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Barriers and enablers to deprescribing in people with a life-limiting disease: A systematic review: — Source link

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Running head: Barriers and enablers to deprescribing

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Abstract

Background: Knowing the barriers/enablers to deprescribing in people with a life-limiting disease is crucial for the development of successful deprescribing interventions. These barriers/enablers have been studied, but the available evidence has not been summarized in a systematic review.

Aim: to identify the barriers/enablers to deprescribing of medications in people with a life-limiting disease.

Design: systematic review, registered in PROSPERO (CRD42017073693).

Data sources: A systematic search of MEDLINE, Embase, Web of Science, and CENTRAL was conducted, and extended with a hand search. Peer-reviewed, primary studies reporting on barriers/enablers to deprescribing in the context of explicit life-limiting disease were included in this review.

Results: 1026 references were checked. Five studies met the criteria and were included in this review. Three types of barriers/enablers were found: organizational, professional and patient (family) related barriers/enablers. The most prominent enablers were organisational support (e.g. for standardized medication review), involvement of multidisciplinary teams in medication review, and the perception of the importance of coming to a joint decision regarding deprescribing, which highlighted the need for interdisciplinary collaboration and involving the patient and his family in the decision making process. The most important barriers were shortages in staff, and the perceived difficulty or resistance of the nursing home resident's family - or the resident himself

Conclusions and implications of key findings: The scarcity of findings in the literature highlights the importance of filling this gap. Further research should focus on deepening the knowledge on these barriers/enablers in order to develop sustainable multifaceted deprescribing interventions in palliative care.

Keywords

Drug utilization, deprescriptions, palliative care, systematic review

Key Statements

What is already known

- Barriers/facilitators to deprescribing have been studied in older adults with a normal life-expectancy
- Few studies on this topic were conducted in a population with a life-limiting disease

What this paper adds

The most prominent barriers/facilitators to deprescribing in the specific context of a life-limiting disease were:

- Organizational support
- Interdisciplinary communication and collaboration
- Communication with the patient and family

Implications for practice

- Deprescribing interventions require a whole system approach for successful implementation
- Education and training of healthcare professionals should provide more insight in the negative consequences of polypharmacy
- Care goals and treatment targets, such as deprescribing of medications, should be discussed with the patient and family

Introduction

People with a life-limiting disease are often confronted with a high symptom and drug burden. Research has demonstrated that these people use a mean number of medications between 7 and 11, with a prevalence of polypharmacy (5-9 chronic medications) of 25% to 84%, and 28% to 69% excessive polypharmacy (>= 10) (1-3). In these people, medications for symptom relief are often combined with medications to treat their life-limiting disease and comorbidities, and with medications for long-term prevention (3). The latter category is usually considered to be inappropriate at the end of life, because of a lack of short-time benefit. Moreover, drug-drug interactions with medications for symptom relief (e.g. with anti-emetics, neuroleptics) are common (4-6). Earlier studies have found a relatively high prevalence of medications for long-term prevention: e.g. 8% to 22% for lipid modifying agents (7, 8), 23% for anticoagulants (2, 7), 10% to 56% for anti-platelets (1, 2, 7), 58% for anti-hypertensives (1), and 20% to 36% for anti-dementia in people with advanced dementia (8, 9). Discontinuation of inappropriate medications or deprescribing would reduce the drug burden, decrease the number of drug-drug interactions, and might improve quality of life in people with a life-limiting disease (3, 10-12).

The term ‘deprescribing’ is used to describe the process required for safe and effective cessation of medication (13). Deprescribing is the process of withdrawal of an inappropriate medication, supervised by a healthcare professional with the goal of managing polypharmacy and improving outcomes (14). Following from this definition, end-of-life non-treatment decisions, such as not initiating a curative treatment when death is imminent (e.g. chemotherapy, antibiotics) are not considered as deprescribing. Deprescribing can be defined as ‘the systematic process of identifying and discontinuing drugs in instances in which existing or potential harms outweigh existing or potential benefits within the context of an individual patient’s care goals, current level of functioning, life-expectancy, values, and preferences’ (15). Earlier studies have demonstrated physical and cognitive benefits, and no significant harm, to be related to deprescribing of anti-hypertensives, benzodiazepines, neuroleptics, and statins in patients with a life-limiting disease (16-18).

Five relevant systematic reviews about the topic of deprescribing were published earlier (19-23), three of which focused on barriers/enablers of deprescribing in people with a normal life-expectancy (19, 22, 23). One systematic review focused on the use of preventive medications in patients with reduced life-expectancy (21), and one on the discontinuation of preventive medications in older adults with a life-limiting disease (20). However, the barriers/enablers to deprescribing in people with a life-limiting disease were not described in these reviews.

