Patient Forecasts for Pipeline ARVs: Adults

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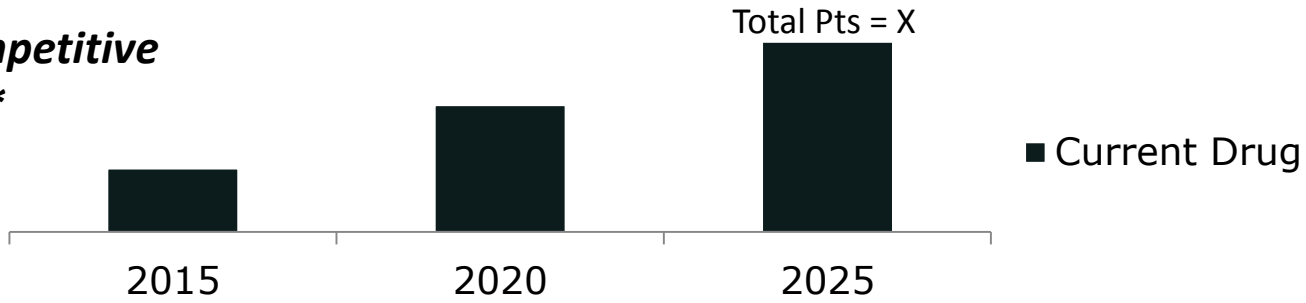
CLINTON HEALTH ACCESS INITIATIVE

Agenda

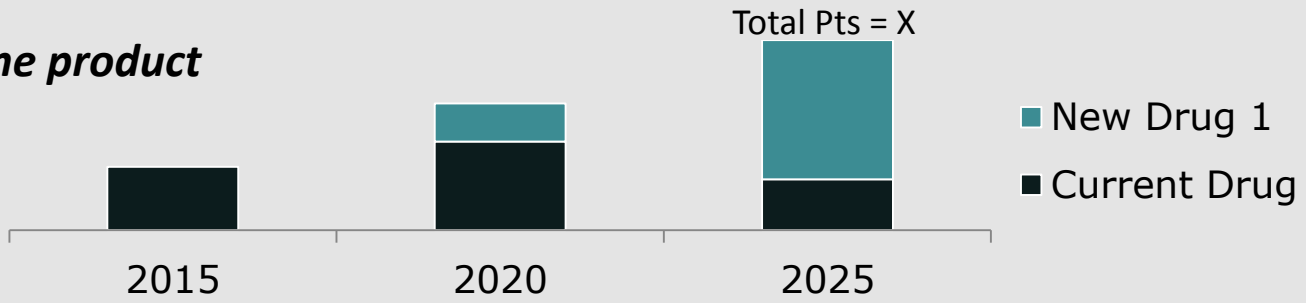
- General approach
  - Variables considered
  - Uptake curves
  - Justifying uptake curve choice
- High level assumptions in approach
- Patient forecasts with product specific assumptions

General Approach: Start with Projected Patient Numbers with Status Quo; Layer In Uptake of New Products as They Become Available

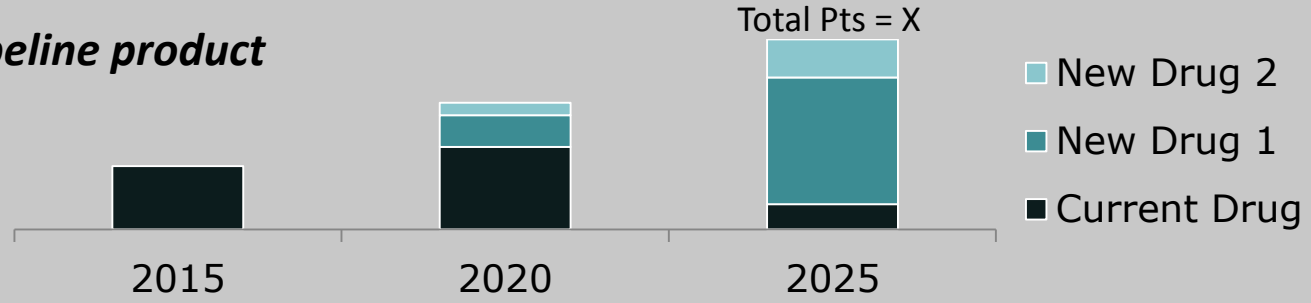
1) Baseline forecast for competitive set assuming status quo*



2) Forecast with first pipeline product



3) Forecast with second pipeline product



- Separate aggressive/moderate/conservative uptake against (i.e. taking from patients who would have otherwise been on) previously introduced drug(s)
- For each competitive pair, separate uptake curve amongst new vs. existing pts

*Note: CHAI typically does 5-year forecasts, the latest ending 2018. 2019-2025 baseline patient numbers were extrapolated by using moving 3 year avg. growth rates to calculate total patients on ART and then assuming projected 2018 drug splits would hold

3 Primary Variables to Consider

Anticipated price differential

Financial incentive for MoHs to encourage uptake and change procurement decisions

Relative clinical improvement

Question of only initiating new patients vs. also actively switching existing patients

