Appendix S1: Search Strategy

exp Polypharmacy/

exp Inappropriate Prescribing/

exp Potentially Inappropriate Medication List/

exp Multimorbidity/

polypharma*.ti,ab.

multi*-morbidit*.ti,ab.

multi-medication*.ti,ab.

"multiple medication*".ti,ab.

((multi-drug* or multidrug*) adj2 (prescrib* or prescription* or regimen* or therap* or treatment*)).ti,ab.

multimedication*.ti,ab.

((concomitant* or concurrent* or unnecessary or excess* or multip*) adj1 (medicine* or medicat* or prescrib* or prescription* or pharmaco* or drug*)).ti,ab.

1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11

exp Deprescriptions/

((beer* or shan? or mclead?) adj3 criter*).ti,ab.

("fit for the aged" adj3 (criter* or list? or instrument or classif*)).ti,ab.

((forta or rasp or priscus) adj3 (criter* or list? or instrument)).ti,ab.

(stopp criter* or stopp list?).ti,ab.

exp Prescriptions/

deprescrib*.ti,ab.

deprescript*.ti,ab.

((discontinu* or withdraw* or reduc* or remov* or cease* or cessation or stop or review*) adj3 (drug* or pharmaco* or prescription* or prescrib* or medicine* or medicat*)).ti,ab.

13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21

12 and 22

(barrier* or facilitat* or enabl* or promote or promotion or promoted or hinder* or block* or obstacle* or restrict* or restrain* or obstruct* or inhibit* or impede* or delay* or constrain* or hindrance* or prevent*).ti,ab.

23 and 24

((inappropriate or appropriate or incorrect or quality or improv* or unnecessary or safe* or unsafe) adj3 (medicine* or medicat* or prescrib* or prescription* or pharmaco* or drug*)).ti,ab.

(over-prescrib* or "over prescrib*" or "under prescrib*").ti,ab.

"medication appropriateness index*".ti,ab.

(prescrib* adj cascade*).ti,ab.

26 or 27 or 28 or 29

12 and 24 and 30

25 or 31

limit 32 to (english language and humans and "all adult (19 plus years)")

limit 33 to yr="2000 -Current"

Appendix S2:

Screening tool: Polypharmacy, multimorbidities and deprescribing (Review)

Primary research question:

1. What are the barriers to, and facilitators of, safe deprescribing strategies?

Secondary research questions:

2. (a) What 'conditions' (of population, setting or components of interventions) are associated with safe deprescribing? (b) What *configurations* of these 'conditions' are associated with safe deprescribing?
3. (a) What deprescribing strategies are available? (b) How can safe deprescribing be supported during intervention design or implementation?

Questions - key elements	
Population (P) and Conditions (c)	**Included:** Patients and prescribers. **Patients:** with multiple morbidities and polypharmacy (i.e. 2 or more long-term health conditions and prescribed 4 or more medications). **Support workers for patients**: Paid or unpaid carers or support workers / families. **Prescribers**: GPs, doctors, pharmacists, consultants, nurses, health practitioners, health care practitioners, health personnel, educators, policy-makers, healthcare service planners, multi-disciplinary teams.
	Excluded: child and adolescent patients aged < 18 years.
Interventions (I)	**Included**: electronic and non-electronic safe deprescribing interventions such as (but not limited to): • Medication reviews, medication review clinics and / or continuous medicine reviews • Computerised decision support, computerised systems • Education programmes for prescribers or patients • Specific prescribing audits • Prescribing incentive schemes • Regulatory interventions • Pharmaceutical care • Pharmacist-led interventions • Visual identification of medicines • Multidisciplinary case reviews • Beers list / PRISCUS list / STOPP criteria • Medication Appropriateness Index.
	Excluded: Medication errors (ME) (ME only – without deprescribing component).
Settings	**Included**: any setting including primary, secondary, tertiary and community settings. Transitional care e.g. patient's home to hospital; A&E to hospital ward; hospital to care homes. **Levels**: all levels: individual, organisational, national (including high-level strategies) and international.
	Excluded: End-of-life care settings. Antibiotics (as more appropriate to reviews of antimicrobial stewardship).
Outcomes (O)	**Included:** Barriers and enablers to safe deprescribing. Barriers and enablers may be organisational, professional and or patient (family)-related. **Examples of barriers (list not extensive)**: prescriber beliefs, attitudes, knowledge, skills, behaviour, disagreements over `appropriateness' of cessation, absence of a `process' for cessation, patient (family)-related resistance, work setting (e.g. staff shortages), health system, cultural factors, medication reviews happening outside of general medical practices with poor information flow into the practice. **Examples of enablers (list not extensive)**: organisational support (e.g. for medication review), involvement of multi-disciplinary teams, joint agreement over `appropriateness' of cessation, presence of a `process' for cessation, prescribing incentive schemes, pharmacists based in general medical practices and also employed by them.
Study design	**Included:** any study design and reviews / expert papers of interventions reporting barriers or facilitators to the implementation of the intervention. Studies published in English language.
	Excluded: editorials, commentaries, conference abstracts or posters, thesis, dissertations, book chapters, single case studies.

Table S1: Summary of included studies

First author, Year, Country	Study aims and objectives	Study design, methods and participants	Barrier themes reported	Facilitator themes reported	MMAT score
Ailabouni, 2016 New Zealand	To investigate general practitioner (GP) perceived challenges to deprescribing in residential care and the possible enablers that support GPs to implement deprescribing.	Qualitative. Semi-structured interviews 10 GPs	GPs have to balance a multitude of factors including the disease(s) the patient may have, the benefit-risk profile of medicines prescribed, the patients' personal views and the opinions of other prescribers. Clinical decisions may be based on very scarce clinical information. Uncertainties regarding applying evidence-based medicine, lack of access to user-friendly evidence-based deprescribing guidelines, fear of consequences. Social influences - residential staff, families / carers, other prescribers. Policy / process: communication issues at transfer points of healthcare, fragmented care at points of transfer, unclear discharge summaries, lack of communication between hospital physicians and GPs, chaotic prescribing environment and nursing home policies, time and funding constraints.	Multi-disciplinary approach to reducing polypharmacy and inappropriate medication use by carrying out comprehensive medicine reviews. Collective efforts to deliver patient-centred care - including their family / carers in the process. Involvement of pharmacists in the multi-disciplinary approach. Adequate re-imbursement for GPs in residential care. Better communication between physicians at health interfaces. Deprescribing guidelines, GP education and GP empowerment.	*****
Alhusein 2018 UK	To explore the pharmaceutical care needs of, and service provision to, older people with sensory impairment (visual, hearing and dual impairment) on prescribed polypharmacy (≥4 medicines) in Scotland.	23 older people with sensory impairments. 30 community pharmacy personnel	Patient-level barriers at all stages of the pharmaceutical journey including: Changing appearance of medications. Lack of training. Lack of contact. Patients masking sensory impairments. Difficulties communicating. Lack of time. Patients not understanding pharmacist. Lack of suitably trained staff. Patients not understanding medications. Lack of (availability) assisted technologies. Safety concerns. Pharmacy environment. Problems ordering and storing medications.	Staff being aware of the needs of people with sensory impairments. Good relationships between pharmacists and patients. Patients disclosing their sensory impairments to the pharmacist. Giving patients time. Well-staffed pharmacists. Use of consulting rooms. Patients understanding their medications. Patients understanding pharmacy teams. Accessible pharmacy environments. Availability of assistive technologies.	*****
Anderson, 2017 Australia	To explore the views of GPs and Consultant Pharmacists (CPs)	Qualitative. Focus groups.	Themes were common to both GPs and CPs. Major theme 1: Uncertainties confronting clinicians when assessing and older patient	Working through uncertainties. Strategies adopted included targeting medicines that are easier to deprescribe in the first instance,	*****

