Research Priorities for Differentiated Care

ICAP Grand Rounds, 23 May 2017

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Outline

- Why we need new approaches to HIV service delivery?

- Differentiated care- what is it? what is it not?

- What do we know, and what do we need to learn when it comes to differentiating care?

- Priorities for differentiated care research
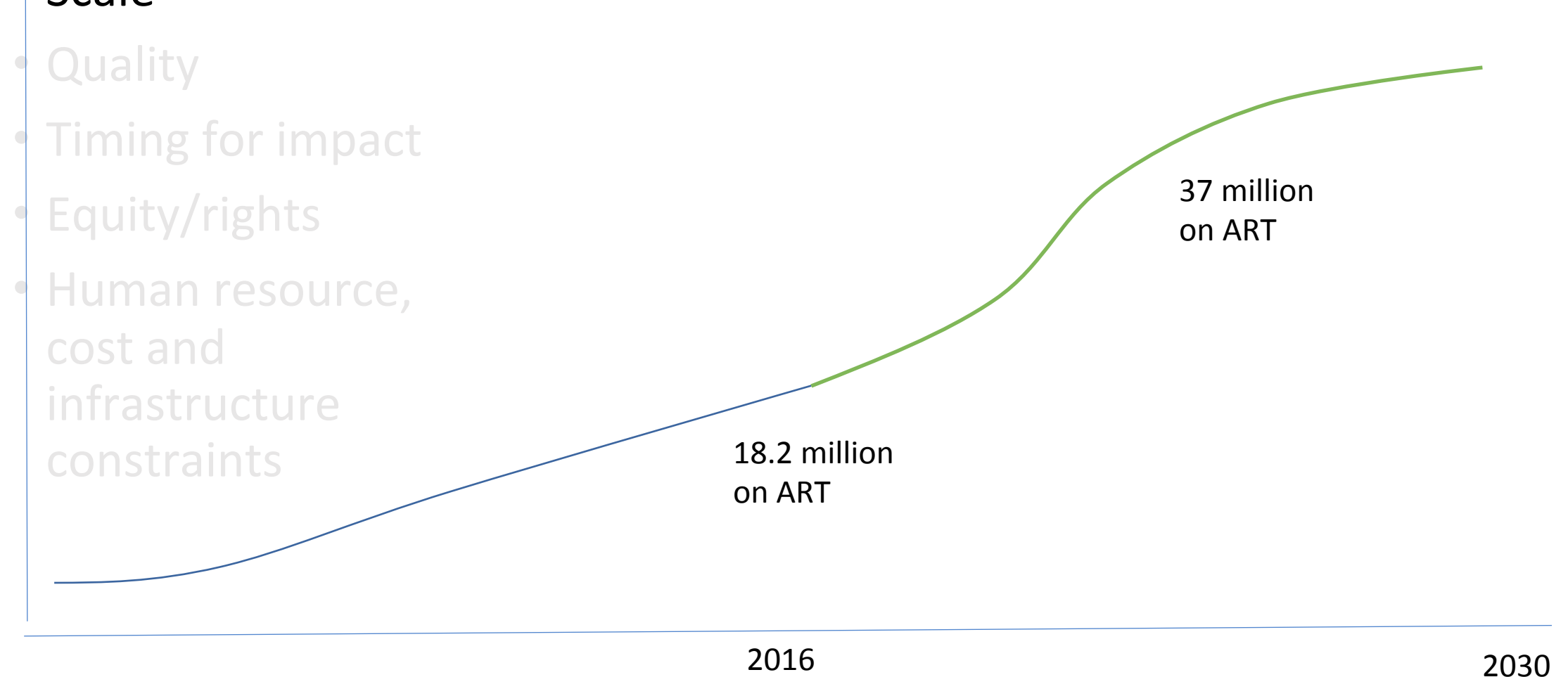
- Conclusions

Why do we need new approaches?

- Scale
- Quality
- Timing for impact
- Equity/rights
- Human resource, cost and infrastructure constraints

Why do we need new approaches?

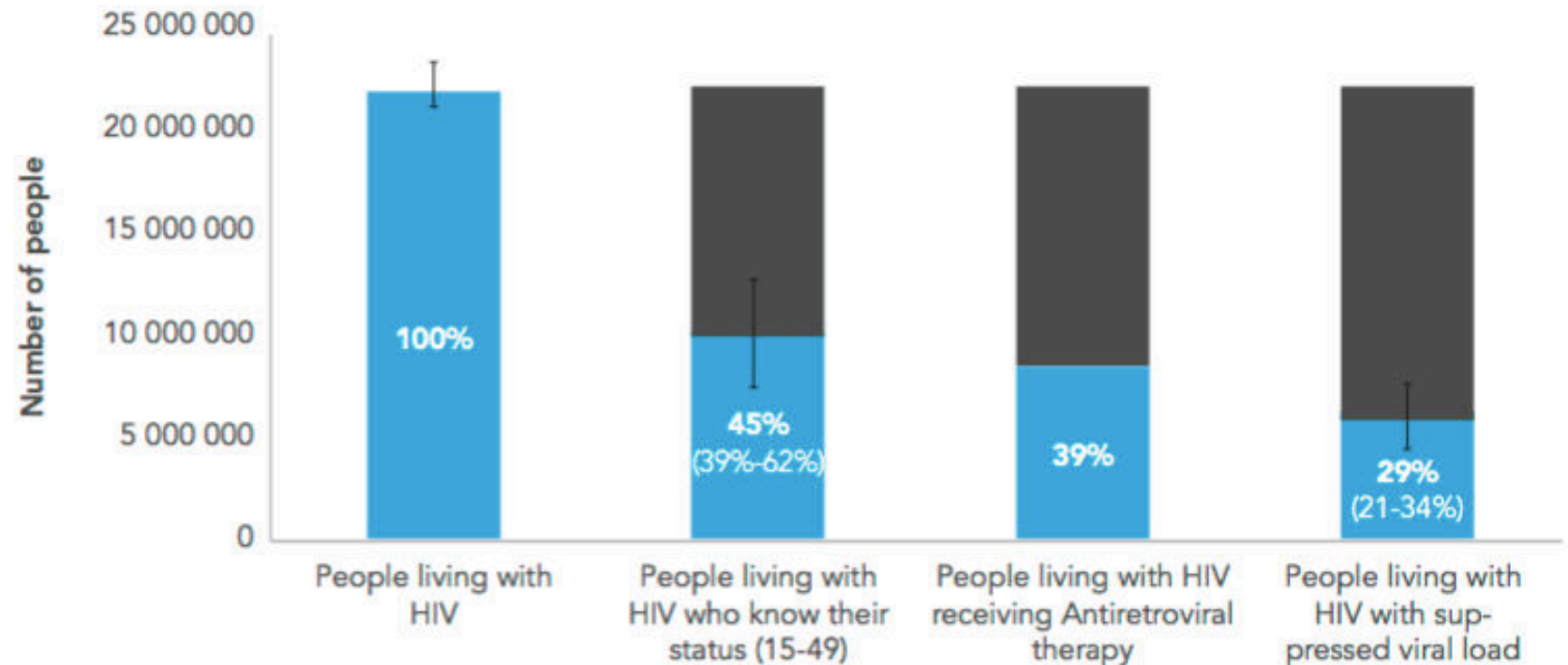- Scale
- Quality
- Timing for impact
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- Human resource, cost and infrastructure constraints

37 million on ART

18.2 million on ART

2016

2030

Why do we need new approaches?

- Scale
- **Quality**
- Timing for impact
- Equity/rights
- Human resource, cost and infrastructure constraints


ABBREVIATED HIV TREATMENT CASCADE FOR ADULTS IN SUB-SAHARAN AFRICA AGED 15 YEARS OR MORE, 2013
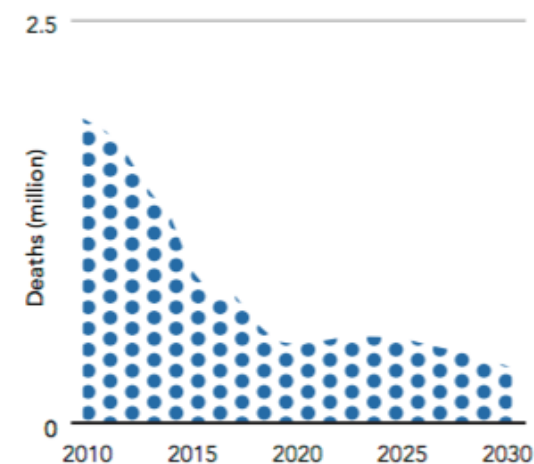
Why do we need new approaches?

- Scale
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90-90-90 by 2020 if we want to achieve 2030 UN goals for reducing new infections and deaths

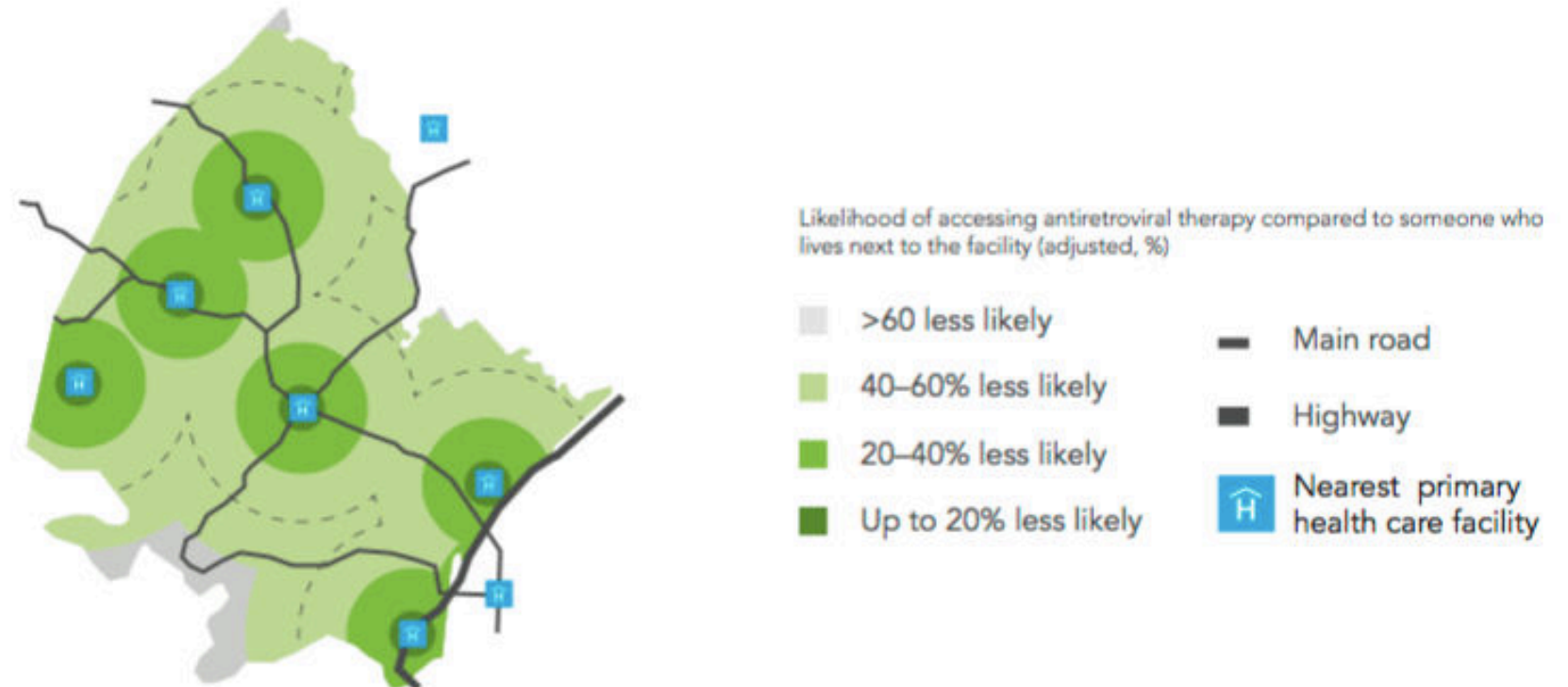**New HIV infections in low- and middle-income countries (millions)**
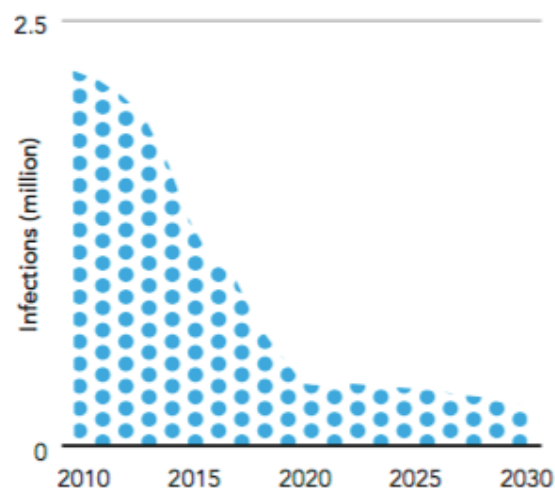
AIDS-related deaths in low- and middle-income countries (millions)

