The CQUIN Learning Network

Annual Meeting

Introduction of New ARVs in the Context of DSD

Nandita Sugandhi M.D.
ICAP at Columbia University

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HIV LEARNING NETWORK
The CQUIN Project for Differentiated Service Delivery

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Columbia University
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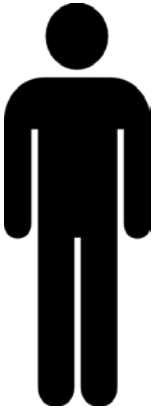
Objectives

- Introduction of a new optimal ARV: Dolutegravir
- Considerations for new ARV introduction in the context of DSD
  - Sub-populations
  - Clinical characteristics
  - Context

What is an optimal ARV

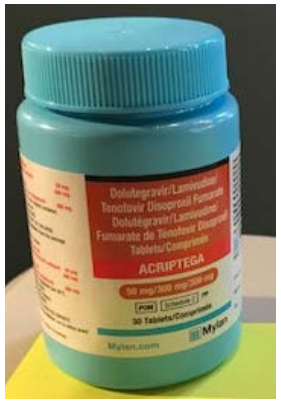
- Effective
- Low toxicity
- Well tolerated and easy to take
- Durable/high genetic barrier to resistance
- Better sequencing/switching
- Harmonized across populations
- Reduced cost



2016 WHO Guidelines: ART recommendations for adults and adolescents included dolutegravir (DTG)

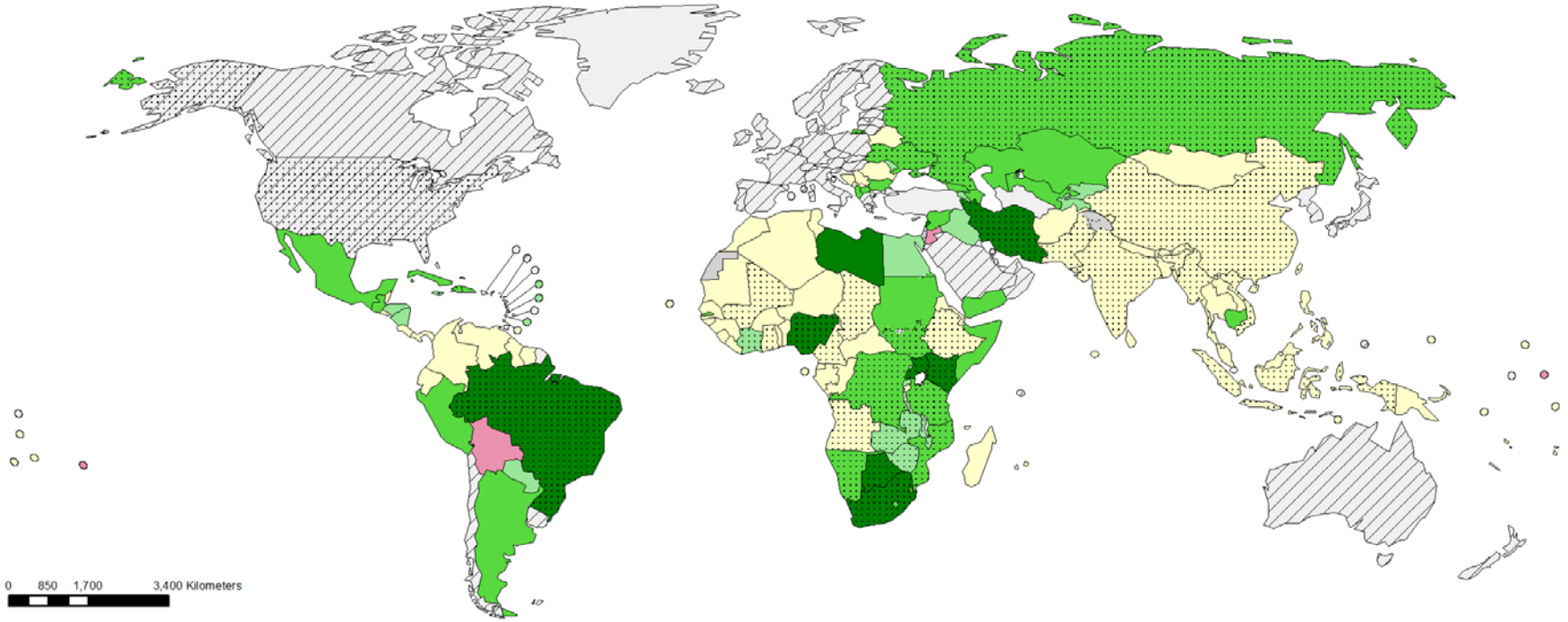
	PREFERRED	ALTERNATIVE
First-line ART	TDF + XTC + EFV	AZT + 3TC + EFV (or NVP) TDF + XTC + **DTG** TDF + XTC + EFV_{400} TDF + XTC + NVP