Table S1: Summary of included studies

	about inappropriate polypharmacy and the reasoning they apply to deprescribing in primary care; and to identify factors that support or inhibit this cognitive process.	32 GPs and 15 CPs	with potentially inappropriate polypharmacy. Sub-theme 1.1: weighing unmeasurable harm against benefit. Minor sub-themes to 1.1: patient heterogeneity and complexity; incomplete medical information; lack of evidence (inadequate research in older poly-medicated adults); time and resource constraints for GPs. Sub-theme 1.2: strategies / circumstances that mitigate uncertainty. Minor sub-themes to 1.2: low risk strategies; patient and / or carer attitudes; patient relationship (barrier for CP); interprofessional relationships and communication. Major theme 2: risk as a frame of reference. Sub-theme 2.1: deprescribing as a risk to be avoided / reconciled; risk tipping points; self-efficacy. Minor sub-themes to 2.1: fear of unknown / harm from deprescribing; proactive strategies to facilitate deprescribing; low-hanging fruit; clear triggers; confidence and experience.	adopting a gradual approach to changing medicine regimens and deferring to patients in making a deprescribing decision. Examples of `easy deprescribing options' included statins, proton pump inhibitors and complementary medicines. However, participants acknowledged that targeting `low hanging fruit' like this may deliver easy wins but may sidestep drugs with potential to do more harm. Consideration of relationships e.g. GP / patient relationship was critical to better assessing harms and benefits and committing to the process of deprescribing. Good working relationships between GPs and CPs facilitated timely, collaborative deprescribing decisions. Better evidence that deprescribing is safe and effective and decision support provided in a format that is easily accessible at point of care for use in discussions with patients was offered by participants as a key facilitative strategy. Tipping points e.g. clear trigger points to change medications and using these to take action. Past experience and confidence.	
Anthierens, 2010 Belgium	To describe GPs' views and beliefs on polypharmacy in order to identify the role of the GP in relation to improving prescribing behaviour.	Qualitative. Semi-structured interviews. 65 GPs	4 main themes that influence polypharmacy: patient related, GP related, evidence-based medicine, and specialist related factors. Patient related factors include: side effects, difficulty keeping an overview of exact intake of medication of their older patients, dangers of self-medication by patients changing their own regimes and importance of compliance, patients not being inclined to stop using drugs they've used for a long time. GP factors include - easier to start a new treatment for every new complaint without evaluating the existing medication schedule, the need for	Need for new tools that are easier to use in primary care and simple approaches such as working in close collaboration with skilled pharmacist or peers for medication review. Need for GP training in geriatric pharmacotherapy. Need to optimise educational approaches, computer assisted approaches, medication review by clinical pharmacists, geriatric medicine services, multidisciplinary and multifaceted approaches. Updating knowledge and info alone not enough though. There's a need for change in attitude	*****

Table S1: Summary of included studies

			GPs to have a list of priority medication, GPs feel under pressure from guidelines to prescribe preventive drugs even if impacts of polypharmacy outweigh the possible benefits, increased risk of interactions. Also, shortcomings in their pharmacological knowledge and info available that is not that accurate or up-to-date. Absence of communication between different prescribers in different settings.	and behaviour of GPs and they need tools for this.	
Bell, 2017 Norway	To investigate nurses' and pharmacists' perceived learning experience after participating in IMRs in primary health care for up to two years.	Qualitative. Focus groups and telephone interviews. 13 nurses and 4 pharmacists	Previous studies have pointed to a lack of mandate for the pharmacist's role, the time the pharmacist was on site and funding of the pharmacists as barriers for pharmacists participating in interprofessional teams in primary health care. The main barrier identified by this present study was if there were delayed or deficient documentation about the patient's condition given to the pharmacist prior to the IMRs. Funding for IMRs is dependent on the municipalities' willingness to pay for the pharmacist and can be a limitation for the continuation of IMRs in primary care. Evidence suggests that the physician has a pivotal role in decisions making about the prescribed medicines. No surprise, when the physician is not present at the IMR, the interviewees in this study said that they learned less. Shift work and part-time positions in addition to nurses spending little time with home dwelling patients, made it difficult to collect the relevant patient information.	Interprofessional collaboration (between nurses, pharmacists and physicians). Involvement in interprofessional medication reviews facilitate learning and greater understanding about the roles of other HCPs. Find common time and booking meeting facilities for interdisciplinary case conferences, in home-based care and in rural municipalities. Involvement of patients in decisions about their healthcare. Authors had not found not any studies investigating such a solution in IMRs challenges.	*****
Cadogan, 2015 UK	To identify the underlying barriers to, and enablers of,	Qualitative. Face-to-face semi-	Eight key domains were identified, perceived to influence prescribing and dispensing of appropriate polypharmacy: 'Skills', 'Beliefs	Four Behaviour Change Techniques (BCTs) were selected for inclusion in an intervention for GPs or pharmacists: 'Action planning',	*****

Table S1: Summary of included studies

	prescribing/dispensing appropriate polypharmacy and to frame these barriers and enablers in terms of theoretical domains of behaviour change to support intervention development. The underpinning theoretical model was the Theoretical Domains Framework (TDF)	structured interviews. 15 GPs and 15 CPs	about capabilities', 'Beliefs about consequences', 'Environmental context and resources', 'Memory, attention and decision processes', 'Social/professional role and identity', 'Social influences' and 'Behavioural regulation'.	'Prompts/cues', 'Modelling or demonstrating of behaviour' and 'Salience of consequences'. An additional BCT ('Social support or encouragement') was selected for inclusion in a community pharmacy-based intervention in order to address barriers relating to interprofessional working that were encountered by pharmacists.	
Clyne, 2017 Rep. of Ire.	To explore patients' beliefs about and attitudes towards medication, within a population of community-dwelling older patients with polypharmacy, and explore factors that might influence medication beliefs.	Mixed methods. 196 patients (mean age 76.7 years, 54% male) with mean of 9.5 medications per patient	Patients with poor knowledge of their medications. Older people with poorer health literacy. Medication taking is often characterised by uncertainty, elements of risk, and information asymmetry between patients and GP (GP with more info than patients creating an imbalance of power). Lack of guidelines, involvement of multiple prescribers, patients' strong beliefs in medicines. Findings highlight that strong beliefs can mask a complex interplay of positive and negative patient attitudes, in the context of limited knowledge and a willingness to stop medications.	Trust in the GP may enable patients to negotiate the uncertainty and complexity of polypharmacy. Patients more willing to cease medications when recommended by a physician they trust. Patient trust may facilitate a willingness to tolerate polypharmacy in a context of uncertainty and may equally influence a patient's willingness to deprescribe.	****
Dalleur, 2014 Belgium	To explore general practitioners' (GPs) perceptions regarding the use of the STOPP&START tool in their practice.	Qualitative. Focus groups. Use of vignettes. 27 GPs involved in 3 focus groups.	Barriers to using the tool: The tool is difficult to implement. The application of the tool is time-consuming. The patient might disagree with treatment modifications. Diverging views between general practitioners concerning the usefulness of the tool, its comprehensiveness, and relevance of the criteria. GPs often feared that patients would disagree to change	The tool was considered as a decision support aid and a way to improve security, as it drew attention on main inappropriate prescribing events. It allows a systematic revision of the patient's therapy. Participants reported that STOPP would help GPs to withdraw useless drugs, which was perceived to be particularly welcome in poly-medicated patients, and that	*****

Table S1: Summary of included studies

		Brainstorming sessions included pharmacists, hospital pharmacists, GPs and geriatricians.	their treatment, as they were attached to their medications. The layout of the tool was also suboptimal according to GPs and should be improved to become more interactive. ICT support needed. Training also needed.	START would help them remembering to prescribe required medications. This medication review was considered as essential by the participants but currently insufficiently achieved. Educational role of the tool mentioned and associated with the improvement in the use of the GPs' skills. To improve implementation of the tool, most GPs reported that several adaptations were needed, including: better availability, adaptation to the practice of the GPs and individualization to their actual needs, flexibility and updates to address new molecules, and evolution of knowledge. Involving the patients as `partners in optimizing treatment' was also mentioned. Multi-disciplinary working: GPs thought that effectiveness could be increased by working with other healthcare professionals such as physician colleagues, geriatricians, (clinical) pharmacists, nurses from nursing homes, and medical trainees. However, not all participants agreed to discuss the treatment of their patients with other professionals.	
Djatche, 2018 Italy	To assess the perceptions of primary care physicians on deprescribing for elderly patients and potential barriers to deprescribing that physicians experience in the Local Health Authority (LHA) of Parma, Emilia Romagna, Italy.	Quantitative. Paper survey 160 GPs	The study highlighted that although many physicians in the LHA of Parma felt confident about deprescribing, there were many barriers that discouraged them from undertaking this process. Most respondents (78%) reported they were comfortable deprescribing preventive medications, yet only half (53%) were comfortable deprescribing guideline-recommended therapies. Lack of evidence on discontinuing preventive medicines and concern about withdrawal side effects were reported to impede deprescribing by more than one-third	Increased awareness about deprescribing among current and future clinicians would help them appreciate the scope of inappropriate medication use as a population health issue and recognize the barriers they may encounter. Educational workshops about how to effectively deprescribe can help physicians better understand how to communicate with other providers and address patients' concerns. Utilizing available medication or class-specific deprescribing tools with a monitoring plan could help ease clinicians into the decision-making process. Imperative that physicians	***

