# Blood Screening|Transfusion
## *Future Product Market Concepts*

September, 2013

# Opportunities Exist to Grow the Transfusion Testing Business

- Current blood screening markets are for the most part mature, leading to flat to single digit revenue growth.
- Therefore, one can potentially reinvigorate transfusion test growth through three initiatives
  - **Facilitate decentralized donation in developing countries and certain regions (e.g., India, rural China)**
  - **Investigate serology for donation - in addition more revenue in developed markets, likely a good entre and beachhead into developing markets**
  - **Grow traditional, centralized sales in developing countries, and local donation sites where economically feasible and allowed by regulation, including NAT conversion and menu expansion**

# Potentially reinvigorate transfusion test growth through three initiatives

- **Facilitate decentralized donation in developing countries, and some developed markets (e.g., India, rural China)**
  - **"Non-tracked" incremental market from NAT $280 million**
  - **Incremental revenue at the same rate as developed country donations per capital ("developed-equivalent") $2,725 million (of which $2,100 million in middle healthcare spending / capita countries)**
  - **Partner to get to decentralized locations**
  - **Add other assays for high-incidence areas, beyond typical screening, where incidence is high (e.g., dengue fever)**
- **Investigate serology for donation - in addition more revenue in developed markets, likely a good entre and beachhead into developing markets**
- **Grow traditional, centralized sales in developing countries, and local donation sites where economically feasible and allowed by regulation, including NAT conversion and menu expansion**
  - **Mandates requiring NAT in China, India, and Russia**
  - **"Tracked" incremental market from NAT conversion with current menu $400 million**
  - **Incremental new tests, such as HAV, HEV, dengue fever, and parvo virus (for plasma screening)**

# WORLDWIDE OPPORTUNITY

# International Blood Donations Provide Testing Opportunities

- 92 million blood donations every year
  - *50% collected in high-income countries with only 15% of the world's population,* leading to a developed-country total equivalent market of 310 million donations.
- Approximately 8000 blood centers in 159 countries *report* on blood donations.
  - Average, annual blood donations per blood center in high-income countries is 30,000 versus 3700 low-income countries
- Only 62 countries have national blood supplies entirely from voluntary, unpaid blood donations.
- 39 countries in the list were unable to screen all blood donations for one or more of these transfusion-transmissible infections: HIV, hepatitis B, hepatitis C and syphilis.
- 106 countries have national guidelines for appropriate clinical use of blood.
- Only 13% of low-income countries have a national hemovigilance system to monitor and improve safe blood transfusion.

