

Review Article

Polypharmacy

Ruckmani A

Professor and Head, Dept. of Pharmacology, Chettinad Hospital & Research Institute, Chettinad Academy of Research & Education, Chennai, India.



Dr. A. Ruckmani graduated (MBBS) from Madurai Medical College, earned PG Diploma in Dermatology from Madras University and M.D in Pharmacology from Dr.MGR Medical University. She is a practicing general physician. She has been teaching Pharmacology from 1990 onwards. She is currently Professor & Head, Dept. of Pharmacology, Chettinad Hospital & Research Institute. Her areas of research interest include toxicology, renal failure, rheumatoid arthritis, cancer, traditional systems of medicine and medical ethics. She has published more than 50 papers in indexed national and international journals. She has guided UG, PG as well as PhD research projects.

Corresponding author - Prof.Dr.Ruckmani A - (ruckmani.nirmal@gmail.com)

Chettinad Health City Medical Journal 2018; 7(4): 137 - 143

This article focuses on the discussion of the term "Polypharmacy", the rationality of polymedication, its limitations, the understanding of the concept in other systems of medicine and suggestions to minimize polymedication.

The term "Pharmacy" is derived through French and Medieval Latin from Ancient Greek word, *phármakon*, which means "a drug", "charm" and "enchantment."¹

Pharmacy is the art, practice, or profession of preparing, preserving, compounding, and dispensing medical drugs.² However, today, the pharmacies perform only the function of storing and dispensing of drugs. In common usage, pharmacy refers to a shop or hospital dispensary where approved medicinal drugs are sold.

Pharmacy practice also includes clinical services, reviewing medications for safety and efficacy, and providing drug information.

The term 'Poly' in English refers to more than one. Hence, Polypharmacy means more than one pharmacy and it may mean, getting drugs from more than one pharmacy. The pharmacy can dispense modern drugs, drugs of traditional medical systems or other systems, in which case polypharmacy may mean getting drugs of different systems of medicine from more than one pharmacy.

The concept of "polypharmacy" is said to have originated more than a century ago,³ but it has gained importance only in the recent past due to the prevalence of multiple medical disorders in individual patients.

Currently polypharmacy does not refer to multiple pharmacies, but multiple medications. However, there is no consensus about the meaning and definition of the term.⁴

According to WHO, the definition of polypharmacy is "the administration of many drugs at the same time or the administration of an excessive number of drugs" (WHO, 2004). WHO has not specified the number of drugs. The use of five or more medications is considered polypharmacy by most of the authors.^{5,6}

In patients suffering from cardiovascular disorders, even using more than two cardiovascular drugs is considered polypharmacy.⁷

If number of drugs is the criterion to define polypharmacy, then, if a patient takes a single tablet of a fixed drug combination like antitubercular formulation containing four first line drugs along with Paracetamol and Ranitidine can it be considered polypharmacy? If one takes, along with less than five tablets, an herbal extract which contains many active ingredients, can it be considered polypharmacy? In both cases, the number of drugs taken is more than five though the number of tablets is less than 5. Therefore, both may be regarded as polypharmacy.

As the term polypharmacy is used to refer to multiple medications rather than multiple pharmacies, the term "polymedication" may be more apt than polypharmacy. Polymedication can be due to using:

1. Multiple medications of modern system of medicine
2. Combination of drugs of modern and other systems of medicine like Siddha or Ayurvedha

Let us first consider multiple medications of the modern system of medicine.

