MALARIA VACCINE DEMAND ISSUES

Overview Malaria Vaccines Globally

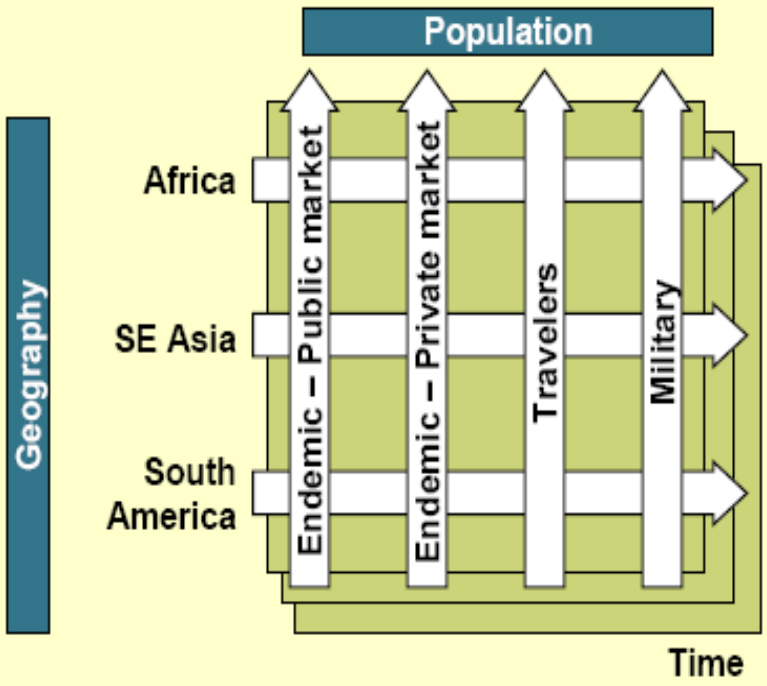
Please note that much of the following is based on the work of Boston Consulting for BMGF

- 1 Pivotal Phase 3 Trial (RTS,S/AS01, GSK/MVI)
- 14 other projects in clinical evaluation with 17 at advanced pre-clinical stage globally
- Clinical projects: about 1:1 Pre-erythrocytic/Blood-stage
- Clinical challenge model plays key role
- Renewed interest in Transmission-blocking & *P. vivax* vaccine development - mainly at pre-clinical stage

Malaria vaccine demand analysis

INCLUDES PUBLIC AND PRIVATE MARKETS IN MALARIA-ENDEMIC AREAS OVER TIME AND ACROSS DIFFERENT POSSIBLE PRODUCTS

Project scope covers broad range of populations and endemic geographies from 2010 to 2025



Flexibility built into design so that project broadly relevant for malaria vaccine community

Analysis for malaria vaccines in general, not for any one specific vaccine

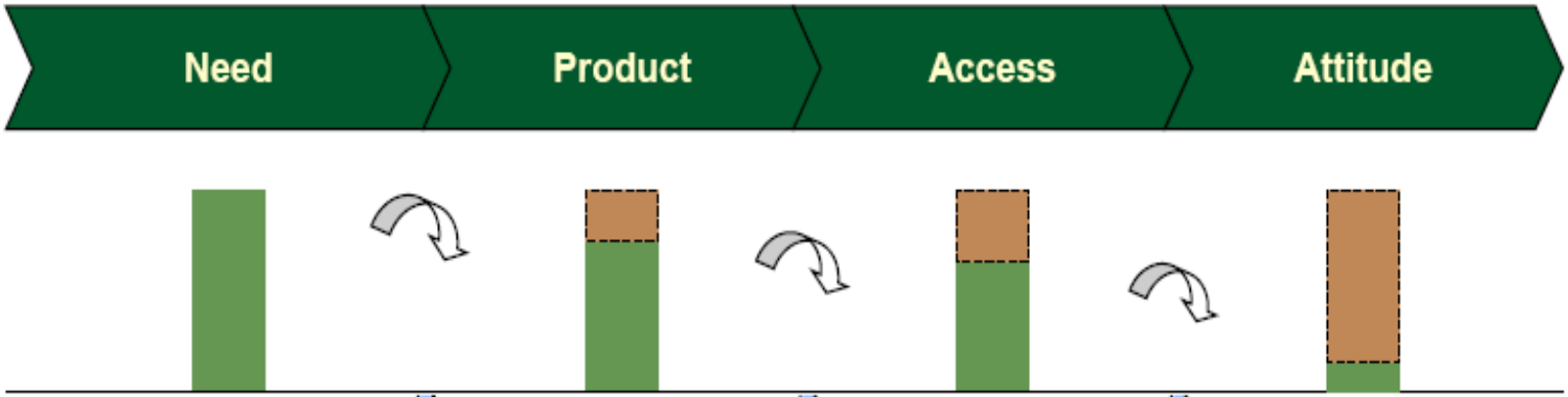
- Overall evaluation of demand drivers and adoption hurdles
- Includes demand forecasting and "tipping points" for various product profile scenarios (e.g., duration, efficacy, cost)

Market assessment conducted at one point in time, but structure allows ongoing insights to be developed as new information becomes available

- Attributes of a vaccine
- Attitudes with respect to particular product profile requirements
- Funding available for malaria

Malaria vaccine demand analysis

PROJECT DRIVEN BY DEMAND LEAKAGE FRAMEWORK



	Need	Product	Access	Attitude
Description	Number of people who would benefit from a malaria vaccine	Number of people for whom this vaccine suitable	Number of people with access to medical care and able to pay for vaccination	Number of people likely to get vaccinated given government/personal stance and vaccination strategies
Example factors	• Size of population with significant malaria mortality and disease burden • Size of traveler population • Size of relevant military population	• Species (P. falciparum or P. vivax) • Pediatric indication	• Country healthcare expenditure per capita • Infrastructure, e.g., beds per 1000 people • Percent of children under 12 vaccinated for measles	• Government support of current prevention and treatment • Individual compliance with current prevention and treatment

Malaria vaccine demand analysis

FOCUS ON PREVENTION VS. TREATMENT VARIES BY GEOGRAPHY

Most African Countries Emphasize Prevention while More Developed Countries Promote Early Diagnosis and Treatment

Strategy / Area	Population at risk and attitude	Donor perspective	Prevention	Diagnosis and treatment
Africa	• Children under 5 and pregnant women most vulnerable • Majority of country • Common disease: part of daily life	• Some funds for subsidized ITN, IPT, ACT, etc	• ITN subsidies • IPT with SP piloted • Lower focus on spraying and clean-up	• First line varies (CQ, SP and Amodiaquine) facing resistance • Shift to ACTs • Limited diagnostic equipment
SE Asia	• Adults and children • Biggest problem in border areas • Focus of local govt	• Wealthier countries less reliant on donor support	• Residual spraying in selected districts • Use of larvivorous fish to control vector	• Rapid diagnosis / presumptive treatment based on geography • High resistance; some must use ACT first line
South America	• Adults and children • Biggest problem in border areas • Perceived to be "under control"	• Wealthier countries less reliant on donor support	• Spraying & clean-up in high risk/border areas • No ITN, indoor spray due to outdoors-resting vector	• Faster response from diagnostic facilities • Species specific treatment • Goal: treatment within 24 hours

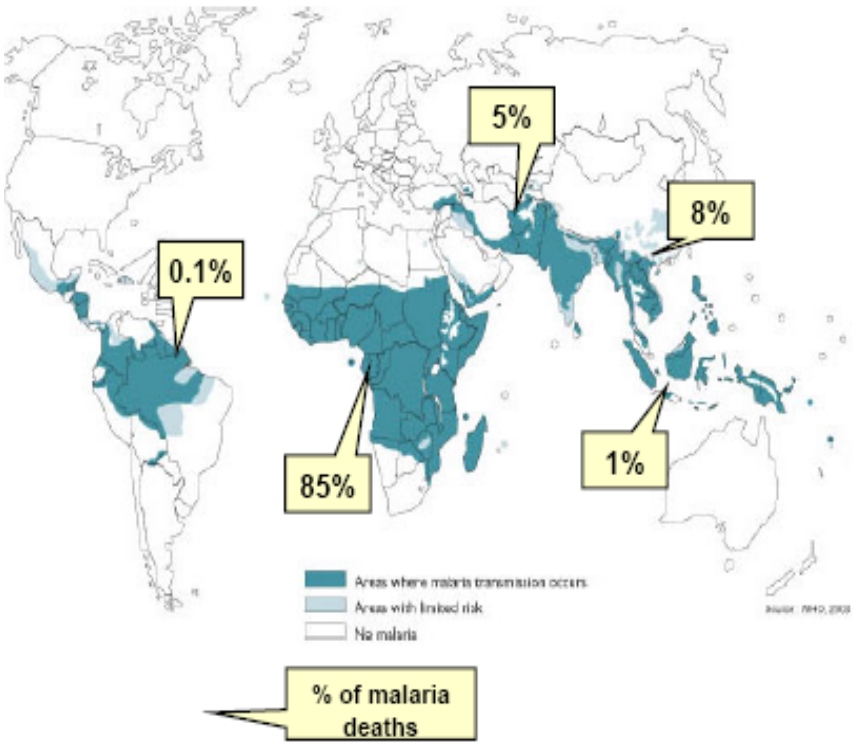
Difficulty in controlling malaria burden, especially in Africa

Malaria vaccine demand analysis

PRIMARY INTERVIEWS FOCUSED ON MALARIA-ENDEMIC REGIONS ACROSS THE GLOBE

Included Both P. vivax and P. falciparum Endemic Regions

Malaria-endemic regions are geographically concentrated



P. falciparum of increasing importance in Africa and SE Asia

Africa dominated by P. falciparum
- 5 to 10% of cases are P. vivax
- Increasing drug resistance to this more severe species makes P. falciparum a focus area

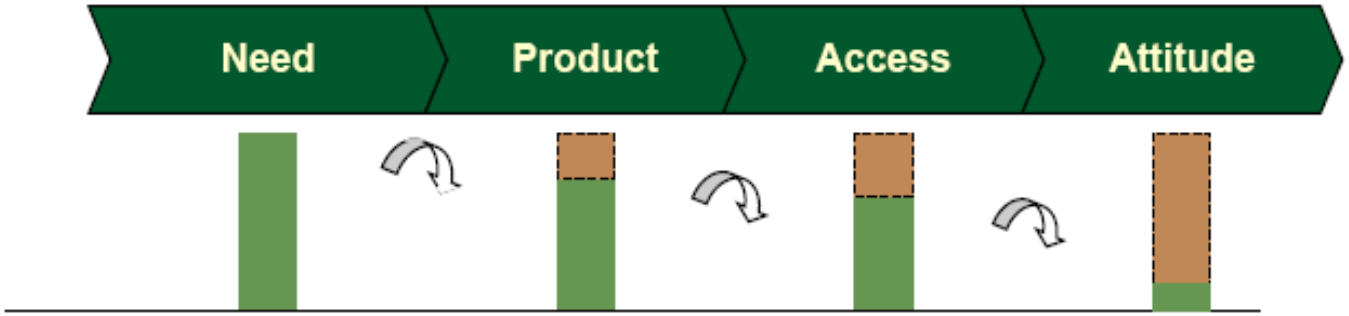
Growing importance of P. falciparum in India
- 20% of cases in 1980 to 45% in 2000

