

Genital inflammation test for HIV prevention and reproductive health

Lindi Masson, Burnet Institute
on behalf of the GIFT-Africa Consortium



SEXUAL AND REPRODUCTIVE HEALTH **FOR WOMEN**

A rapid point-of-care test to improve management of sexually transmitted infections and bacterial vaginosis in women.

Disclosures

- Co-inventor with Jo-Ann Passmore on European and South African patents for a method for diagnosing an inflammatory condition in the female genital tract.
- Recipient of SAMRC SHIP, EDCTP and TIA grants to develop and test the GIFT device.
- Recipient of SAMRC, NRF, PRF, and Carnegie Corporation grants to identify novel BV biomarkers using proteomics.



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WP1, 2 and 5: Overall project management, device development and marketing

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WP4: Implementation strategy and impact

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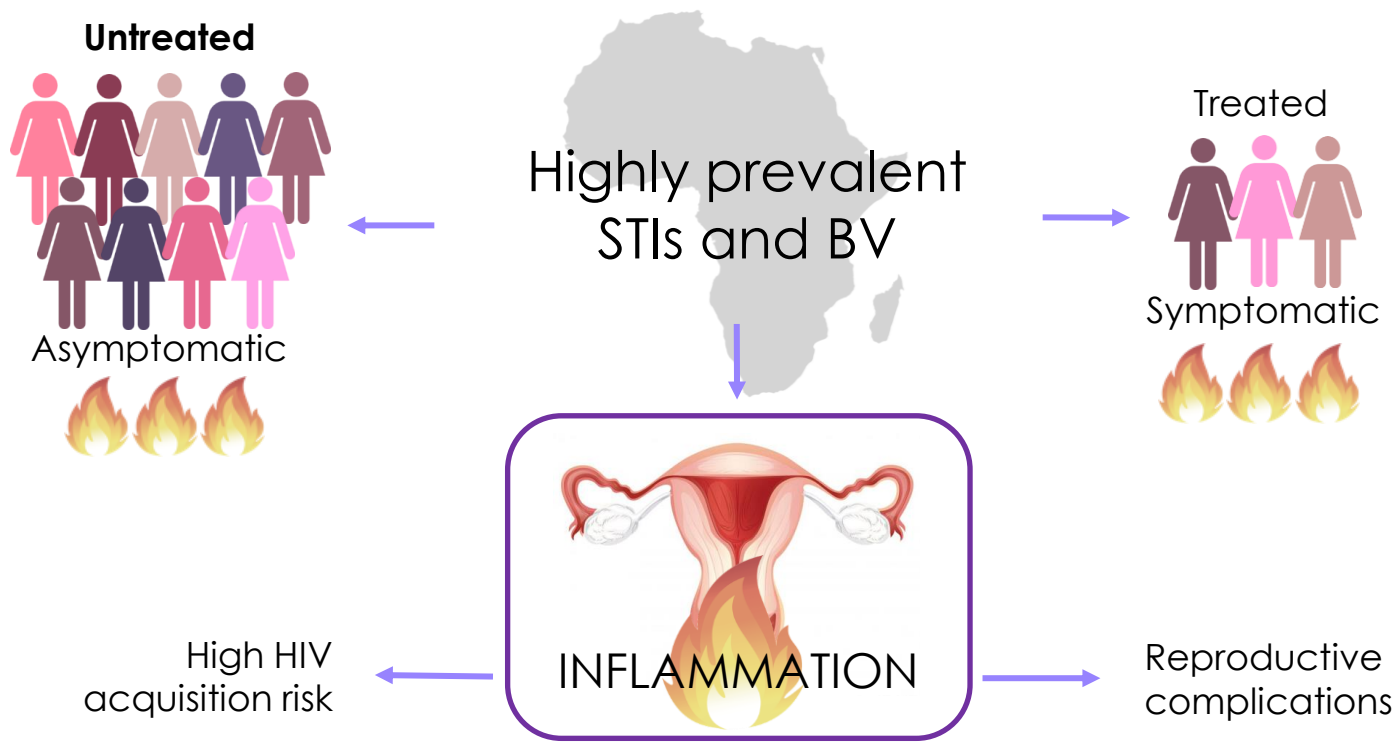
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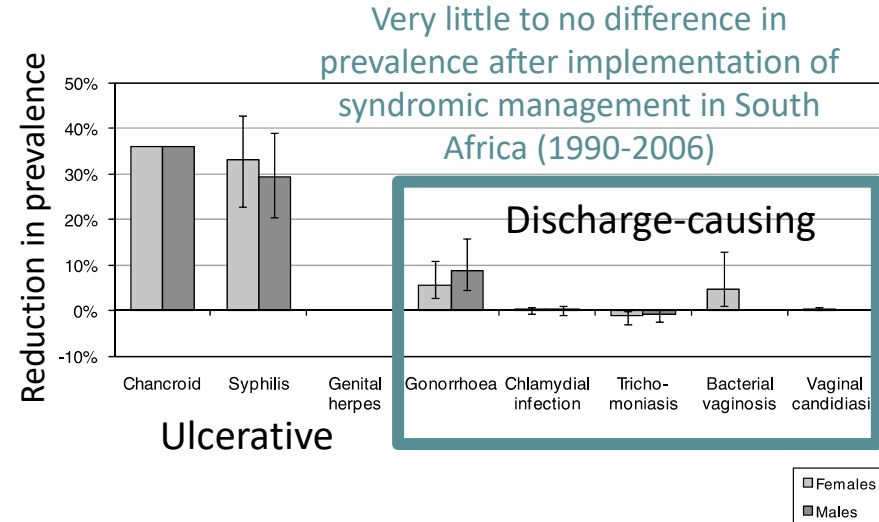


