Forecast vs Reality: are we on course?

Aastha Gupta, Medicines Patent Pool

Boniface Dongmo, World Health Organization

Vincent Habiyambere, World Health Organization

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Introduction

- Last year we presented methodology of MPP-WHO forecasts
- Presented full forecast at AMDS meeting, Geneva
- Forecasts published in PLOS ONE in October 2016
- Today: recap of the methodology and status check on validity of assumptions and results of the forecast

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Recap:
Forecasting Methodology & Assumptions

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Forecast Scenarios

Scenario 1: Conservative uptake of new ARVs

- Conservative timelines are projected for ongoing clinical study results to be available
- WHO guidelines do not prioritize new products based on lack of clinical data
- New products when launched show a low uptake in initial years

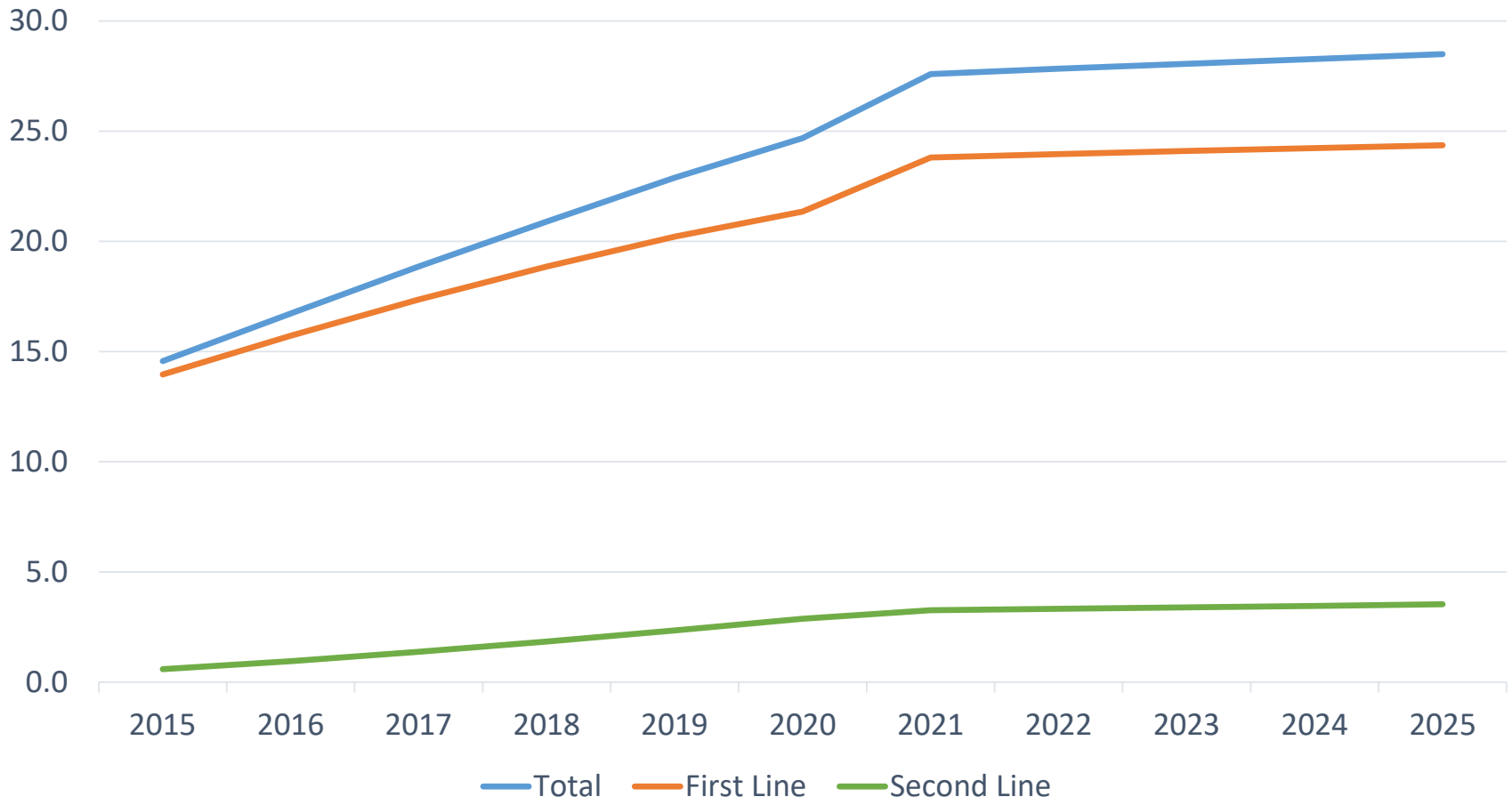
Scenario 2: Likely use of new ARVs

- Clinical study results are available in a timely manner
- WHO guidelines recommend new products, initially as alternate regimens till clinical data is made available, later progressing to preferred options

Scenario 3: Aggressive adoption of new ARVs

- WHO Guidelines recommend aggressive use of new products; DTG and TAF become preferred options recommended in 1st line soon after launch

