



# Structural factors and the HIV prevention and treatment cascades: where are we?

Sinead Delany-Moretlwe &  
James Hargreaves

On behalf on

The STRIVE Biomedical Working Group



## Structure of talk

Introduction: STRIVE in the time of cascades

Biomedical HIV prevention tools can't do it on their own



Structural factors can be addressed within programmatic time frames with evidence-based interventions

Innovative new studies are needed to understand and respond to structural barriers to HIV prevention

Discussion

## Introduction: STRIVE in the time of cascades

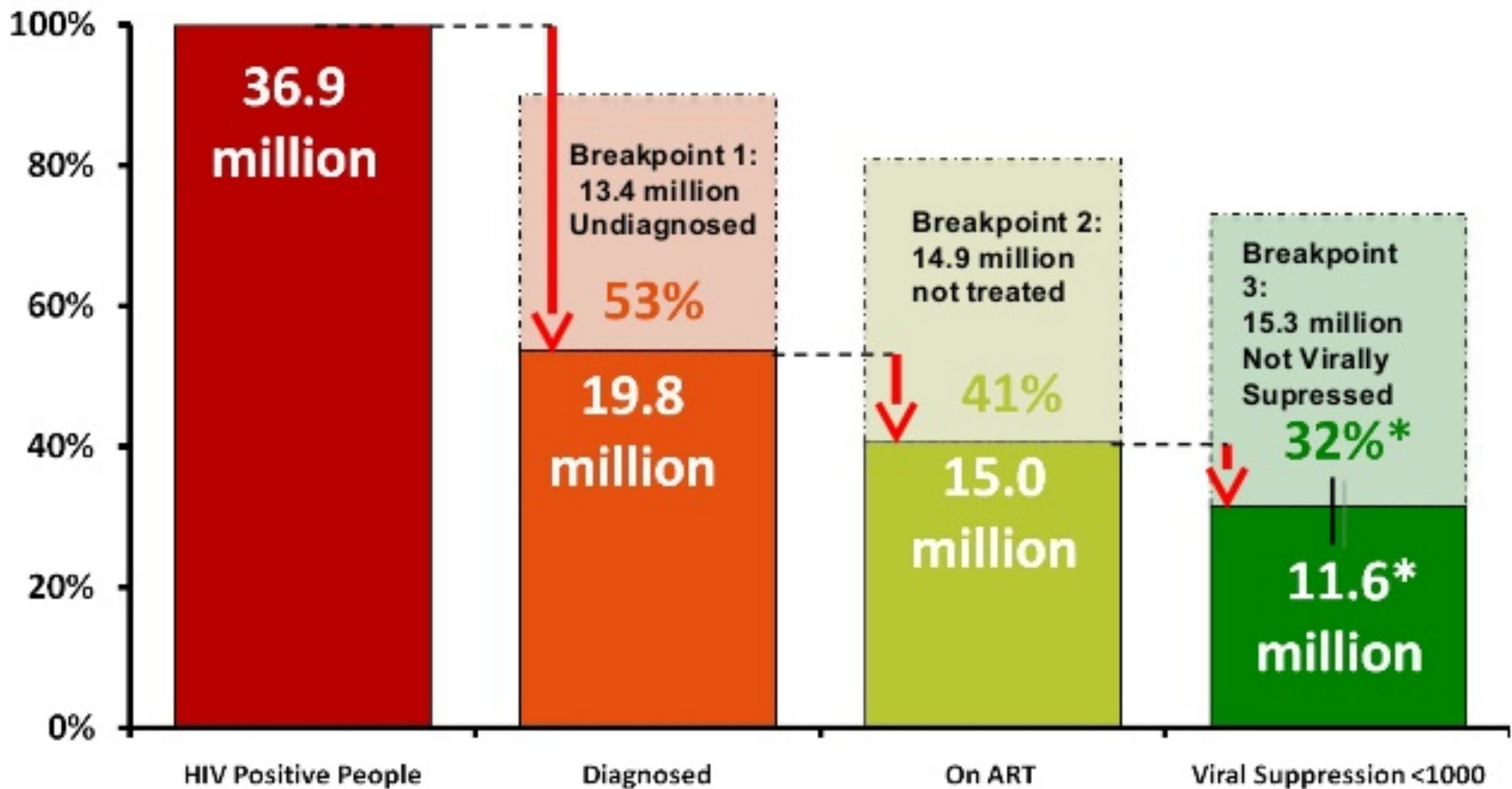
There is an unmet need for HIV prevention, both through primary prevention and treatment-as-prevention, particularly in key populations.

HIV prevention has been dominated by behaviour change, but structural factors have acted as a barrier

Recent advances in knowledge about biomedical prevention offers real promise for reducing HIV incidence at a population-level – if sufficient coverage achieved.