Most women with STIs or bacterial vaginosis (BV) don't have symptoms but have high levels of vaginal inflammation



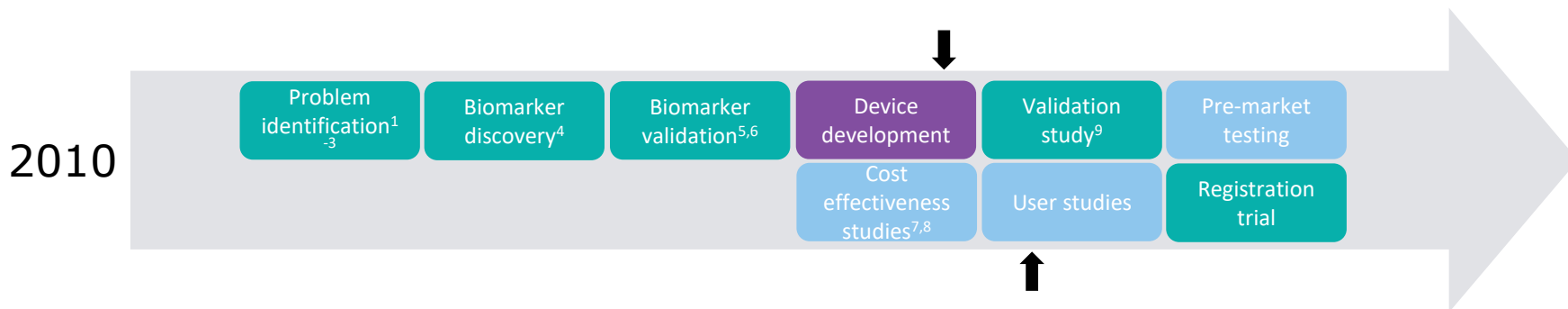
Women with STIs or non-optimal microbiomes are managed syndromically in resource-limited settings

- Recommended by WHO in the 1990s
- Pros:
 - Inexpensive
 - Lab facilities, specialized staff and equipment not needed
 - Patients are given immediate treatment
- Cons:
 - Most women don't have symptoms
 - Frequent overtreatment



We don't have low-cost and accurate alternatives for most STIs and BV or a way to detect vaginal inflammation

To reduce the risk of HIV infection and improve reproductive health in women by developing a **low-cost point-of-care screening test** to identify vaginal inflammation caused by STIs or BV



