Healthcare in South Africa

South Africa has a two-tier health care system

- The private health system is costly and used mostly by middle to high income individuals and families (services about 8 ,9 million people, mostly covered by about 80 medical aids).

- The public health care system services to about 80% of the population mainly at the 435 government hospitals

GDP on Healthcare

- 6.68 percent in 2002
- 8.58 percent in 2020,

……..An average of 7.58 % in this period

- This is 4 % higher than the WHO's recommended spending for a country with similar socioeconomic status
- Despite this high expenditure, health outcomes are still trailing in comparison with similar middle-income countries

Healthcare Resources in South Africa

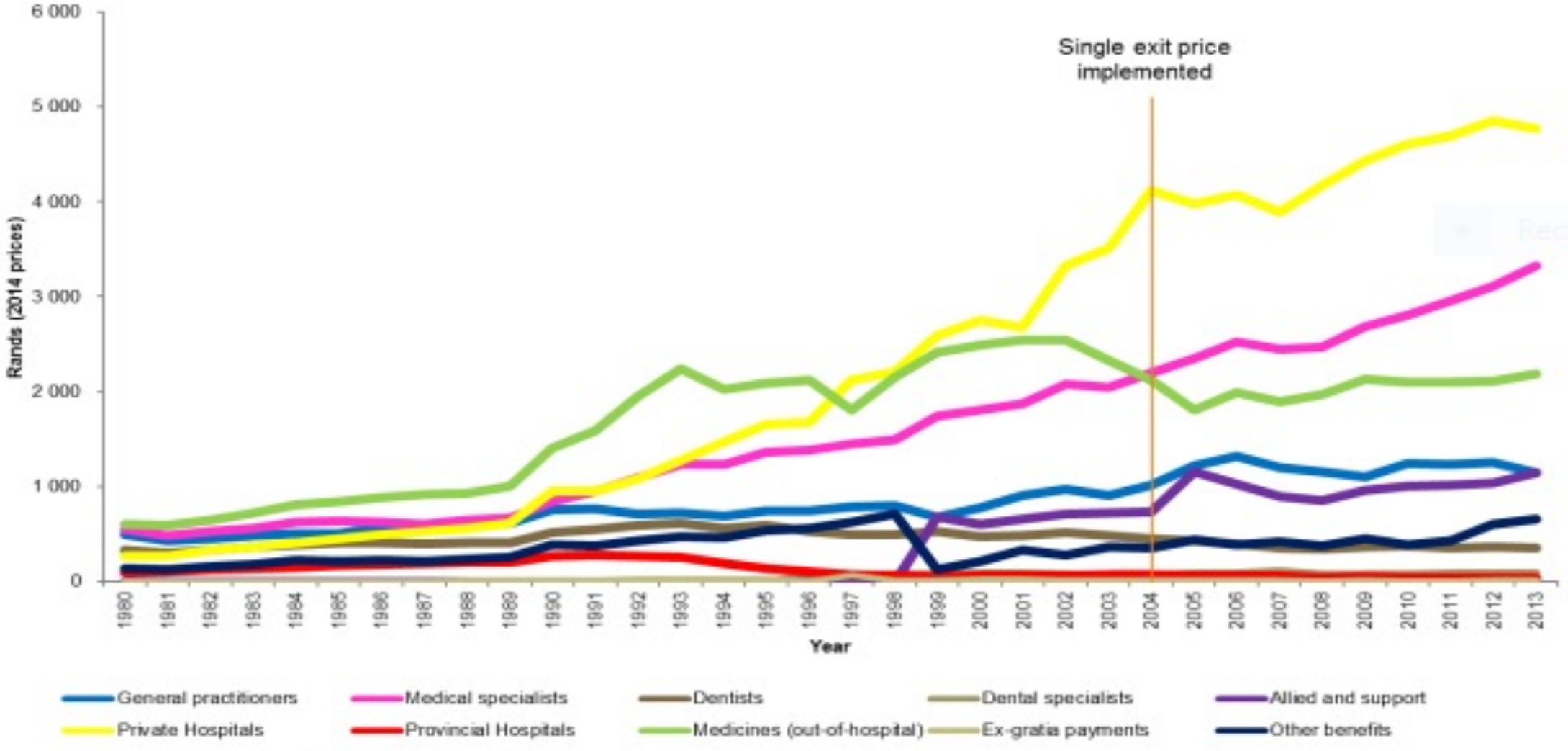
Healthcare Resources (South Africa 2012-2016)	2012	2013	2014	2015	2016
Total Hospitals	687	694	701	708	715
Public Hospitals	418	422	426	430	435
Private Hospitals	269	272	274	277	280
Hospitals beds	131,929	133,246	134,575	135,918	137,274

Healthcare personnel in South Africa

Healthcare Personnel (South Africa 2012-2016)	2012	2013	2014	2015	2016
Total Physicians	38,444	39,445	41,132	42,323	43,425
Total Dentists	5,613	5,667	5,824	5,998	6,147
Total Pharmacists	12,998	13,401	13,364	13,479	13,878
Total Nurses	248,736	260,698	270,437	278,617	287,458

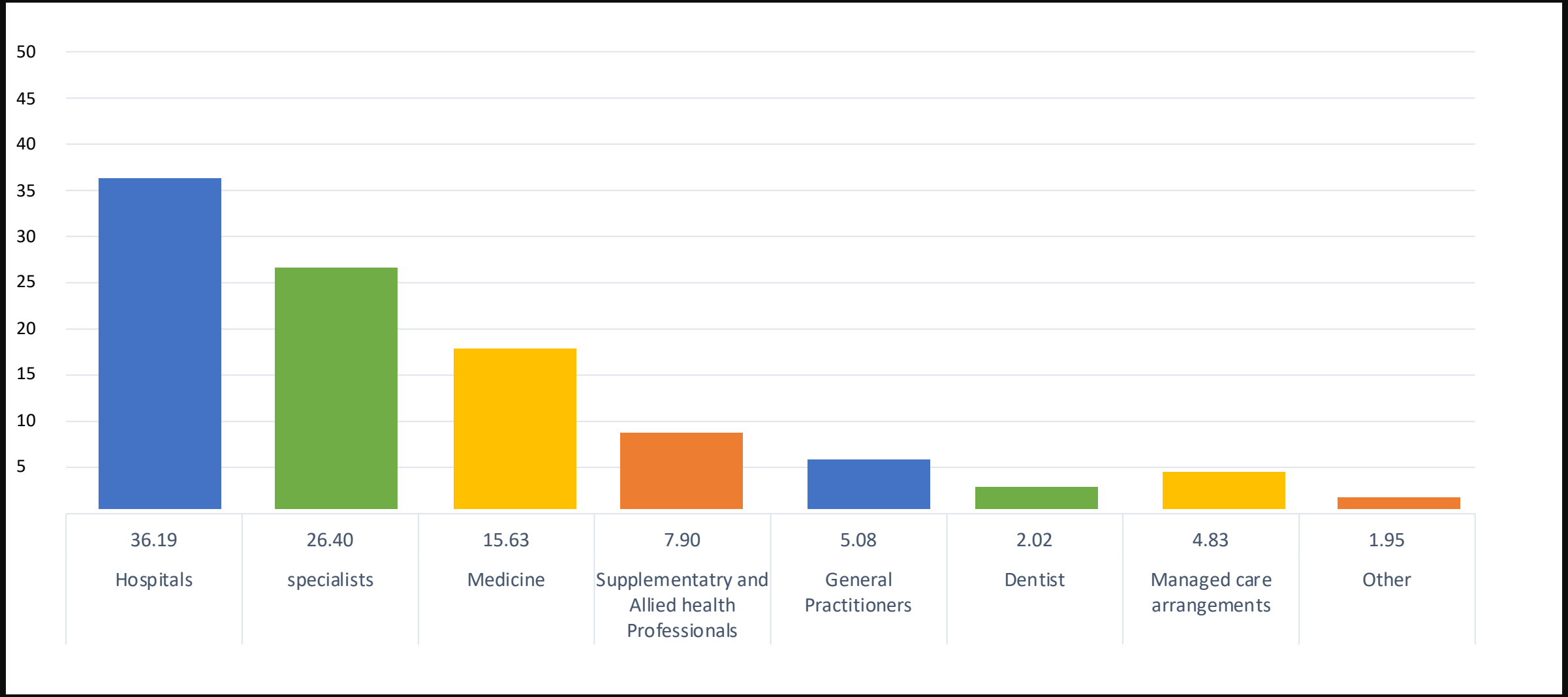
Pharmacies - Academic	**10**
Pharmacies - Consultant	**16**
Pharmacies - Manufacturing	**293**
Pharmacies - Public Hospitals	**763**
Pharmacies - Pvt Hospitals	**308**
Pharmacies - Retail	**4,114**
Pharmacy Groups - Afrimed	**21**
Pharmacy Groups - Alphapharm (Independent)	**417**
Pharmacy Groups - Arrie Nel (Independent)	**114**
Pharmacy Groups - Clicks (Corporate)	**765**
Pharmacy Groups - Clinix (Hospital)	**8**
Pharmacy Groups - Courier	**11**
Pharmacy Groups - Dis-Chem (Corporate)	**270**
Pharmacy Groups - Essential Health	**7**
Pharmacy Groups - Health and Home	**17**

Figure 1. CLAIMS EXPENDITURE, PER BENEFICIARY PER ANNUM FROM 1980 TO 2013 (2014 PRICES)

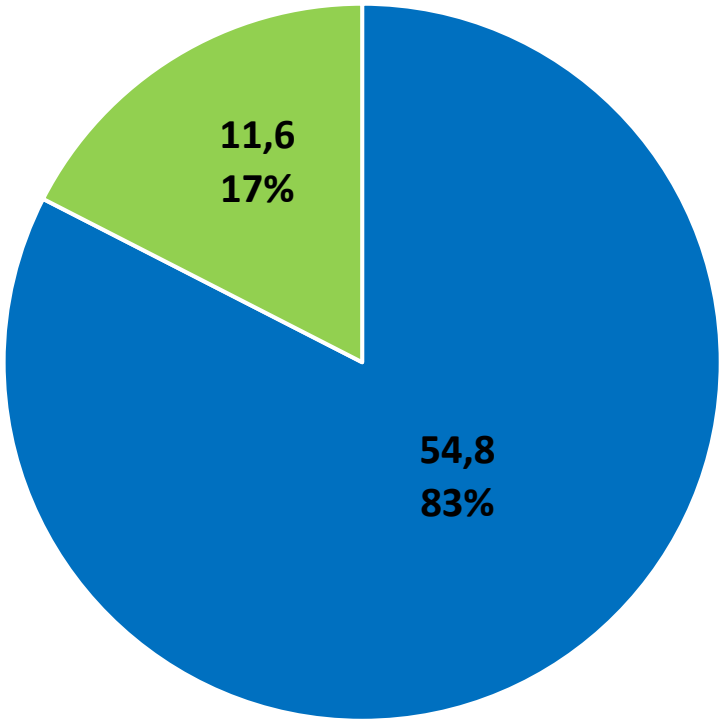


Source: Health Market Inquiry Analysis using data from Council for Medical Schemes