Number of people on ART: UNAIDS Fast Track Report



Source: UNAIDS Fast Track Report

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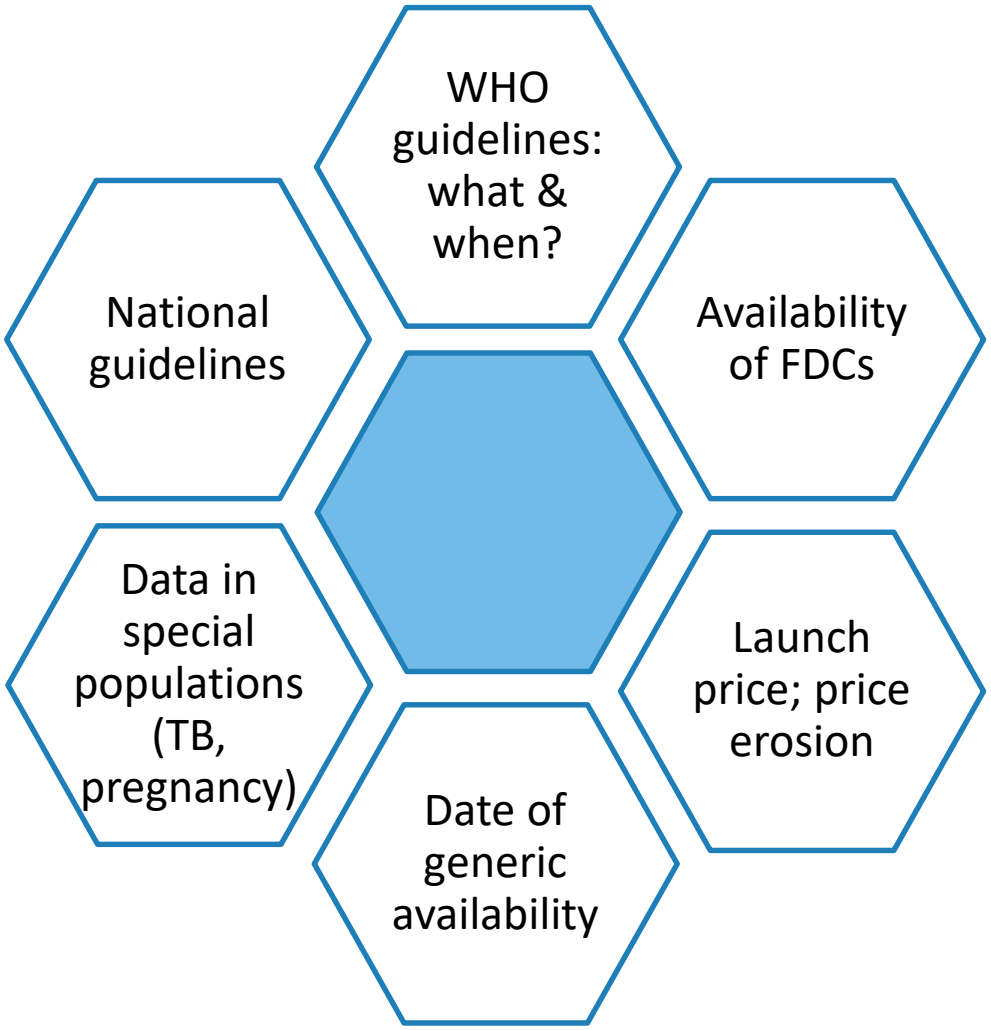
Key Variables



