Forecasting pipeline ARVs

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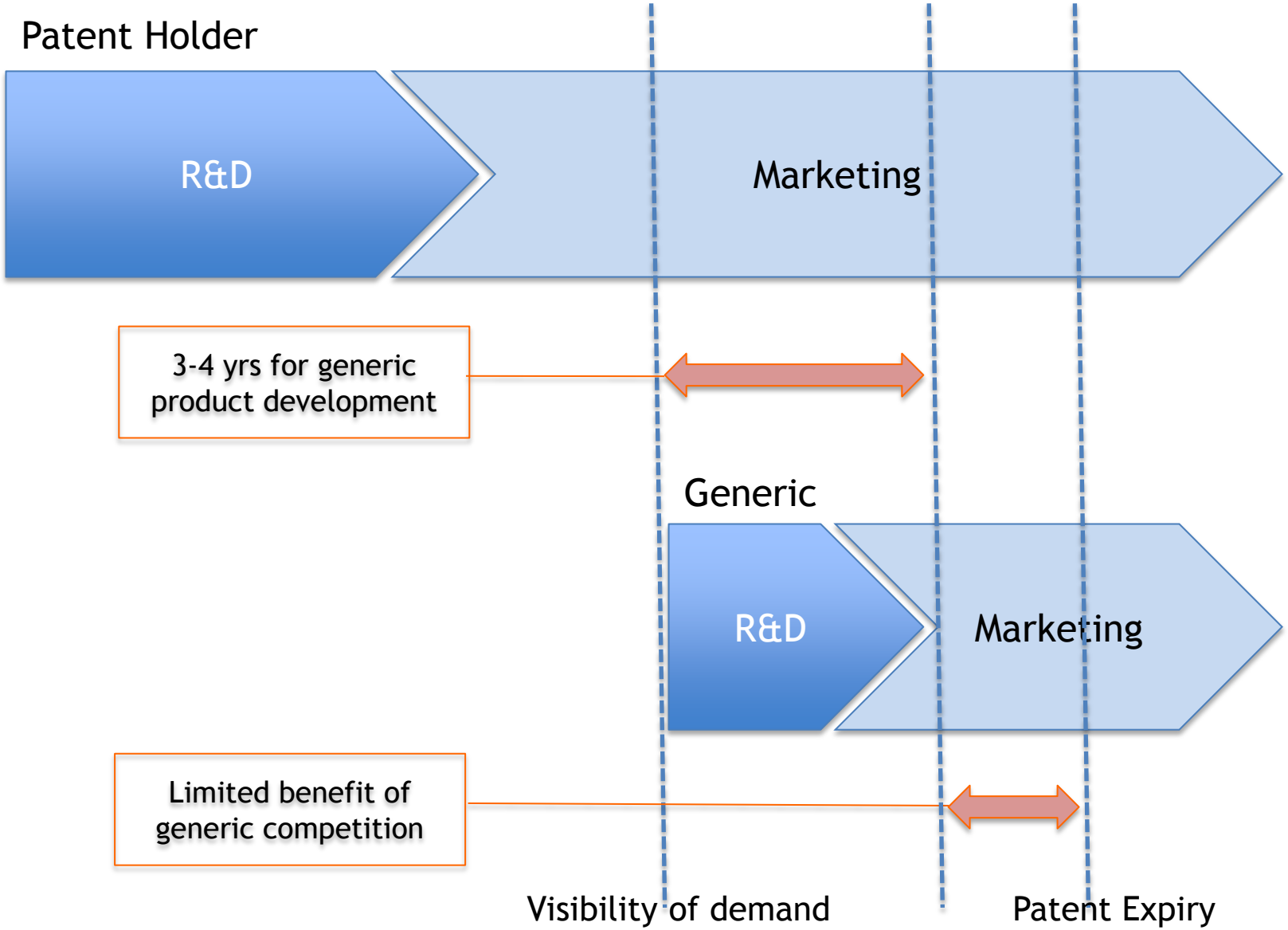
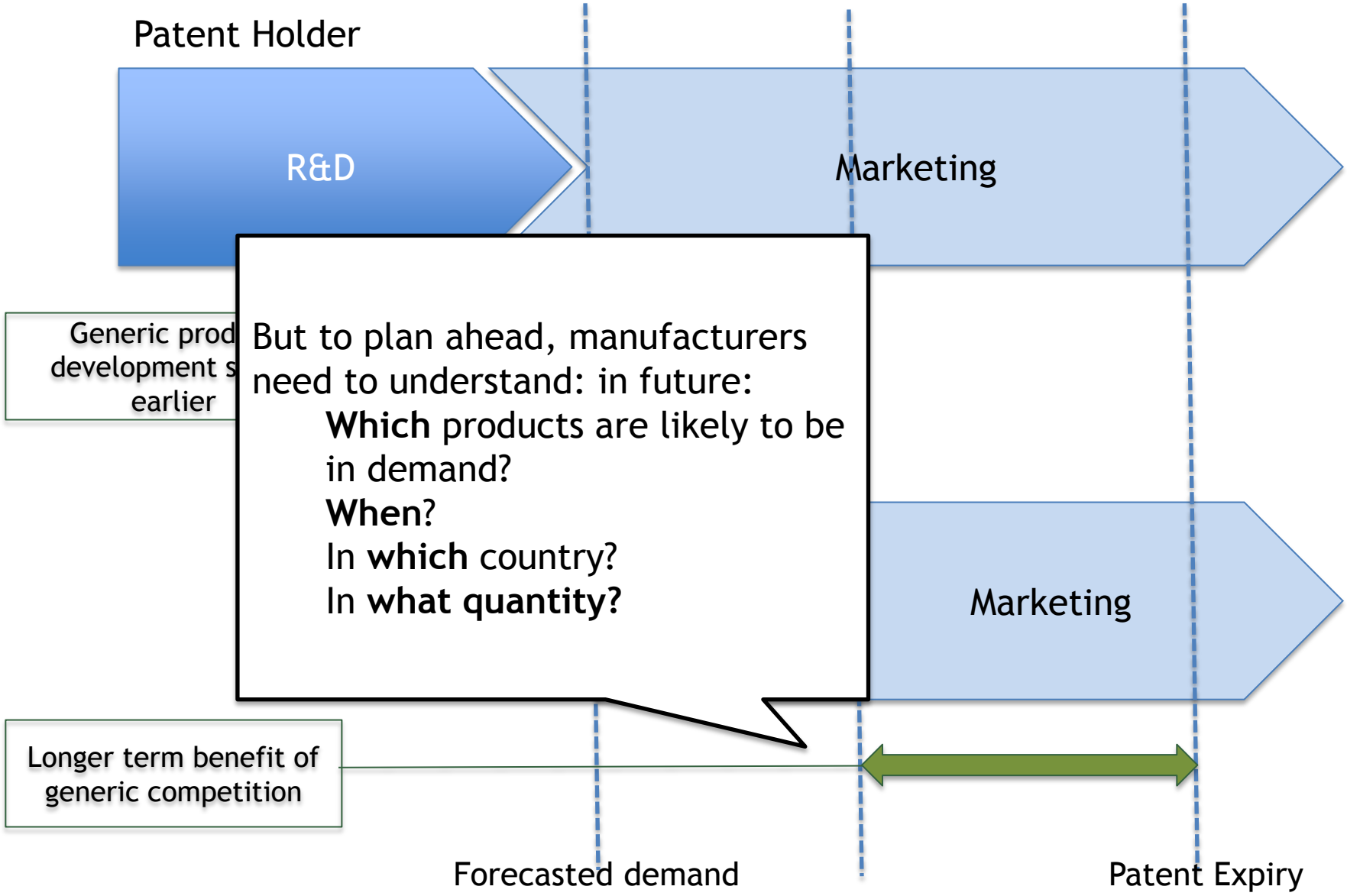
Presently: lack of visibility causes a gap between demand and generic production for new drugs