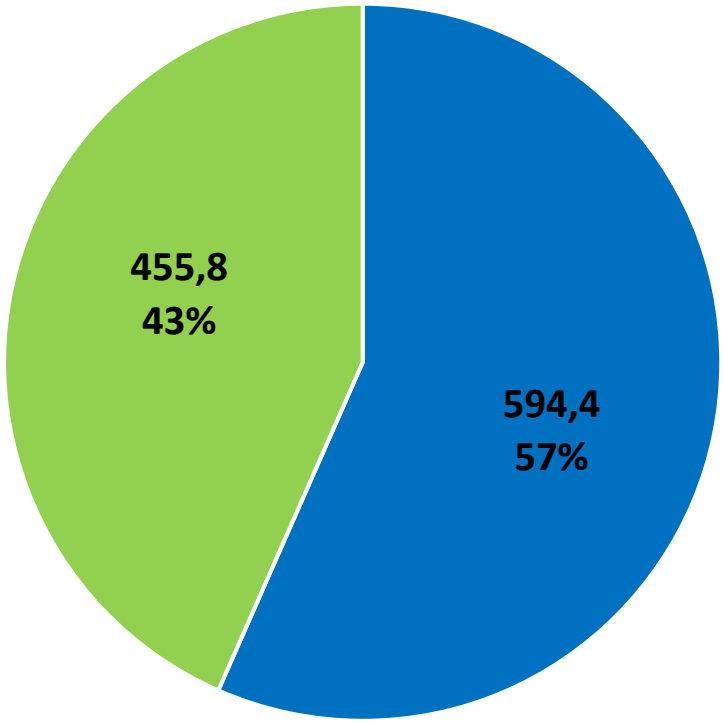
Total spend per discipline (CMS)



Total Pharmaceutical Market



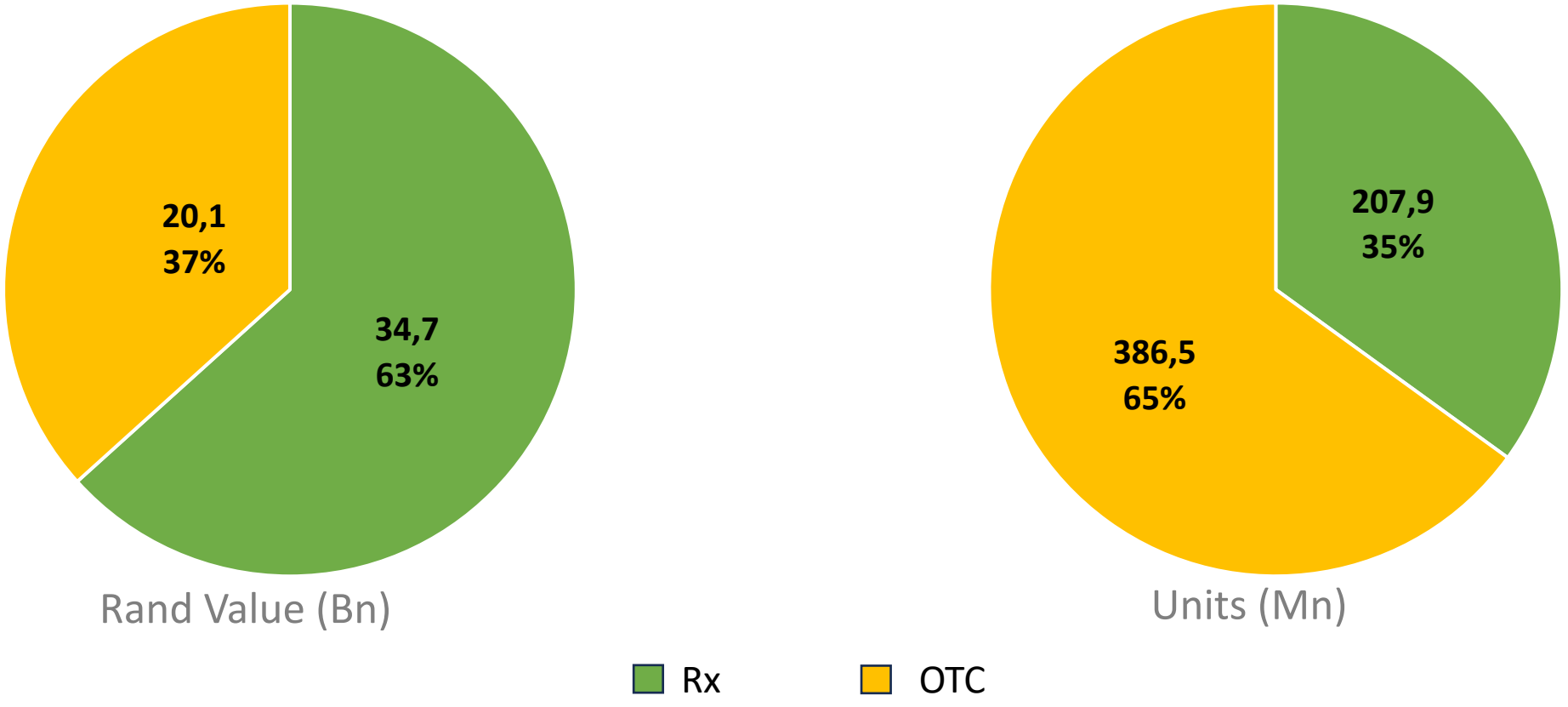
Rand Value (Bn)



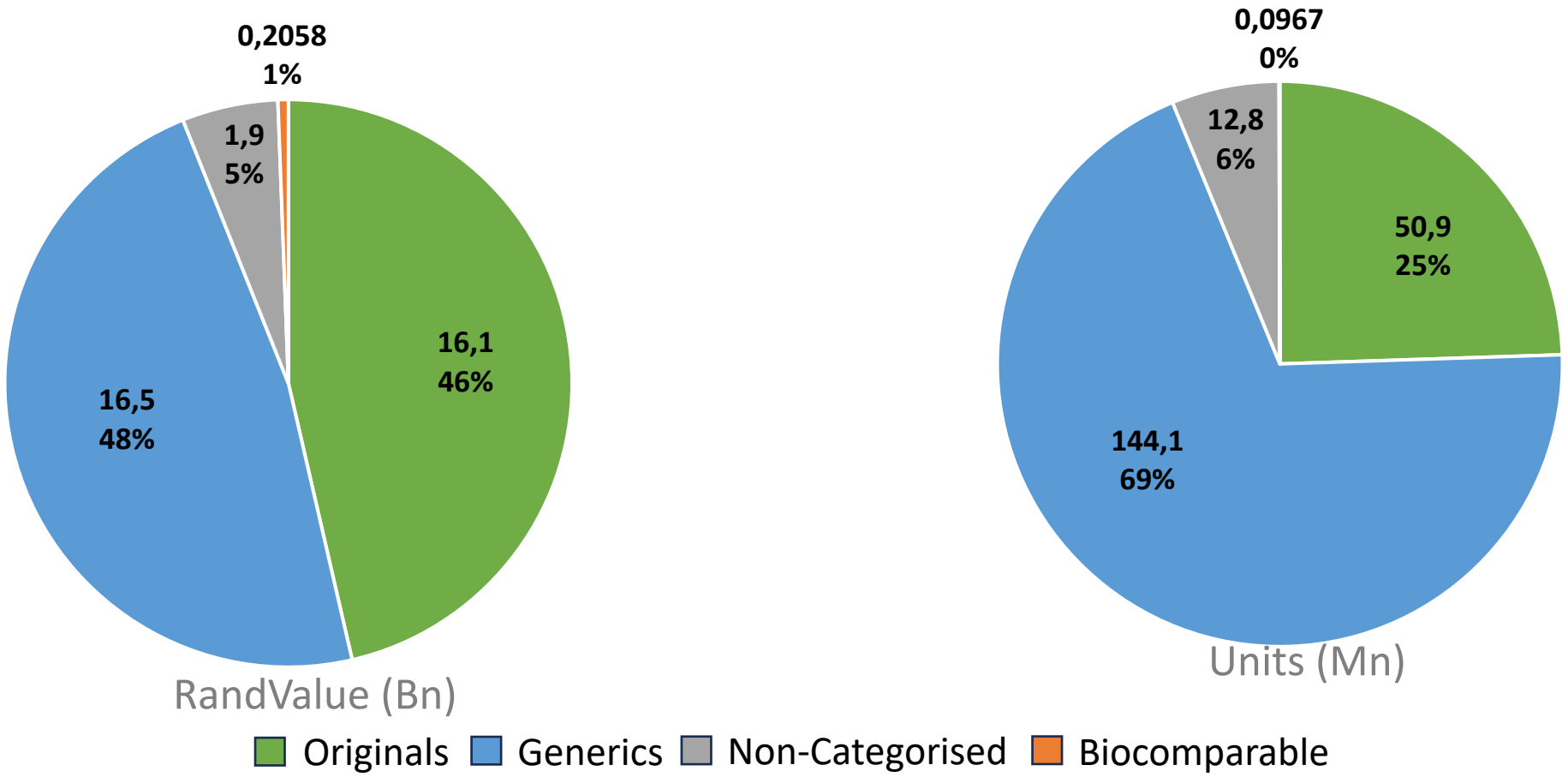
Units (Mn)

Private State

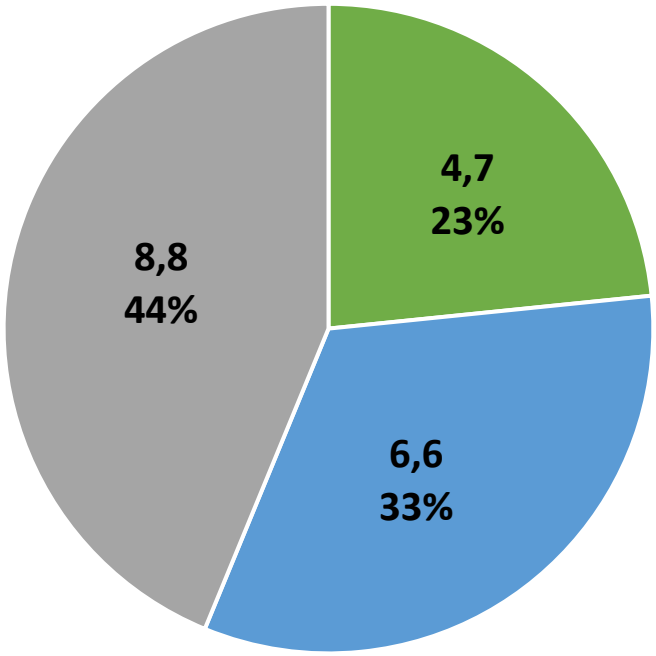
Private Market



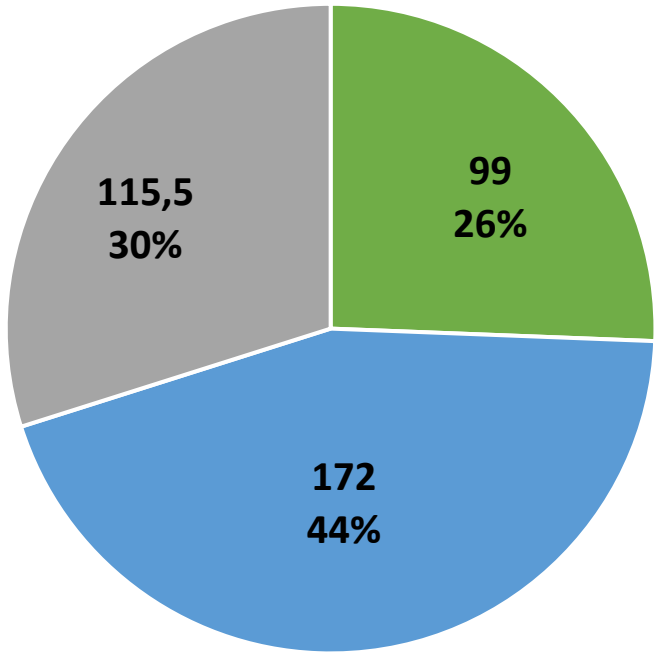
Prescripion medicines



OCT Category



RandValue (Bn)



Units (Mn)

Originals Generics Non-Categorised

Generic substitution of drugs

What is generic substitution?