Polypharmacy is grouped under different types:

- a) Appropriate polypharmacy⁸
- b) Problematic polypharmacy⁸
- c) Simultaneous polypharmacy⁹
- d) Cumulative polypharmacy⁹
- e) Continuous polypharmacy^{9,11}

a) Appropriate polypharmacy refers to prescribing for a patient with multiple medical problems where the selection of drugs is optimized based on the best available evidences and prescribed for the utmost benefit of the recipient. E.g: prescribing medications for a patient with hypertension, diabetes and ischemic heart disease with antidiabetic, anti-hypertensive and cardioprotective drugs.

b) Problematic polypharmacy is prescribing multiple medications inappropriately where the given combination may cause risk/ harm to the patient. E.g. Prescribing drugs to counteract the potential side effects of other drugs, like giving antiulcer medication (PPIs especially, Pantoprazole) along with anti-microbial or antihypertensive drugs, which are not known to cause gastritis. Most of the patients suffering from cardiovascular and metabolic syndrome take PPIs continuously everyday

along with other drugs as they are not advised to stop PPI by the physician. Patients are also unable to stop PPI for fear of rebound acidity. The long-term toxicity of PPIs may result in malabsorption of calcium and magnesium which could lead to bone fractures or cardiac abnormalities. The 2013 ACG guidelines have given a warning about the risk of increased *C. difficile* infection and community-acquired pneumonia in patients taking long term PPIs.

Problematic polypharmacy can also be called as inappropriate polypharmacy as the medications which could eventually be cumulatively toxic are used indiscriminately.¹⁰

c) Simultaneous polypharmacy denotes the number of drugs simultaneously taken by a patient on a given day. For example, prescribing antimicrobial, antipyretic, antiemetic, antiulcer and antihistamine for a patient with fever may be considered simultaneous polypharmacy.

d) Cumulative polypharmacy is the sum of different medications administered generally over a given period of time like three months to twelve months.

e) Continuous polypharmacy indicates limited number of medications taken regularly for a prolonged period.¹¹ Life-long therapy for diabetes, hypertension and Ischemic heart disease are examples of continuous polypharmacy.

Factors influencing Polypharmacy

1) Coexisting morbidities

It is very common at present to see patients suffering from multiple medical problems. When a patient suffers from hypertension, diabetes, dyslipidemia and ischemic heart disease, it is inevitable that he/she has to be prescribed multiple drugs. In this situation polymedication is a necessity. However, the physician has to carefully select the drugs in order to avoid adverse effects due to drug interactions.

2) Geriatric age group

The life expectancy is increasing globally. In India it was 67.14 years in 2012, and in 2018, it has improved to 68.8 years.¹² The population living beyond 60 years is projected to increase significantly from 104 million in 2011, to 174 million in 2026.¹³

The older population is liable to suffer from multiple disorders – diabetes, hypertension, cardiovascular disease, parkinsonism, Alzheimer's, renal dysfunction and others. Hence, it is essential for them to be prescribed with multiple medications. As the renal and hepatic function decline with age, dose adjustment is necessary to prevent the occurrence of adverse effects in this vulnerable population.

3) Vulnerability of physicians

The physician's practice of prescribing more drugs than the necessary ones contributes to polymedication, which can be due to the pressure from the pharmaceutical agents to promote certain drugs.

4) Insurance

Coverage of expenditure of treatment by medical insurance can persuade both the physician and patient to adopt polypharmacy.

5) Symptomatic treatment

The patient is simply treated for the symptoms rather than the cause of the symptoms. Multiple symptoms could be due to one cause like diabetes or depression. For example, drugs are prescribed for each of the symptoms such as body pain, fatigue, headache, body weight changes and lack of sleep, all of which are associated with diabetes or depression. Such treatment of symptoms will not be treatment of the disease itself.

6) Non-availability of the information on the drugs prescribed previously

Most of the time it may not be possible to find out why a particular drug was prescribed earlier. The current examination of the patient may not indicate the necessity to administer such a drug. The treating physician may continue the same drug to avoid withdrawal effects.¹⁴ Consider, for example, continuing a patient on Insulin even when the blood sugar remains consistently controlled with oral antidiabetic drugs.

7) Consulting multiple Physicians

Each physician prescribes from the perspective of his/her own specialty without taking into consideration the drugs prescribed by the other physicians. An orthopedist prescribes an antiulcer medication along with an analgesic, and a general physician prescribes antimicrobial and antiulcer drugs for respiratory infection in a diabetic patient. Ultimately, the patient has two antiulcer medications even when he or she does not suffer from gastritis. It is common to see antiulcer medication being prescribed in most of the prescriptions.