# Achieving TasP coverage: The treatment cascade

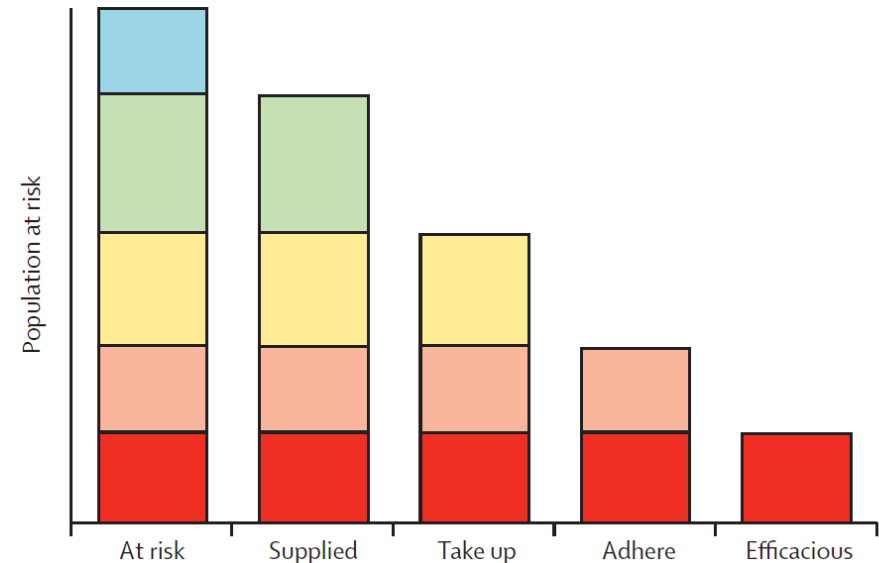
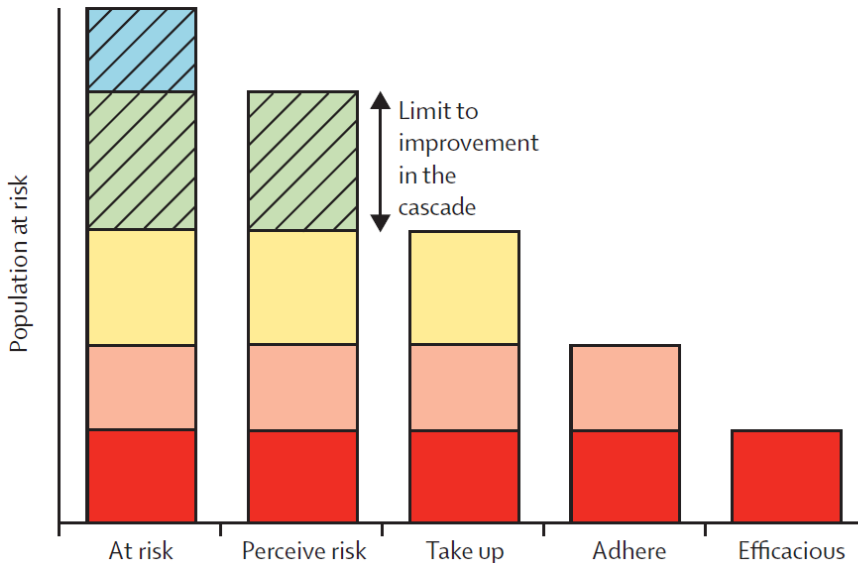


# Achieving prevention coverage: The prevention cascade

**A Client-centric prevention cascade**


**B Intervention-centric prevention cascade**

▨ Do not perceive risk   
 ▨ Ignore prevention technology   
 ■ Remain unaffected   
 ■ Leave/return   
 ■ Lack of adherence or fidelity   
 ■ Lack of efficacy  
■ Lack availability   
■ Lack of uptake



## STRIVE BMWG questions


Will structural factors act as barriers to the success of biomedical prevention tools, and if so how, why and among who?



Can programmes address structural factors in order to optimise the impact of biomedical HIV prevention?

## Message 1

Biomedical HIV prevention tools can't do it on their own

- 
- The inverse equity hypothesis
  - STRIVE review

## The inverse equity hypothesis



“New interventions will initially reach those of higher socioeconomic status and only later affect the poor.”