Table S1: Summary of included studies

			of physicians. When medications were initially prescribed by another physician, 40% of physicians reported hesitance in deprescribing them. About half of physicians (45%) did not feel comfortable deprescribing when patients/caregivers believed that continuation of the medication was needed. Lack of time and difficulty engaging patients/caregivers in the deprescribing process were cited as barriers by about one in four physicians. There was no strong correlation between physicians' confidence and attitudes or barriers associated with deprescribing.	take the time to conduct a comprehensive review of the medications that their patients are taking, including those prescribed by other provider.	
Farrell, 2015 Canada	To engage physicians, pharmacists and nurses in identifying and prioritizing medication classes where evidence-based deprescribing guidelines would be of benefit to clinicians.	Quantitative. Descriptive. Online survey. 65 geriatrics experts (36 pharmacists, 19 physicians, 10 nurse practitioners)	Health care providers work in a culture that facilitates diagnosing and prescribing, and that pays relatively little attention to deprescribing or reducing chronic medications. This can lead to overtreatment and drug-related illness. Other: More guidance needed e.g. on use of Proton Pump Inhibitors. Deprescribing should be an aspect in all treatment guidelines (including preventative meds). Clinicians need assistance with negotiating changes with patients, finding non-pharmacologic approaches to manage symptoms and managing the process of tapering.	The Delphi consensus process identified five priority drug classes for which expert clinicians felt guidance is needed for deprescribing. The classes of drugs that emerged strongly from the rankings dealt with mental health, cardiovascular, gastroenterological, and neurological conditions. The results suggest that deprescribing and overtreatment occurs through the full spectrum of primary care, and that evidence-based deprescribing guidelines are a priority in the care of the elderly.	****
Farrell, 2018 Canada	To determine whether the use of deprescribing guidelines would change the perception of self-efficacy and also whether such changes might differ depending	Quantitative. Descriptive. Emailed survey. 50 primary care physicians	It was learned from users that implementation of deprescribing guidelines was facilitated by use of the associated algorithm in routine quarterly medication reviews by a pharmacist and physician in Long Term Care (LTC). Conversely, no such routine process was mandated for patients in Family Health Teams (FHTs); this, in combination	The use of a guideline algorithm providing a structure and approach for deprescribing appears to improve self-efficacy for certain deprescribing tasks.	**

Table S1: Summary of included studies

	on practitioner type, practice site or specific guideline.		with competing priorities and short patient appointments were barriers to widespread guideline implementation in this type of primary care setting.		
Fried, 2017 USA	To examine the effect of the Tool to Reduce Inappropriate Medications (TRIM), a web tool linking an electronic health record (EHR) to a clinical decision support system, on medication communication and prescribing.	Quantitative. RCT. 128 older people aged 65 years and over, prescribed 7 or more medications	Not described.	Patients who received TRIM had significantly more active participation and medication-related communication than controls. The clinicians of patients who received TRIM demonstrated significantly more facilitative and medication-related communication than clinicians of control patients, and a significantly larger proportion made a medication-related recommendation. TRIM had a direct effect on patients but an indirect effect on clinicians, with the patients' active communication style promoting a more participatory communication style among their clinicians. The lack of a direct effect on clinician communication may help to explain the finding that the use of TRIM was not associated with changes in patients' medication regimens. Although clinicians in the intervention group responded to patients' questions and concerns about their medications, they were no more likely than those in the control group to implement the specific recommendations provided in the TRIM feedback.	***
Garfinkel, 2018 Israel	To evaluate efficacy and safety of poly-de-prescribing (PDP) based on the Garfinkel method in older people with polypharmacy.	Quantitative. Descriptive. 122 patients in the intervention group (PDP) and 55 in the non-	The main barrier to de-prescribing was the family doctor's unwillingness to adopt PDP recommendations. In 48 out of 55 (87%) NRs, the GP (sometimes specialists) refused to discontinue medications. In the 122 patients of the PDP group, GPs adopted the PDP plan completely, mostly or partially in 86, 20 and 5 patients, respectively (91%). In six cases (3.3%) the patient/family decided to adopt	There is an issue here as to who takes responsibility for managing or slowing down of 'the epidemic'? Geriatricians and GPs play a major role (preferably in cooperation with pharmacists) as their hands write prescriptions. We need to change from disease-oriented approaches and internalize the fact that for older people, we have no reliable 'guidelines' for most diseases/drugs, no proof that	****

Table S1: Summary of included studies

		responder group (NR)	the PDP recommendations despite their doctor's refusal to comply. Extract from DISCUSSION: For most medications, the positive benefit–risk ratio becomes non-existent or reversed, in correlation to the extent of the VOCODFLEX characteristics; the severity of 'the epidemic' increases in correlation to exactly the same characteristics and the extent of polypharmacy. The problem is further aggravated due to 'prescription cascades' where symptoms resulting from ADEs are perceived as representing 'new diseases'. This perpetuates the iatrogenic vicious cycle of over-diagnosis, useless evaluations, hospitalizations, overtreatment and 'the epidemic'. Possible contributors are for-profit diagnostics and drug companies. Other contributing factors are 'defensive medicine' attitudes of automatically 'following orders', implementing whatever guidelines we do have in all older people, until death.	prescribing would be better than non-prescribing. Authors conclude: Only an integrated global effort from health professionals, policymakers and consumers, all committed to improving health through optimizing medicines, including involvement from the general press and social networks, can win the war against 'the epidemic'.	
Green, 2019 Australia	To investigate clinician-perceived barriers and facilitators of reducing polypharmacy and PIM use in people with dementia	Qualitative. Semi-structured interviews. Face to face or video conferencing. 21 clinicians from 16 different clinics (19 physicians and 2 nurse practitioners)	Heightened barriers for patients with dementia and coexisting conditions. Lack of data - lack of clinical trial data for people with dementia, comorbidities, polypharmacy and lack of evidence of efficacy for older adults. Concerns about harming patients by stopping medications. Tendency to continue preventive medications until patients reached advanced dementia. Difficulties determining whether patient with dementia benefitting from medications. Uncertainty over identifying adverse effects. Reliance on caregiver's assessment of benefits / harms and clinicians needing caregivers to be	Use of pre-printed materials such as flowcharts to illustrate the risks and benefits of treatment options. Educational resources and communication guides to help clinicians deprescribe unnecessary medications. Patient-directed materials to help prime patients and caregivers for discussions about medications. Disease-specific clinical practice guidelines. Access to interdisciplinary services. Communication with other clinicians involved in a patient's care. Electronic medical records. On-site pharmacists to review patients' medications and provide guidance on tapering regimens or drug interactions. Other	*****

