Risks versus benefits related to the possible implementation of a malaria blood-screening test

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Probabilistic Modeling Risk/Benefit of New Donor Populations

- **Current U.S. policy includes deferral of:**
  - **Travelers – malaria endemic countries in last year**
  - **Immigrants – from malaria endemic countries < 3 yrs**
  - **Donors that had malaria – asymptomatic < 3yrs**

- **Goal: Use probabilistic model to evaluate potential risks / benefits and uncertainties of:**
  - **Current policy**
  - **Universal NAT Testing Scenario**
  - **Universal Antibody Testing Scenario**

Probabilistic Modeling

- Rather than single numbers or "point estimates"

- Employs statistical distributions for INPUT PARAMETERS - represents uncertainty of data

- Monte Carlo method chooses a value from each distribution as the "single number" for ONE iteration and generates OUTPUT as distributions

- Model is run thousands or millions of iterations and single "aggregate" OUTPUT distributions reflecting uncertainty and variability are generated

Uncertainty

- Arises from lack of or limited data for an input parameter(s)
- Assumptions used in model – add to uncertainty
- Lack of information or data for estimating –
  - Self deferral for travelers to / immigrants from malaria areas,
  - effectiveness malaria deferrals,
  - Donation rates of travelers / immigrants,
  - NAT test sensitivity,
  - Antibody test sensitivity, etc.
- Uncertainty represented as confidence intervals about mean estimated outcomes

Malaria Risk in the United States

- 1,325 reported cases of Malaria identified in the U.S. in 2004 (CDC, MMWR 2006)

- All but 4 cases imported

- ~ 50% cases were *Plasmodium falciparum*

- Transfusion transmitted malaria (TTM) rate is low
  - ~ 0.25 cases per million units collected

# Possible Risks (Costs) and Benefits of Malaria testing of blood

- Risks (Costs)
  - **Additional malaria units, transfusion transmitted malaria (TTM), etc.**
  - **Costs of testing entire supply (>14 million units / yr)**
  - **Costs of re-testing units**
  - **Loss of blood donors and blood units**
  - **Costs of recruiting donors**

- **Benefits**
  - **Number of additional donors gained**
  - **Detection of additional malaria units from non-deferred donors**

Overview of Model Components
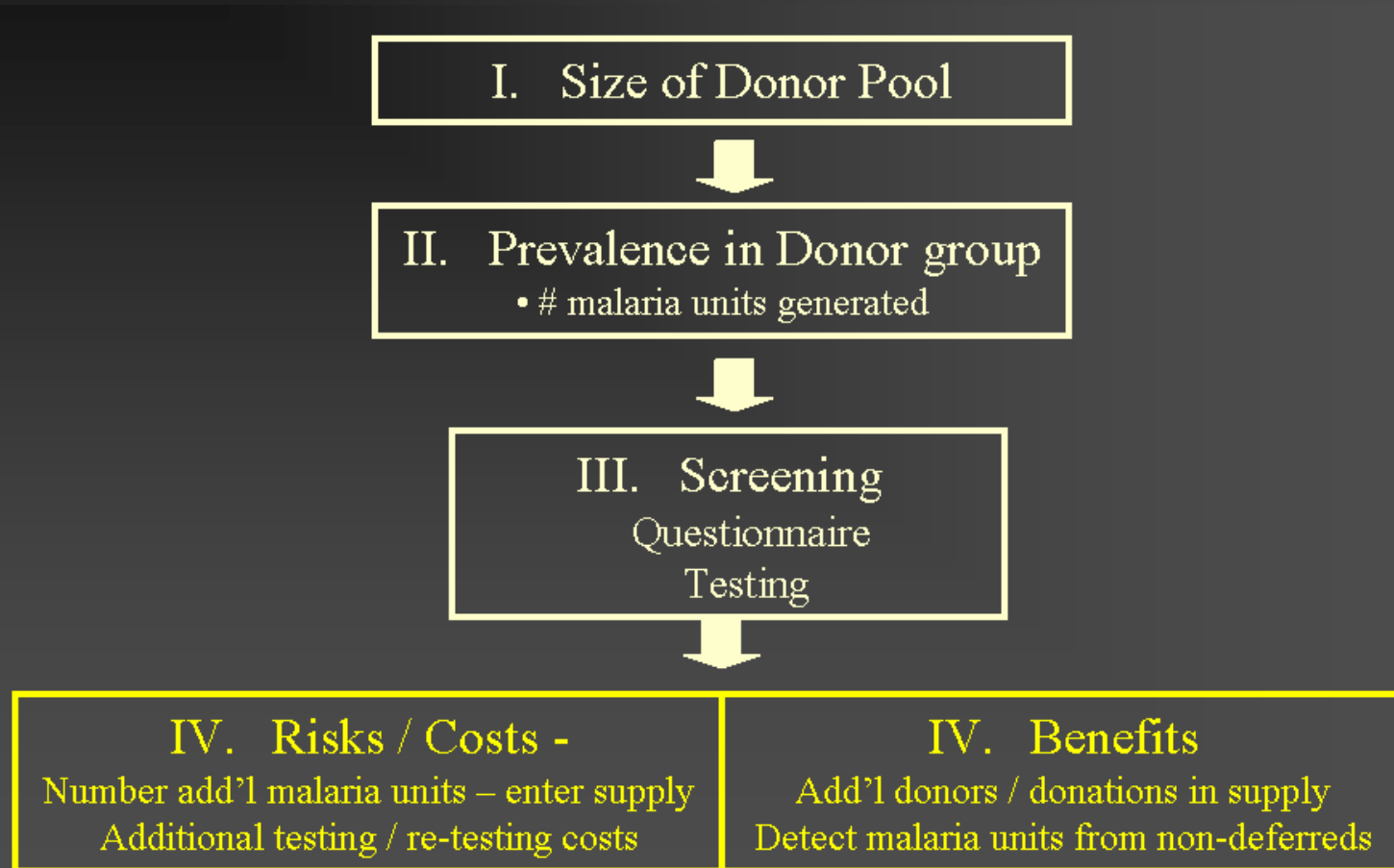
I. Estimation Size of Donor Pool