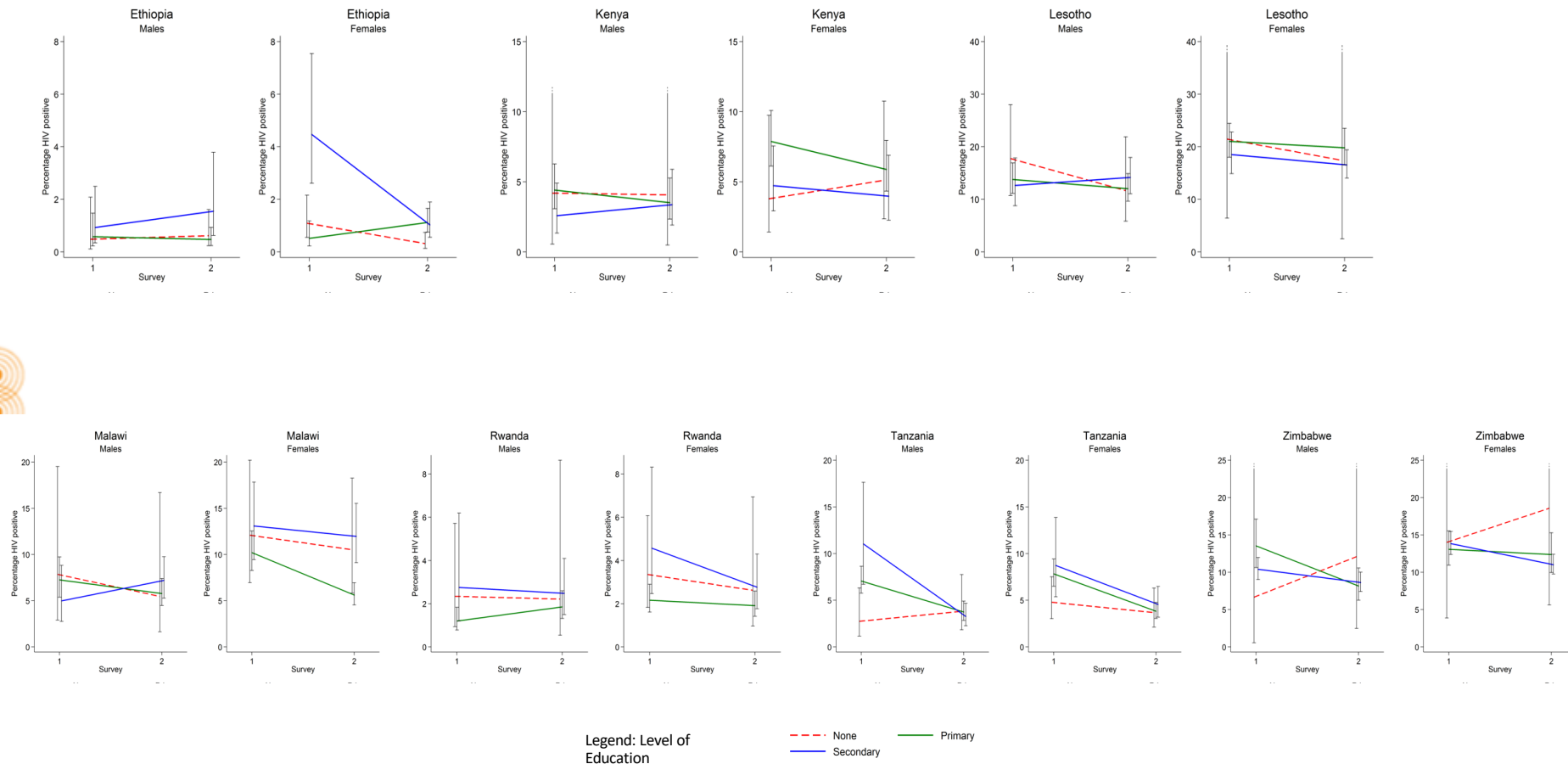


# Tanzania

	Males			Females		
	No Education	Primary Education	Secondary education or higher	No Education	Primary Education	Secondary education or higher
Year	HIV (%)	HIV (%)	HIV (%)	HIV (%)	HIV (%)	HIV (%)
2003	4.2	6.5	7.3	5.8	8.1	9.3
2007	5.5	4.7	3.4	6.0	7.0	4.9
<b>RD%*</b>	31.0	<b>-27.9</b>	<b>-53.4</b>	3.4	<b>-13.8</b>	<b>-47.3</b>

Interaction terms year-education p=0.07, from Hargreaves and Howe AIDS (2010)

Figure 1. Changes in HIV Prevalence among men and women aged 15-24 years with different levels of educational attainment between earlier (2003-5) and later (2008-12) nationally-representative population-based surveys in seven sub-Saharan African countries .





# **STRIVE review of reviews**

## Selection of factors

- Gender inequality and violence,
- Alcohol use
- Stigma,
- Poverty or socio-economic status, and



## Methods

- Systematic scoping review of the literature to map existing understanding of the potential for selected factors to act as a barrier
- Prioritized systematic reviews i.e. review of reviews.
- Search strategies were conducted using MeSH terms and keyword searches specific to the cascade.
- Two key databases were searched: Pubmed/MEDLINE and ISI Web of Science.
- Titles, abstracts, and full texts of published reviews were screened for inclusion by two reviewers.
- Assessed the type and direction of the evidence for each of the four outcomes based on study design and direction of reported findings

# Violence and fear of violence limits the success of HIV treatment cascade

## HIV testing and linkage to care

Gender inequality undermines women's decision making autonomy about HIV testing  
*Musheke, 2013*

Fear of partner violence prevented some women from accessing testing, but other studies showed no difference in uptake or access by IPV status. One study suggested that IPV motivates HIV testing  
*Kouyoumdjian 2013*

Fear of violence prevented disclosure  
*Kouyoumdjian 2013*

## ART initiation

- IPV was associated with inability to access care and treatment, although one outlier did not show an association. *Kouyoumdjian, 2013*
- IPV was associated with lower 'current ART use' among women in meta-analysis. *Hatcher, 2015*
- Women were reluctant to, or did not include at all, their male partners in PMTCT services due to fear of violence. *Morfaw, 2013*

## Adherence and Retention in care

- IPV reduced odds of women adhering to ART by half. *Hatcher, 2015*
- Partner abuse associated with poor medication adherence leading to poor treatment outcomes (VL, CD4+). *Pantalone, 2014*
- IPV associated with treatment discontinuation in two studies  
*Kouyoumdjian, 2013*
- Some evidence for increased loss to follow up  
*Hatcher, 2015*

Limited data for PrEP but emerging evidence for similar patterns

## Socio-economic status

### HIV testing and linkage to care

- Transport costs, distance to health facility, food shortage, patient-related time constraints were the main reported economic barriers to linkage to care  
*Obermeyer, 2007*  
*Govindasamy, 2012*
- Unstable housing associated with poor health service utilisation  
*Leaver 2007*

### ART initiation

- Influenced by travel time/distance, lack of consistency and co-ordination across services, and the limited involvement of the community in the programme planning process  
*Hlarlaithe, 2014, Posse, 2008*

### Adherence and retention in care

Housing instability was a significant predictor of non-adherence to HAART  
*Leaver, 2007*  
Transport costs and distance impeded continuity in HIV care.  
*Govindasamy, 2012*  
Food insecurity is an important barrier to ART adherence and provision of food can improve adherence  
*de Pee 2014, Singer, 2015*

# Stigma

Consistent findings that stigma is a barrier to

- Access and uptake of testing and linkage to care *Obermeyer, 2007; Mahajan, 2008; Ferguson, 2012; Musheke, 2013; Levy, 2014; Posse 2008*
- Adherence and retention in care *Mahajan, 2008; Katz, 2013; Colombini, 2014*
  - No reviews showing impact on clinical outcomes apart from PMTCT *Mahajan, 2008; Hlarlaithe, 2014;*
- Less but emerging evidence of ART stigma associated with poor PrEP adherence in placebo-controlled trials
- Mediated largely through fear of disclosure of status