Source: WHO

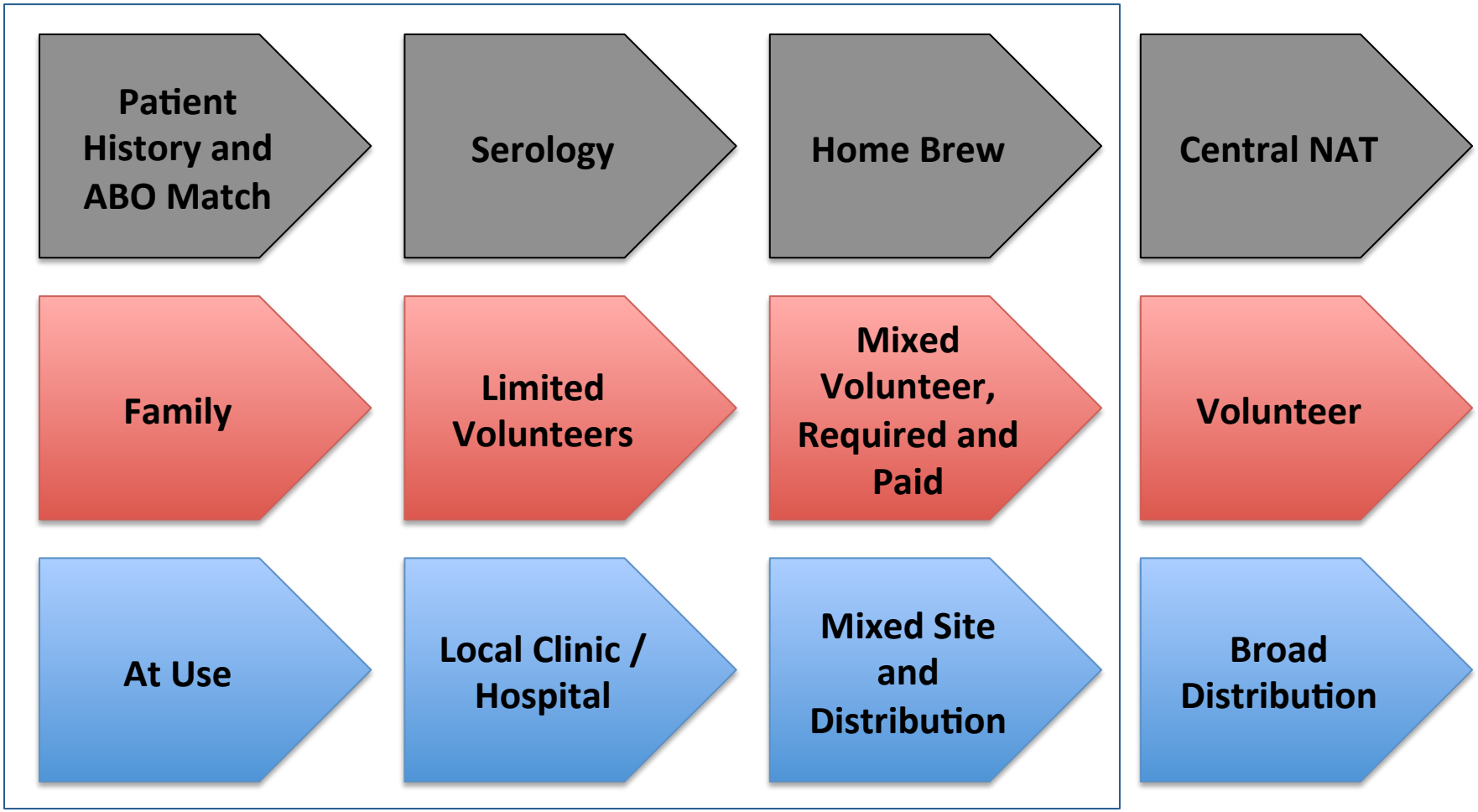
# Donation Systems in Developing Countries Show Clinical Need

- 50% of donations in high-income countries with only 15% of the world's population, leading to a developed-country total equivalent market of 310 million donations.
- 39 countries (of 159 reporting) unable to screen all blood donations for one or more of these transfusion-transmissible infections: HIV, hepatitis B, hepatitis C and syphilis.
- Only 13% of low-income countries have a national hemovigilance system to monitor and improve safe blood transfusion.