¹Masson, Passmore, et al., STI, 2014

²Masson, Passmore, et al., CID, 2015

³Mlisana, Masson, Passmore, et al., JID, 2012

⁴Masson, Passmore, et al., STI, 2016

⁵Masson, Barnabas, Passmore, et al., STI, 2019

⁶European (14809984.9) and South African (2016/03606) patents

⁷Kairu, Masson, Passmore, Sinanovic, et al., STD, 2021

⁸Smith, Masson, Passmore, Sinanovic, et al., Frontiers Public Health, 2023

⁹ClinicalTrials.gov identifier: NCT05723484

Biomarkers discovery: Three markers of inflammation (IL-1 α , IL-1 β , IP-10) identified as predictors of STIs/BV

Cohort	Sample type	Model Classification	True STI*/BV diagnosis (n)		Sensitivity	Specificity	PPV	NPV	Correctly classified (%)
			Pos	Neg					
HIV negative women	Vaginal lavage	Pos	102	16	72	81	86	64	76
		Neg	39	70					
HIV positive women	Vaginal lavage	Pos	24	0	80	100	100	54	84
		Neg	6	7					
HIV negative women	Signs and symptoms	Pos	27	7	19	92	79	40	46
		Neg	115	78					

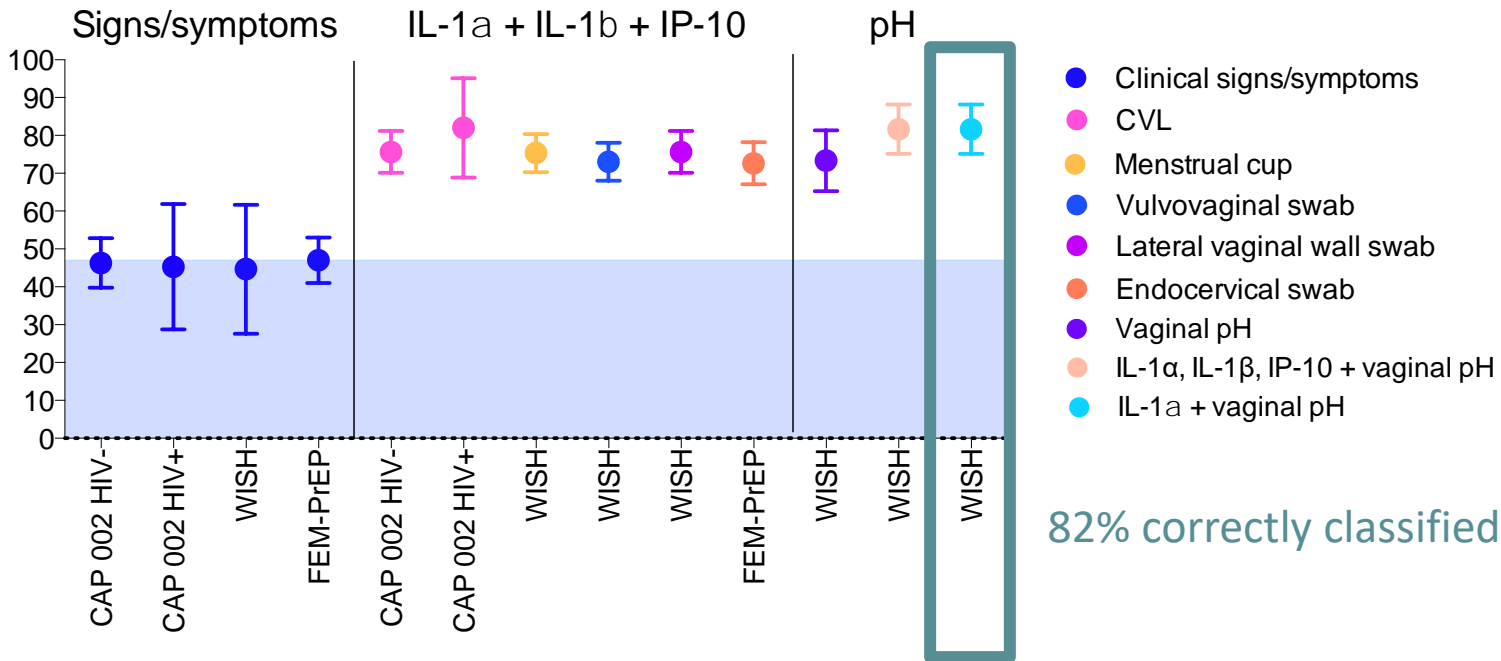


