

Performance Art: Deciding on Acceptable Sensitivity and Specificity for HIV Self Tests

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Goals of this Talk

- To describe the evolution of thinking that led to the approval by the US Food and Drug Administration of the first over-the counter home-use rapid HIV test
- To appreciate the flexibility that can (should?) be exercised to meet a critical public health need

Assessing HIVST



Goal

Recognizing that no test is 100% and 100% specific, demonstrate that it is safe and effective for its intended use



HOW THE US FDA APPROVED AN HIVST

Why HIVST for the US?

Number of Americans
newly diagnosed with HIV
infection each year



~50,000

Number of HIV-infected
people in the U.S.



1.2 MILLION

HIV-infected people in the
U.S. who do not know
they are infected



1 in 5

OraQuick® In-Home HIV Test System



Expected Performance

(FDA Blood Products Advisory Committee)

- Professional use test:
 - Sensitivity and specificity $\geq 98\%$ as the lower bound of the 95% confidence interval
- Self test:
 - Sensitivity and specificity $\geq 95\%$ as the lower bound of the 95% confidence interval
- Rationale:
 - Expected decrease in performance in the hands of non-professionals

Home-Use Test Performance as a Measure of Safety and Effectiveness



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graph LR; A([TEST PERFORMANCE]) --> B([SAFETY AND EFFECTIVENESS])
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TEST PERFORMANCE

SAFETY AND
EFFECTIVENESS

Professional Test Performance

(OraQuick ADVANCE® HIV-1/2 Antibody Test with Oral Fluid Specimens:
Package Insert)

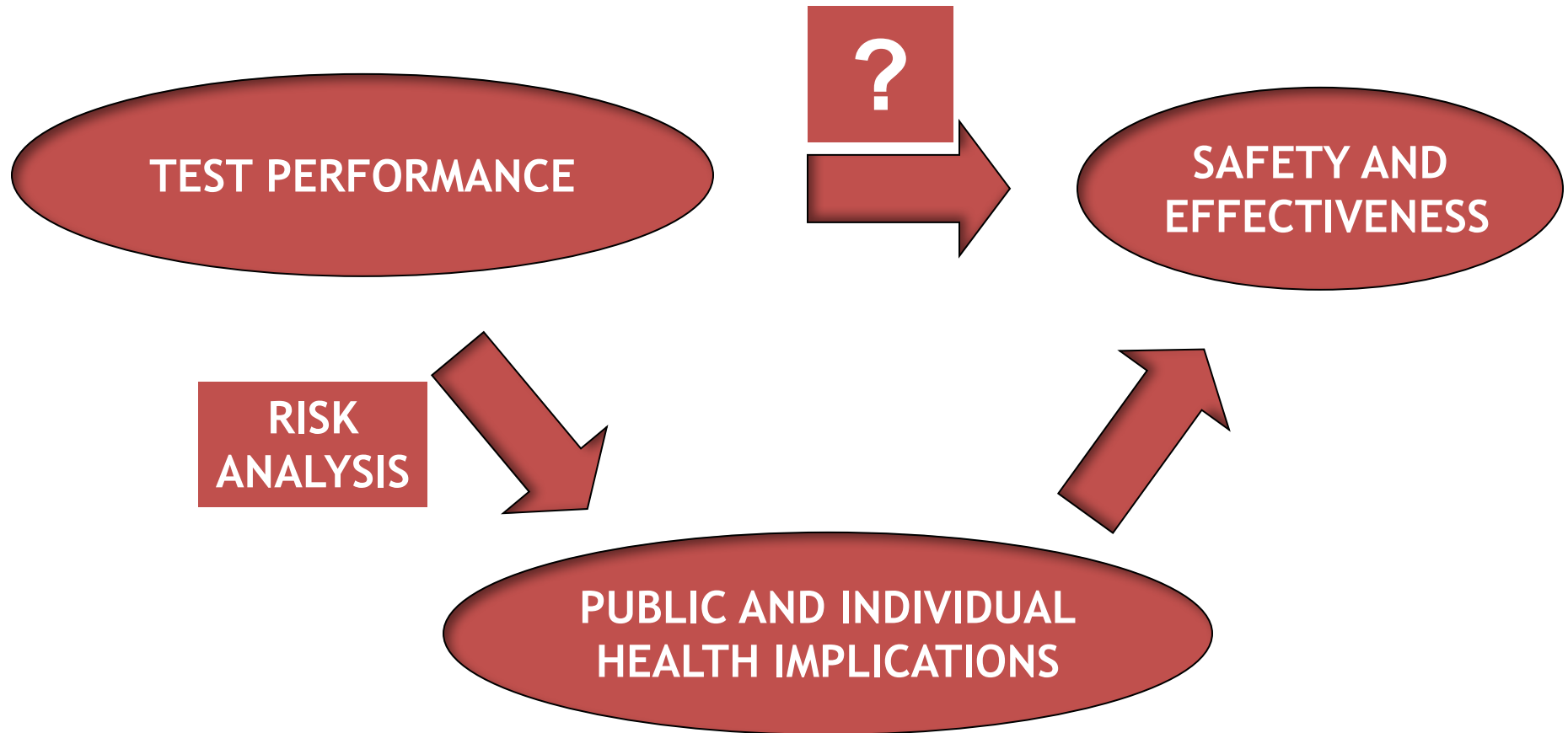
	Performance of the OraQuick ADVANCE® Rapid HIV-1/2 Antibody Test (2-sided 95% CI)	BPAC Minimum Recommended Performance
Specificity	99.8% (99.6 - 99.9%)	98% (lower bound of the 95% CI)
Sensitivity	99.3% (98.4 - 99.7%)	98% (lower bound of the 95% CI)