8) Withholding information by patients

Patients take treatment from more than one physician without informing the details of medication prescribed by the other physicians. Sometimes the patients take drugs of modern medicine as well as those of other systems of medicine such as Siddha and Ayurvedha which may result in drug interactions. Certain herbal products like soya, garlic, Ginkgo biloba can interact with warfarin metabolism.¹⁵

In addition, the patients may be taking multivitamins on their own. Even as prescription of proton pump inhibitors with antidiabetic or antihypertensive drugs has become a routine, prescription of multivitamins with multiminerals has also become a common practice.

9) Self medication

Easily available information on the internet emboldens the patients to choose drugs for themselves. Moreover, patients consume many health medicines such as natural preparations thus increasing the number of drugs.

10) Over the counter drugs

Patients are also likely to take OTC drugs in addition to the drugs they take regularly. This can add to polymedication. OTC drug formulation like antacids can inhibit the absorption of other drugs.

11) Taking medication on the advice of the staff in the pharmacy

Drugs are issued to patients by the sales person in the pharmacy without a prescription. As the dispensing person in the medical shop will not be able to diagnose,

wrong drugs may be issued resulting in problematic polymedication.

12) Fixed drug combinations (FDCs)

Fixed drug combinations usually contain more than one drug. Some of the commonly available combinations include Amoxicillin and Clavulanic acid, Furosemide and spironolactone, Telmisartan and hydrochlorothiazide, Metformin and Glimepiride. If a patient takes all these four formulations, the number of drugs taken will not be four, but eight though the tablets are four. Though this will not count as polypharmacy (as the number of drug combinations is only four), it is still polymedication as the number of drugs exceeds five.

The above discussion shows that the causes for polymedication are multifactorial.

Rationality of polypharmacy:

1) Concurrent treatment of multiple medical problems: As discussed earlier, when patients suffer from multiple problems multiple medications become mandatory to give relief from suffering.

2) Prevention of ADRs: The side effect of one drug is counteracted by another drug (Hypokalemia that could be caused by digoxin can be prevented by coadministration of ACE inhibitors and both are indicated in congestive cardiac failure). Thiazide diuretic is administered with potassium sparing diuretic to avoid potassium deficiency that can be caused by thiazide diuretic.

3) Dose and toxicity reduction: The dose of individual drugs can be reduced in order to reduce toxicity. For example, in cases of autoimmune disorders like rheumatoid arthritis, along with low doses of corticosteroids, steroid sparing drugs like methotrexate could reduce toxicity and benefit the therapeutic outcome.

4) Prevention of drug resistance as in tuberculosis and anti-HIV therapy in which polymedication is approved.

5) Prevention of risk factors : Drugs are given prophylactically to prevent risk factors for a particular disease. "Polypill" was a concept introduced by Wald and Law in 2003, and the pill composed of a statin, thiazide, β -blocker, ACE inhibitor, folic acid, and aspirin. It was predicted that such a polypill could reduce the risk of Ischemic heart disease by 88% and stroke by 80% in the geriatric population.¹⁶

6) Reduction in the cost: Though polymedication can increase the cost of drug therapy, replacing costlier drugs with less costlier ones with equal efficacy will reduce the cost and improve the rationality of multiple drug use.

Limitations of polypharmacy:

1) ADRs due to drug interactions

In addition to adverse effects caused by individual drug therapy, inappropriate combinations can cause adverse effects due to drug interaction. The analysis of prescriptions of older patients carried out in Sweden revealed that those prescribed 5 to 7 drugs daily were 4 times more likely to experience a drug-drug interaction; those taking 8 to 10 medicines

8 times and those taking 14 to 16 medicines were 20 times more likely to experience adverse reactions due to drug interactions.^{17,18} In adults above the age of 55, daily consumption of five or more drugs is found to be associated with risk of impaired mobility and global cognition, independent of the comorbidities and of the pharmacological class.¹⁹

The prevalence of hepatic cytochrome enzyme-mediated, drug-drug interaction was 80% in a prospective cohort study conducted among adults taking five or more medications and the risk increased to 100% when the number of drugs was twenty or more.