Table S1: Summary of included studies

			available and skilled in decision-making. Nonpharmacological therapies deemed too onerous for patients with dementia. Tensions between advocating for the patient and helping caregivers. Perceived caregiver guilt leading to clinicians continuing preventive medications. Giving medications seen as `doing something for the patient'. Not doing so, perceived as giving up. Patients / carers expecting to be given something often led to a prescription. Cognitive biases could cause clinicians to withhold treatments. Therapeutic inertia. System barriers e.g. lack of time to discuss medications, different health providers involved in care plan. Acceptance of other prescribers' recommendations even if they had doubts.	interdisciplinary services e.g. social workers to assist caregivers access resources (although access to such services were far from universal). Approaches to discussing medications: some clinicians were explicit with caregivers about medications for patients with life-limiting illness. Others suggested stopping meds could enhance quality of life and others focused on long-term benefits of medications within mentioning life expectancy.	
Hansen, 2019 Republic of Ireland	Explores the views of community pharmacists on their potential involvement in reducing PIP and determines the challenges to its implementation	Qualitative - semi-structured interviews 18 pharmacists interviewed (n= 15 urban and n= 3 rural)	Despite beliefs about capability and responsibility for reducing PIP structured medication, reviews and recommendations about stopping medications do not form a routine part of daily practice for community pharmacists in Ireland. Pharmacists expressed uncertainties about the extent of what their role in reducing PIP should be. They described a reluctance to work outside of their current role and to challenge prescribing decisions taken by GPs, such as recommending drug discontinuation. When asked specifically about stopping medications, pharmacists in our study described uncertainty of where final responsibility for PIP avoidance lies. Collaboration between pharmacists and GPs was challenged by (i) a lack of understanding of each other's professional role in combination with (ii) the busy professional	Having access to diagnoses and comorbidities would increase the clinical relevance of pharmacist recommendations and improve communications with other healthcare providers. Sharing patient clinical data was suggested as one fundamentally important way to improve communication and collaboration between community pharmacists and GPs. Pharmacists in the study welcomed more education and guidelines on reducing PIP. These guidelines should ideally give instructions on the steps following the identification of a PIP, be up-to-date and be used by all, including prescribers. There is a need to design guidelines that meet the needs of healthcare professionals in busy medical and pharmacy clinical practice in terms of content, instructions and relevance. The majority of barriers and facilitators identified in this study	*****

Table S1: Summary of included studies

			practice environment and (iii) the absence of a shared platform with patient information. To date, there is no centralised system in which patient information is shared between community pharmacies and GP practices in the Republic of Ireland.	fall under the TDF domains of environment, knowledge, social professional role and social influences. The design of future interventions should target these domains.	
Harriman, 2014 Canada	To identify common challenges (amongst GPs) to discontinuing medications and to explore current deprescribing practices.	Quantitative. Descriptive. Online or printed self-administered survey. 30 GPs	Original prescriber concerns: Reluctance to deprescribe was reported when the family physician (FP) was not the original prescriber of the medication. This may be due to a lack of confidence in their own deprescribing knowledge and experience or being unclear about the indication for the specific medication chosen by the specialist. Furthermore, there is little published evidence for effective deprescribing practices to guide FPs in discontinuing medications. Organisational challenges: FPs reported that their reluctance to act was increased by organizational challenges to discussing deprescribing (e.g., time constraints, family unavailability) and concerns about the possible consequences. The organization of primary care in nursing homes in Vancouver may also hinder deprescribing. "If it ain't broke, don't fix it!" The fear of making any change in a relatively stable patient that could cause destabilization, negative symptoms, or, even worse, death, is understandable. FPs in this study are aware of the benefits of deprescribing, yet half of them said they do not use a systematic approach or evidence-based method when discontinuing medications (due to the barriers described).	A multidisciplinary team approach to deprescribing is needed, where the work is shared by various members of the health care team. Barriers should be targeted and further research into polypharmacy reduction practices should be undertaken.	*

Table S1: Summary of included studies

Heser, 2018 Germany	To gain insight into contextual factors that might lead to chronic Potentially Inappropriate Medication use.	Qualitative. Semi-structured face-to-face interviews. 52 patients	Barriers to deprescribing: PIM is not rated as problematic medication. Patient does not care about side effects of medication. Alternative treatments are not used. Resistance against cessation of PIM. Dependency or failed discontinuation of PIM. Ageism by patient.	Besides certain health-related behaviours (e.g., own obligation to report to GP) and medication-related attitudes and knowledge (e.g., awareness of side effects and interaction of medicines), patient-GP-interactions that were characterised by mutual agreements on drugs (e.g., concerning dosage or discontinuation of a drug) might be advantageous to reduce the probability of chronic PIM use.	*****
Kennedy, 2015 USA	To determine the impact of integrating pharmacists into patient-centered medical homes	Quantitative. Non-randomised. 8 pharmacists in 7 sites	Not described.	There was clear value in integrating pharmacists into primary care teams. Their inclusion prevented adverse drug events, avoided costs, and improved patient outcomes. Primary care providers should consider pharmacists well suited to offer direct patient care, population-based management, and prescriber education to their practices. To be successful, pharmacists must have full permission to document findings in the primary care practices' electronic health records.	*
Linsky, 2015a USA	To understand providers' beliefs and attitudes about polypharmacy and medication discontinuation	Qualitative. Face-to-face semi-structured interviews. 20 prescribers at two sites (11 physicians, 3 nurse practitioners, 6 pharmacists)	Patients uncertain as to why they were taking medications. Providers maintaining the status quo if they had no clear reason to stop a medication. The presence of multimorbidities inhibited discontinuation. Impaired cognition effected clinical decision making with uncertainties that recommended changes would be understood and implemented. Limited patient knowledge was challenging for clinicians to ensure medication adherence. Hesitation to alter regimens prescribed by other providers. Difficulty communicating between providers. The complexity of the deprescribing process seen as additional work compared to	Patient age can trigger deprescribing because of concerns around polypharmacy, decline in drug metabolism, or shifts in risk-benefit ratio due to changes in perceived life expectancy. Patient knowledge about their condition and medications often facilitated conversations about ceasing medications. Clinicians felt additional contact with the patient to obtain an updated medication list is essential for prescribing decisions. Providers felt that their professional identity made them responsible for providing appropriate, comprehensive care and are accountable for medication decisions. Physicians felt that nurses and pharmacists could aid in medication reconciliation to allow	*****

Table S1: Summary of included studies

			medication renewal. Providers burdened by external directives and policies. Mixed views on influence of IT e.g. electronic medical records could lead to discontinuation of medications but inaccurate lists led to uncertainties and providers were wary of burdensome electronic reminders or alerts.	more time for other clinical issues. Pharmacists embraced the opportunity for a better schedule capacity and longitudinal monitoring that expanded their role and facilitated deprescribing.	
Linsky, 2015b USA	To identify key patient elements that contribute to shared clinical decision making about intentional medication discontinuation	Qualitative. Focus groups and interviews. 27 patients	Patients expressed that even though they did not like taking medications they remained adherent because they had trust in their health care provider. Patients were concerned about the potential adverse effects of not taking their medications. Patients put a lot of trust in their doctor's knowledge and expertise despite wanting to reduce their medications. Patient's lack of training meant that patients would follow doctor's orders despite wanting to take fewer medications. Patients indicated that they had not experienced a provider recommending discontinuing a medicine. However, there were also instances where patients were told to stop a medication but this was not updated on their record.	Majority of patients expressed a desire to take fewer medications. Patients wished to be monitored to see how their body responded to medications. Patients wanted to take a more active role in the decision-making process with a need for more information on their medications, the rationale for taking them and the potential side effects.	*****
Linsky, 2017 USA	To determine preferences for interventions that would improve providers' ability to discontinue medications.	Quantitative. Descriptive. Survey (self-administered). 326 prescribers (physicians, nurse practitioners, physical assistants and pharmacists)	Not described.	One survey question presented 15 potential changes to medication-related practices and respondents ranked their top three choices for changes. Among the 326 respondents who provided rankings, the top choice for a change that would help improve their ability to discontinue medications was "Requiring all medication prescriptions to have an associated 'indication for use.'" This preference was followed by "Assistance with follow-up of patients as they taper or discontinue medications is performed by another member	***

Table S1: Summary of included studies

				of the Patient Aligned Care Team (PACT)" and "Increased patient involvement in prescribing decisions". Also indicated: "Improved information exchange with all VA and non-VA pharmacies to confirm medication reconciliation", improving medication reconciliation, the benefit of additional time with patients, and explicit clinical guidelines and criteria for deprescribing.	
Linksy, 2018 USA	To characterise which patients are more or less likely to report discontinuing medications	Quantitative. Descriptive. Self-administered survey. 803 patients	Taking more medicines, seeing a VA clinical pharmacist, and placing greater trust in one's prescriber were associated with lower likelihood of discontinuation.	Strongest prediction of having discontinued a medication was provider recommendation, followed by patients requesting to stop a medication. Respondents with higher education, greater interest in deprescribing, and those who prefer shared decision-making were also more likely to report discontinuation. A provider's recommendation increases discontinuation as many patients perceive control of medications to fall within realm of the prescriber. It also highlights the importance of patient-provider communication that should occur to determine whether continuing or discontinuing a medication is the best course of action for the patient. Patients have their own opinions about medications and the impact of any effects. Patient initiation of the deprescribing conversation is likely to alleviate any clinician misperceptions that might hinder deprescribing - such as thinking the patient might feel abandoned by such a suggestion.	***
Luijks, 2012 The Neths	To explore GPs' considerations and main objectives in the management of multimorbidity and to	Qualitative. Focus groups (n=5) 25 GPs	Presence of mental-health problems regarded as a complicating factor in multimorbidity management and `Diagnostic overshadowing'. Cognitive impairment of patients with multimorbidity impeding	Patient-centredness. Shared decision-making. Continuity of care. A personal, long-standing, patient-doctor relationship was a major facilitator in the management of	*****