Why do we need new approaches?

- Scale
- Quality
- Timing for impact
- **Equity/rights**
- Human resource, cost and infrastructure constraints

LIKELIHOOD OF ACCESSING ANTIRETROVIRAL THERAPY, RELATIVE TO DISTANCE FROM HEALTHCARE FACILITY, KWAZULU NATAL, SOUTH AFRICA

Likelihood of accessing antiretroviral therapy compared to someone who lives next to the facility (adjusted, %)

- >60 less likely
- 40–60% less likely
- 20–40% less likely
- Up to 20% less likely

- — Main road
- — Highway
- Nearest primary health care facility
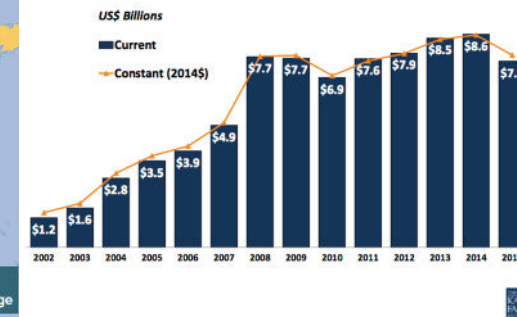
Cooke et al, BMC Public Health 2010
UNAIDS, 2016

Why do we need new approaches?

- Scale
- Quality
- Timing for impact
- Equity/rights
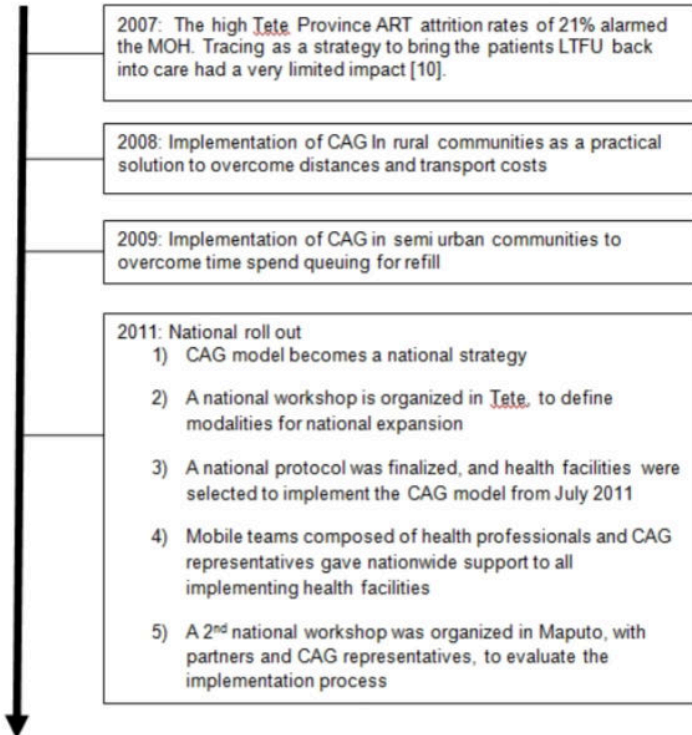
- Human resource, cost and infrastructure constraints

Health systems delivery innovators to the rescue? The example of community adherence groups (CAGS)..

2007: The high Tete Province ART attrition rates of 21% alarmed the MOH. Tracing as a strategy to bring the patients LTFU back into care had a very limited impact [10].

2008: Implementation of CAG In rural communities as a practical solution to overcome distances and transport costs

2009: Implementation of CAG in semi urban communities to overcome time spend queuing for refill

2011: National roll out
1) CAG model becomes a national strategy
2) A national workshop is organized in Tete, to define modalities for national expansion
3) A national protocol was finalized, and health facilities were selected to implement the CAG model from July 2011
4) Mobile teams composed of health professionals and CAG representatives gave nationwide support to all implementing health facilities
5) A 2nd national workshop was organized in Maputo, with partners and CAG representatives, to evaluate the implementation process

- Scale
- Quality
- Timing for impact
- Equity/rights
- Human resource, infrastructure and cost constraints

Cumulative Incidence: LTFU

"belonging to a group strengthens people, they become very strong in groups "

Decreased visit frequency

Decroo et al, TMIH 2014
Rasschaert et al, PLOS One 2014
Jobarteh et al, PLOS One 2016
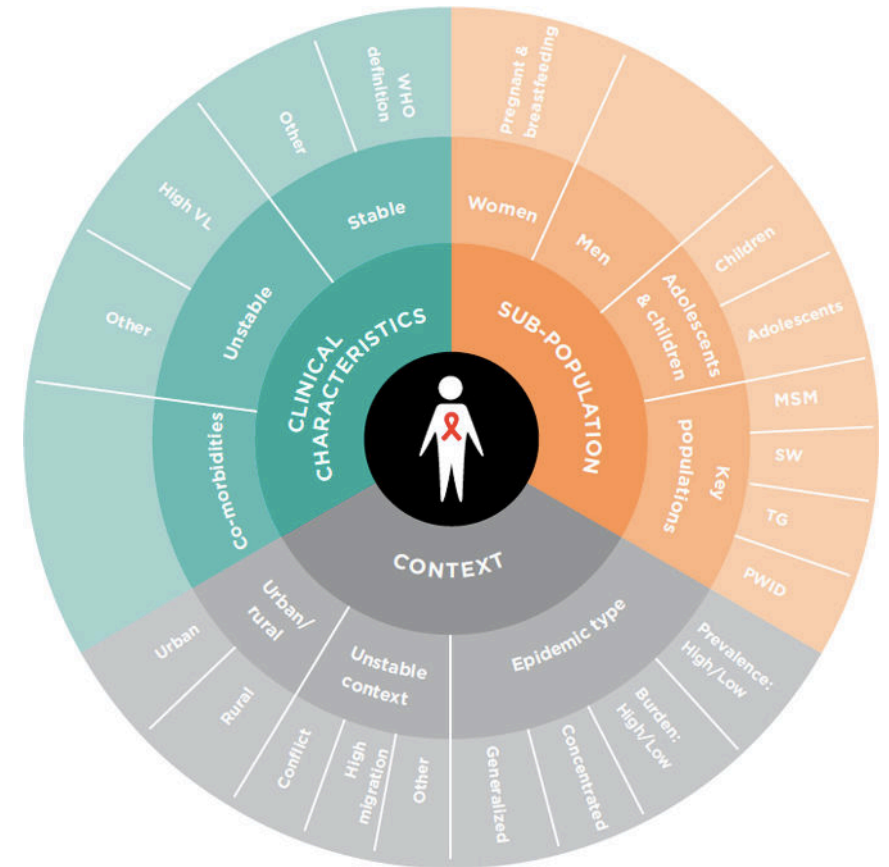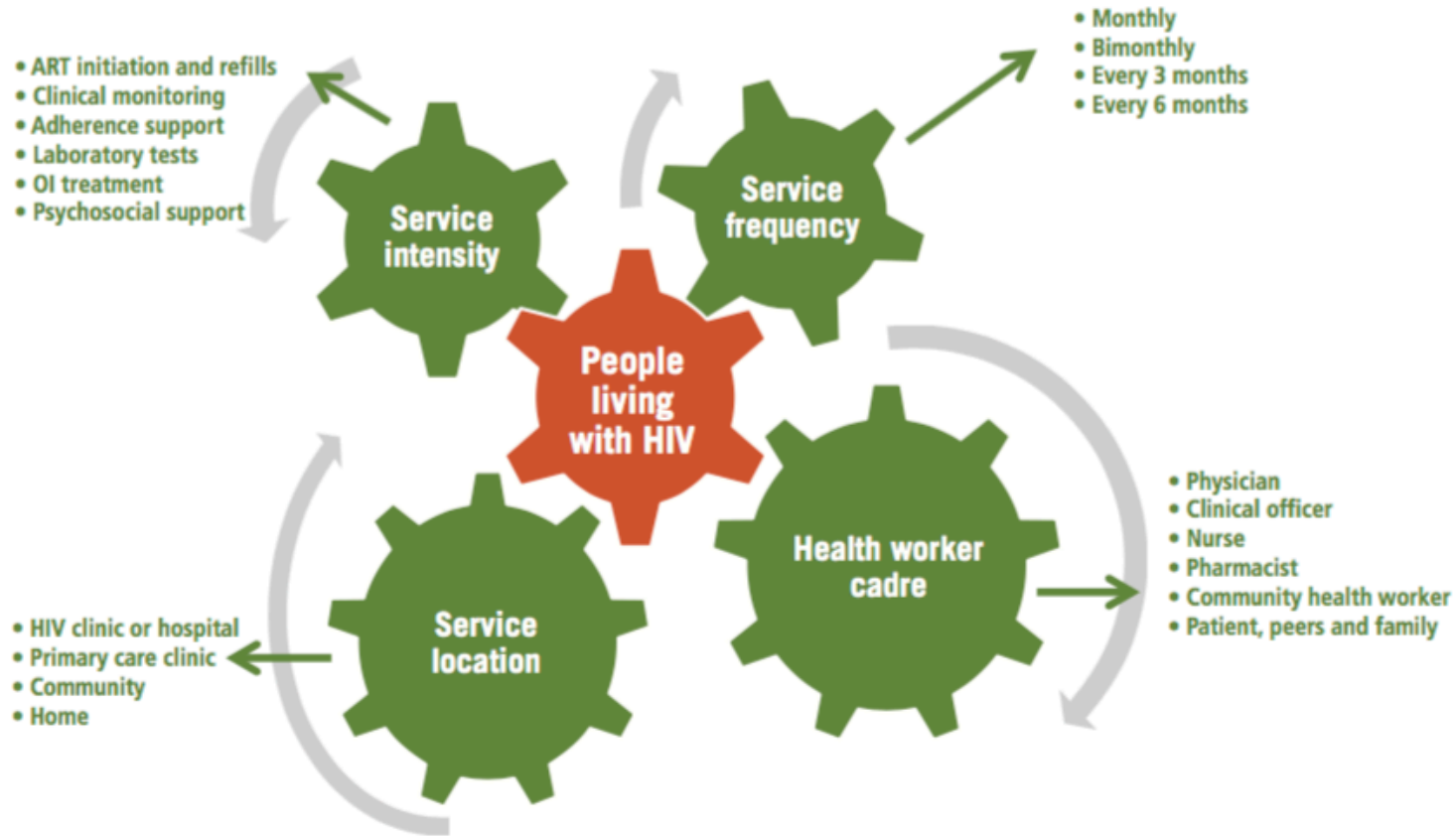
What is differentiated care?