Source: WHO

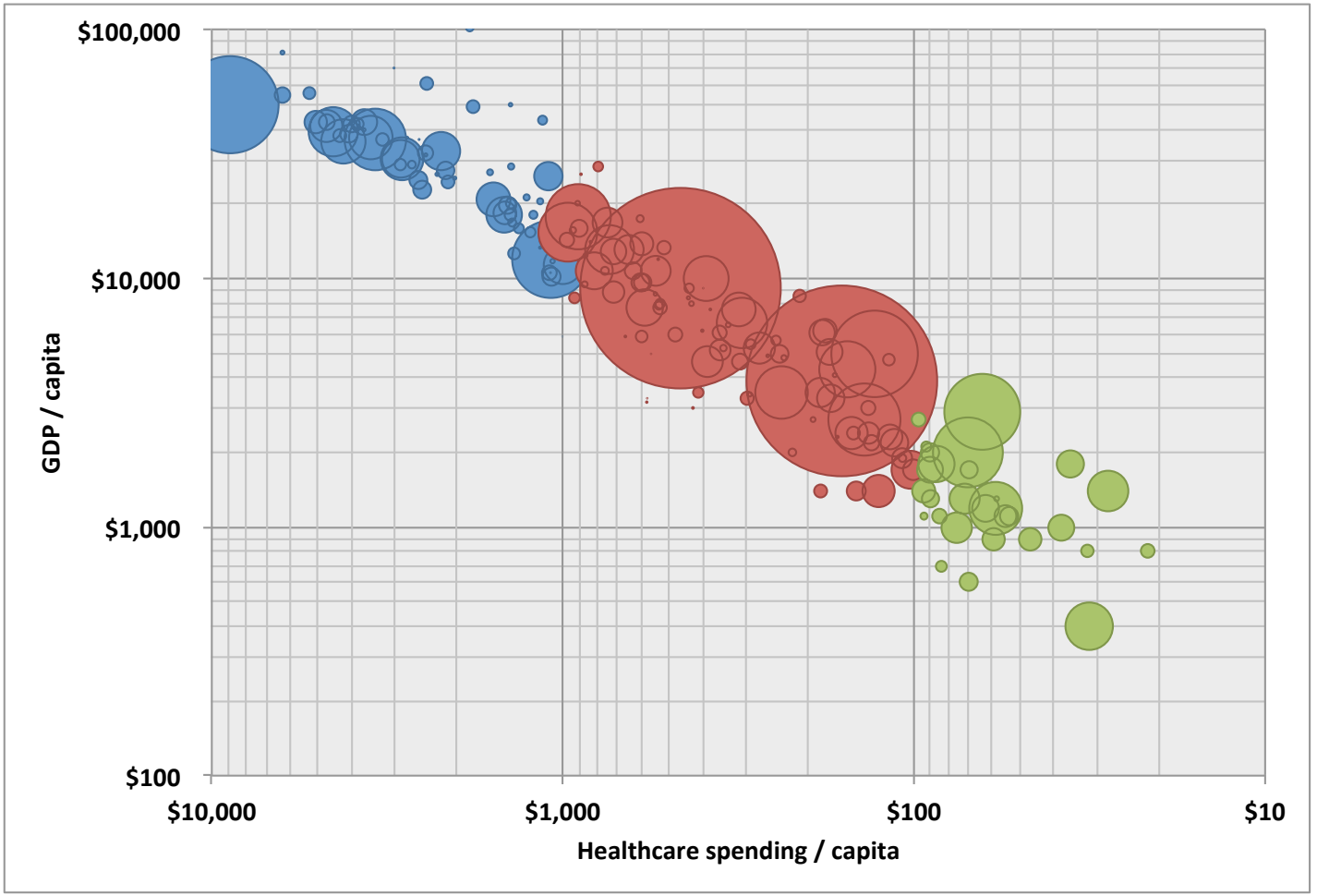
A CENTRAL CONCEPT

# POC Needed before Testing, Sourcing, and Distribution of Blood Fully Evolved



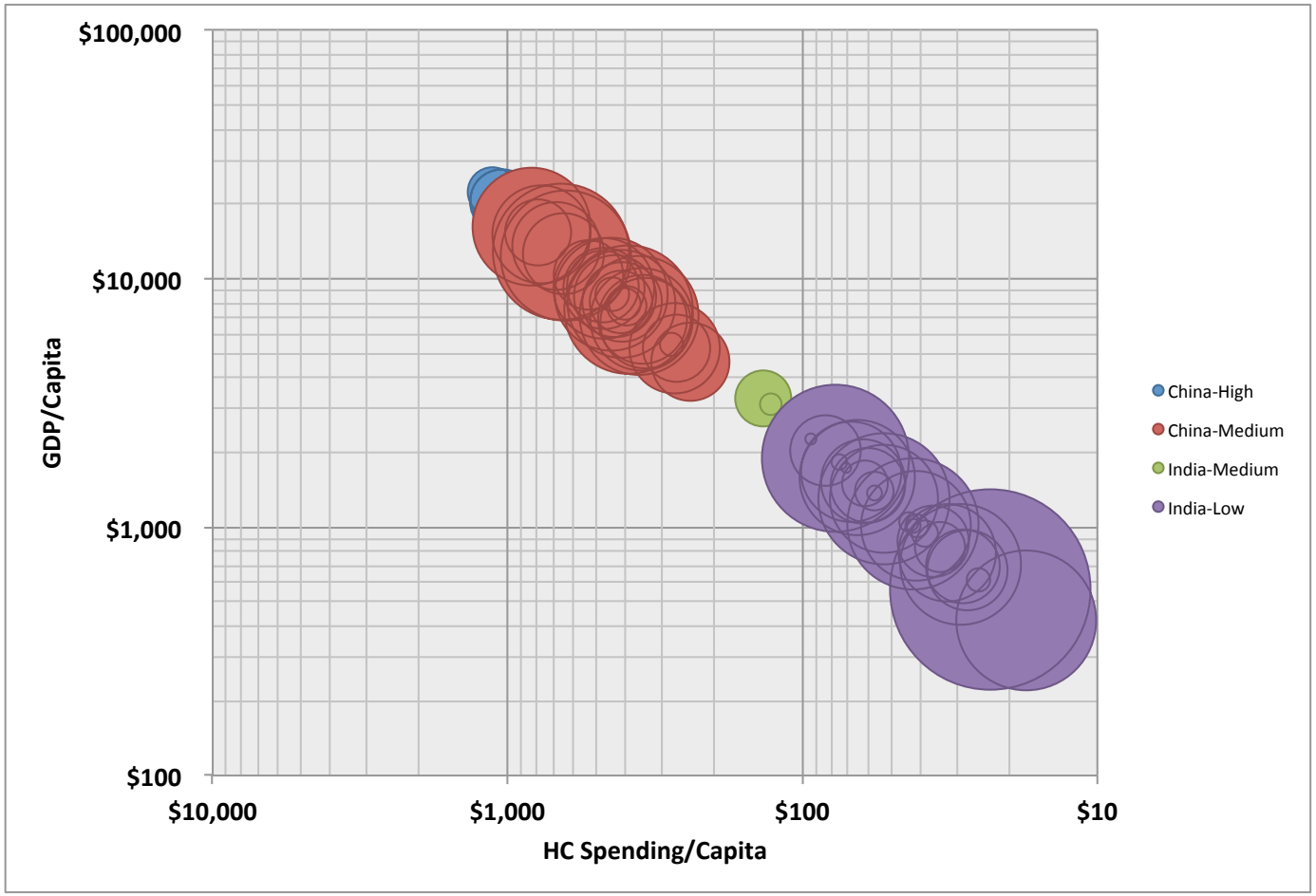