P. falciparum accounts for nearly 80% of cases in the Mekong region of SE Asia

Eastern Europe, Caucasus, and Brazil predominantly P. vivax

Malaria vaccine demand analysis

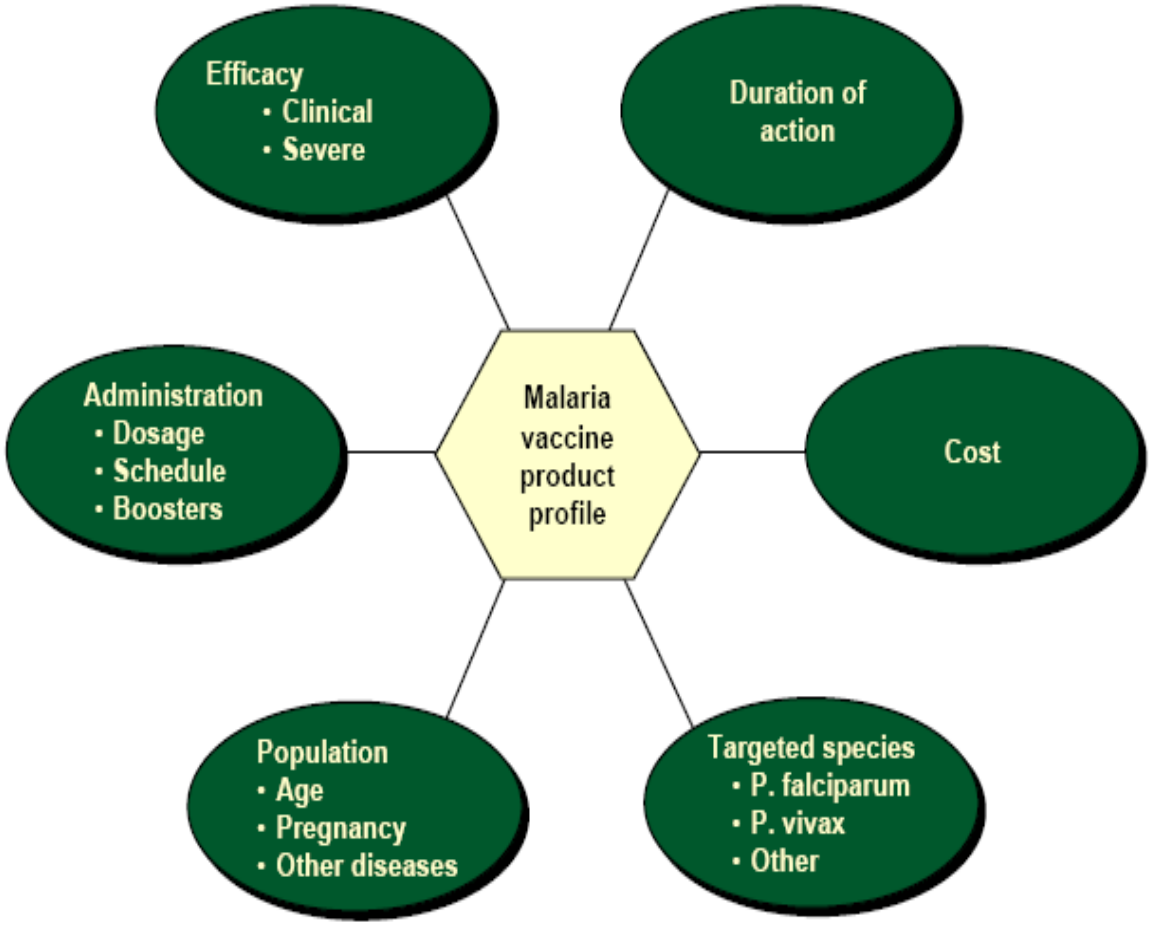
ENDEMIC COUNTRY DEMAND LARGELY DRIVEN BY PUBLIC MARKET



	Need	Product	Access	Attitude
Public market	• Population of endemic country	• Product profile	• Coverage of target pop. • Donor funding • Hurdles to adoption	• Decision making and attitudes of government, KOLs
Private market	• Population of endemic country	• Product profile	• Private clinic access • Income levels	• Individual attitudes
Travelers	• Travelers to endemic countries	• Product profile	• Seek advice before traveling	• Prefer vaccine vs. prophylaxis
Military	• Worldwide militaries	• Product profile	• Military budget	• Vaccinate all vs. deploying vs. none

Malaria vaccine demand analysis

SIX CHARACTERISTICS OF PRODUCT PROFILE ARE KEY DEMAND DRIVERS



Malaria vaccine demand analysis

PUBLIC MARKET VACCINE MUST BE COST EFFECTIVE, FINANCIALLY SUSTAINABLE, AND EASY TO ADMINISTER

Attribute	Impact on demand	Details	Comments
Efficacy	High	• Minimum efficacy desired against clinical disease vary from 30% in W Africa to 50% in E Africa to 80% in SE Asia	Countries will compare efficacy against ITNs and other preventative tools
Duration	Medium	• Duration factors into cost effectiveness - minimum of 1 year	Benefit of protecting children early in life, until they develop partial immunity Duration impacts cost
Cost	High	• Cost/efficacy needs to compete with existing interventions • May require donor funding, but countries need sustainable solution	Financial sustainability a huge issue
Species	High	• P. falciparum most important in Africa and Asia vs. P. vivax in Brazil	We're most concerned about P. falciparum—it is the most deadly
Population segment	Low	• Relevant to infants, children, and pregnant women in Africa vs. adults in SE Asia, S America	Pregnant women and under fives are highest priority
Administration	High	• Prefer to give vaccine with existing EPI schedule	Only realistic way to implement vaccine is through EPI schedule

Malaria vaccine demand analysis

MALARIA VACCINE SEEN AS PROMISING, BUT WOULD SHARE AVAILABLE DONOR RESOURCES WITH EXISTING INTERVENTIONS

Donors are highly interested in a vaccine...

- Donors routinely cite a vaccine as a very exciting possibility
- Donors fund significant amounts of vaccine R&D

"DFID maintains an active interest in vaccine research" -DFID

"A vaccine will be a very attractive investment for the donor community" -USAID

...but total funding unlikely to increase drastically

- Total malaria and vaccine funding may not change with partial efficacy vaccine

"There is only one pot of money for all healthcare interventions" -UNICEF

"USAID dollars given to the Vaccine Fund will likely not increase in response to a new malaria vaccine" -USAID

..and current solutions are unlikely to disappear

- Current tactic of portfolio approach to malaria unlikely to disappear with vaccine introduction

"No one measure is a magic bullet—need to work with what we have" -USAID

"We would not want to see a vaccine hindering the use of ITNs; the world has worked so hard to get people to use them" -USAID

Allocation of funding within prevention and control portfolio likely to be determined by vaccine product profile

Malaria vaccine demand analysis

EVEN WITH DONOR FUNDING, SOME CONCERN ABOUT KEY STAKEHOLDERS WILLINGNESS TO ACCEPT A MALARIA VACCINE

8 Reasons Commonly Cited

	Reasons for Reduced Interest	Rationale	Relevant Geographies
1	No need for a vaccine	Countries with better control over malaria may view need for a vaccine as less urgent	Brazil, Thailand
2	Do not trust vaccine due to prior failure	Community may be less willing to support a new malaria vaccine based on history of SPF66	Thailand; Africa—high awareness, but less impact due to high burden
3	Inadequate infrastructure	Pragmatic concerns regarding ability to reach population, i.e. staff training, cold chain needs, etc.	Mozambique, Tanzania, Nigeria; likely an issue throughout Africa
4	Do not want to spend for non-nationals	Government unlikely to unilaterally spend money on malaria control for migrants and refugees	
5	Need local data to prove effectiveness	Some countries emphasize importance of testing the vaccine in-country	Most countries
6	Difficult decision making	States or regions highly autonomous in decision-making, particularly regarding health interventions	Nigeria, India
7	Partial efficacy vaccine may decrease credibility	Vaccinated people who contract malaria could decrease credibility of entire immunization program	Most countries
8	Partial efficacy vaccine complicates messaging	Must communicate benefit of partial efficacy in promotion materials and to trainers	Most countries

Malaria vaccine demand analysis

PRIVATE MARKET MOST CONCERNED THAT VACCINE BE HIGHLY EFFICACIOUS

Attribute	Impact on demand	Details	Comments
Efficacy	High	• Most important factor given need to proactively seek out vaccine; efficacy has to warrant the time and money invested	Private market acceptance likely with high efficacy
Duration	Medium	• Minimum one year	
Cost	Medium	• Cost less of an issue than in public market for wealthy individuals, but still significant for groups choosing among interventions	Cost of vaccine would have to be comparable to current interventions for use in the private market
Species	High	• Vaccine for P. falciparum more important given severity of disease	
Population	Medium	• Private market vaccine applicable to adults as well as other high risk groups	
Administration	Low	• Individuals seeking a vaccine in the private market are more likely to comply with multiple doses / boosters	

Malaria vaccine demand analysis

KEY TAKEAWAYS
Private Market

Product profile varies from public market requirement

- Higher efficacy threshold given availability of alternatives (minimum 50%)
- Administration restrictions lower due to routine doctor visits
- Cost less sensitive than for public market

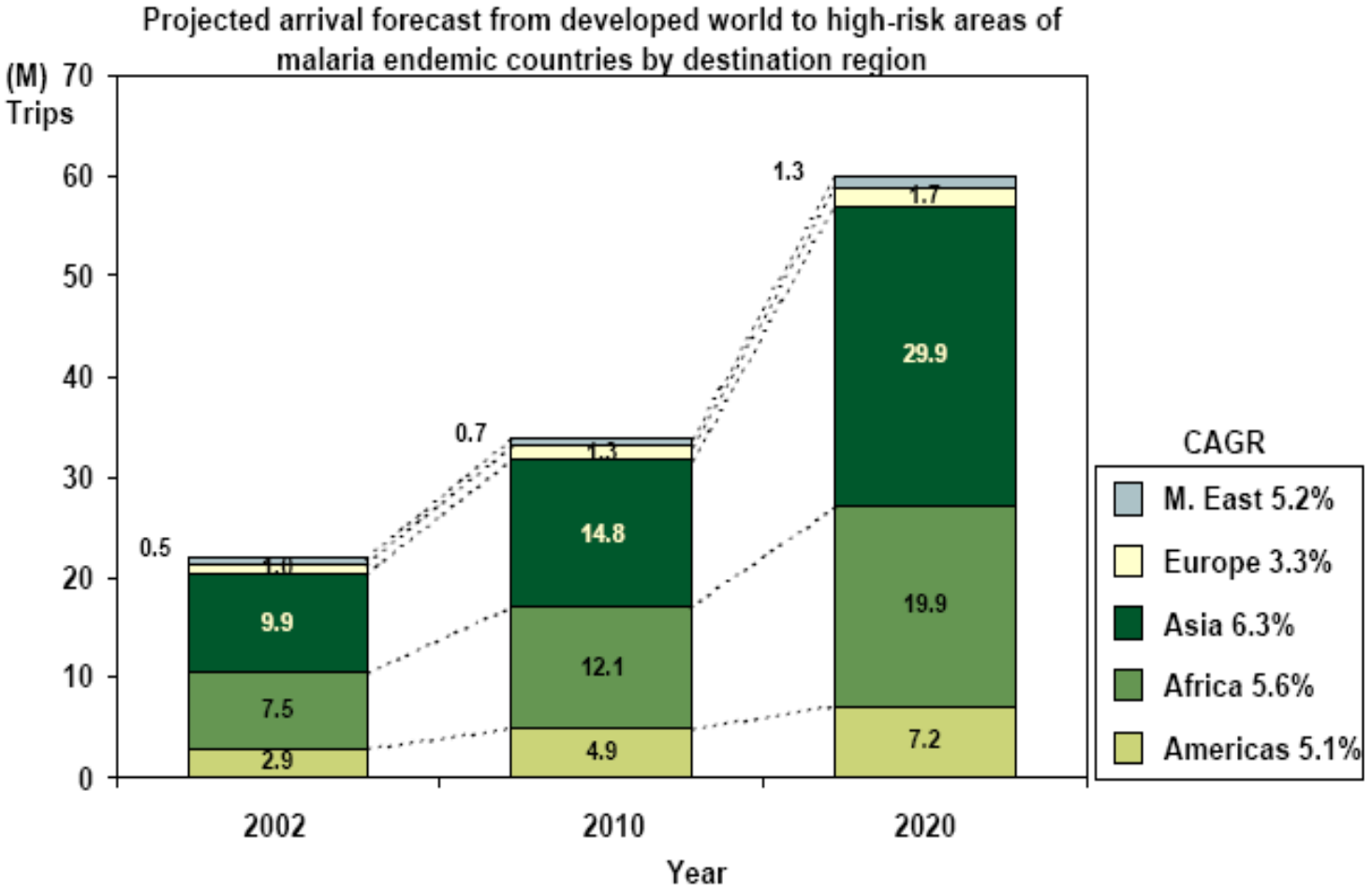
Access and wealth constraints limit private market to subset of populations

