PEPFAR Priorities & HIV Drug Resistance: Where are we heading and what has us worried

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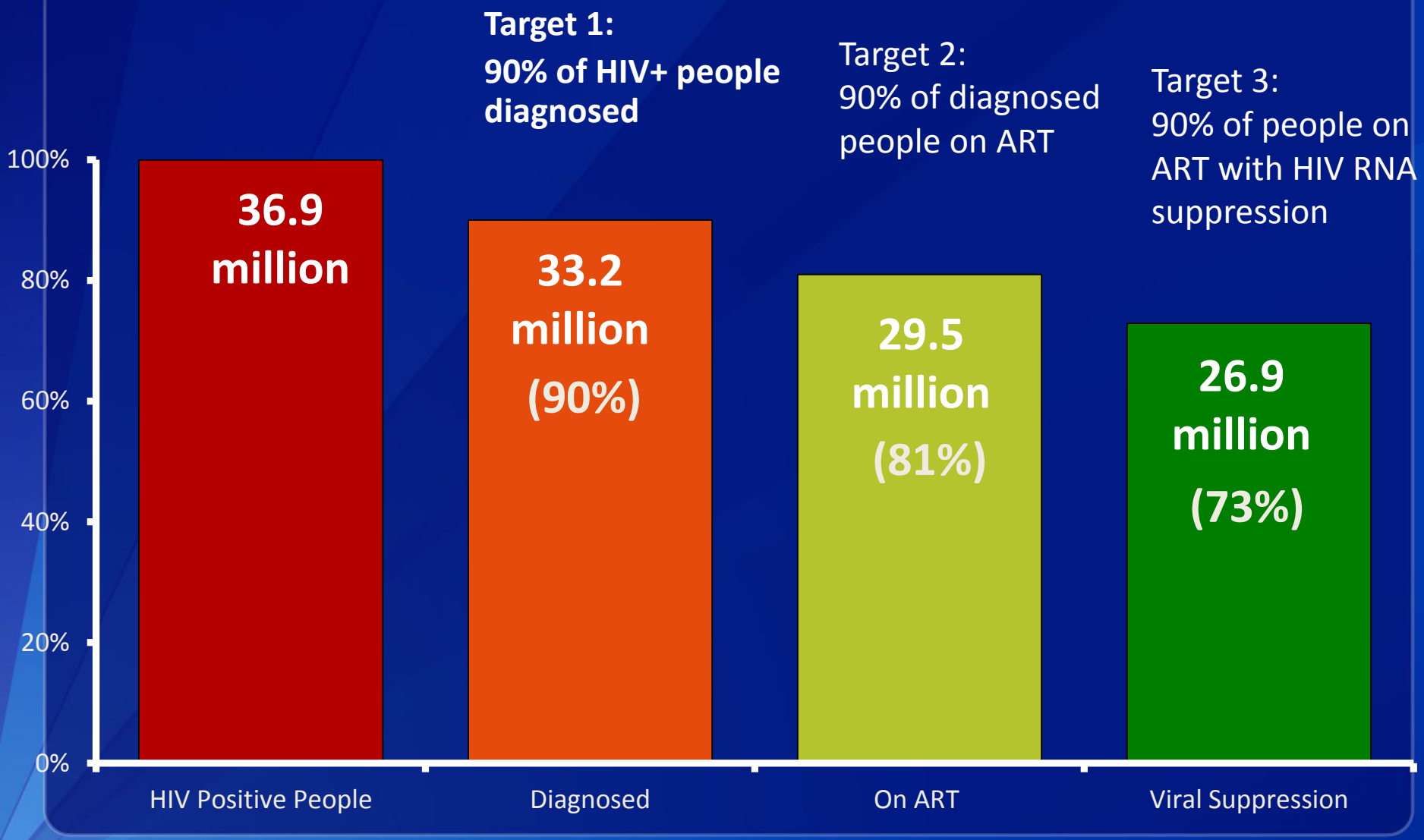
President's Emergency Plan for AIDS Relief (PEPFAR): A brief history

- **Phase 1 (2003-2008): Emergency response**
  - Delivering prevention, care, & treatment services
  - Building and strengthening health systems to deliver HIV services
- **Phase 2: (2008-2013): Shift to sustainable response**
  - Shared responsibility & country-driven programs
  - Scaling up ART, Prevention of Mother-to-child transmission (PMTCT), and voluntary male circumcision (VMMC) for impact
- **Phase 3: (2013-): Controlling the epidemic**
  - Quality, oversight, transparency, & accountability for impact
  - Accelerating core interventions (ART, PMTCT, VMMC) for epidemic control

