

WHO Malaria Vaccine Forum: Challenges in translating research results to implementation

Meredith McMorrow, MD, MPH, FAAP
Malaria Branch, Division of Parasitic Diseases
Centers for Disease Control and Prevention



Acknowledgements

Rob Newman (IPTp)

S. Patrick Kachur (Equity-effectiveness)

Jane Crawley (Research to program)

Larry Slutsker and John Gimnig (ITN)

The findings and conclusions in this presentation are those of the author and do not necessarily represent the views of the Centers for Disease Control and Prevention.

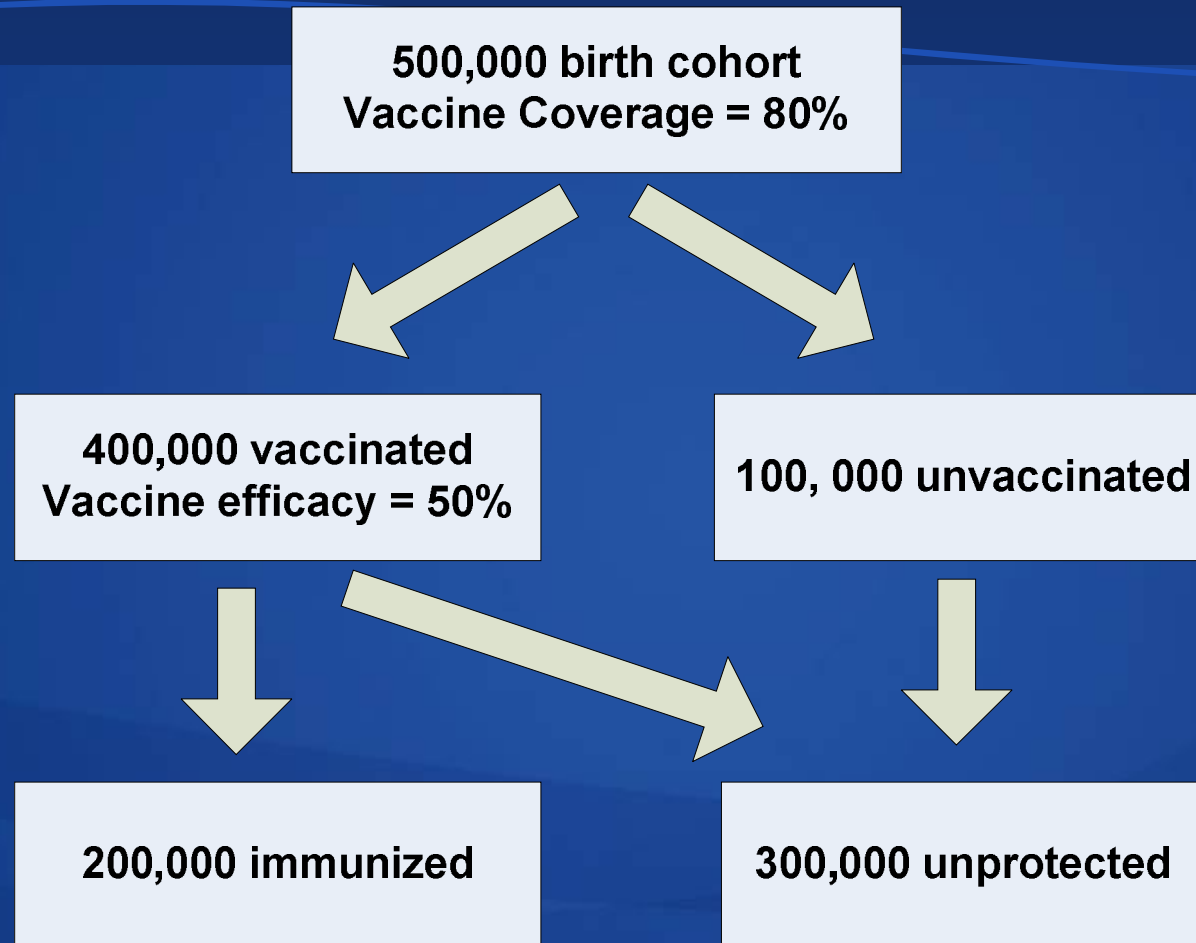


Outline

- **Efficacy and Effectiveness**
 - Defining malaria vaccine efficacy
 - Implementation challenges
 - Equity effectiveness
- **Successful program implementation**
 - Necessary elements
 - IPTp in West Africa
 - Tale of the ITN
- **When is an intervention ready for implementation?**
- **Additional challenges for malaria community**
 - Fever = Malaria
 - Diagnostics