A CENTRAL CONCEPT

# Targeting Should Occur in Highest Population at the Right Stage



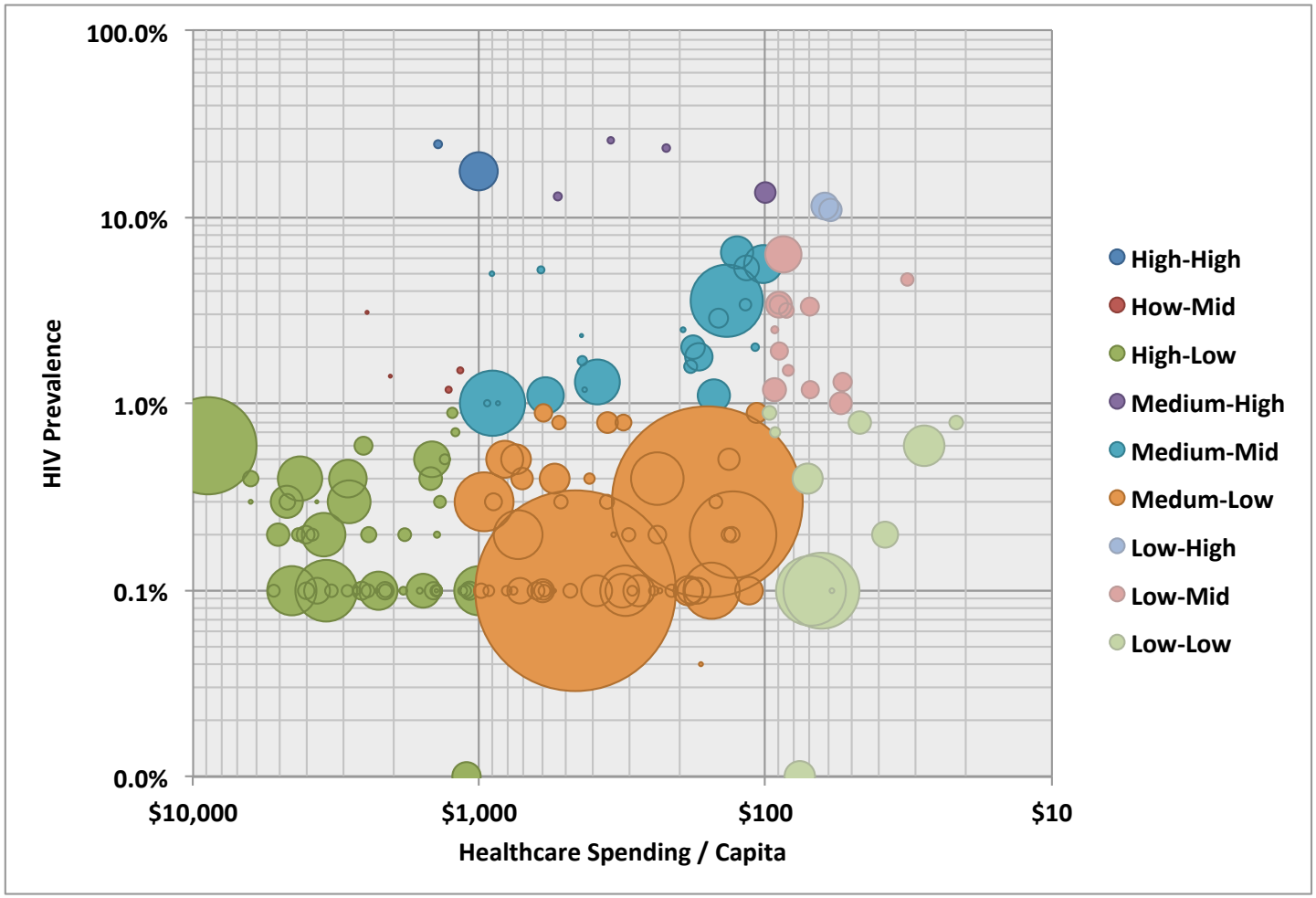
A CENTRAL CONCEPT

# China and India Should be Considered