one specific PD that fits all similar cases of agitated behaviour in dementia. They explained this by the heterogeneity of patients with agitation in dementia, where each patient exhibits different behaviour, has different needs and may also respond differently to the same treatment.

G1-F2: ‘I wouldn’t say that I can manage with one drug. Or with three, or four drugs. Erm… yes, it is actually more complicated in practice.’

Reanalysis of problem and cause
The physicians indicated that when (previous) guideline-treatment failed, they would first reanalyse the situation. They said they considered what had already been done and whether the advice in the guideline had been sufficiently tried. In addition, they indicated that they wanted to have a full understanding of the patient’s behaviour and to look for underlying causes or other leads.

E17-F4: ‘I actually always start with an analysis, why does this resident actually show this behaviour?’

Physicians pointed out several factors they considered during the analysis. These included (a) specification of the agitation, (b) person-related factors and (c) underlying causes.

Specification of the agitation
Physicians described that they tried to specify the agitation. They considered the type, the severity and the occurrence of the agitated behaviour. The different types of agitation that were mentioned included aggression, nocturnal agitation, disinhibited behaviour, sexual disinhibition, compulsive behaviour, constant request of attention, repetitive
Table 1. Characteristics of focus group (FG) participants

|               | FG 1 (n = 6) | FG 2 (n = 7) | FG 3 (n = 5) | FG 4 (n = 6) | FG 5 (n = 7) |
|---------------|--------------|--------------|--------------|--------------|--------------|
| Specialty     |              |              |              |              |              |
| Elderly care physicians (n = 22) | 6            | 3            | 5            | 4            | 4            |
| Old-age psychiatrists (n = 4)     | 3            | 1            |              | 1            |              |
| Geriatricians (n = 5)             | 1            | 2            | 2            |              |              |
| Sex           |              |              |              |              |              |
| Female gender (n)                  | 5            | 3            | 4            | 5            | 6            |
| Work setting  |              |              |              |              |              |
| Nursing home | X            | x            | X            | x            | x            |
| Hospital      |              |              |              | x            |              |
| Psychiatry    | x            | X            |              | x            |              |
| Extramural    | x            | x            | x            | x            | X            |

*Because most participants worked in more than one setting, we have only indicated roughly which settings were represented rather than specific numbers. If there was a clear overrepresentation of one setting, this is shown ‘in bold’ (X).*

Figure 1. Code tree of main themes and their interrelation.

calling/shouting and motor restlessness. Next to the type of agitation, they mentioned to consider the severity of the behaviour. Lastly, they also took into account the actual condition and situation in which the agitation occurred.

E3-F1: ‘We have behavioural consultations with the multidisciplinary team every week, and we always try […] to explore, like, what type of behaviour are we actually talking about.’

Person-related factors
Physicians stated that it is very important to know the person in front of you to better understand their behaviour. They explored the patients’ biography, personality and coping strategies.

E9-F2: ‘And then you ask, gosh, what kind of person did he use to be, what is his life history? What kind of training? What was his coping strategy? What
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was meaningful! And a very important one: is this someone with a need for autonomy or not? And did he experience any traumas?

Underlying causes
It was indicated that there is usually something underlying the agitation. Physicians said they considered psychiatric or somatic underlying causes and also external provoking factors.

E10-F3: ‘Right, because agitation usually follows from something. Usually there’s something of… erm… at the root of it, isn’t there? Anxiety, or depression or…’

Multiple different psychiatric causes were mentioned as possible underlying causes. These include anxiety, depressive symptoms, psychotic symptoms, post-traumatic stress disorder (PTSS)/trauma, personality disorder, obsessive compulsive disorder and intellectual disability.