82% of women with vaginal inflammation detected

Biomarker validation across cohorts and sample types

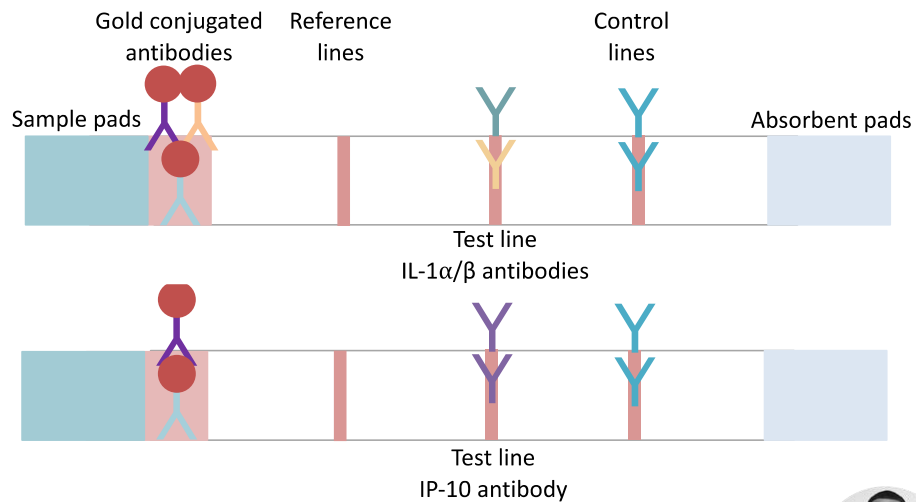


Percentage of women correctly classified



82% correctly classified

Device development



Ashley Uys, Lyndon Mungur, Darryl Uys



Device development

IL-1 β
441
combinations

IP-10
85
combinations

IL-1 α
841
combinations



IP-10
2

IL-1 α
4

IL-1 β
4

- 6 buffers
- 9 recombinant standards
- pooled and individual clinical samples



Monalisa Manhanzva and
Fezile Khumalo, UCT



Device development

Controls

IL-1 α	clone 5/2	clone 5/9
Neg control	0	0
Pos control	9	10
Pos control	9	10

IL-1 β

	clone 19/18	clone 19/20
Neg control	0	0
Pos control	10	10
Pos control	9	9

IP-10

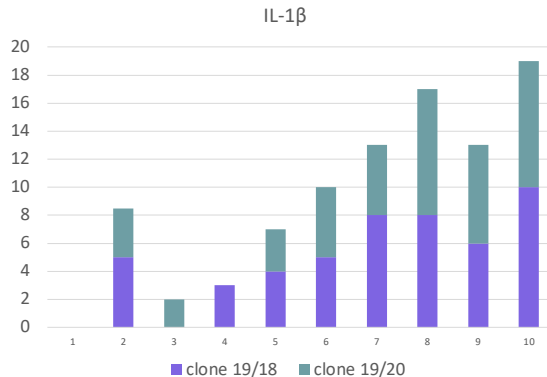
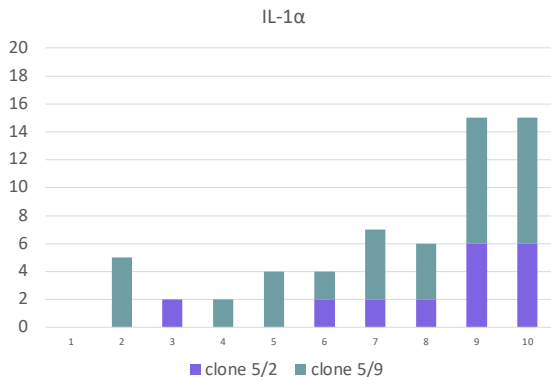
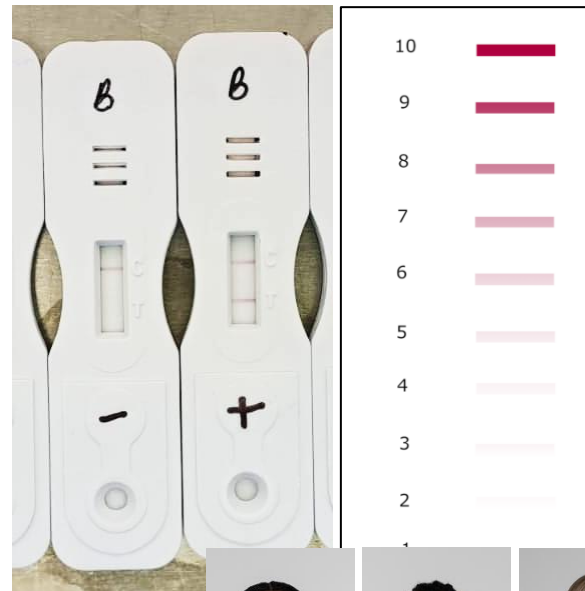
	clone 6/5	clone 3/5
Neg control	0	0
Pos control	10	10
Pos control	9	7
Pos control	7	10