- A "best in class" integrase inhibitor
- Once-daily dosing
- Well tolerated and low toxicity
- High genetic barrier to resistance
- Affordable options now available
  - DTG 50mg)
  - TDF/3TC/DTG (TLD)



US$ 75 per patient per year

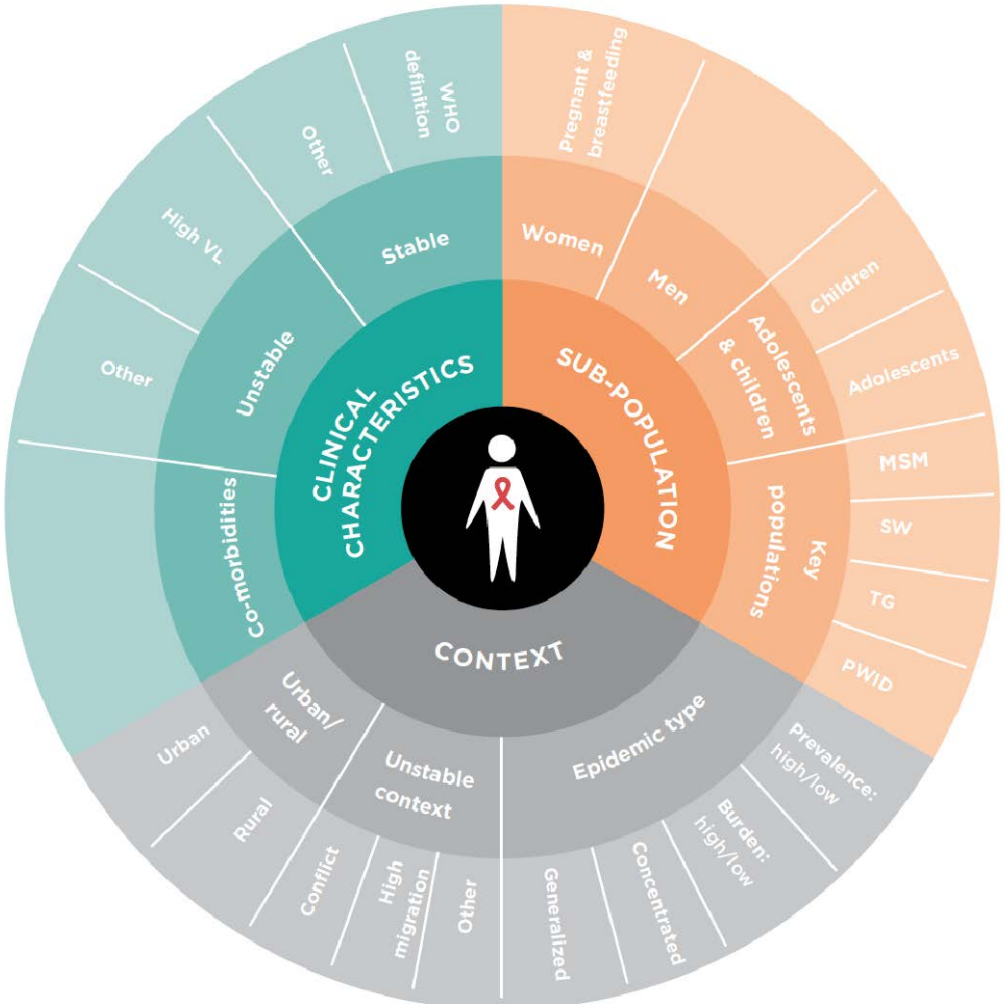
TDF/3TC(FTC)/EFV as the preferred first line ARV combination among adults and adolescents and initial shifts towards Dolutegravir (DTG) in low- and middle-income countries (situation as of November 2017)



Data Source: World Health Organization
Map Production: Information Evidence and Research (IER)
World Health Organization

World Health Organization

Introduction of new treatment options in the context of Differentiated Service Delivery