# Alcohol

## Testing and linkage to care

- Evidence on the impact of alcohol use and HIV service utilization was variable *Azar, 2010*
- Alcohol use negatively affects all steps of the treatment cascade. *Vagenas, 2015*

## ART initiation and use

- Strong and consistent evidence that alcohol use undermines adherence and treatment outcomes. *Hendershot, 2009; Azar, 2010; Gari, 2013; Nakimuli-Mpungu, 2012; Vagenas, 2015;*
- Worse outcomes with non-communicable co-morbidities *Grodensky, 2012*

Limited evidence for effects on ART-based prevention

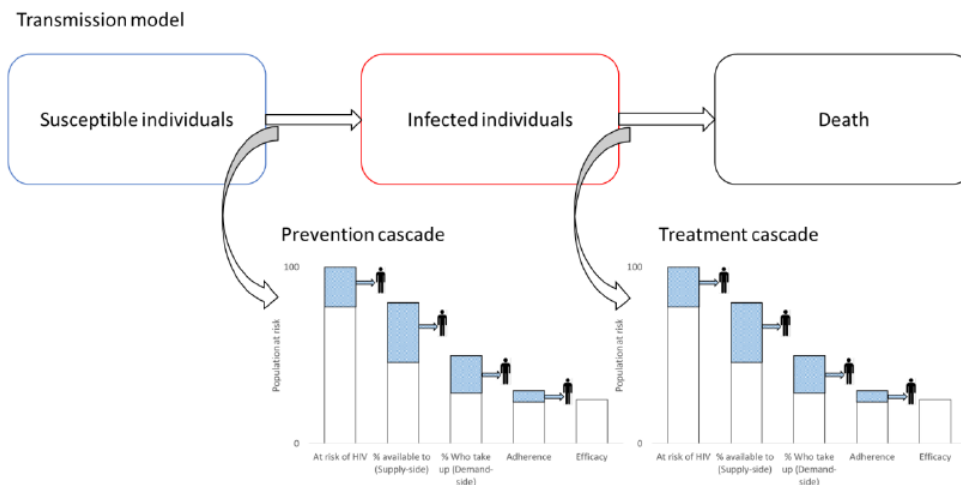


## Conclusions

- Evidence that each of these structural factors influence elements or all of the cascade
- In some cases the evidence is mixed – related to definition of the structural factor
- Evidence more limited for prevention interventions e.g. PMTCT, PrEP, PEP – but emerging and similar trends
- Evidence for impact on clinical/population-level impacts if limited – where it exists, outcomes are poorer

# Implications

- In designing ART-based prevention interventions, need to identify evidence-based interventions that address these structural factors
- Test combination interventions to optimise ART benefits in populations at risk – key is an understanding of those factors that are most influential



## Message 2

**Structural factors can be addressed within programmatic time frames with evidence-based interventions**

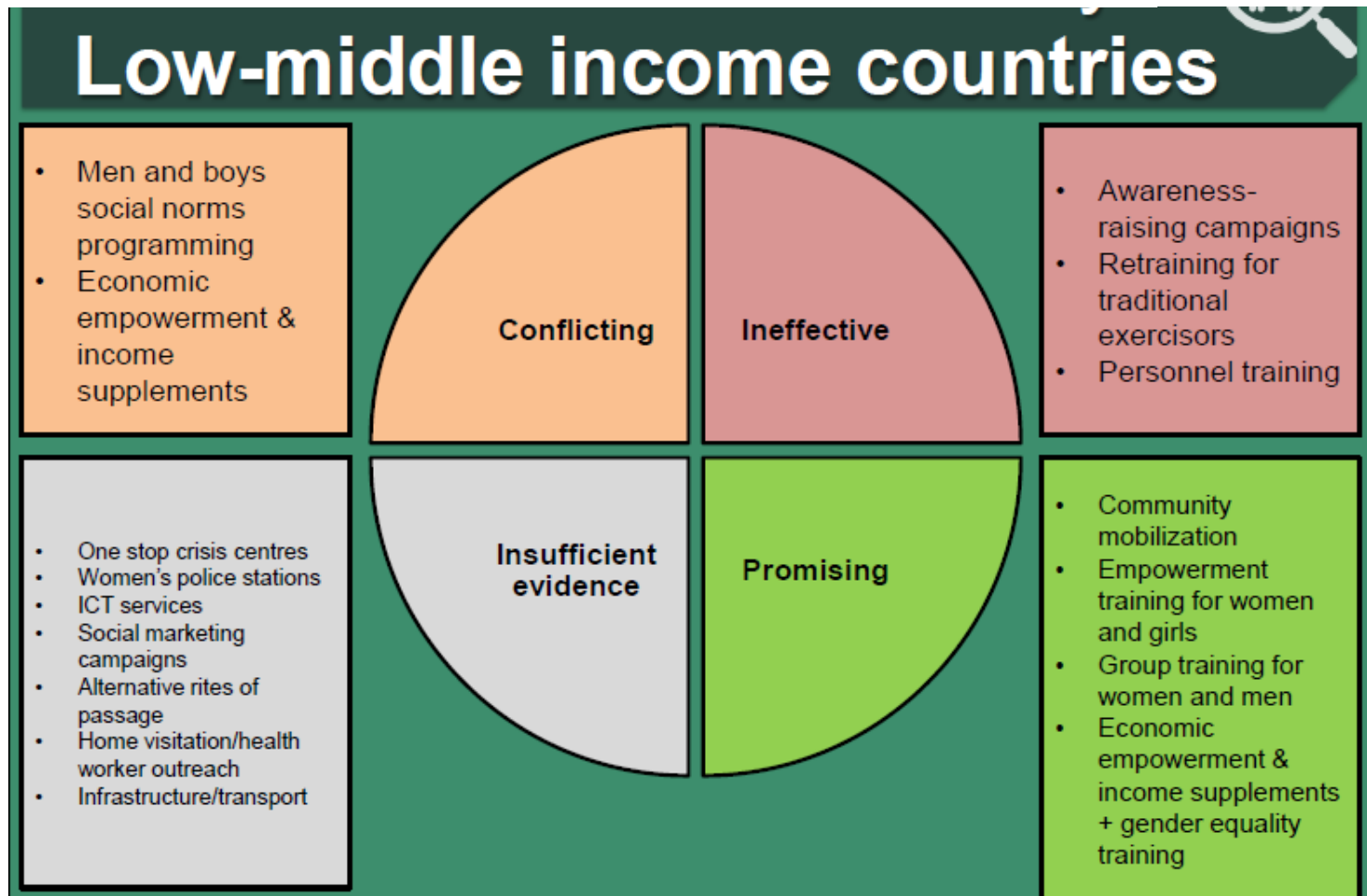
- 
- Examples from the literature
  - The Prevention Cascade