The author knows of a patient prescribed with diltiazem and metoprolol for hypertension, was advised to have a cardiac pacemaker by a cardiologist, as the patient's heart rate (HR) was below forty. However, when diltiazem was replaced with Telmisartan (ARB), it resulted in improvement in HR the next day and in a few days HR became normal and the patient did not require pacemaker. Identification of such complications due to drug interaction is a mandatory skill required to prevent unnecessary treatment as well as anxiety to the patient.

2) Drug Burden

Drug Burden Index was the tool used by Hilmer et al. to quantify the medication load. They had carried out a cross-sectional study in the geriatric population taking anticholinergics and sedatives and concluded that the combination of these two drugs reduces the functional ability of the older people over a period of five years.²⁰ Polymedication carries a higher risk in the older population due to the presence of multiple medical problems.

3) Organ toxicity

The two organs that could commonly get affected adversely due to medication overload are the liver and kidneys.

In a study conducted in Germany based on the data gathered from nursing homes, the authors observed that polypharmacy (5-9 drugs) and excessive polypharmacy (≥ 10 drugs) could cause severe renal failure.²¹

The duration of polypharmacy seems to be associated with occurrence of acute renal failure in elderly patients with multiple chronic diseases.²²

Drug-induced hepatotoxicity is a well known adverse effect. The hepatotoxicity will be aggravated with polypharmacy and the severity of hepatic damage can be high in alcoholics.

4) Failure of therapy

The failure of therapy on certain occasions could be due to the combination of drugs used. A patient with diabetes and rheumatoid arthritis (RA) was prescribed prednisolone along with hydroxy chloroquine and leflunamide. This patient was on Metformin 500 mg twice a day. Her blood sugar was normal initially, but later it remained elevated. She was advised to take Inj. Insulin. The poor control of blood sugar could be due to the administration of prednisolone. In such patients substituting prednisolone with other DMARDs would be a better alternative. Hence, identifying the cause of failure of treatment is essential in order to avoid

substituting prednisolone with other DMARDs would be a better alternative. Hence, identifying the cause of failure of treatment is essential in order to avoid polymedication.

5) Drug resistance

If the optimum dose and duration of the therapy of an antimicrobial is not followed by the patient, there is a chance for developing multidrug resistant organisms. The emergence of MDR tuberculosis could be due to this reason.

Multi-drug resistant tuberculosis is due to inadequate or improper administration of anti TB drugs. When the patients recover from the acute phase, they tend to stop taking their medication due to the long duration of treatment. As the eradication of TB bacteria is incomplete, the organisms develop resistance to drugs. When the patients report with recurrence of symptoms, the organisms may not respond to first line drugs already given and in addition they become highly contagious and spread the disease.

6) Compliance to treatment

When multiple drugs are prescribed with complicated regimen (like before food, after food, along with food, before breakfast, at bedtime, once a day, once a week etc), it is difficult for the patients, especially for those elderly who may have memory disturbances, to adhere to the therapeutic regimen. Poor compliance with treatment is common among the elderly suffering from multiple disorders such as diabetes, dyslipidemia, hypertension, Ischemic heart diseases, stroke, parkinsonism and osteoarthritis as they may have to take several drugs on a single day. Both under medication and over medication are possible, hence the treating physician should choose only drugs which are absolutely essential. Even for the younger population, it would be difficult to follow the complex drug regimen.