Generic substitution is the term applied to the

……..substitution of a prescribed branded drug

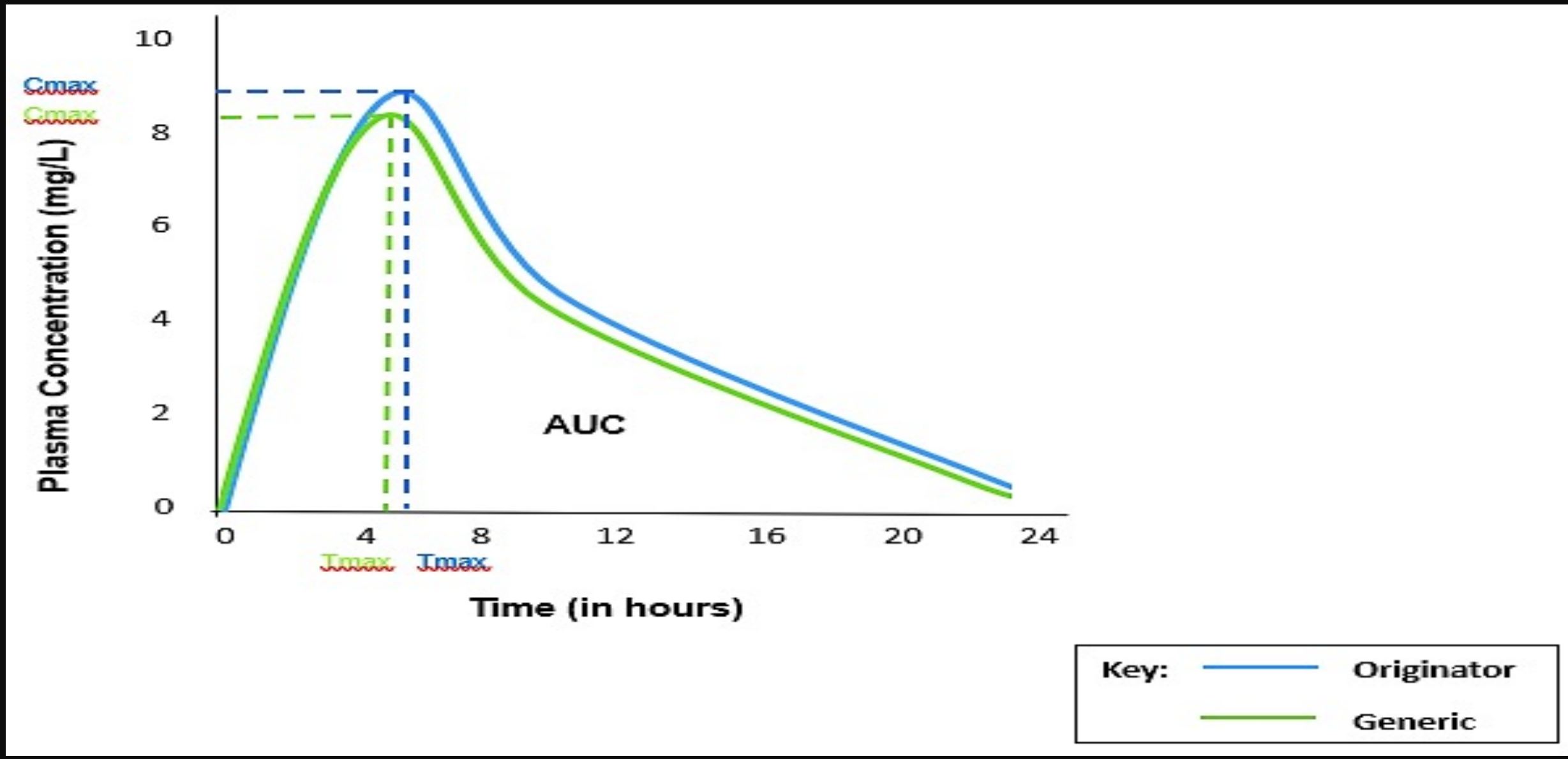
……..by a different form of the same active substance

Generic medications must fulfil certain requirements

- Must imitate brand-name drugs with respect to strength, effect, dosage, form, administration, quality and safety with that of the active substance and be equivalent to the reference product within narrow margins.

- These stringent requirements mean that there should be very little concern among prescribers and the general public about the quality and comparability of generics to the branded products

Bio-equivalence to originator



Advantages of generic substitution

Reducing costs:

- More generic entrants usually drive cost down to the advantage of cost containment and cost to the patient
- Less marketing involved than branded drugs, making generics cheaper
- On average, first to market generics are about 15 to 20 % less than branded drugs, depending on if a clone exists
- With more entrants, prices drop even further (for example, for statins where there are more than 10 generics, prices of generics, and even the originator drugs, are now about one tenth of the original price)

Advantages of generic substitution

Availability:

- Because many manufacturers have access to active ingredients, it is more widely available.

- Manufacturer’s target big therapeutic areas, and therefore there are many generic entrants

Important pre-requisites

Quality:

- They should be the exact copy of their brand name counter-parts (CEP versus DMF APIs, South Africa regulated, but many other African countries are not)

Regulatory approval should be strict for :

……Good manufacturing processes (dossier quality)

……Bio-equivalence

……Nitrosamine content

Generic drugs in USA

- Generic drugs were first introduced USA 1962
- In 1984, the Drug Price Competition and Patent Term Restoration Act gave the FDA statutory authority to approve generic versions of innovator drug products approved after 1962 as safe and effective

(Ref: Henderson, 1992).

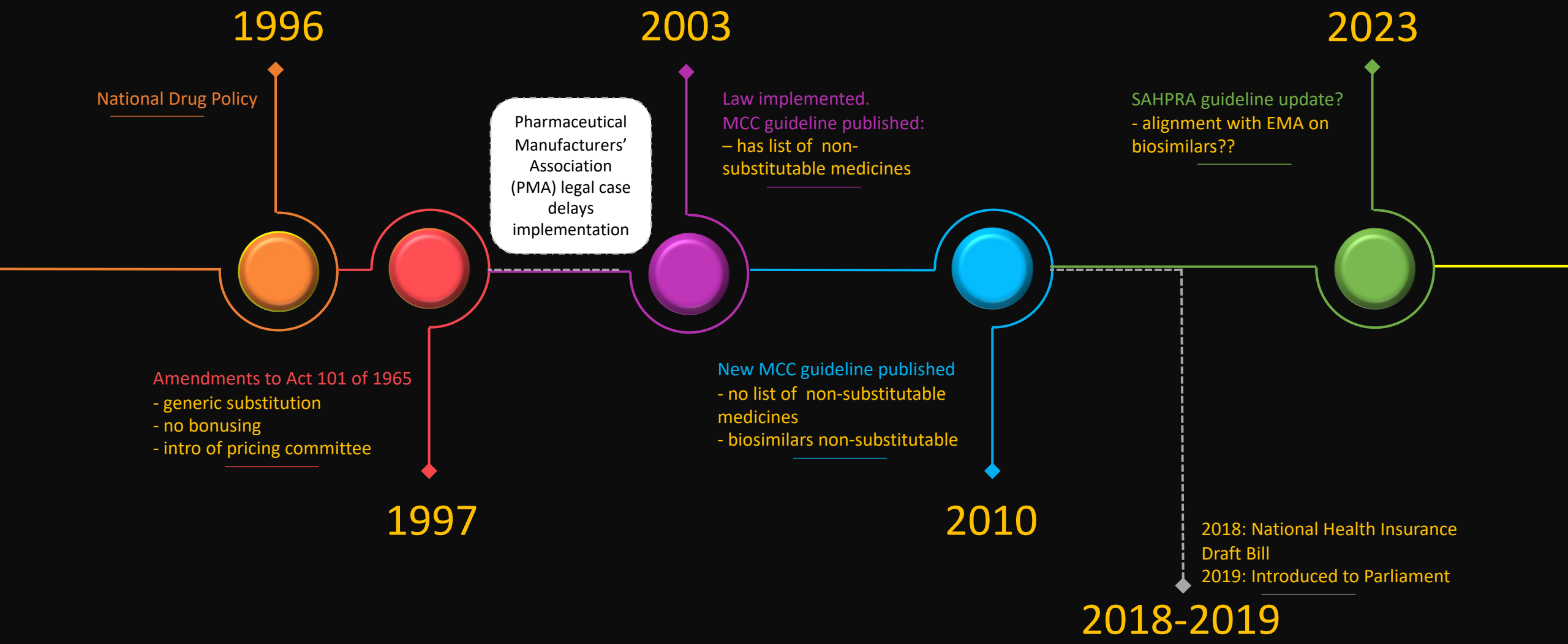
Generic drugs in UK

Generic substitution was raised as a means of reducing the NHS medicines bill in 1983

The proposal was not implemented, but an initiative to encourage generic prescribing resulted in a change in doctors' prescribing habits to generics

By 1993 generic products accounted for 11% of the NHS expenditure on drugs and 41% of the volume.

Generic Substitution in South Africa



Law Implemented - 2003

The implementation of the Act required the assistance of many role players, including the :

- **Department of Health,**
- **Medical practitioners,**
- **Pharmacists, and**
- **Administrators of medical aid schemes.**

Law Implemented - 2003

- The mandatory offer of generic substitution came into effect in May 2003 with safegaurds
- In the event that a generic equivalent existed, it was mandatory that pharmacists offer generic substitution, which the patient could accept or refuse.
- In addition, the law allowed the prescriber to indicate ‘no substitution’ on the prescription. In such cases, the pharmacist was prohibited from substituting the brand prescribed with a lower priced version.
- Medicines Control Council (MCC)) was required to provide a ‘non-substitutable list’.
- A second Amendment Act in 2002 added an obligation on the pharmacist to take reasonable steps to inform the prescriber that a substitution had occurred.

Section 22F of Act 101 of 1965

No substitution may take place in the following cases:

- **The patient forbids substitution;**
- **The prescriber writes "no substitution" in his or her own handwriting next to each line item;**
- **The generic is more expensive than the ethical product; or**
- **The medicine is declared non-substitutable by the Authority.**

MCC Guideline - 2003

“MCC recommended that substitution should not occur when prescribing and dispensing "generic medicines that:

i. **have a narrow therapeutic range;**
ii. **have been known to show erratic intra and interpatient responses;**
iii. **are contained in dosage forms that are likely to give rise to clinically significant bioavailability problems, e.g. extended or delayed release preparations, as well as those known to be super bioavailable; or**
iv. **are intended for the critically ill and/or geriatric and paediatric patient.”**

MCC Guideline - 2003

List of medicines that have on occasion, been known to present bioequivalence problems and should ideally not be interchanged with other "generics"

Alendronate tablets or capsules
Amiodarone tablets or capsules
Atenolol tablets or capsules
Carbamazepine tablets
Chlorpromazine tablets
Dexamethasone tablets
Diethylstilboestrol tablets
Digoxin tablets
Disulfiram tablets
Ethinyl Oestradiol tablets
Fluoxymesterone tablets
Furosemide tablets
Glibenclamide tablets
Hydralazine, Hydrochlorothiazide and Hydrocortisone Acetate injection
Isoproterenol Metered Dose inhaler
Isoethrane Metered Dose inhaler
Isosorbide Dinitrate sustained release tablets and capsules
Itraconazole tablets or capsules
Levodopa tablets and capsules
Nifedipine: all extended/delayed release formulations
Oestrogens, Conjugated tablets
Oestrogens, Esterified tablets
Penicillin G Benzathine injection
Phenytoin tablets and capsules
Phytomenadione injection
Prazosin Hydrochloride tablets 5mg
Prednisolone tablets
Prednisolone Acetate injection
Prednisolone Tebutate injection
Prednisone tablets
Promethazine tablets
Propylthiouracil tablets
Reserpine tablets
Reserpine and Chlorothiazide combination tablets
Reserpine and Trichloromethiazide combination tablets
Sotalol tablets or capsules
Tamoxifen tablets of capsules
Theophylline controlled release tablets/capsules
Triamcinolone tablets
Trichloromethiazide tablets
Warfarin Sodium tablets

MCC Guideline - 2010

- New guideline removes the list of non-substitutable medicines: possibly due to tightening of bioequivalence requirements for narrow therapeutic index medicines
- Biosimilars are non-substitutable
  - Biosimilars are not generic products and cannot be identical to their reference products.
  - Further, the formulations may be different and this can have a profound effect on their clinical profiles.
  - In addition, a biosimilar does not necessarily have the same indications or clinical use as the reference product.
  - Therefore, given current science, they cannot be considered interchangeable with the reference product or products of the same class.