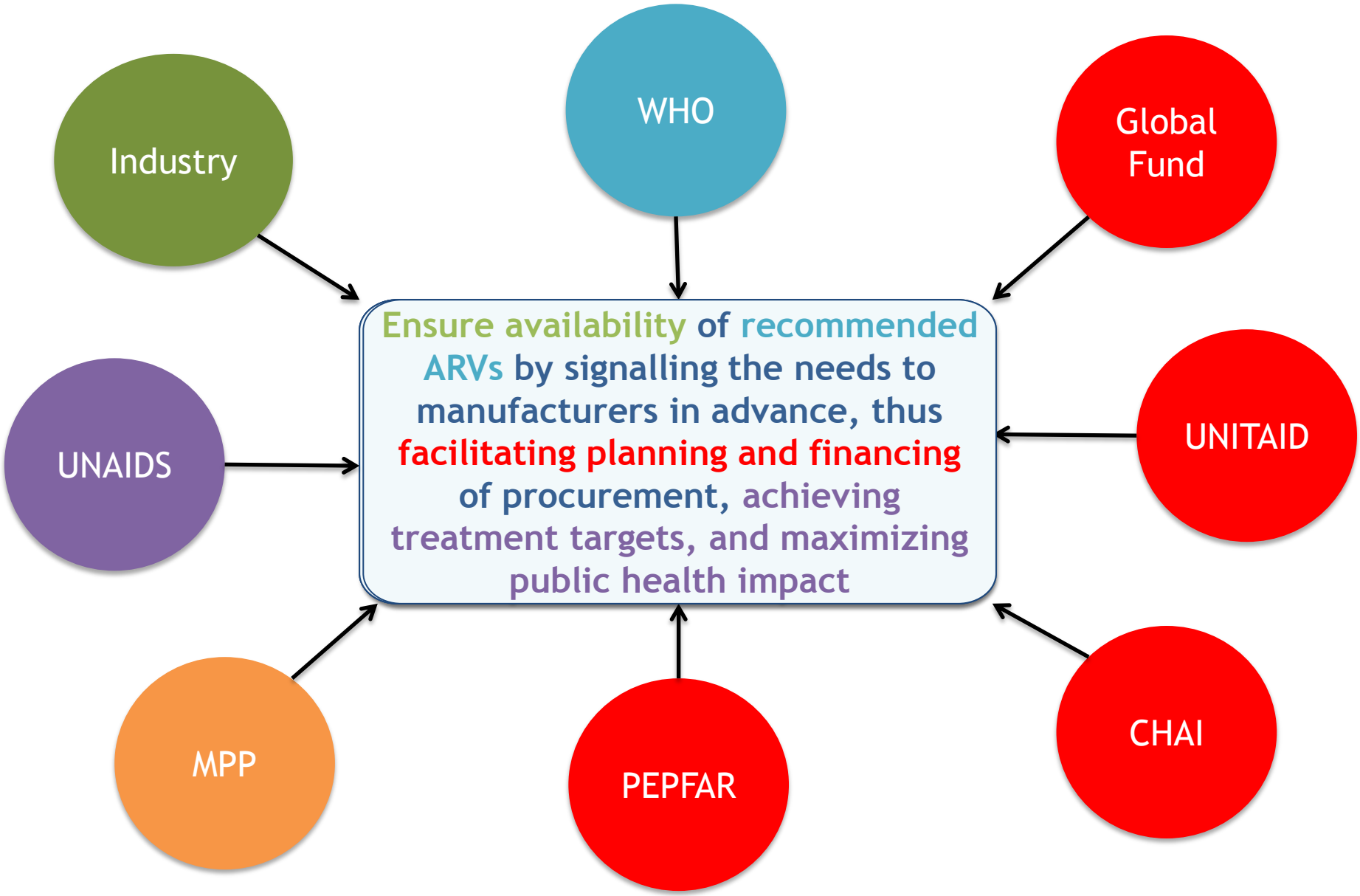
Creating early visibility of demand (forecasts) can speed benefits of generic competition