- "Differentiated care is a client-centered approach that simplifies and adapts HIV services across the cascade, in ways that both serve the needs of PLHIV better and reduce unnecessary burdens on the health system."

  - Grimsrud et al, JIAS 2016

σιμπλιφιχατιον τασκ σηιφτινγ δεχεντραλιζατιον,
χομμυνιτψ-βασεδ χαρε οπτιμιζεδ χαρε
πατιεντ-χεντερεδ χαρε νεεδσ-βασεδ χαρε

Differentiated care- putting the patient at the center of care

Grimsrud, JIAS, 2016
Duncombe, J Trop Med 2013

What is differentiated care NOT?

- Differentiated care is not a silver bullet that is guaranteed to improve outcomes and reduce costs

- It is not entirely new, and it is not comprised of a single model

- It is not the end- rather it is one means to the "ends" that we care about: coverage, quality and impact

Opinion: If carefully, yet boldly implemented, monitored and studied, the principles of differentiated care could help to transform care systems for the benefit of individuals and public health

What progress is being made in moving towards more differentiated care?

- Rapid spread of programmatic interest and generation of pilot data
- Emerging data on effectiveness and cost-effectiveness from randomized evaluations of differentiated care models
- Emerging data from M&E of ongoing and expanding pilot programs
- New guidance from WHO, national governments and funders
  - Community of practice emerging- CQUIN
- Comparatively little implementation science

High-level questions

- How can we use differentiated care as a tool to help us improve quality (retention/VL suppression), coverage and impact?

- How can we strike the right balance between simplicity of delivery while allowing for flexibility/innovation?

- How can we create a less medicalized system for healthy patients, while maintaining levels of safety and not doing harm?

- How can we better leverage community spirit to create stronger and more sustainable support structures for long-term adherence and stigma reduction?

- Can we use these gains to spare unnecessary use of resources and allow for greater scale?

"Implementation research plays an important role in identifying barriers to, and enablers of, effective global health programming and policymaking, and leveraging that knowledge to develop evidence-based innovations in effective delivery approaches"

- Fogarty International Center

"Implementation research does not isolate the effects from the context – rather it focuses precisely on the interaction between the intervention and the context"
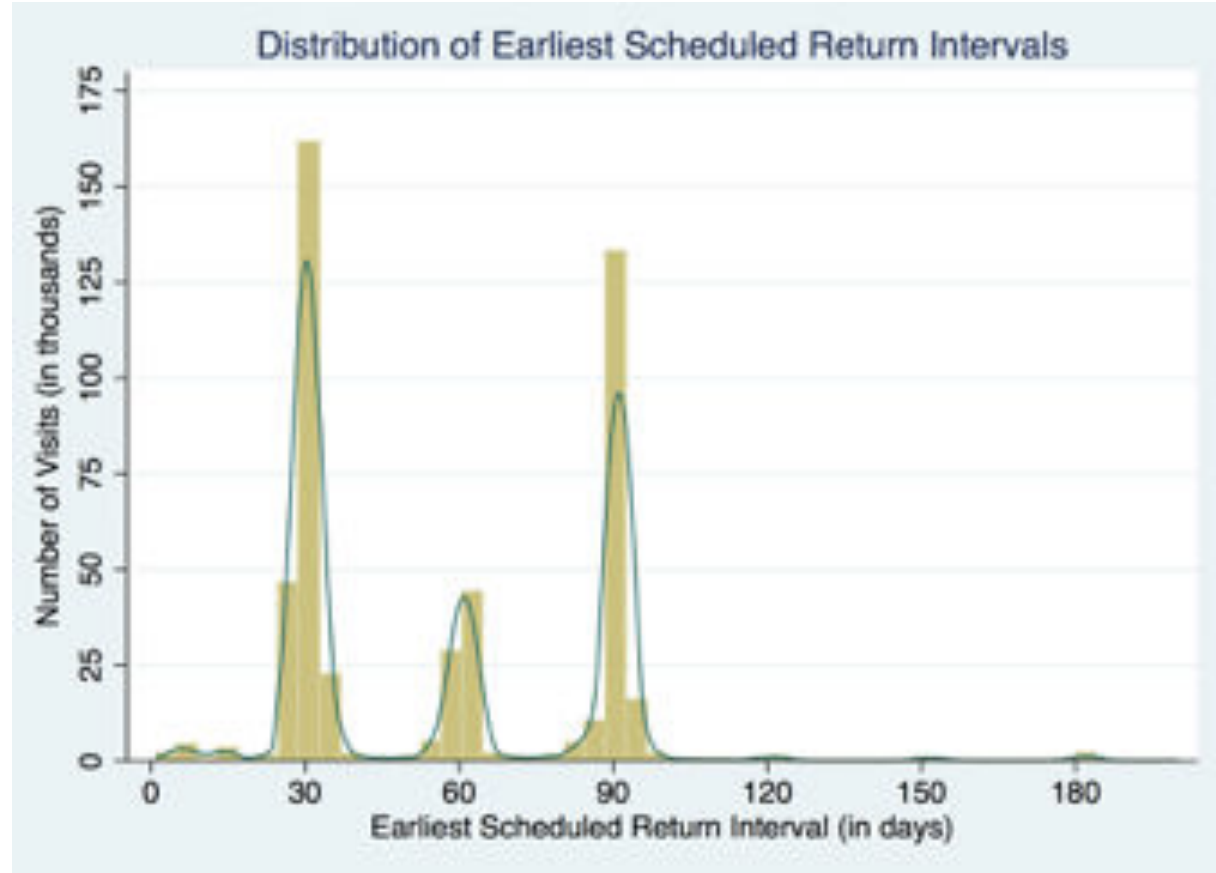
- Allotey TDR 2011

What are some priorities for differentiated care implementation research?

- Visit spacing
- Model selection/deployment – "guided choice"
- Patient experience to drive demand for differentiated/better care
- Special patient populations
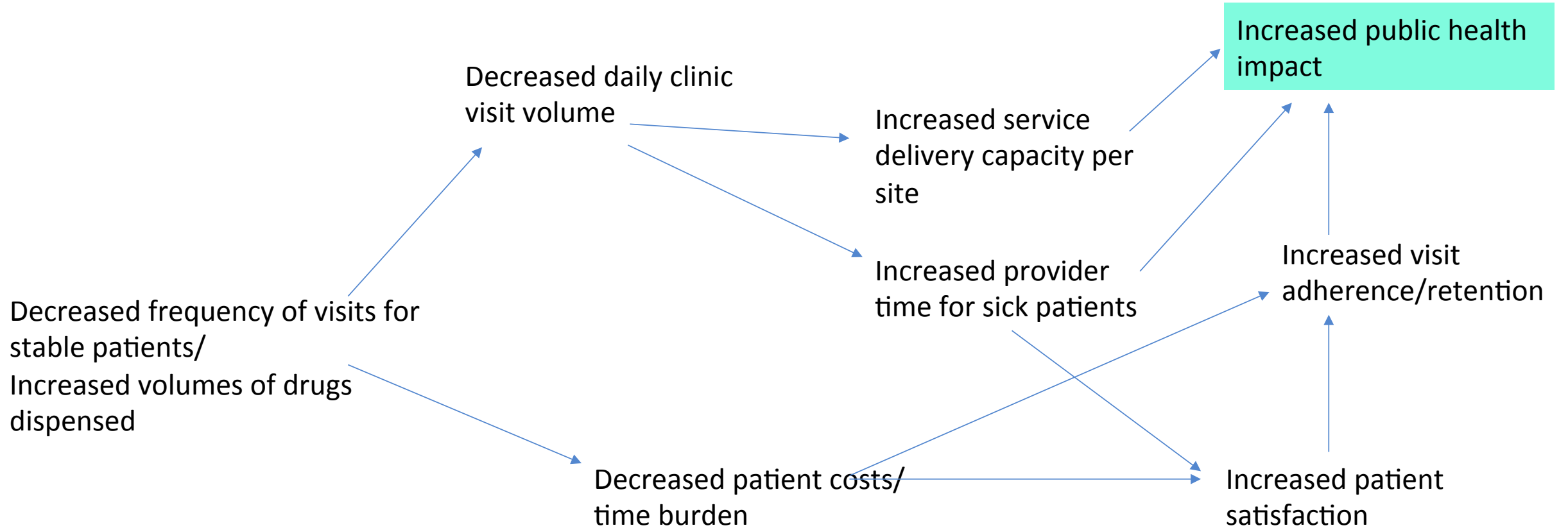- The science of differentiated care scale-up

Visit spacing anyone?

- The standard of care in most settings: frequent visits to clinic/pharmacy
    - Is the standard of care making people non-adherent to visits?
- Spacing of visits is arguably the simplest form of differentiated care
- Yet, it is under-implemented in most settings..