PEPFAR supports UNAIDS Fast Track Targets for Ending the AIDS Epidemic by 2030

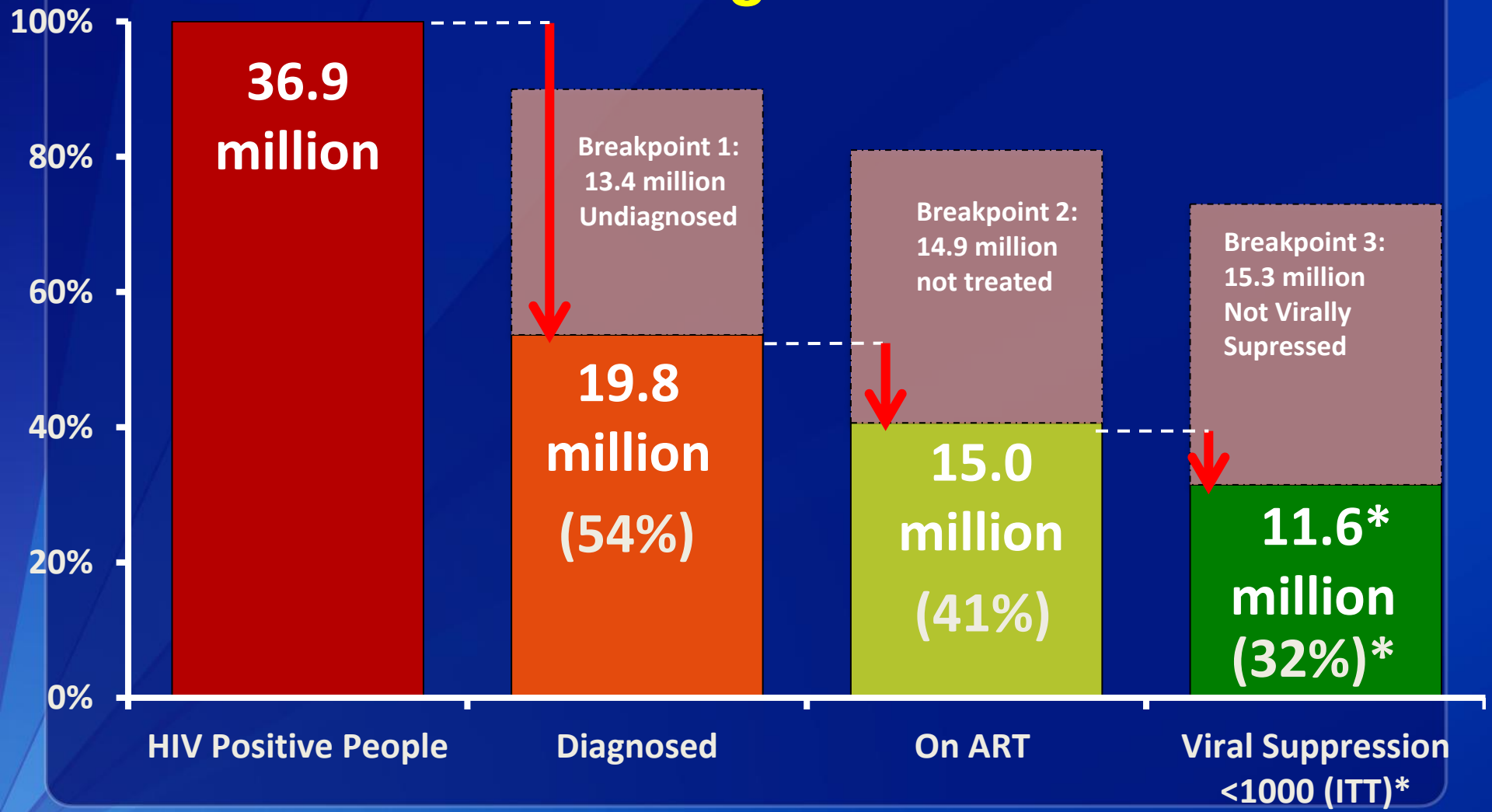
UNAIDS: 2014

UNAIDS 90-90-90:
HIV Treatment Targets for 2020 with Global Estimates (2014)



Levi J, et al. IAS 2015. Abstract MOAD0102.

