







REVIEW

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The burden of polypharmacy and potentially inappropriate medication in Nigeria: a clarion call for deprescribing practice

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Abstract

Background: Polypharmacy and potentially inappropriate medications (PIMs) could cause adverse drug events leading to poor health outcomes. This burden is addressed through deprescribing practice. However, data on deprescribing practices are lacking in Nigeria, where the healthcare systems are fragile.

Aim: This review aimed to summarise the literature on the burden of polypharmacy and PIMs and identify the need for deprescribing practice in Nigeria.

Method: A systematic search of the literature was conducted on MEDLINE through PubMed (Public Medline), Google Scholar, and a manual search of included articles to identify information on deprescribing, polypharmacy, and PIMs in Nigeria from the inception of the database to date. Relevant information from the articles was summarised and presented as subsections in the manuscript.

Results: In this review, we reported the burden of polypharmacy, PIMs, and the need for deprescribing practice in Nigeria. The estimated prevalence of polypharmacy was up to 23.8% among older patients with chronic disorders. Polypharmacy and PIMs have been reported to be a significant cause of medication non-adherence, drug addiction, drug interactions, adverse drug reactions, hospitalisation, morbidity, and mortality. Thus, there is the need to consider deprescription practice in the country.

Conclusion: This review revealed that polypharmacy and PIMs are common in Nigeria. Therefore, there is a need for deprescribing practice to improve drug safety in the country. This could be achieved through patient education, increasing awareness of deprescribing practice among the healthcare professionals, and ensuring adherence to the core prescribing indicators of the World Health Organization (WHO) and National Standard Treatment Guidelines.

Keywords: Polypharmacy, Deprescribing, Nigeria

Introduction

Polypharmacy is a global phenomenon with an increasing public health problem (Schenker et al. 2019). Polypharmacy refers to the use of multiple medications in a patient, usually a geriatric. While the most commonly

used definition of polypharmacy is on five or more medications; the definitions are variable (Masnoon et al. 2017). Polypharmacy may be defined as the use of more medicines than are clinically necessary for a patient's comorbidities (Zarowitz et al. 2005). The rate of polypharmacy is increasing in developing countries like Nigeria due to the growing number of older adults (Tanyi et al. 2018). In Nigeria, the number of older individuals taking five or more prescription or over-the-counter medications varies from 25 to 35% (Akande-Sholabi et al. 2018a).

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Potentially inappropriate medications are medications for which the risks outweigh the benefits, especially in the presence of more effective alternatives (Renom-Guiteras et al. 2015). Polypharmacy and PIMs are associated with an increased risk of adverse drug reactions, hospitalisation, morbidity, and mortality (Reeve 2020).

Polypharmacy and PIMs could therefore benefit from an informed deprescribing process. Deprescribing is the practice of withdrawing an unnecessary medication to reduce polypharmacy and optimise outcomes monitored by a healthcare professional (Reeve 2020). The deprescribing process involves taking a history of drugs, identifying unnecessary medication, acknowledging the need to stop a medication, preparing and carrying out the medication's removal, and tracking outcomes during and after withdrawal (Reeve 2020).

There is emerging evidence that deprescribing is safe and helpful, but it can be challenging to incorporate deprescribing into clinical practice (Reeve 2020; Reeve et al. 2017). Several challenges to deprescribing have been identified from both the health practitioners' and patients' perspectives, including a shortage of resources to support deprescribing practice (Zechmann et al. 2019; Conklin et al. 2018). Thus, several tools have been created to help clinicians implement deprescribing practices (Reeve 2020). Despite the increasing prevalence of polypharmacy and PIM in Nigeria, there is limited application of controlled mechanisms like the deprescribing practice.