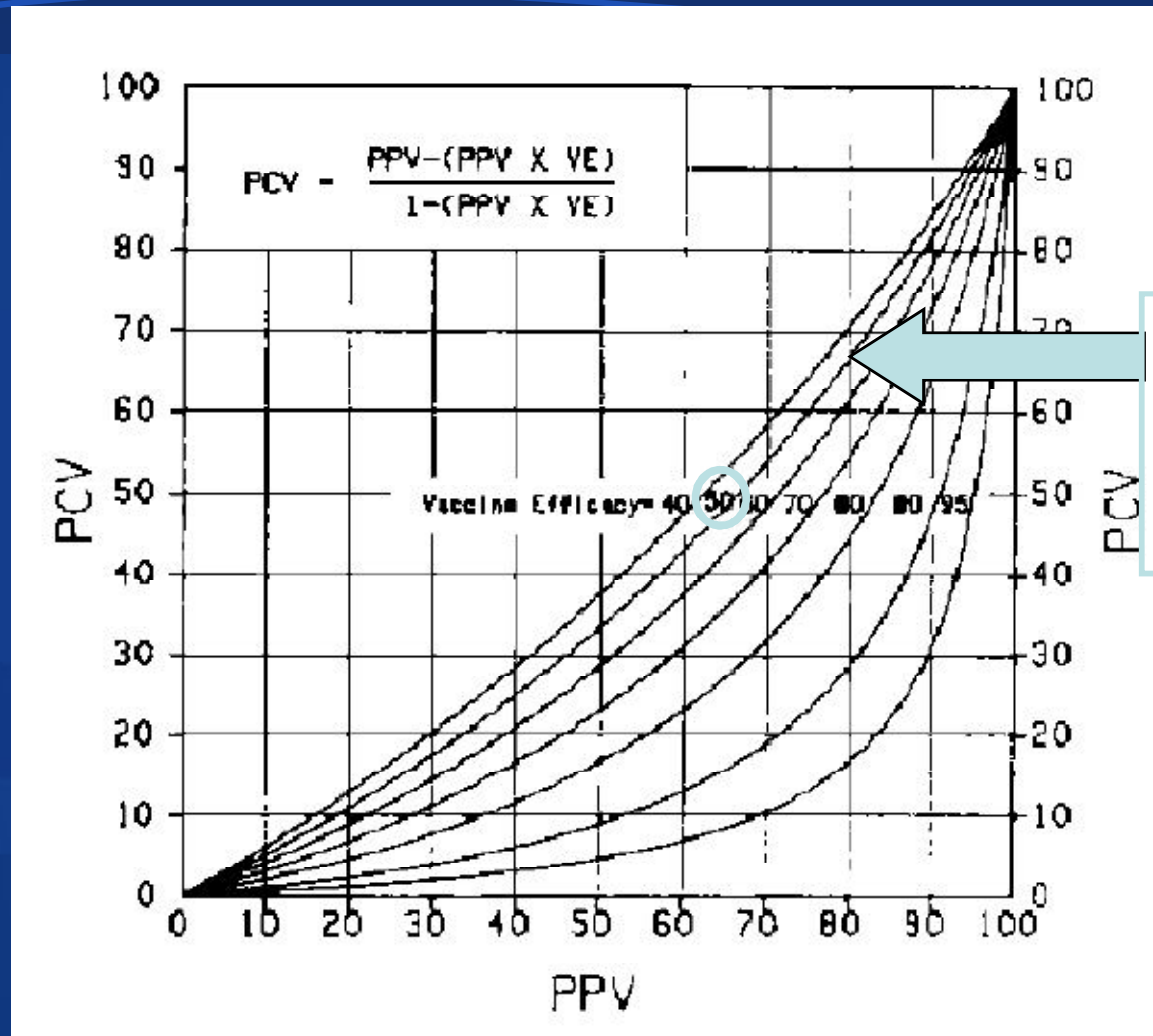
Efficacy to effectiveness



Population Immunity = 40%



Percent of population vaccinated vs. percent of cases vaccinated



With 80% coverage,
~ 2/3 of cases will
have been
vaccinated

Orenstein et al. Bull WHO, 1985.