Hypothesis of underlying cause and treatment goal
Closely related to the previous theme, many physicians stated that they usually did not treat the agitation itself but they regarded it as a symptom of underlying cause(s). To decide on a PD treatment outside the guideline prescribing recommendations, physicians mentioned making hypotheses about underlying causes and formulating corresponding treatment goals as a strategy. As mentioned before, underlying causes consisted of underlying psychiatric or somatic causes, external causes and personal factors. The stated treatment goals usually consisted of the pharmacological mechanism of action of a drug, for example sedation or mood stabilisation.

P2-F2: ‘So to what extent do we actually treat [laughs], a fairly general question, agitation or treat those target symptoms of anxiety… erm… trauma. For that is what I hear you all say. We don’t treat the agitation at all, but we try to find out what the underlying target symptom is [E7 nodding vigorously, E9 saying yes] that makes people agitated.’

Some physicians said that a hypothesis of an underlying psychiatric cause could support their choice of PD treatment, because they could then use the corresponding guideline recommendations. They would use these other guidelines even if a patient did not meet the diagnostic criteria.

P2-F2: ‘Even… erm… if someone doesn’t fully meet the criteria for depression or fully meet the criteria for psychosis. Then we still do apply those guidelines.’

Also, it was mentioned that hypotheses were adjusted to support PD choices.

E10-F3: ‘Then I think… then I might try to stay within the guideline with a bit of creative accounting with diagnoses [laughs].’

Considerations regarding drug choice
One of the reasons they did this is the ‘Care and Compulsion Act’, a Dutch law that makes it inconvenient for physicians to start out-of-guideline prescriptions.

E13-F3: ‘Yes, then you have to go searching around the internet, don’t you? And look up all of the guidelines. My colleagues want to do so too, because… erm… they also find the Care and Compulsion Act a difficult roadmap in that context.’

The physicians reported that they sometimes used a combination of PDs for treating the underlying or provoking cause of the agitation and treating the symptoms of agitation itself. Especially when treatment of the underlying cause would take time to work, or when the agitation was severe and one of the treatment goals was to ensure safety first. Sometimes they used a combination of PDs for better effect.

E5-F1: ‘Combinations… erm… you have to give benzos at the onset to take the edge off for a while and to give the client the feeling that something really is changing and then meanwhile you have time to adjust your SSRI.’

Patient-related
The physicians indicated that patient-related factors, such as type and stage of dementia, medical history, comorbidities, co-medication and person-related factors play a role in their choice and dosage of medication.

E8-F2: ‘And that is also important, that choice of drug also depends on the co-morbidity of the people and also the polypharmacy administered at our institution. That is also something to… erm… take into consideration.’

For example, when a patient already had extrapyramidal symptoms or walking difficulties they would be more cautious about starting certain PDs.

E7-F2: ‘As soon as I see someone… erm… walking very badly or who I believe to be at an early stage of vascular parkinsonism I’m not going to give haloperidol and, in fact, I like to steer away from risperdal [risperidone]. And, so, I turn to alternative drugs.’

Environment-related
The setting in which a patient resides influenced the decision-making. For example, physicians indicated to choose other PDs for patients residing at home than for NH residents receiving 24/7 supervision.

E14-F3: ‘I usually don’t do so in the home situation, because you have far less control over… erm… the use of your medication, don’t you? And…’
Physicians indicated they mostly prescribe on the basis of shared decision-making with the patient or their family. In addition, they described they sometimes felt pressured by caregivers to prescribe medication. This seemed to be a pressured feeling to prescribe ‘something’, rather than it influenced the choice of PD prescription itself.

E19-F5: ‘Of course, it is a whole process and you take them along with it, but... once in a while, a pill for the nurse, like they say, that still happens.’

It was also mentioned that the timing of consultation influenced PD choice. Physicians indicated that it frequently occurred that they were asked for a consultation too late.

P2-F2: ‘We also do a lot of consultative work from our clinic. And my experience is that we first come in when the nursing home has had it up to HERE [gestures with her hand high].’