- Wealthiest segment of population likely to purchase all relevant interventions
  - i.e. residual spraying along with ITNs, a vaccine, and ACT purchases
- Only small fraction of remaining population can afford typical vaccine costs and this group will likely have to decide among interventions
  - i.e. only 0.03% of Nigeria privately purchases $12 Hep B vaccines
- However, small fraction of large country is still a substantial population (~600,000 Indian citizens purchase Hep B)
- Proximity to clinics and regulations on private sales of vaccines also limit demand
  - many countries have <300 clinics able to administer a private vaccine

Cultural expectation of publicly-provided health services translates to some individuals not seeking private vaccination, even if they can afford it

Malaria vaccine demand analysis

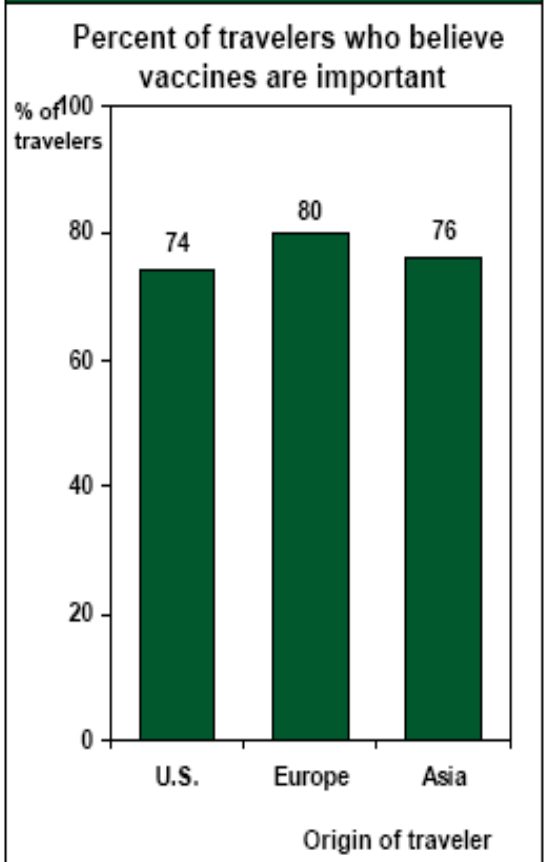
INTERNATIONAL TOURISM TO ENDEMIC REGIONS PROJECTED TO INCREASE OVER THE NEXT 15 YEARS



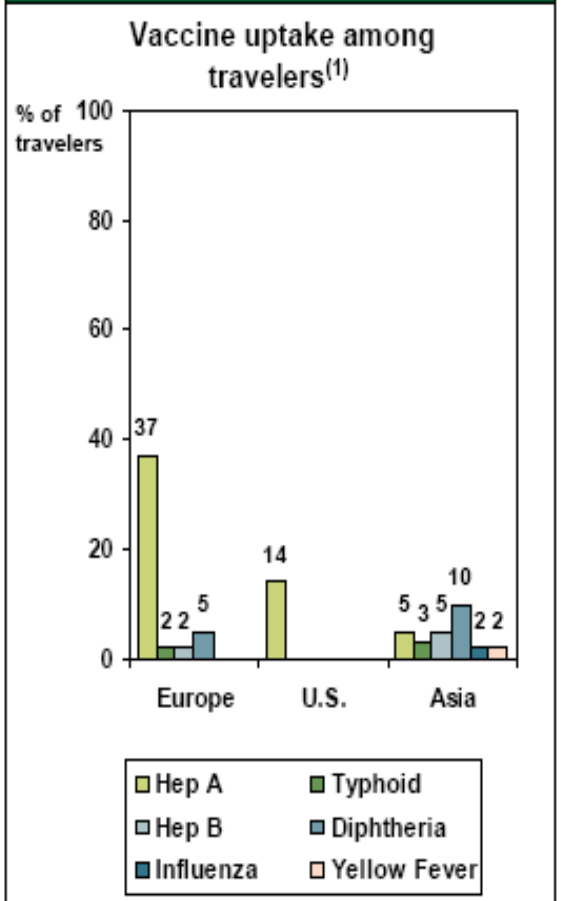
Malaria vaccine demand analysis

ALTHOUGH TRAVELERS THINK HIGHLY OF VACCINES, FEW USE THEM TO PROTECT AGAINST INFECTIOUS DISEASES

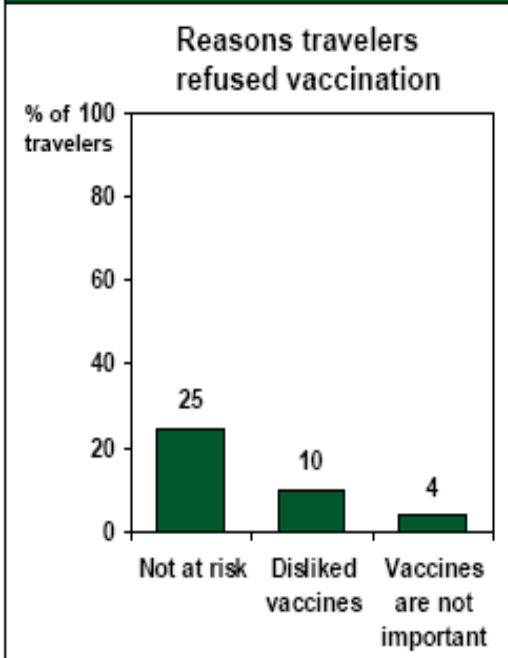
Vaccine opinion rate high among travelers ...



...but Hep A uptake is low



Variety of reasons drive low uptake



Vaccine concerns included:

- Side effects
- Cost
- Pain
- Belief that they are useless

Malaria vaccine demand analysis

TRAVELER VACCINE UPTAKE DEPENDS ON ITS PROFILE

Attribute	Impact on demand	Details	Comments
Efficacy	High	• Would need to be at least as efficacious as prophylaxis (98%) • Potential risk of misuse of standby treatment with lower efficacy • Previous low efficacy vaccine (cholera) had low uptake	"From a public health perspective, there is very low tolerance for risk with travelers"- CDC
Duration	Low	• Short nature of "average trip" decreases importance of long duration vaccine	"A 30% efficacy vaccine is too low. It would be a hard sell"- Canadian KOL "Cholera vaccine has been highly ineffective"- CDC
Cost	Medium	• Price sensitivity may depend on health-care system and drug coverage in home country • Cost relative to chemo-prophylaxis will likely drive demand • Travelers seem less price-sensitive if side effects of chemo-prophylaxis could be avoided	"Cost of treatment is a hurdle for a lot of people"- CDC
Species	Medium	• Falciparum primary requirement for travelers • However, lack of vivax efficacy could hurt vaccine credibility or generate negative impressions	
Administration	High	• Time required between administration and departure will be key driver in vaccine usefulness given wide variation in planning habits observed	"There is a general public dislike to taking tablets- U.K." KOL "People are still afraid of needles"- KOL
Education	High	• Increasing population that seek pre-travel medical advice could heavily influence number that can receive vaccine • Traveler attitudes towards vaccines vs. tablets also important	

Malaria vaccine demand analysis

KEY TAKEAWAYS
Travelers Market

Frequency of international travel to high-risk malaria areas is growing

- 22 MM arrivals in 2002 and 60 MM projected in 2020

Traveler behavior varies significantly in chemoprophylaxis use, pre-travel planning habits, duration of trips, and attitudes toward vaccines

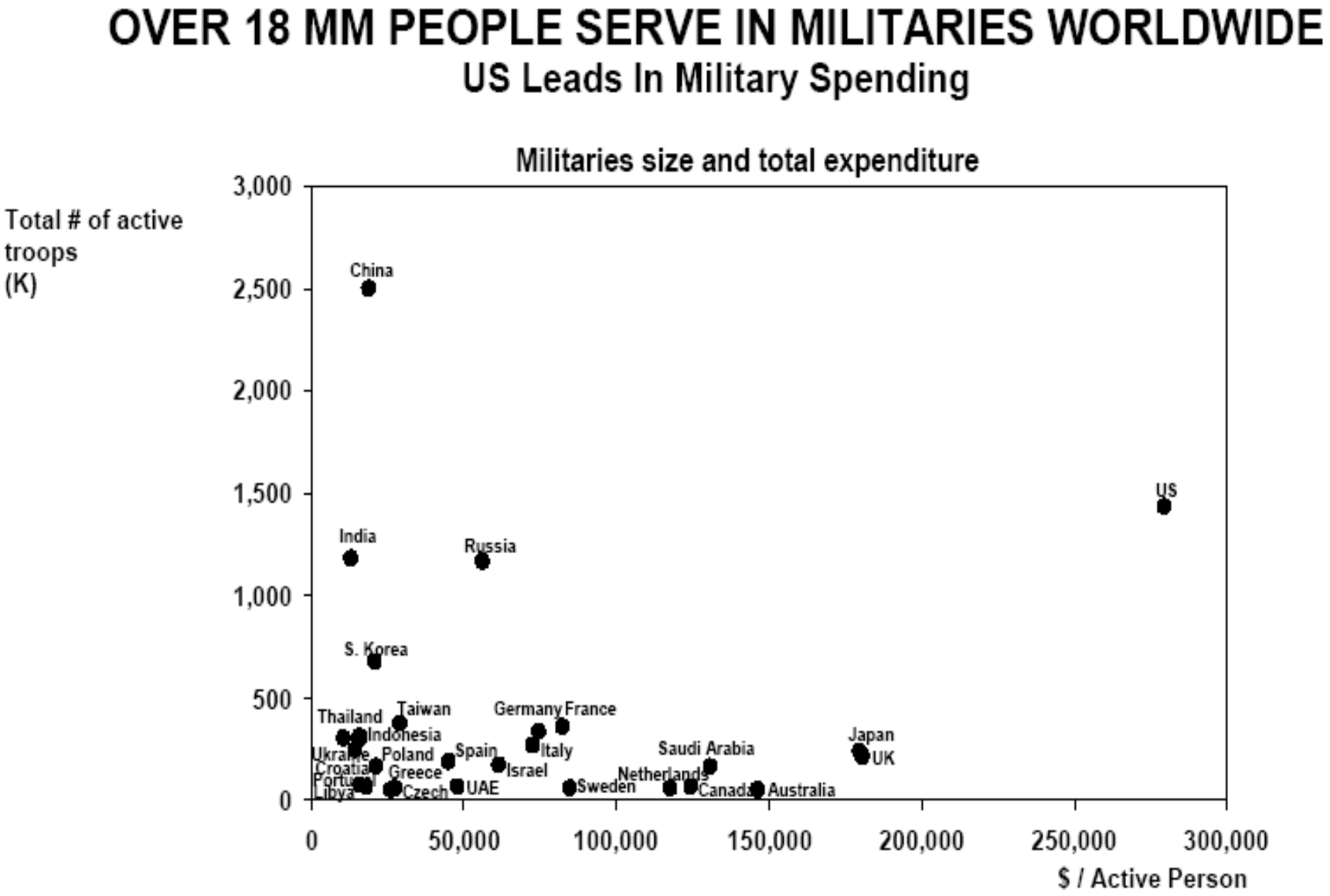
- 78% of European travelers to high-risk malaria areas take prophylaxis vs. 46% of American travelers to high-risk malaria areas take prophylaxis
  - however, in low risk areas, prophylaxis use by Europeans lower than by Americans
- 30-50% of travelers plan trips 4-8 weeks in advance
- > 50% of travelers spend less than 2 weeks in destination region