Multiple competing barriers and enablers can influence a patient and physician's decision to stop or reduce a medication, such as beliefs, knowledge, attitudes of the prescriber and the patient (19, 23). Barriers and enablers to deprescribing in people with a life-limiting disease have been studied before, but the available evidence has not been summarized in a systematic review yet. Knowing these barriers and enablers is crucial to guide the development and implementation of sustainable deprescribing interventions. Therefore, the purpose of this systematic review is to identify factors that facilitate and/or hinder deprescribing of medications in people with a life-limiting disease.

Methods

This systematic review was performed conform to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) standardized guidelines to ensure quality and clarity (24). The protocol of this systematic review was developed according to the Cochrane Guidelines for review protocols and the PRISMA statement for protocols (25, 26). This protocol was registered in PROSPERO (registration number: CRD42017073693) and can be accessed at https://www.crd.york.ac.uk/PROSPERO.

Eligibility criteria

No limits were placed on the type of methods used in the studies (quantitative, qualitative or mixed), nor on time/date, nor on language for full texts.

Inclusion criteria

- Peer-reviewed, primary studies reporting original data, with a clearly formulated research question, and an abstract in English

- Population: people with any of the following life-limiting diseases: advanced cancer, heart failure, COPD, renal failure, dementia, and/or receiving palliative care
- Scope of the study: deprescribing of medications in the context of explicit life-limiting disease
- Topic: barriers and/or enablers to deprescribing

Exclusion criteria

- Case reports, case series, letters to the editor, and opinion papers

Search methods

Firstly, four electronic databases were systematically searched for relevant studies: MEDLINE (via the PubMed interface), Embase, Web of Science, and CENTRAL (Cochrane Central Register of Controlled Trials) from date of inception until 12th September 2017. A combination of controlled vocabulary and free text words was used to search in titles and abstracts. The final keywords used were ((deprescri* or (withholding treatment and drug prescription) or ((discontinuati* or withdrawal or cessation or tapering or stop*) and (medication or drug treatment))) AND (challeng* or enabler* or facilitat* or barrier* or belief* or perception* or attitude* or perspective* or preference* or insight* or view* or health knowledge) AND (frail elderly or palliative care or dementia or chronic obstructive pulmonary disease or advanced cancer or heart failure or renal failure or life-limiting disease or life-threatening disease or limited life-expectancy). The full electronic search strategy for MEDLINE can be found in appendix 1. Secondly, the cited and citing references of the included studies were checked via Web of Science. Thirdly, the first author of every included study and ten known experts in the field of deprescribing were contacted for additional peer-reviewed studies. Finally, the most recent issues (September 2016-September 2017) of Drugs & Aging and Journal of the American Geriatrics Society (JAGS) were hand searched for more articles.

Data collection and analysis

Selection of studies

In a first phase, the selection was based on title and abstract, and in a second phase, on full-text. In both phases, selection was performed by two independent reviewers (KP and RVS), using the Covidence tool (27). Disagreement about the relevance of studies was resolved by discussion, and where necessary a third reviewer (ME) was consulted for arbitration.
Endnote X8 citation management software was used for deduplication of references. Multiple reports of the same study were collated.

Data extraction and management

Characteristics of the included studies were extracted using a self-developed data extraction form. One reviewer (KP) extracted data on country, type of research, method, research question (aim), setting, participants, and scope of the study. These data were checked by the second reviewer (RVS). Two reviewers (KP and RVS) independently extracted data on barriers/enablers. Discrepancies between reviewers were discussed and where consensus could not be reached, a third reviewer (ME) was consulted for arbitration.
Data on the topic of this review were classified as barriers and/or enablers to deprescribing of medications in the context of explicit life-limiting disease. Barriers and enablers were reported as mentioned in the article. Where information was missing or clarification was needed, authors of primary studies were contacted, using email addresses on the study's publication.

Quality assessment

The quality assessment was conducted by two reviewers (KP and RVS) independently. Disagreement was resolved by discussion, and if necessary a third reviewer (ME) was consulted for arbitration. The quality of studies was appraised using the Critical Appraisal Skills Programme (CASP) (28). Since no CASP tool was available for cross-sectional studies, the Critical Appraisal Checklist for Cross-Sectional Study, and the JBI Critical Appraisal Checklist for Analytical Cross-Sectional Studies were used (29, 30). The assessment tools used in this

systematic review are different from the protocol. Instead, we chose quality assessment tools that were best fit and comprehensive for the studies we had selected. Total quality assessment scores for all studies were presented as scores on a scale from 0 to 10. The individual studies were categorized as high-quality studies (scores from nine to ten), medium-quality studies (scores from six to eight), and low-quality studies (scores equal to five or less).