World Health Organization

medicines patent pool

Forecasts can be useful for multiple stakeholders



Forecast for pipeline ARVs built on current work

- Consolidated forecast: for both pipeline AND current ARVs for 10 years
- Draws from and builds upon existing forecasts
- Accounts for current and likely use of ARVs, technical/medical aspects and country/regional information
- Allows better definition of markets

Forecasting Model

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Background

- Extent and timing of public health usage of ARVs, especially new drugs, was a key area for the MPP to understand when we commenced our licensing work with originator and generic companies
- MPP started its forecasting exercise in 2011, including all ARVs but focusing on new drugs
  - Prioritisation of voluntary licences with originators to achieve key public health objectives
  - Early visibility by generic manufacturers on new ARVs: portfolio planning and prioritisation
  - Resulting in timely development of required FDCs
- To further supplement this, MPP requires knowledge of futuristic FDCs which would be needed in resource limited settings
- Consultations with WHO HIV department and the TAC team to understand FDCs needed in future, scenario building and refine assumptions on uptake
- Consultations with other stakeholders in the TWG

MPP's Concluded Agreements

abbvie

- Lopinavir (paed)
- Ritonavir (paed)

Bristol-Myers Squibb

- Atazanavir

GILEAD

- Cobicistat
- Elvitegravir
- Emtricitabine
- Tenofovir Alafenamide
- Tenofovir Disoproxil

MERCK

- Raltegravir (paed)

NIH

- Darunavir related

ViiV Healthcare

- Abacavir (paed)
- Dolutegravir

Roche

- Valganciclovir (pricing agreement)

MPP has concluded licence agreements with 6 patent holders and a pricing agreement

medicines patent pool

Out-Licensing Partners and Agreements

AUROBINDO

- Cobicistat
- Elvitegravir
- Emtricitabine
- Quad
- Abacavir (paed)
- Atazanavir
- Tenofovir Alafenamide

Cipla

- Cobicistat
- Elvitegravir
- Emtricitabine
- Quad
- Dolutegravir
- Tenofovir Alafenamide
- Atazanavir

DESANO

- Atazanavir
- Tenofovir
- Cobicistat
- Emtricitabine
- Tenofovir Alafenamide
- Dolutegravir

Emcure SUCCESS THROUGH INNOVATION

- Cobicistat
- Elvitegravir
- Emtricitabine
- Quad
- Atazanavir
- Dolutegravir
- Tenofovir Alafenamide

HETERO

- Cobicistat
- Elvitegravir
- Emtricitabine
- Quad
- Dolutegravir
- Tenofovir Alafenamide

LAURUS Labs

- Cobicistat
- Elvitegravir
- Emtricitabine
- Quad
- Tenofovir
- Dolutegravir
- Tenofovir Alafenamide

MICRO LABS

- Dolutegravir

Mylan

- Dolutegravir

Shasun

- Cobicistat
- Elvitegravir
- Emtricitabine
- Quad
- Tenofovir

Shilpa

- Cobicistat
- Elvitegravir
- Emtricitabine
- Quad
- Tenofovir

MPP is currently running 52 development projects with 10 partners

medicines patent pool

Principles of the Model

- Currently does not include estimates of number of people who may need PrEP (e.g. number of IDUs at high risk of HIV acquisition) or TasP
- Borrows average usage forecast from currently available forecasts till 2018
- Borrows epidemiological estimates from available estimates till 2018
- Assumptions:
  - Linear regression on market share increase
  - Healthy and timely generic competition
  - Introduction of new drugs based on projected development timelines of generic manufacturers and estimated inclusion in WHO Guidelines
  - Price considerations: lower priced medicines would potentially have higher usage
  - Country inclusion: accounts for all low and middle income countries including those with well established ARV treatment programs such as Brazil
  - Accounts mainly for the public market