Home-Use Test Performance

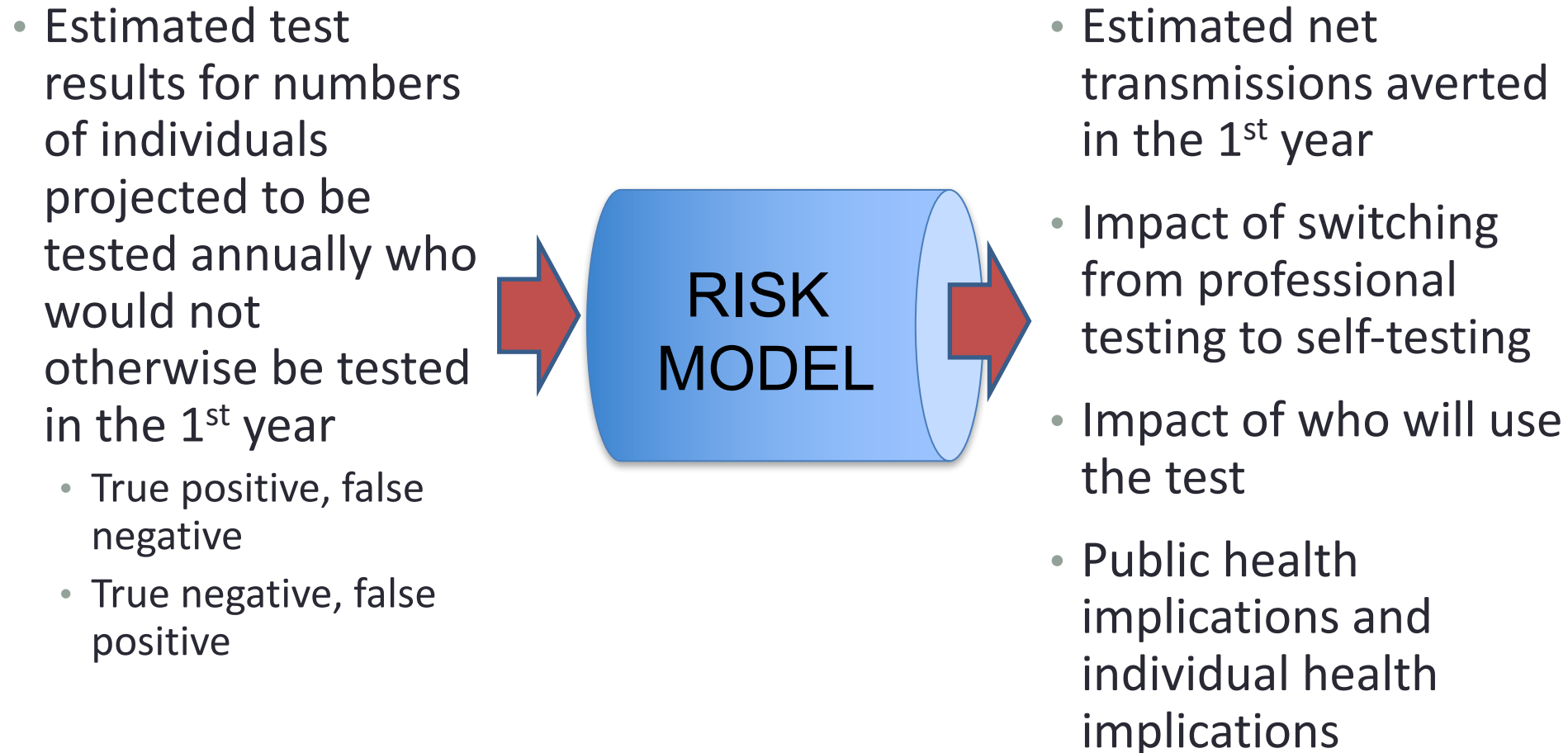
(OraQuick® In-Home HIV Test for Oral Fluid Specimens: Data shown at Blood Products Advisory Committee, May 2012)