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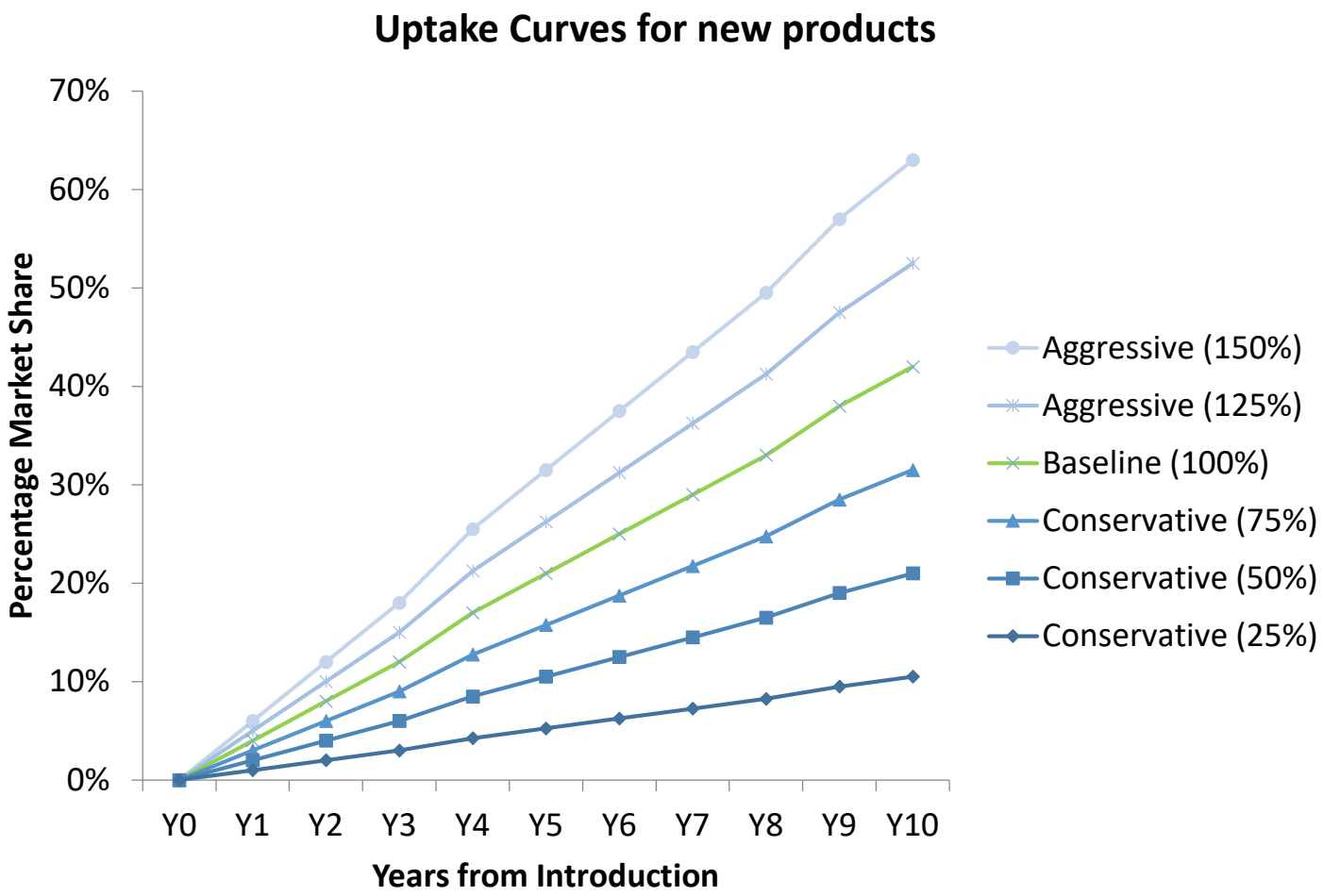
Uptake curves



- Baseline = historical use trend for TDF per GPRM, linearized
- Other uptake curves are based on the above
- Each new product follows one of these curves based on the scenario and based on each product
- At different times, one product may follow different curves, taking into account higher or lower usage of drug with each year (example in next slide)

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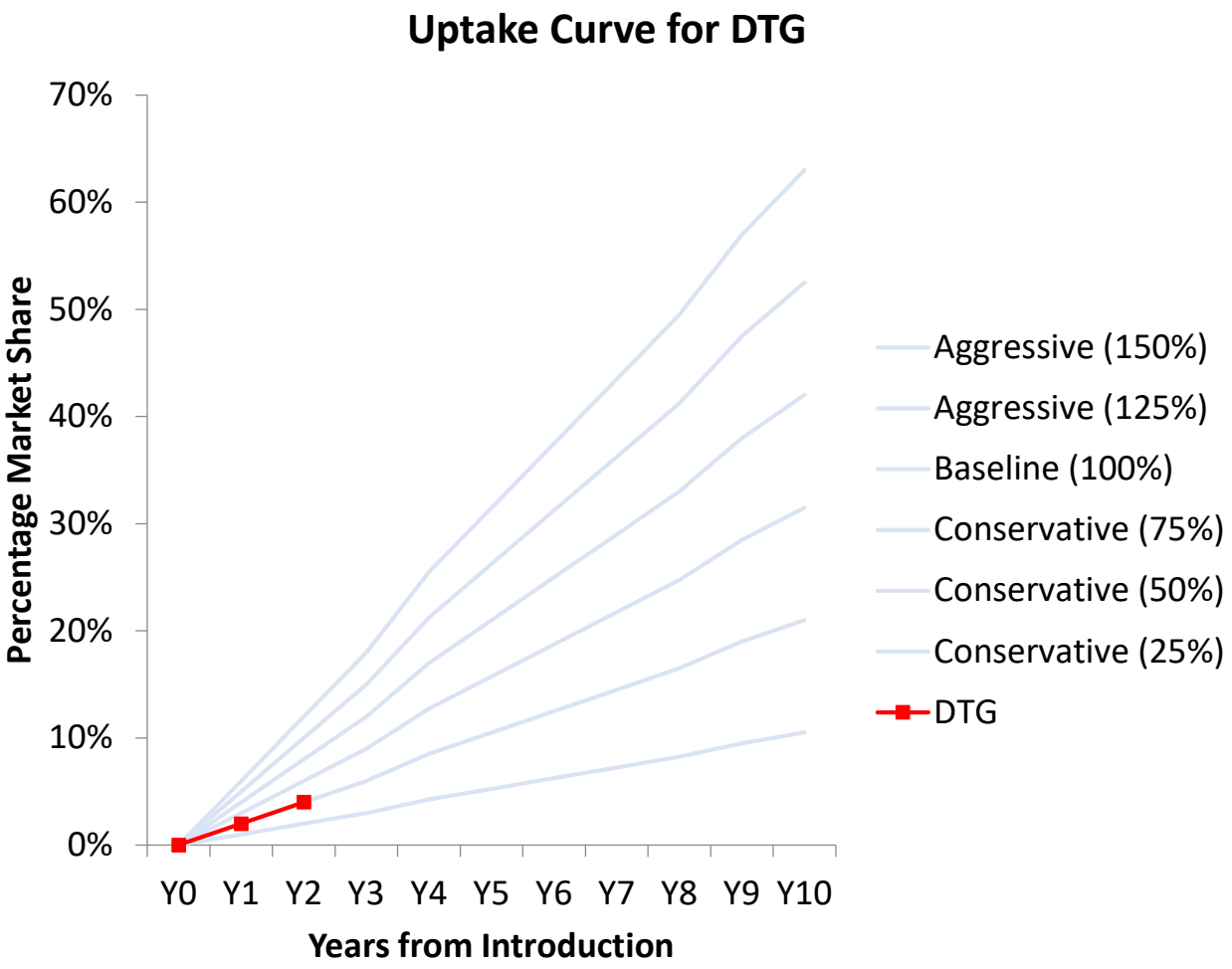
Example of Uptake curve used for DTG in first line treatment