Pools

IL-1 α	clone 5/2	clone 5/9
Neg pool	0	0
Pos pool	5	6

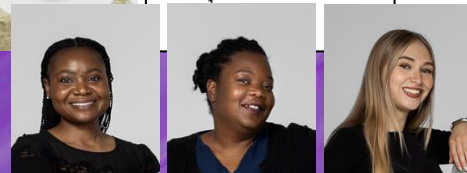
IL-1 β

	clone 19/18	clone 19/20
Neg pool	0	0
Pos pool	5	5
Pos pool	6	8

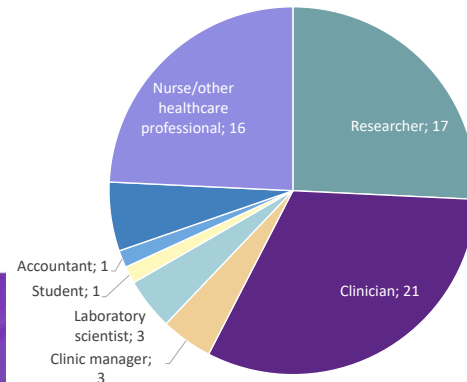
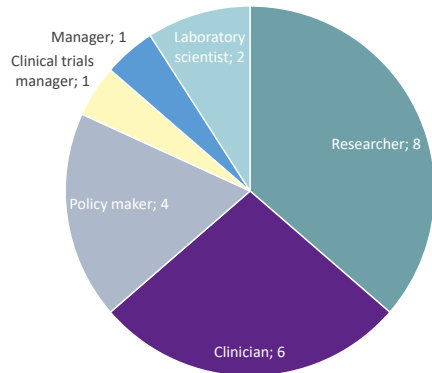


Increasing biomarker concentration (ELISA)

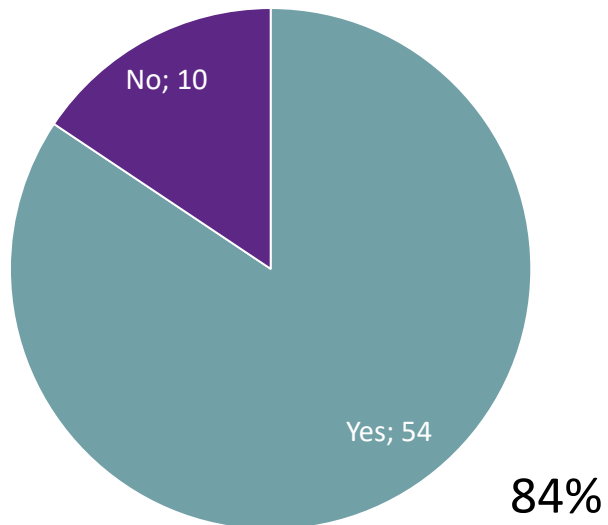
Monalisa Manhanzva, Fezile Khumalo, Micaela Lurie, UCT