Table S1: Summary of included studies

	explore factors influencing their management of multimorbidity.		management and medication adherence. Difficulties from conditions interacting with each other. Practical problems: time, polypharmacy considered harmful but hard to reduce, difficulties coordinating and maintaining an overview of medication. The need to adapt management of multimorbidity to the patient's personal circumstances and preferences and socioeconomic conditions. Adhering to strict guidelines contradicts perception of an individual as a unique person with specific combination of conditions. Fragmented care. Disease-centred approach insufficient because multiple conditions and corresponding advices need integration and coordination. Searching for a balance between a patient's disease and illness. Responsibilities - variation in responsibilities allocated to themselves [GPs] when care provision to patients with multimorbidity was shared with other medical specialists.	multimorbidity. Tailoring care to the individual. Integrated approach.	
Mc Namara 2017 Australia	To explore approaches to multimorbidity management, and perceived barriers and enablers to deliver appropriate medications management for community-dwelling patients with multimorbidity and polypharmacy, from a broad range of healthcare professional	Qualitative. Semi-structured interviews 26 HCPs. Of which, 14 prescribers and 12 practices in primary care.	GPs felt that limited time prevented them from incorporating personal preferences into decision-making. Disability and poor health literacy. Patients reluctant to ask questions. Guidelines focused on individual diseases. Junior doctors lacking experience and nurses reporting receiving conflicting advice from different prescribers. HCP were not aware of prognostic tools. Ethical concerns and litigation fears from denying treatment. No clear method of assessing adherence to modified treatment plans. Deprescribing was not a priority for GPs with limited time with patients. There was a reluctance to interfere	Shared decision-making to improve adherence. Pharmacists and nurses improving the knowledge of patients regarding their medications and addressing concerns and personal preferences. GPs and nurses felt that home medical reviews conducted in collaboration with pharmacists were helpful in optimising treatment.	*****

Table S1: Summary of included studies

	(HCP) perspectives in Australia.		with other HCPs prescribing due to a fear of disturbing therapeutic relationships especially among young doctors. Patient resistance. GPs not having access to up-to-date information after hospital discharge. No one assuming responsibility for optimising care plans due to poor coordination of care. A poor level of government renumeration for GPs and pharmacists conducting home medical reviews.		
Mantelli, 2018 Switzerland	To determine whether, how, and why Swiss GPs deprescribe for this population (frail, oldest-old).	Quantitative. Descriptive. Survey.	Not described.	GPs most commonly rated four factors as "important" or "very important" in their decisions about deprescribing: 'risk of a medication' (99%); 'benefit of a medication' (98%); 'quality of life' (98%); and, 'life expectancy of the patient' (96%). Many GPs mentioned the importance of patients' wishes and priorities, and that their own 'assessment of cost/benefit of a medication' and 'drug interactions' could influence their decision to deprescribe. CVD history influences GP prescribing decisions. Conclusions: Swiss GPs were willing to deprescribe cardiovascular preventive medication when it lacked indication but tended to retain pain medication. Developing tools for GPs to assist them in balancing the risks and benefits of medication in the context of patient values may improve deprescribing activities in practice.	***
Ng, 2017 Singapore	To elucidate patients' attitudes towards the number of medications they were taking and identify factors that might influence	Quantitative. Descriptive. 136 patients (41% female, aged between 45 and 84 years)	Having a discount card for medications. Paucity of deprescribing guidelines concerning patients with multi-morbidities for physicians.	If advised by the doctor, 93.4% of participants were willing to stop one of their medications. This was associated with a younger age (< 65 years), not have a discount for medications, and having a higher physician trust score. Although a significant proportion of participants were comfortable with the number	***

Table S1: Summary of included studies

	acceptance of deprescription.			of medications that they were taking (82.4%) and believed that all their medications were necessary (88.8%), 72.8% still had the desire to reduce the number of medications they were taking. A quarter of participants (25.0%) felt that they might be taking one or more medications that they no longer needed, and 30% felt that one or more of their medications were giving them side effects. Patients' willingness to stop a medication had a strong association with the patient's desire to take fewer medications. The patients' desire to reduce medications was positively associated with whether the doctor indicated possibility of stopping the medication.	
Palagyi 2016 Australia	To explore perceptions of medication use and the concept of deprescribing in long-term care facilities (LTCFs)	Qualitative. Focus groups and interviews with GPs, pharmacists, nurses, residents and relatives in three LTCFs in NSW, Australia Nine focus groups with residents (n=25), relatives (n=16), and LTCF staff (n=19) from three LTCF. A tenth focus	Inadequate communication between healthcare providers. A lack of review meant that medications were being continued after the condition had subsided. A lack of medical charts which provided a barrier to initiating medication change. Pharmacists felt that the currently established two-year gap between medical reviews was too long. Medical reviews were not conducted face-to-face and GPs stated that they were more likely to apply recommendations of a medical review that was conducted by a pharmacist with contact with the patients, rather than using an automated review. Time constraints and a shortage of health professionals – GPs were only able to provide part-time support to LTCF. A lack of knowledge of medicine indications, actions and potential adverse effects by residents and their families created apathy towards polypharmacy. GPs were not confident deprescribing for diseases such as	Electronic medical records and ability to use practice software for LTCF patient records. GPs felt that relatives needed to be educated in order to manage their expectations and initiate discourse.	*****

Table S1: Summary of included studies

		group was held with 8 GPs who provided care to residents of LTCFs in the study region. Four pharmacists completed semi-structured interviews.	dementia and Alzheimer's where there was a lack of guidelines. A lack of skilled staff specifically nursing staff, who do not have the education to document medication side effects. Residents and relatives put a complete trust in the GP and their management should not be questioned. GPs were cautious of making medication changes particularly when trying to manage a families expectations to keep their relative alive. GPs were concerned about the legal risks of not implementing the recommendations from non-commissioned medication reviews despite not being a legally binding document. An attitude of "if it ain't broke, don't fit it".		
Reeve, 2018 UK	To explore what factors enable or limit health professionals in delivering individually tailored prescribing (ITP) in every day practice.	Quantitative. Descriptive. 419 healthcare professionals	ITP seen as integral part of patient-centred practice, but ITP lacks clarity amongst healthcare professionals (HCPs). ITP is not prioritised. HCPs lack time, headspace and energy to be engaged in ITP. Much of the training and support comes from experiential learning and peer support. HCPs have concerns over making defendable decisions and getting practice advice on how to translate ideals of care into practice. The importance of feedback to patients and learning from patients but lack of continuity of care and the need for more formal monitoring / feedback systems in place to recognise this complex form of practice.	Need for training, support, interpretive practice. Need to prioritise ITP in primary care practice. Need to raise understanding and awareness of ITP as legitimate role of expert clinical generalist role. Need for feedback mechanisms, monitoring through peer reflection, continuity with patients, and consideration of the impact of formal monitoring on care. The study highlights the importance of patient understanding of the model of care as a potential enabler and barrier to deprescribing.	*****
Reeve 2018 USA	To explore the attitudes of older US adults toward deprescribing.	Mixed methods 1981 Medicare beneficiaries	Most older adults reported that their medications were necessary, and a substantial proportion expressed concern over stopping a medication that they had been taking for a long time. Contradictory beliefs (about being willing to have a	Majority of Medicare beneficiaries were willing to have a medicine deprescribed if their physician said it was possible. Physician can have a strong influence on patient attitudes toward deprescribing. Discussion of concepts essential for reaching an informed decision	*****