Estimated Global Progress to 90-90-90 Targets



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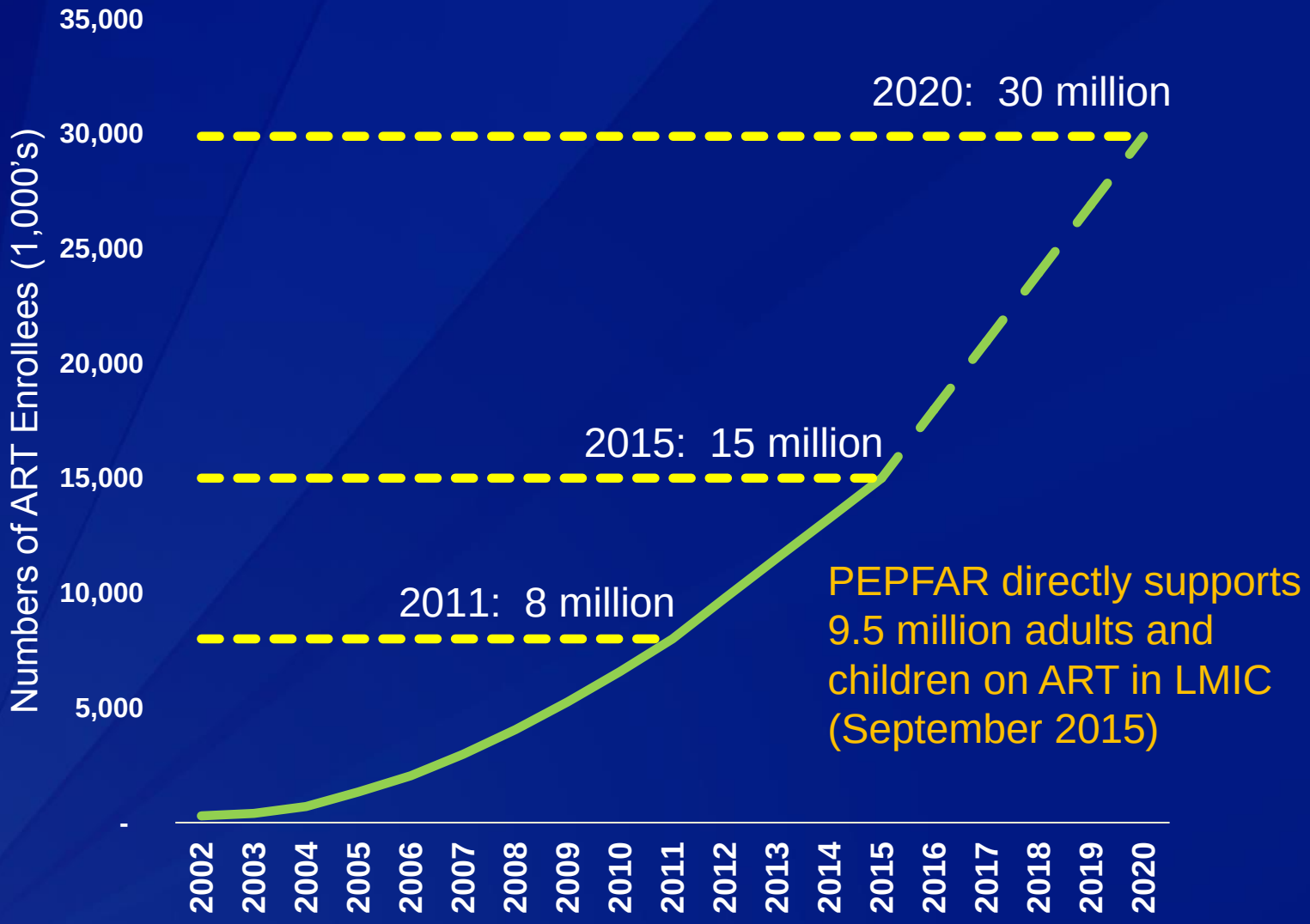