Data analyses

Because of the nature of the topic of this systematic review, the results were reported in a pragmatic and descriptive way with textual data from the studies included.

Results

Study selection

The electronic searches resulted in 1134 potentially eligible records retrieved from the four databases. After removing 108 duplicates, 1026 records were assessed for eligibility based on title and abstract. Full text of the 13 articles that appeared to potentially meet the inclusion criteria were sought (31-43). Full text screening of those 13 records resulted in the exclusion of eight articles because they did not meet the inclusion criteria (31-36, 38, 43). The remaining five articles were included in this review (37, 39-42). Checking the cited and citing references of the included studies in Web of Science did not lead to any additional studies, nor did the hand search in Drugs & Aging and JAGS. The first authors of the included studies and ten known experts in the field of deprescribing were contacted by email. This resulted in one additional manuscript, which reported on the same study as Sawan et al. [2017] and, thus, both manuscripts were collated (39, 44). Figure 1 provides more details on the study selection results.

(Figure 1.)

Characteristics and quality assessment of relevant studies

Only five studies were found, of which two were qualitative studies (39, 42, 44), two were quantitative cross-sectional studies using a survey design (37, 40), and one was a secondary analysis of baseline data from a pragmatic clinical trial (41).

Quality scores ranged from six to eight on a scale of ten for the quantitative studies. Both qualitative studies scored a nine out of ten. Based on these scores, all quantitative studies were appraised as medium-quality studies and both qualitative studies as high-quality studies.

(Table 1.)

Barriers and enablers towards deprescribing

Different types of barriers and enablers were found, and categorized as organizational, professional and patient/family related barriers and enablers. Two studies reported on organisational and professional barriers/enablers (39, 40, 44), one study on professional and patient/family related barriers/enablers (42), one study only reported on organisational barriers/enablers (37) and one study only described patient/family related barriers/enablers (41). Table 2 provides a detailed overview of the barriers/enablers identified in the literature.

(Table 2.)

Organizational barriers and enablers

Contextual factors: Shortages in staff levels and lack of organisational support were described as barriers in one study: e.g. inadequate staffing and training when handling behavioural disturbances caused reliance on psychotropic medications and hindered deprescribing (39, 44). The same study found that formally organized events, supported by the NH management, were enablers (39, 44). This was the case for drugs and therapeutic committee meetings when they were utilized by managers to highlight the overuse of psychotropic medications or for case conferencing of individual residents, and for pharmacist led medication management reviews. Moreover, one study found that discontinuation of medication as part of the hospice care plan can be an enabler to deprescribing: 80% of hospice medical directors would recommend

deprescribing of cholinesterase inhibitor and N-Methyl-D-Aspartic Acid receptor antagonists in these circumstances (40).

Care setting: One study found that the patient's residence was an enabler: simvastatin and quetiapine were more likely to be discontinued in hospitalized patients with dementia (37).

National healthcare system: One study found that the national healthcare system can be a barrier as well as an enabler (37).

Professional barriers and enablers

Perceived patient related characteristics*:* Two studies described the perceived difficulty or resistance of the nursing home resident's family - or the resident himself - as a barrier (39, 40, 44). One study described communication with the resident and his family as an enabler: explaining the pros and cons of psychotropic medications facilitated deprescribing (39, 44).

Perceived medication related characteristics*:* Physicians' perceived benefits of medications and negative effects of deprescribing were described as barriers in one study (40). Another study described negative reactions of NH staff towards the prescriber as a barrier: physicians felt that cessation of psychotropic medications was unwelcomed by NH staff because they feared escalation of behavioural and sleep disturbances, resulting in an increase in their workload (39, 44). One study found that the acknowledgement that medications were burdensome interventions was an enabler (42).

Perceived knowledge*:* One study found that nursing assistants' uncertainty about their level of medical knowledge was a barrier to provide any input in medication review, while this input was found to facilitate deprescribing of psychotropic medications (39, 44).

Interdisciplinary communication: Two studies found that interdisciplinary communication can be a barrier as well as an enabler, e.g. the complexity of care can hinder discussing changes in medication, a collegial attitude of physicians towards involvement of NH staff in medication review facilitates deprescribing of psychotropic medications (39, 42, 44).

Patient/family related barriers and enablers

Perceived medication related characteristics: One study found that the patient's perception of potential risks and concerns can be a barrier towards deprescribing. On the contrary, the patient's perception of potential benefits was found to facilitate deprescribing (41). Another study described the volume of medications and difficulties with swallowing as enablers (42).