Let us discuss the following prescription (Table 1) given to a patient above 60 years of age. The content of the prescription is reproduced exactly how it was written:

Sl.no	Name of the drug	Dose	Frequency	
1.	Metoprolol tab	50 mg	1 OD	After meal
2.	HCO tab	200 mg	1 BD	After meal
3.	Mecovit tab		1 OD	After meal
4.	Azathioprine	50 mg	1 BD	After meal
5.	Clopidogrel	75 mg	1 OD	After meal
6.	Montelukast chewable	5 mg	1 OD	After meal
7.	Citicoline tab	500 mg	1 BD	After meal
8.	Defacort tab	6 mg	½ OD	After meal
9.	Omeprazole cap	20 mg	1 BD	Before meal
10.	Aerocort inhaler 200	One puff	1 BD	After meal
11.	Ecosprin tab	75 mg	1 OD	After meal
12.	Amlodipine tab	5 mg	1 OD	After meal
13.	Losartan tab	50 mg	1 BD	After meal
14.	Iron, B12, folic		1 OD	After meal
15.	Metformin tab	500 mg	1 OD	After meal
16.	Atorvasatin tab	20 mg	1 hs	After dinner
17.	Vit. D3 sachet	60000 IU	Weekly	After meal
18.	Sulphasazine tab	500 mg	2 BD	After meal
19.	Telmisartan tab	40 mg	1 hs	After meal
20.	Pregabalin tab	75 mg	1 hs	After dinner

Table 1 : Sample prescription 1

In this prescription, the total number of drugs prescribed is twenty. After meal refers to which meal is not given. The formulation is provided after the drug name where as it has to be given before the drug name. This is clearly a case of polypharmacy. Multiple drugs are prescribed for rheumatoid arthritis, metabolic disorder and hypertension. While the four anti rheumatoid drugs may eventually increase the blood pressure, the glucocorticoids may increase both blood pressure and glucose level. Sulfasalazine and Deflazacort may aggravate peptic ulcer. The absorption of iron may be affected by Omeprazole. The lack of improvement in this patient could be due to these interactions.

The second prescription given below (Table 2) was given to a middle-aged woman who suffered from chronic pain in the neck and joints.

The content of the prescription is exactly reproduced from the original prescription.

Sl.No	Name of the drug	Dose	Frequency
1.	Levorid	1 mg	1/7 am
2.	Allegra	120 mg	1 /7 pm
3.	Bromhexine	8 mg	1 - 1 - 1
4.	R - Cinex	600/300	1/30 minutes before breakfast
5.	Ethambutol	600 mg	2/25 minutes before breakfast
6.	Liv- 52		2-0- 2 after food
7.	Shelcal	500 mg	1- 0- 0
8.	Rocathiol	0.25 mcg	0 - 0 - 1
9.	Thyrox	25 mcg	1/30 minutes breakfast
10.	Flunarin	5 mg	1/after breakfast
11.	Becozinc		1- 0- 0
12.	Roxid	150 mg (14)	1- 0 - 1
13.	Ciplox from 8 th day	500 mg (30)	1 - 0 - 1
14.	Canditrol from 8 th day	100 mg (180)	0 - 0 - 2
15.	Libotryp from 10 th day		1/8 pm daily non stop
16.	Shallaki from 1 st day itself	400 mg	1-1-1 after food

Table 2 : Sample prescription 2

It is a complicated prescription containing sixteen drugs (two antimicrobials, antifungal, antitubercular drugs, combination of amitriptyllin and chlordiazepoxide, two antihistamines, calcium, Liv 52, Shallaki and others) from more than one system of medicine. The formulation of the drugs is not provided. The patient has to remember which day and time she should take these drugs.

Libotryp is a combination of Chlordiazepoxide and Amitriptyllin. Chlordiazepoxide is a benzodiazepine which is given for insomnia to produce sleep. It has been advised to take this medication "non-stop" and duration of the therapy is not mentioned. Though the two antihistamines -Allegra (fexofenadine) and Levorid (levocetirizine) are grouped under least sedative antihistamines, they also cause sleep. Most often patients complain of excessive sedation when Levocetirizine is prescribed alone. Amitriptyllin is an antidepressant with sedative effects. When these four drugs are given together what would be the extent of sedation they would cause? In fact, this particular

patient stopped all the medications and she switched over to alternative system of medicine.