Nigeria is a developing country in West Africa with a reported poor healthcare system (Muanya and Onyenucheya 2021). The country has a population of about 200 million population, with a doctor to patient ratio of 1:5,000 (higher than the WHO recommendation of 1:600) (Muanya and Onyenucheya 2021). The country is battling with chaotic drug distribution systems, poor patients' compliance with medical authority, and healthcare workers to professionals' ethics (Boluwaduro 2021; Muhibi 2010). Therefore, in this review, we report the burden of polypharmacy and PIMs, and identified the need for deprescribing practice in Nigeria.

Main text

Literature selection method

A search strategy using the following terms both as medical subheading (MeSH) and free text as (all fields) was developed. The search terms used included: "polypharmacy"[MeSH Terms] OR "polypharmacy"[All Fields], "potentially inappropriate medication list"[MeSH Terms] OR "potentially inappropriate medication list"[All Fields] OR ("inappropriate prescribing "[MeSH Terms] OR "inappropriate prescribing"[All Fields] OR "inappropriate prescription"[All Fields])" deprescriptions "[MeSH Terms] OR "deprescriptions"[All Fields] OR

"deprescription"[All Fields]"Nigeria"[MeSH Terms] OR "nigeria"[All Fields] OR "nigeria s"[All Fields]. Relevant studies were also identified manually from the reference lists of the included articles. Additional information was also retrieved from Google Scholar using the following search expression "polypharmacy, potentially inappropriate medication, deprescribing in Nigeria." Based on previous recommendations, only the first 200 search results from the Google scholar search were considered for inclusion (Reeve et al. 2017). The search strategies employed in the systematic search of the literature in PubMed and Google Scholar are provided in "Appendix A".

Eligibility criteria

The studies included in this review were in peer-reviewed journals from the year 1980 to 2022, which were available in the English language. The chosen studies were those that focused on "polypharmacy, potentially inappropriate medication and deprescribing in Nigeria."

Results and discussions

The burden of polypharmacy and PIMs in Nigeria

In Nigeria, polypharmacy is common in clinical practice settings. Patients using between six and twelve medications have a higher risk of adverse drug events than patients with a lower quartile of drug use (Steinman et al. 2006). Akande and Ologe found that polypharmacy (particularly involving injectable formulations) and under-usage of life-saving drugs were common at a secondary healthcare facility in the North-central region of the country (Akande and Ologe 2007). The major risk factors for polypharmacy were reported as age, level of education, and diagnosis (Igbinomwanhia et al. 2017). The burden of polypharmacy had several clinical effects on the patients, ranging from medication non-compliance, addiction to drug interactions (Igbinomwanhia et al. 2017).

Antibiotics and antimalarials are often prescribed unnecessarily with little consideration for resistance and the development of adverse drug events (ADEs) (Nduka et al. 2017; Oshikoya et al. 2008). Antibiotics are among the most commonly misused medicines in Nigeria, and this poses a high risk of bacterial resistance, and adverse drug reactions, among other consequences (Akin-yandenu and Akinyandenu 2014).

Fadare et al. (2018) used Beer's criteria to assess the prevalence of PIMs being prescribed to elderly Nigerian outpatients (65 years and above) in a rural south-west Nigerian hospital. They used a prospective cross-sectional study to assess drug-use indicators for 220 patients using WHO's guidelines, while the Beers criteria were employed to detect PIMs. Their findings

showed that a total of 837 medicines were prescribed to the patients (i.e. 3.8 ± 1.3 drugs per patient), and 56 patients (i.e. 25.5% of total patients) were identified with at least one prescribed PIMs (Fadare et al. 2013). The identified PIMs were antihistamines, non-steroidal anti-inflammatory drugs (NSAIDs), and amitriptyline (Fadare et al. 2013). Similarly, the prevalence of PIMs prescribed to elderly patients in two tertiary health-care centres in South-Western Nigeria was estimated using Beers' and STOPP (Screening Tools of Older Person's Prescription) criteria. According to Beers' criteria assessment, the results showed that 30.3% of the 350 evaluated patients had at least one prescribed PIMs (Fadare et al. 2015a). Simultaneously, the STOPP criteria showed that 15.7% of the patients had at least one potential encounter with PIMs (Fadare et al. 2015a).