Distribution of Earliest Scheduled Return Intervals

Mody et al, CROI 2017

Conceptual framework- visit spacing

Decreased daily clinic visit volume

Increased service delivery capacity per site

Increased public health impact

Decreased frequency of visits for stable patients/
Increased volumes of drugs dispensed

Increased provider time for sick patients

Increased visit adherence/retention

Decreased patient costs/ time burden
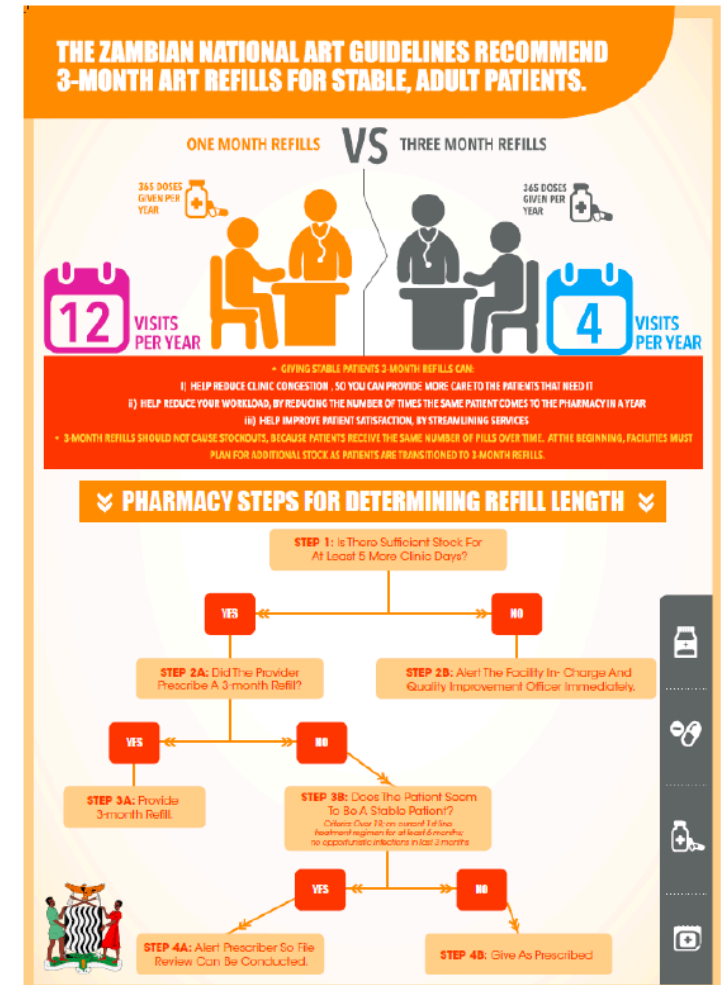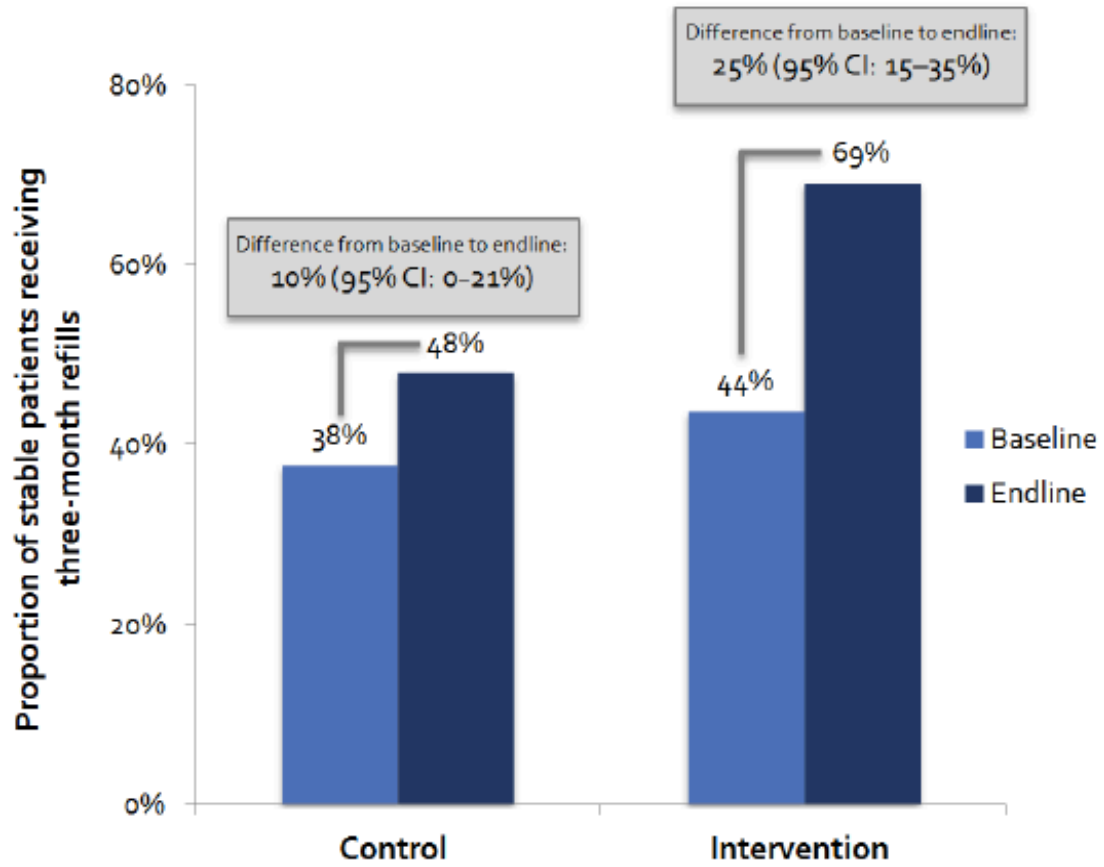
Increased patient satisfaction

Spacing visits and refills

- MSF evaluated a strategy of six-monthly appointments (SMA) for stable ART patients in Chiradzulu District, Malawi
- Stable patients (aged ≥15, on first-line ART ≥12 months, CD4 count ≥300, No OI, not pregnant/breastfeeding
- **Clinical assessments 1-2 months → 6 months. ARV refills 3 months**
- Median time from SMA eligibility to enrolment was 6 months (interquartile range 0-17 months). The cumulative probability of death or loss to follow-up five years after first SMA eligibility was 56.3% (95% CI: 52.4-60.2%) among those never SMA enrolled; 13.9% (95% CI: 12.5-15.6%) among early SMA enrolees and 8.1% (95% CI 7.2-9.0%) among late SMA enrolees.
- One third of patients returning to routine care at some point
- Unable to control for selection bias and differences among those who did and did not enroll in the program

Cawley et al, AIDS Durban 2016
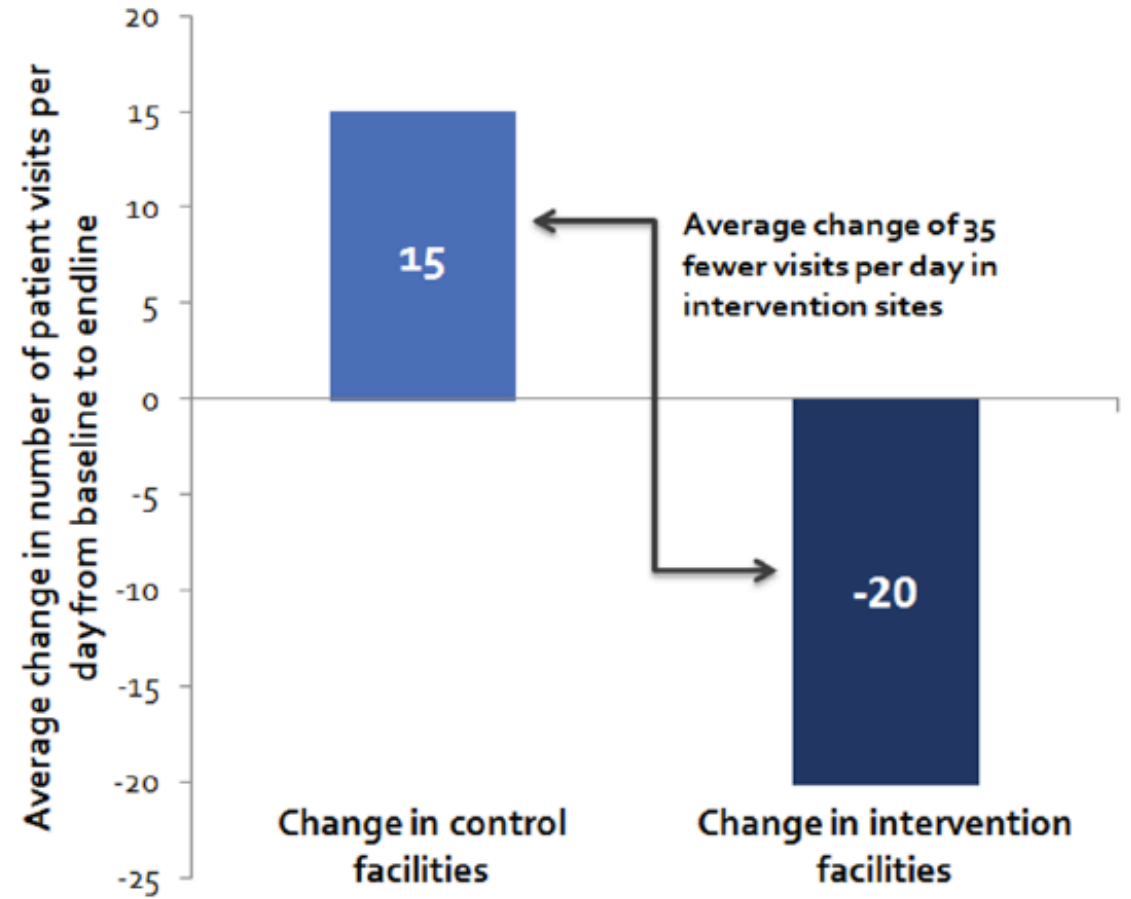
Cluster RCT of Visit Spacing- Zambia MOH/ CHAI

- 16 facilities- control vs intervention

- Intervention: Pharmacist job aide, QI officer, checklists, troubleshooting, forecasting tool (control too)

- Primary outcome: mean change in the proportion of patients receiving three-month refills between baseline and end-line for each facility

- 3-month follow-up

McCarthy, et al, 2017 PLOS One

Proportion of patients receiving 3-month refills

Average change in visits per day/site

Difference from baseline to endline:
25% (95% CI: 15–35%)

69%

44%

Difference from baseline to endline:
10% (95% CI: 0–21%)

48%

38%

Proportion of stable patients receiving three-month refills

80%
60%
40%
20%
0%

Baseline
Endline

Control
Intervention

Average change in number of patient visits per day from baseline to endline

20
15
10
5
0
-5
-10
-15
-20
-25

15

-20

Average change of 35 fewer visits per day in intervention sites

Change in control facilities
Change in intervention facilities

McCarthy, et al, 2017 PLOS One

Retrospective analysis of visit-spacing- Zambia

- Stable HIV-infected patients on ART (**On ART>180 days, CD4>200 cells/µL for 6 months, No TB diagnosis in past 6 months**)
- Presented for routine follow-up between January 1, 2013 – July 31, 2015 at one of 63 CIDRZ-supported clinics in Zambia

Patient Characteristics	
Total Patients, N	127,448
Total Visits, N	1,113,211
Male Sex, N, (%)	43,200 (33.9)
Age, years, median (IQR)	38 (32 - 45)
Years Since ART Initiation, median (IQR)	2.3 (0.8 - 4.8)
CD4 count, cells/µL, median (IQR)	425 (309 - 585)
First Line ARV Regimen, N, (%)	119,338 (97.9)
Province, N, (%)	
Eastern	23,013 (18.1)
Lusaka	68,186 (53.5)
Southern	18,683 (14.7)
Western	17,547 (13.8)
Retention History	
Visits Missed by >14d, %, median (IQR)	19.0 (6.7 - 36.4)
Patients with an episode of LTFU, N, (%)	41,678 (33.8)
Medication Possession Ratio, %, median (IQR)	88.6 (77.8 - 96.5)

Mody et al, CROI 2017

Spacing visits

Patients whose earliest scheduled return to clinic was at 6 months were less likely to:
- miss their next visit (aOR 0.23)
- have a gap in medication (aOR 0.50)
- become LTFU by their next visit (aOR 0.48) compared to those scheduled to return at 1 month.