## Violence against women and girls 1

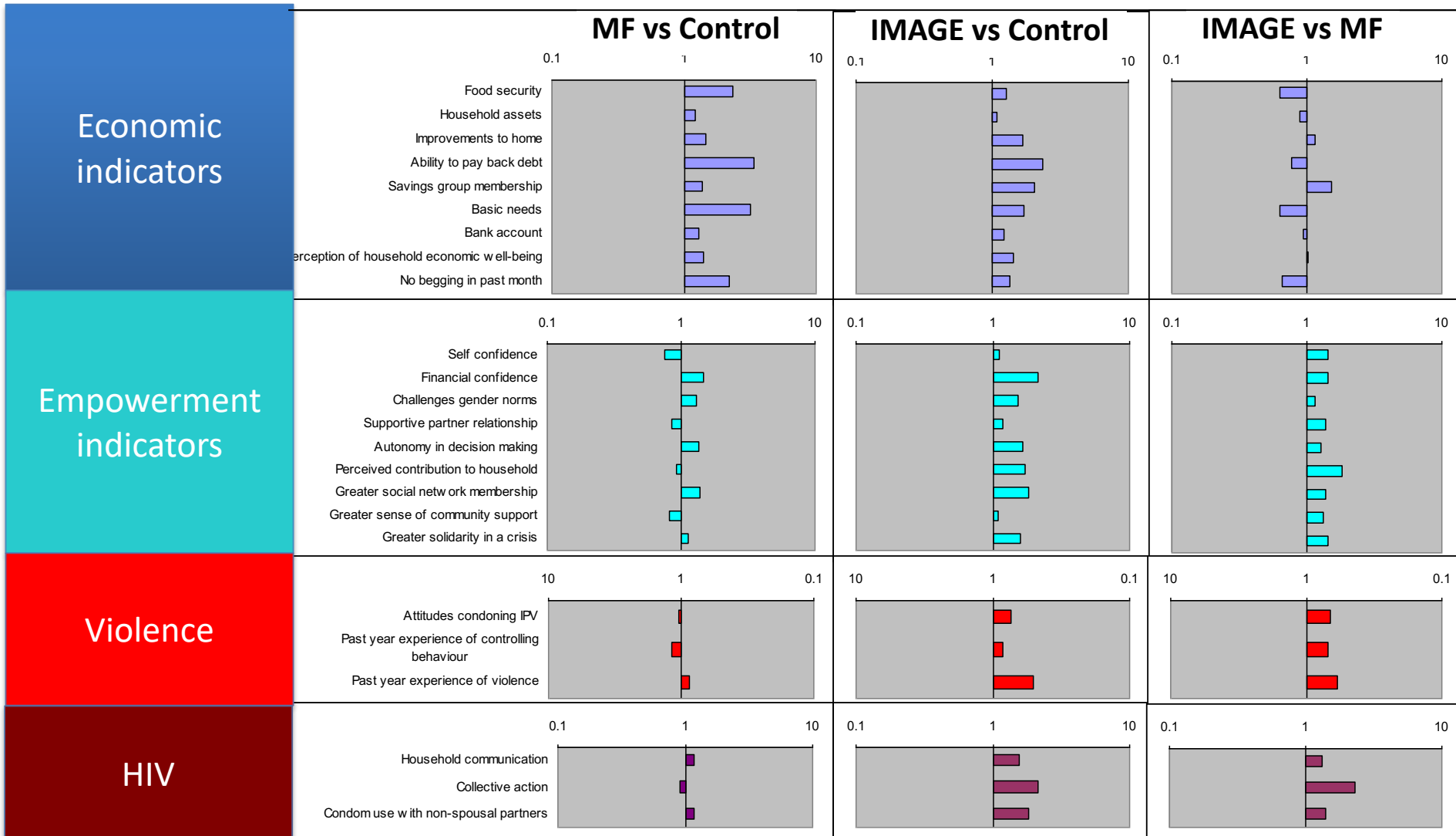


# Prevention of violence against women and girls: what does the evidence say?

Mary Ellsberg, Diana J Arango, Matthew Morton, Floriza Gennari, Sveinung Kiplesund, Manuel Contreras, Charlotte Watts



# South Africa: Microfinance combined with Gender training (IMAGE) improved range of indicators



Source: Kim, Watts et al 2008 WHO Bulletin

## Review article

# A systematic review of interventions to reduce HIV-related stigma and discrimination from 2002 to 2013: how far have we come?