Malaria vaccine efficacy

- Typically vaccine efficacy is considered the ability to prevent disease
- Phase II malaria vaccine trials have reported:
 - Delay in time to first infection
 - Protective efficacy against any parasitemia
 - Protective efficacy against fever and parasitemia > 0 parasites/ μ L
 - Protective efficacy against fever and parasitemia $> 1500/2500$ parasites/ μ L
 - Protective efficacy against severe malaria
 - Protective efficacy against all-cause hospitalizations
 - Protective efficacy against malaria-related hospitalizations
- What should be the standard for malaria?
- How do we ensure that decision makers understand the vaccine efficacy measure?



Malaria vaccine effectiveness

- **Affected by:**
 - **Initial vaccine efficacy**
 - **Coverage with 1, 2, and 3 doses**
 - 1 and 2 dose recipients partially protected?
 - **Decrease in efficacy over time**
 - Waning immune response may shift mortality curve
 - No evidence in Mozambique trial
 - **Host factors**
 - **Intensity of malaria transmission**
 - **Seasonality**



Implementation challenges (I)

- **Access to immunization services**
 - AFRO: DTP3 coverage 57-73% (2002-2006)
 - Countries with <50% DTP3 coverage are not eligible for GAVI support for new vaccine introduction
- **Decreasing incidence of malaria**
 - Potential impact on vaccine uptake
- **Diagnostic accuracy**
- **Provider education**
 - Behavior change necessary
 - Differential diagnosis of febrile illness
- **Caregiver confidence in vaccination**
 - Adverse events
 - High percentage of cases vaccinated