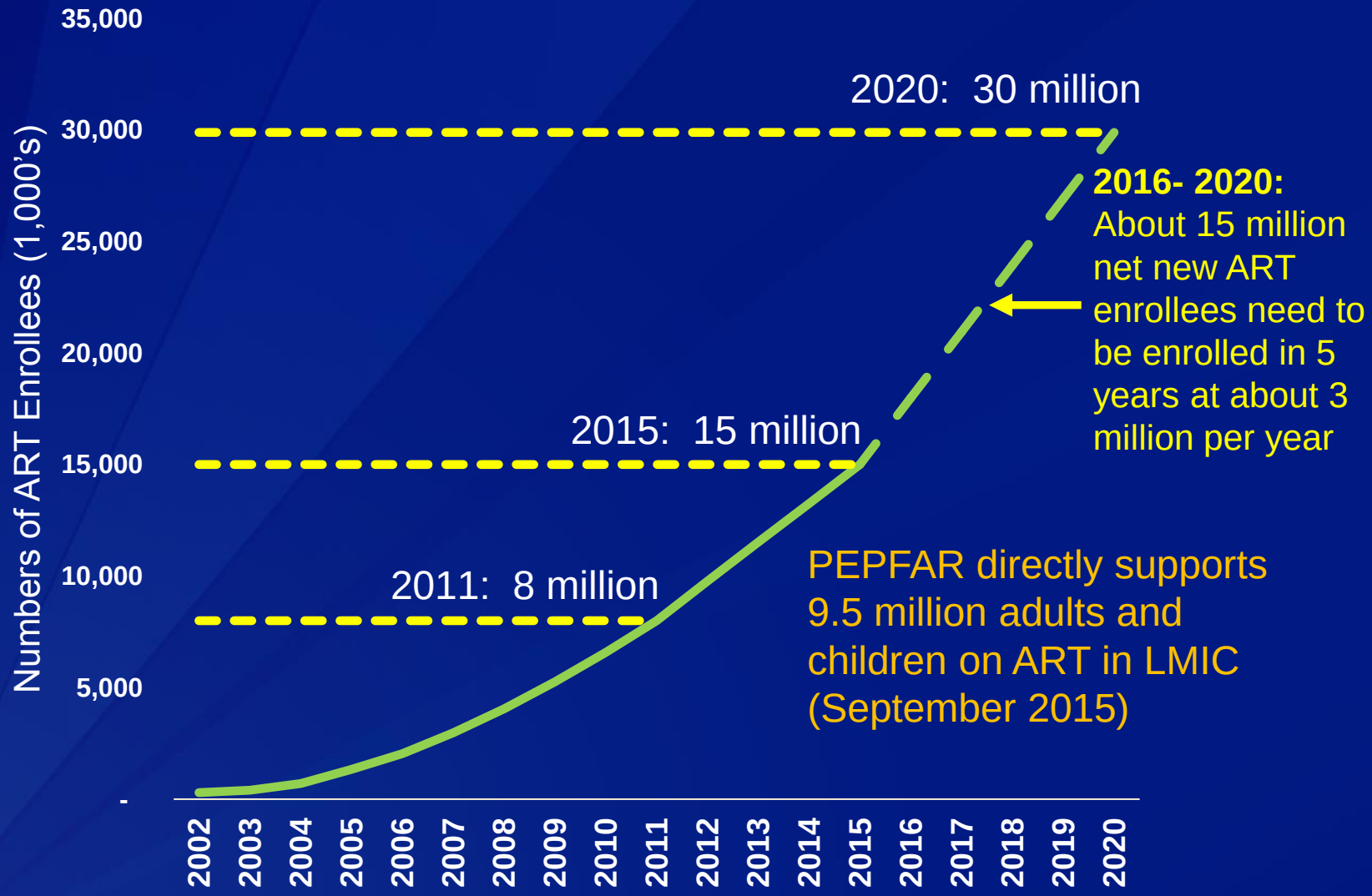
Global Estimates of Cumulative ART Enrollees Since 2002 and Targets for 2020