Introduction of 3 Scenarios

Considered three possibilities:

Scenario 1: Status Quo

- WHO Guidelines remain consistent with current guidelines
- New products when introduced show only a marginal uptake
- Use of Integrase Inhibitors (INIs) limited to 3rd line

Scenario 2: Likely Use

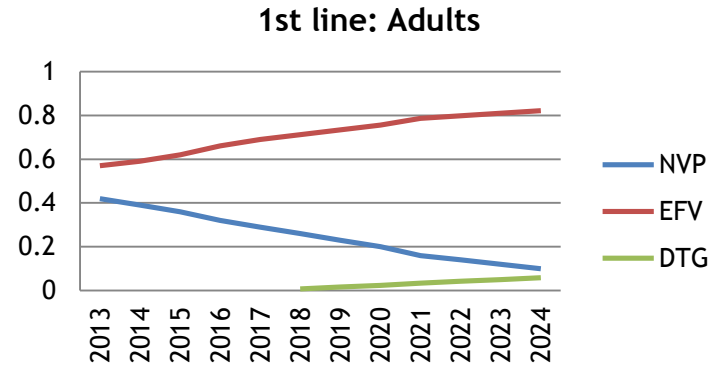
- WHO Guidelines accept and recommend new products using the treatment optimisation framework
- New products have a good uptake; assumed that new FDCs such as those containing DTG, TAF and heat stable DRV/r are made available as generics
- Use of INIs is recommended as preferred options in 2nd and 3rd line in initial years, and later progressing to 1st line use (when more safety data is available)

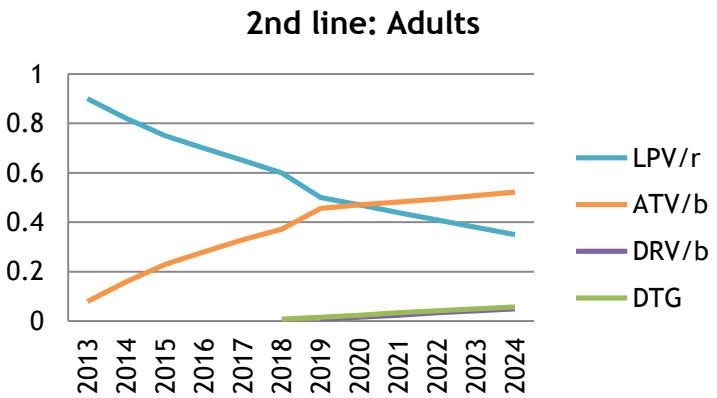
Scenario 3: Aggressive Adoption

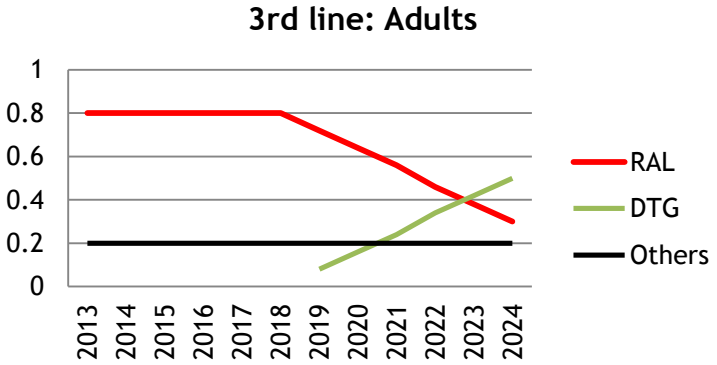
- WHO Guidelines recommend aggressive use of new products
- Use of INIs as preferred option recommended in 1st line

Adults

Scenario 1: Status Quo







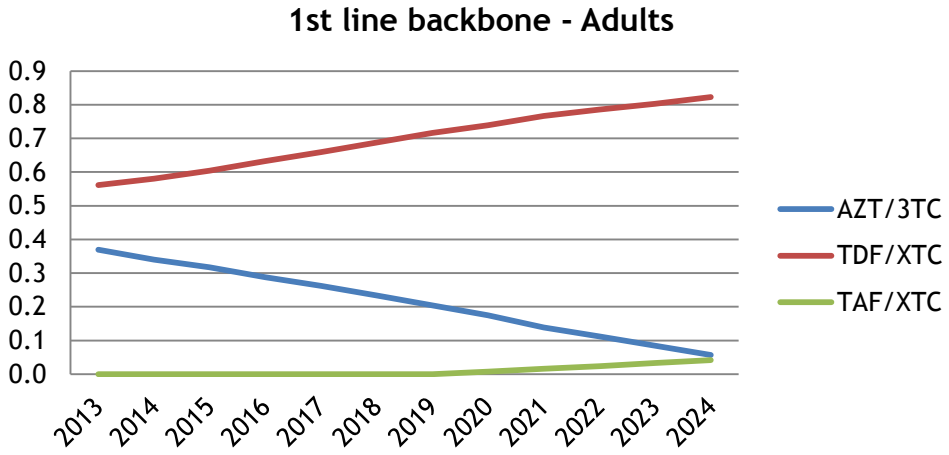
Guidelines remain consistent with current recommendations