Table S1: Summary of included studies

			medication deprescribed but also thinking that their medications are necessary) reflect a combination of traditional deference to physician recommendations coupled with a medical culture focused on prescribing and starting medications rather than deprescribing.	about deprescribing with older adults. Clinicians should be reassured about broaching the topic of deprescribing with their older patients. Deprescribing should be undertaken within the framework of patient-centred care and shared decision-making. Increased public awareness about deprescribing also necessary. Need to challenge status quo which encourages continuation of medications. Canadian study suggests fewer than 10% of people aware of the term deprescribing. Choose Wisely Campaign. `Less is more'.	
Riekert, 2018 Germany	To examine how GPs experienced the use of the PRIMA-eDS tool, how they adopted recommendations and GPs' ideas on future implementation of the tool.	Qualitative. Face-to-face interviews. 21 GPs	Tool considered time-consuming. Some GPs delegated data entry to healthcare assistants. Not all GP practices had access to internet which complicated data entry in which case data entry was done at home. Data entry was not always carried out whilst the patient was present. Switching between software was inconvenient and sometimes content needed to be printed or written down for it to be added. Patient not always asked about symptoms and medical conditions and info instead estimated or transferred from patient files. Technical problems. Patients were sometimes fearful of negative effects when changing long-term medications and feared changes were due to cost-cutting measures rather than to the objective of improving care. GPs had not followed recommendations because alternatives / recommendations had already been tested and GP / patient felt this was not the optimal way of treatment. GPs regarded medications as necessary. GPs / patients had other priorities. GPs feared changing medication	Tool easier and faster to use after a period of familiarisation. GPs felt majority of patients taking part in the trial of the tool were open-minded and cooperative towards recommended changes in medication. Some patients were happy about taking fewer drugs. GPs felt that patients involved in the trial liked being closely connected with the GP and liked the extra attention / extensive care. GPs positive about the CMR and described as useful, trustworthy with well-chosen recommendations that support the GP, although, some GPs thought the recommendations were either `too tame' or hard to realise. Some GPs were not able to follow recommendations and at times, discontinued medications had to be restarted - but the decisions made were made more consciously and necessity of medications confirmed. Several GPs reported well-tolerated and lasting changes in medication.	*****

Table S1: Summary of included studies

			could get complex. GP lacked motivation to reconsider medications that had been prescribed for years. GPs did not want to diverge too far away from standard guidelines. Some GPs found recommendations not comprehensible or applicable. Patients perceived as barrier to discontinue medications. Other: GPs less likely to change prescriptions made by other professionals. Also, infrastructure issues resulting in delays or event forgotten medication changes.		
Schopf, 2018 Germany	To explore elderly patients' and general practitioners' (GPs') perceptions of communication about polypharmacy, medication safety and approaches for empowerment.	Qualitative. Face-to-face and telephone semi-structured interviews. Patients (n=6) and GPs (n=3)	Changes made by other specialists, self-medication or discontinuation of medication by the patient not being communicated to the GP by the patient resulting in inaccurate plans. A lack of courage, fear, pain, forgetfulness, embarrassment, lack of trust in the GP, a perception that side-effects were less important in old age and no desire for more information were factors for patients. The GP is seen at the main responsibility for decision making. Partly reviewed medical plans. A lack of patient knowledge about their medications hinders communication between the patient and GP. Legal concerns and a lack of time were barriers to deprescribing. Patients fear that their condition may worsen, they take too much of the GPs time and concerned if medication is prescribed by another specialist. Patients reported a lack of discussion about medication or the possible risk of side-effects for medications that are taken for a long time. Patients wanting to appear obedient to maintain a good relationship with their GP.	Friendliness of GP and continuity of care by the same GP were important in promoting open discussion. GPs feel they are responsible for explaining the reasons for deprescribing and to motivate the patient. Interventions to improve patients' communication skills and address issues of polypharmacy need designing. GPs might support patients by `inviting' their contribution. The friendliness of the GPs and continuous care by the same GP might promote an open discussion. The behaviour of the GP is important in supporting patients' openness about discussions about their medications. One GP thought a public campaign might motivate patients to address difficult topics during consultations. Another GP suggested patients come prepared for the consultation by, for example, informing themselves by reading up on the subject and / or bringing medication plans and relevant documentation from other providers. The Internet was seen as an important source of information and relatives as an important means of support.	**

Table S1: Summary of included studies

			Trust in the GP acts as a double-edged sword: can promote open communication about medications but can also prevent patients from asking questions.		
Schuling, 2012 The Neths	To explore how experienced GPs feel about deprescribing medication in older patients with multimorbidity and to what extent they involve patients in these decisions.	Qualitative. Focus groups. Use of vignettes. 3 focus groups in which 12, 8 and 8 GPs participated respectively.	GPs felt that patients do not have a problem with polypharmacy or with medication burden. Patients are reluctant to cease medications. GPs are not fully aware of the problems that patients experience. Patients underreport possible adverse effects. GPs reluctant to initiate a discussion about deprescribing because it could be seen as a sign of being given up on. GPs felt that level of education and old age were barriers to discussing deprescribing. GPs had trouble in identifying possible adverse effects in patients with multimorbidities. The real area of concern was how to manage the long-term use of preventive medication. A lack of evidence of the effects of preventative medication and a need for clear information on the benefit/risk of these medications. GPs were not aware of patient's treatment preferences. GPs feel forced by guidelines to prescribe multiple medications. Medication lists for new patients are not exchanged and are inconsistent. Communication between providers is poor. Some GPs indicate that patients cling to their extensive medication list. GPs acknowledge that they may not be fully aware of the actual problems patients may experience. GPs may be reluctant to initiate a discussion about deprescribing because of concerns that patients may interpret this as a sign of being given up on.	GPs saw it as their duty to provide necessary information on treatment choices. The relationship between GP's and local pharmacists was an important factor when a GP was looking for support when making decisions regarding medication reviews.	*****

Table S1: Summary of included studies

			Some GPs think that confronting a patient with a discussion about life expectancy versus quality of life is not ethical. However, others believed that such a discussion could have a positive effect on their relationship. GPs vary in their belief on the effects of preventative drug therapy in older patients. Some GPs mention patient characteristics (low education and old age) as a barrier to the patient's understanding of the issue. GPs experience difficulties in identifying ADEs and take the patient's judgement seriously. The real area of concern for the participants was how to manage the long-term use of preventive medication. The problem of the lack of evidence of the effects of preventive medication in the very elderly is paramount. GPs indicate a strong need for clear information on the benefit/risk ratio of preventive medication in the very old and often frail. However, even if such information were available, some participants feel incompetent in risk communication, and others consider this information not helpful for actual shared decision-making. All participants admit they were seldom aware of their patients' treatment preferences. GPs feel forced by current guidelines to prescribe many different medicines: they appear to pile the recommendations of one guideline on another instead of prioritizing. Participants claim they often feel guilty when their adherence to guidelines is not up to scratch. A new patient entering the practice list is welcomed as an opportunity to review their medication. Some GPs complain about an		

Table S1: Summary of included studies

			inadequate overview of the patient's medication. In multimorbidity, several healthcare providers are involved in a patient's treatment and communication is sometimes poor. Cooperation with prescribing medical specialists who represent 'their' guideline is a barrier to deprescribing. In addition, most GPs work closely with a local pharmacist: the task perception of such pharmacists was an important factor when a GP was looking for decision support in medication review. Findings suggest that GPs tend to avoid discussing withdrawal of preventive medication with their elderly patients. Their beliefs concerning patients' support, even justify, this policy. Even though GPs support a patient-centred approach, they do not inquire into patients' preferences or discuss treatment goals. Current guidelines focus on management of a single disease and do not take into account the problem of multimorbidity. Prioritization is needed but GPs do not feel empowered to do so.		
Sinnott, 2015 The Rep. of Ireland	To explore how GPs make decisions when prescribing for multimorbid patients, with a view to informing intervention design.	Qualitative. Face-to-face interviews. 21 GPs	Negotiating conflicts between GP, patient's requests and specialists' recommendations. Lack of guidance and reliance on `best guesses'. Lack of time pushed some GPs' into a default position to `maintain the status quo' rather than interfere with the medication regimes - unless clear adverse drug effects. Fear of medico-legal repercussions or negative responses from patients and or their next of kin. Use of medications considered `justified' because they were initiated by a specialist or recommended in guidelines. GPs assumptions that multi-morbid patients	GPs, when faced with difficult decisions, elected to have a practice discussion about it to bounce ideas off other colleagues and to reach a consensus. Follow-up return consultations.	*****