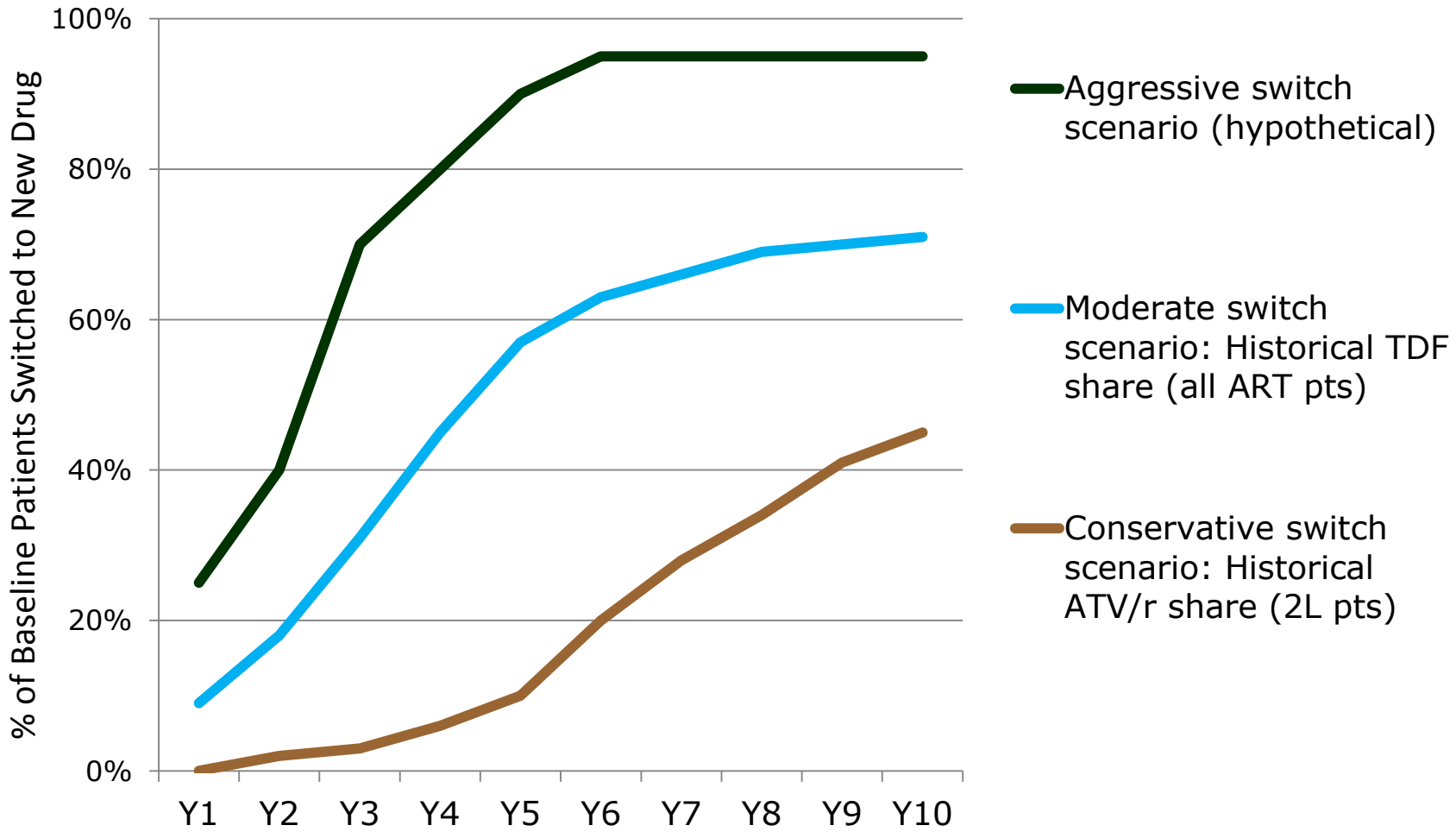
Anticipated Launch Year

Likely first availability of SRA-approved new product in LMICs with WHO guideline inclusion (equivalent FDC as incumbent)

Taken together with an uptake curve, we can estimate total number of patients on each product in any given year

3 Possible Uptake Curves Considered for Each Competitive Pair; 2 Based on Historical Analogs

Uptake Curves



Scoring System to Justify Uptake Curve Choice

a) Anticipated price relative to incumbent

+ 0-25% less

++ 25-50% less

+++ >50% less

b) Clinical improvement relative to incumbent

+ Slightly better AE profile

++ Significantly better AE profile OR greater viral suppression/less resistance

+++ Significantly better AE profile AND greater viral suppression/less resistance

Also considered, but with lower importance:

c) Substitutability – major clinical/scientific reason to not switch patients?

+ Different class of drug (e.g. DTG vs. EFV)

++ Same class of drug, but different end active ingredient (e.g. DRV vs. ATV)

+++ Same end active ingredient (e.g. TAF vs. TDF)

High Level Assumptions to Avoid Pitfall of False Precision with Many Variables Involved

- For each new product, there is **one primary patient segment per line of treatment** (i.e. competitive set) worth forecasting – use outside that represents further upside
- Clinical data for new products (in context of anticipated use) will be ≥ incumbents; expect **rapid inclusion in WHO Guidelines** released immediately post-SRA approval
  - Where SRA approved in even numbered year, WHO inclusion assumed to be next odd numbered year when updated guidelines are released
  - Choice of uptake curve will reflect preferred/alternate status and timing of inclusion in local guidelines
- **Rapid country-level registration** and availability once SRA approval secured
- **Negligible uptake** of new products **without** introduction as FDCs that represent the **same/lower pill burden** as incumbent products for major regimens
  - i.e. only launch year of equivalent FDC considered in forecast
- Relative **price differentials** between products will **remain largely the same** during the forecast period
  - Any changes not substantial enough to warrant changing initial uptake curve choice
- **VL testing** will be assumed to **not significantly change number of 2L patients** overall as net effect of VL testing in the real world remains to be seen
  - CHAI's baseline forecast based on this assumption

Four Competitive Sets are Most Apparently Relevant to Model for Adults in GA-LMICs

1 Replacing 1L TDF

Established Product
- TDF

New Entrants
- TAF

2 Replacing 1L EFV & NVP

Established Products
- EFV 600mg and NVP

New Entrants
- EFV 400mg and DTG

3 Replacing 2L TDF & AZT

Established Products
- TDF and AZT (+3TC/FTC)