Key demand drivers are efficacy, timing of immunization, education, duration of trip

- Vaccine must be as effective as available prophylaxis (~98%)
- Vaccine most useful if effective within a month of travel due to travel planning habits
- Market likely limited by number of people who seek pre-travel health advice from a physician
- Vaccine most useful for people who remain in destination for long periods of time (over 1 month)

Ultimate demand will depend on product profile trade-offs with available prophylaxis options

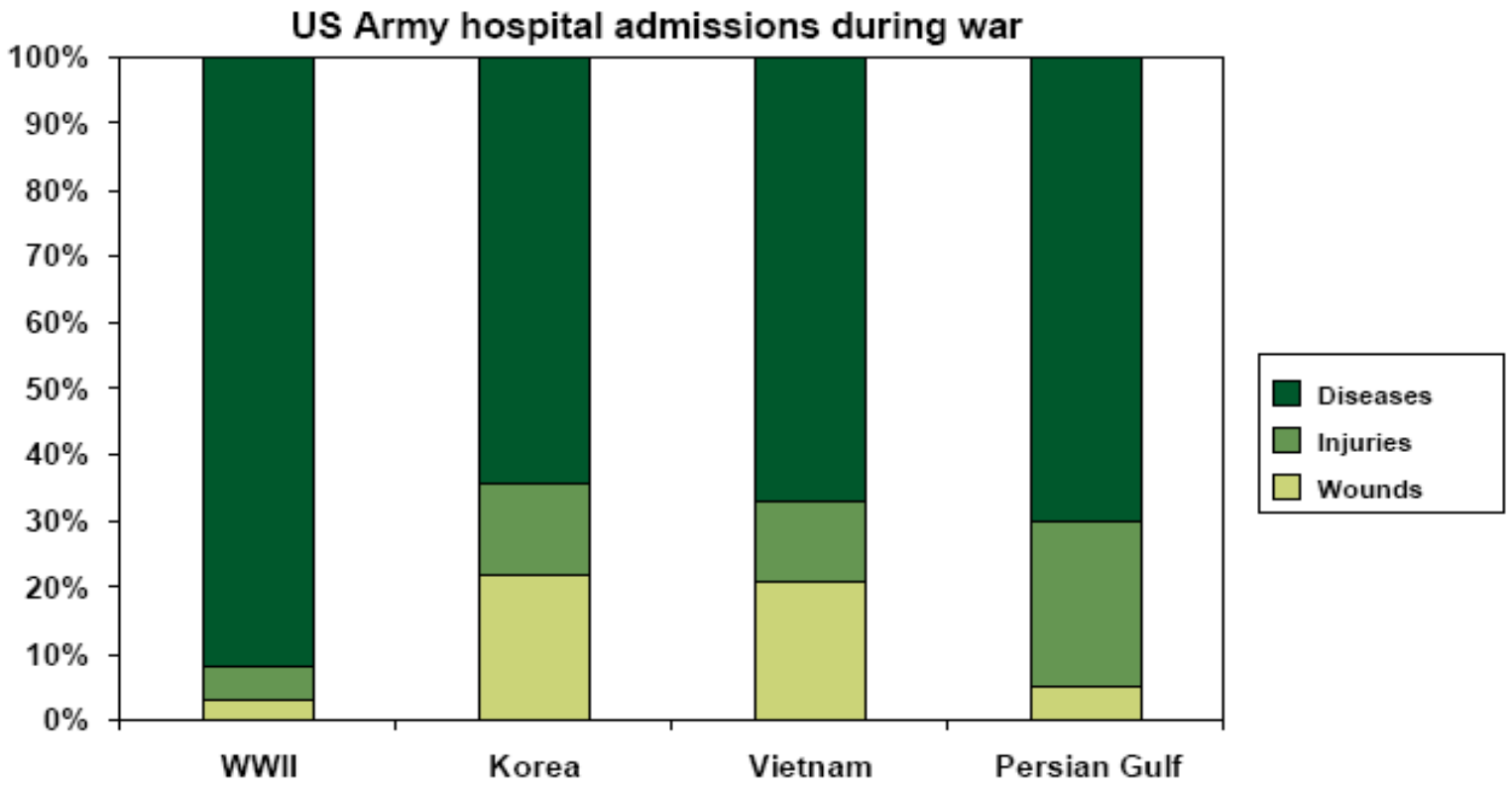
Malaria vaccine demand analysis



Malaria vaccine demand analysis

ILLNESS IS A SERIOUS ISSUE FOR MILITARIES

More Soldiers Die From Diseases Than from Wounds and Injuries



In Somalia and Operation Restore Hope, malaria was the No. 1 cause of casualties

Malaria vaccine demand analysis

MILITARIES ACTIVELY VACCINATE THEIR TROOPS

All troops receive

United States	United Kingdom
Influenza	Meningococcal C
Measles	Polio
Meningococcal (A,C,Y,W-135)	Tetanus
Mumps	Diphtheria
Polio	Yellow Fever
Rubella	Hepatitis A
Tetanus	Typhoid
Diptheria	TB
Hepatitis A	

"The military currently gives Hep A vaccine to all its soldiers. They made major purchases in recent years and the only reason they did so was because Hep A was a major problem in North Africa during World War II" –KOL

Troops deploying to high risk areas receive

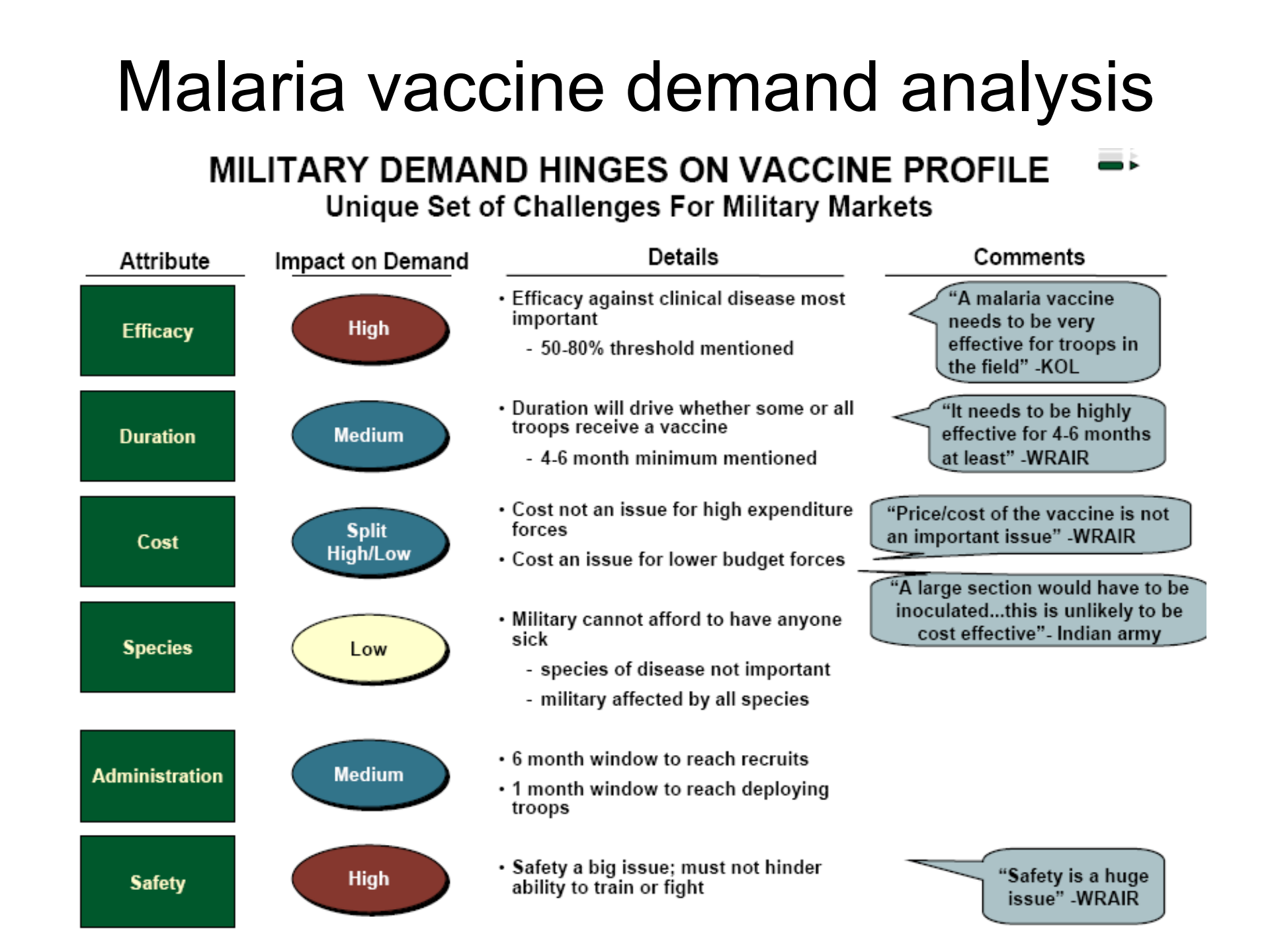
United States	United Kingdom
Yellow Fever	Meningococcal A
Typhoid	Japanese Encephalitis
Japanese Encephalitis	Rabies
	Encephalitis (tick)
Occupational Risk:	
Hepatitis B	Occupational Risk:
Plague	Hepatitis B
Rabies	Rubella
Varicella	
Small Pox	
Anthrax	

"Soldiers deployed to Korea had to take the anthrax vaccine, those travelling to Kuwait took the small pox vaccine, those going to Kenya received the yellow fever vaccine and some going to Asia received the JE vaccine" -WRAIR

Comfort with vaccination as a prevention technique could drive demand for a potential malaria vaccine

- "The most efficient, cost-effective and easiest way to prevent any infectious disease is with a vaccine" –Naval Medical Research Institute

Malaria vaccine demand analysis



Malaria vaccine demand analysis

KEY TAKEAWAYS
Military Market

Preparedness is essential to maintaining an alert force

- Malaria incidence is problematic for militaries
  - largely due to low chemoprophylaxis compliance from extended deployments

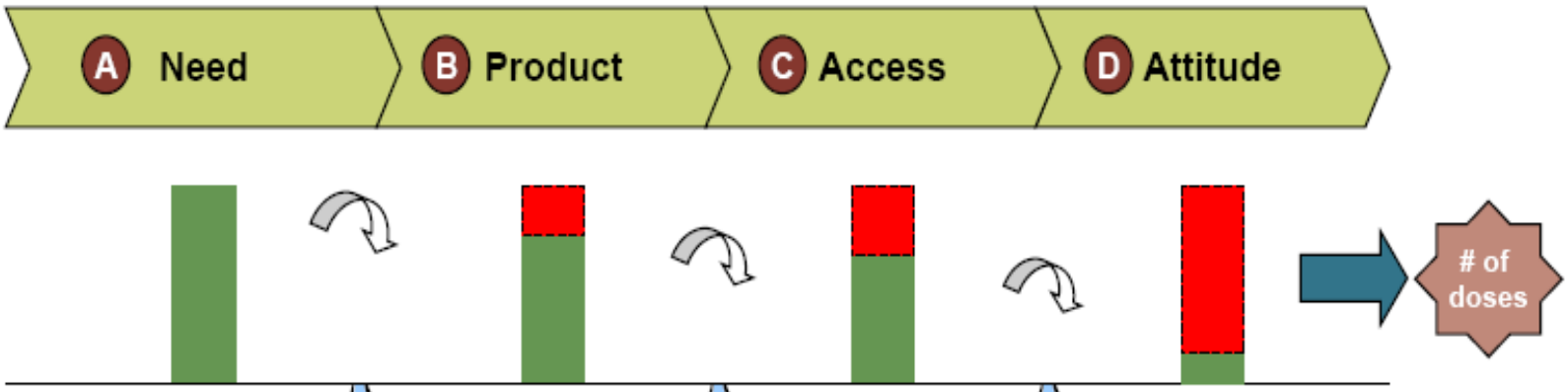
Vaccine used regularly as preventative tool