by Region



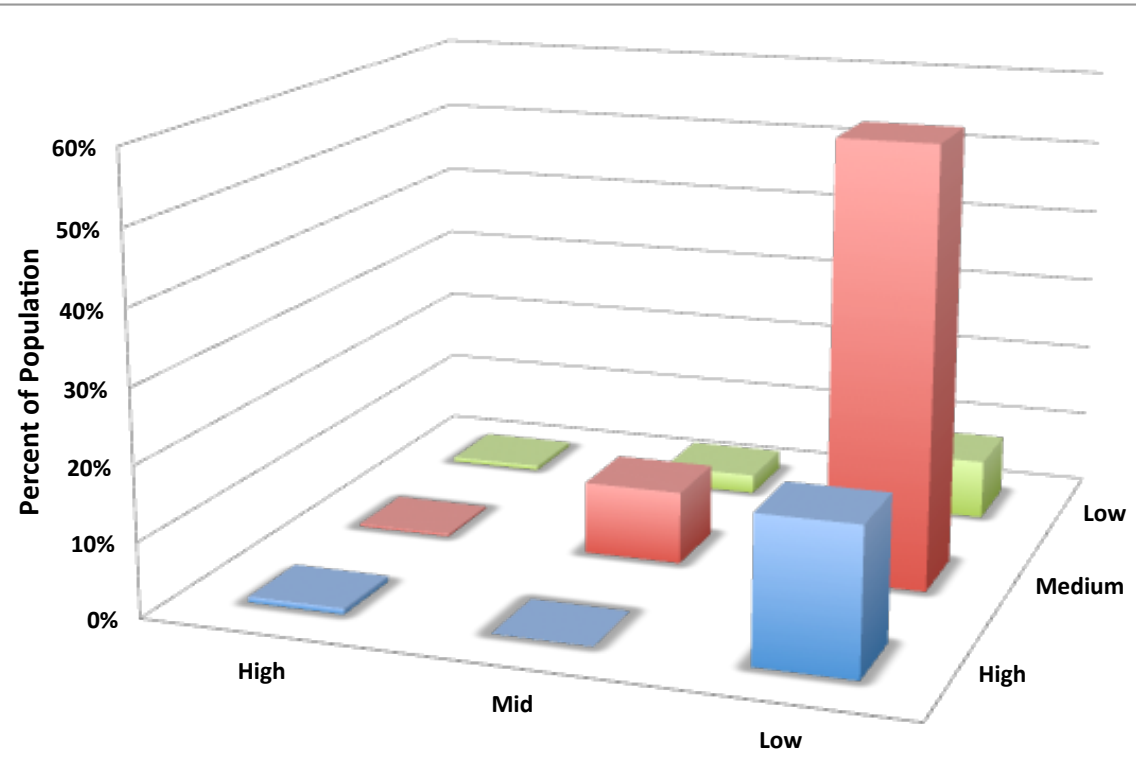
A CENTRAL CONCEPT

# Example - Country Prioritization by HIV Prevalence



A CENTRAL CONCEPT

# Target Countries with Medium HC