New Entrants
- DTG

4 Replacing 2L PIs

Established Products
- LPV/r and ATV/r

New Entrants
- DRV/r

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New Entrants
- DRV/r

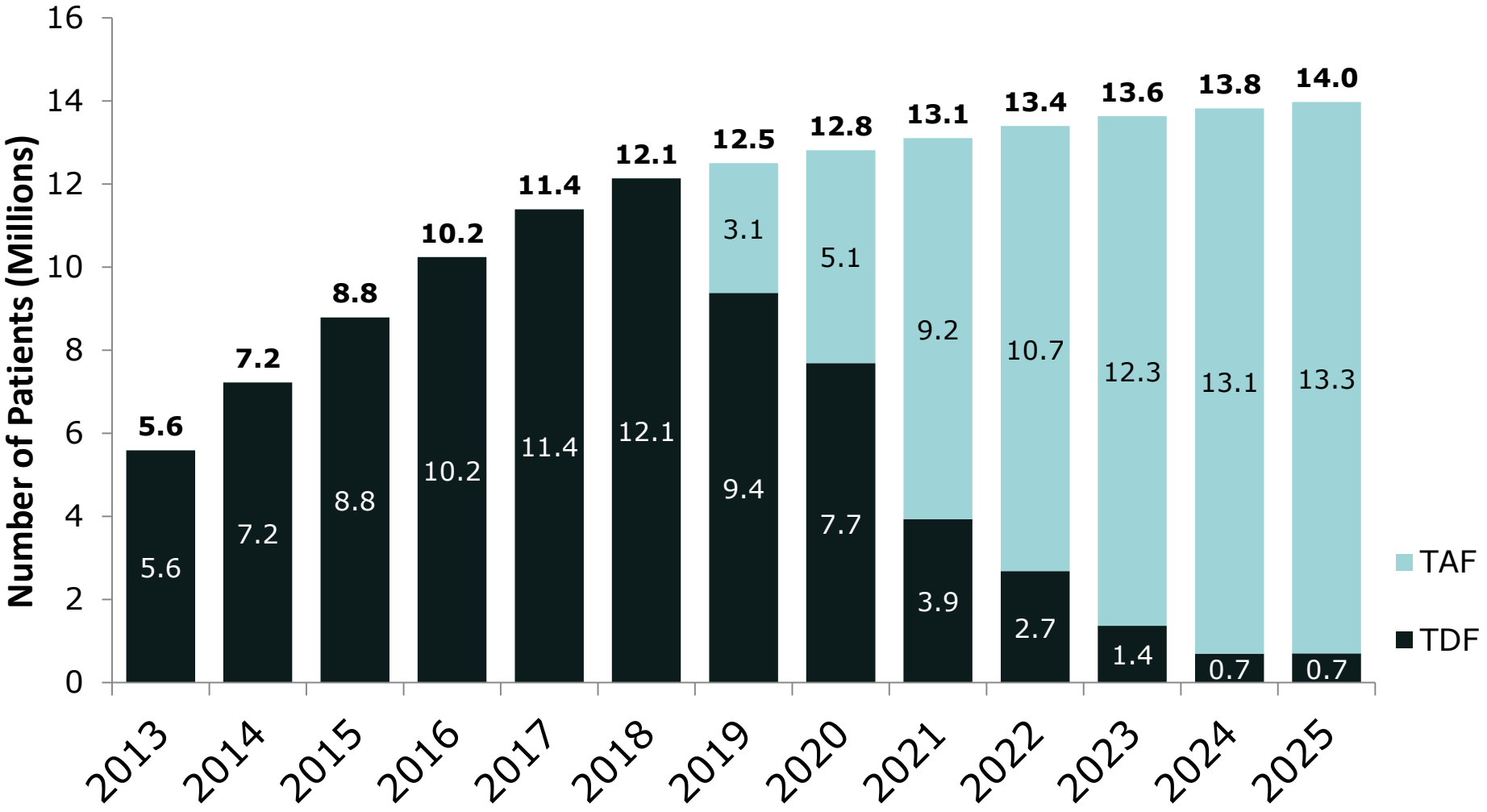
Adult 1L Backbone – Replacing TDF

	TAF
LMIC Launch Year *(of equivalent FDC)*	2019 *(2018 SRA approval)*
	vs. TDF or TDF(xb)
Price Differential	**+++**
Clinical Improvement	**+**
Substitutability	+++
Uptake curve choice: ***new patients***	Aggressive
Uptake curve choice: ***existing patients***	Aggressive

KEY	Price relative to incumbent	Clinical Improvement relative to incumbent	Substitutability
	+ 0-25% less	+ Slightly better AE profile	+ Different class of drug
	++ 25-50% less	++ Significantly better AE profile OR greater viral suppression/less resistance	++ Same class of drug, but different end active ingredient
	+++ >50% less	+++ Significantly better AE profile AND greater viral suppression/less resistance	+++ Same end active ingredient

TAF Expected to Rapidly Account for Vast Majority of First Line Tenofovir Patients

Patient Forecast for Replacement of 1L TDF, 2015-2025



Note: For each year, sum of all segments in bar chart reflects projected patient totals for current drug(s) shown for pertinent setting in the absence of newer drugs being introduced

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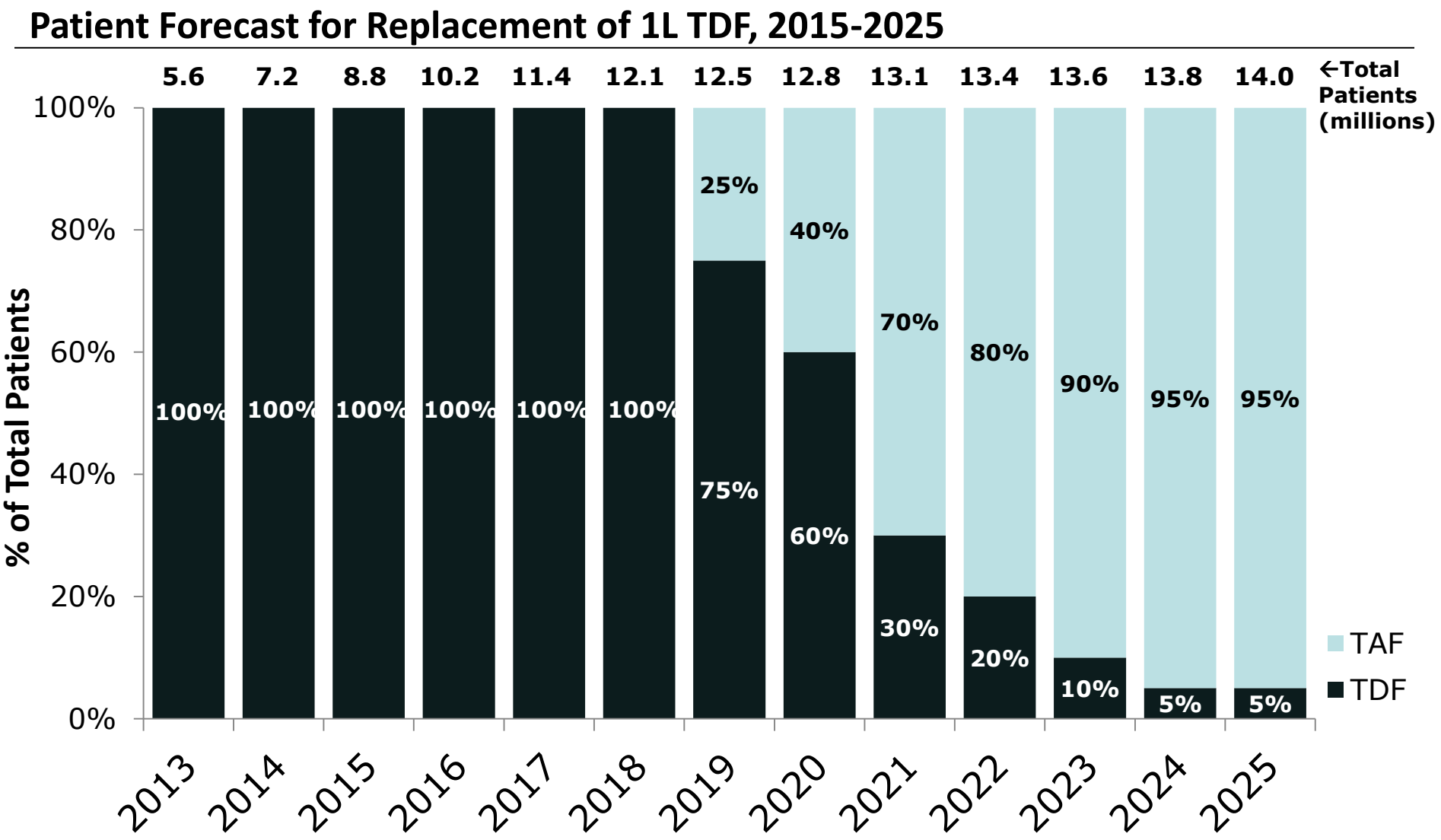