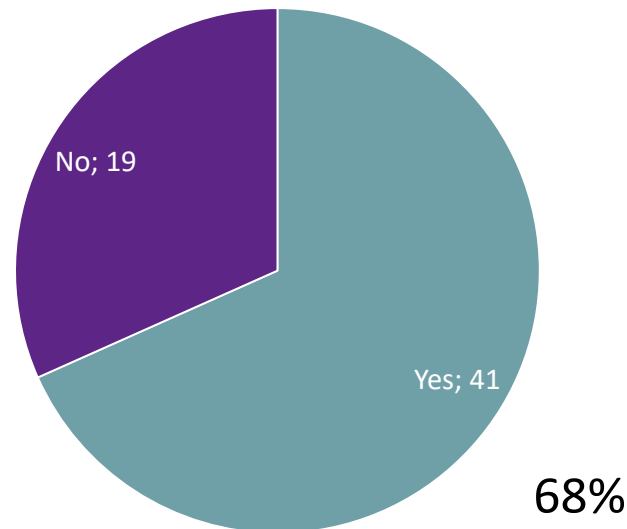
Stakeholder interviews to evaluate GIFT implementation strategies



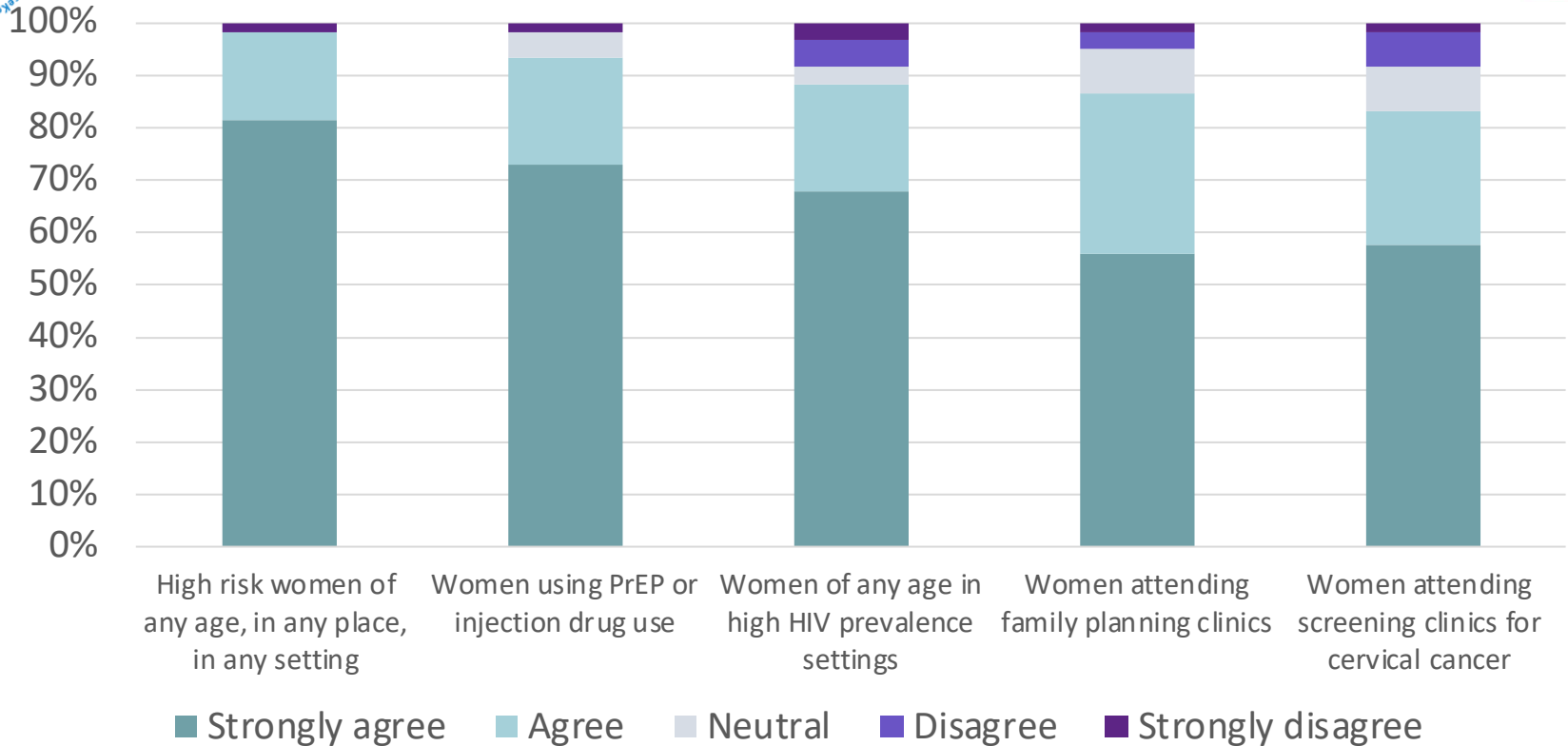
Would you offer sexually active, asymptomatic women screening with GIFT?