PEPFAR directly supports 9.5 million adults and children on ART in LMIC (September 2015)

Courtesy of Andrew Auld

Global Estimates of Cumulative ART Enrollees Since 2002 and Targets for 2020



Courtesy of Andrew Auld

PEPFAR HIV PREVENTION AND TREATMENT TARGETS

PREVENTION

25% REDUCTION

2016

By the end of 2016, achieve a **25 percent reduction** in HIV incidence among adolescent girls and young women (aged 15-24) within the highest burden geographic areas of 10 sub-Saharan African countries.

40% REDUCTION

2017

By the end of 2017, achieve a **40 percent reduction** in HIV incidence among adolescent girls and young women (aged 15-24) within the highest burden geographic areas of 10 sub-Saharan African countries.

11 MILLION

2016

By the end of 2016, PEPFAR will provide **11 million** voluntary medical male circumcisions for HIV prevention, cumulatively.

13 MILLION

2017

By the end of 2017, PEPFAR will provide **13 million** voluntary medical male circumcisions for HIV prevention, cumulatively.

TREATMENT

11.4 MILLION

2016

By the end of 2016, PEPFAR will support a total of **11.4 million** children, pregnant women receiving B+, and adults on life-saving anti-retroviral treatment, of which **7.2 million** are directly supported by PEPFAR funding and **4.2 million** are supported through technical assistance, jointly with partner countries.