1. Sub-populations
2. Clinical characteristics
3. Context

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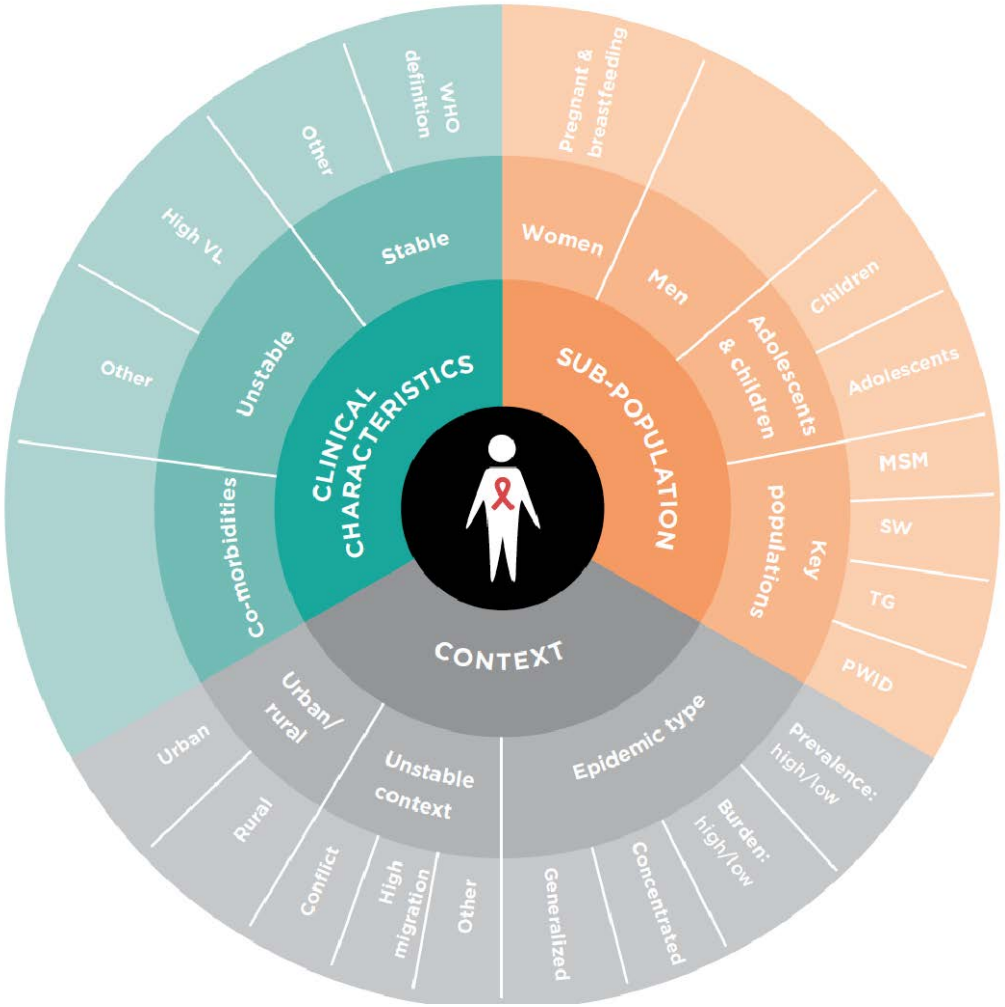

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Sub-populations and considerations for DTG

Considerations for use of DTG in first line ART		
✓	Newly initiating patients	Superior to EFV and boosted PI's in newly initiating patients
✓	Patient currently on first line ART (NNRTI or bPI based)	Patients currently on 1st line may substitute for NNRTI or bPI
✓	Pregnant women	Increasing evidence to support regular dosing in pregnancy and no differences in pregnancy/birth outcomes compared with EFV (programmatic cohort studies)
✓	Patients on TB treatment	Can be dosed 50mg twice-daily during rifampicin-containing TB treatment (pK data). More data expected at CROI2018 (Additional DTG 50mg tablet needed)
✓	HIV-2	Effective in both HIV-1 and HIV-2
✓	Women using family planning	No interaction with hormonal contraception
✓	HCV co-infection	No interaction with Hepatitis C treatment (e.g direct acting antivirals)
✓	IVDU	No drug interaction with OST
✗	Infants and younger children	Currently only approved for children ≥ 6 yrs/ ≥ 15kg