EMA position on biosimilars - 2023

- On 21 April 2023, the European Medicines Agency (EMA) released a joint statement with Heads of medicines Agencies (HMA) on interchangeability of biosimilars in the EU.

- A recent on-line article from Cipla suggests that SAHPRA may be reconsidering their position on non-substitutability of biosimilars in line with the EMA's position:

SAHPRA Position on biosimilars - 2023

- "SAHPRA has now finally agreed to amend the guideline and publish a statement to declare that biosimilars are interchangeable with their reference products (or vice versa) and also with other biosimilars of the same reference medicine."

- Extracted from: https://ciplabiosimilars.co.za/articles/new-position-of-sahpra-on-interchangeability

- No guideline has been published by SAHPRA to date.

Uptake of generics in South Africa

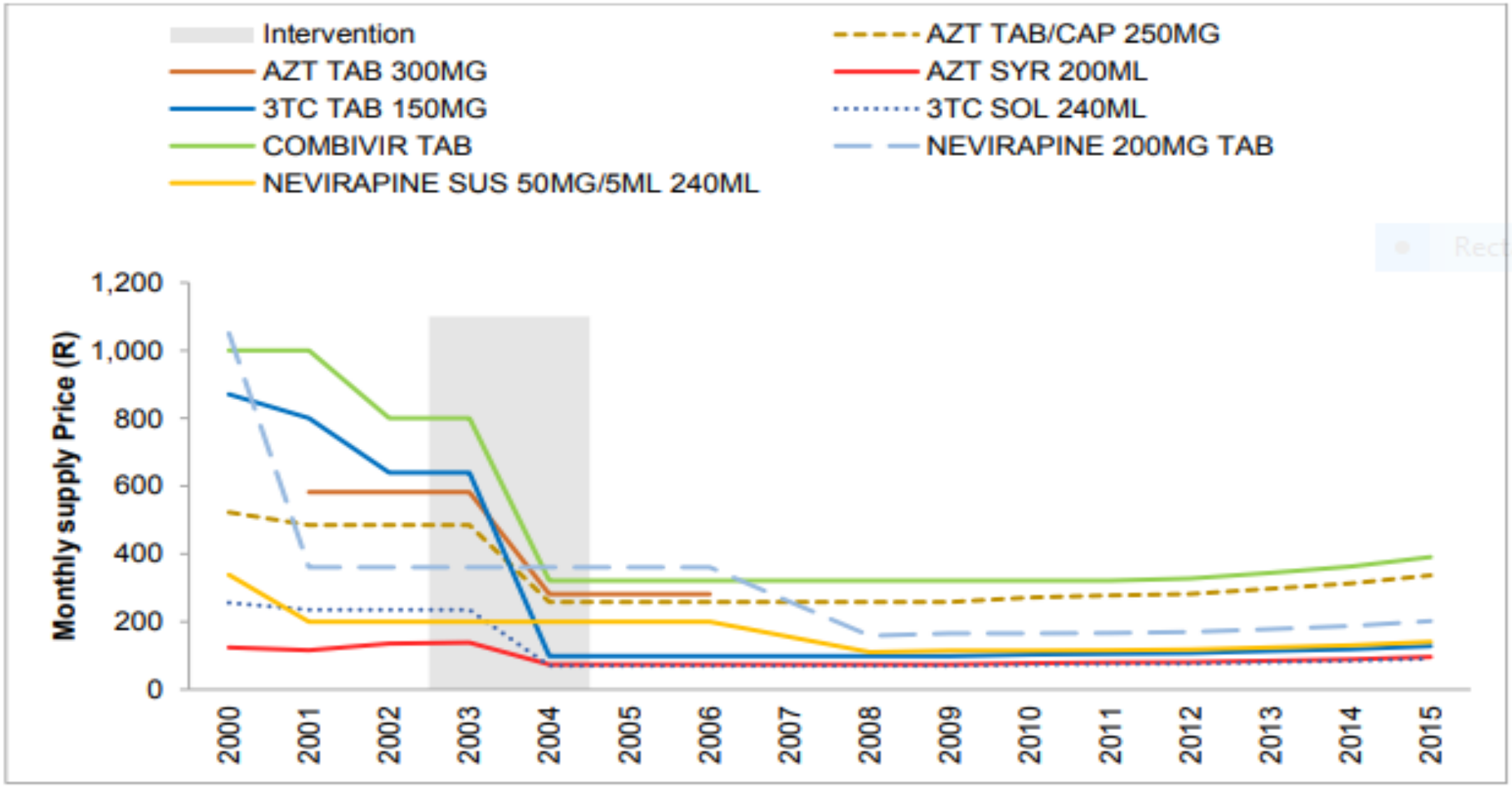
	2004	2015	2019	2020	2021
Generic utilization rate	38,3%	56,2 %	62.7 %	63.2 %	62.4 %* (63,7 %)
% of products paid for where the patent had expired	Not available	Not available	77.5 %	78,0%	76,7%
Generic uptake**	Not available	76.5 %	80.8 %	81.1%	81.3%

***This decline in generic utilisation results from the introduction of COVID-19 vaccines that are classified as originals with valid patents. Bracketed figure is if COVID vaccines are not considered)**

****This indicates the proportion of instances where a generic equivalent was available and was used.**

Data available in the public domain: Mediscor (medical scheme administrator) annual reports; Gray et al., 2017

Figure 2. Price movements of ARV's following intervention to promote the entry of generics



Source: MedPrax (Pty) Ltd

Pricing in South Africa

- Bangalee and Suleman, 2016 and Truter et al., 2015 examined South African prices of cardiovascular and proton pump inhibitors, respectively.
- Concluded that the South African policies such as generic substitution appeared to be working,
- Both concluded that South African prices could be lower considering international prices.

Counterfeit medicines

- Substandard and counterfeit medicines are available in South Africa.
- These medicines are usually manufactured by highly organised criminal groups that are often involved in cross-border trafficking.
- The products can be bought online, in tuck shops or at street markets.
- Sometimes they find their way into legitimate supply chains, cropping up in registered pharmacies and hospitals.

Counterfeit medicines

- Usual incriminents are medicines for erectile dysfunction, weight loss, antidepressants, anabolic steroids, antibiotics and pain killers

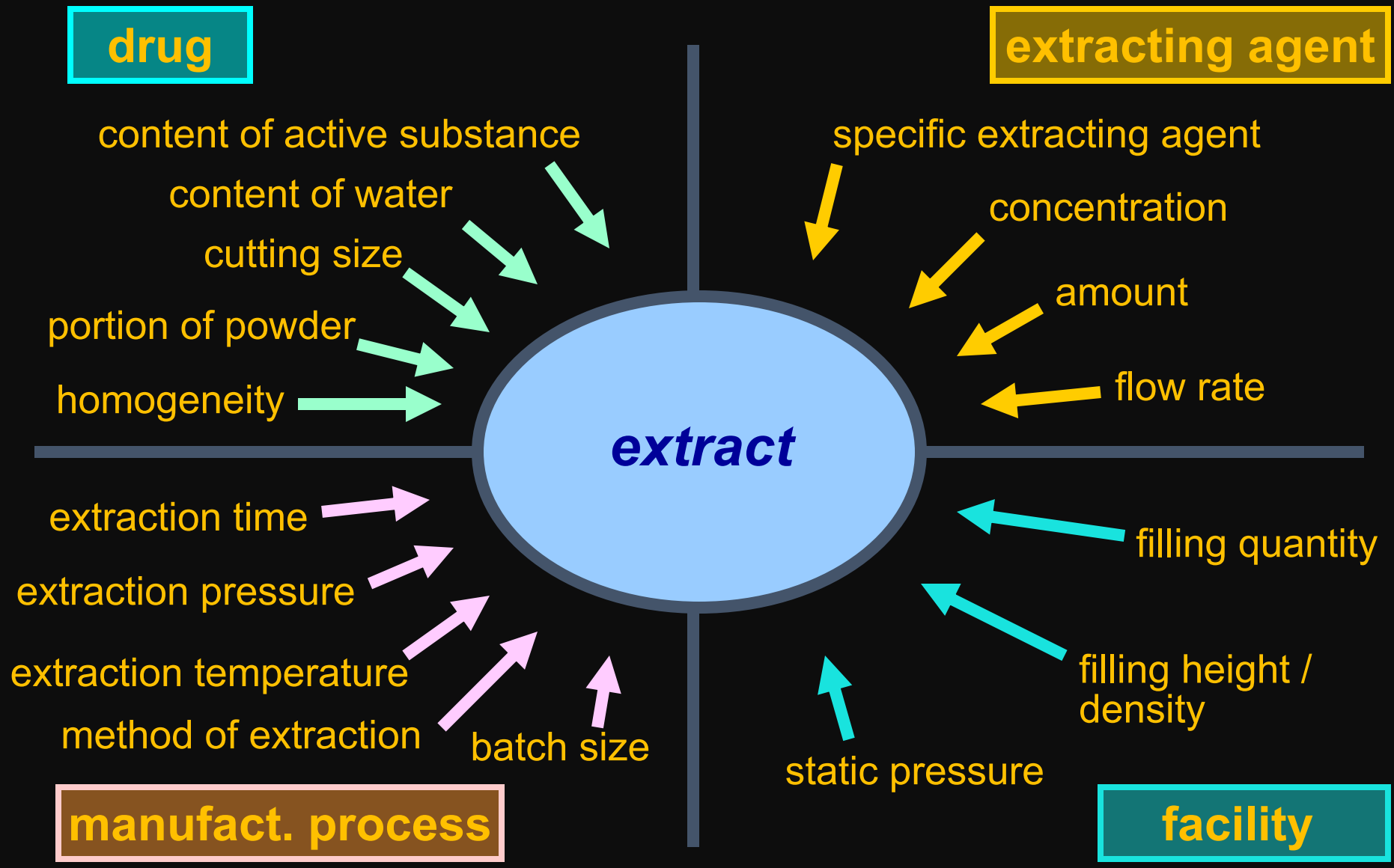
- South Africa is lagging behind in having a specific pharmaceutical crime and anti-counterfeit legal framework, which has far-reaching consequences