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Other Considerations for 1L TAF Forecast

- Timing of TAF launch in LMICs (i.e. generic SRA approval, inclusion in WHO guidelines) highly dependent on availability and acceptability of clinical data from cobicistat-unboosted studies
  - Current TAF/FTC switching study in virologically suppressed rather than treatment naïve patients
- Uptake shown assumes licensing agreements that allow combination with all agents, including DTG
- Dose-reduced TDF (TDF(xb)) has potential to provide cost savings bridge to eventual availability of TAF
  - Clinical data yet to be developed

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Established Products
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New Entrants
- EFV 400mg and DTG

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New Entrants
- DTG

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Replacing 2L PIs

Established Products
- LPV/r and ATV/r

New Entrants
- DRV/r

Adult 1L – Replacing EFV 600 and NVP

	EFV 400mg		DTG		
LMIC Launch Year *(of equivalent FDC)*	2017 *(2017 SRA approval)*		2017 *(2017 SRA approval)*		
	vs. EFV 600	**vs. NVP***	**vs. EFV 600**	**vs. NVP***	**vs. EFV 400****
Price Differential	+	+	+++	++	++
Clinical Improvement	+	++	+++	+++	++
Substitutability	+++	++	+	+	+
Uptake curve choice: *new patients*	Moderate	Moderate	Aggressive	Aggressive	Moderate
Uptake curve choice: *existing patients*	Moderate	Conservative	Moderate	Moderate	Moderate

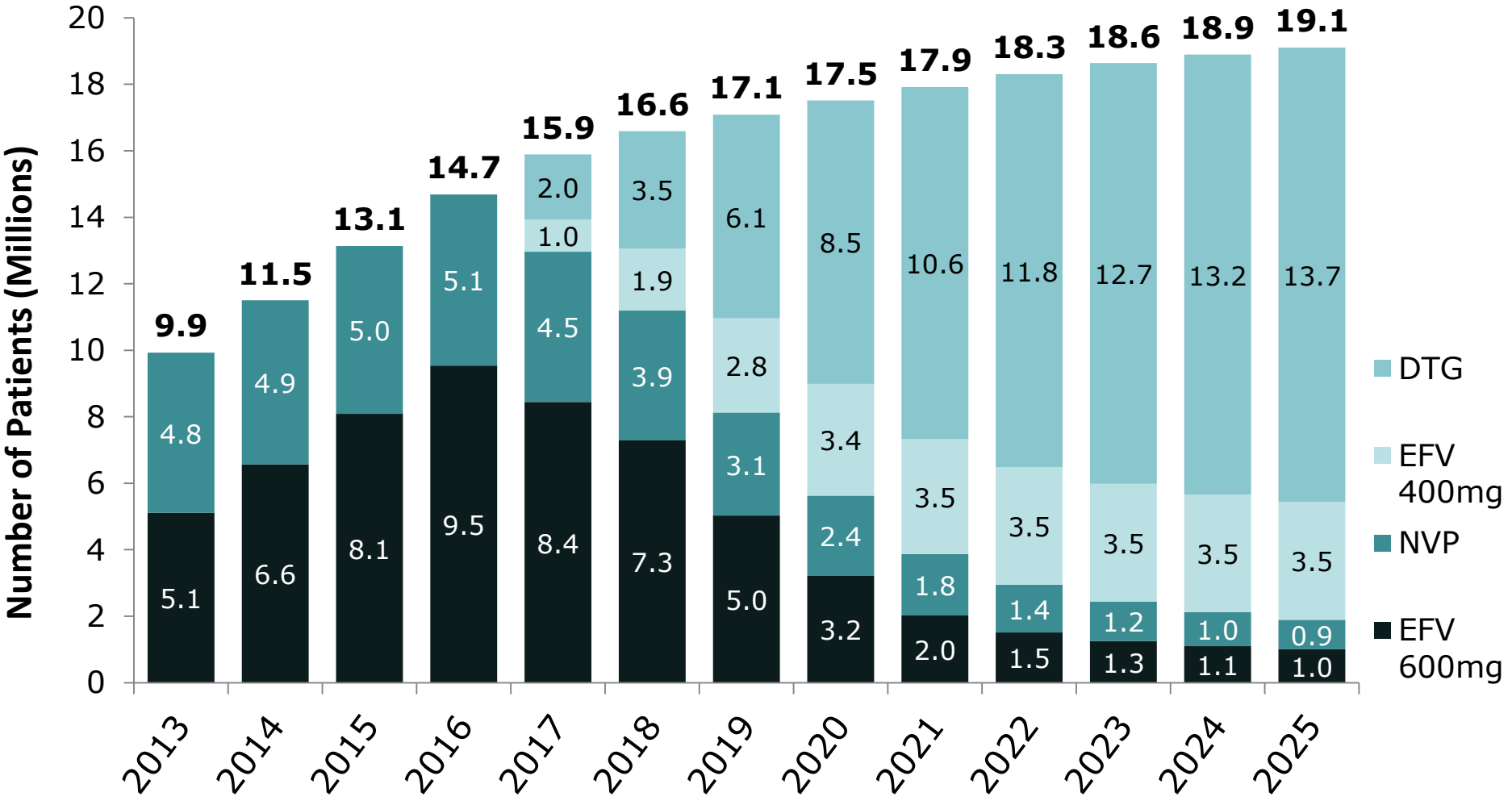
*NVP pts. who would not have otherwise been switched to EFV 600mg