The model uses different uptake curves for DTG for 1st line ART post its introduction in 2017 (likely scenario)

- Initial uptake is conservative = 50% of baseline
  - DTG recommended as alternate use in first line (as per WHO Guidelines 2015)
  - FDCs not available initially
  - Country registrations and uptake is limited
  - Price comparable with EFV

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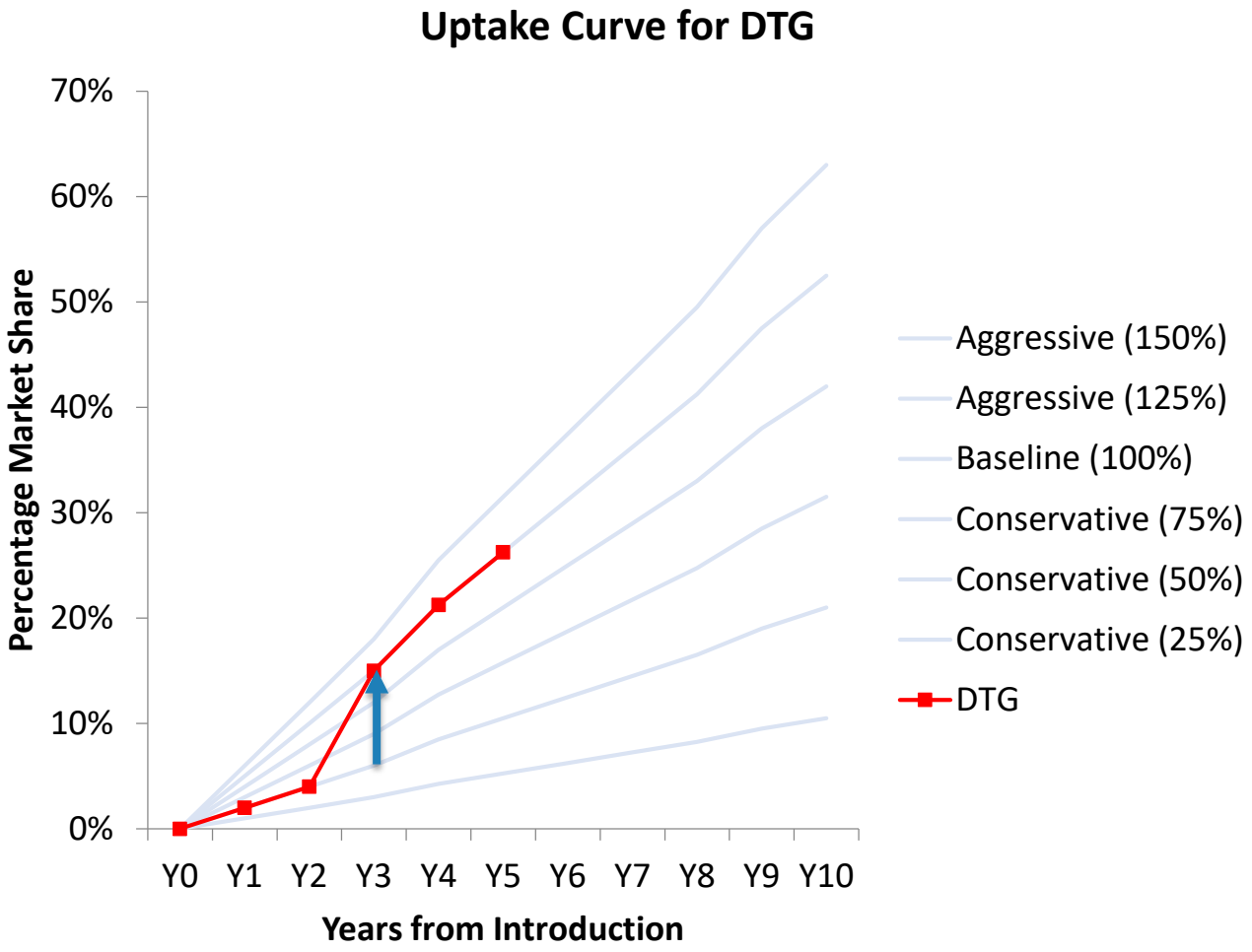
Example of Uptake curve used for DTG in first line treatment