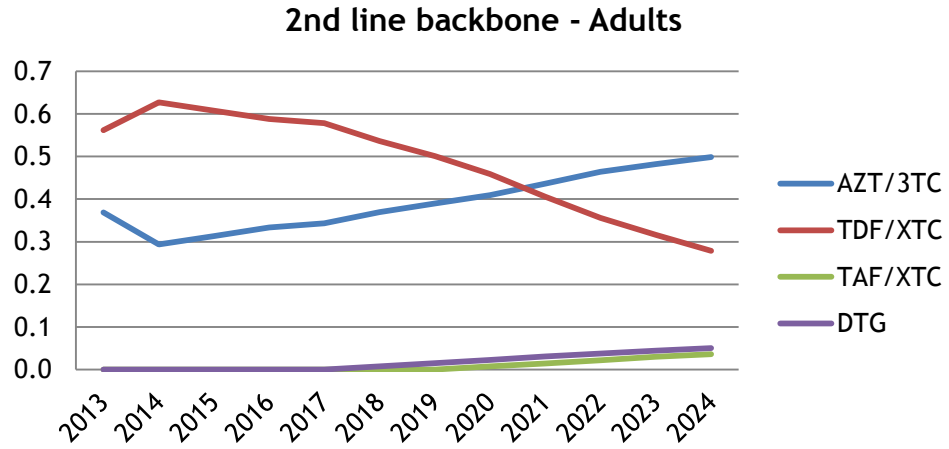
In this scenario:

- 1st line:
  - INI-based regimens used minimally in 1st line
  - As per current recommendations, use of NVP declines and EFV increases
- 2nd line
  - LPV continues to be the main option initially
  - ATV is used due to the potential low cost and once daily dose
  - DRV/r in combination with DTG is used marginally
  - DTG used marginally with NRTIs
- 3rd line
  - DTG slowly replaces RAL in 3rd line

This scenario is less likely, as generics are already developing low cost FDCs which may be compelling for potential use in developing countries

Status Quo: Backbones

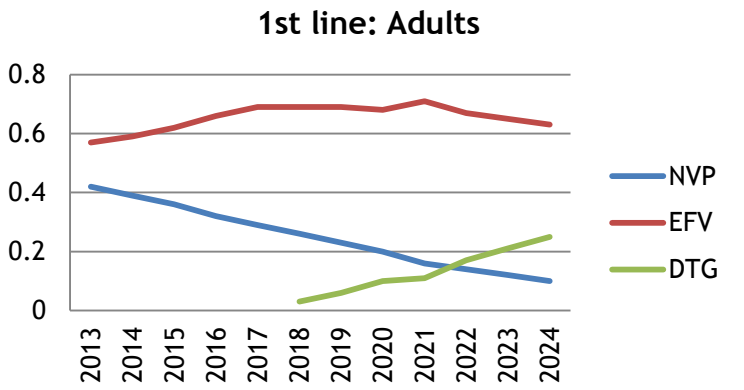


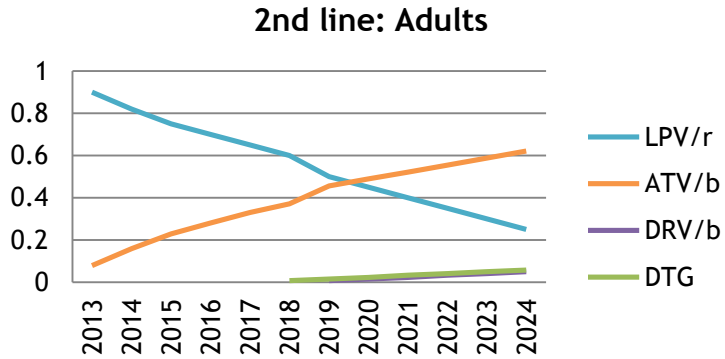


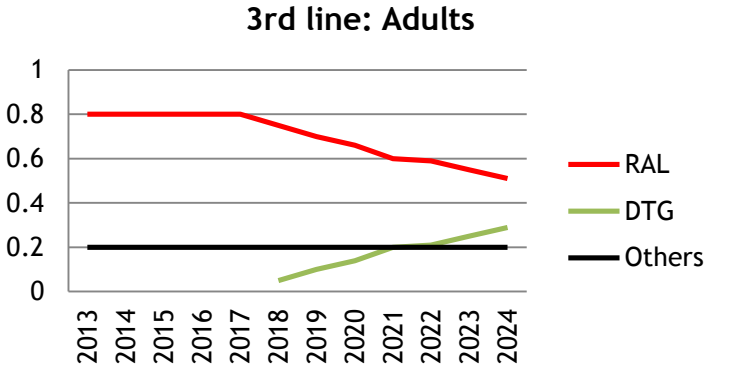
Consistent with current Guidelines

- Uptake of TDF increases further, consolidating its positions as the main backbone in 1st line
- Due to higher use of TDF in 1st line, AZT becomes preferred option in 2nd line
- Minimal uptake of TAF from 2020, taking share from TDF
- DTG introduced marginally in 2nd line with PIs