Anne L Stangl<sup>§,1</sup>, Jennifer K Lloyd<sup>2</sup>, Laura M Brady<sup>1</sup>, Claire E Holland<sup>2</sup> and Stefan Baral<sup>2</sup>

Considerable progress made over the last decade.

- The number, geography and complexity of interventions have notably expanded.
- Studies that showed reductions of HIV-related stigma were of high quality
  - 90% reported reductions in stigma
  - 75% used 2+ strategies

Current evidence is strongest for interventions with:

- students, health care workers, and community members; and
- interventions using structural and counseling-based

## “Best buy” policy interventions to reduce alcohol-related harm (WHO)

- Regulate production, wholesaling and serving of alcoholic beverages that places reasonable limitations on the distribution of alcohol and the operation of alcohol outlets in accordance with cultural norms (WHO, 2009)
- Reduce the impact of marketing, particularly on young people and adolescents, is an important consideration in reducing harmful use of alcohol.
- Use pricing policies to reduce underage drinking, to halt progression towards drinking large volumes of alcohol and/or episodes of heavy drinking, and to influence consumers' preferences.



# Mapping interventions to the prevention cascade



<b>Demand side</b>			
<b>Targets for prevention programmes</b> <ul style="list-style-type: none"> <li>• Risk perception</li> <li>• Awareness and positive attitudes towards direct mechanisms of HIV prevention</li> <li>• Social norms</li> </ul> <b>Interventions</b> <ul style="list-style-type: none"> <li>• Information and education campaigns</li> <li>• Peer-based prevention programmes</li> </ul> <b>Platforms for delivery at scale</b> <ul style="list-style-type: none"> <li>• Schools, media, community</li> </ul> <b>Policies</b> <ul style="list-style-type: none"> <li>• Quality assurance programmes, policies that support age-appropriate sex education</li> </ul>	<b>Supply side</b>		
	<b>Targets for prevention programmes</b> <ul style="list-style-type: none"> <li>• Availability and accessibility of direct mechanisms of HIV prevention (especially products and procedures)</li> </ul> <b>Interventions</b> <ul style="list-style-type: none"> <li>• Mass condom distribution</li> <li>• Needle-syringe exchange programmes</li> <li>• Integrated health service delivery of HIV prevention</li> </ul> <b>Platforms for delivery</b> <ul style="list-style-type: none"> <li>• Health sector, private sector</li> </ul> <b>Policies</b> <ul style="list-style-type: none"> <li>• Overcoming legal barriers to supplying prevention products, mainstreaming, task sharing</li> </ul>	<b>Adherence</b>	
		<b>Targets for prevention programmes</b> <ul style="list-style-type: none"> <li>• Behavioural self-efficacy and agency</li> </ul> <b>Interventions</b> <ul style="list-style-type: none"> <li>• Longitudinal behavioural counselling.</li> <li>• Interventions targeting social determinants of behaviour such as cash transfers, livelihood programmes, empowerment programmes</li> <li>• Incentives</li> </ul> <b>Platforms</b> <ul style="list-style-type: none"> <li>• Health sector, development sector partners</li> </ul> <b>Policies</b> <ul style="list-style-type: none"> <li>• Co-financing, monitoring of police treatment of key populations</li> </ul>	<b>Direct mechanisms of HIV prevention</b>
			<b>Prevention behaviours</b> <ul style="list-style-type: none"> <li>• Abstinence, sero-sorting</li> </ul> <b>Prevention products</b> <ul style="list-style-type: none"> <li>• PrEP, male and female condoms</li> </ul> <b>Prevention procedures</b> <ul style="list-style-type: none"> <li>• Voluntary medical male circumcision</li> </ul>

Approaches to increase coverage and to translate trial efficacy to population effect

**Figure: Targets for prevention programmes along the HIV prevention cascade**  
Prevention targets with some examples of interventions, platforms for delivery, and policies.

## The HIV prevention cascade: integrating theories of epidemiological, behavioural, and social science into programme design and monitoring

James R Hargreaves, Sinead Delany-Moretlwe, Timothy B Hallett, Saul Johnson, Saidi Kapiga, Parinita Bhattacharjee, Gina Dallabetta, Geoff P Garnett

“Direct mechanisms”:  
29 Reviews (98 primary  
studies [34 RCTs])

Prevention products: PreP  
(6), Condoms (4), VMMC  
(64), STI reduction (7),  
Microbicides (12),  
Vaccines (5)

Prevention behaviours:  
abstinence, sero-sorting  
(not included in this  
review)

“Demand” focused interventions: 40 Reviews (108 primary  
studies [24 RCTs])

IEC approaches (54); Peer-based approaches (54)

“Supply” interventions: 12 Reviews (35 primary studies [6 RCTs])

Mass Condom Distribution and associated policies (20); Needle / Syringe  
programmes and associated policies (6); Health system policies: Integration of  
family planning and HIV (6); STI Control (3)

“Use” interventions: 16 Reviews (51 primary studies [26 RCTs])


Counselling approaches (40); Social determinants approaches: cash transfers  
(3); microfinance (8)