Variety of approaches for prioritizing patients for DTG

Country	DTG eligibility criteria					Pregnancy during DTG use	TB during DTG use	Use VL for DTG substitution
	ART naive	NNRTI intolerance	NNRTI exposure/ contra indication	PW	TB			
Botswana	✓	✓	✗	✓	✓	Stay on DTG	Stay on DTG (double dose)	✗
Brazil	✓	✓	✗	✗	✗	Switch to RAL	Switch to RAL	✗
Kenya	✗	✓	✗	✗	✗	Switch to EFV	Stay on DTG, (double dose)	✓
Nigeria	✗	✓	✓	✗	✗	Switch to EFV or ATV/r	Switch to EFV or LPV/r	✓
Uganda	✓	✓	✗	✗	✓	Switch to EFV or ATV/r	Stay on DTG (double dose)	✓

Sub-populations and considerations for DTG

Population	Rationale
Newly initiating patients	Simple programmatic approach
Patients on suboptimal 1st line regimens (e.g. AZT/3TC/NVP)	Supports harmonization across populations and reduces use of suboptimal regimens
Patients on TDF/3TC/EFV experiencing side effects	Better tolerated regimens may improve adherence
Acute HIV infection Newly diagnosed pregnant or breastfeeding women	Benefit of rapid reduction in viral load
Adolescents	Benefit of high genetic barrier to resistance

Harmonizing paediatric treatment

- Currently approved in children ≥ 6 yrs/ ≥ 15kg (EMA)
- Ongoing work to establish dosing in younger children and infants as well as using dose of 50mg OD in children ≥25kg*
- **Available in 50mg, 25mg and 10mg tablets**
- Generic formulations in development of DTG and ABC/3TC/DTG

Paediatric DTG Dosing (EMA)	
Body weight (kg)	Dose
15 to less than 20	20mg OD
20 to less than 30	25mg OD
30 to less than 40	35mg OD
40 or greater	50mg OD

* TDF/3TC 300mg/300mg already recommended in children ≥30kg. Use of DTG 50mg in this age group would enable use of TLD

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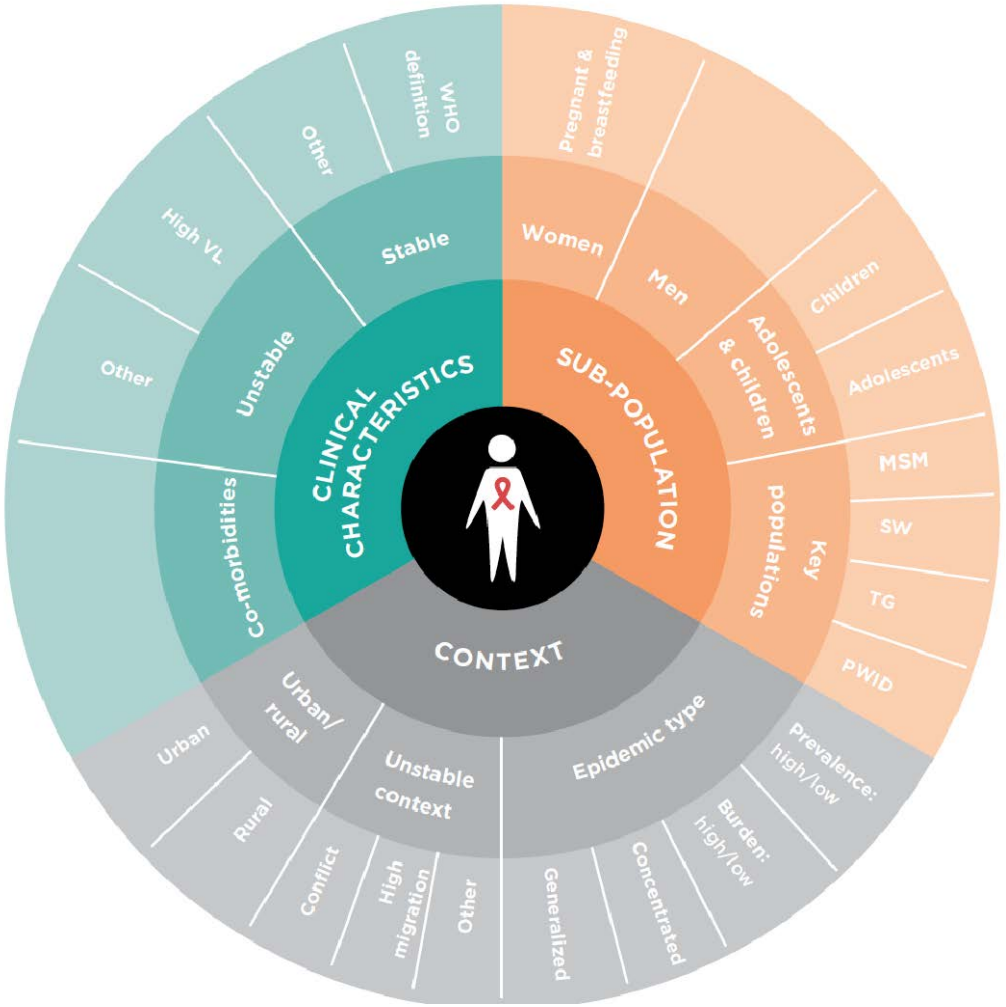