Saka et al. (2018) used 2015 updated Beers' criteria to evaluate PIMs, drug–drug interactions, and the inter-relation between these two issues with polypharmacy among Nigerian elderly patients (≥ 60 years) with chronic conditions. The study involved a retrospective evaluation of medicines prescribed to elderly patients, a total of 352, at Olabisi Onabanjo University Teaching Hospital, Sagamu, Ogun State, Nigeria. The authors found that the PIMs and drug–drug interaction incidences were 35.2% and 5.7%, respectively, and the majority (54.5%) of the participants received polypharmacy. They also found that PIMs were significantly associated with drug–drug interactions and polypharmacy (Saka et al. 2018). In a similar investigation, Akande-Sholabi et al. (2018b) employed the Beers' 2015 criteria to determine the prevalence of PIMs and to describe their associated factors among 400 elderly patients with comorbidities that attended University College Hospital, Ibadan, Nigeria. They found that 81.5%, 17.7%, and 0.8% of the respondents were using one, two, and three PIMs, respectively, most of which happened to be NSAIDs (commonest) and benzodiazepines (Akande-Sholabi et al. 2018b).

To evaluate the extent of inappropriate antibiotics usage, a cross-sectional, retrospective evaluation of the drugs' prescribing pattern in public secondary and tertiary hospitals was recently conducted in Nasarawa State, Nigeria (Helma et al. 2020). A total of 2800 participants' records were accessed and evaluated during 10 years. The researchers used WHO's prescribing indicators and Strengthening Pharmaceutical System/United States Agency for International Development (SPS/USAID) to identify the irrational antibiotic usage. The results indicated a high deviation of most of the WHO or SPS/USAID prescribing indicators' optimal values, suggesting irrational antibiotic prescribing in Nasarawa State, Nigeria (Helma et al. 2020).

Saka et al. (2019) compared the prevalence of potentially inappropriate prescribing (PIP) and determined the associated factors among older patients at University teaching hospitals in Nigeria and South Africa. PIP among 680 participants was evaluated using the 2015 American Geriatrics Society-Beers Criteria. The PIP among participants from Nigeria and South Africa was found to be (124/352; 35.2%) and (97/328; 29.6%), respectively (Saka et al. 2019). The study further reported that hypertension was significantly associated with PIP. These findings suggest the need for considering deprescribing practice among the older population.

In another research, Akande-Sholabi et al. (2020) identified potentially inappropriate prescribing in ambulatory elderly patients and compared the appropriateness of guidelines; Beers' and screening tool of older person's prescription (STOPP)/screening tool to alert right treatment (START) criteria to detect potentially inappropriate prescribing among the elderly. The 2015 American Geriatrics Society (AGS)-Beers Criteria and version 2 of the STOPP and START were subsequently used to identify the PIP and potential prescribing omissions (PPOs). The study reported an average of 4.2 medications per patient prescription. The Beers criteria identified 26.5% PIP, while STOPP criteria identified 57.1% PIP. START detected 29 PPOs in 15 (4.4%) of the patient's prescriptions. Polypharmacy was significantly associated with PIP in both Beers and STOPP criteria (Akande-Sholabi et al. 2020). These studies demonstrate the extent of PIP and polypharmacy even when assessed using standard screening tools.

Overall, the literature suggests that poor compliance to core prescribing indicators of the World Health Organization (WHO) and the Nigerian Essential Drug List prescriptions/National Standard Treatment Guideline aggravated the PIMs problems in Nigeria (Chijoke-Nwauche et al. 2018). Therefore, there is a need for interventions to address these growing public healthcare problems in the country.