- Uptake from Year 3 = 125% baseline
  - Study results in special populations are available and positive
  - Generic FDCs available
  - WHO guidelines shift the product to a preferred treatment in first line
  - More national approvals
  - Price of single agent falls

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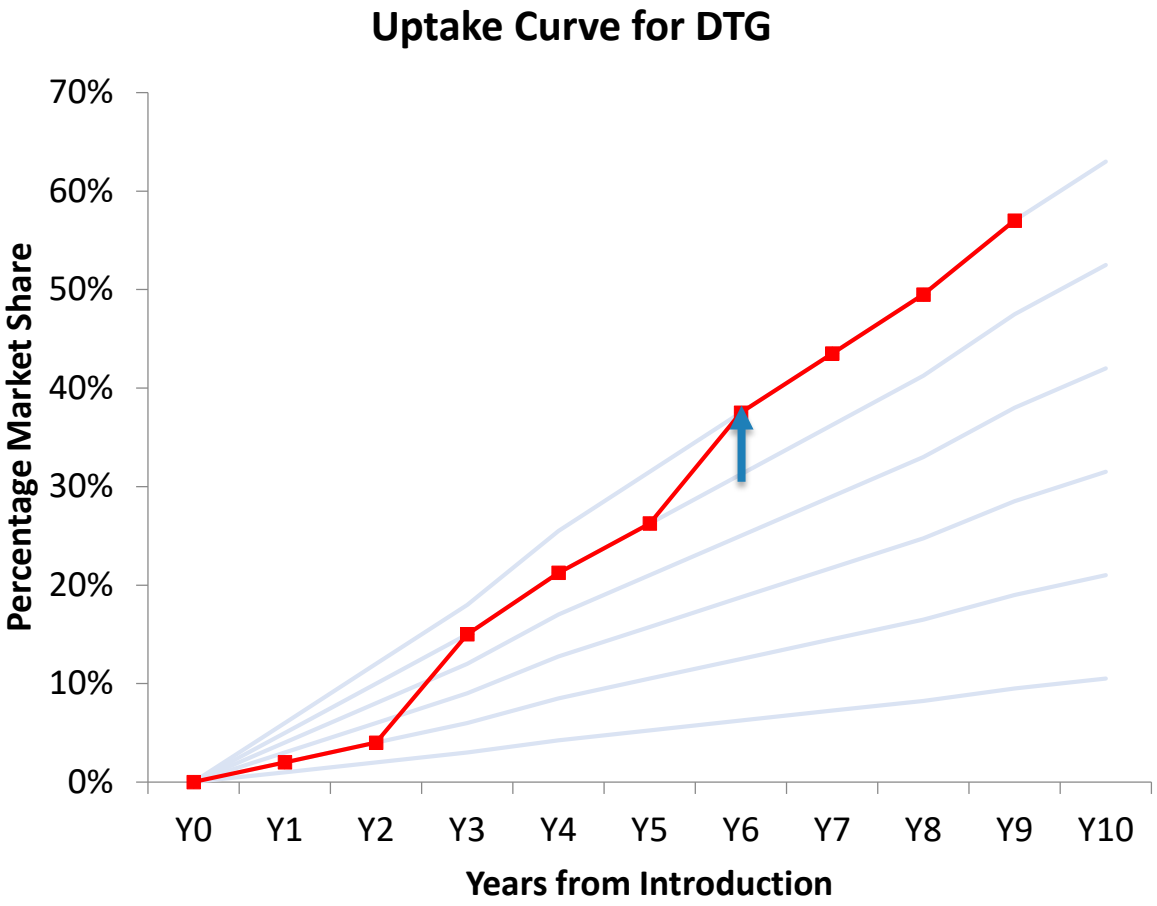
Example of Uptake curve used for DTG in first line treatment



- Uptake from Year 6 = 150% baseline
  - Price drop of generic FDCs
  - More national approvals
  - Widespread country level use

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Assumptions on Likely Scenario

Date of Introduction (>1 Gx)

- DTG 50mg: Q4-2017
- DTG FDCs: Q3-2018
- TAF FDCs: Q1-2019

Price Differential

- Launch Price:
  - DTG & TAF priced at par with EFV & TDF respectively
- Future pricing basis historical erosion trends