Scenario 2: Likely Use







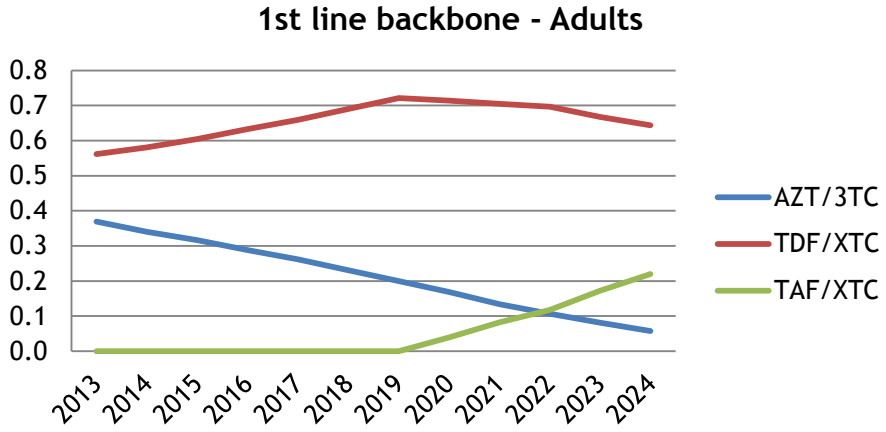
bPIs: recommended in in 2nd line and 3rd line either with NRTIs or with INIs.
New INIs: initially in 2nd & 3rd line; recommended in 1st line after 3-4 years of introduction

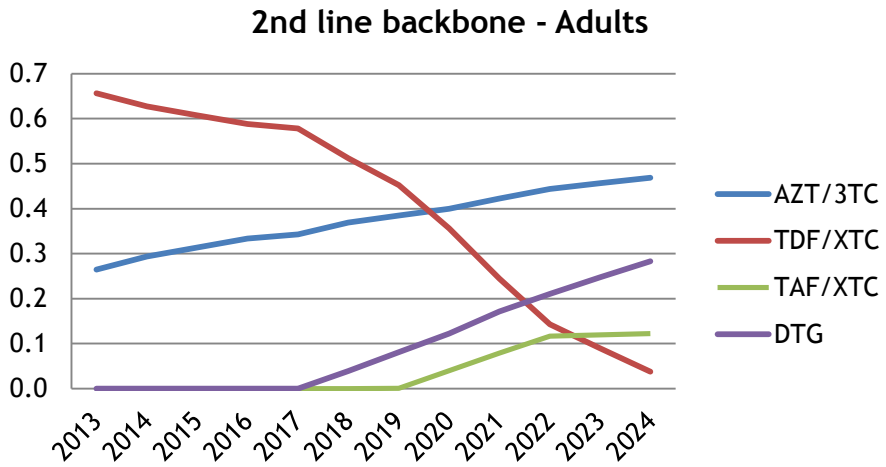
In this scenario:

- 1st line
  - Continues to be NNRTI based initially
  - INI-based regimens used minimally in initial years, then increase
- 2nd line
  - Development of co-formulations of bPI with INI (trials in plan)
  - bPIs used with either NRTIs (as per current Guidelines) or with INIs (such as DTG)
- 3rd line
  - Mainly RAL-based, DTG uptake increases initially, then then stabilizes

This may be a likely scenario in the initial years. Clinical trials of bPI+INI regimens in experienced patients underway.