Phytopharmaceuticals medicines

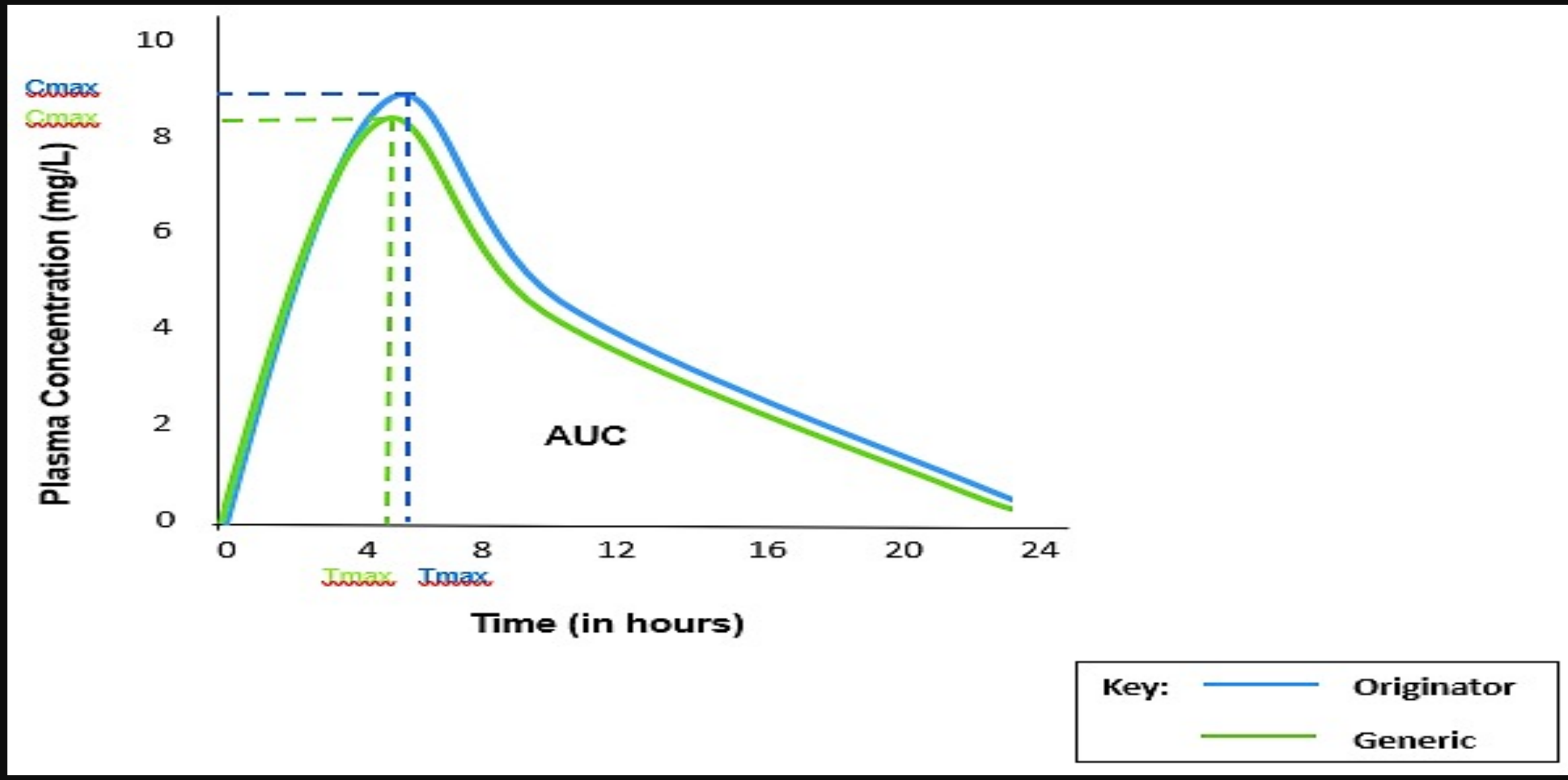
Phytopharmaceutical medicines

- Phytopharmaceutical are medicines of natural origin,
- With unique extracts
- Manufactured in a unique way

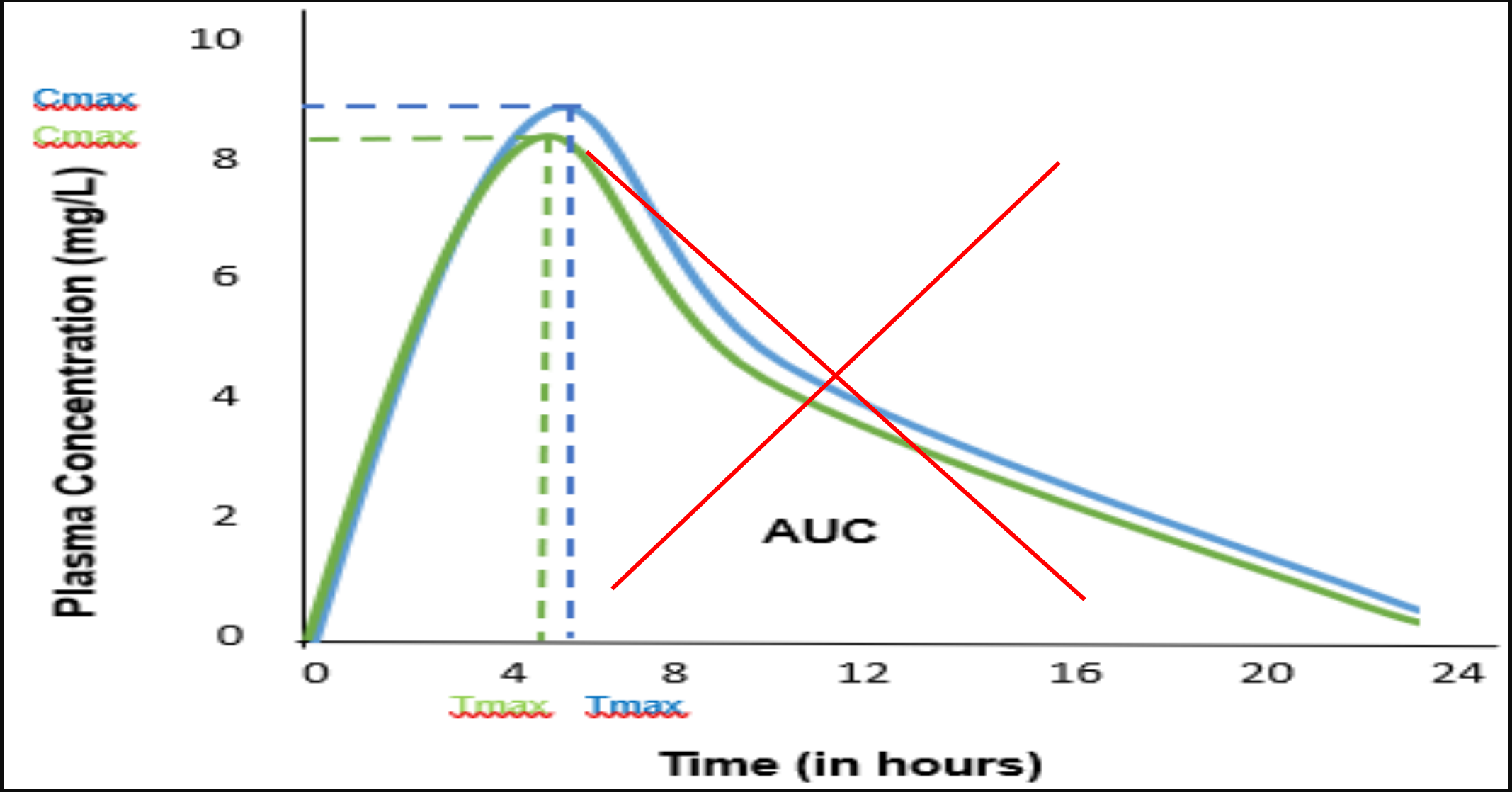
Dependency of the composition of a extract from manufacturing and quality parameters



Bio-equivalence to originator



Bioequivalence not possible due to several active




Probiotics

One’s phenotypic make-up is a result of:

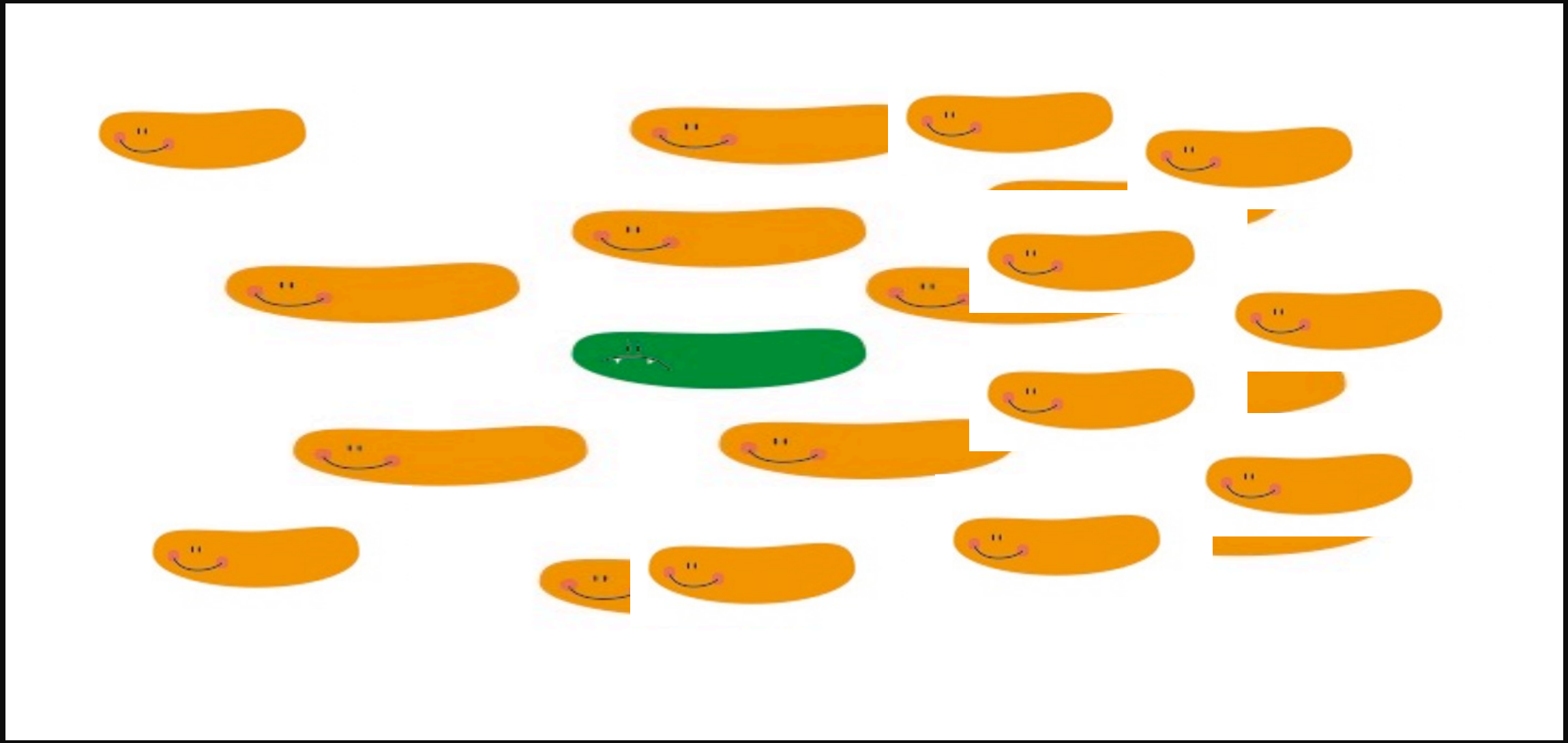
- Genotype
- Environment

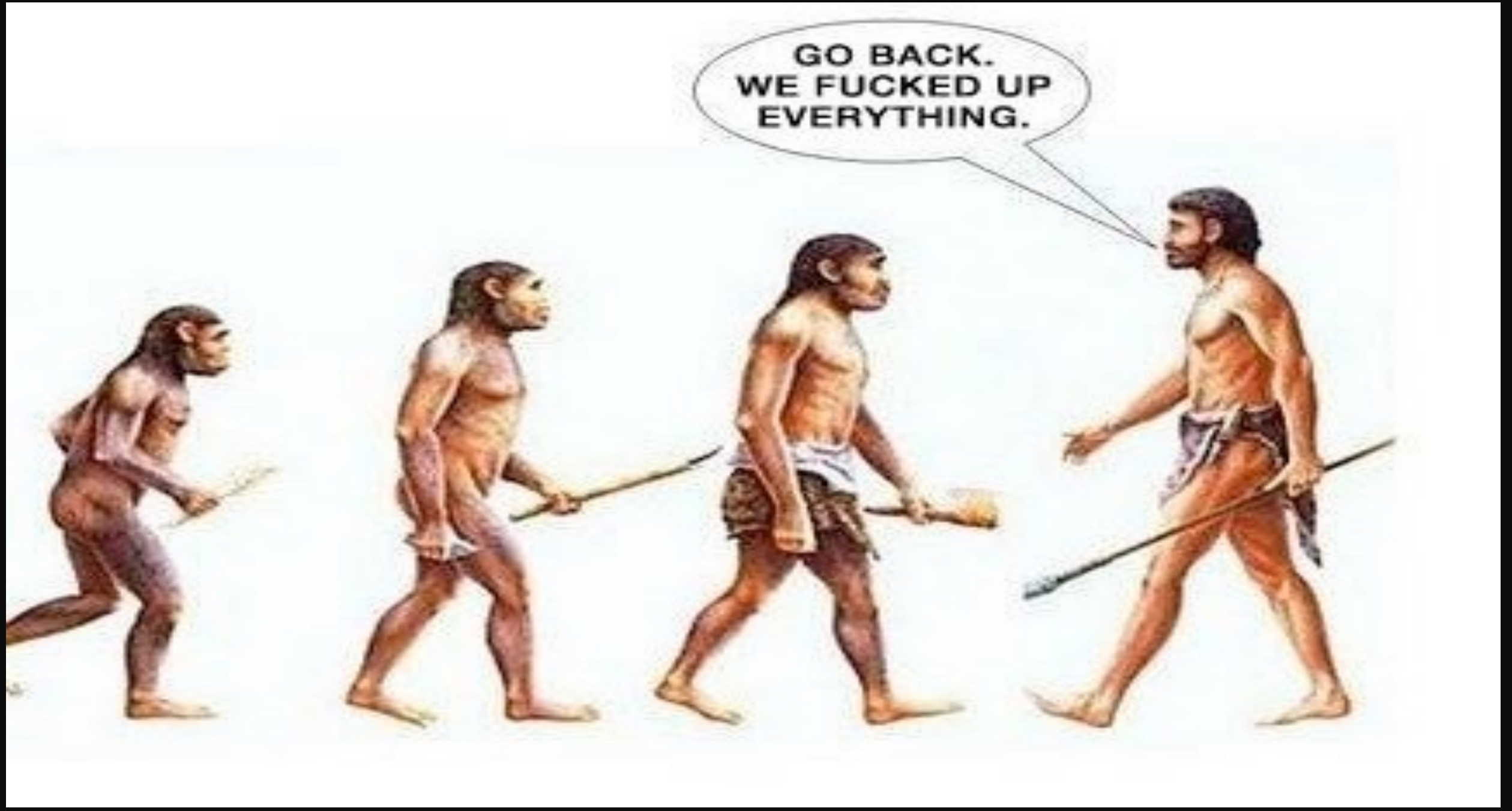
……..Your early childhood circumstances

……..Your lifestyle (Both impact on one’s microbiome)

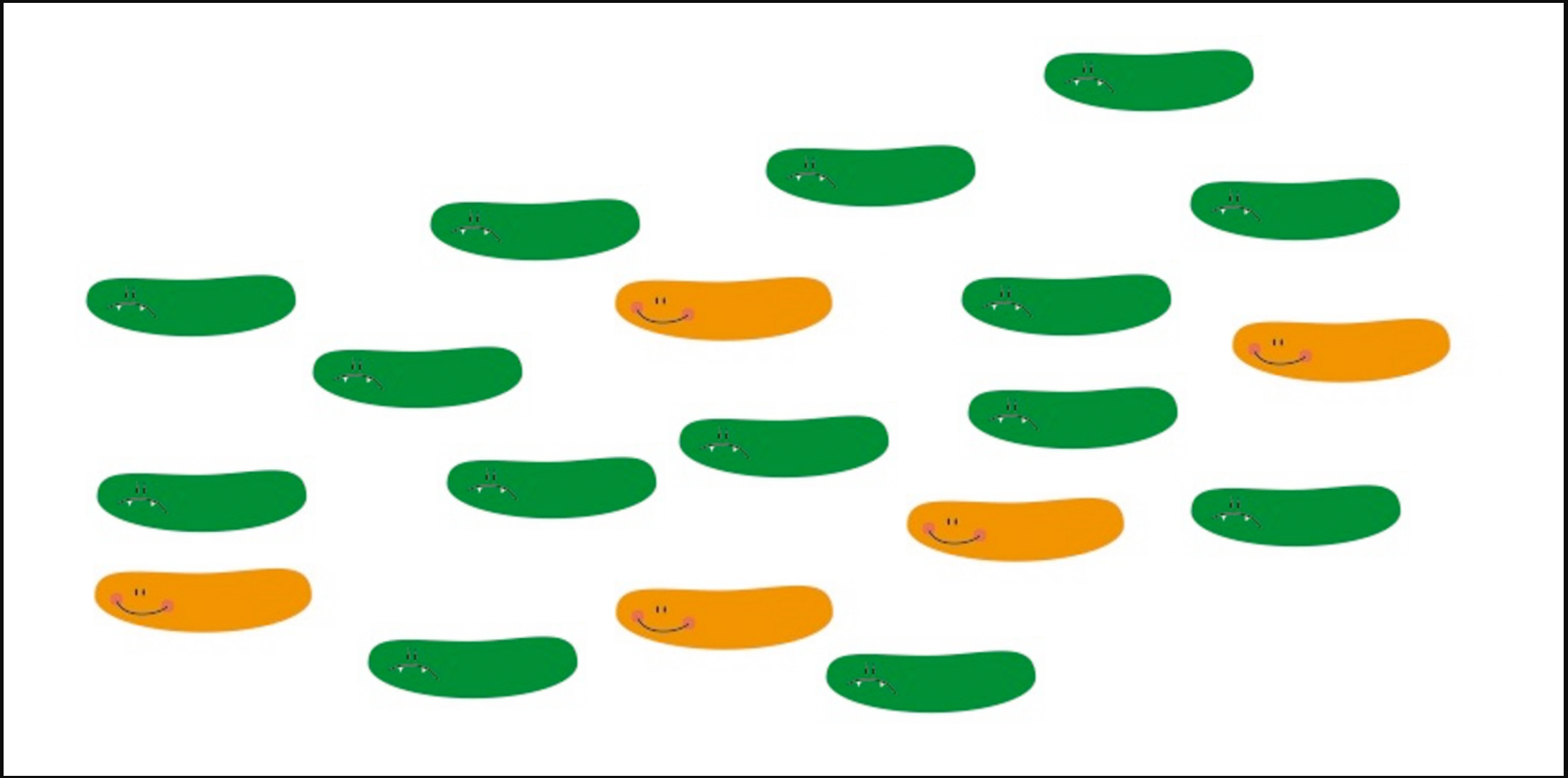
1. Diet
2. Weight
3. Exercise
4. Mental well being

20 to 1 is good




GO BACK.
WE FUCKED UP
EVERYTHING.

Modern way of living - Dysbiosis



Dysbiosis leads to disease susceptibility

- Dysbiosis (perturbations in the composition of the microbial communities may result in disrupted interactions between microbes and host

- A number of non-communicable diseases, such as, infantile colic, IBS, IBD, other auto-immune diseases, obesity, CVD, CNS degenerative diseases etc, have been associated with alterations in gut microbiota

Microbiota unique for an individual

1. There is no optimal gut microbiota composition

2. Each individual is unique, and harbours his or her own distinctive pattern of bacterial composition in terms of species and strains

Can probiotics modify gut microbiota?

- Probiotics have been used to treat a variety of diseases for decades.

- The impact of probiotics probably does not reside in their ability to change microbiota, but rather in sharing genes and metabolites, supporting challenged microbiota, and directly influencing epithelial and immune cells.

World Gastroenterology Organisation Global Guidelines

Probiotics and prebiotics

February 2023

Use of probiotics- what do the guidelines say?

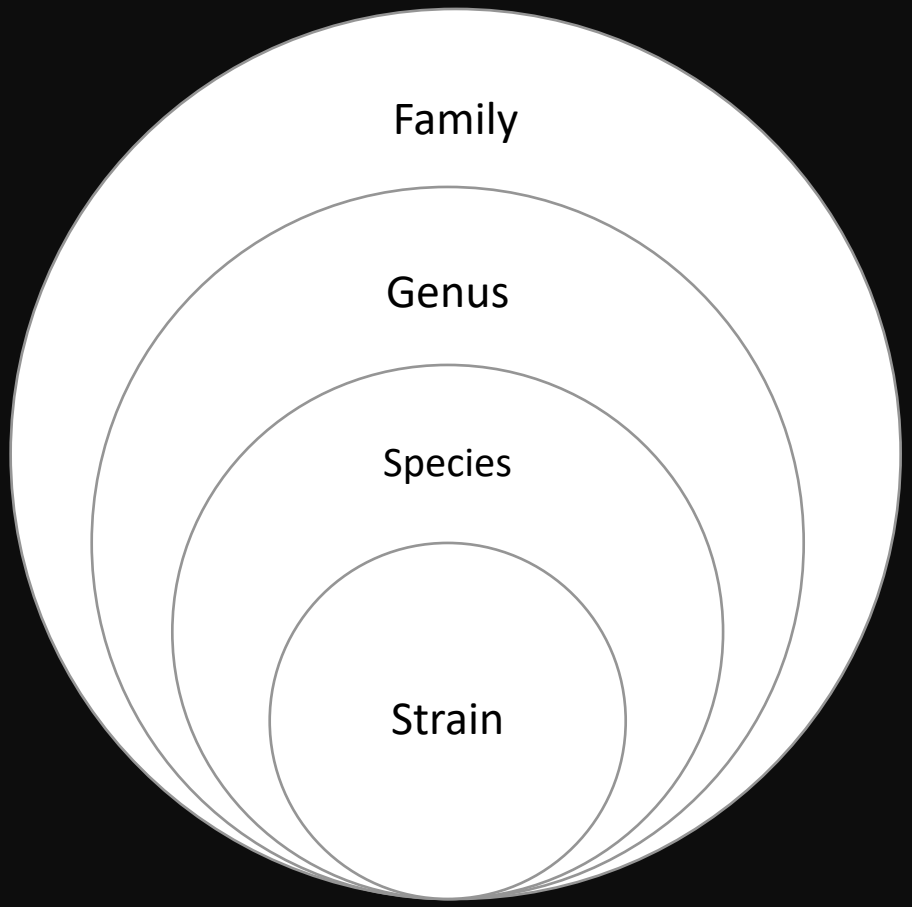
- Recommendations for probiotics, clinically, should tie a specific strain or strains to specific diseases
- The claimed benefits must be based on human studies with acceptable level of evidence
- Strain designations for probiotics are important, because the most robust approach to probiotic evidence is to link benefits to specific strains or strain combinations of probiotics at the effective dose.
- Some strains will have unique properties that may account for certain neurological, immunological, and antimicrobial activities.