**Incl. pts who would have otherwise been on EFV 600mg

KEY	Price relative to incumbent	Clinical Improvement relative to incumbent	Substitutability
	+ 0-25% less ++ 25-50% less +++ >50% less	+ Slightly better AE profile ++ Significantly better AE profile OR greater viral suppression/less resistance +++ Significantly better AE profile AND greater viral suppression/less resistance	+ Different class of drug ++ Same class of drug, but different end active ingredient +++ Same end active ingredient

DTG Likely to Represent Majority of Patients in 1L Who Would Have Otherwise Been on NNRTIs

Patient Forecast for Replacement of 1L NNRTIs, 2015-2025



Note: For each year, sum of all segments in bar chart reflects projected patients totals across current drugs for pertinent setting in the absence of newer drugs being introduced

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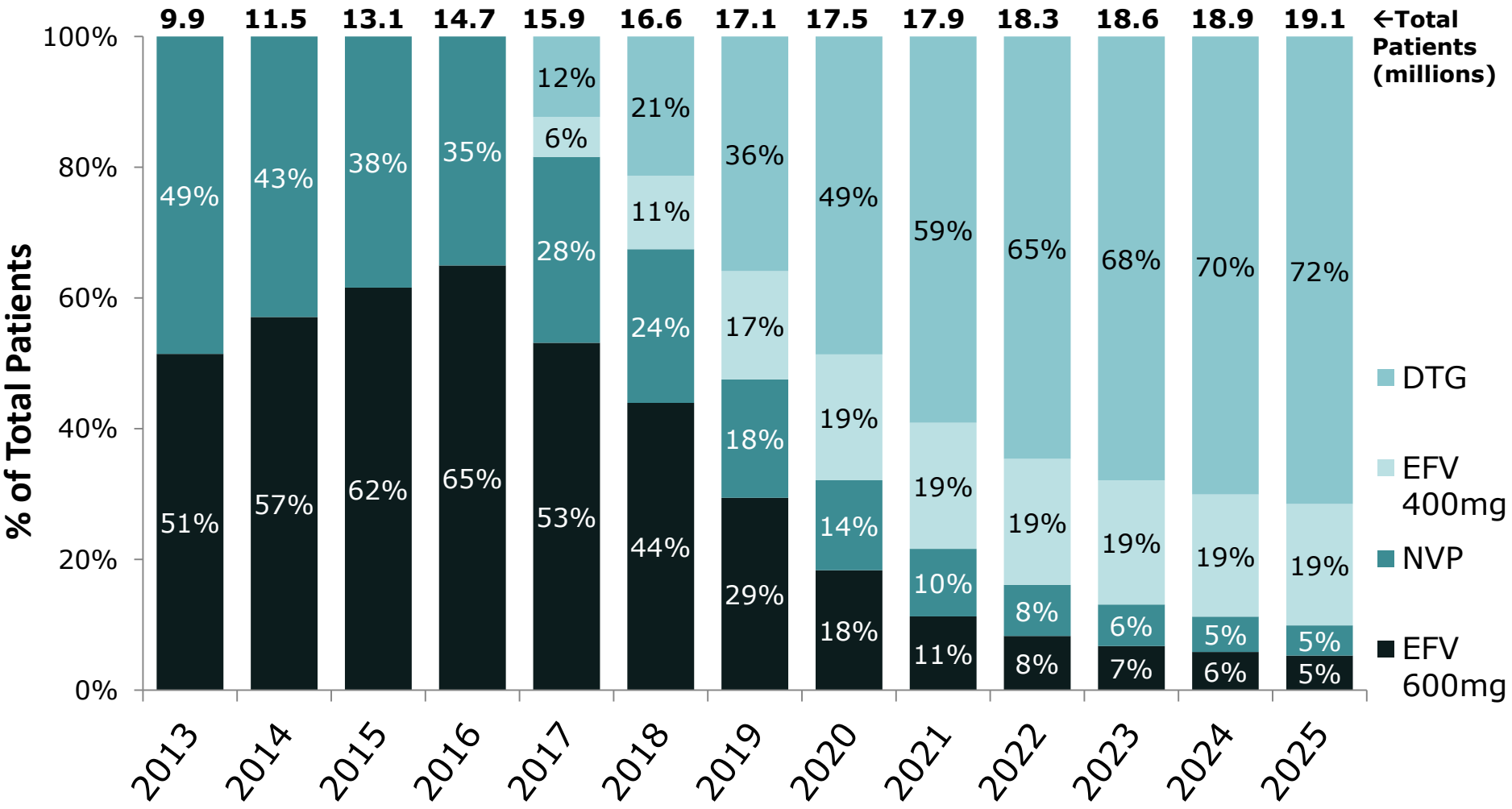
Patient Forecast for Replacement of 1L NNRTIs, 2015-2025



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Caveats to 1L DTG & EFV 400mg Forecast

- Timing of DTG launch in LMICs (i.e. generic SRA approval, inclusion in WHO guidelines) highly dependent on availability and acceptability of clinical data from studies with tenofovir
  - Limited H2H data of TLE vs. TLD
- Uptake shown assumes licensing agreements that allow combination with all current and future 1L backbone agents, including TAF
- Possibility that EFV 400mg could be perceived as a "developing world-only" or inferior product, reducing MoH receptivity

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Established Products
- EFV 600mg and NVP

New Entrants
- EFV 400mg and DTG

3

Replacing 2L TDF & AZT

Established Products
- TDF and AZT (+3TC/FTC)