Clinical Assumptions

- Positive study results for DTG & TAF in TB co-infection and pregnant women
  - Including potential drug-drug interaction of TAF with RIF
- WHO Guidelines recommend new ARVs: first as alternate and then as preferred

Country Level Uptake

- New products come on National Guidelines within one year from WHO recommendation
- Use starts shortly thereafter

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Validity of Assumptions Today

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Date of Introduction

Assumptions

Date of Introduction (>1 Gx)

- DTG 50mg: Q4-2017
- DTG FDCs: Q3-2018
- TAF FDCs: Q1-2019

Scenario Today

DTG 50mg:

- One generic in market
- Three more filed in Q4-16

TDF/3TC/DTG:

- Two generics have filed by Feb-17

TAF FDCs:

- No filings yet

Forecast assumptions valid

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Country filing plans

Planned Filing	DTG 50mg	TLD
Number of countries	80	70
% PLHIV coverage in countries open for generic supply	97.5%	96.8%

Number of Countries	DTG 50mg	TLD
Where 1 to 3 companies plan to file	55	48
Where > 3 companies plan to file	25	22

With more visibility from licensees in the coming months, a wider coverage is expected

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Price Differential

Assumptions

Price Differential

- Launch Price:
  - DTG & TAF priced at par with EFV & TDF respectively
- Future pricing basis historical erosion trends

Scenario Today

2016 prices

- DTG 50mg @ $44/year
- EFV 600mg @ $36.2/year
  - = 20% premium in year of introduction, with one generic in market; no FDCs

DTG price at a slight premium; may change as more generics and FDCs come to market in the coming months

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Clinical Assumptions

Assumptions

Clinical Assumptions

- Positive study results for DTG & TAF in TB co-infection and pregnant women
  - Including potential drug-drug interaction of TAF with RIF
- WHO Guidelines recommend new ARVs: first as alternate and then as preferred

Scenario Today

Studies underway for DTG and TAF

(See next two slides)

WHO Guidelines 2016 recommend DTG in first-line (alternate) and third-line ARV treatment

Forecast assumptions valid

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New ARVs and TB drugs: Current Studies

DTG & TAF STUDIES IN TB

Study	Drug	Intervention	Major outcomes	N	Country	Expected Completion
INSPIRING (ING117175)	**DTG**	Safety /efficacy of DTG vs EFV in PLHIV with TB confection using RIF (50 mg DTG twice daily vs 600 mg EFV once daily during TB treatment)	VL at 24 and 48 weeks, CD4 changes, treatment discontinuation, AEs; HIVDR	**125**	Argentina, Brazil, Mexico, Peru, Russian Federation, South Africa, Thailand)	**Q4 2017**
SSAT 075	**TAF**	TAF and TDF pK in presence of RIF (HIV negative patients)	TDF DP levels	**20**	South Africa	**Q4 2017**

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New ARVs in Pregnancy: Current Studies

DTG & TAF STUDIES IN PREGNANT WOMEN

Study	Drug	Intervention	Major outcomes	N	Country	Expected Completion
DOLPHIN 1	**DTG**	DTG pK in pregnant women with HIV	pK data in 3rd trimester and 2 weeks postpartum; maternal VL at delivery	**60**	South Africa Uganda	**Q4 2017**
DOLPHIN 2	**DTG**	DTG safety/efficacy/ tolerability in pregnant women with HIV	pK data 3rd trimester and 18 weeks post partum, maternal VL at delivery, breast milk sterilization	**250**	South Africa Uganda	**Q1 2021**
ING200336	**DTG**	DTG pK and safety in unintended pregnancies in ARIA study (DTG/ABC/3TC vs ATV/r+ TDF/FTC)	pK data in 2nd and 3rd trimester; pK in neonates, maternal and infant adverse events; adverse pregnancy outcomes, maternal disease progression and fetal transmission	**25**	Spain, Russia, UK, USA	**Q1 2019**
WAVES OLE	**TAF**	TAF safety/efficacy/ tolerability in pregnant women with HIV (TAF/FTC/EVGc vs ATV/r +TDF/FTC)	Maternal VL at 48 weeks	**583**	Belgium, Dominican Republic, France, Italy, Mexico, Portugal, Puerto Rico, Russia, Thailand, Uganda, USA, UK	**Q2 2017**
IMPAACT P1026s	**DTG TAF**	DTG and TAF pK in women with HIV on ART > 20 weeks of pregnancy and post partum	pK data (during pregnancy and post partum), pK data in neonates, maternal:cord blood ration, maternal and infant AEs, adverse pregnancy outcomes	**100**	Argentina, Botswana, Brazil, Puerto Rico, South Africa, Thailand, Uganda, USA	**Q3 2017**
IMPAACT P2010	**DTG TAF**	DTG and TAF safety/efficacy in women with HIV starting ART at 14-28 weeks of pregnancy (DTG+ TAF/FTC vs DTG/TDF/FTC vs EFV/TDF/XTC)	Maternal VL at delivery, adverse pregnancy outcomes, maternal toxicity, SAB, foetal deaths, infant AEs, mother-infant ARV transfer at birth and from breast milk	**549**	Argentina, Botswana, Brazil, Puerto Rico, South Africa, Tanzania, Thailand, USA, Zimbabwe	**Q3 2018**
PANNA	**DTG TAF**	DTG and TAF safety/efficacy in women with HIV receiving ART and < 33 weeks of pregnancy	PK data in week 33 of pregnancy and 4-6 weeks after delivery, pK data in neonates; maternal VL and fetal transmission; maternal and infant AEs; adverse pregnancy outcomes	**32**	Belgium, Germany, Ireland, Italy, Netherlands, Spain, UK	**Q4 2020**