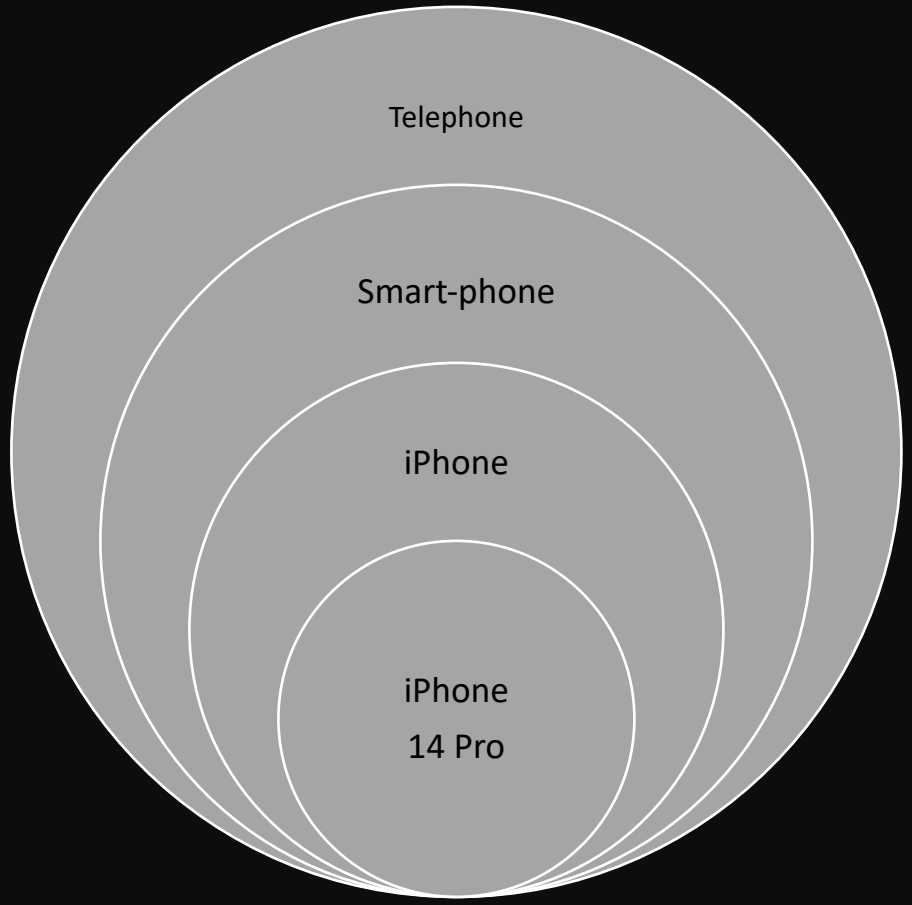
Genera, species and strains

- **A probiotic strain is identified by the genus, species, subspecies (if applicable) and an alphanumeric designation that identifies a specific strain.**

- **In the scientific community, there is an agreed nomenclature for microorganisms—for example, *Lactobacillus casei* DN-114 001 or *Lactobacillus rhamnosus* GG or lactobacillus reuteri 17938**

Classification of bacteria





Strain Specificity

	Bacteria	Something to read
Family	**Lactic acid bacteria**	**Literature**
Genus	***Lactobacillus***	**Printed book**
Species	***Lactobacillus reuteri***	**Novel**
Strain	***L. reuteri* DSM 17938**	**The Lord of the Rings**

Pharmaceutical forecast for the future

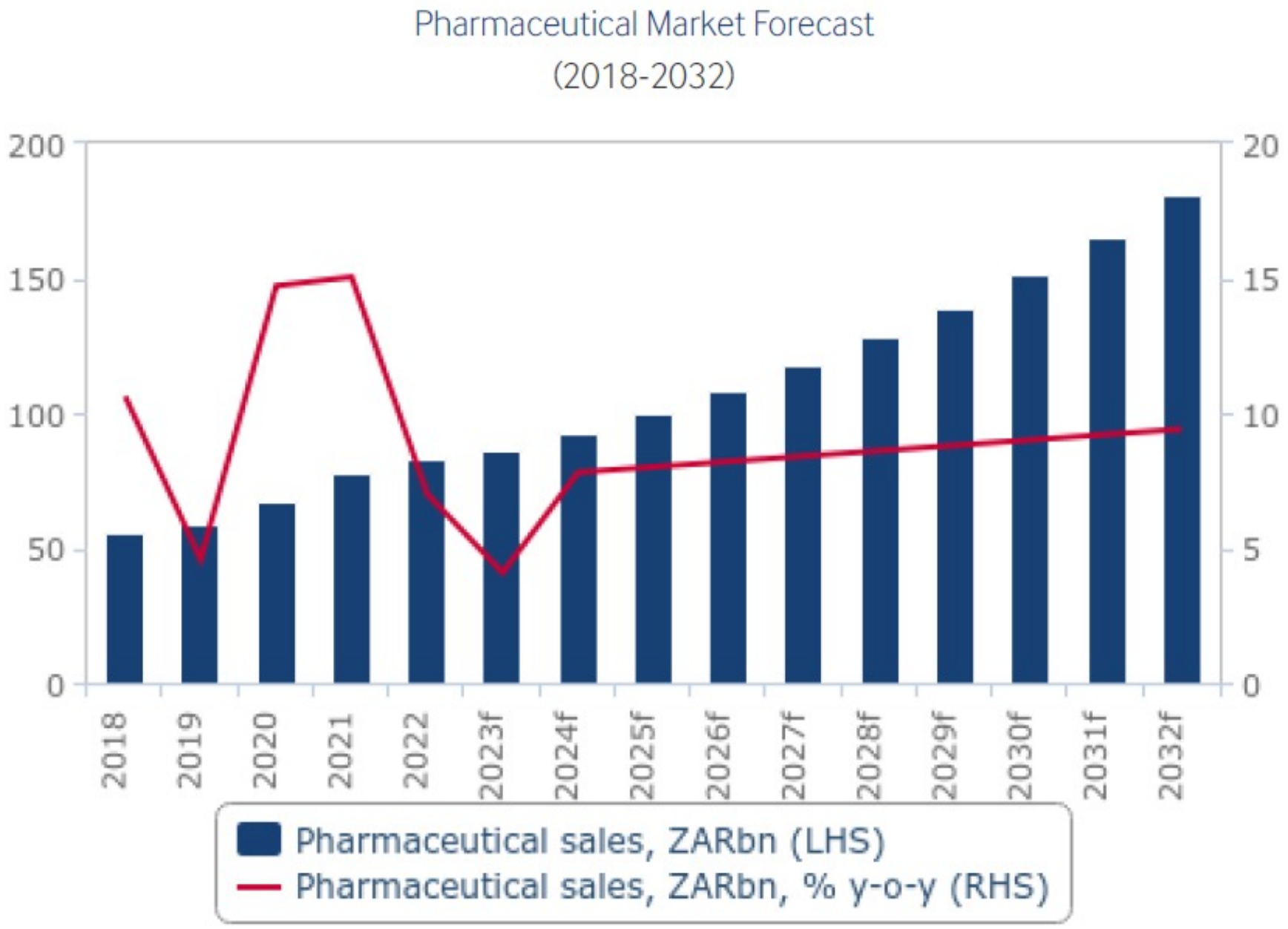
NHI

SA Government is set to establish universal healthcare (NHI)

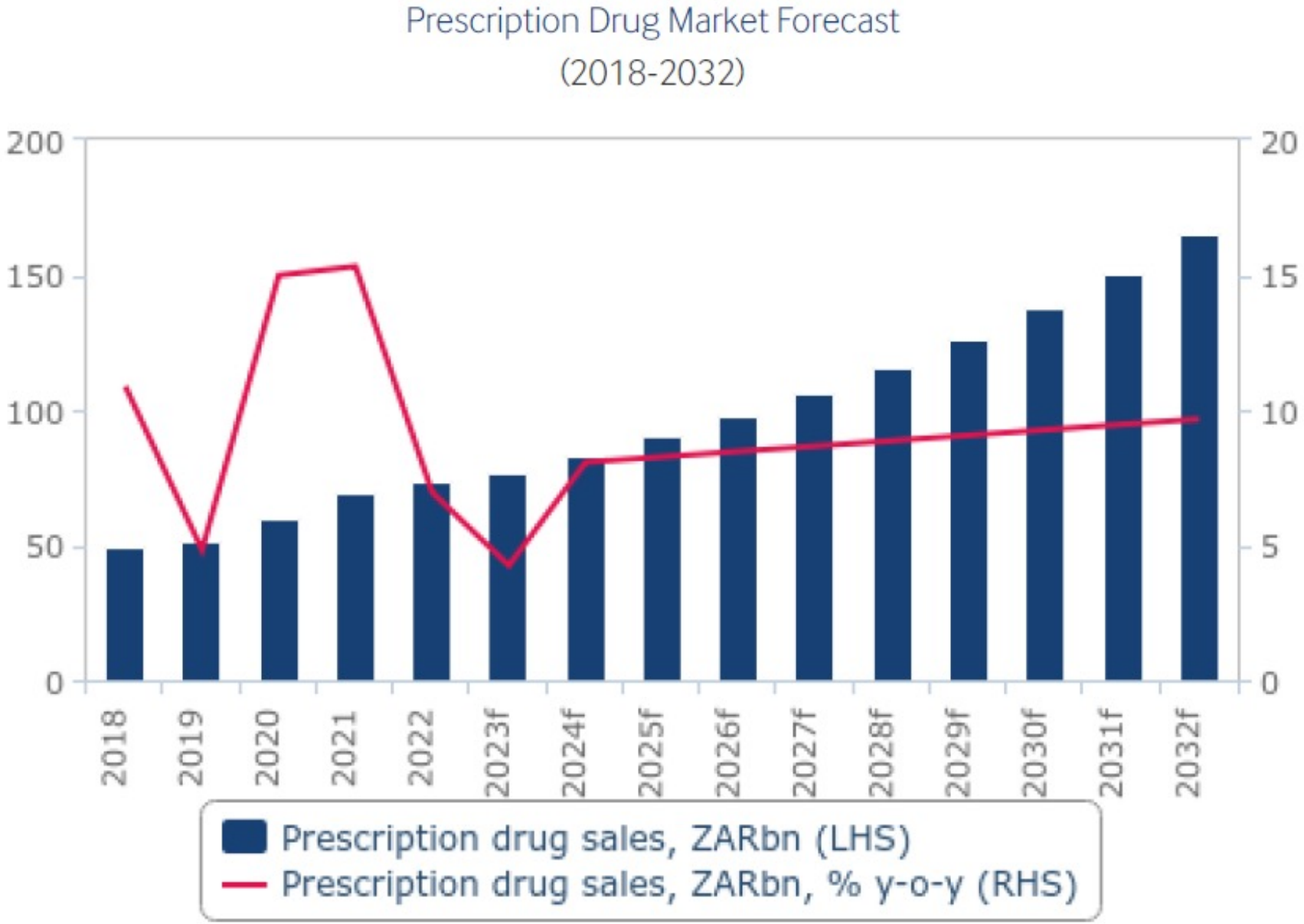
- **Is it a right or a privilege ????**
- **South Africa's 435 government hospitals are presently not optimal**
- **Financial affordability**

NHI

- Implementation is expected to take up to15 years,
- Still delays even with these timelines
- A single financing system will pose significant challenges for the entire system of medicines selection, procurement, distribution, and use, in which pharmacists will play a central role.
- Pharmacy policy specialists will play a key role to the implementation, design, and operation of this potentially huge single system



f = BMI forecast, Source: DESA/UNSD United Nations Comtrade Database, local news sources, domestic companies, BMI



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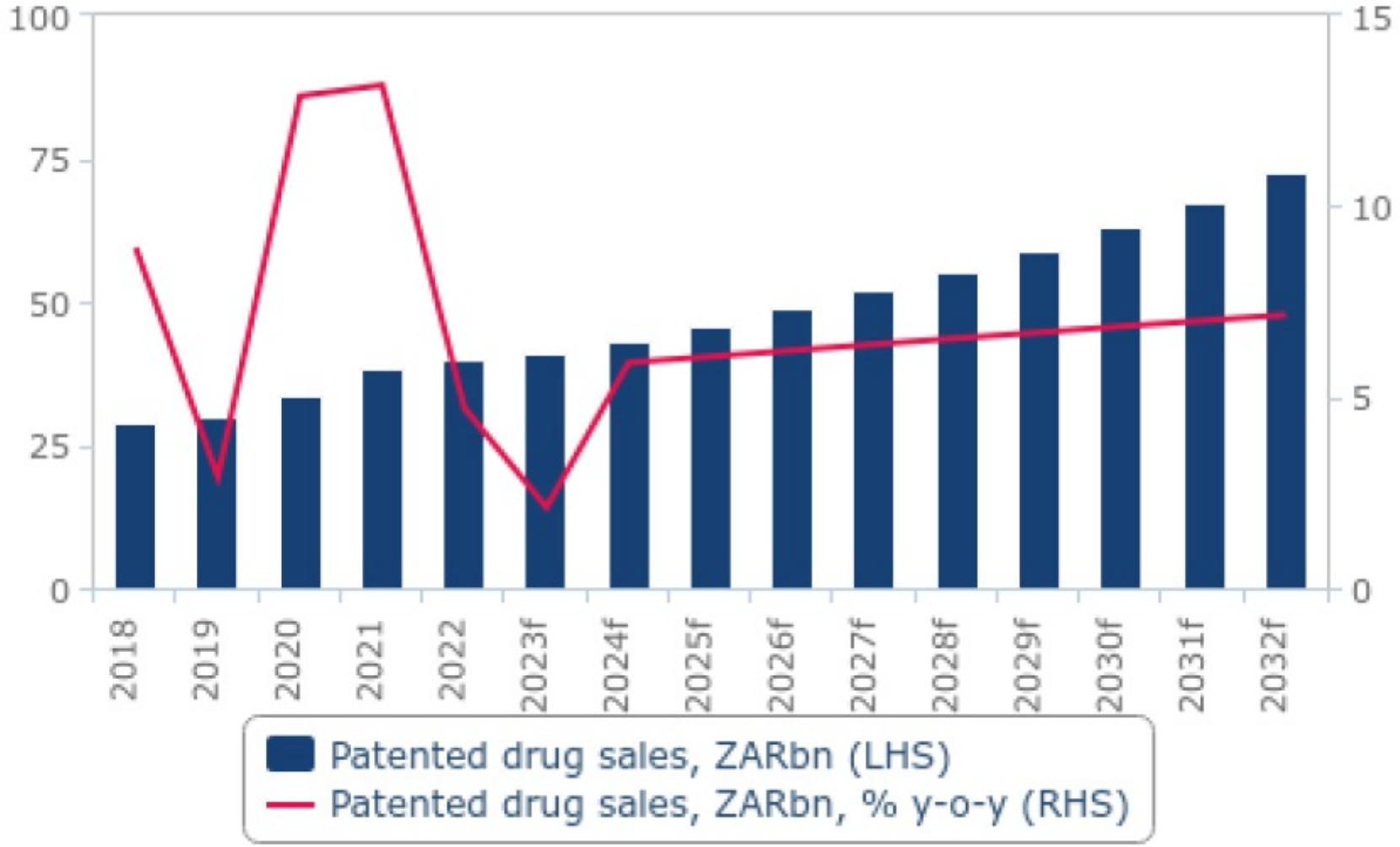
Patented Drug Market Forecast
(2018-2032)