Communication with healthcare professionals: One study found that a mismatch of expectations between healthcare professional and patient and carer regarding treatment was a barrier (42). The same study described shared decision making as an enabler (42).

Discussion

Main findings

To the best of our knowledge, this is the first study providing a systematic overview of the existing literature about barriers and enablers to deprescribing in people with a life-limiting disease. Only five studies, describing three different types of barriers/enablers were found: organizational, professional and patient/family related barriers/enablers. The most prominent factors were organisational support (e.g. for standardized interdisciplinary medication review), interdisciplinary communication and collaboration, and communication with the patient and his family.

Interpretation in the context of literature

Research on the barriers/enablers to deprescribing of medications in people with a life-limiting disease is scarce, which is highlighted by this limited collection of findings from the literature. Deprescribing of potentially inappropriate medications (PIMs) is more intensely studied in the broader context of older adults with a normal life-expectancy, with regard to type of intervention as well as to its barriers/enablers (23, 45). These findings are not entirely transferable to a population with a limited life-expectancy and to palliative care, since the medical focus on long-term profit changes entirely into a focus on the different aspects of comfort of the individual. In this context, all medications for primary and secondary prevention are eligible for deprescribing, while restrictions regarding addiction (e.g. to opioids) are

irrelevant when short-term benefit and comfort have absolute priority. Nevertheless, we found some similarities. As in studies in older adults we found that pharmacist led medication reviews may improve prescribing appropriateness (46, 47). Furthermore, involvement of multidisciplinary teams (e.g. audit and feedback at multidisciplinary meetings) and regulatory policies (e.g. mandatory pharmacy services in NHs), which were acknowledged as enablers for deprescribing in this review, positively affected inappropriate prescribing in other studies (19, 46, 48, 49). One important barrier regarding multidisciplinary meetings that was not described in any of the selected studies for this review is the limited time available for GPs and other healthcare professionals to discuss goals of care and to closely monitor patients after treatment discontinuation. Deprescribing is time consuming, and additional time is required to implement a strategic approach to deprescribing (48-50). The average primary care physician consultation length varies internationally from 48 seconds to 22.5 minutes, which is likely to negatively affect patient care (51). Finding additional time to participate in multidisciplinary meetings aiming to review and deprescribe unnecessary medications is a critical impediment for physicians' willingness to attend these meetings (48). Concordant with the findings of Dilles et al. (2013), we found that the input of nurses in medication review, i.e. by reporting their observations of symptom and drug burden, may facilitate medication changes (52).

Consistent with Turner et al. (2016), both interdisciplinary communication and communication with the patient and/or his family (e.g. in case of resistance towards deprescribing) were considered to be challenging for healthcare professionals (53). Earlier research has demonstrated that NH residents and their families have minimal experience in discussing and questioning prescribing decisions with the physician (48). Residents and their families appear to have strong expectations about medications keeping them alive or prolonging their life, which can result in fear of deprescribing (48). Physicians fear to upset patients and their families if their recommendations to deprescribe are misinterpreted as a sign that they are giving up on the patient, or as withdrawal of care (49, 50). Moreover, they fear that patients experience a deterioration in their health or a potentially preventable outcome shortly following deprescribing (49, 50). Discussing medication related issues and involving the patient (and his family) in prescribing and deprescribing decisions might counterbalance these potential

misbeliefs and misinterpretations. In this study, the perceived value of interdisciplinary collaboration and involving the patient and his family in the decision making process was highlighted by the perception of the importance of coming to a joint decision regarding deprescribing interventions. This was found to be essential for successful implementation of interventions aiming to reduce inappropriate medication use in earlier research (46).

Our results are similar in many respects to those from previous studies on barriers/enablers of deprescribing in people with a normal life-expectancy (19, 22, 23), but we did not find any specific barriers/enablers to deprescribing in the context of explicit life-limiting disease or palliative care. This finding supports our assumption that the same barriers/enablers to deprescribing play a role in palliative care as in general care. However, these barriers/enablers might be more compelling and urgent in palliative care, due to the patient's limited life-expectancy. In this context, we would like to point out some relevant issues. Firstly, the probability of drug-drug interactions with medications for symptom relief should facilitate deprescribing of futile medications which lack short-term benefit in palliative care, but this was not described as an enabler in any of the studies included in this systematic review (12). It remains an open question whether this is an indication of prognostic uncertainty or an unreasonable tenacity to continue treatment that has no benefit, regarding the use of preventive medications in patients with a life-limiting disease. Secondly, advance care planning embedded in routine and standard care in the facility should provide opportunities to discuss patient preferences regarding care goals and treatment targets, and facilitate deprescribing of preventive medications. Shega et al. (2009) found that discontinuation of medications at the time of hospice enrolment facilitated deprescribing for patients with advanced dementia, but also reported that three-quarters of families have difficulty stopping these therapies (40). Moreover, this enabler was described in none of the other studies. Finally, this raises the important question whether conversations about deprescribing are more difficult in a palliative care context compared to general care. One of the most important reasons for continuing futile treatment is lack of communication between the medical team and the patient and/or his family. It is therefore strongly recommended that options regarding futile treatment and palliative care are discussed with the patient and his family (54). Although the prescriber is