**Physician-related factors**

Physicians stated that their own experience and competence also played an important role in their PD choices. For example, they indicated that their personal experiences, derived from previous PD treatment of agitation in dementia, is of influence.

E19-F5: ‘I sometimes say yes, it is n = 1, it is your experience. And sometimes you have someone... who had a different experience again that someone did well on quetiapine and then you continue that [...]’

But also the advice they got from colleagues played a role. Some ECP’s indicated that old-age psychiatrists advised other PDs than they usually prescribed themselves.

E13-F3: ‘We have begun steering away from mirtazapine, due to our psychiatrist. Because he... erm... came up with a very sad story about it seriously disrupting REM sleep. So... erm... we try not to use it as much.’

**Drug-related**

Physicians named several drug properties that are important for PD choices. These properties included: the effects and side effects, receptor binding profiles, administration forms, dosage options and other properties.

E1-F1: ‘You do indeed make a breakdown of the agitated behaviour, and then you look at your effect profile and your side effect profile for the drug. And that, for me, entails, let’s say, a factor of choice.’

They described that the side effects of several PDs are so undesirable that they do not prescribe these drugs at all.

P4-F5: ‘I don’t ever give it [clomipramine] to people with dementia, because of its anticholinergic effects and all those other side effects.’

Physicians indicated that they sometimes want to make use of the side effect of a PD, for example; the libido-inhibiting side effect of some PDs to treat sexual disinhibition. Also, sedating properties of several PDs were often mentioned, sometimes as a desired effect and other times as an unwanted side effect of the PD. In addition, they stated to be cautious for paradoxical reactions of PDs.

G5-F5: ‘Yes, on the other hand, you can... a person can also become extra anxious if you also sedate them so that they completely lose control [others nodding along].’

Several times considerations regarding the receptor binding profiles were mentioned. Some physicians based their specific PD choices largely on these pharmacodynamics.

E9-F2: ‘Yes, I don’t use benzos anymore. I only use 5HT2A antagonists. So, that’s a low dose of quetiapine, mirtazapine, trazodone... erm... right’.

Other drug properties that were frequently mentioned were the different administration forms. Sometimes PD choice was based on the ability of the drug to administer it intramuscular, nasal or (sometimes hidden) as drops in a drink.

E6-F1: ‘But as has also been said, if you really have escalations, then midazolam. Right, even if it’s only because you have to inject it at some point.’

Some physicians said they chose a specific drug because they saw a benefit in the dosing interval. Also, it was considered how a drug should be dosed in order to see effect. Physicians considered whether it is feasible to carry out necessary checks related to certain medication, for example, blood tests when prescribing clozapine. In addition, they said to consider how quickly the drug should work and whether the drug should be long-acting or short-acting.

E5-F1: ‘Well, as an escape, I very often choose midazolam because it’s relatively short-acting, [...] Erms... yes, oxazepam is also... if you want... erm... short-term anxiety... if someone is panicking and you want to cut short the anxiety [...] and it can be used at an early stage, or reasonably soon after the onset of the anxiety that you observe, then often oxazepam. If you want to get a more steady state throughout the day, you shouldn’t do it with oxazepam, you had better use lorazepam or diazepam.’

**Trial and error**

In each of the focus groups physicians indicated that while they carefully considered which PD to prescribe, many times it just came down to trying out what works. They described this process as ‘trial and error’.

E19-F5: ‘Yes, I don’t use benzos anymore. I only use 5HT2A antagonists. So, that’s a low dose of quetiapine, mirtazapine, trazodone... erm... right’.
They described many difficult cases in which they had to keep searching for medication that could possibly improve the situation somewhat.

E1-F1: ‘Yes, then you introduce something at a certain point, like, well, there is also this you could use, with a completely different side-effect profile, but yes, at a certain point it’s its trial and error. You still want to do something to keep those people at home.’

Physicians indicated that in general, PD treatment for agitation in dementia is very challenging. However, especially when treatment fails after trying multiple PDs, the feeling of hopelessness arises.