Likely Use: Backbones

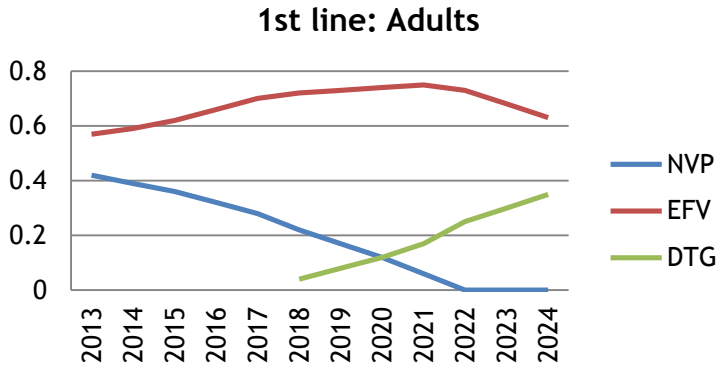


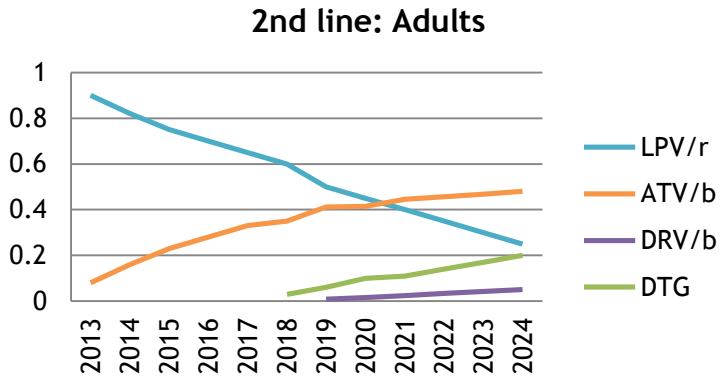


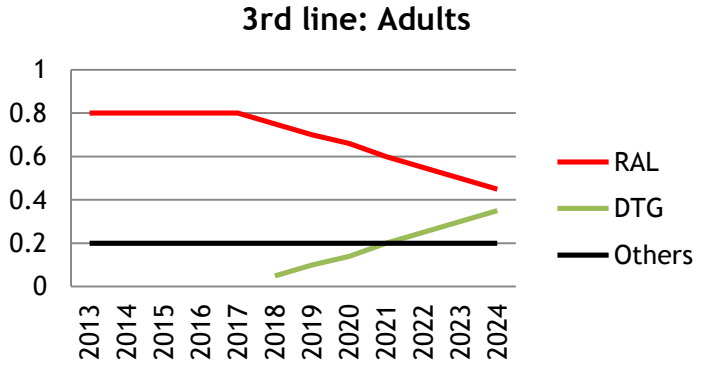
Introduction of INI in 2nd line

- Uptake of TDF increases further, consolidating its positions as the main backbone in 1st line
- Due to higher use of TDF in 1st line, use of AZT increases in 2nd line, however, the market is shared with TAF as well as DTG
- Medium uptake of TAF from 2020, mainly taking share from TDF in 1st and 2nd line
- DTG used in 2nd line with PIs (mainly with DRV)

Scenario 3: Aggressive Adoption







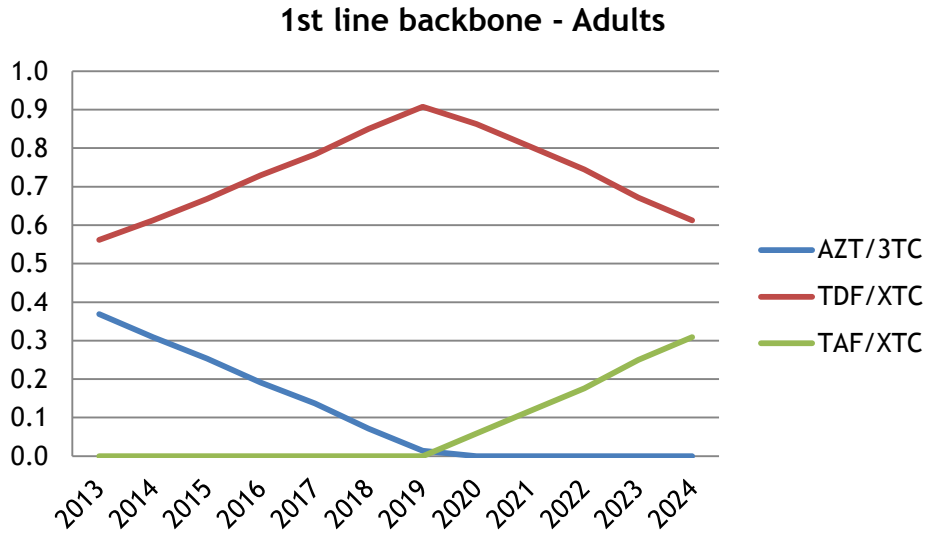
INIs recommended in 1st line based on low cost and FDC availability

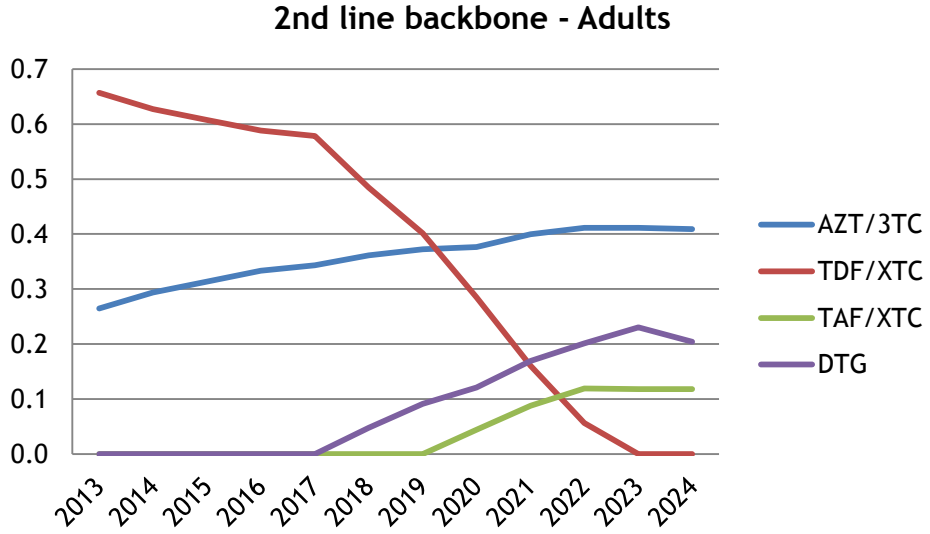
In this scenario:

- 1st line
  - DTG is rapidly used in 1st line from year 2018, becoming the main option
- 2nd line
  - LPV/r is replaced steadily by ATV/r due to lower cost and once daily regimen
  - bPIs used with either NRTIs (as per current Guidelines) or with INIs (such as DTG)
- 3rd line
  - Mainly RAL-based; DTG is used by patients who have not used it in 1st line

This scenario may be a reality in future once WHO gets more data with respect to INIs on TB co-infection and use in pregnant women