responsible for making decisions about deprescribing of futile medications, consent from the patient or his legal representative is still necessary. In this context, the healthcare team needs to take up their responsibility to start a discussion.

Strengths and limitations

We conducted this systematic review according to the methodology of the Cochrane Handbook of Systematic Reviews of Interventions (25). The Covidence tool was used for the selection of studies to ensure a systematic approach (27).

A few limitations apply to this study. Firstly, all barriers and enablers were described in only one study, except for the perception of difficulty or resistance of the resident's family which was described as a barrier in two studies (39, 40, 44), and interdisciplinary communication which was described as a barrier as well as an enabler in two studies (39, 42, 44). Hence, a grading of the barriers/enablers was not possible. Secondly, the different methods used in the studies complicated summarizing - quantitative and qualitative - findings and did not allow to pool data across the studies for meta-analysis. Thus, the results were reported in a pragmatic and descriptive way.

Implications for practice and research

A whole system approach supported by the organization, involving the patient and his family in the decision making process regarding deprescribing, and an interdisciplinary approach towards medication use are necessary for successful implementation of any deprescribing intervention. The same elements are crucial in an end-of-life context. Moreover, it is crucial that prescribers are aware of polypharmacy-related harm at the end-of-life, such as drug-drug interactions with medications for symptom relief. Hence, education and training of healthcare professionals should provide more insight in the negative consequences of polypharmacy.

Furthermore, care goals and treatment targets, such as deprescribing of medications, should be discussed with the patient and his family. Timely initiation of these conversations is necessary to make sure patients' wishes and preferences are known before the patient loses his cognitive

capacity to make his own decisions. Healthcare professionals should focus on communication strategies to facilitate shared decision making regarding medication use and deprescribing.

Conclusion

Three different types of barriers and enablers to deprescribing of medications in people with a life-limiting disease were found: organizational, professional and patient/family related barriers/enablers. The most prominent factors were organisational support, interdisciplinary communication and collaboration, and communication with the patient and his family. The scarcity of findings in the literature regarding barriers/enablers to deprescribing of medications in people with a life-limiting disease highlights the importance of filling this gap. Further research should focus on deepening the knowledge on these barriers/enablers in order to develop sustainable multifaceted deprescribing interventions in palliative care.

Declarations

Authorship

All authors meet the criteria for authorship as stated by the International Committee of Medical Journal Editors authorship guidelines.

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Declaration of conflicting interest

The authors declare no conflicts of interest with respect to the research, authorship, and/or publication of this article.