Should a positive GIFT result be followed by diagnostic tests for common STIs and BV?

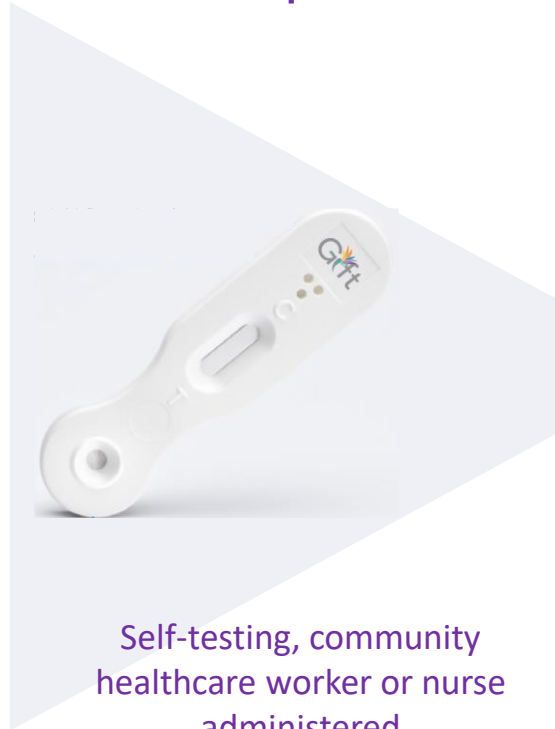
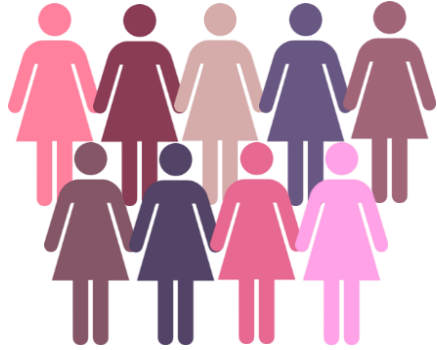


Who would you screen with GIFT?



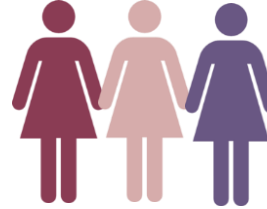
Implementation

High risk women or women accessing family planning, PrEP, cervical cancer screening