INPUT DATA:

- ~ 8 - 9 million — Total Annual number blood donors
- ~ 27.4 million — US travelers to malaria countries
- ~ 382,000 — Immigrants from malaria countries
- ~ 60 % — Population qualified to donate
- 5 % — Donation rate general population
- 1.7 — Annual donations per donor per yr
- ~ 14 million — Total number blood donations per yr

OUTPUTS:

- > 880,000 — Donors per year travel to malaria country
- > 730,000 — Donors – self defer for malaria risk
- > 150,000 — Donors – deferred by questionnaire

II. Estimation of malaria infection prevalence potential new donor groups

- **INPUT DATA :**
- 95 - 99%   Effectiveness of Questionnaire screen
-                     (effectively lowers malaria prevalence in donors)

- **OUTPUTS:**
- ~   42   Potential mean malaria <u>donors</u> per year*
- ~   71   Potential mean malaria <u>donations</u> per yr*
- ~   3   Malaria units – not deferred per yr

  *Most are removed by donor screening

III. Testing Scenarios: Universal Nucleic Acid Test (NAT)

- **Test all donations using NAT**

- **Travelers (< 1yr) and Immigrants (< 3yr) to Malaria endemic countries**
  - **Assumed there was a one month window period (WP) – donors with malaria not detected**

- **All other donors**
  - **Assumed no window period**

- **Test Sensitivity assumed 99% - 100% sensitive**

III. Testing Scenarios: Universal Antibody testing

- **Travelers ($\leq$ 3 months) to Malaria countries**
  - **Assumed a 3 month WP – test may not detect malaria**

- **Travelers (> 3 months) to Malaria countries**
  - **Test sensitivity – assumed to vary by species**

- **Immigrants ($\leq$ 3yr) to Malaria countries**
  - **Assumed no WP**

- **All other donors**
  - **Assumed no WP**

III. Universal Antibody testing (cont'd)

- **Travelers (> 3 months) to Malaria countries**
  - **Adjust test sensitivities for (>3 mo) traveler population by occurrence of species in geographic regions traveled**

- **(1) Assumed Test Sensitivity:**
  - **P. falciparum**   **94% - 99.5%**
  - **P. vivax**   **75% - 100%**
  - **Others**   **50% -   75%**

(2) Occurrence of species in travelers by region

	Pf	Pv	Other
Africa	82%	10%	7%
Asia	11%	83%	6%
Americas	36%	57%	6%
Others	10%	76%	14%
All regions	63%	30%	7%

IV. Results: potential risks and benefits of alternative screening methods

Current Policy	Risks (5th, 95th perc)			Costs of screening	Benefits (5th, 95th perc)	
	Blood units lost	Donors removed	Malaria units – not removed		Malaria units removed	Potential donors gained
Self deferred	1,276,000	729,000	na	Assumed low	58 (48-79)	na
Questionnaire deferred	207,000	150,000	3 (1 – 5)		9 (3 - 18)	na
Total: Self + Questionnaire	1,483,000	879,000	3 (1 – 5)	Costs for recruiting	67 (48 - 90)	na

Blood units collected per year in US = ~ 14 million

IV. Results: potential risks and benefits of alternative screening methods

	Blood units collected	Risks (5th, 95th perc)				Benefits (5th, 95th)	
		Blood units lost	Donors removed	Malaria units – not removed	Costs of screening	Malaria units removed	Potential donors gained
Current	~ 14 million	**1,483,000**	**879,000**	3 (1 – 5)	Assumed low Costs for recruiting	67 (48 - 90)	na
NAT testing	15,761,616	**66** **(46 – 87)** (benefit)	**40** **(30 – 51)** (benefit)	5 (2 – 9)	Costs >14 million tests Re-testing of units	66 (46 – 87)	~ 880,000
Antibody testing	15,760,264	**1,418** (954 – 1912) (benefit)	**890** (600 – 1200) (benefit)	10 (4 - 16)	Costs >14 million tests Re-testing of units	61 (43 - 81)	~ 880,000

Key Uncertainties

- Overall there is uncertainty for many of model inputs

- Would expect Malaria prevalence in donors with travel history (<1yr) or immigrant – Malaria countries to be leading contributor to uncertainty

- Variability in malaria species by region over time

- Sensitivity of test that would by used

Conclusions from Malaria model

- Current policy – many donors (~ 150,000) deferred
- or ~ 880,000 donors if include self-deferrals

- Antibody testing – fewer donors deferred(~1,400)
- NAT testing – even fewer deferred (66)

- However, testing has <u>significant costs</u> associated with testing / re-testing >14 million units / yr

- But, testing scenario there may be a net gain of
- ~ 880,000 donors

Conclusions from Malaria model (cont'd)

- Need further exploration of costs of each option
  - Testing
  - Re-testing
  - Recruitment of donors

- Validate assumptions (with data) on test sensitivities

- Peer review of Model
  - Assumptions, data used, etc.

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