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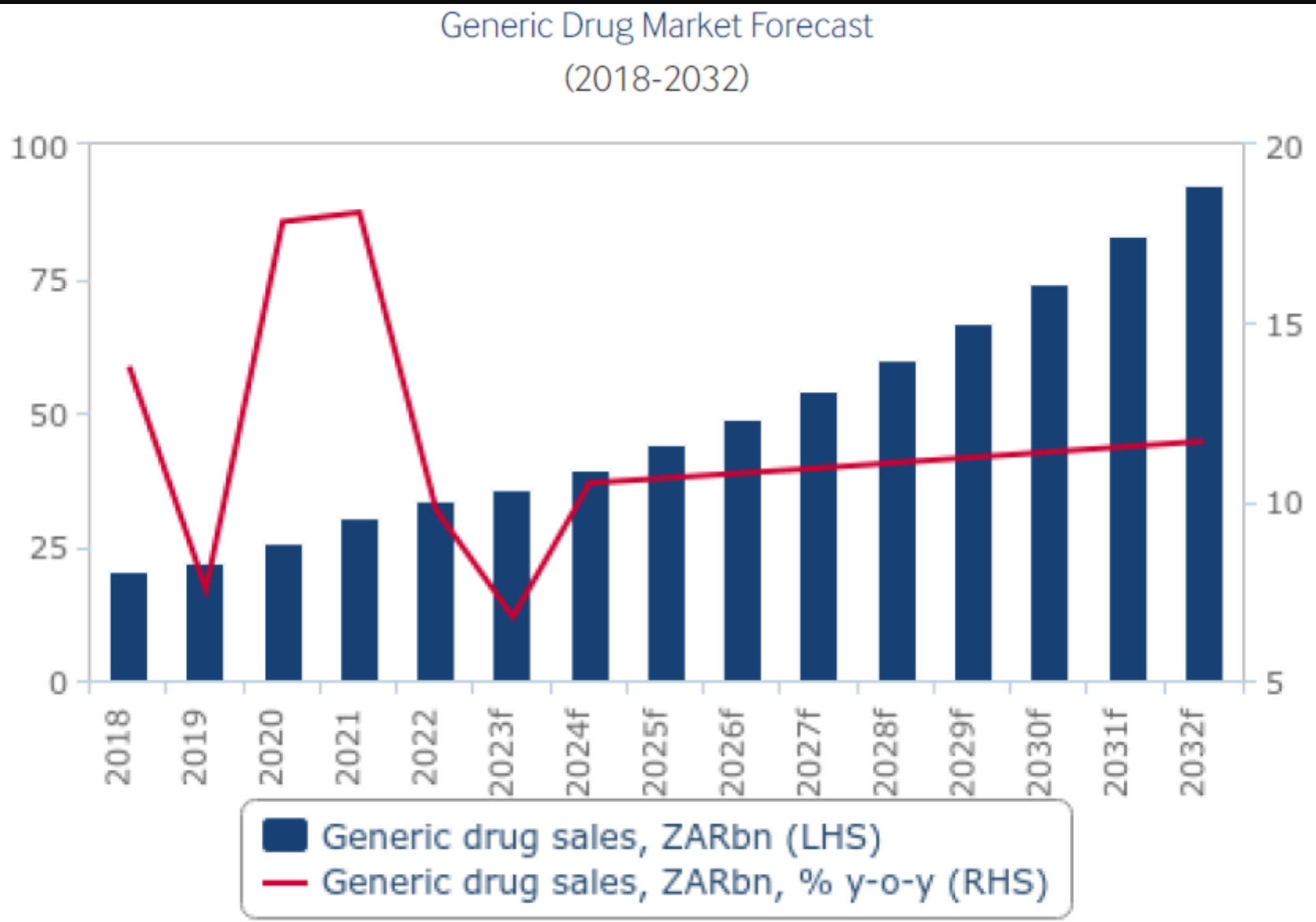
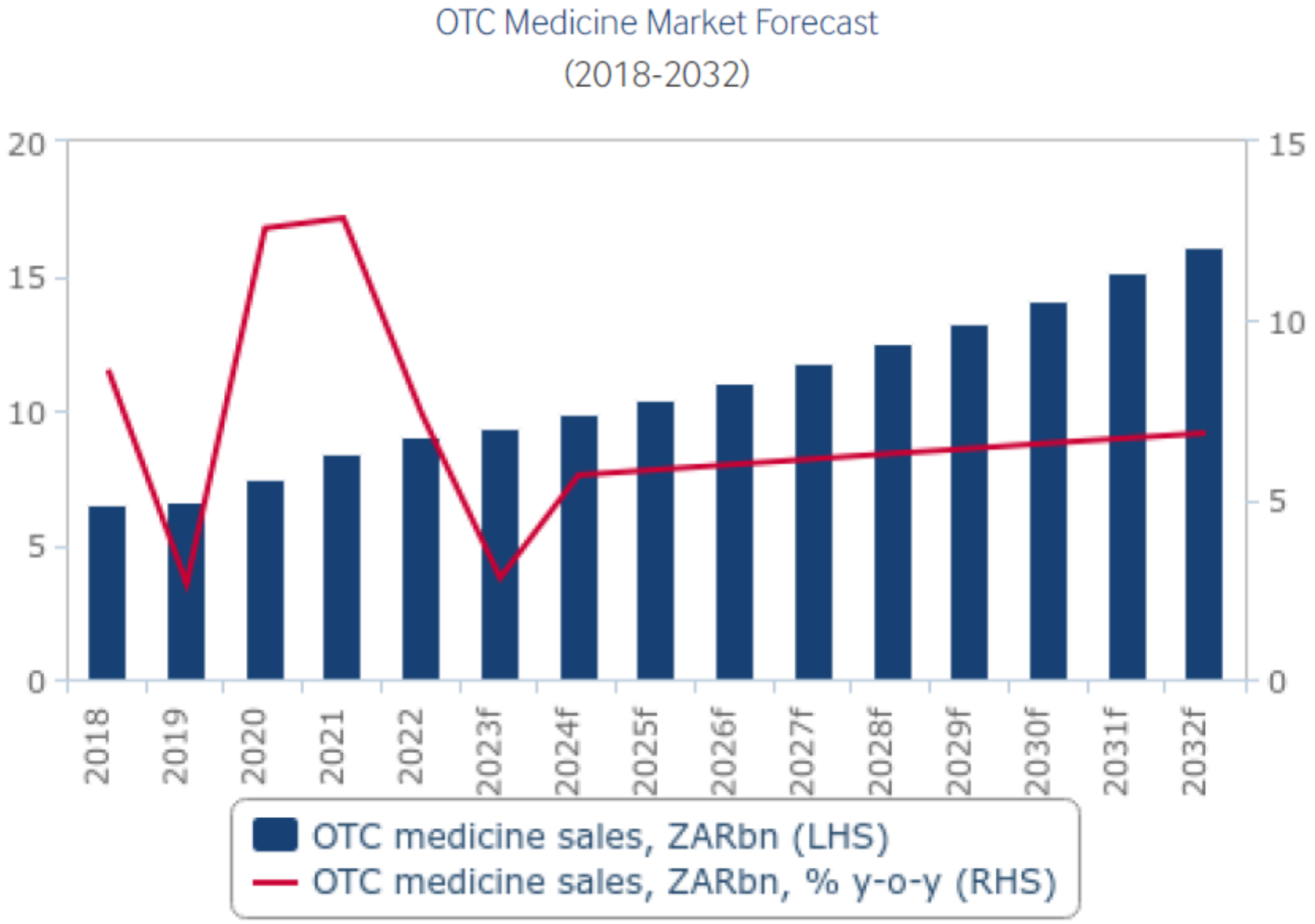


f = BMI forecast. Source: National sources, BMI



f = BMI forecast. Source: DESA/UNSD United Nations Comtrade Database, local news sources, domestic companies, BMI

PIMART

- Pharmacist-Initiated Management of Antiretroviral Therapy (PIMART) is a type of pharmacist-initiated therapy which aims to allow pharmacists to join nurses and clinicians in the fight against the rising HIV infections in South Africa.

- In addition, PIMART will help address the lack of adherence to treatment by persons living with HIV (PLWHA), and the high number of avoidable HIV-related deaths by allowing them access to antiretroviral treatmen

PRIMARY CARE DRUG THERAPY (PCDT)

- A pharmacist who has completed the PCDT supplementary training and has been issued with the relevant section 22A(15) permit.

- He can then offer certain PCDT services according to the list of conditions published by the National Department of Health from time to time.

PCDT

Consultation with patients, in an approved primary health care setting, and includes:

(i) comprehensive patient history taking;

(ii) physical examination (excluding internal and external genitourinary examination);

(iii) assessment of diagnosed and undiagnosed conditions listed in the Primary Health Care (PHC) Standard Treatment Guidelines (STG) and Essential Medicines List (EML);

(iv) ordering, conducting and interpretation of applicable diagnostic and laboratory tests for the purposes of (iii) above;

(v) interpretation of the assessment/diagnosis;

(vi) decision on safe and appropriate therapy;

(vii) prescribing of medicines for the conditions identified for the purposes of PCDT as per PHC STG and EML List published by the National Department of Health from time to time;

(viii) monitoring of the outcomes of therapy; and

(ix) referral to another health care provider where necessary

Summary

- Generic substitution of branded products has played an important role in limiting the cost of medicines in South Africa
- South Africa's strict regulatory requirements have ensured that marketed generics are bioequivalent to branded products,and meet the standards of safety, efficacy and quality
- Adoption by medical specialists for conditions of concern.
- Demonstration of comparability between biological products presents challenges, but with the registration of biosimilars in EU, will SA follow.

Summary

- Quality biosimilars will provide patients with life-saving medicines (traztuzumab, adalumimab, pembrolizumab, rituximab)
- Phyto pharmaceuticals have different extraction processes and many actives and cannot be genericized
- Certain probiotic strains have been proven to provide benefit for certain disease condition and should not be substituted
- South Africa needs more vigorous measures to control counterfeit medicines

Thank you for your attention