Table S1: Summary of included studies

			preferred not to be involved in decisions. GPs assumptions that patients would be unable to understand and so would just worry. GPs difficulties talking to multi-morbid patients about stopping medications as they feared this would be interpreted by the patient as a withdrawal of care and potentially damaging the doctor-patient relationship. Lack of timely access to and communication from specialists or because of a single disease rather than a generalist approach to the patient. Lack of relational continuity of care could affect management (especially in larger GP practices).		
Strassner, 2018 Germany	To identify determinants (barriers and facilitators) for the implementation of polypharmacy recommendations in general practice	Qualitative. Interviews and focus groups. Interviews with 24 GPs, 4 other medication specialists, 1 pharmacist, 3 nurses, 6 medical assistants. Focus groups with 17 professionals	General determinants: lack of time and reimbursement and range of patient factors. Patients using high number of over-the-counter medications and unwilling to report their medication completely. Lack of continuity of care in nursing homes with high staff turnover and in patients with migration background who frequently spent several months of the year in their home countries. The lack of carers available for patients not able to care for themselves. `Hierarchy of prescribers' meaning that GPs may have inhibitions to question prescriptions from clinicians or specialists. Lack of collaboration / info exchange between prescribers, pharmacists and nursing homes. Problems in changing of medications when transferring care between hospital to community.	Multi-faceted interventions targeting barriers in different areas are needed to achieve meaningful improvement in the management of polypharmacy, but they are difficult to implement. Pharmacological expertise, improving patient involvement, practice organisation and communication training might be relevant elements. Also, continuity of care, and collaboration was easier to establish in smaller rural areas with fewer stakeholders.	*****
Turner 2016 Australia	To rank factors that GPs, nurses, pharmacists and residents perceive as	Mixed Methods. Nominal Group	None reported	GPs ranked evidence for deprescribing as the most important factor. Ability to communicate the need to deprescribe to residents and their families was second most important. Nurses	*****

Table S1: Summary of included studies

	most important when deciding whether or not to deprescribe medications.	Technique (NGT). 56 participants (19 GPs, 11 residents / reps, 12 nurses, 14 pharmacists)		ranked GP receptivity to deprescribe as a priority, followed by the ability to advocate for the resident. Pharmacists ranked 'clinical appropriateness of the prescribed therapy' and 'difficulty in determining the residents' goals of care' as the two most important factors. Residents ranked 'wellbeing of the resident' which included the capacity to question GPs about medications, to continue medications they believed made them feel well, and cease medications that caused side effects. 'Continuity of nursing staff' was the second most important factor.	
Van Middelaar, 2018 The Neths	To explore general practitioners' (GPs) routines and considerations on (de)prescribing antihypertensive medication (AHM) in older patients, their judgement on usability of the current guideline and needs for future support.	Qualitative. Semi-structured face-to-face interviews. 15 GPs	Barriers to deprescribing antihypertensive medication in older people: deprescribing may give the impression of giving up on a patient, the drug gives a patient a sense of control. Reducing or discontinuing antihypertensive medication was not easily decided upon. Some GPs were influenced by regret and fear that a patient might have a stroke after deprescribing the medication. They hesitated to discontinue - even if the patient was terminal - to avoid the impression of giving up on the patient or depriving them of a sense of being in control with blood pressure measurements. They aim to avert the risk of non-fatal stroke and accompanying functional limitations in the last phases of life.	Enablers to deprescribing antihypertensive medication in older people: prolonged achievement of target blood pressure, risk of side effects, risk of falling, patient preference, increase in quality of life, terminal illness.	*****
Van Summeren, 2017 The Neths	To determine proposed and observed medication changes when using an Outcome Prioritisation Tool (OPT) during a medication review in	Quantitative. Intervention trial. Descriptive. 14 GPs and 63 patients	In patients who prioritised 'maintaining independence' as most important, GPs proposed to stop various preventive medication, such as statins and antihypertensives. Few of these proposed changes were observed at follow-up, and one may question whether stopping preventive	Stopping medication appeared to be easier for patients who prioritised 'reducing other symptoms' as the most important health outcome, compared with patients who prioritised 'remaining alive' or 'maintaining independence' as the most important. A stepwise reduction of medication may be a	***

Table S1: Summary of included studies

	older patients with multimorbidity with polypharmacy. A secondary aim was to explore the relationship between the prioritised health outcome of patients and the type of medication change, such as a stop, a dose adjustment, or a switch.		medication is in line with the patient's prioritisation. GPs may have had difficulty in deciding which medication might be stopped when patients prioritise 'maintaining independence' as most important. In contrast, in patients who judged 'reducing other symptoms' as most important, such preventive medication was often stopped as proposed.	good approach to stop symptom-relieving medication. Further research is needed to determine whether patients benefit from a medication review with an outcome prioritisation tool. www.optool.nl	
Wallis, 2017 New Zealand	To explore the views of primary care physicians on the barriers and facilitators to deprescribing in everyday practice	Qualitative. Face-to-face and telephone semi-structured interviews. 24 GPs	Physicians described `swimming against a tide' of patient expectations, medical culture of prescribing, and organisational constraints. Prescribing was the easy option. Patients expected there to be "a pill for every ill". Uncertainty around which medicines patients were taking and why. Poor information between providers. A lack of evidence regarding best prescribing practice for older people with multimorbidities. Fear of preventable adverse effects following deprescribing. Wanting to maintain relationships with patients and their families and not wanting to appear like they were "giving up on them". Young inexperienced physicians were reluctant to cease medications prescribed by others. Fast pace and competing demands of the practice. Fragmented care made deprescribing difficult due to poor information between providers and a lack of trust in short-term therapeutic relationships. Single diseased focused	Physicians felt they had a duty to do what was right for the patient. Organisational changes recommended by participants including: incentivisation for annual medicines review, computer alerts to prompt physicians' memories, computer systems to improve info sharing between different prescribers, improved access to non-pharmaceutical therapies, research to build the evidence-base in multi-morbidity, education, training, ready access to expert advice and user-friendly decision support, regularly updated guidance for the management of common comorbidities, tools and resources to assist with the communication of risk to patients, and activating patients to become more involved in meds management and alert to the fact that `less might be better than more'.	*****

Table S1: Summary of included studies

			guidelines and limited availability of non-pharmaceutical alternatives.		
Weir, 2018 Australia	To explore decision making about polypharmacy with older people and their companions	Qualitative. Face-to-face, semi-structured interviews 30 older people and 15 of their companions	Three types of patients identified: Type 1: Patients attached to their long-term medications. These patients tended to have negative attitudes to deprescribing: concerns / fears over their health condition worsening as a result of deprescribing and preference for continuing their medication and maintaining the status quo. These patients could not recall a discussion about deprescribing being initiated by their doctor. Patients had high trust in the doctor for decision-making about their medicines. Type 2: ambivalent towards medicines. Mixed attitudes. Valued their medicines but disliked side effects and willing to consider deprescribing. Awareness of options and preference for shared decision-making. Type 3 were frail and did not give their medicines much thought. Openness to deprescribing but only if doctor thought best. Preference to defer to the doctor. Limited knowledge about medicines. Type 1 had companions that were either dominant or had equal partnership in decision-making. Type 2's companions were more collaborative / more actively involved in decision-making. Type 3's companions were managing patients medicines (so much so that in some cases they were the only ones who knew about the medicines).	Importance of recognising the various types of patients and that not all patients confirm to an `ideal' patient standard. Also, important to consider the varying roles of companions and how this relates to communication between doctors and patients. Importance of doctors initiating deprescribing discussions as study shows many patients are open to have such discussions - especially if benefits made clear by a knowledgeable doctor in whom they trust and with whom they have a quality doctor / patients relationship. The participant types identified in this study suggest that deprescribing should be tailored to older adults' understanding of their medicines, their attitudes towards medicines and deprescribing, and their preferred participation in decision-making. Educating clinicians about the potential benefits and harms of medicines in older people, as well as training/guidance for deprescribing, is also important, as many patients will simply follow their doctors' advice unquestioningly.	*****
Wermeling, 2014 Germany	To describe factors and motives associated with the continuation of inappropriate	Qualitative. Semi-structured interviews.	Default prescribing of PPIs in hospital. Doctors who continued to prescribe PPIs seemed to do so almost every time a NSAID, (non-steroidal anti-inflammatory drug) is	`Discontinuing' GPs (i.e. those GPs more likely to not prescribe / deprescribe' were more aware of prescription guidelines, which specify the necessity of PPI usage. More informed GPs	*****