12.9 MILLION

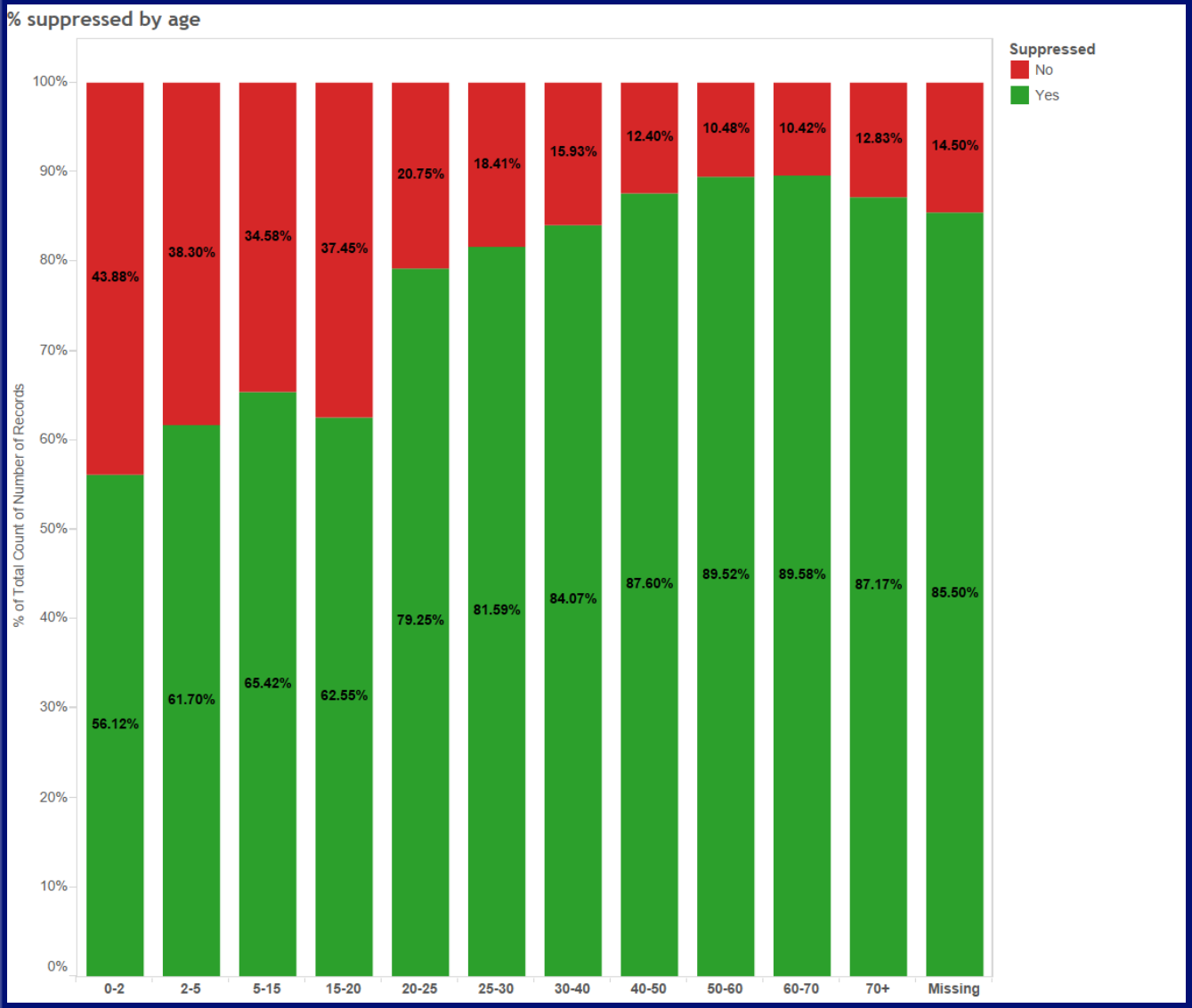
2017

By the end of 2017, PEPFAR will support a total of **12.9 million** children, pregnant women receiving B+, and adults on life-saving anti-retroviral treatment, of which **8.5 million** are directly supported by PEPFAR funding and **4.4 million** are supported through technical assistance, jointly with partner countries.

PEPFAR

PEPFAR realities and HIVDR risk

- **Single drug regimen for 1st-line ART (primarily Tenofovir/XTC/Efavirenz)**
  - No baseline drug resistance testing with limited surveillance data on pre-treatment DR
  - HIVDR surveys suggest patients failing NNRTI-based 1st-line regimens are likely to suppress with adherence to 2nd-line ART
- **Recommended use of PI-based 1st-line regimens in younger children very limited (primarily AZT/3TC/NVP)**
  - Achieving adequate levels of ARVs in children also challenging as weight fluctuates with growth and control of HIV
- **Limited use of routine viral load monitoring**
  - Identification of treatment failure with switch to PI-based 2nd-line uncommon (~5%) and likely after prolonged maintenance of failing regimens even with routine viral load monitoring
  - Most PEPFAR-supported countries have plans for implementation of routine VL monitoring over next 5 years but pace variable



Kenya 2015 Viral Load Data

- Includes all indications for VL (routine or suspected failure)

Source: NASCOP website, accessed May 1, 2016

Test & Start/Treatment for All: Mitigating HIVDR risk in PEPFAR programs

- **Routine VL monitoring**
- **Better program data: Expanded availability of PEPFAR MER & SIMS Data**
  - Systematic mandatory collection of VL suppression data at the subnational level
  - Also available genotype data?
- **Better regimens: Dolutegravir +/- TAF?**
- **Availability of palatable PI regimens for children**
- **Alternate service delivery models to improve retention on ART**
- **Case-based surveillance of virologic failures using sampling methodologies**