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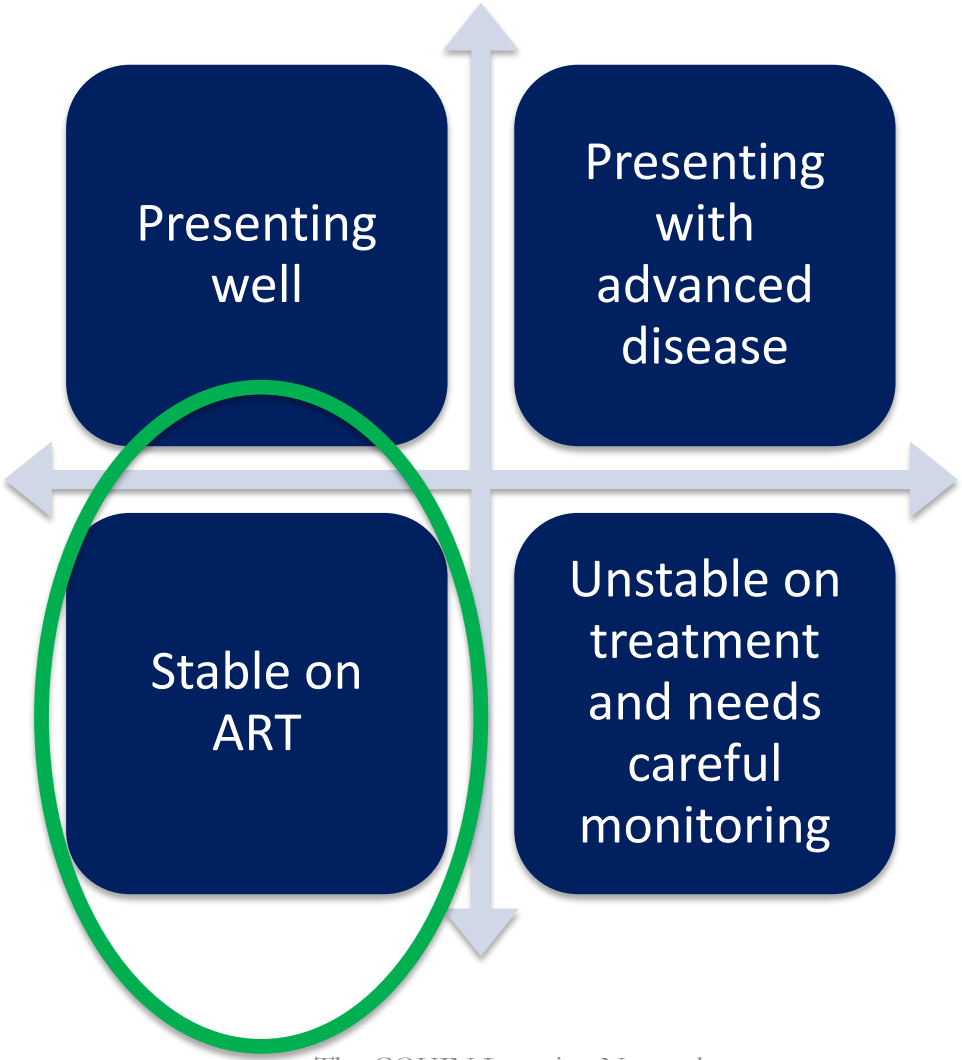
Clinical characteristics and considerations for DTG



Prioritized for transition?

- Clinical appointment spacing
- Multimonth dispensing
- Task sharing
- Community ART distribution

Increased risk of IRIS?