	Incidence		Prevalence		Condom use		HIV testing	
	Number of studies	Quality assessment rating	Number of studies	Quality assessment rating	Number of studies	Quality assessment rating	Number of studies	Quality assessment rating
<b>Demand-side interventions</b>								
Effect of IEC interventions focused on young people <sup>2-31</sup>	3 (1)	B4	1 (1)	B4	28 (7)	A3	--	--
Effect of IEC interventions focused on men <sup>31,32,39-42</sup>	--	--	--	--	9 (3)	A2	1 (0)	C1
Effect of IEC interventions focused on women <sup>31,33</sup>	--	--	--	--	2 (2)	B3	--	--
Effect of IEC interventions using mass media <sup>31,32,34</sup>	1 (1)	B3	--	--	9 (1)	B4	--	--
Effect of IEC interventions focused on people who use drugs <sup>35,33,34</sup>	--	--	--	--	4 (3)	A1	--	--
Effect of peer-based interventions focused on young people <sup>6,8,29,31,35,36,37-39</sup>	1 (1)	B4	--	--	11 (0)	C2	2 (0)	C1
Effect of peer-based interventions focused on MSM <sup>39-36</sup>	--	--	--	--	3 (1)	B1	1 (0)	C1
Effect of peer-based interventions focused on female sex workers <sup>9,34,32,36,37-44</sup>	3 (1)	C4	4 (0)	C4	22 (3)	B2	3 (0)	C1
Effect of peer-based interventions focused on people who use drugs or alcohol <sup>12,28,30,31,45-47</sup>	2 (2)	B4	1 (1)	B4	5 (2)	B3	--	--
Effect of peer-based interventions with no population focus <sup>9,18,32,28,30,31,33,41</sup>	--	--	--	--	10 (2)	B1	1 (0)	C1
<b>Supply-side interventions</b>								
Effect of interventions that integrate HIV services into routine care <sup>41,41</sup>	--	--	--	--	1 (0)	C1	5 (0)	C1
Effect of clean needle or syringe programmes <sup>45,50</sup>	2 (0)	C3	6 (0)	C1	--	--	--	--
Effect of condom distribution interventions <sup>7,9,15,28,29,44,51</sup>	--	--	3 (0)	C1	20 (5)	A1	--	--
Effect of community-level STI interventions <sup>52</sup>	3 (3)	A4	--	--	1 (1)	B4	--	--
<b>Adherence interventions</b>								
Effect of couples-based counselling <sup>46,53-57</sup>	1 (0)	C1	--	--	9 (3)	A1	4 (3)	A3
Effect of HIV testing and counselling <sup>34,51,51,54,58</sup>	1 (1)	B4	--	--	8 (1)	B2	3 (2)	B1
Effect of individual-level counselling <sup>54,55,22,24,37-39</sup>	1 (1)	B3	--	--	12 (7)	A1	2 (1)	B3
Effect of HIV-positive prevention counselling <sup>11,24,53,55,59,60</sup>	--	--	--	--	7 (4)	A3	--	--
Effect of microfinance interventions <sup>61-64</sup>	1 (1)	B4	--	--	8 (4)	A3	1 (1)	B1
Effect of cash transfer interventions <sup>65</sup>	2 (2)	B4	2 (2)	B1	1 (1)	B4	--	--
<b>Direct mechanisms</b>								
Medical male circumcision for heterosexual route risk (female to male) <sup>66-74</sup>	38 (3)	A1	--	--	--	--	--	--
Medical male circumcision for heterosexual route risk (male to female) <sup>75</sup>	7 (1)	B3	--	--	--	--	--	--
Male circumcision men who have sex with men route individual-level studies <sup>75,76,78</sup>	19 (0)	C3	--	--	--	--	--	--
Condoms (heterosexual) individual-level studies <sup>79-84</sup>	4 (0)	C1	--	--	--	--	--	--
Oral PrEP (overall) individual-level studies <sup>85-84</sup>	6 (6)	A2	--	--	--	--	--	--
Microbicide prophylaxis individual-level studies <sup>88,71,89-90</sup>	12 (12)	A3	--	--	--	--	--	--
STI treatment individual-level studies <sup>44,84,89,91-93</sup>	7 (7)	A4	--	--	--	--	--	--
HIV vaccine individual-level studies <sup>71,90</sup>	5 (5)	A3	--	--	--	--	--	--

	3 or more RCTs (might also include observational studies)	1-2 RCTs (might also include observational studies)	No RCTs; only observational studies
Consistently showed effectiveness	A1	B1	C1
Largely, but not consistently, showed effectiveness	A2	B2	C2
Mixture of beneficial and ineffective or harmful results	A3	B3	C3
Consistent ineffective or harmful results	A4	B4	C4

## Message 3

Innovative new studies are needed to understand and respond to structural barriers to HIV prevention

- 
- Stigma and TasP
  - EMPOWER

HIV stigma : negative stereotypes, leading to a separation of “us” from “them” and status loss

Attitudes and behaviours of community members and health workers are determinants of stigma experienced by PLHIV and other vulnerable groups

Experienced and internalised stigma are negative outcomes, human rights infringements and can lead to poor mental health

Stigma can act as a barrier to HIV prevention, testing, linkage to care and adherence

## Stigma and Universal Test and Treat hypotheses

Universal Test and Treat may change levels of HIV-related stigma



HIV-related stigma may undermine the effectiveness of Universal Test and Treat

Universal Test and Treat may change the forms of HIV-related stigma







## Measuring stigma

Harmonised consensus items – STRIVE measurement brief (Stangl et al)

Parallel approach

– Eg “Talk badly”