The rationale for deprescribing practice

Deprescribing is a purposeful and systematic activity carried out to control polypharmacy, remove PIMs, and enhance patient outcomes (Page et al. 2016, 2018a; Scott et al. 2015, 2017). The goal of producing a beneficial outcome distinguishes deprescribing from actions such as the omission of an indicated prescription by the prescriber or the patient's non-compliance with prescribed therapy (Page et al. 2018b). When more than one medicine is indicated for deprescribing, the rule of thumb is to discontinue each drug at an interval. These are withdrawn consecutively at monthly intervals to ensure that any change in clinical signs or symptoms can

be attributed to just one medication (Page et al. 2018b). However, two or more medications can be removed concurrently in possible adverse drug reactions or a limited chance of an adverse drug withdrawal event (ADWE, for example, with supplements).

Polypharmacy stresses the need for medication review by the prescriber, thereby leading to deprescribing. In addition, multimorbidity also plays a vital role in justifying the practice of deprescribing. When there are many chronic disease conditions in patients, the number of drug–disease interactions increases, leading to drugs meant for a particular disease condition affecting a chronic disease condition (Schuling et al. 2012). Another important reason leading to medication discontinuation is when patients have multiple prescribers and visit numerous healthcare centres. These can lead to miscommunications about patients’ medication between the prescribers, which give rise to the use of drugs that would have been discontinued or deprescribed to avert adverse events (Ailabouni et al. 2016). Optimising healthcare centres and prescribers could help minimise the rate of medication non-adherence (Reeve and Wiese 2014).

Discontinuation of medications should always prioritise older patients, given these patient populations have a high risk of polypharmacy, the transition of care, and multiple prescribers (Reeve et al. 2015). The high proportion of older patients in Nigeria could call the need for improving deprescribing practice in the country.

There is scanty information on Nigerian prescribers’ awareness regarding appropriate prescribing and the screening tools for the elderly. This prompted some researchers to assess Nigerian physicians’ knowledge about screening tools for PIMs for the elderly. The study revealed that although around 105 (85%) of the respondents

indicated confidence in their ability to prescribe medications to elderly patients appropriately, only 20% and 15.6% of the respondents knew about Beer’s and STOPP criteria, respectively (Fadare et al. 2019). This indicated a gross lack of knowledge among Nigerian physicians about screening tools for PIMs, and potentially implementing the deprescribing practice at healthcare facilities. This gap in knowledge and practice necessitates the call for deprescribing practice by physicians in Nigeria. Figure 1 illustrates an overview of deprescribing practice in Nigeria.

Implications of deprescribing practice in Nigeria

Minimising harms related to polypharmacy

Polypharmacy has been independently associated with drug-related hospital admission in Nigeria (Adedapo et al. 2020). Although deprescribing practice could reduce adverse events due to polypharmacy, a major challenge could be the influence (through incentives) of pharmaceutical sales representatives on doctors to prescribe multiple drugs to patients (Fadare et al. 2018). Therefore, improved awareness of the rationale of prescription and professional ethics are needed among doctors to ensure patient safety.

Improving medication non-adherence

A conceptual model has shown a relationship between polypharmacy and medication (non) adherence (Marcum and Gellad 2012). The literature suggests that medication non-adherence occurs in up to 55% of elderly patients receiving multiple medications (Zelko et al. 2016). In Nigeria, the prevalence among people with chronic illness ranges from 40.0 to 60.8% (Usman et al. 2019; Adisa et al. 2011; Chukwujekwu and Adesokun 2017). Even though it could be hypothesised that deprescribing could