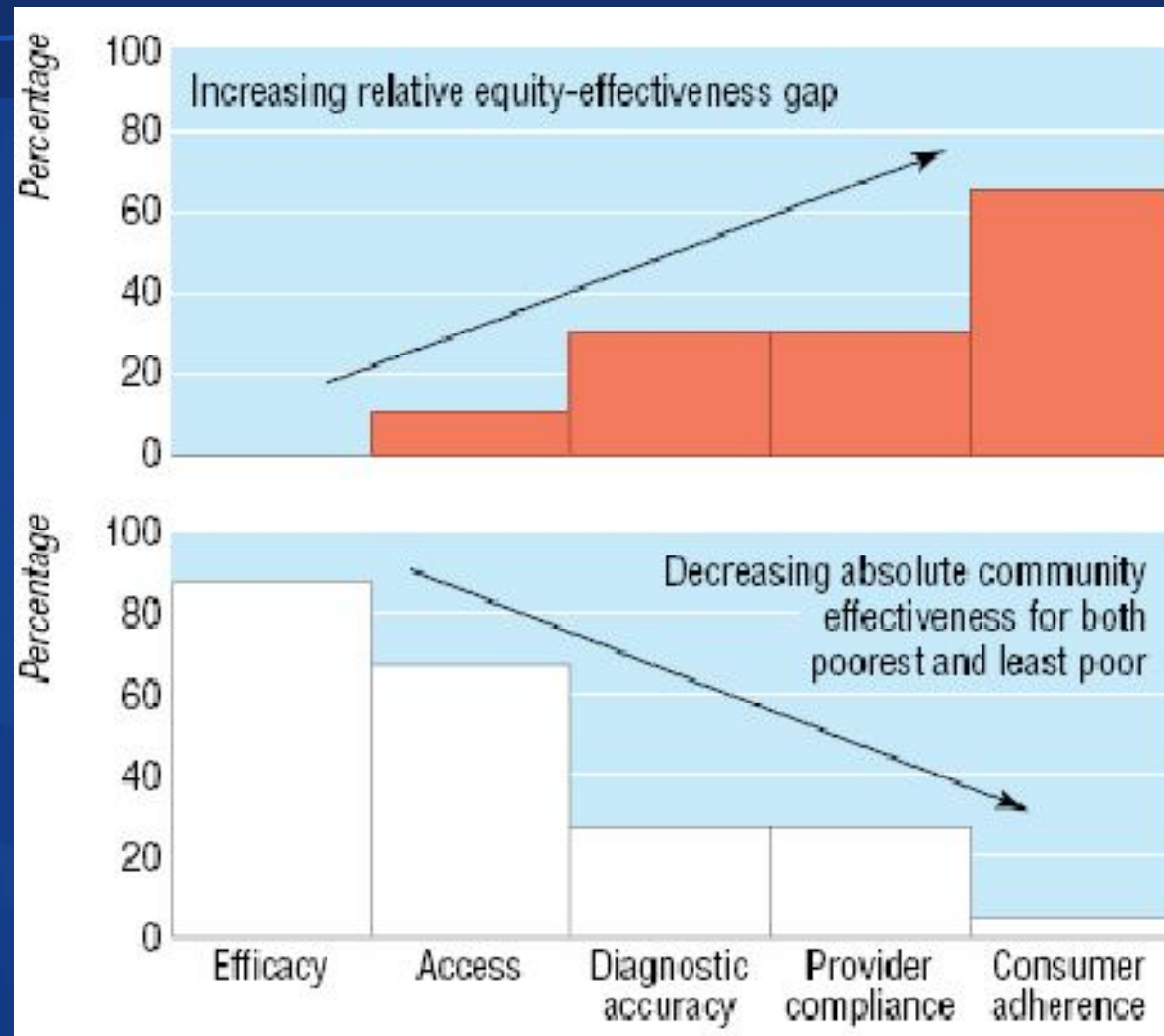


Implementation challenges (II)

- **Potential impact on other malaria control interventions**
 - Potential perception vaccine confers protection therefore don't need ITN, etc.
- **Resource allocation**
 - Currently GAVI requires co-financing by grant recipient
 - 15-30 cents per dose for most SSA countries
 - Given low efficacy and potential high cost, how will MoH weigh vaccine cost against investment in other malaria control interventions
- **Targeted implementation**
 - Limited resources may dictate limited vaccine introduction
 - Introduction of vaccine in areas with high disease burden, limited access to other malaria control interventions, other criteria?
 - Challenge of monitoring and evaluating impact



Equity-effectiveness



Tugwell et al. BMJ, 2006.



Malaria vaccine efficacy similar to other malaria interventions

- **IPTp**
 - Protective efficacy 43% against LBW, 38% against severe antenatal anemia, 66% against placental parasitemia (Garner and Gülmezoglu, Cochrane Review, 2006)
- **ITNs**
 - Protective efficacy 50% against clinical malaria and 45% against severe malaria in stable transmission areas (Lengeler, Cochrane Review, 2008)
- **IPTi**
 - Protective efficacy 30% against clinical malaria, 15% against anemia and 37.6% against malaria-related hospital admissions in pooled analysis (Grobusch et al. COID, 2007)



Given the challenges inherent in implementing an intervention with potentially low effectiveness, how do you build a consensus to promote policy change and successful implementation?



Necessary elements for successful program implementation

1. Convincing body of evidence
2. Clear, timely WHO policy recommendation
3. Political endorsement
4. Widespread availability of relevant commodities
5. Adequate financing mechanisms
6. Training materials and other supports
7. Experience of pilot implementation
8. Sub-regional networks for information exchange
9. Monitoring and evaluation plan
10. Feedback from M&E to inform research and policy agenda



Success: IPTp in West Africa

1. Convincing body of evidence

- Multiple East Africa trials demonstrate efficacy in 1990's
- Local data generated from rapid assessments in 3 countries and clinical trial in Mali

2. Clear, timely WHO policy recommendation

- WHO expert committee recommends IPT and ITNs for all pregnant women in malarious areas (2000)

3. Political endorsement

- Abuja Declaration (2000)