Demand will hinge on vaccine characteristics

- Safety is key
  - troops must be able to train and fight without side effects or risks
- Militaries will immunize segments of personnel based on vaccine profile
  - All troops vs. troops deploying to high-risk areas
- Efficacy against clinical disease is critical
  - militaries cannot afford illness; "a sick soldier is a useless soldier"
  - vaccine must compete with prophylaxis compliance levels (50-80%)
- Cost not an issue for militaries with high expenditures (i.e. US, UK, Japan), but may significantly affect demand from militaries with smaller budgets

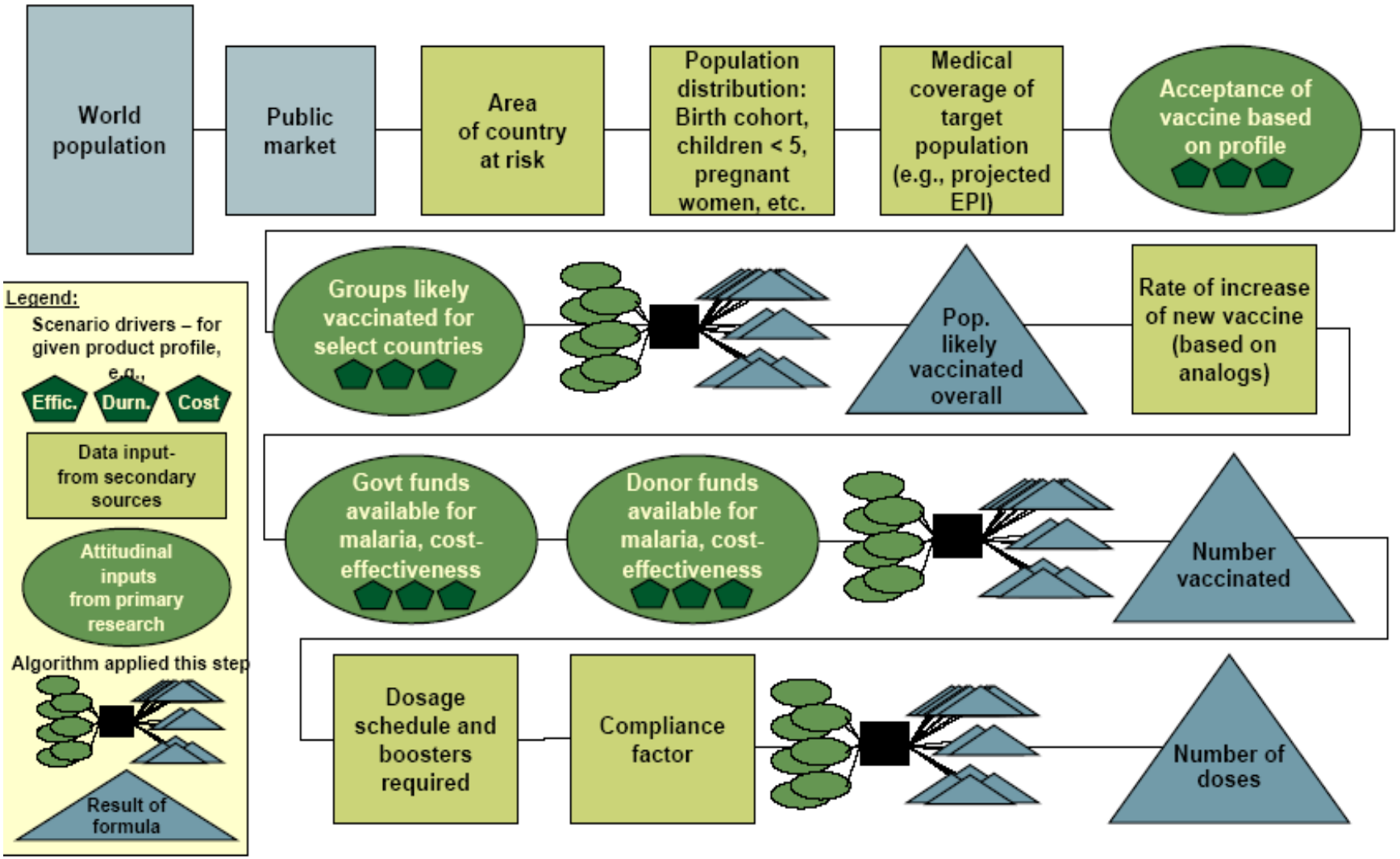
Malaria vaccine demand analysis

MODEL FOLLOWS THE DEMAND LEAKAGE FRAMEWORK FOR ASSESSING MARKET POTENTIAL



Public:	Which countries?	How does product profile influence?	Target population coverage / donor funding available?	Vaccinate none versus high risk versus infants versus children versus all?	How many doses of vaccine in a given year does this translate into?
Private:	Which individuals?	How does product profile influence?	Private clinics/ ability to pay?	Use private market for vaccine?	
Travelers:	Which travelers?	How does product profile influence?	Individuals seek pre-travel advice?	Prefer nothing versus chemo-prophylaxis or vaccines?	
Military:	Which militaries?	How does product profile influence?	Military budget sufficient?	Vaccinate none versus all versus deployed only?	

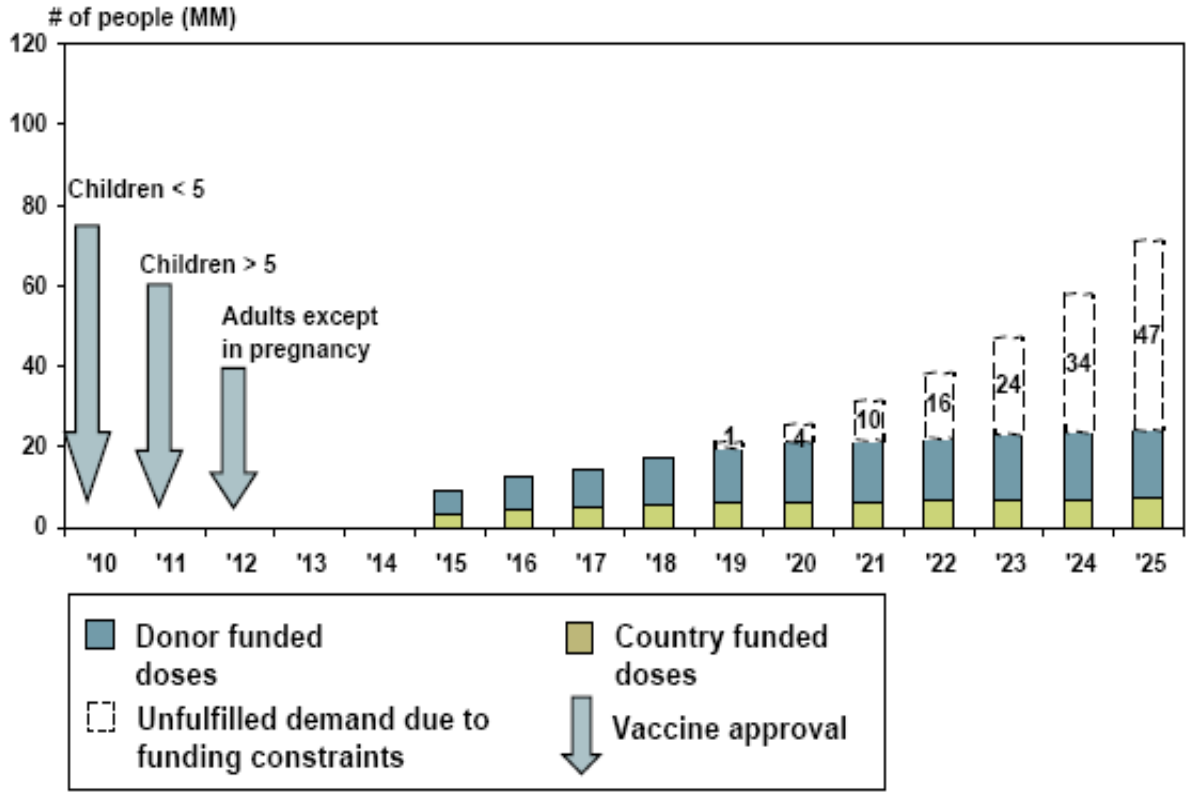
Malaria vaccine demand analysis



Malaria vaccine demand analysis

FUNDING GAP INCREASES OVER TIME FROM 1 MM PEOPLE IN 2019 TO 47 MM PEOPLE IN 2025

Vaccine demand likely to be funded at current donor activity levels (2010-2025)



Note: Assuming current levels of donor activity in the future

Key messages

Countries unable to fully self-fund demand

- As majority of demand for a 50% efficacious vaccine is from high burden, low income countries

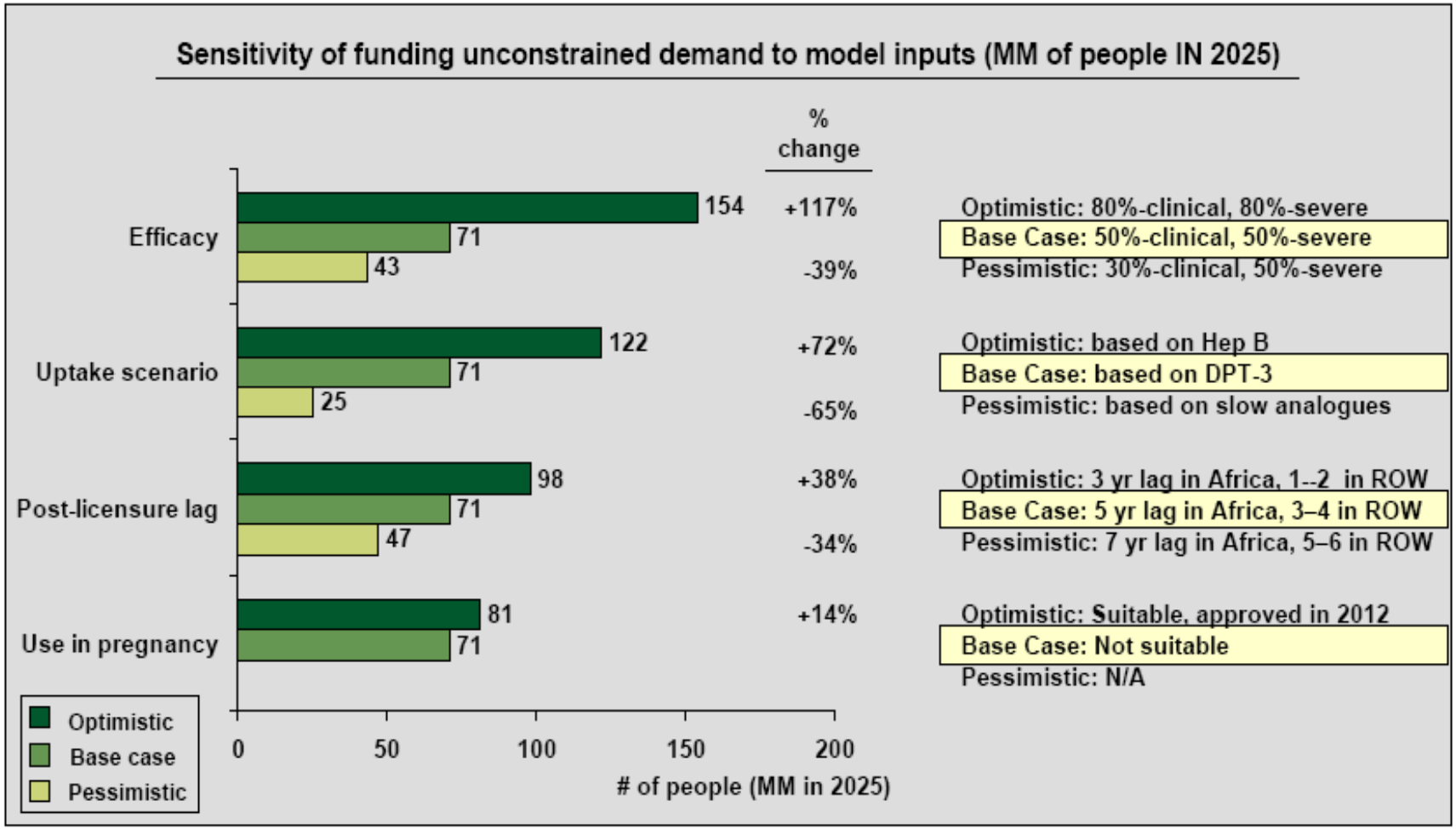
Donor activity at current levels insufficient to vaccinate all people who could be reached