New Entrants
- DTG

4

Replacing 2L PIs

Established Products
- LPV/r and ATV/r

New Entrants
- DRV/r

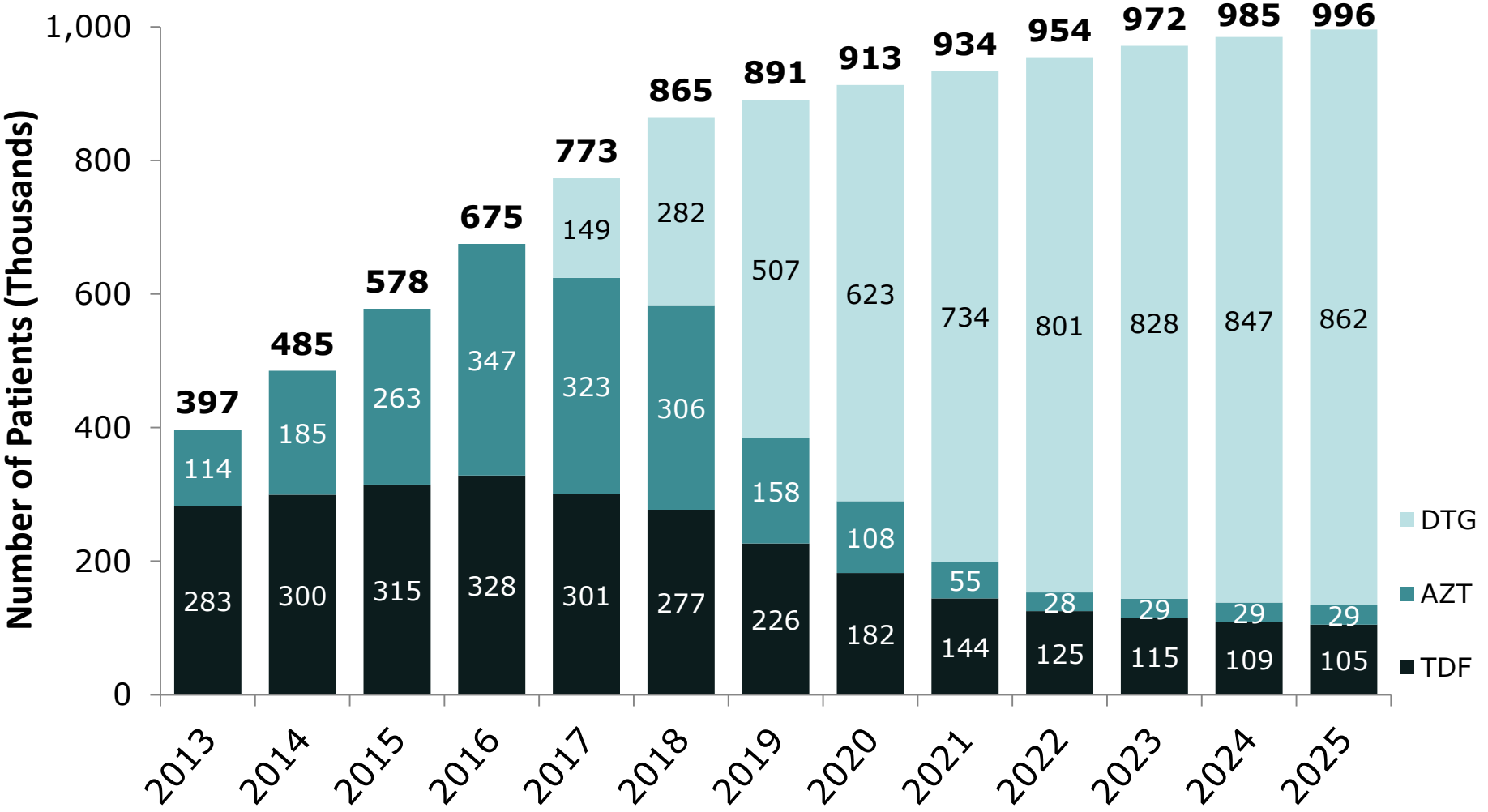
Adult 2L – Replacing TDF and AZT (+3TC/FTC) in Combination with PIs

	DTG	
LMIC Launch Year *(of equivalent FDC)*	2017 *(2016 SRA approval)* *(single would be equivalent to dual NRTI in this setting)*	
	vs. TDF	**vs. AZT**
Price Differential	+++	+++
Clinical Improvement	++	+++
Substitutability	+	+
Uptake curve choice: ***new patients***	Aggressive	Aggressive
Uptake curve choice: ***existing patients***	Moderate	Aggressive

KEY	Price relative to incumbent	Clinical Improvement relative to incumbent	Substitutability
	+ 0-25% less ++ 25-50% less +++ >50% less	+ Slightly better AE profile ++ Significantly better AE profile OR greater viral suppression/less resistance +++ Significantly better AE profile AND greater viral suppression/less resistance	+ Different class of drug ++ Same class of drug, but different end active ingredient +++ Same end active ingredient