E10-F3: ‘It is so terribly complicated at times. Yes, sometimes we all are so powerless.’

Most physicians feel that in such cases the guideline leaves them few options.

**Last resort: sedation**

In each of the focus groups physicians said that in some cases, even though they tried all kinds of PDs, they could not resolve the agitated behaviour. They said that in that case, sedation was the only option left.

G3-F4: ‘Those people who are so therapy-resistant, yikes. [...] Very, very severe aggression and agitation. But for the safety of the people around them you can actually do nothing more than sedate. And that is often with a lot of... erm... benzos. [E18 and E17 nodding emphatically] And then these people can indeed no longer eat, no longer drink, no longer safely receive medication. And those people often die really quickly, at least, that is what we see at the hospital.’

This stage of agitated behaviour in dementia was called refractory, which led to the consideration of (palliative) sedation.

E14-F3: ‘So then I actually think that you... erm... are entitled to say that it is refractory and we are going to reduce that burden of suffering.’

These situations were described as difficult, in which they felt powerless because they could not solve the agitated behaviour. However, they also indicated an analogy with serious physical illness which could help put it into perspective.

E13-F3: ‘I find that in family consultations, I often say, like you have to realise that if you have lung cancer and you are at the end of your life and you are suffocatingly out of breath and in great pain, then everyone understands that you can get medication for that, and also if you get confused, that you can be helped with painkillers and sometimes with sedation. Dementia is, of course, also a horribly fatal condition. With... erm... massive destruction of your brain. There is simply no way out, sometimes.’

**Discussion**

In this study, we explored how physicians specialised in dementia care decide on PD treatment for agitated behaviour in dementia when treatment according to guideline prescribing recommendations is not sufficient. This study illustrates five interrelated main themes reflecting physicians’ considerations in the decision for such PD treatments: reanalysis of problem and cause, hypothesis of underlying cause and treatment goal, considerations regarding drug choice, trial and error and last resort: sedation.

Physicians’ approach to PD treatment outside the guideline prescribing recommendations (Figure 1) resembles the ‘methodical approach’ as described in (inter)national guidelines for the treatment of challenging behaviour in dementia and the ‘WHO 6-step’, a method developed by the World Health Organization to stimulate and teach rational prescribing of drugs [5, 37]. This can be expected as physicians are trained to use these methods. However, this approach as shown in Figure 1 probably represents an ideal situation, where it is more likely that in practice not all steps are completed every time. For example, in case of severe agitation, drugs with insufficient effect may be quickly switched to another without (proper) reanalysis.

Our results suggest that physicians only treat the agitation itself when it is severe or acute. In other cases of (unexplained) agitated behaviour, the agitation is regarded as a symptom of underlying causes (such as underlying psychiatric causes like psychosis or depression) and physicians try to treat these underlying causes instead. This approach is in accordance with an article by Volicer et al. [38], which underlines the importance of treating the primary cause instead of the peripheral symptoms. A hypothesis of underlying causes as treatment goal then guides physicians’ PD choices. However, our participants indicated that underlying causes of agitated behaviour were often not clear, resulting in diagnostic uncertainty. Some physicians seem to cope with this uncertainty by stretching diagnostic criteria of possible psychiatric underlying causes. PD treatment is then justified by other (psychiatric) guidelines. After all, the Diagnostic and Statistical Manual of Mental Disorders (DSM) criteria have not been validated for psychiatric disorders if there is an underlying neurocognitive disorder. Some physicians also described to adjust their hypothesis in order to justify PD choices. We found both these processes to be enhanced by the current Dutch legislation; the ‘Care and Compulsion Act’ which stimulates physicians to prescribe PDs according to a guideline. Similar findings of justifying PD treatment have been reported internationally, for example Kerns et al. [39] reported that as a consequence of policies, primary care physicians adjusted their diagnosis to better support PD treatment for NPS in dementia.