Gap increases over time as potential coverage increases faster than ability to fund a vaccine

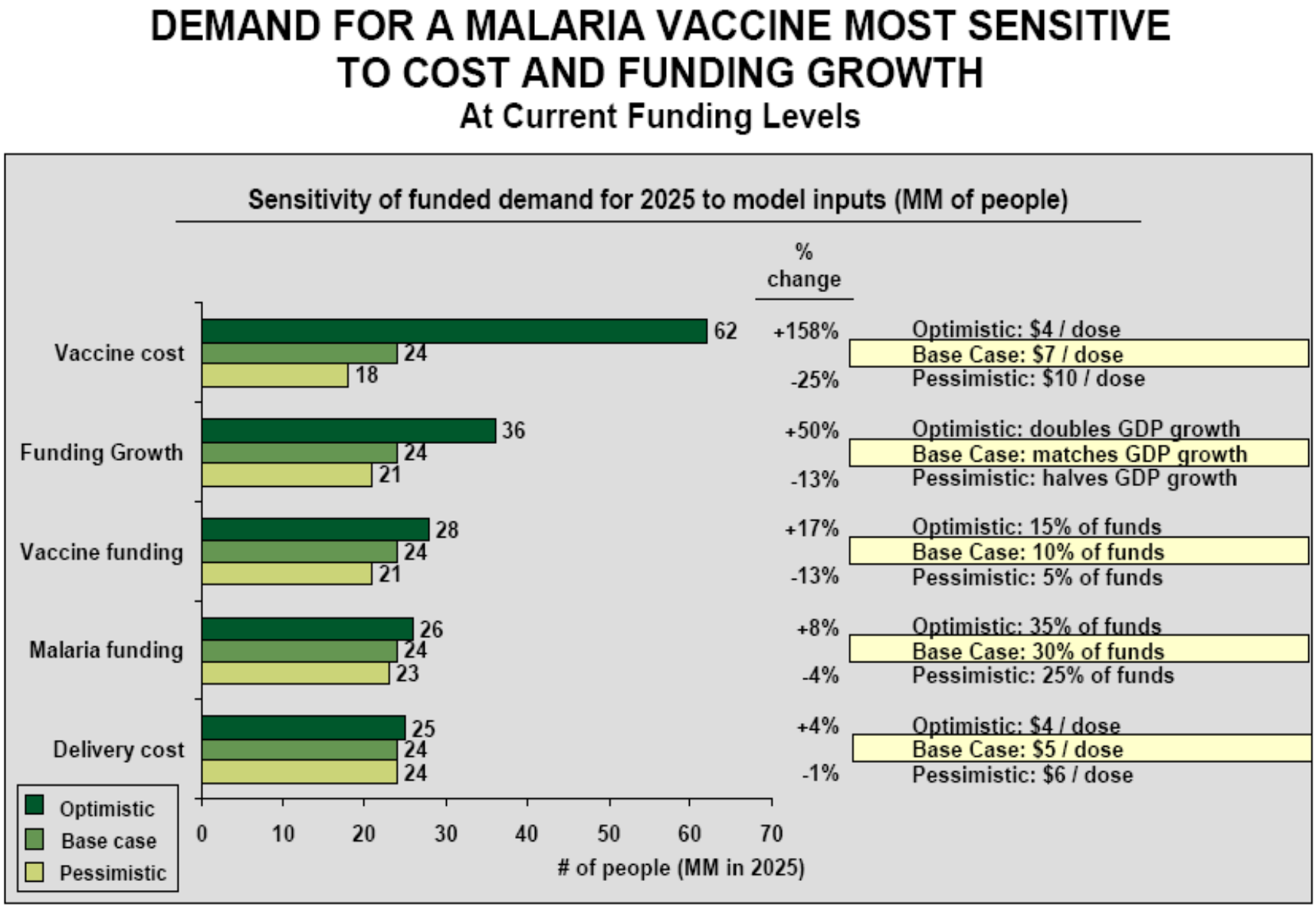
Malaria vaccine demand analysis

DEMAND FOR A MALARIA VACCINE MOST SENSITIVE TO EFFICACY AND UPTAKE SCENARIOS

For Demand Unconstrained By Funding Availability

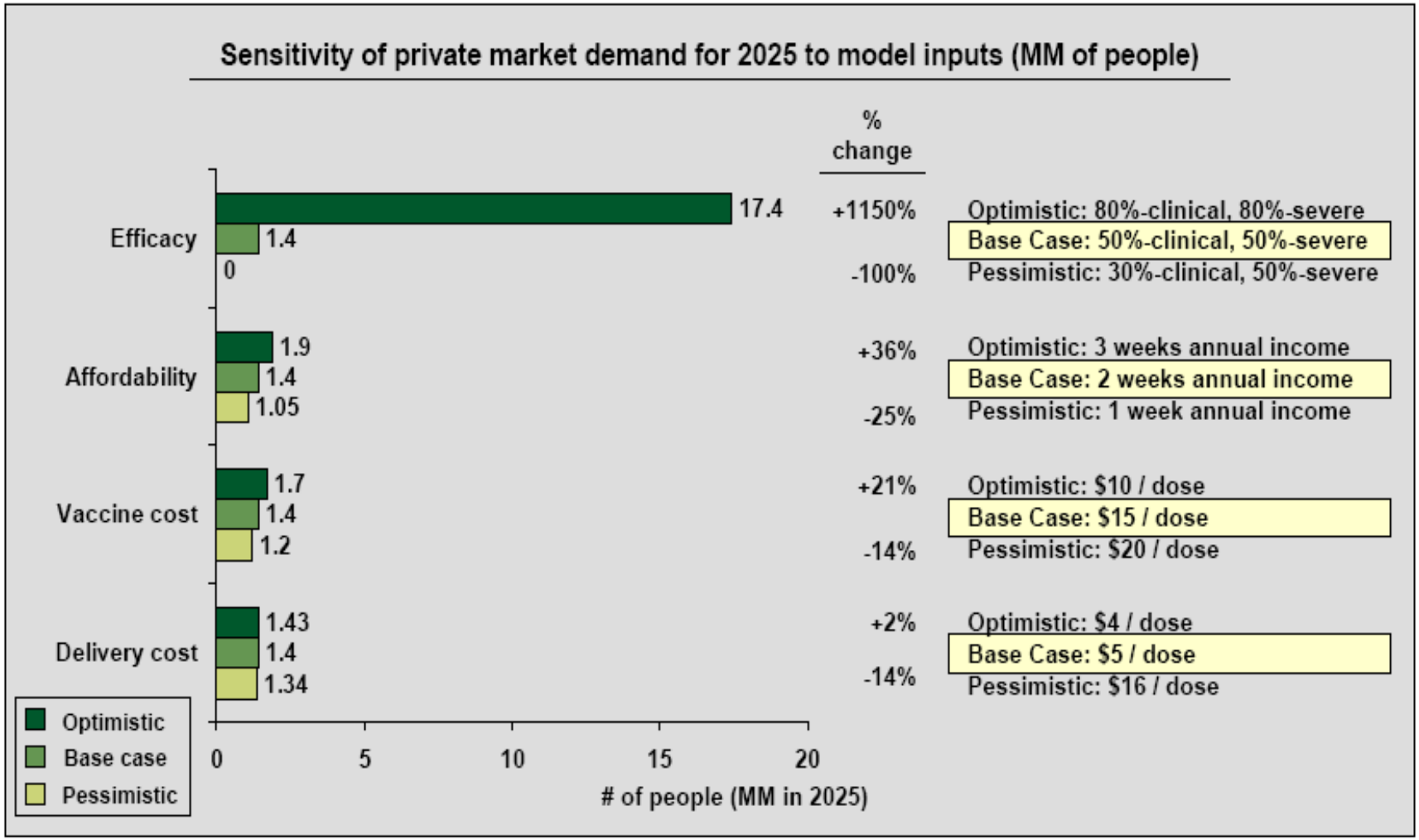


Malaria vaccine demand analysis



Malaria vaccine demand analysis

PRIVATE MARKET DEMAND FOR A MALARIA VACCINE MOST SENSITIVE TO EFFICACY

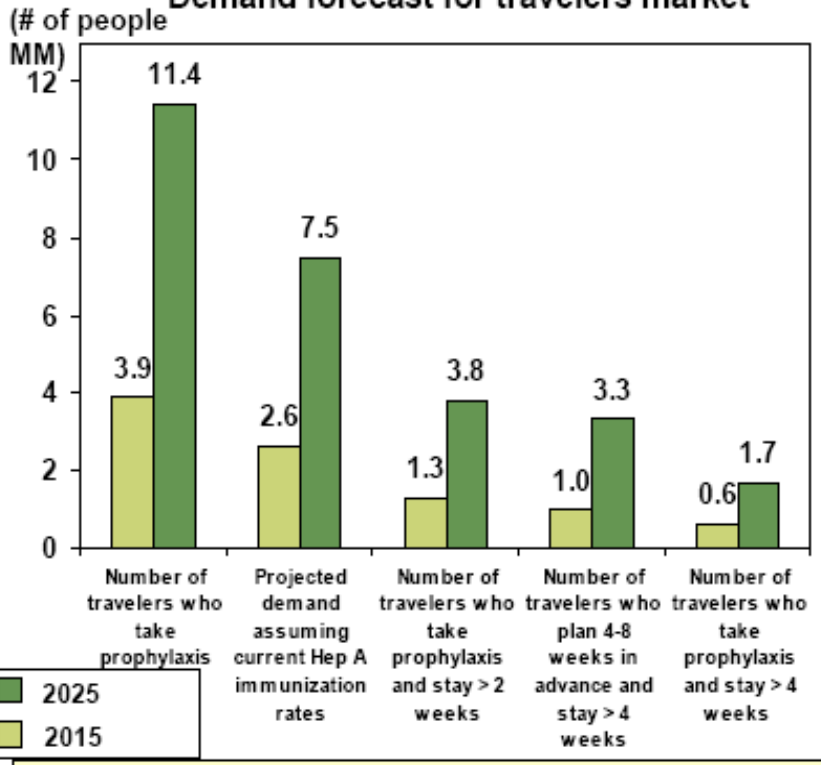


Malaria vaccine demand analysis

TRAVELERS MARKET LIKELY TO RANGE BETWEEN 1.7 AND 3.3 MM PEOPLE IN 2025

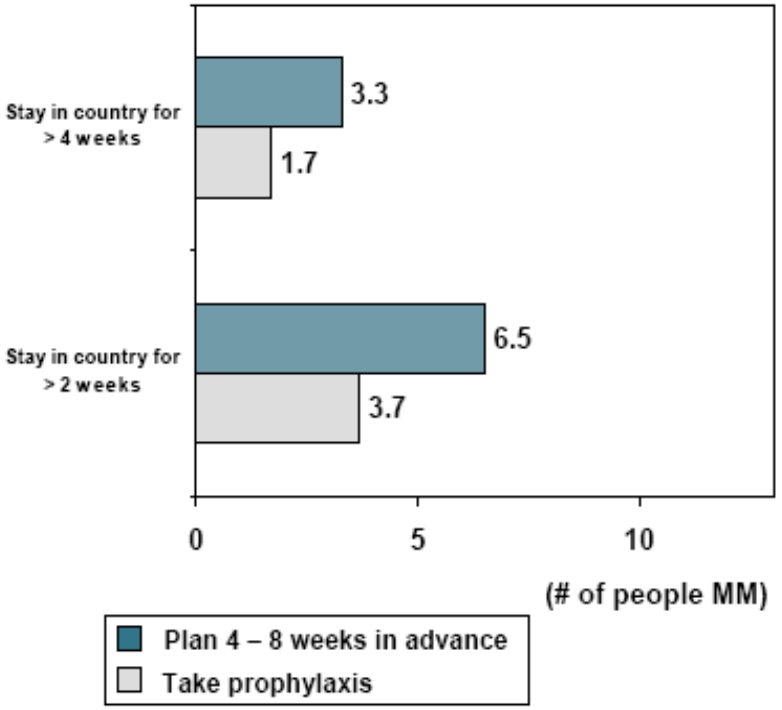
Demand ranges from 1.7 MM to 3.3 MM people in 2025

Demand forecast for travelers market



Demand sensitivity highest to time in-country required to generate interest in vaccine

Sensitivity analysis for travelers market (2025)



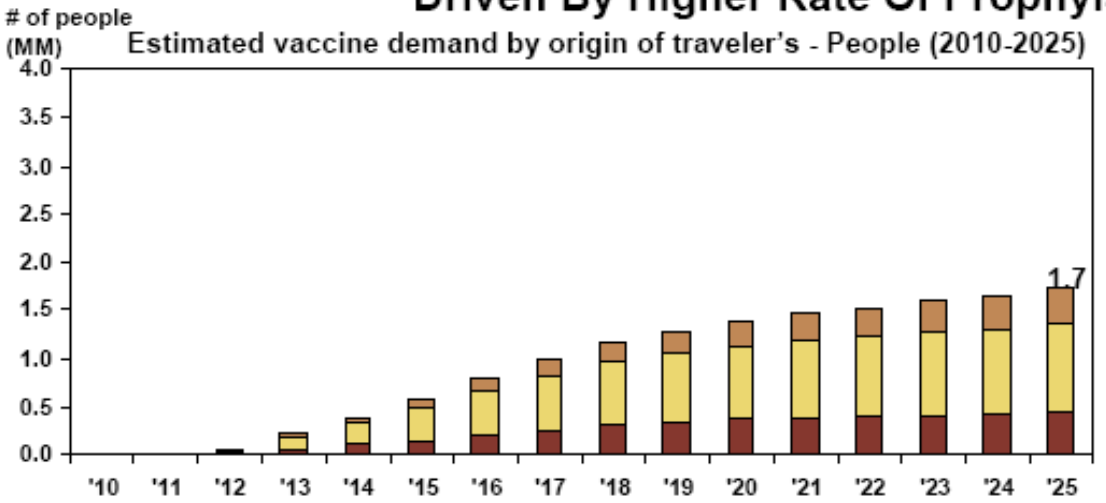
Peak demand likely to be in the range of 1.7 and 3.3 MM people in 2025

- However close to 100% efficacious vaccine required