Theory and data informed approach to item grouping

# Initial Findings from HPTN071 (PopART)

## Stigma in the Health Facility

- Space is important
- HCWs LWH



## Stigma in the community

- Vulnerable groups and PLHIV

## Stigma and uptake of the testing and treatment interventions

- Home-based testing
- Early ART

## Stigma prevalence in PLHIV ( $n=3859$ )

HIV stigma outcomes	Total	South Africa ( $n=1704$ )	Zambia ( $n=2155$ )	<i>P</i>
<b>Current internalised stigma</b> Responding Agree or Strongly Agree to any of 3 items	868 (22.5%)	310 (18.2%)	558 (25.9%)	<0.001
<b>Experienced any stigma in past year</b> Responding Once, A few times or Often to any of 5 items	853 (22.1%)	320 (18.8%)	533 (24.7%)	<0.001
<b>Experienced health setting stigma in past year</b> Responding Once, A few times or Often to any of 3 items	280 (7.3%)	148 (8.7%)	132 (6.1%)	0.002
<b>Any stigma last year</b> Yes to current internalised stigma, experienced any or health setting stigma in last year	1371 (35.5%)	503 (29.5%)	868 (40.3%)	<0.001

## Primary Objectives:

To evaluate the feasibility, acceptability and safety of:

- integrating screening and linkage-to-care for GBV and stigma within HIV counselling and testing for AGYW, and
- supporting PrEP acceptance, effective use (adherence) and retention in care through adherence clubs that include a four-session empowerment curriculum, compared to counselling and SMS support alone, in HIV negative AGYW

**Population:** 600 sexually-active HIV-negative AGYW 16-24 yrs in Johannesburg, South Africa and Mwanza, Tanzania

*Completed follow-up mid-Feb 2018; anticipated results mid-2018*

# Study Design



HCT+ GBV screening  
AGYW age 16-24 years



HIV positive and/or risk of immediate harm - refer

Enrol HIV negative

Accept oral PrEP (N=500)

Decline oral PrEP

Randomisation

Standard of Care  
N=250

Empowerment clubs + standard adherence support (N=250)

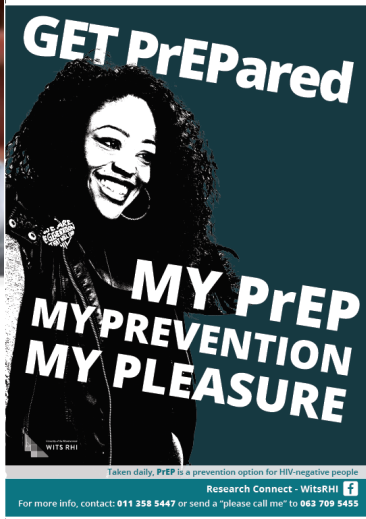
Standard of Care

Empowerment clubs + standard adherence support



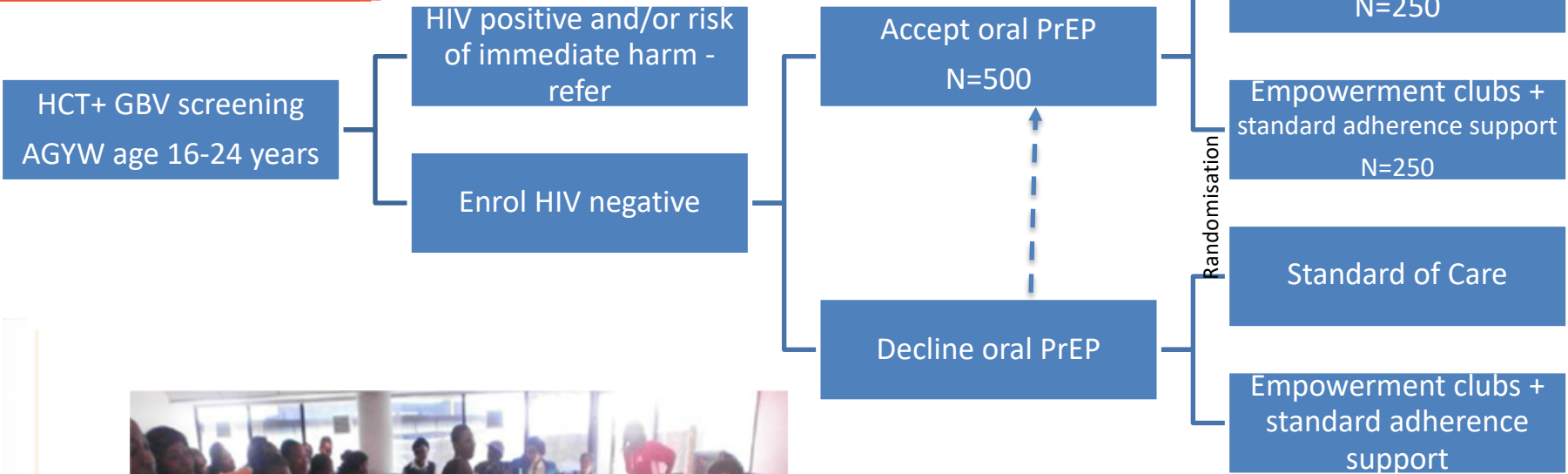
Get PrEPared: What African women need to know!

7.	Test Result Counselling	
8.	STI/HIV treatment or prevention options	2-5
12.	Risk reduction plan	
13.	Disclosure and Partner Referral	5-10
<b>Second Session Time</b>		<b>24-47</b>
<b>Total Time</b>		<b>51-92</b>



Taken daily, PrEP is a prevention option for HIV-negative people.  
Research Connect - WitsRHI  
For more info, contact: 011 258 5447 or send a "please call me" to 062 709 5455

# Study Design (cont.)



Adherence club




Stakeholder engagement and community dialogues

## Discussion

- Biomedical interventions will not achieve the ambitious targets to end AIDS without addressing structural factors that shape HIV risk and undermine uptake and effective use
- Structural factors can be addressed within programmatic time frames with evidence-based interventions
- We must now integrate strategies to address structural factors within HIV biomedical prevention and evaluate at scale



# Acknowledgements



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