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Country Transition Plans

Assumptions

Country Level Uptake

- New products come on National Guidelines within one year from WHO recommendation
- Use starts shortly thereafter

Scenario Today

- Multiple countries procuring DTG 50mg: Botswana, Kenya, Nigeria, Uganda, Ukraine, CIS countries

Forecast assumptions valid

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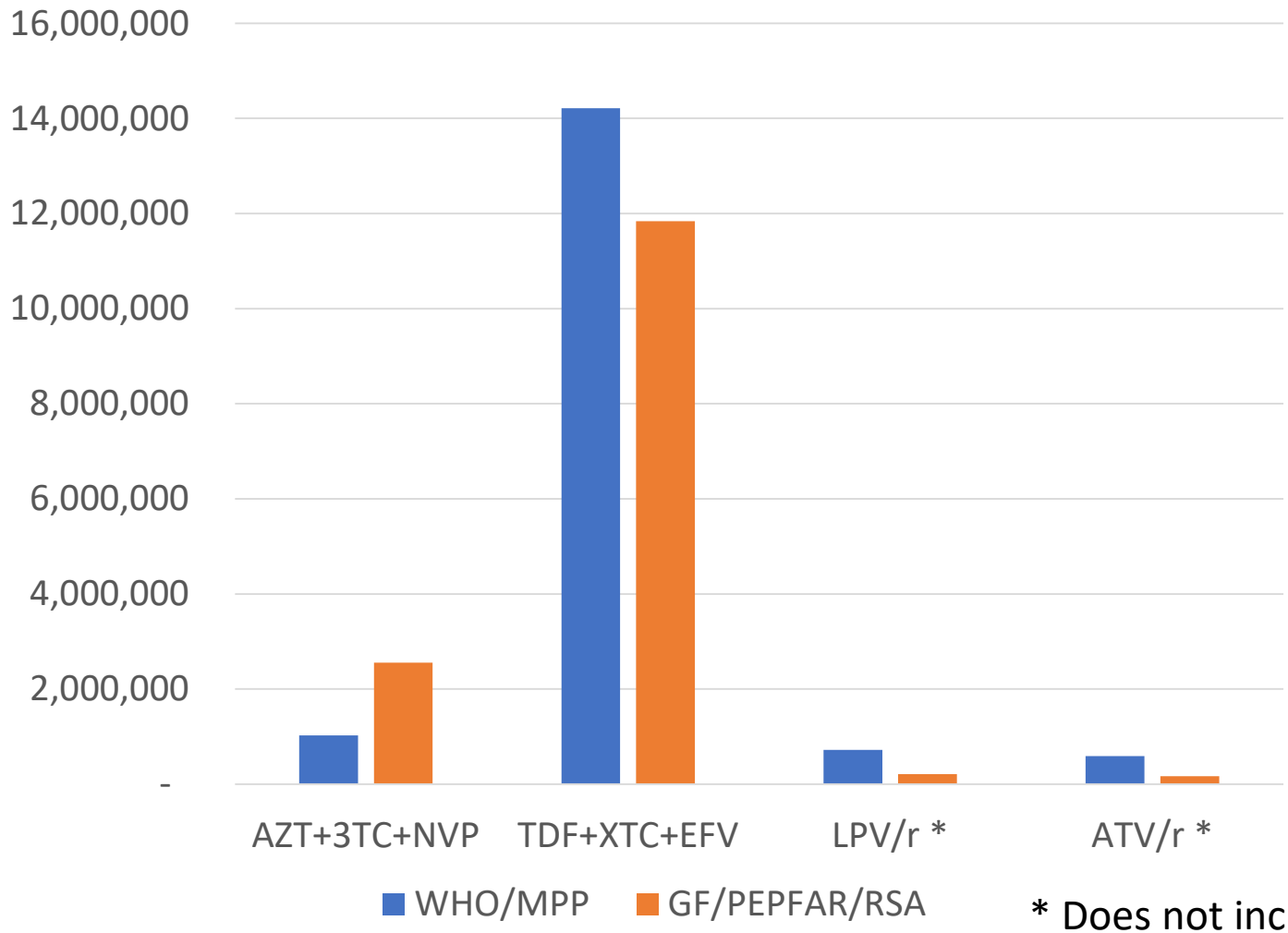
Validity of Results