The reason for prescribing both Ciprofloxacin and Roxithromycin is not known. For this particular patient, antitubercular therapy involving multiple drugs is a necessary one. But the rationale for the prescription of the non-tubercular drugs is not evident. For such patients drugs should be selected in such a way that there are no untoward drug interactions.

7) Latrogenesis

Complications due to drug interaction and adverse drug reaction can be diagnosed as new disease and treated. Hyperglycemia induced by long-term administration of steroid or IV infusion of dextrose is diagnosed as diabetes for which anti-diabetic drugs are prescribed. Subsequently, patients develop hypoglycemia and get treated with IV infusion of dextrose. This is one of the common problems encountered when patients consult multiple physicians as well as when drug history is not considered properly.

8) Cost

It is obvious that more drugs means more expense. On an average, a lower income group patient who is prescribed Metformin, Glimepride, Voglibose, Telmisartan and Metoprolol has to spend at least Rs. 1300 / month. Patients with cardiac diseases will have to spend even more, especially when they are prescribed multivitamins, calcium, vitamin D and antiulcer medication.

9) Failure of analysis before issue of prescription by the physicians

It is mandatory that every physician should review his/her prescription for potential drug interaction and the necessity for choosing a particular drug. It is very common to see a prescription having the following drugs for a patient with hypertension, and diabetes with acute exacerbation of bronchial asthma along with lower respiratory infection:

- Tab. Metoprolol 25 mg bd
- Tab. Telmisartan 40 mg bd
- Tab. Metformin 500mg bd
- Tab. Glimepride 1mg bd
- Tab. Pantoprazole 40 mg once a day/ twice a day
- MDI with Salmeterol and Fluticasone
- Tab. Amoxicillin with Clavulanic acid (500+ 125 mg) 625 mg bd for 5 days
- Cough expectorant containing Salbutamol and Ambroxol for 5 days

It is possible to say whether the above mentioned prescription is right or wrong. Right from one perspective wrong from another.

Let us discuss the benefits and risks of these drugs one by one.

Metoprolol, a beta blocker is proved to be useful in hypertension. But can it be given for a patient with diabetes? The physician should inform the patient to check blood sugar level periodically whenever he/she feels fatigue and headache as the other features of hypoglycemia such as palpitation and tremors will be masked by metoprolol.

Pantoprazole is a drug which is likely to figure in almost all prescriptions. The approved indications for Pantoprazole are Erosive esophagitis, GERD and Zollinger Ellison syndrome. Instead of pantoprazole, patients may be advised to take antiulcer medication if they develop gastritis after consulting the physician.

Salbutamol present in the expectorant can increase the heart rate and BP which can reduce the action of metoprolol and telmisartan. In addition, salmeterol and fluticasone in the MDI can produce a similar effect. The failure to control BP and blood sugar could be due to such drug combinations.

Using multiple medications from other systems of medicine:

It is common for a patient to develop fever during the course of treatment for life style diseases for which he/she will already be on multiple medications. If it is dengue fever, the patient takes Nilavembu Kudineer (NK). NK is a combination of nine medicinal plants. Among them the important one is *Andrographis paniculata*.

As it is a polyherbal formulation, it can be considered polymedication. Several lehiyagkaL and ChooranagkaL are used in therapy in Siddha and Ayurvedhic systems of medicine. As the ingredients in each of these preparations have their own individual actions complementing each other producing a synergistic effect. Each individual plant extract contains multiple phytochemicals. When a polyherbal formulation is consumed, the patient will be taking multiple ingredients. When such preparations are accepted, polypharmacy used in modern medicine can also be accepted as a rational therapy provided the combinations of drugs produces no harm to the patient.

Thus the problems that could occur with polymedication are adverse effects due to drug interactions including treatment failure in addition to high cost and poor compliance to treatment. The adverse effects can range from mild to severe ones like renal and hepatic and CNS toxicity.

How to reduce polymedication

1) Intelligent polypharmacy with rational combination:

We can intelligently combine drugs in such way that the benefits of the drugs prescribed would outweigh the risks associated with each medicine as well as with the combination of drugs.²³

E.g:

1. HAART for HIV infection
2. Anti TB regimens
3. Anticancer therapy

The above combination of drugs, though not risk free, is life saving to the patients. We have to carefully balance between risk and benefit of such polymedications.