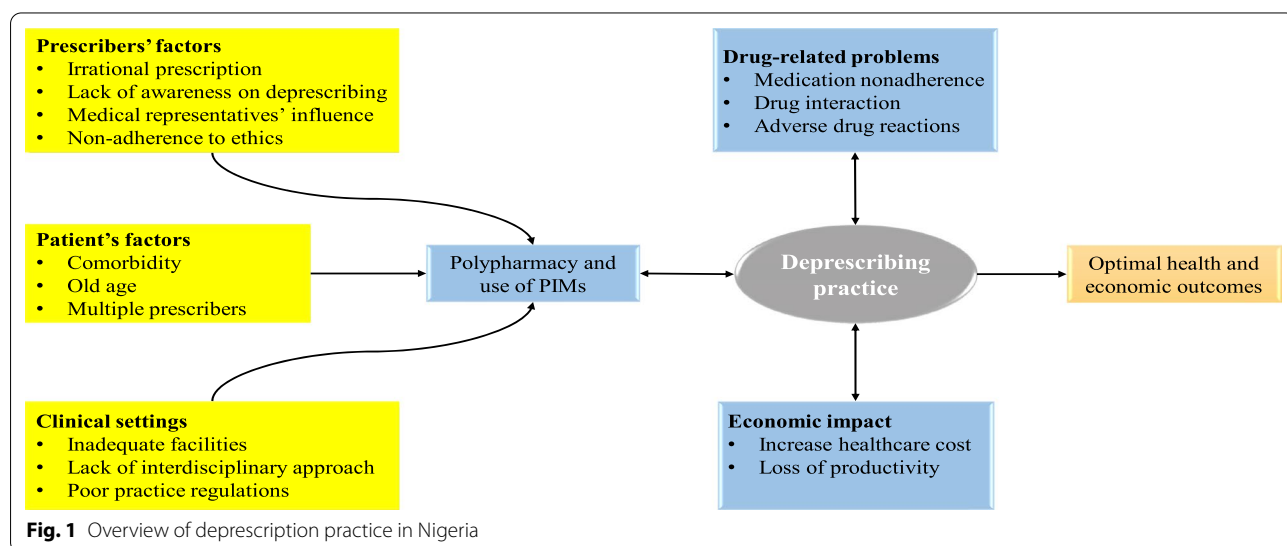


Fig. 1 Overview of description practice in Nigeria

improve medication adherence, a systematic review of the literature showed that there is insufficient evidence to demonstrate that deprescribing practice improves medication adherence (Ulley et al. 2019). Therefore, while more evidence is needed, implementing deprescribing practices in Nigeria could improve medication adherence and subsequent optimal healthcare outcomes.

Reducing harm related to PIMs, falls, and ADR

Deprescribing has the potential to resolve adverse drug reactions (ADR), reducing adverse events such as drug interactions, incorrect indications, drug-related falls, and potentially inappropriate medications (PIMs). In Nigeria, the use of PIMs among older patients was up to 15.7–46.5% (Eze and Olowu 2011; Eze and Olowu 2011; Fadare et al. 2015b); the prevalence of falls and ADR among older people was 23% (Bekibele and Gureje 2010) and up to 10.7% (Aderemi-Williams et al. 2015), respectively. Also, ADR was associated with prolonged hospital stays (Fasipe et al. 2019). Thus, deprescribing practice in clinical settings could reduce these figures in Nigeria. Discontinuation of medications should always prioritise older patients, given these patient populations have a high risk of polypharmacy, the transition of care, and multiple prescribers (Reeve et al. 2015). The high proportion of older patients in Nigeria could call the need for improving deprescribing practice in the country. However, there is scanty information on Nigerian prescribers' awareness regarding appropriate prescribing and the screening tools for the elderly. The gap in knowledge and practice necessitates the call for deprescribing practice by physicians in Nigeria.

Economic benefits

Prescribing multiple drugs to inappropriate patients could contribute to unnecessary healthcare expenditure. In Nigeria, 70% of the population is poor (Kale 2012), and about 90% are not insured with over-reliance on out-of-pocket drug expenditure (Aregbeshola 2016). Discontinuing inappropriate medicines through deprescribing can reduce one-fifth of the total cost of drugs (Morin et al. 2019).