- Sensitive to in-country stay assumptions, cost and administration schedule

Malaria vaccine demand analysis

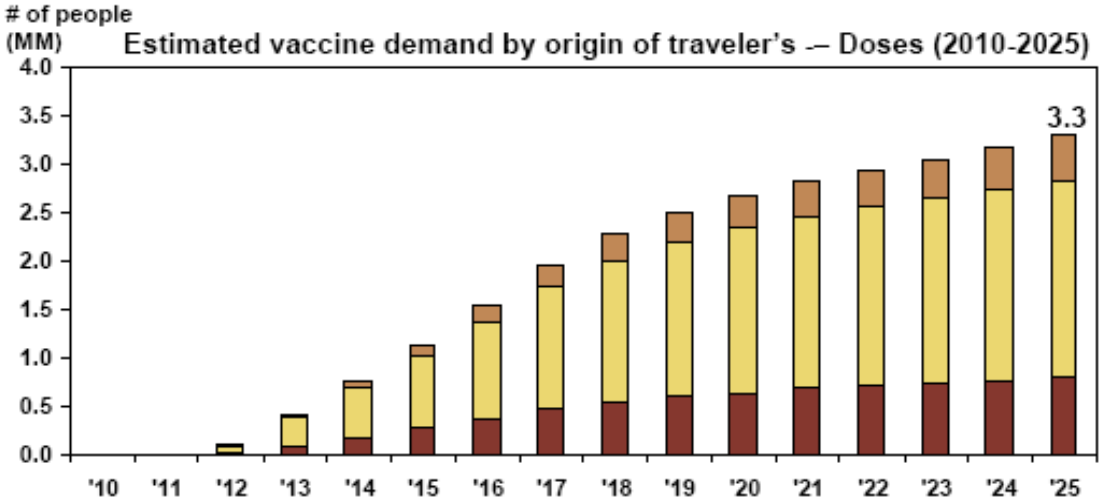
60% OF DEMAND IN TRAVELERS MARKET LIKELY TO BE FROM EUROPEAN TRAVELERS

Driven By Higher Rate Of Prophylaxis Use



Base Case

Demand based on travelers who take prophylaxis for malaria and stay longer than 4 weeks in country



Demand based on travelers who plan 4-8 weeks in advance and stay > 4 weeks

Americans
Europeans
Asians

Note: Assuming one arrival per traveler per country per year

Malaria vaccine demand analysis

PEAK ANNUAL DEMAND FOR A MALARIA VACCINE IN THE MILITARY RANGES FROM 0-13 MM THROUGH 2025

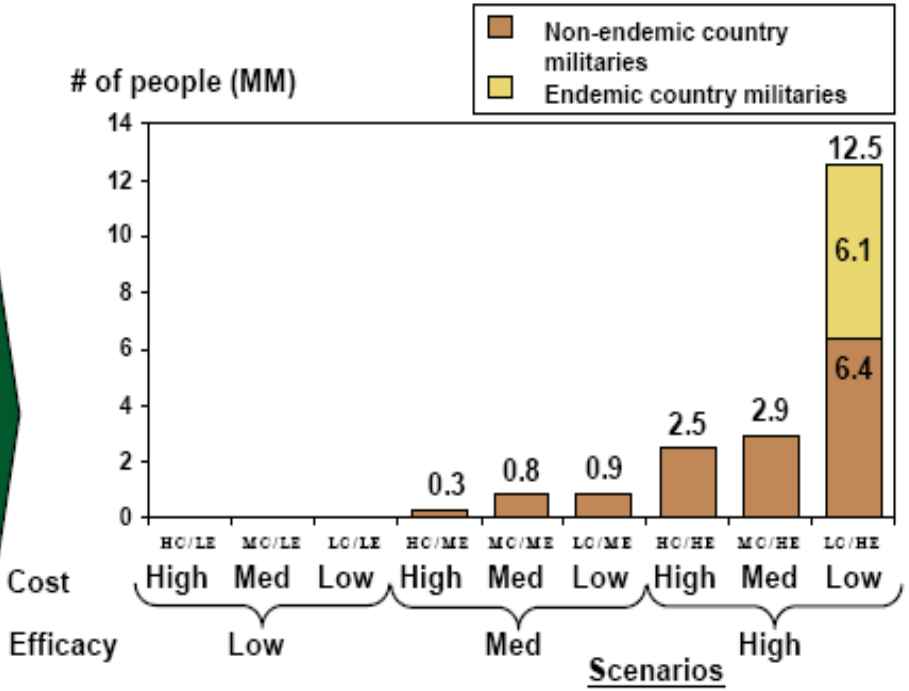
2025 Scenarios

Efficacy Against Clinical Disease

	<$20	$20-$100	>$100
> 80%	12.5MM	2.9MM	2.5MM
50- 80%	0.8MM	0.8MM	0.3MM
< 50%	0	0	0

Total Vaccine Cost

Significant impact of efficacy on demand



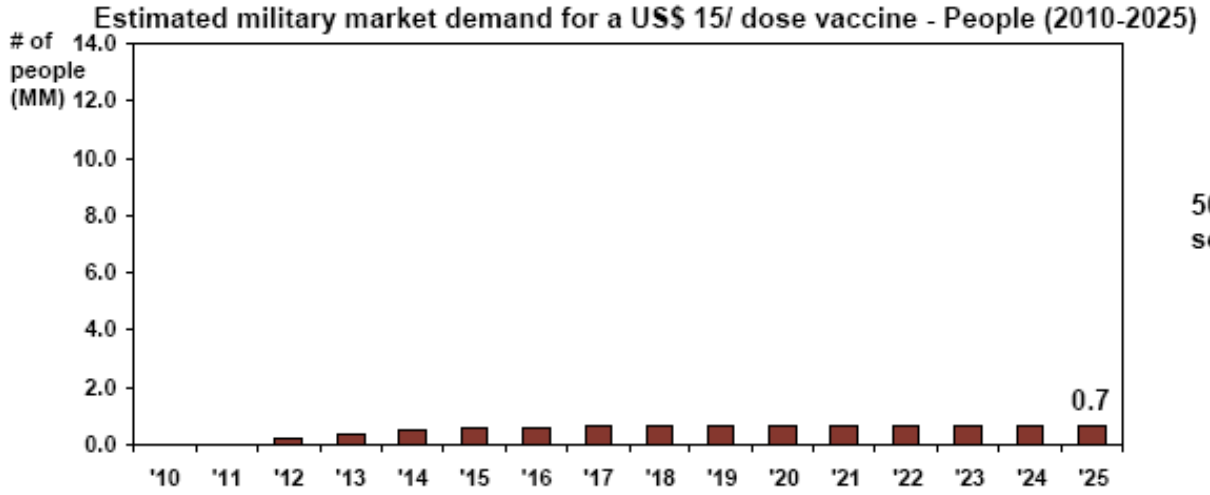
Key:
Cost: Low - < $ 20, Med - $ 20 – 100, High - > $ 100
Efficacy: Low - < 50%, Med – 50 – 80%, High - > 80%