2) Adapting the following criteria for drug selection:

In drug selection, the following factors may be taken into account: safety and efficacy of the drug with regard to age, gender, pregnancy, lactation and coexisting morbidities like renal or hepatic dysfunction.

The need of drug therapy: Before starting any new drug therapy the physician has to ascertain whether pharmacotherapy is needed for the patient. It is well known that mild hypertension and diabetes can be controlled with non-pharmacological management.

The economy of the drug: Less costlier drugs which are equally effective have to be chosen instead of more expensive ones.

Availability: The drugs prescribed should be available in the nearby pharmacy. Otherwise, the patient has to go from one pharmacy to another to get the prescribed drugs. In the process, the patient's treatment is likely to be delayed and the drugs may get substituted with the alternatives.

3) Following Beers criteria

Beers criteria are generally applicable to geriatric population. The American Geriatrics Society (AGS) has updated the Beers Criteria for rational use of drugs in older people. It gives a detailed list of drugs to be avoided in the older population.²⁴

4) Prevention of prescribing cascade^{25,26}

Prescribing cascade refers to prescribing additional drugs to treat the adverse effects of other drugs. According to Kalish et al, a "prescribing cascade occurs when a new medicine is prescribed to 'treat' an adverse reaction to another drug in the mistaken belief that a new medical condition requiring treatment has developed." Prescribing cascade is a major problem causing polypharmacy. The physicians should be able to differentiate between an adverse effect and the onset of a new disease.

5) '4 R' principle

The 'R' principle followed in animal research can be applied in the selection of drugs also. The principle of Refine, Reduce, Replace or Remove can be followed in the selection of drugs, especially when polymedication is necessary.

1. Refine the selection of drugs which are action-specific with least side effects.
2. Reduce the number of drugs to a minimum.
3. Replace with non-pharmacological management wherever possible, especially for lifestyle-related disorders.
4. Remove the patient from drug therapy as early as possible.

Conclusion:

The term polymedication is the appropriate alternative term for polypharmacy. Polymedication is more common among the elderly. It should be adopted only when it is absolutely essential and beneficial to the patient. Polymedication becomes inevitable for those suffering from multiple disorders. However, it carries a higher risk of causing adverse effects as well as inconvenience and extra cost. Proper diagnosis, drug history and rational combination of drugs would prevent unnecessary polymedication. The 4'R' principle of Refine, Reduce, Replace or Remove can be applied in the selection of drugs.

In itself, polymedication is neither a peril nor a boon. Its rationality or irrationality depends on the physician. In the hands of a good physician, it can prove to be a boon too!

Acknowledgements: The author thanks Dr. R.Arunkumar, Professor, Department of Pharmacology and Dr.E.Madhavi, Associate Professor, for their valuable inputs to the article, and Dr. E. Madhavi for helping in the preparation of the manuscript.