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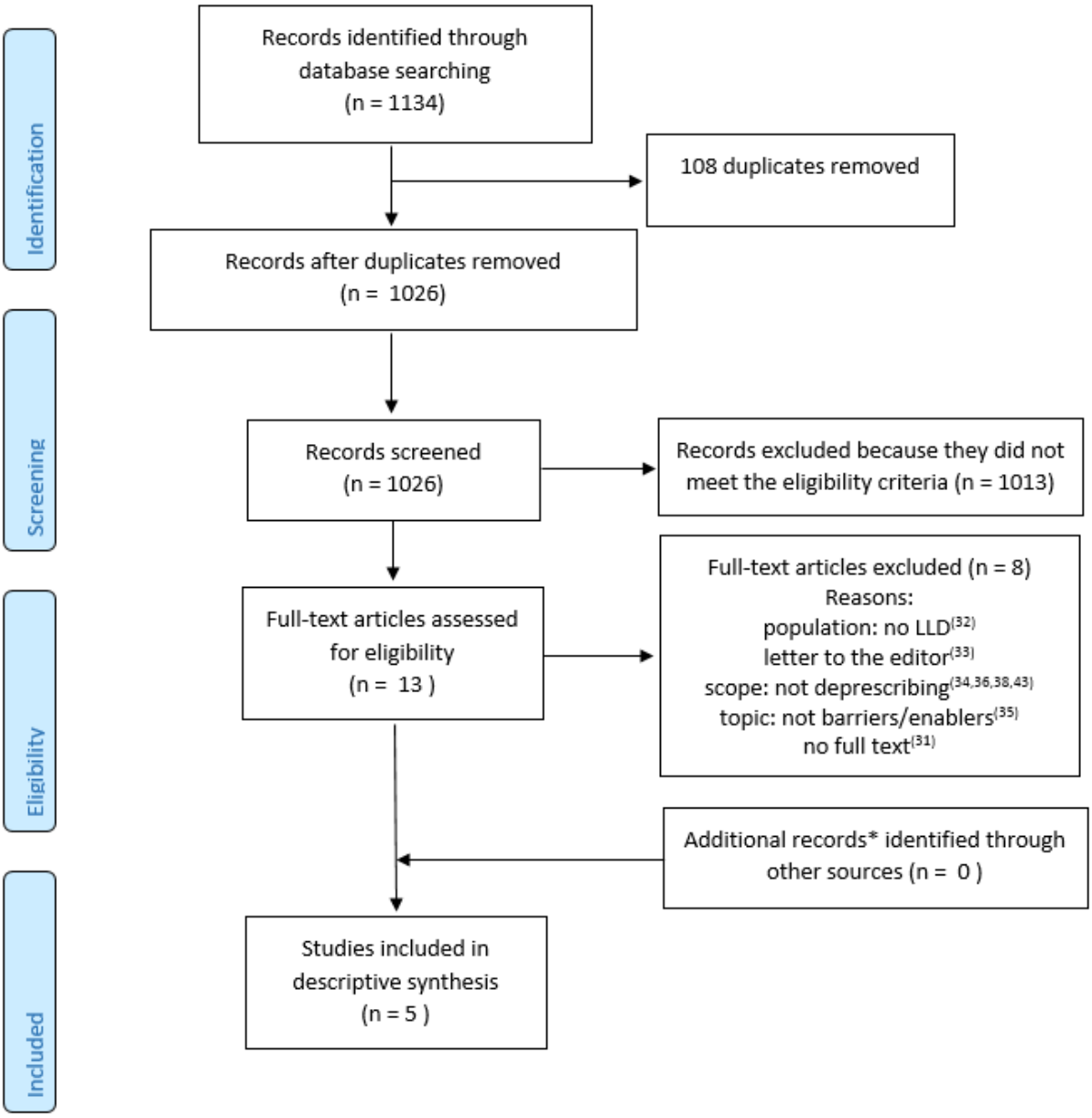
Figure 1: Flow diagram with the study selection results.



*one additional manuscript was found (44) reporting on the same study as one of the already included manuscripts (39). Both manuscripts were collated.

	Study (year)	Country	Type of research	Research question / aim	Method	n	Setting	Participants	Scope of the study	Quality assessment*
A	Parsons et al. (2014) (37)	Northern Ireland (NI) & Republic of Ireland (RoI)	Quantitative (cross-sectional survey)	To evaluate the extent to which patient-related factors and physicians' country of practice influence decision-making regarding medication use (continuing or discontinuing) in patients with end-stage dementia	Factoral survey design comprising four vignettes	662	Primary care (general practice) and hospitals (geriatric medicine)	General practitioners (GPs) and hospital physicians in NI and RoI	Withholding or continuation /discontinuation of key medications in patients with end-stage dementia	8
B	Shega et al (2009) (40)	USA	Quantitative (cross-sectional survey)	To describe hospice medical directors practice patterns and experiences in the use and discontinuation of cholinesterase inhibitors and	Mail survey with multiple choice questions and hypothetical vignettes	152	A random sample of 500 hospice sites in the USA	Hospice medical directors	Discontinuation of cholinesterase inhibitors and NMDA receptor antagonists in hospice patients that meet the	7

				NMDA receptor antagonists in hospice patients that meet the Medicare hospice criteria for dementia					Medicare criteria for dementia	
C	Sawan et al. (2016 & 2017) (39, 44)	Australia	Qualitative	To explore how visible artefacts in nursing homes influenced the prescribing and use (initiation, administration, monitoring, continuation, and cessation) of psychotropic medicines and how these artefacts were operationalized across nursing	Semi-structured interviews	40	8 high care, low care, and high care specific dementia nursing homes	On-site and visiting staff (managers, registered nurses, nursing assistants, GPs, pharmacists, specialist medical practitioner)	Use of psychotropic medicines for management of BPSD (Behavioural and Psychological Symptoms of Dementia) in nursing homes	9