Days Late to Next Visit by Earliest Clinic Return Interval
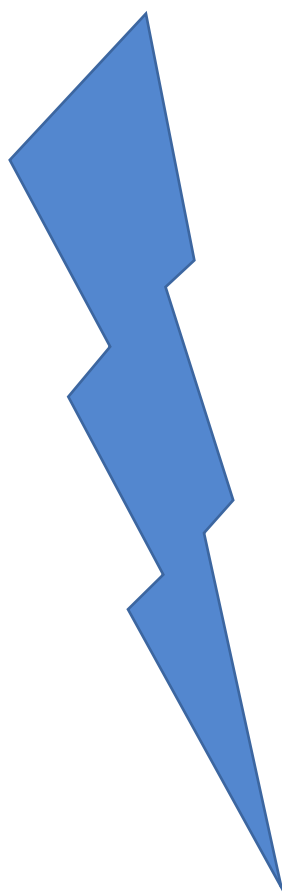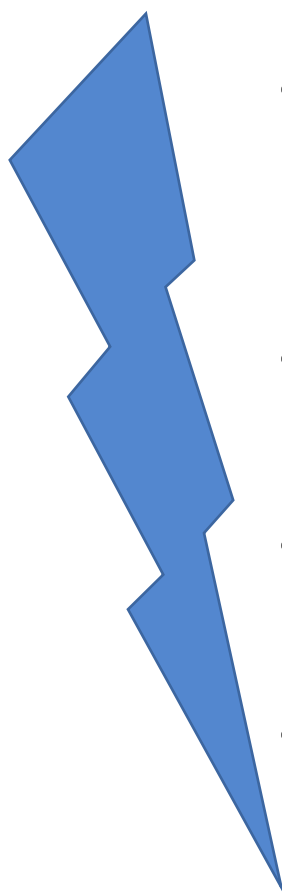
Mody et al, CROI 2017
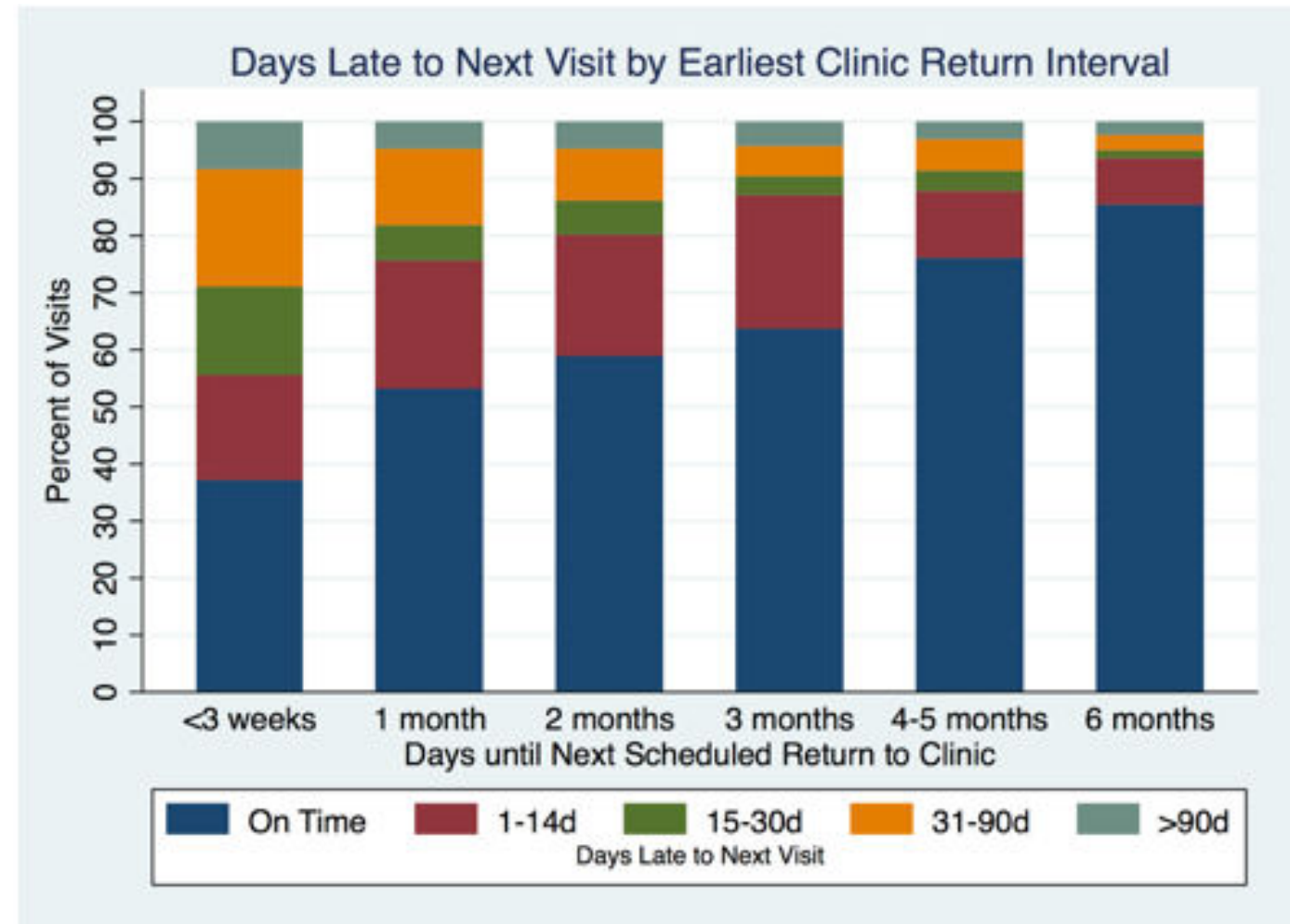
Visit spacing

- These three studies suggest the feasibility and likely effectiveness of 3-6 month appointments
  - Further supported indirectly through CAGs, which facilitate individuals being seen clinically only every 6 months
- Also suggest that visit-spacing may require additional strategies in order to promote its uptake among providers
- Although gaps in our knowledge base- seems to be little justification for not simply aligning refills with appointments at 6 months for stable patients and this is broadly endorsed by WHO
- Where do we go from here?
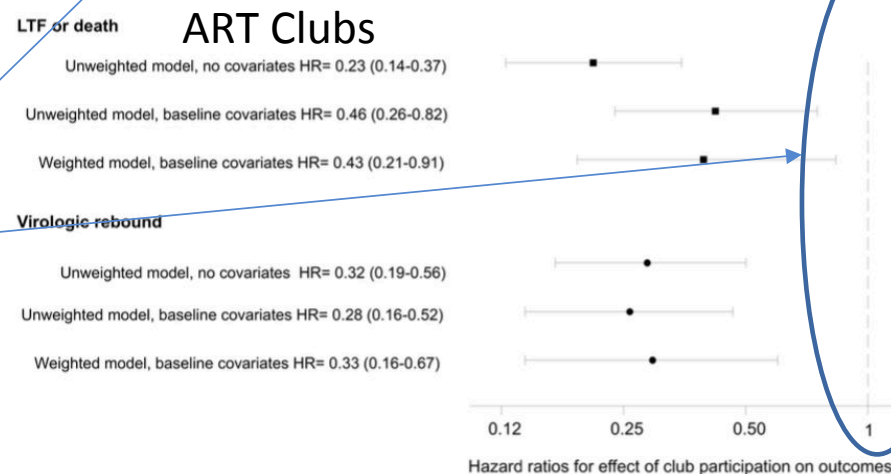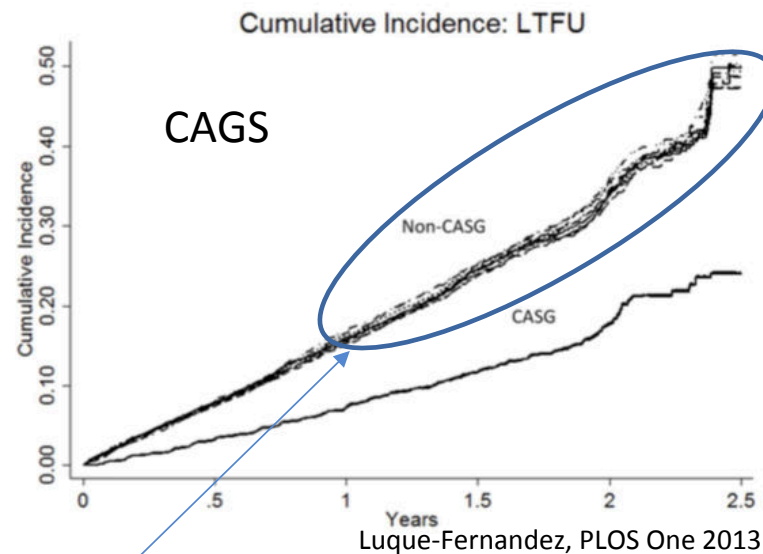
Visit spacing research agenda

- What are the most effective quality-improvement approaches to drive and sustain the shift to 6-month visits/refills?
  - Strategy studies nested in broader scale-up? What elements are most important and linked to the best outcomes?
- How can lab performance (e.g., VL) be streamlined/aligned with visits in a way that does not defeat gains made through visit spacing?
- Systems interventions that use technology more effectively to ensure adequate stocks?
  - e.g., real-time monitoring of pharmacy refill scheduling- trend towards shorter refill periods is likely a good functional indication of drug insecurity..

Visit spacing research agenda, cont'd

- Any qualitative evidence of disconnection to health facility/ adherence support?
  - How can technology be employed to address this? 2-way SMS?
- How can excess capacity be most effectively re-deployed? Shift resources to community support/SMS, etc?
- What is the appropriate visit frequency for kids at various stages of their treatment?
- 1-year visit-spacing for the healthiest 15 million? Is it safe? What is needed to accompany it? RCT's required..

Effective selection/deployment of differentiated care models

- We have multiple models that have proven effective in add'n to visit spacing

- CAGS: 91.8% retention at 4 years

- ART adherence groups: 94% retention at 1 year

  (For those who have opted in)

- Further emerging model effectiveness data from MSF, CIDRZ, etc

- What about those that don't opt-in for whatever reason?

Cumulative Incidence: LTFU

CAGS

Non-CASG

CASG

Luque-Fernandez, PLOS One 2013

LTF or death — ART Clubs

Unweighted model, no covariates HR= 0.23 (0.14-0.37)

Unweighted model, baseline covariates HR= 0.46 (0.26-0.82)

Weighted model, baseline covariates HR= 0.43 (0.21-0.91)

Virologic rebound

Unweighted model, no covariates HR= 0.32 (0.19-0.56)

Unweighted model, baseline covariates HR= 0.28 (0.16-0.52)

Weighted model, baseline covariates HR= 0.33 (0.16-0.67)

0.12   0.25   0.50   1

Hazard ratios for effect of club participation on outcomes

How can we introduce greater flexibility into health systems in order to address the heterogeneous needs and preferences of individuals in need of life-long care?