Self-testing, community healthcare worker or nurse administered

Women with inflammation caused by STI or BV

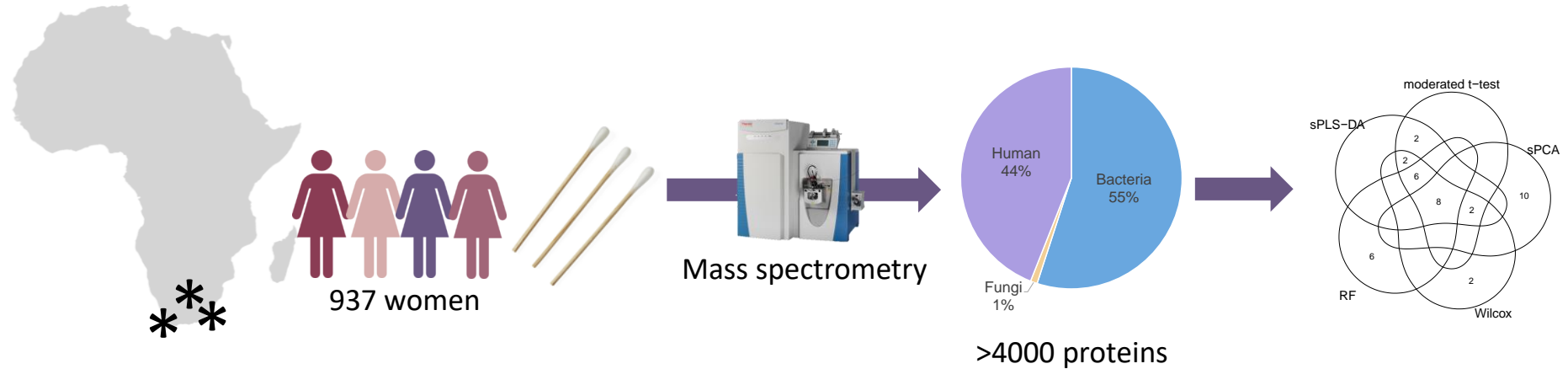


Context-specific management depending on available resources



- Etiological tests if available, but what if not available?
- Refer for PrEP in high HIV prevalence settings

Identifying new infection-specific biomarkers using metaproteomics



Two proteins that identify women with BV with 96% and 92% accuracy

Next steps

Optimize device

Device evaluation in 675 women

Validated device

Economic evaluation

User experience

Decision tree

Discrete choice experiments

(Kairu, et al., STD, 2021
Smith, et al., Frontiers Public Health, 2023)

Implementation
plan

Premarket testing

Marketing plan

Registered trial

CE Mark/
SAHPRA

Validate new biomarkers of BV

Identify new biomarkers of preterm birth using metaproteomics in Australian women

(Brown et al., Microbiology Australia, 2022)

Thank you!



Genital inflammation test for HIV prevention

CLINICAL SAMPLES
 HIGH PREVALENCE asymptomatic STI & BV
 182 SA YOUNG WOMEN
 up to 5 visits
 THOUSANDS OF SAMPLES

ANTIBODY SCREENING
 selection of optimal pairs
 1P-10 2
 10-30 4
 10-30 4
 NB: STABILITY OF ANTIBODIES OVER TIME... @ room temperature



Untrained individuals need to be able to READ it...
SELF ADMINISTERED
 WE KNOW IT WORKS!
 REDUCE COST & COMPLEXITY

BUFFER SELECTION



RECOMBINANT PROTEINS



Clinical Trials
 FAMILY PLANNING CLINIC
 225 WOMEN
 18-35 YEARS OLD
 ALL WILL BE TESTED WITH GIFT DEVICE AT FAMILY PLANNING SERVICES POINT OF CARE
 ZIMBABWE
 MADAGASCAR
 SOUTH AFRICA
 SCREENING for INFLAMMATION, STI & BV in ASYMPTOMATIC WOMEN
 WILL NOT BE USED FOR DIAGNOSIS

1 DELPHI SURVEY
 ESSENTIAL DEVICE ATTRIBUTES
 - ACCURACY
 - SENSITIVITY
 - EASE OF USE
 - AFFORDABLE
 Consensus from expert opinions
2 QUALITATIVE RESEARCH
 BARRIERS
 - LACK OF PROVIDER AWARENESS
 - AVAILABILITY
 - COST



DEVELOP A FEASIBLE, ACCEPTABLE & ECONOMICALLY FEASIBLE STI/BV MANAGEMENT ALGORITHM WHICH INCLUDES GIFT INTEGRATED INTO NATIONAL GUIDELINES

3 DISCREET CHOICE EXPERIMENT (D.C.E)
 PATIENT PREFERENCES for various attributes of STI management
 FACTORS INFLUENCING patients' decisions to manage STI management
 PROBABILITY of patient prioritizing

4 DECISION TREE ALGORITHM
 WHO should be screened?
 DEVELOP ALGORITHM DIAGNOSTIC STEPS
 MANAGEMENT STEPS

5 ECONOMIC EVALUATION
 ECONOMIC FEASIBILITY
 - HEALTH SYSTEM COSTS
 - UNIT COSTS PER PERSON
 - COSTS for DIFFERENT SCALE-UP SCENARIOS



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