				homes, from the perspective of on site and visiting staff						
D	Tjia et al. (2017) (41)	USA	Quantitative (cross-sectional, but using baseline data from a multicentre, pragmatic clinical trial)	To quantify the perceived benefits and concerns of statin discontinuation among patients with life-limiting disease (LLD)	Questionnaire (nine self-developed questions regarding patients' perceptions about discontinuing statins)	297	10 academic medical centers and 5 community-based hospice / palliative care organizations	Cognitively intact patients with LLD, 62% cancer patients, 14% COPD, 8% cardiovascular disease, 4% renal disease, 12% other	Discontinuation of statins	6
E	Todd et al. (2016) (42)	UK	Qualitative (phenomenology)	To explore the lived experience of patients, carers and healthcare professionals in the context of medication use in life-limiting illness (LLI)	In-depth interviews	36	Day care centre at a specialist palliative care unit	12 patients with a life-expectancy <18 months (7 cancer patients, 2 COPD, 1 heart failure, 2 other disease); 12 healthcare professionals (3	Medication use in LLI and deprescribing of statins	9

								palliative medicine consultants, 3 advanced nurse practitioners, 6GPs), 12 carers (all family members of the patient)		

Table 1. Characteristics and quality assessment of relevant studies

**CASP for qualitative studies (28), Critical Appraisal Checklist for Cross-Sectional Study for Surveys (30), JBI Critical Appraisal Checklist for Analytical Cross-Sectional Studies (29). Total quality assessment scores for all studies presented as scores on a scale from 0 to 10.*

	Barriers	Enablers
Organizational	***Contextual factors:*** →shortages in staff levels at night time hindered deprescribing of psychotropic medications[C] →involvement of nursing assistants in care decisions involving psychotropic medications not supported by management hindered nursing assistants to participate while such participation contributed to cessation[C] ***Care setting:***	***Contextual factors:*** →when discontinuation of cholinesterase inhibitors and NMDA receptor antagonists is a part of the hospice care plan for patients with advanced dementia, those medications are more likely to be discontinuated[B] →formally organized drugs and therapeutic committee meetings (e.g. MAC meetings in Australia, audits, case conferences) raised awareness of GPs to review the continued use of psychotropic medications[C] →pharmacist led medication review can be used as a lever to implement changes such as cessation of psychotropic medications[C] →formal case conference meetings with families at NH admission to discuss the resident's medication history often resulted in cessation[C] →positive attitude of NH management towards non-pharmacological treatment of behavioural and sleep disturbances resulted in NH staff highlighting the need to review continuation of psychotropic medications to the GP when the welfare of the resident became a concern[C] →support of management for interdisciplinary participation in medication review contributed to cessation of psychotropic medications[C] ***Care setting:***

	/	→Place of residence: when the patient was resident in hospital (compared with resident at home or in a nursing home (NH)) it was more likely that simvastatin and quetiapine would be discontinued in patients with dementia at the end of life[A]
	National healthcare system: →Physician's country of residence: if the physician practiced in Republic of Ireland (RoI) (compared with Northern Ireland (NI)) it was less likely that quetiapine was discontinued in patients with dementia at the end of life[A]	***National healthcare system:*** →Physician's country of residence: If the physician practiced in hospital in RoI (compared with NI) it was more likely that donepezil hydrochloride and memantine hydrochloride were discontinued in patients with dementia at the end of life[A]
Professional	***Perceived patient related characteristics:*** →perceived difficulty or resistance of family regarding deprescribing can be a barrier for physicians to discontinue cholinesterase inhibitors and NMDA receptor antagonists[B] →resistance from the resident's family or the resident himself was challenging for the NH staff and GPs when attempting to withdraw psychotropic medications[C]	***Perceived patient related characteristics:*** →NH staff found it important to explain the pros and cons of use of psychotropic medications to the resident and his family to facilitate withdrawal[C]

	Perceived medication related characteristics: →physicians were significantly less likely to recommend discontinuing cholinesterase inhibitors and NMDA receptor antagonists if they belief that these therapies have positive effects[B] →physicians were significantly less likely to recommend discontinuing cholinesterase inhibitors and NMDA receptor antagonists if they belief that discontinuation has negative effects[B] →once treatment with psychotropic medications was initiated, most GPs felt that cessation was unwelcomed by NH staff as it would result in escalation of behavioural and sleep disturbances and increase their workload[C] ***Perceived knowledge:*** →nursing assistants' uncertainty about their ability to participate in medication review because of their level of medical knowledge was perceived as a barrier to provide any input in medication review (such participation contributed to cessation of psychotropic medications)[C] ***Interdisciplinary communication:***	***Perceived medication related characteristics:*** →the acknowledgement that medications were burdensome interventions facilitated a willingness to rationalize them in this context[E] ***Perceived knowledge:*** / ***Interdisciplinary communication:***