DTG Will Likely Replace all 2L TDF & AZT use by 2025

Patient Forecast for Replacement of 2L TDF & AZT, 2015-2025



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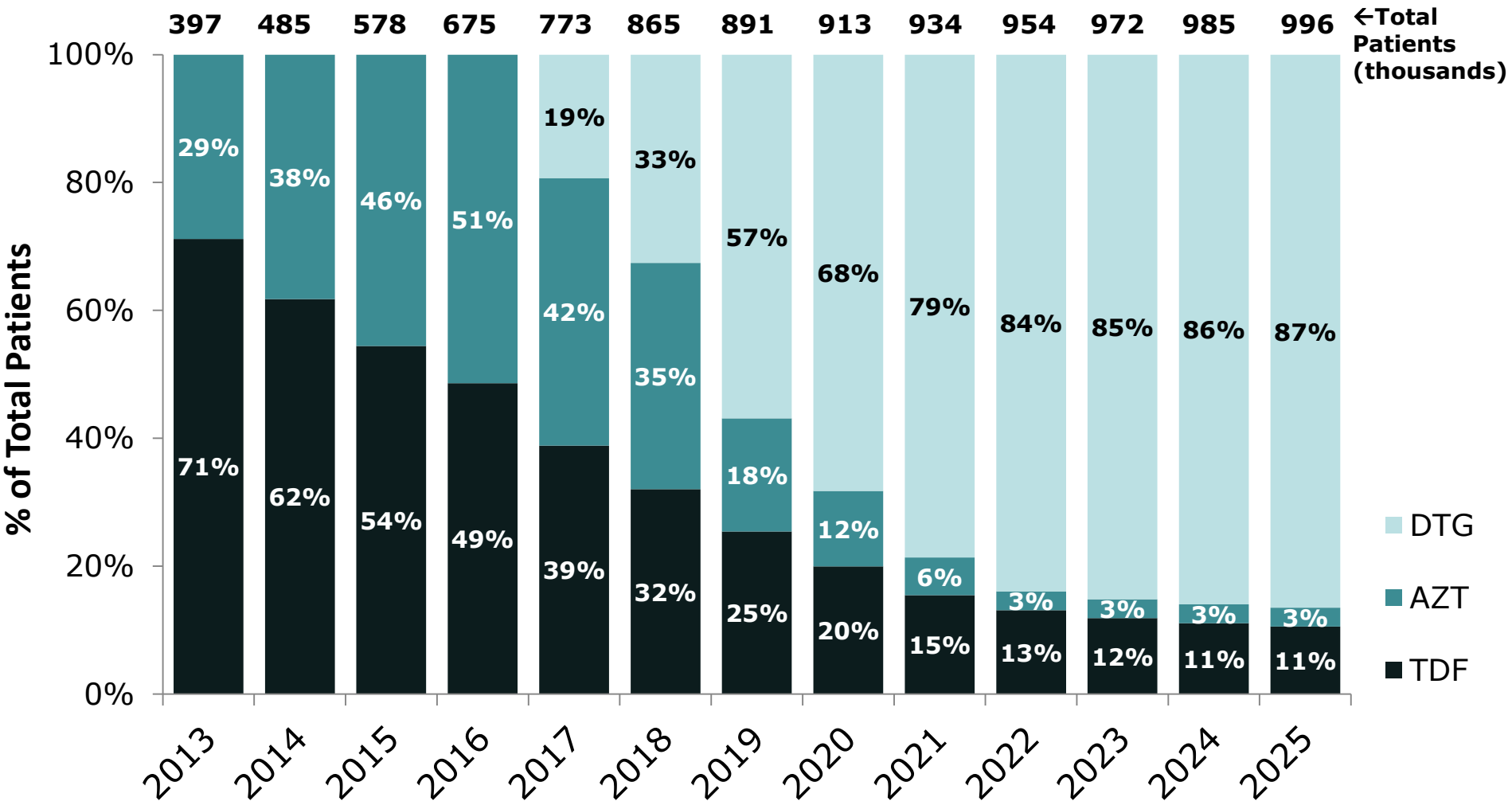

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Other Considerations for 2L DTG Forecast

- Possibility of DTG being included as an alternative option in 2015 guidelines, leading to some use in LMICs prior to 2017
- Even faster uptake of DTG in 2L possible if FDCs with PIs (one-pill, once-a-day) become available, further reducing pill burden relative to today's 2L regimens (2 pill minimum)

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New Entrants
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New Entrants
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- TDF and AZT (+3TC/FTC)

New Entrants
- DTG

4

Replacing 2L PIs

Established Products
- LPV/r and ATV/r

New Entrants
- DRV/r

Adult 2L – Replacing ATV/r and LPV/r

	DRV/r	
LMIC Launch Year *(of equivalent FDC)*	2016 (2015 guideline inclusion)	
	vs. LPV/r	**vs. ATV/r**
Price Differential	+	+
Clinical Improvement	+++	++
Substitutability	++	++
Uptake curve choice: *new pts*	Aggressive	Moderate
Uptake curve choice: *existing pts*	Moderate	Conservative

KEY	Price relative to incumbent	Clinical Improvement relative to incumbent	Substitutability
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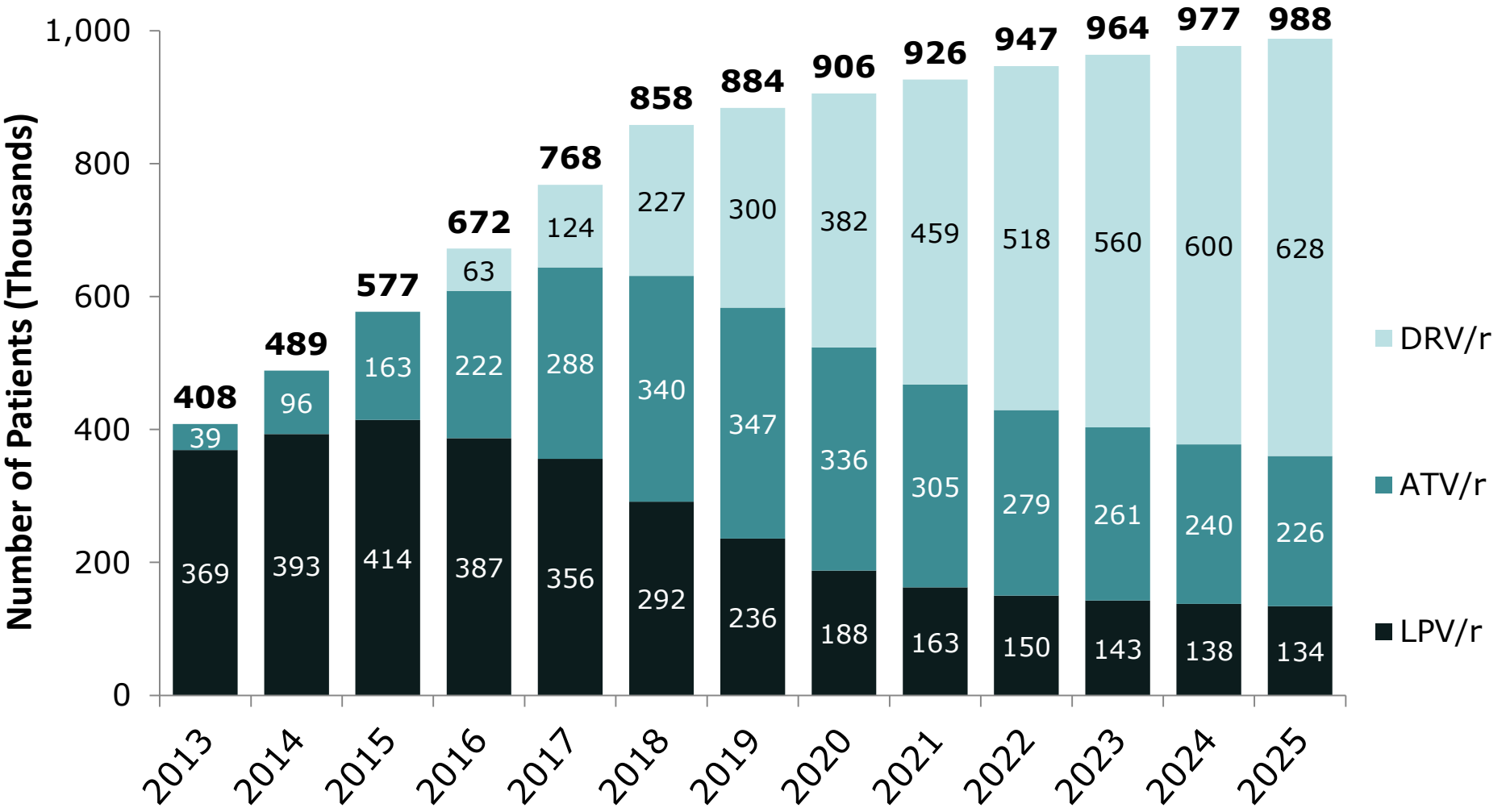
DRV/r Could Represent Majority of 2L PI Patients by 2025