Aggressive Adoption: Backbones

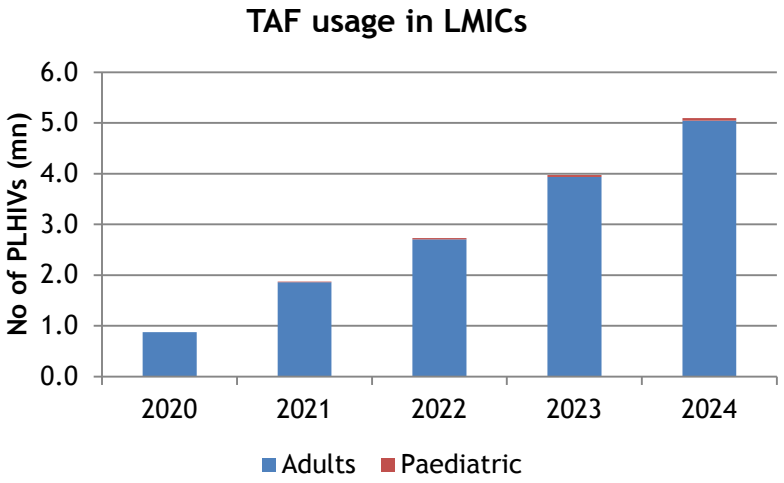


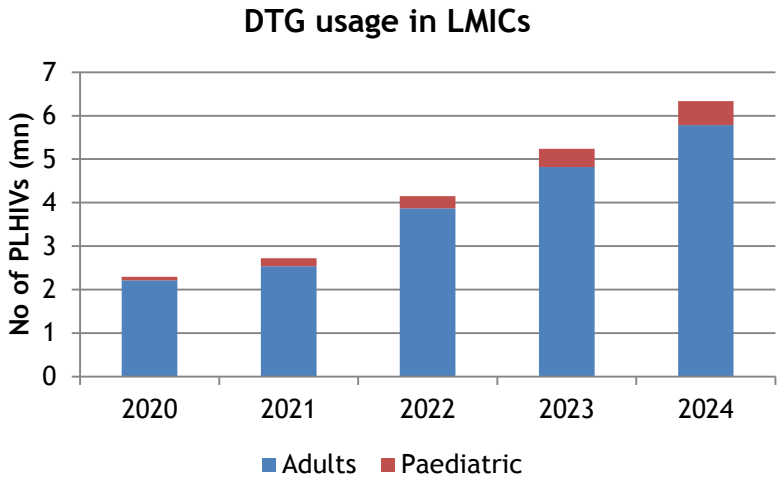


Introduction of INI in 2nd line

- Uptake of TDF increases, becoming the main backbone in 1st line, and being replaced later by TAF
- Due to higher use of TDF in 1st line, AZT becomes preferred option in 2nd line
- High uptake of TAF from 2020, taking share from TDF and AZT
- DTG used in 2nd line with PIs (mainly with DRV)

New Products in LMICs





- Above graphs show likely uptake of TAF and DTG
- The two products show quite significant number of people on treatment, going upto >5mn in 5 years for TAF and >6mn for DTG

medicines patent pool

Formulations Usage for Adults

PLHIVs using each formulation	2018	2019	2020	2021	2022	2023	2024
NVP/AZT/3TC	3,025,000	2,716,000	2,425,000	1,963,000	1,736,000	1,502,000	1,264,000
NVP/TDF/XTC	1,964,000	1,763,000	1,574,000	1,274,000	1,127,000	975,000	820,000
EFV/AZT/3TC	1,690,000	1,430,000	1,157,000	917,000	583,000	285,000	-
EFV/TDF/XTC	11,550,000	12,009,000	11,717,000	11,920,000	11,075,000	10,276,000	9,638,000
EFV/TAF/XTC	-	-	723,000	1,528,000	2,040,000	2,855,000	3,492,000
LPV/r/AZT/3TC	240,000	218,000	217,000	218,000	214,000	200,000	182,000
LPV/r/TDF/XTC	328,000	251,000	186,000	116,000	58,000	28,000	3,500
LPV/r/TAF/XTC	-	-	21,000	39,000	53,000	48,000	42,000
ATV/r/AZT/3TC	149,000	199,000	236,000	284,000	338,000	393,000	453,000
ATV/r/TDF/XTC	203,000	229,000	202,000	152,000	92,000	55,000	9,000
ATV/r/TAF/XTC	-	-	22,000	50,000	85,000	94,000	104,000
DRV/r/AZT/3TC	-	3,000	5,000	9,000	13,000	17,000	21,000
DTG/TDF/XTC	-	1,182,000	1,913,000	2,017,000	2,991,000	3,449,000	3,865,000
DTG/TAF/XTC	-	-	109,000	243,000	528,000	939,000	1,410,000
DTG/LPV/r	25,000	44,000	62,000	82,000	94,000	100,000	101,000
DTG/ATV/r	16,000	40,000	67,000	107,000	148,000	196,000	252,000
DTG/DRV/r	15,000	38,000	60,000	91,000	106,000	132,000	157,000
RAL/DRV/r	228,000	229,000	230,000	220,000	224,000	216,000	203,000

Thank You