The legal implication of deprescribing in Nigeria

The legal implication of deprescribing has been discussed in the literature (Barnett and Kelly 2017a, b). In some cases, deprescribing can harm such as withdrawal syndrome from discontinuing antipsychotic medicines, disease relapse, or deterioration of a disease condition. Severe damage due to deprescription without patient consent could lead to legal litigation. In Nigeria, according to the Codes of medical ethics, it is "medical negligence" to change the treatment course of a disease without the consent of the patient (when such consent

is necessary) (Ende et al. 2017). Although the literature proposes a Model Reform Act on medical negligence litigation in Nigeria (Obafemi 2017), deprescribing without consent can potentially result in medical negligence litigation. This is possible because about 1.1% of all medical malpractice cases are reported to the court in Nigeria (Abugu and Obalum 2018).

In summary, the high rate of polypharmacy and PIM may be contributed by many factors such as those related to prescribers (irrational prescriptions, lack of awareness of the deprescribing practice, the influence of medical representatives, and non-adherence to practice ethics), patients (comorbidity, old age, and visiting multiple prescribers), and clinical settings (inadequate facilities, lack of interdisciplinary approach, and poor practice regulations). In the absence of deprescribing practice, these factors could lead to adverse events such as medication non-adherence, drug interactions, and ADRs. It will also increase healthcare costs and loss of productivity. Therefore, implementing deprescribing practices could minimise these burdens and improve optimal health and economic outcomes (Fig. 1).

Recommendations for deprescribing practice in Nigeria

1. There is a paucity of data related to deprescribing practice in Nigeria. Adequate knowledge about the problem could guide the development of targeted interventions. Thus, future research is needed to explore the rate of this practice among prescribers, healthcare settings, patient populations, drug classes, and different disease conditions.
2. Data from prospective cohort studies or controlled trials in Nigeria could assist in providing evidence for the health and economic impact of deprescribing practice on the patients and healthcare system in the country.
3. There is also the need for improved awareness and utilisation of the use of appropriate deprescribing tools such as Beer's Criteria and STOPP among prescribers for rational drug prescription at healthcare facilities. Also, developing screening tools that are most suitable for the Nigerian population and healthcare setting may create a good foundation for deprescribing practice research in Nigeria.
4. Provision of computerised decision support tools ("passive and active referential information as well as reminders, alerts, and guidelines" or "computer applications designed to aid clinicians in making diagnostic and therapeutic decisions in patient care") (Monteiro et al. 2019) could facilitate deprescribing practice in Nigeria.

5. Continuing educational professional (CEP) courses of prescribers should be updated to include de-prescribing practice. This will keep them abreast of the current trends and the urgent need to implement them appropriately. Also, incorporating courses specific to appropriate prescriptions in the curriculum of medical students could assist in providing a foundation of knowledge for future prescribers.
6. An interdisciplinary approach among health practitioners would assist in implementing deprescription practice in Nigeria. For example, a patient’s medication review by competent pharmacists could detect polypharmacy and use of PIMs, which, when the prescriber is alert, can lead to deprescription and consequent optimal healthcare outcomes.

Conclusions

The burden of polypharmacy and the use of PIMs are common in Nigeria. The literature demonstrates that deprescribing practice could address healthcare and the economic burden related to polypharmacy and the use of PIMs. Therefore, there is a need for interventions to improve awareness and educate the prescribers about the need to implement deprescribing practices at healthcare facilities in the country. The intervention measures should include more research to identify the problems for targeted solutions.