References

- 1) <https://www.etymonline.com/word/pharmacy>.
- 2) <https://www.merriam-webster.com/dictionary/pharmacy>.
- 3) Duerden, M., Avery, T., & Payne, R. Polypharmacy and medicines optimization. Making it safe and sound. 2013. Kingsfund. London.
- 4) Mortazavi SS, Shati M, Keshtkar A, Malakouti SK, Bazargan M, Assari S. Defining polypharmacy in the elderly: a systematic review protocol. *BMJ Open*. 2016;6(3):e010989.
- 5) Gnjidic D, Hilmer SN, Blyth FM, Naganathan V, Waite L, Seibel MJ et al. Polypharmacy cut off and outcomes: five or more medicines were used to identify community-dwelling older men at risk of different adverse outcomes. *J Clin Epidemiol*. 2012;65(9):989-95.
- 6) Jokanovic N, Tan EC, Dooley MJ, Kirkpatrick CM, Bell JS. Prevalence and factors associated with polypharmacy in long-term care facilities: a systematic review. *J Am Med Dir Assoc*. 2015;16(6):535.e1-12.
- 7) Yong TY, Lau SY, Li JY, Hakendorf P, Thompson CH. Medication prescription among elderly patients admitted through an acute assessment unit. *Geriatr Gerontol Int*. 2012;12(1):93-101.
- 8) Aronson JK. In defence of polypharmacy. *Br J Clin Pharmacol*. 2004;57(2):119-20.
- 9) Fincke BG, Snyder K, Cantillon C, Gaehde S, Standring P, Fiore L et al. Three complementary definitions of polypharmacy: methods, application and comparison of findings in a large prescription database. *Pharmacoepidemiol Drug Saf*. 2005;14(2):121-8.
- 10) Rupert Payne, Martin Duerden. Polypharmacy – appropriate, problematic or both? *Prescriber*. 2015;26(4):31-34.
- 11) <http://www.irdes.fr/english/issues-in-health-economics/204-polypharmacydefinitions-measurement-and-stakes-involved.pdf>.
- 12) <https://www.worldlifeexpectancy.com/india-life-expectancy>.
- 13) vikaspedia.in/social-welfare/senior-citizens-welfare/senior-citizens-status-in-india.
- 14) Masnoon N, Shakib S, Kalisch-Ellett L, Caughey GE. What is polypharmacy? A systematic review of definitions. *BMC Geriatr*. 2017;17(1):230.

- 15) Ge B, Zhang Z, Zuo Z. Updates on the clinical evidenced herb-warfarin interactions. *Evid Based Complement Alternat Med.* 2014;2014:9573-62.
- 16) Wald NJ, Law MR. A strategy to reduce cardiovascular disease by more than 80%. *BMJ.* 2003 Jun 28;326(7404):1419. Erratum in: *BMJ.* 2006 Sep;60(9):823. *BMJ.* 2003;327(7415):586.
- 17) Steinman MA. Polypharmacy and the balance of medication benefits and risks. *Am J Geriatr Pharmacother.* 2007;5(4):314-6.
- 18) Johnell K, Klarin I. The relationship between number of drugs and potential drug-drug interactions in the elderly, a study of over 600,000 elderly patients from the Swedish prescribed drug register. *Drug Saf.* 2007;30(10):911-8.
- 19) Langedard A, Pothier K, Morello R, Lelong-Boulouard V, Lescure P, Bocca ML et al. Polypharmacy Cut-Off for Gait and Cognitive Impairments. *Front Pharmacol.* 2016;7:296.
- 20) Hilmer SN, Mager DE, Simonsick EM, Ling SM, Windham BG, Harris TB et al. Drug burden index score and functional decline in older people. *Am J Med.* 2009; 122(12):1142-1149.e1-2.
- 21) Dorks M, Herget-Rosenthal S, Schmiemann G, Hoffmann F. Polypharmacy and Renal Failure in Nursing Home Residents: Results of the Inappropriate Medication in Patients with Renal Insufficiency in Nursing Homes (IMREN) Study. *Drugs Aging.* 2016;33(1):45-51.
- 22) Chang YP, Huang SK, Tao P, Chien CW. A population-based study on the association between acute renal failure (ARF) and the duration of polypharmacy. *BMC Nephrol.* 2012;13:96.
- 23) Ginpreet Kaur. Polypharmacy: The past, present and the future. *J Adv Pharm Technol Res.* 2013;4(4):224-5.
- 24) American Geriatrics Society 2015 Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults. By the American Geriatrics Society 2015 Beers Criteria. *J Am Geriatr Soc.* 2015;63(11):2227-46.
- 25) Rochon PA, Gurwitz JH. Optimizing drug treatment for elderly people: the prescribing cascade. *BMJ.* 1997;315(7115):1096-9.
- 26) Rochon PA, Gurwitz JH. The prescribing cascade revisited. *Lancet.* 2017;389 (10081): 1778-1780. Erratum in: *Lancet.* 2017;389(10085):2192.