Adherence support or switch needed?

Are stable patients still "stable" after transitioning to a new ARV?

- Is more frequent clinical monitoring needed and for how many visits?
  - Will need for frequent appointments be a disincentive to switch
  - Will demand for a new drug overwhelm facilities that are trying to decongest

- Is available supply adequate and reliable enough to give multimonth prescriptions?

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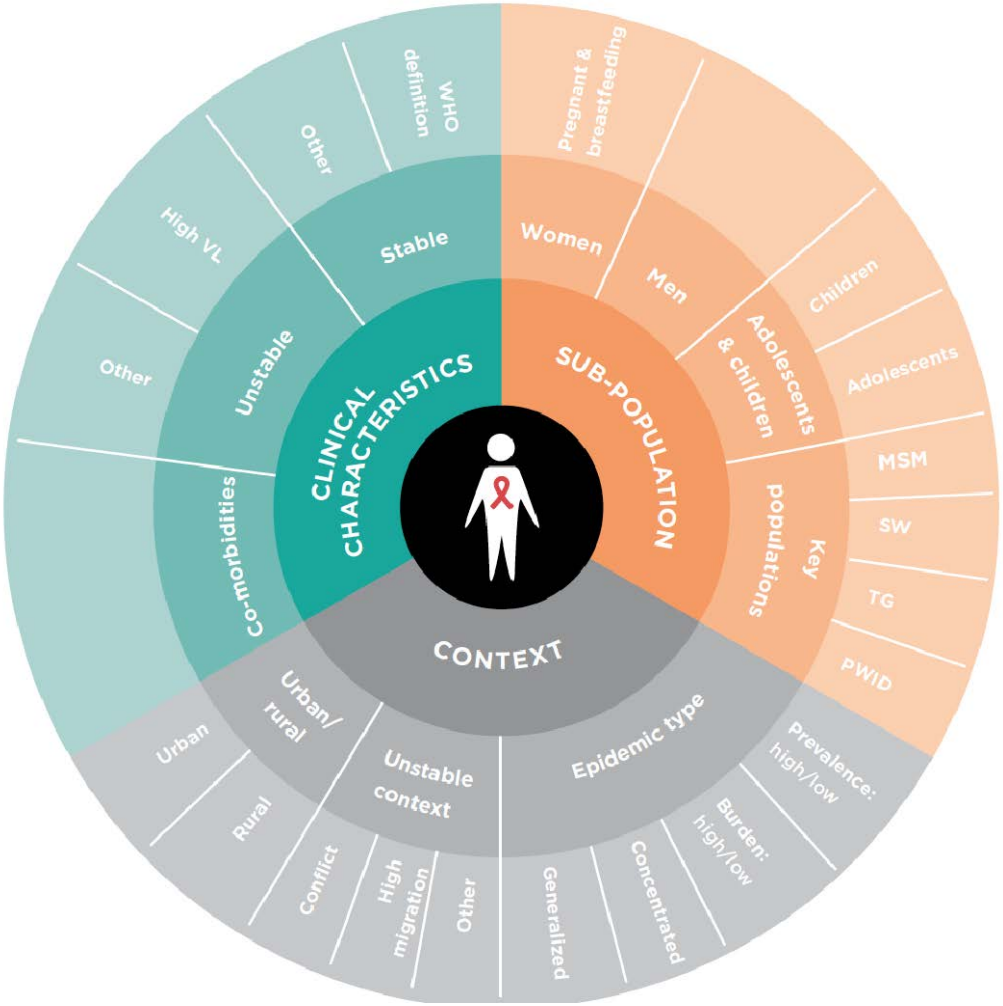

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Context and considerations for the introduction of DTG

- Who is able to prescribe and monitor patients transitioning to DTG
- Should patients be transitioned and monitored at the health facility or in the community
- How do we communicate our transition plans and provide timey updates
- What should be done for migrant populations
  - Regional and subnational harmonization

Conclusion:

- New recommendations are not implemented in isolation and planning should take this into account

- Service delivery questions to ask when introducing new ARVs:
  - **Who** should be prioritized for new ARVs?
  - **When** and **how** frequently is monitoring needed?
  - **Where** should new ARVs be prescribed, dispensed and monitored?
  - **How** much stock and supply security is needed to support multimonth prescribing of new ARVs?

Thank you!

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https://optimize.icap.columbia.edu/