- How well are we adapting/differentiating care based on empiric evidence of the most influential barriers?
- What if we explicitly took into account empiric data on patient barriers when deciding what models would be most effective at the individual or site level?

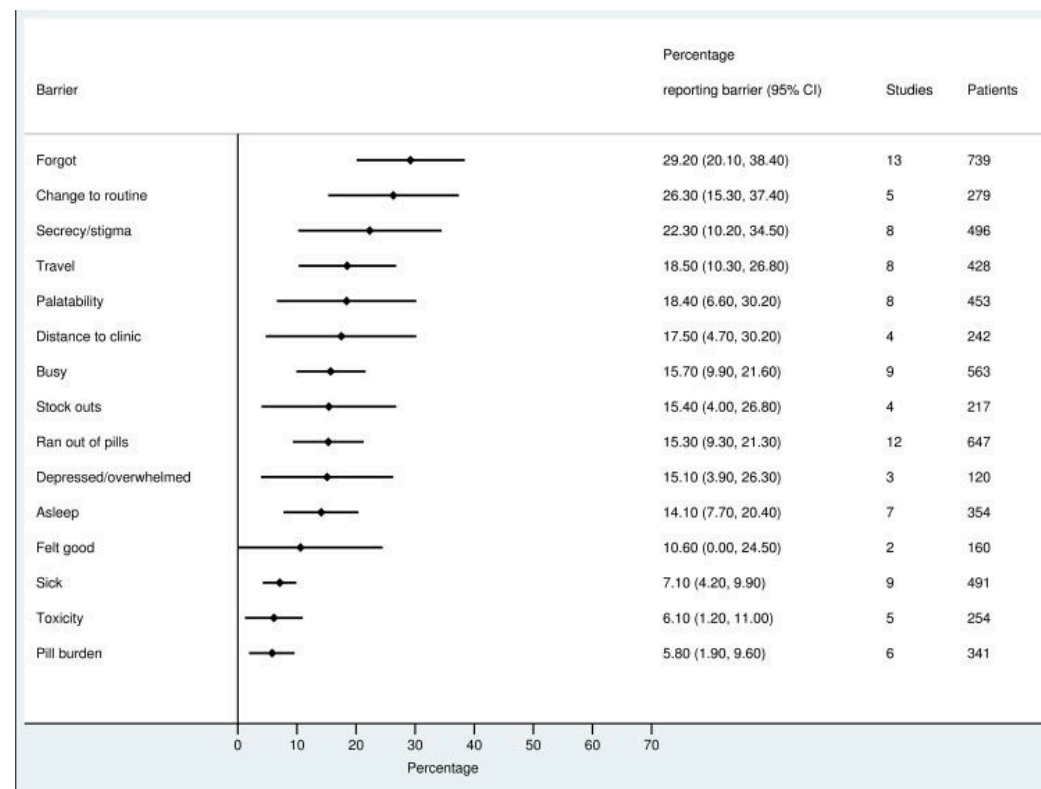**Patient-Reported Barriers to Adherence to Antiretroviral Therapy: A Systematic Review and Meta-Analysis**
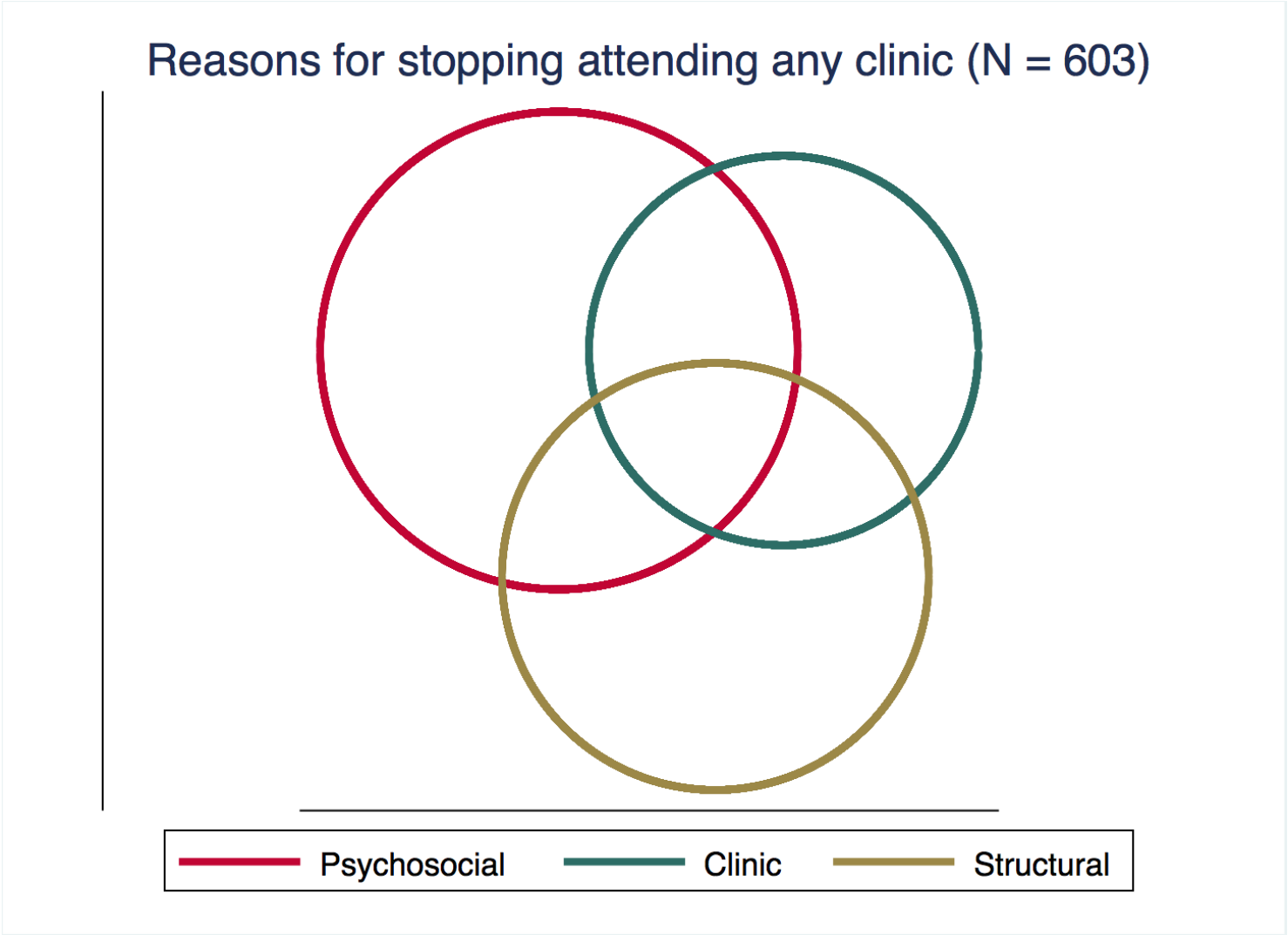
Zara Shubber,[1] Edward J. Mills,[2] Jean B. Nachega,[3,4,5] Rachel Vreeman,[6,7] Marcelo Freitas,[8] Peter Bock,[9] Sabin Nsanzimana,[10,11] Martina Penazzato,[12] Tsitsi Appolo,[13] Meg Doherty,[12] and Nathan Ford[12,14,*]

Barriers to Care and 1-Year Mortality Among Newly Diagnosed HIV-Infected People in Durban, South Africa

Ingrid V. Bassett, MD, MPH,*†‡§‖ Sharon M. Coleman, MS, MPH,¶ Janet Giddy, MBChB, MFamMed,#
Laura M. Bogart, PhD,§‖**†† Christine E. Chaisson, MPH,¶ Douglas Ross, MBChB, MBA,‡‡
Moses J. E. Flash, BA,‡ Tessa Govender, MSc,# Rochelle P. Walensky, MD, MPH,*†‡§‖$$
Kenneth A. Freedberg, MD, MSc,*†‡§‖‖‖¶¶ and Elena Losina, PhD‡§‖‖‖##***

Barrier		Percentage reporting barrier (95% CI)	Studies	Patients
Forgot		29.20 (20.10, 38.40)	13	739
Change to routine		26.30 (15.30, 37.40)	5	279
Secrecy/stigma		22.30 (10.20, 34.50)	8	496
Travel		18.50 (10.30, 26.80)	8	428
Palatability		18.40 (6.60, 30.20)	8	453
Distance to clinic		17.50 (4.70, 30.20)	4	242
Busy		15.70 (9.90, 21.60)	9	563
Stock outs		15.40 (4.00, 26.80)	4	217
Ran out of pills		15.30 (9.30, 21.30)	12	647
Depressed/overwhelmed		15.10 (3.90, 26.30)	3	120
Asleep		14.10 (7.70, 20.40)	7	354
Felt good		10.60 (0.00, 24.50)	2	160
Sick		7.10 (4.20, 9.90)	9	491
Toxicity		6.10 (1.20, 11.00)	5	254
Pill burden		5.80 (1.90, 9.60)	6	341

Percentage (0, 10, 20, 30, 40, 50, 60, 70)

Understanding the nature of individual barriers to care

Reasons for stopping attending any clinic (N = 603)

Psychosocial — Clinic — Structural

BetterInfo Study- Patient reported reasons for stopping care by clinic among the lost (and traced)