Pediatric ADR Surveillance: South Africa

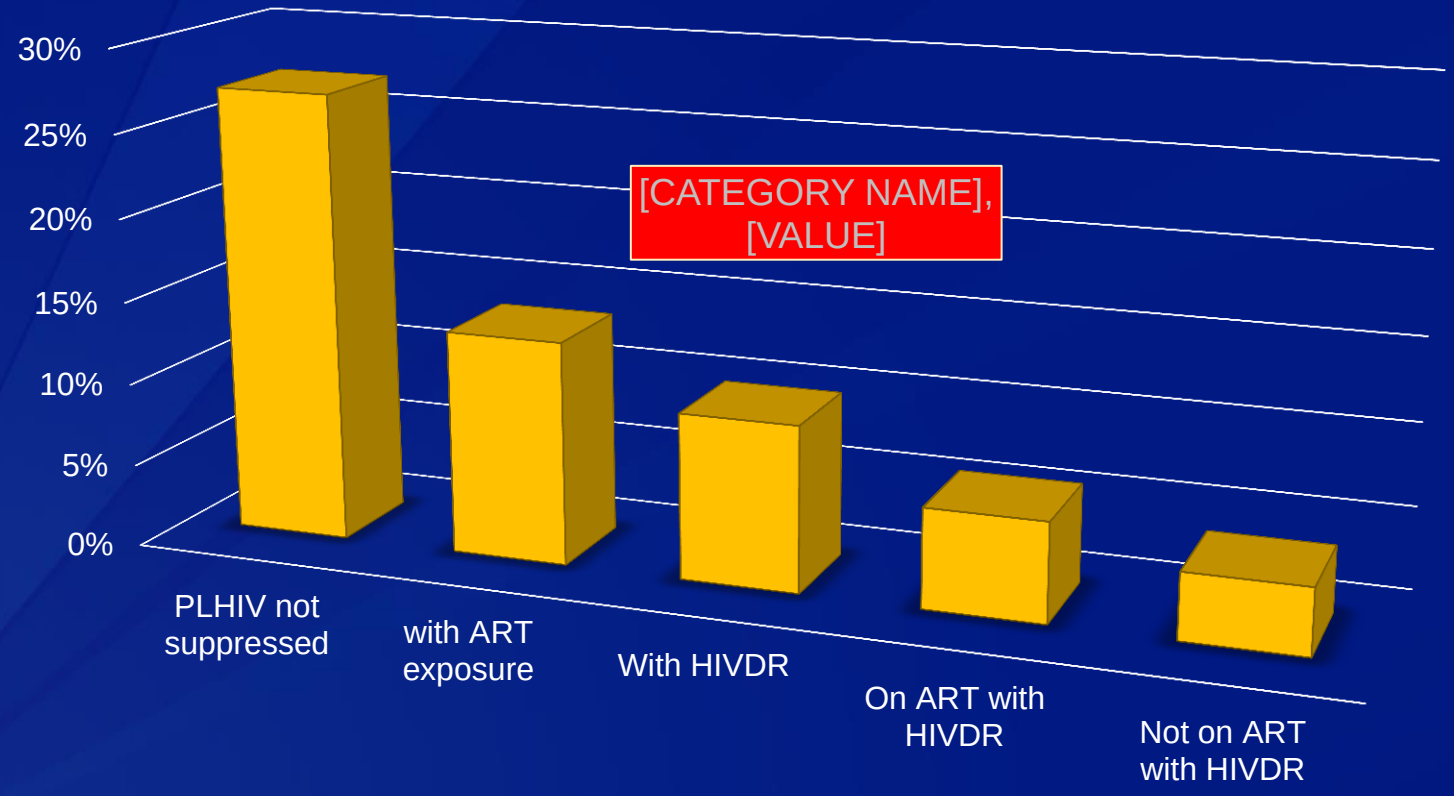
- **A list of facilities with >100 VL samples from children 1-19 yo with >1000 copies/ml was generated**
- **45 sites were randomly selected stratified by province**
- **Sample size of 1475 gives adequate power to determine prevalence of HIVDR (with 95% CI width of ≤ 10%) by four age groups (<5, 5-<10, 10-<15, 15-19)**
- **Facility will obtain new specimen for genotype from children with VF**
- **Major limitations:**
  - Selection of larger sites (may not be nationally representative)
  - Unclear what success rate for obtaining specimens will be

As we move towards 2020 goals (and beyond) what has us worried?

- **Pace of scale-up of routine viral load monitoring**
  - DBS remains an issue and point-of-care VL still not ready for implementation
- **Barriers/reluctance to prescribing of second-line ART**
- **Increasing likelihood of PLHIV rotating in and out of care**
- **Concurrent uptake of PrEP**
- **Ongoing stigma/disclosure issues impacting adherence for children/adolescents**
  - Impact of adolescents transitioning to adults

PEPFAR realities that need to be managed as we achieve 90-90-90

Over 3 million or at least 1/3 of all PLHIV not suppressed will likely have HIVDR...



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PEPFAR realities that need to be managed as we achieve 90-90-90

- Continued progress to 95-95-95 needed to fully achieve and maintain epidemic control but predicted levels of ongoing TDR threatens our ability to eliminate HIV transmission by 2030
- Increasing ART exposure at the population level will likely increase the proportion of PLHIV not suppressed with HIVDR
- Once PLHIV are identified and linked, focus needs to be on suppression and retention to mitigate risk
- Limited availability of palatable PIs and/or 2nd-line ART for children

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What do we (still) need to know?

- What is the likely impact of transition to INSTI-based regimens (especially DTG)?
- What is the consequence of failing to identify and act upon VL results between 20-1000 copies/ml?
- What proportion of PrEP failures will be due to acquired or transmitted drug resistance?
- What is the impact of minority variants and subtypes on treatment outcomes in large population settings?

What do we (still) need to know?

- **Do policy changes based on HIVDR surveillance results achieve a net positive impact?**
- **What populations would most benefit from early adoption of new technologies that allow for individual HIVDR testing?**
  - Adolescents
  - Pregnant and breastfeeding women
  - PMTCT failures (infants)
  - PLHIV in and out of care
- **Is it operationally feasible for ART programs in LMIC settings to incorporate multiple ARV options based on perceived HIVDR risk?**

HIV DR Intelligence:

More Critical than Ever

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Thank You

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