Number of PLHIV on ART by regimen: WHO-MPP projections vs. GF/PEPFAR/RSA demand in 2017 for existing products



- GF/PEPFAR/RSA account for ~80% of market
- Includes double and triple FDCs
- Main product TDF+XTC+EFV: variance of 17%
- LPV/r and ATV/r: with information from RSA, the two projections would likely be close

* Does not include RSA data

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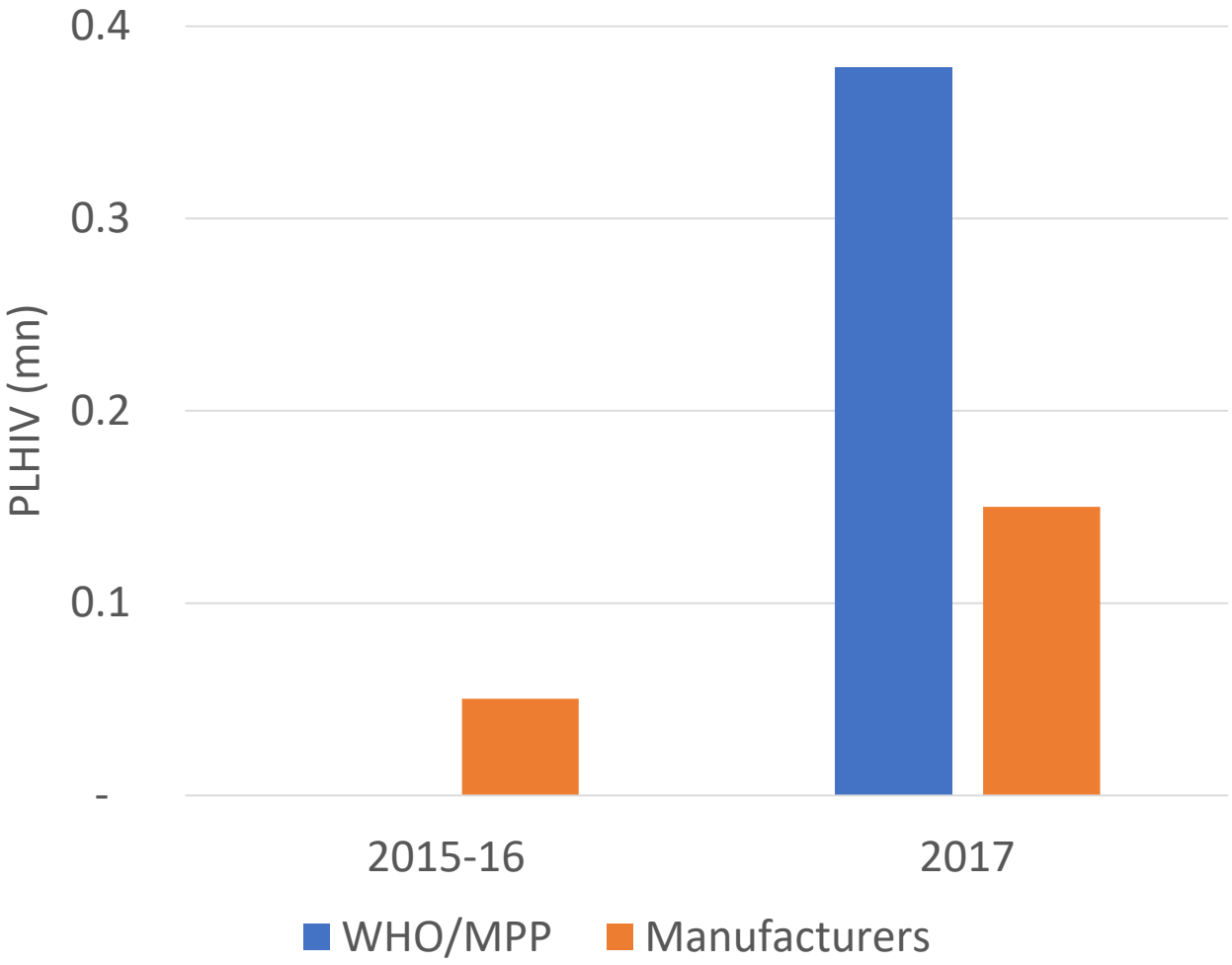
WHO-MPP projections vs. visible uptake from manufacturers for DTG so far



- 2015-16: data from existing suppliers of DTG and ARV Use Survey
- 2017: data from existing suppliers of DTG, based on current demand visibility as at end Q1 2017

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Conclusion

- Forecast assumptions are on track
- Positive developments:
  - Low price point @$44 pppy
  - >95% coverage for national registrations
  - DCGI approval to waive local clinical trials for FDCs on WHO EOI; will help get FDCs to market faster
- We need more for increased uptake:
  - Clinical studies for TAF and DTG to allow WHO to add TAF on Guidelines and to make DTG a preferred regimen
  - Fast track in-country approvals
  - WHO collaboration procedure – possibility of extension to countries not under agreement
  - Encourage countries to use new ARVs faster

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