Appendix A

PubMed Search Strategies

#1	11,430	"Polypharmacy"[MeSH Terms] OR "polypharmacy"[All Fields]
#2	8460	"Potentially inappropriate medication list"[MeSH Terms] OR ("potentially"[All Fields] AND "inappropriate"[All Fields] AND "medication"[All Fields] AND "list"[All Fields]) OR "potentially inappropriate medication list"[All Fields] OR ("inappropriate prescribing"[MeSH Terms] OR ("inappropriate"[All Fields] AND "prescribing"[All Fields]) OR "inappropriate prescribing"[All Fields] OR ("inappropriate"[All Fields] AND "prescription"[All Fields]) OR "inappropriate prescription"[All Fields])
#3	793	"Deprescriptions"[MeSH Terms] OR "deprescriptions"[All Fields] OR "deprescription"[All Fields]
#4	60,429	"Nigeria"[MeSH Terms] OR "nigeria"[All Fields] OR "nigerias"[All Fields]

#1 + #2 + #3 + #4	105	("Potentially inappropriate medication list"[MeSH Terms] OR ("potentially"[All Fields] AND "inappropriate"[All Fields] AND "medication"[All Fields] AND "list"[All Fields]) OR "potentially inappropriate medication list"[All Fields] OR ("inappropriate prescribing"[MeSH Terms] OR ("inappropriate"[All Fields] AND "prescribing"[All Fields]) OR "inappropriate prescribing"[All Fields] OR ("inappropriate"[All Fields] AND "prescription"[All Fields]) OR "inappropriate prescription"[All Fields]) OR ("polypharmacy"[MeSH Terms] OR "polypharmacy"[All Fields]) OR ("deprescriptions"[MeSH Terms] OR "deprescriptions"[All Fields] OR "deprescription"[All Fields])) AND ("nigeria"[MeSH Terms] OR "nigeria"[All Fields] OR "nigerias"[All Fields])
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Proposed Scopus database Search Strategies

#1	Polypharmacy OR Polymedication
#2	"PIM List" OR "PIM Lists" OR "Potentially Inappropriate Medications" OR "Inappropriate Medication, Potentially" OR "Inappropriate Medications, Potentially" OR "Medication, Potentially Inappropriate" OR "Medications, Potentially Inappropriate" OR "Potentially Inappropriate Medication" OR "Beers Criteria" OR "Beers Potentially Inappropriate Medications" OR "de Beers Criteria" OR "Beers Criteria, de" OR "STOPP (Screening Tool of Older Person's Potentially Inappropriate Prescriptions)" OR "STOPPs (Screening Tool of Older Person's Potentially Inappropriate Prescriptions)" OR "Screening Tool of Older Person's Potentially Inappropriate Prescriptions" OR "STOPP" OR "STOPP START Criteria" OR "Criteria, STOPP START" OR "Criteria, STOPP START" OR "START Criteria, STOPP" OR "START Criteria, STOPP" OR "STOPP START Criteria" OR "Medication Appropriateness Index" OR "Appropriateness Index, Medication" OR "Appropriateness Indices, Medication" OR "Index, Medication Appropriateness" OR "Indices, Medication Appropriateness" OR "Medication Appropriateness Indices" OR "Inappropriate Prescrib*" OR "Inappropriate Prescrib*" OR "Over Prescrib*" OR "Over Prescrib*"
#3	Deprescribing OR Deprescription OR Deprescrib* OR Deprescrip*
#1 + #2 + #3	

Proposed Google Scholar Search Strategies

#1	72	Polypharmacy potentially inappropriate medication deprescribing in Nigeria
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Abbreviations

ADEs: Adverse drug events; ADR: Adverse drug reaction; ADWE: Adverse drug withdrawal event; CEP: Continuing education professional; MeSH: Medical Subject Headings; NSAIDs: Non-steroidal anti-inflammatory drugs; SPS: Strengthening pharmaceutical system; STOPP: Screening tools of older person's prescription; PIMs: Potentially inappropriate medications; PubMed: Public Medline; USAID: United States Agency For International Development; WHO: World Health Organization.

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Author contributions

SBB and AS conceptualised the original idea and co-wrote the manuscript. AIJ, MM, and NA performed the literature review and co-wrote the manuscript. SBB and ZS edited the final draft, and AS critically reviewed the manuscript for intellectual content. All authors reviewed and approved the final version of the manuscript.

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