Table S1: Summary of included studies

	prescriptions of PPIs in primary care	10 GPs.	prescribed. Attitudes to prescribing informed prescribing behaviour. GPs who felt confident to prescribe PPIs did so for a variety of reasons, while many of the `discontinuing' GPs were more concerned about the general use of drugs. Personal experience (of the use of PPIs) might influence the perception of the therapeutic value of PPIs. Role of pharmaceutical industry in stimulating unnecessary drug consumption. Patients requesting PPI medications. Continuing GPs valued the experience of hospital physicians who initiated the PPI. Sometimes a lack of knowledge of the evidence-based recommendations seemed to enhance this positive view of hospital physicians. Also, some GPs suspected that a discontinuation would evoke the patients' distrust towards hospitals. Some GPs valued the competence of (younger) hospital physicians over their own. GPs tended to favour a smooth discharge transition without logistic effort. Prescribing budgets more rigorous in primary care, whereas the hospital is less exposed to these pressures. PPI prescriptions in hospitals driven by the risk that patients could develop stress ulcer syndrome with NSAID treatment.	were more motivated to quit an inappropriate medication (including consideration of expensively branded drugs). This was most obvious when PPIs were a co-medication. GPs' feeling of self-confidence, autonomy and trust in their own decision-making. For discontinuing GPs with such feelings, it was not a major issue to stop the medication.	

Table S2: Barriers and facilitators – primary care: summary of data extracts

Barriers	Facilitators
Cultural level *"more is better"(1-3)* *"if it ain't broke, why fix it?"(4)* *"pill for every ill"(2)* Easier to prescribe than deprescribe – status quo easier (3, 5, 6). Pharmaceutical companies – culture that encourages diagnosis and prescribing (7); and over-the-counter meds (8). **Organisational level** ***Lack of evidence-base and guidance*** Single disease focused guidance (not guidance on multimorbidity and polypharmacy); and the different interactions of different meds are not `tied-up' in guidance (1, 2). Design of Randomised Control Trials (RCTs) – concerns starting medications and not when to stop or how to stop (3). Not involving older people with multimorbidity in RCTs (9). RCTs are designed around the starting of medications, and they do not look at how to cease medications (2, 3, 10). RCTs – do not involve older patients with multimorbidity (9, 11). Recommendations within guidelines are not comprehensible or applicable (12). ***Lack of resources and tools*** Insufficient time / headspace for GPs to discuss deprescribing with patients (3). Community Pharmacists (CPs) had more time for discussions with patients about deprescribing but they lacked detailed knowledge of patients (13-15).	**Cultural level** A "*less is more*" culture is needed (2, 3). Public awareness raising campaign advocated (about the need for a more prudent prescribing culture) (3, 8, 26). **Organisational level** ***Evidence-based guidance*** More RCTs are needed which involve patients with multimorbidity and explore how to stop medications as well as how to start them (6, 9). Better guidance is required on the interactions of different medications in different medical conditions. All guidance needs to include when, and how, to stop different medications (as well as when, and how, to start). For example, painkillers, anti-depressants, Proton Pump Inhibitors, statins (1, 9, 13, 30, 35). Better evidence is required in a format that is easily accessible at point of care for use in discussions with patients (13). ***Tools and resources*** Better tools and resources are required including joined-up systems between hospitals and GPs, and time for medication reviews. (10, 17) Studies have identified a need for a medication-specific tool for shared decision-making in primary care (15, 20, 36). Developing tools for GPs to assist them in balancing the risks and benefits of medication in the context of patient values may improve deprescribing activities in practice (and to remind them when to review), including guideline algorithm (29). CPs resolved uncertainties by posting questions about medication appropriateness rather than making recommendations to GPs to cease PIMs (13, 19). Value in integrating pharmacists in primary care teams (37).

Table S2: Barriers and facilitators – primary care: summary of data extracts

Lack of joined-up electronic clinical decision-making solutions (2, 5, 16-19). Cumbersome and time-consuming deprescribing tools (12, 15, 16). Lack of alternatives to pharmaceutical therapies (20). Technological problems e.g. not all GPs had access to internet and software problems involved in certain tools (12). Primary care budgets more rigorous in primary care, whereas hospitals less exposed to budget pressures (21). **Interpersonal level** ***Uncertainties*** General Practitioners' (GPs') fears of stopping medications prescribed by another prescriber (4, 13). Professional etiquette (2). GPs' fears of side effects from deprescribing – uncertainties over identifying adverse effects (10, 17, 22, 23). Prescribers fear of legal implications (6, 18). Tendency to continue preventive medications until patients reached advanced dementia (9-11, 17, 24, 25). GPs' fear to be seen of `letting go' of patient and of not caring by taking away patient's meds (9, 22). Community pharmacists (CPs) with incomplete patient medical info (13, 19, 25). Patient relationship is a barrier for GPs and CPs (13, 14, 26). GPs' uncertainties over deprescribing medications due to a lack of guidance (2, 5, 13, 27). Contradictory beliefs (3).	**Interpersonal level** ***Knowledge*** Improvements needed in both patient and prescriber knowledge, understanding, education and training around deprescribing (13, 15, 16, 18, 23, 30). Provide GPs with better information and guidance on deprescribing (including risks and benefits) so they are better informed and more confident in their own deprescribing actions (3, 21, 38). Seek guidance from experienced peers and other colleagues (6, 16). Target medications that are easier to deprescribe (13). ***Communication*** Most patients trust GPs and patients who trust GPs are willing and open to discussions about deprescribing (8, 12, 20, 23, 26, 31, 33, 39). GPs need to initiate deprescribing discussions with patients (and they need the time and tools to do this) (13, 38). Guidance needed for GPs on how to start conversations with patients about stopping medications (5). Improved communication needed between GPs and their patients and between different specialists (5, 6, 15, 28). Tipping points are useful e.g. clear trigger points to change medications (13). Multidisciplinary team approach to medication reviews and deprescribing needed (including practice-based discussions) (4, 10, 16). Other professions who challenge physician knowledge seen as a facilitator (14, 15). Continuity of care needed (6, 15, 25, 28, 32). Not just between GP and patient but between GP and pharmacist (13, 16, 40). Close collaboration with pharmacist / peers for medication reviews advocated (10). Common time and booking meeting facilities are needed for interdisciplinary case conferences (14).

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Lack of communication Lack of `correct language' for GPs to initiate discussions on deprescribing (5). Patients with impaired cognition (5). Lack of integrated communication between different prescribers and with patients (2, 5, 6, 8-11, 13, 20, 23, 27, 28). ***Lack of collaboration between GPs and other prescribers and fragmented care*** (including issues with GP locums and part-time GPs and other prescribers on short-term contracts) (10, 14, 15, 19, 28). **Individual level** ***Lack of patient involvement in decision-making*** Patients inability to state reason for their meds (20). Patient / family decisions may be different from GPs / other prescribers (4, 7, 27, 29). Patient may not care about side effects of medications (30). Patient's dependency and addiction to certain medications (30). Patients just following `doctor's orders' and not questioning (20).  Patients with `free' prescriptions / discount card for medications are less likely to cease medications (31). ***Lack of tailored approaches*** – e.g. for patients with sensory impairments; patients with dementia and their carers; patients with mental health issues; different socio-economic conditions; and patients with poor health literacy (15, 32-34).	**Individual level** ***Shared decision-making and patient-centred care*** Patient involvement in decision-making is needed (2, 5, 9, 11, 15, 17, 20, 21, 23, 32, 35, 39). Patient-centred care should be the main priority (3, 11, 32). Patients who are open to discussions about deprescribing also value the extra attention given by GPs if they are involved in decision-making and be more likely to act upon GP's recommendations (although not always) (12). Trust in GP influences a patient's willingness to deprescribe (5, 8, 23, 31, 33). Stopping medications appeared easier for patients who prioritised `reducing other symptoms' as most important health outcome (24). Access to non-pharmacological therapies is needed (2). Patients are not homogeneous. Prescribers are different. Tailored approaches needed (23, 34).

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