4. Widespread availability of relevant commodities

- SP low cost (<\$0.20 for 2 doses)
- First-line treatment in some countries



Success: IPTp in West Africa

5. Adequate financing mechanisms
 - Support from GFATM
6. Training materials and other supports
 - Developed with assistance from technical partners
7. Experience of pilot implementation
 - Pilot projects initiated in 6 countries via UNICEF/ACSD
8. Sub-regional networks for information exchange
 - Creation of RAOPAG
9. Monitoring and evaluation plan
 - Implementation limited by HR capacity issues and concerns about drug resistance
10. Feedback from M&E to inform research and policy agenda



Implementation Delays: Tale of the ITN

- 1. Convincing body of evidence**
 - Multiple African trials demonstrate efficacy in 1980's and 1990's
 - Initial delays due to concern of "rebound" mortality
- 2. Clear, timely WHO policy recommendation**
 - Supported by WHO but no guidelines for distribution until recent position statement supporting highly subsidized or free distribution
- 3. Political endorsement**
 - Abuja Declaration (2000) 60% "coverage"
- 4. Widespread availability of relevant commodities**
 - Relative high cost: bed net ~\$2-3, LLIN ~\$7-10
 - Manufacturing capacity of LLINs increasing, but limited



Implementation Delays: Tale of the ITN

5. Adequate financing mechanisms
 - Long debate over social marketing vs. free distribution
 - Distribution in immunization campaigns becoming standard
6. Training materials and other supports
 - Currently usage ~1/2 ownership
7. Experience of pilot implementation
 - Initial distribution with campaign in Togo 2004, others since
8. Sub-regional networks for information exchange
9. Monitoring and evaluation plan
 - Concerns mounting about pyrethroid resistance
10. Feedback from M&E to inform research and policy agenda



When is an intervention ready for programmatic implementation?

- **<50% efficacy not ideal**
- **Other vaccines being developed**
 - Wait for higher efficacy vaccine?
 - Combine with transmission blocking vaccine?
- **Many unanswered questions**
 - Effect on acquired immunity
 - Effects on malaria transmission and epidemiology
 - Efficacy in areas of different malaria transmission intensity
 - Effect on other malaria control interventions
 - Duration of protection
 - Efficacy in immuno-compromised/malnourished
 - And on...
- **Similar questions resulted in serious delays in ITN and ACT implementation**
- **All questions may not need to be answered before moving to implementation**



If we follow this model...

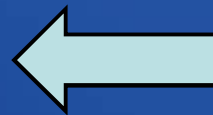
Monitoring &
evaluation



Programmatically
relevant research



Program
implementation



Policy change



*Programmatically relevant research continues
and informs refinements of existing policy*



Additional challenges for the malaria community

- **Improving healthcare infrastructure**
 - Access to care remains an important barrier
 - Healthcare workers need training in differential diagnosis of febrile illness
 - Treatment for non-malarial febrile illness must be equally accessible
- **Improving the quality & reliability of diagnostic testing**
 - Current paradigm of fever = malaria
 - May reduce confidence in malaria vaccine
 - May lead to increased non-malaria deaths
 - Are we ready to move away from clinical to laboratory diagnosis of malaria in some settings?
 - May place children with malaria at risk if diagnosis is unreliable
 - Necessary to invest in diagnostic capacity for other febrile illnesses



Conclusions (I)

- **Low efficacy vaccine will suffer from low effectiveness during programmatic implementation**
 - Coverage of 3 dose vaccine 60-80%
 - Waning immunity
 - Other factors
- **Other malaria interventions have similarly low efficacy, therefore malaria control will ultimately rely on multiple control strategies**
 - How to prioritize interventions with limited resources
 - Should interventions conferring passive protection be prioritized over interventions that require behavior change?



Conclusions (II)

- **Successful program implementation requirements**
 - Body of evidence
 - Political endorsement
 - Available commodities and financing
 - Training materials and supports
 - Successful pilot implementation
 - Forum for sub-regional exchange
 - Monitoring and evaluation feedback for policy change
- **New interventions will have unanswered questions, but research and policy agendas must be separated**
 - Unanswered research questions resulted in significant delays in the implementation of ITNs and ACTs
 - Relevant research should continue to inform policy decisions



Thank you!