Psychosocial ■ Clinic ■ Structural

CIDRZ BetterInfo Study National Dissemination Mtg, 2016
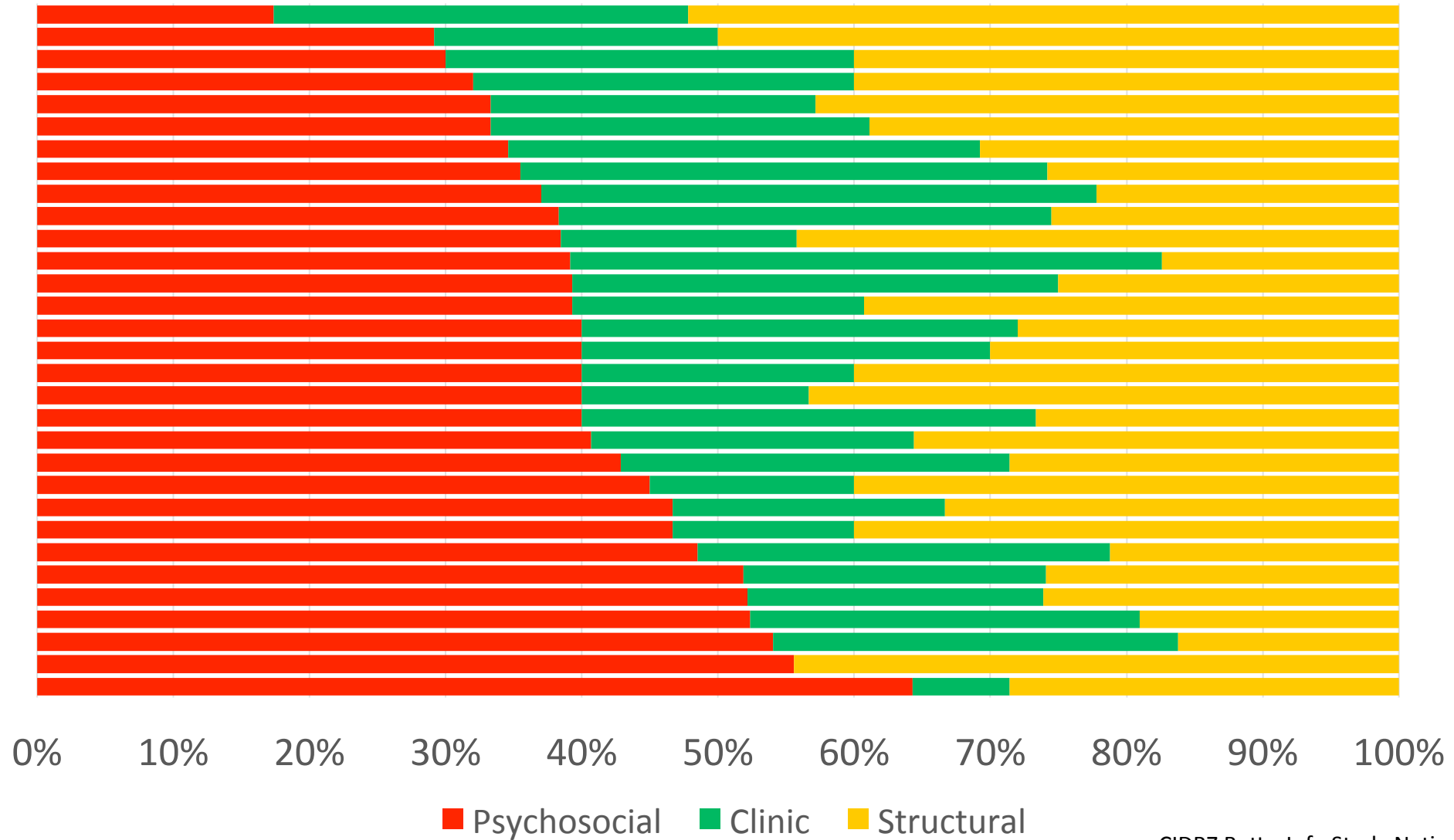
Research agenda around "guided choice" for optimal care differentiation

- Can choice of models be guided by perceived and observed patient needs and health systems capacity?

- Do different models work better for various types of patient needs/barriers?

- Do individuals reporting solely structural or clinic-based barriers to care do best when guided to visit-spacing, whereas those reporting psychosocial barriers may do best in a model incorporating peer-community support?

- Consideration should also be given to how to monitor and screen for model appropriateness as care proceeds..

- Stepwise increases in intensity over time depending on outcomes?
  - E.g., Visit-spacing→ CAGs→more intensive models?
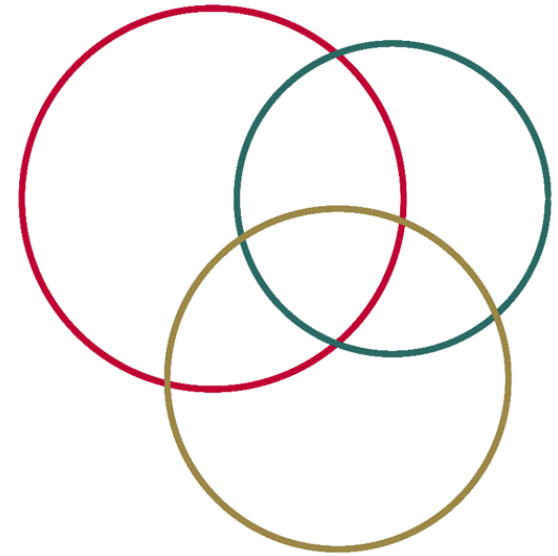
The patient experience: a key driver of demand generation for differentiated care?

- If we believe that patients should be at the center of care, how well are we listening to their voices?

- How can data on the patient experience of care be systematically incorporated into the healthcare delivery system to drive greater:
  - Flexibility
  - Accountability
  - Responsiveness to patient needs
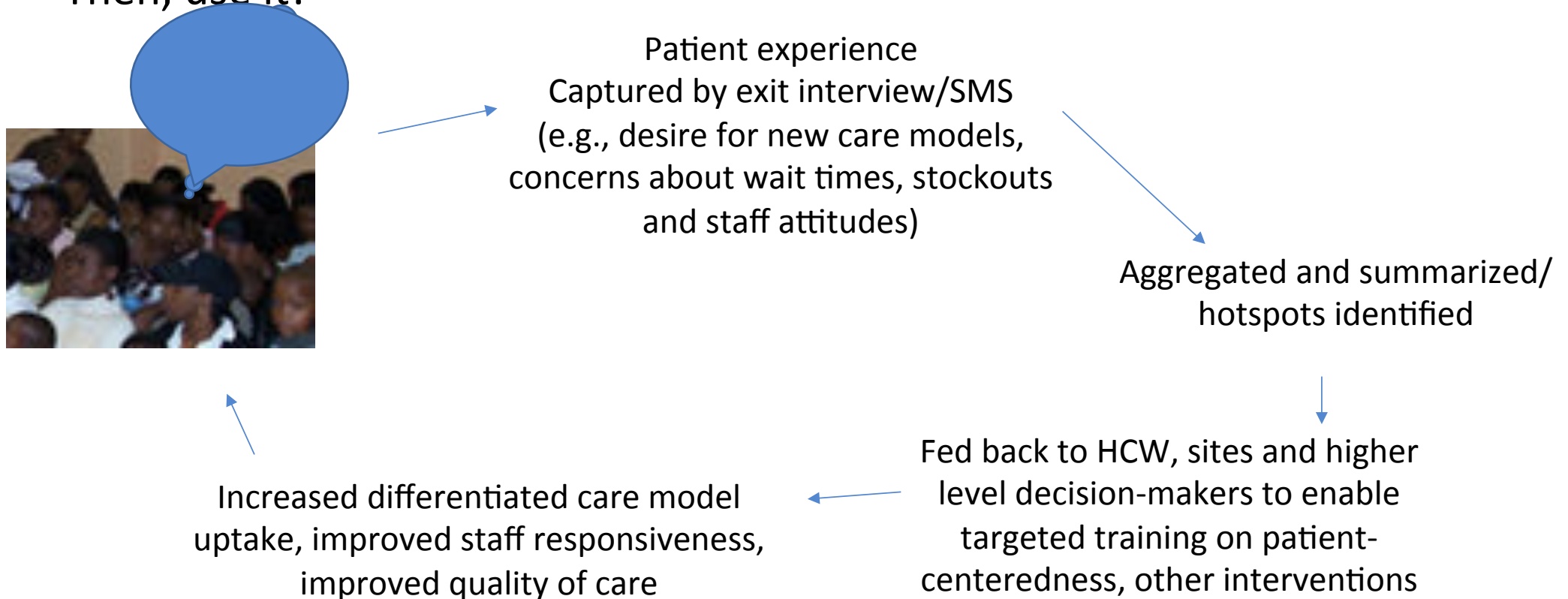 - Uptake of differentiated models of care

Research agenda on the patient experience

- First need to systematically measure the patient experience
  - Patient reported experience measures (PREMs), Patient reported outcomes (PROs)
  - Adapting for lower resource settings- value of routine SMS/exit interviews
- Then, use it!

Patient experience
Captured by exit interview/SMS
(e.g., desire for new care models,
concerns about wait times, stockouts
and staff attitudes)

Aggregated and summarized/
hotspots identified

Fed back to HCW, sites and higher
level decision-makers to enable
targeted training on patient-
centeredness, other interventions

Increased differentiated care model
uptake, improved staff responsiveness,
improved quality of care

Special patient populations..

- Key population friendly models
  - What models are most effective at reducing stigma and enhancing retention and outcomes?

- Adolescents
  - Can wkd/off-hours "club"-type approaches effectively reach and retain adolescents in HIV and RH and other care, and how can this be adapted by MOH given often restrictive HR policies?

- Pregnant and breastfeeding women
  - What is the most effective approach to maintaining continuity of care and social support when women in various models of care become pregnant?
    - E.g., ART clubs, CAGs, visit spacing..

- "Unstable patients"
  - What model of advanced adherence counseling is most effective?
  - What is the most efficient visit schedule and care team to manage patients requiring a switch to second or third line therapy?

- Studies of feasibility, acceptability and effectiveness are needed
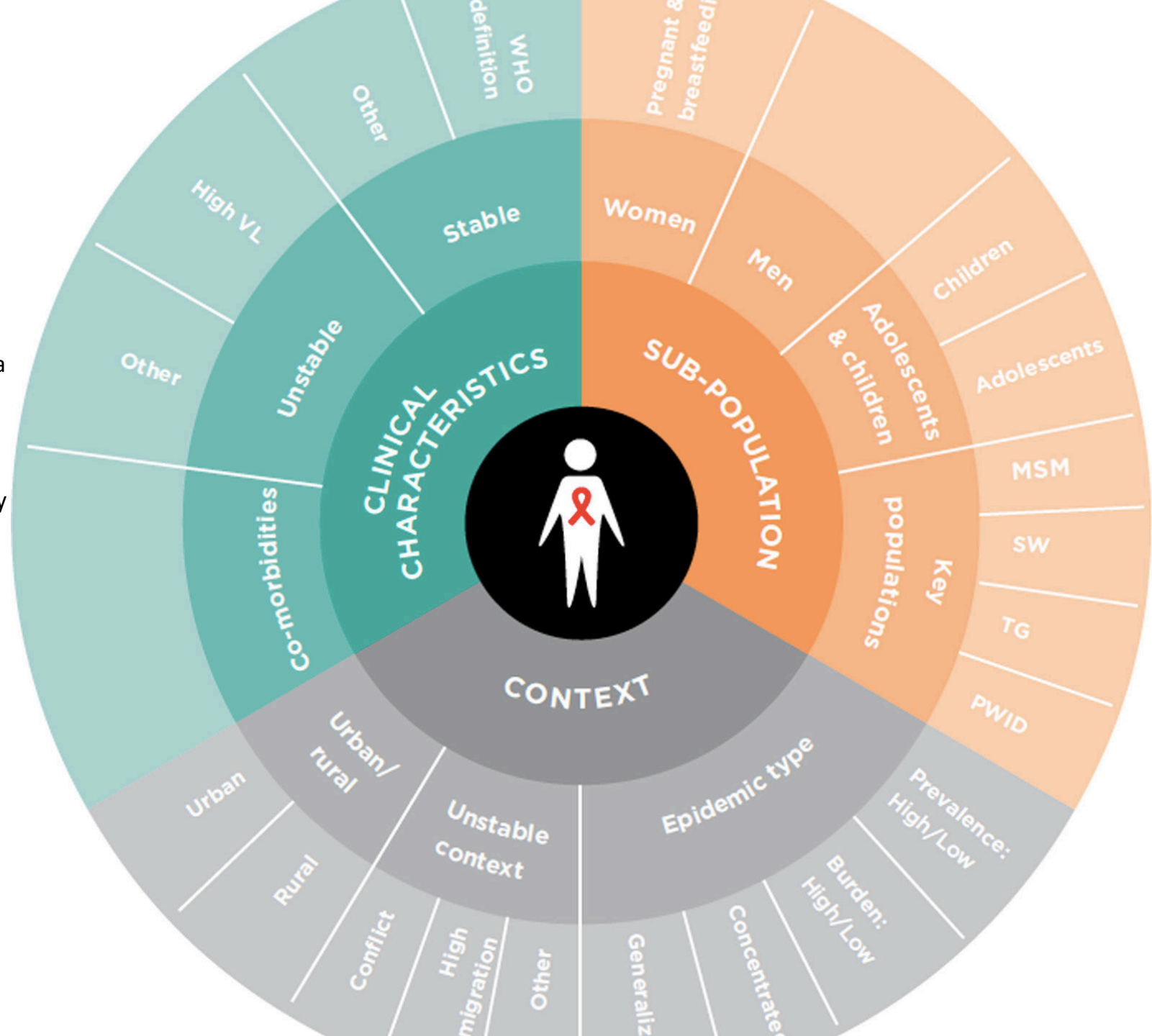
Differentiated care scale-up fidelity - CHAI study in Malawi