	Performance of the OraQuick® In-Home HIV Test Kit (2-sided 95% CI)	BPAC Minimum Recommended Performance
Specificity	99.98% (99.90 - 100%)	95% (lower bound of the 95% CI)
Sensitivity	92.98% (86.64 - 96.92%)	95% (lower bound of the 95% CI)

Home-Use Test Performance as a Measure of Safety and Effectiveness



Very High Level View of FDA Risk Analysis



FDA Projected Outcomes of Testing with the OraQuick® In-Home HIV Test in the 1st Year

(Based on sensitivity and specificity at the 95% confidence interval lower bound)

True Positive	42,000
False Negative	7,000

6 TP : 1 FN

(vs. 62:1)

True Negative	2,700,000
False Positive	3,600

770 TN :1 FP

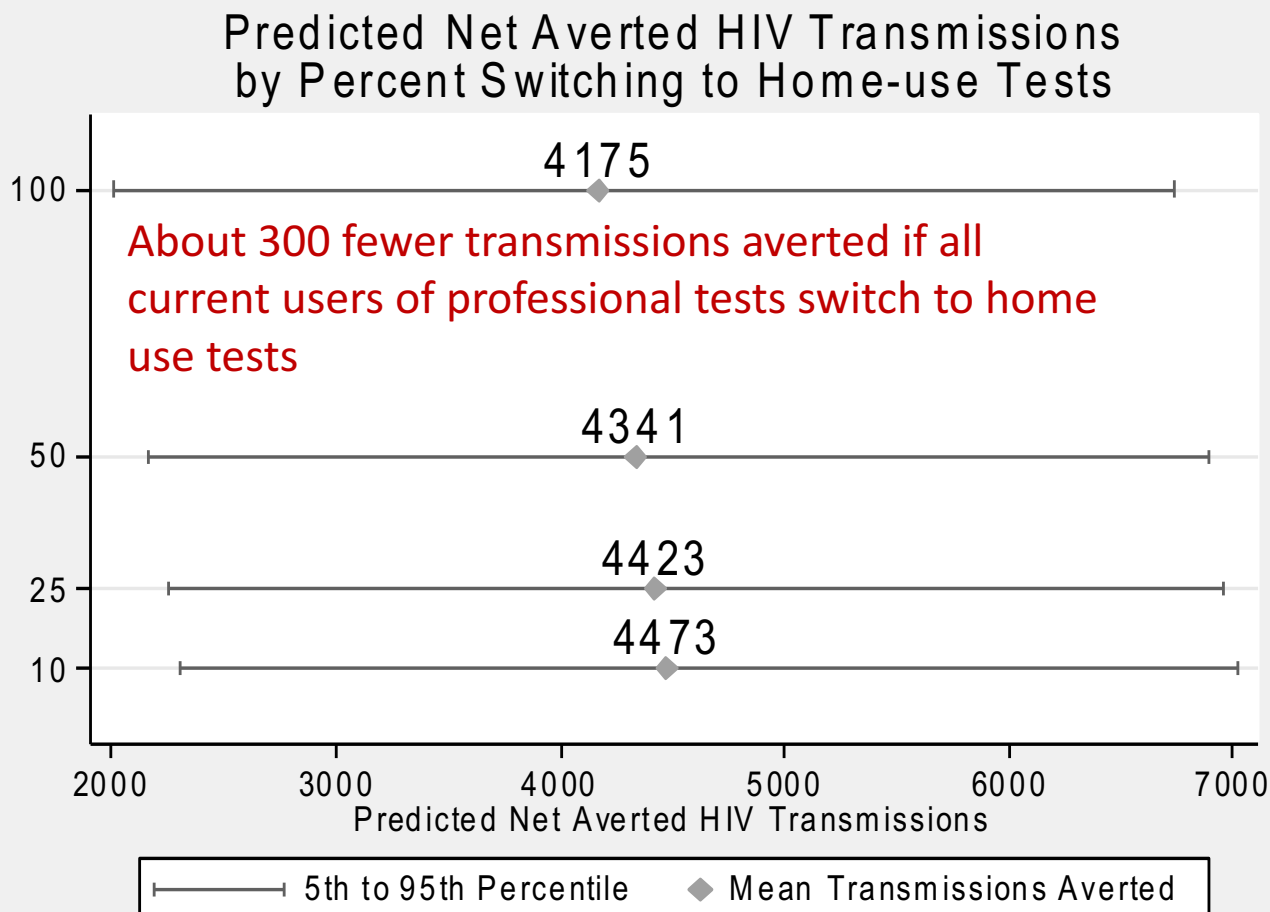
(vs. 249:1)