	→healthcare professionals found communicating with each other frustrating given the complexity of care for patients with life-limiting illness and this was acknowledged as a barrier to change. This challenge was particularly evident for the interfaces between primary, secondary and tertiary care[E] →traditional and hierarchical norms in physicians hinder nurses to present their suggestions for review and cessation of psychotropic medications[C] →absence of GPs in formal drug and committee meetings hindered communication of concerns regarding prescribing of psychotropic medications[C]	→coming to a joint decision between healthcare professional, patient and carer was perceived as important by all participants when considering deprescribing medications[E] →collegial attitude of GPs towards NH staff and their feedback and suggestions facilitated the review and cessation of psychotropic medications[C]
Patient/family related	***Perceived medication related characteristics:*** →potential risks and concerns related to discontinuation[D]: • that they will experience another problem in addition to those they already have • that they have been previously told they should never discontinue their statins • that stopping would mean that all previous effort was wasted • that stopping means that their doctor has given up on treating them • that stopping means that their doctor thinks they are about to die	***Perceived medication related characteristics:*** →potential benefits about discontinuation[D]: • that if they stop their statins, they will spend less money on medications • that if they stop their statins, they will have a better quality of life • that if they stop their statins, they will have fewer symptoms • that if they stop their statins, they may be able to stop other medications that they take →patients with cardiovascular disease as their primary diagnosis were significantly more likely to respond that they may be able to stop other medications if they stop their statins[D]

		→patients with cardiovascular disease as their primary diagnosis were significantly more likely than the two other diagnosis groups to agree that stopping statins may result in fewer symptoms or better quality of life[D] →In many cases, patients were overwhelmed by the volume of medications, which was further exacerbated when patients had difficulty in swallowing medication → facilitated the willingness for change[E]
	Communication with healthcare professionals: →In some cases, when medication was initiated, patients were told that they would be taking this medication for 'the rest of their life': this was literally interpreted by patients that they would be taking the medication until the day they died. This experience created a mismatch of expectations between healthcare professional and patient and carer regarding treatment and appeared to be a significant barrier to deprescribing approaches[E]	***Communication with healthcare professionals:*** →(family) carers would embrace deprescribing approaches, providing the risks and benefits were properly explained and it was done for the benefit of the patient[E] →coming to a joint decision between healthcare professional, patient and carer was perceived as important by all participants when considering deprescribing medications[E]

Table 2. Barriers and enablers to deprescribing identified in the literature

A: Parsons et al. (2014) (37); B: Shega et al. (2009) (40); C: Sawan et al. (2016 & 2017) (39, 44); D: Tjia et al. (2017) (41); E: Todd et al. (2016) (42)
Studies A, B and D are quantitative studies, studies C and E are qualitative studies

Appendix 1: Search strategy MEDLINE

(Deprescription [MeSH] OR potentially inappropriate medication list [MeSH] OR deprescri* [TIAB]) OR (withholding treatment [MeSH] AND drug prescriptions [MeSH]) OR ((discontinuati* [TIAB] OR withdrawal [TIAB] OR cessation [TIAB] OR tapering [TIAB] OR stop* [TIAB]) AND (medication [TIAB] OR drug treatment [TIAB]))

AND

Challeng* [TIAB] OR enabler* [TIAB] OR facilitate* [TIAB] OR barrier* [TIAB] OR belief* [TIAB] OR perception* [TIAB] OR attitude* [TIAB] OR perspective* [TIAB] OR preference* [TIAB] OR insight* [TIAB] OR view* [TIAB] OR health knowledge [TIAB]

AND

Frail elderly [MeSH] OR frail elderly [TIAB] OR frailty [TIAB] OR palliative care [MeSH] OR palliative care [TIAB] OR palliative therapy [TIAB] OR palliative treatment [TIAB] OR dementia [MeSH] OR dementia [TIAB] OR chronic obstructive pulmonary disease [MeSH] OR chronic obstructive pulmonary disease [TIAB] OR chronic obstructive lung disease [TIAB] OR COPD [TIAB] OR heart failure [MeSH] OR heart failure [TIAB] OR chronic heart failure [TIAB] OR chronic heart insufficiency [TIAB] OR advanced cancer [TIAB] OR chronic renal insufficiency [MeSH] OR chronic renal insufficiency [TIAB] OR renal failure [TIAB] OR renal insufficiency [TIAB] OR kidney failure [TIAB] OR kidney insufficiency [TIAB] OR ((life-limiting [TIAB] OR life threatening [TIAB]) AND (disease [TIAB] OR illness [TIAB])) OR limited life-expectancy [TIAB]