Physicians clearly need guidance on the treatment of agitated behaviour in dementia to close the gap between scientific evidence and clinical practice. This is also commonly noted internationally [27, 40]. The heterogeneity of
people with agitation in dementia combined with diagnostic uncertainty and the considerations for personalised PD treatment leads to major treatment challenges for physicians. There is no specific PD that works in all similar cases, which is also commonly noted in the literature [18, 33], and physicians often try multiple kinds of PDs to find a treatment that works. If the few guideline recommended PDs do not work, physicians will try other PDs. As a result, we found that many different PDs are prescribed for various specifications of behaviour, (hypotheses of) underlying causes, and symptomatic treatment goals. The absence or inconsistency of evidence for specific PDs does not rule out individual effects, since the guideline based on randomised controlled trials (RCTs) only concerns average effects in average patients. However, there is also a danger in this way of prescribing: by stretching diagnostic criteria and trial and error, the risk of inappropriate prescribing increases. If on the basis of trial and error a drug is tried which is advised against based on high-quality evidence such as RCTs, this may be considered inappropriate prescribing. To reduce this risk of inappropriate prescribing, it might be beneficial to expand the guideline prescribing recommendations beyond RCT-based prescribing recommendations to give physicians more guidance on PD treatment for agitated behaviour in dementia.

In some cases, all treatment fails, which often leads to frustration and feelings of hopelessness. Especially in the case of refractory symptoms, physicians feel sedation is the only option left. Sedation sometimes ends in intermittent or continuous palliative sedation that eventually leads to death. This difficult process has also been described by Veldwijk-Rouwenhorst et al. [41].

Several factors physicians consider during the reanalysis of agitated behaviour are in accordance with guideline recommendations and reported in previous literature [5, 8, 18, 20, 31, 38]; however, participants’ ‘considerations regarding specific PD choice’ are barely represented in (inter)national guidelines [5, 13, 14, 24–26]. Studies have reported some of these considerations to influence the prescribing of PDs for NPS [8, 30, 32, 33]. In this study, we provide a detailed overview of considerations from physicians’ point of view.

**Strengths and Limitations**

The main strength of this study was the broad group of professionals that participated, with extensive experience in the treatment of severely agitated behaviour in people with dementia in different settings. However, we could only include a few geriatricians and old-age psychiatrists, which could reduce representativeness. A disadvantage of focus group studies is the possibility of socially desirable answers, especially in our focus groups where peers talked about choices that deviate from the guideline. This could have led to physicians’ answers not being representative of reality but of how they would ideally work. However, in each of our focus groups there were physicians who also gave statements that clearly deviated from guideline recommendations and other physicians’ opinions, suggesting that it did not play a major role in our focus groups. Because of the online setting of the focus groups we experienced some technical issues with physicians’ internet connection and audio interference. However, an advantage was that the online setting made it possible to video record facial expressions of all physicians. Thereby non-verbal communication could be added to the transcripts and taken into account during the analysis.

**Conclusion**

Through qualitative exploration, we provided an extensive overview of physicians’ considerations when deciding on PD treatment outside the guideline prescribing recommendations for agitated behaviour in dementia. These considerations give us a better understanding of how physicians deviate from the guideline when treatment according to the guideline prescribing recommendations is not sufficient.

**Recommendations**

We recommend further research into the efficacy of PD treatment in patients with agitated behaviour in dementia, when treated according to a hypothesis of underlying (psychiatric) cause(s) and guideline prescribing recommendations are not sufficient. We suggest to systematically collect and describe cases where this occurs. In addition, we recommend considering less stringent diagnostic criteria for underlying psychiatric disorders of agitated behaviour in dementia (i.e. anxiety and mood disorders), so that medication recommendations from psychiatric guidelines can be used.

**Supplementary Data:** Supplementary data mentioned in the text are available to subscribers in Age and Aging online.

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