Patient Forecast for Replacement of 2L PIs, 2015-2025



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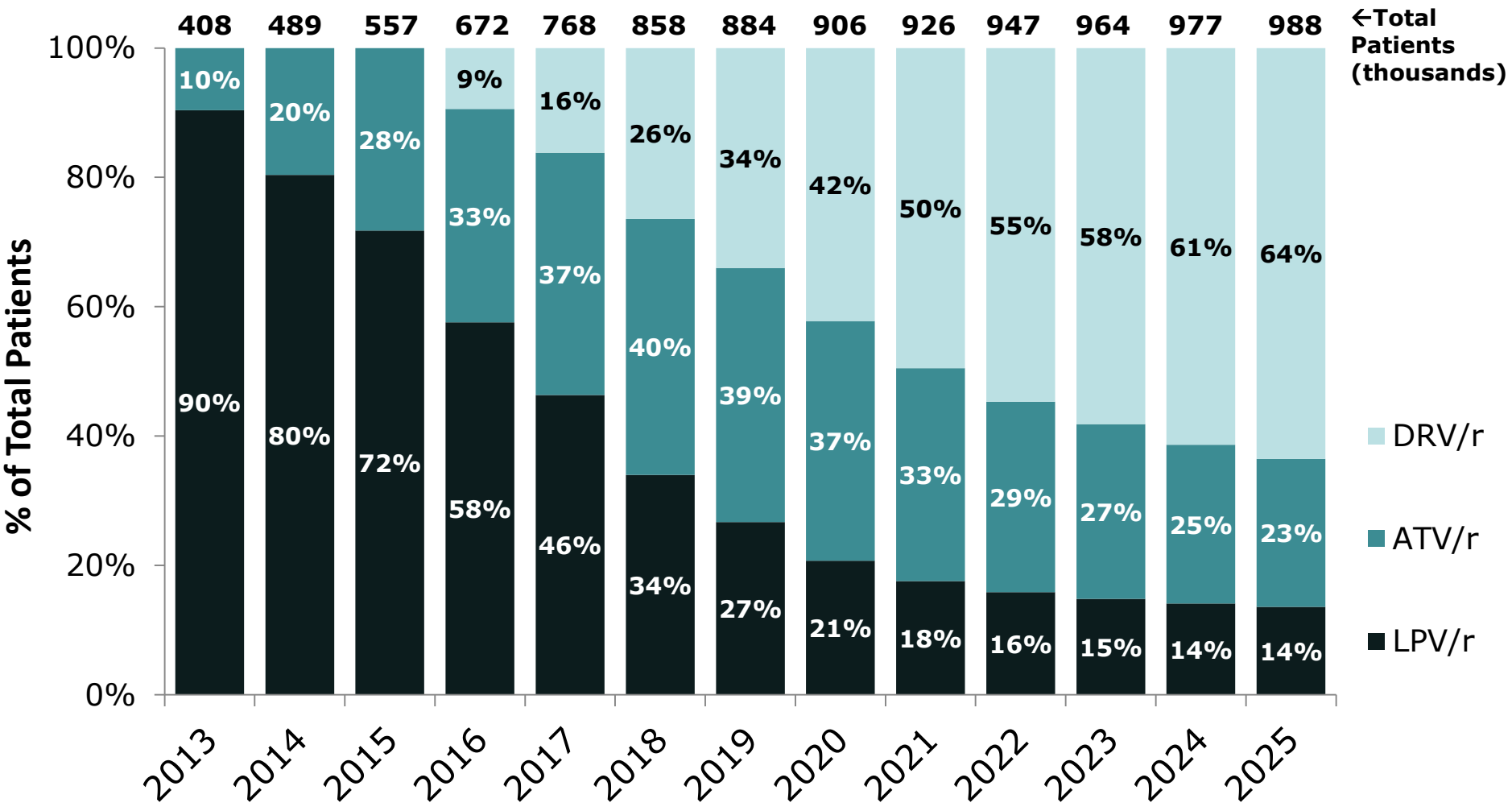

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Other Considerations for DRV/r Forecast

- Uptake of DRV/r highly dependent on presumed price reductions to parity with ATV/r, *at current clinical dosing*
  - Process chemistry improvements and labor cost reductions
- Timing of use in LMICs assumes promotion to preferred/alternate in 2015 WHO guidelines, *regardless of availability of heat-stable FDC at the time*
  - Presumed generic FDC availability by mid-2016
- Even faster uptake of DRV/r possible if:
  a) Dose-reduction efforts pan out, further reducing the price
  b) FDCs with DTG and TDF/3TC and/or TDF/FTC become available, further reducing pill burden relative to incumbent 2nd-line regimens (2 pill minimum)

Conclusions

- **Fast/first movers will benefit** from the opportunity presented by these products as **current drugs are replaced** by cheaper and more efficacious products

- Manufacturers encouraged to position themselves favorably by securing **timely SRA approvals** and country registrations, and preparing **production capacity** as necessary

- Several products identified with clinical and price benefits; however rate of **uptake** will be **highly dependent** on timely inclusion in **WHO guidelines**