Military demand sensitive to efficacy and cost

Malaria vaccine demand analysis

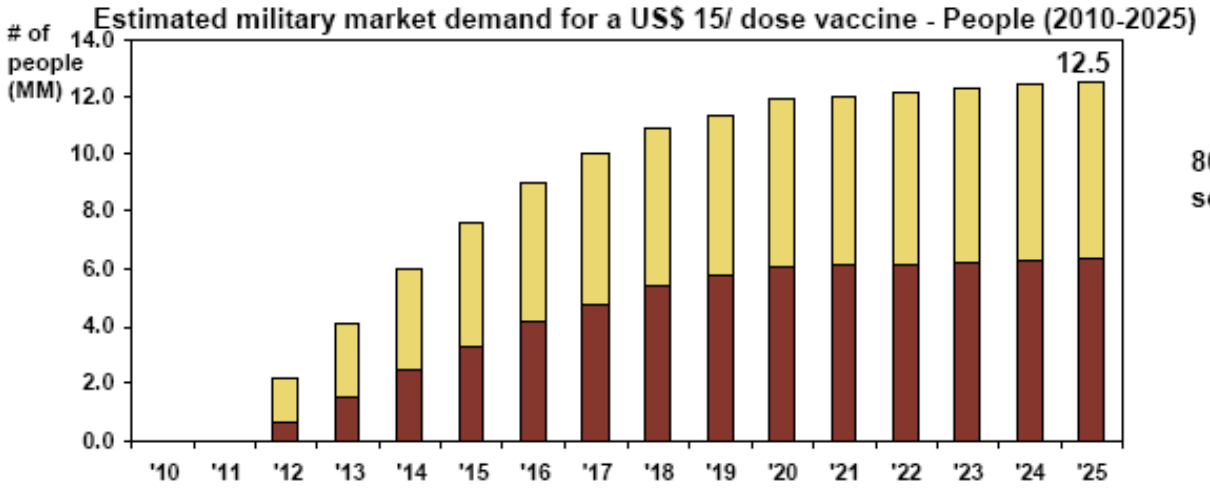
EFFICACY OF VACCINE HAS SIGNIFICANT IMPACT ON MARKET

12.5 MM People Likely to Receive a 80% Efficacious Vaccine



Vaccine efficacy:

50% against clinical and 50% against severe disease



Vaccine efficacy:

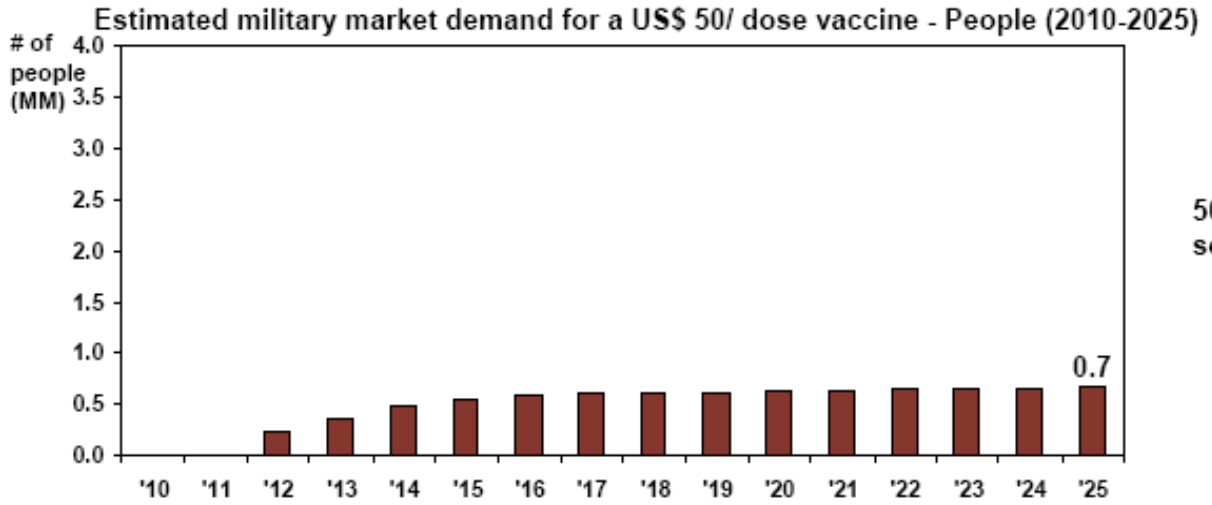
80% against clinical and 80% against severe disease

Non-endemic country militaries

Endemic country militaries

Malaria vaccine demand analysis

DEMAND FOR A US$ 50 / DOSE VACCINE LIKELY TO BE RESTRICTED TO NON-ENDEMIC COUNTRY MILITARIES



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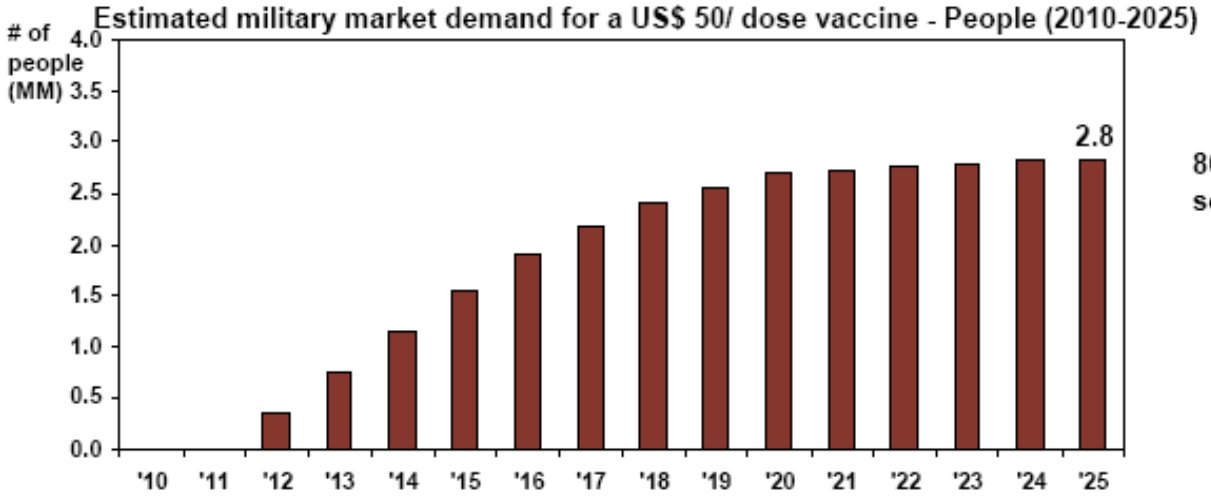


Vaccine efficacy:

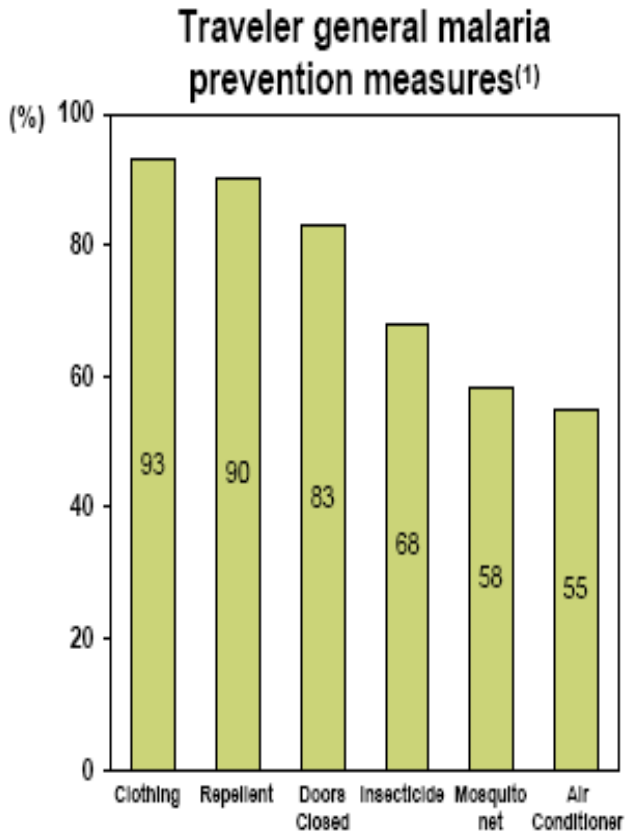
80% against clinical and 80% against severe disease

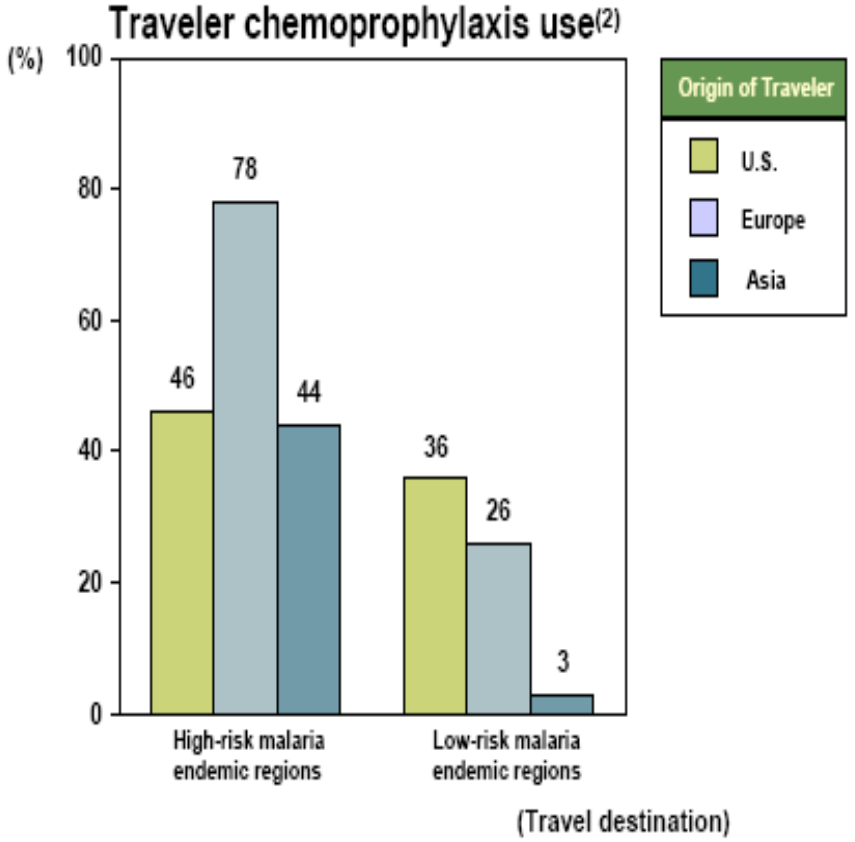
Non-endemic country militaries

Endemic country militaries

Malaria vaccine demand analysis

GENERAL MALARIA PROTECTION IS HIGH AMONG TRAVELERS TO ENDEMIC REGIONS BUT MANY DO NOT TAKE CHEMOPROPHYLAXIS





Malaria vaccine demand analysis

THREE FACTORS MOST INFLUENCE FUTURE SUCCESS OF MALARIA VACCINE

Product profile

Product profile has the strongest influence on demand, as the vaccine must reach stated thresholds to have any uptake

- Efficacy and cost are key drivers, demand in the public market expected to be:
  - 71 MM people with clinical and severe efficacy of 50%, growing to 154 MM at ~80%
  - 50 MM additional people could be funded if cost of vaccine was lowered from $7 to $2 per dose
- P. falciparum component and one year duration are important minimum requirements

Funding

Donor funding can drive demand by stimulating early markets and enabling less wealthy countries' purchase and administration of vaccine

- Public markets will rely heavily on sustainable funding to introduce vaccine
  - uptake only 7 MM people in base case scenario without donor funding
- With strong donor advocacy and implementation support, demand in the public market could reach 290 MM people with clinical and severe efficacy of 80%
- Private markets likely to lag public markets since they do not "turn on" until higher efficacy level reached
  - unlikely to be achieved in first generation vaccine

Influencer support

Support of WHO, academics, and standards-setting organizations are key to vaccine's introduction and credibility

- Support of key third-party organizations can influence lag between licensure and introduction
- Countries and donors both both rely on key opinion leaders and WHO recommendations in deciding on which interventions to support