↑
Professional use
test
↓



Projected Net Transmissions Averted

(Combined Professional and Home Testing)

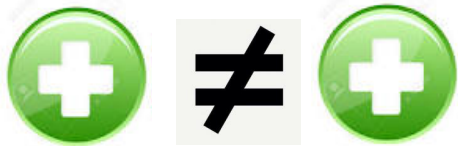


From FDA presentation at Blood Products Advisory Committee, May 2012

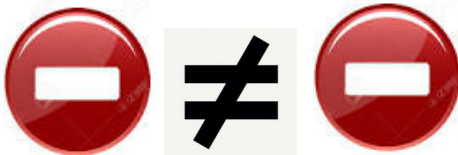
Summary of FDA Assessment

- Based on a risk assessment model, FDA projected a net public health benefit to the OraQuick[®] In-Home HIV Test
 - Net increase in number of HIV infections newly identified in the first year
 - Net transmissions averted
- Individual risk remains in the form of increased numbers of false negative results

Messages to Mitigate Risk



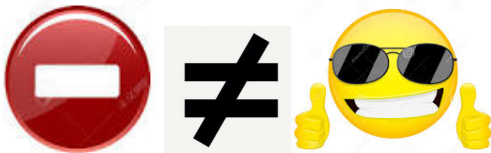
- A positive result with this test does not mean that you are definitely infected with HIV, but rather that additional testing should be done in a medical setting.



- A negative result with this test does not mean that you are definitely not infected with HIV, particularly when exposure may have been within the previous three months.



- Retesting is recommended if you test negative and continue to engage in behavior that puts you at risk for HIV infection.



- A negative result does not mean it is safe to engage in risk behavior for HIV infection.

Generalizing the Approach: Practical Considerations for STAR



- The results of the risk modeling done for the US population do not necessarily carry over to STAR
- Requires its own set of inputs

Challenges



- Where do you draw the line between acceptable and not acceptable?
- Monitoring to determine if the right choices were made

Potential Pitfalls



Concluding Messages



- Be flexible to meet the defined public health need.
- Be rational in your decision-making.
- Considering benefits and risks may take you in directions you don't expect, but sometimes what's not expected is a good thing.
- Be willing to accept risks, but also acknowledge them and mitigate them as much as possible.

THANK YOU!