- **30 ART clinics were sampled purposefully to achieve diversity (4 FTR sites, 8 CAG sites, and 30 MMS sites)**
- **6 data collection methods were used in all sites**

# and type of data	Purpose
32 ART in-charge interviews	• Understand on-the-ground implementation and challenges
30 focus groups with 216 patients	• Explore benefits, challenges and costs for patients
136 health worker surveys	• Explore provider views and experiences with models of care
75,364 patient record reviews	• Understand the percentage of stable patients getting the models
1,473 visit time observations	• Collect wait and servicing times at each step of visit process
30 facility questionnaires	• Document facility characteristics, schedules, lab and stock issues

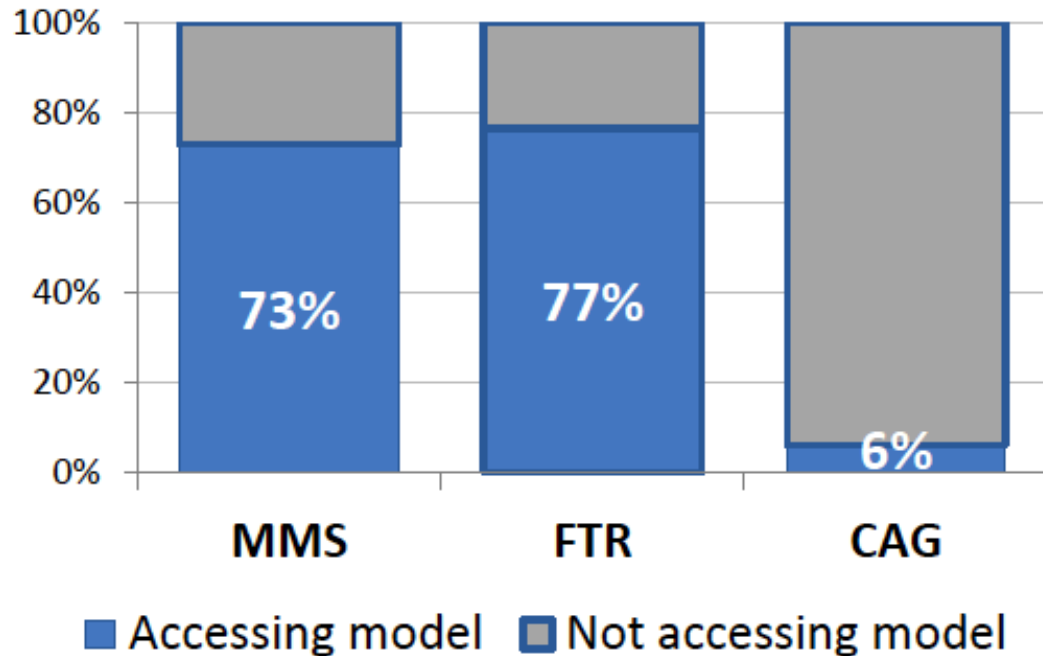**Multi-Month Prescriptions (MMS)**
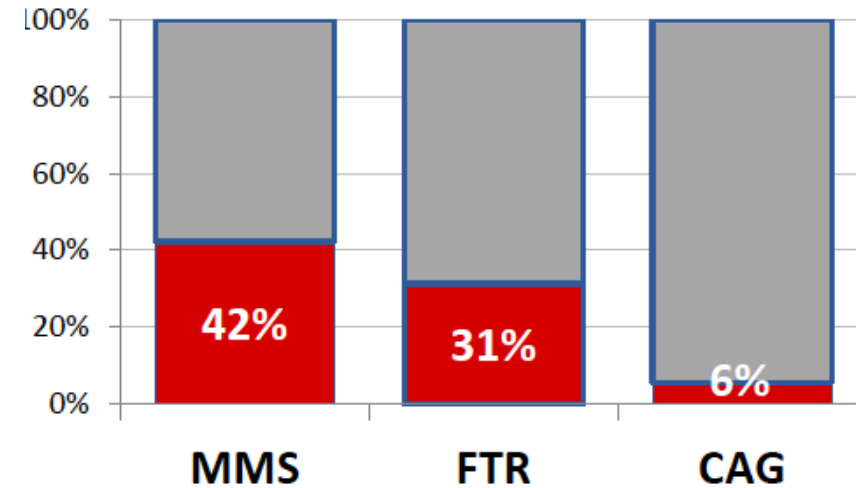
Fast-Track Refills (FTRs)

Community ART Groups (CAGs)

CHAI Project report, 2017

CHAI assessment of multi-month prescribing penetration in Malawi

Percentage of STABLE patients accessing model

- MMS: 73%
- FTR: 77%
- CAG: 6%

■ Accessing model ■ Not accessing model

Percentage of NON-STABLE patients accessing model
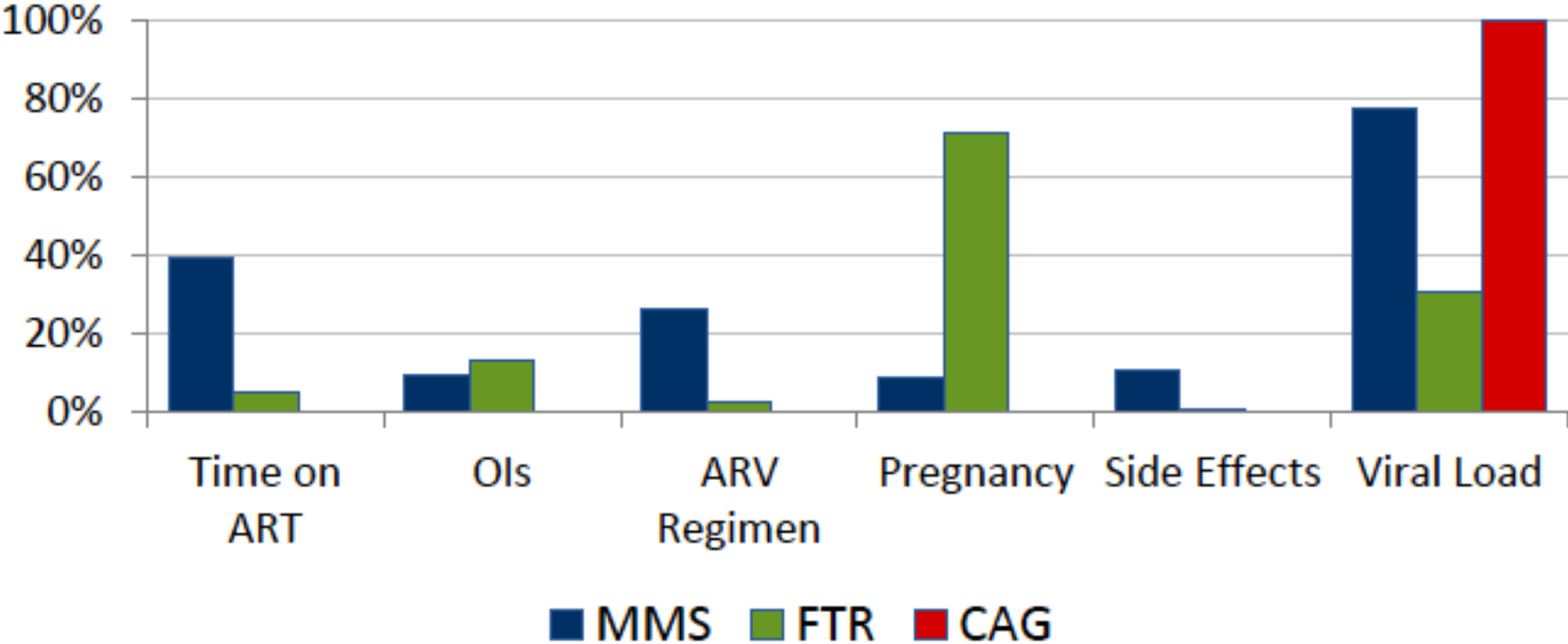
- MMS: 42%
- FTR: 31%
- CAG: 6%

■ Accessing model ■ Not accessing model

Inclusion of non-stable patients:
- Transitioning out of model
- Lack of understanding of criteria
- Patient requests
- Attempt to reduce workload

CHAI Project report, 2017

Percentage of non-stable patients receiving MMS FTRs and CAGs that do not meet each criteria

CHAI Project report, 2017

Research agenda around the scale-up of differentiated care

- In the absence of robust national data systems, how often should we be conducting special studies (CHAI example from Malawi) to assess scale-up fidelity/effectiveness/safety?

- What are the information system features and program indicators that best enable tracking of patient outcomes under different model conditions?

- What alternative strategies can be embedded and tested during scale-up?

- Are high-burden communities with high penetration of differentiated care models experiencing improved outcomes and reduced stigma?

- Are cost-effectiveness projections being met as scale is achieved? How can programmatic expenditure analysis be used to ensure the efficiency of differentiated care scale-up?

Conclusions

- Convergence of demands on the health system require new approaches, including the use of differentiated care principles

- There is an emerging differentiated care research agenda that includes how to make the best of existing models (especially visit spacing) that make the least demands on patients/system

- Emerging data on patient barriers/preferences may be useful to help guide rational site and individual-level deployment/choices of various differentiated care models – opportunities to test the concept of "guided choice"

- The patient experience is an overlooked source of information and should be measured and used/tested as a strategy to drive the uptake of patient-friendly differentiated models and greater responsiveness of the health system to patient needs and preferences

- There are substantial opportunities to tailor differentiated care for special populations that could benefit from greater attention to accelerating evaluations of feasibility, acceptability and effectiveness

- We need the ability to measure the pace and quality of scale-up through incorporation of differentiated care data into existing information systems, yet also need special studies where this is not yet possible

- Studies are needed to assess whether the broader hopes for differentiated care (reduced patient costs, simplicity, stigma, systems costs, etc) are realized when taken to scale

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