Spending / Capita and >1% HIV

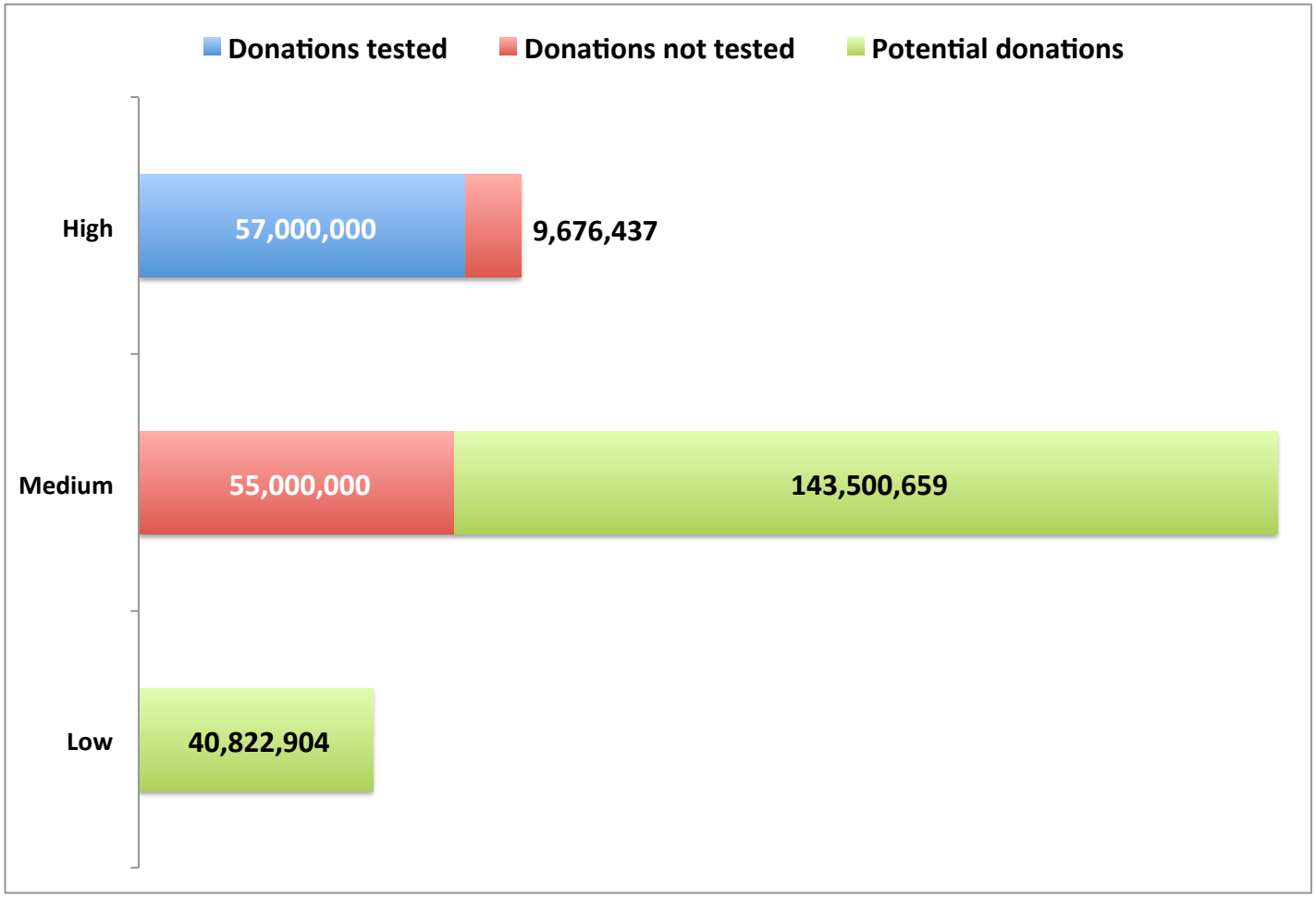



| | High | Mid | Low |
|---|---|---|---|
| High | 1% | 0% | 19% |
| Medium | 0% | 10% | 59% |
| Low | 1% | 3% | 8% |

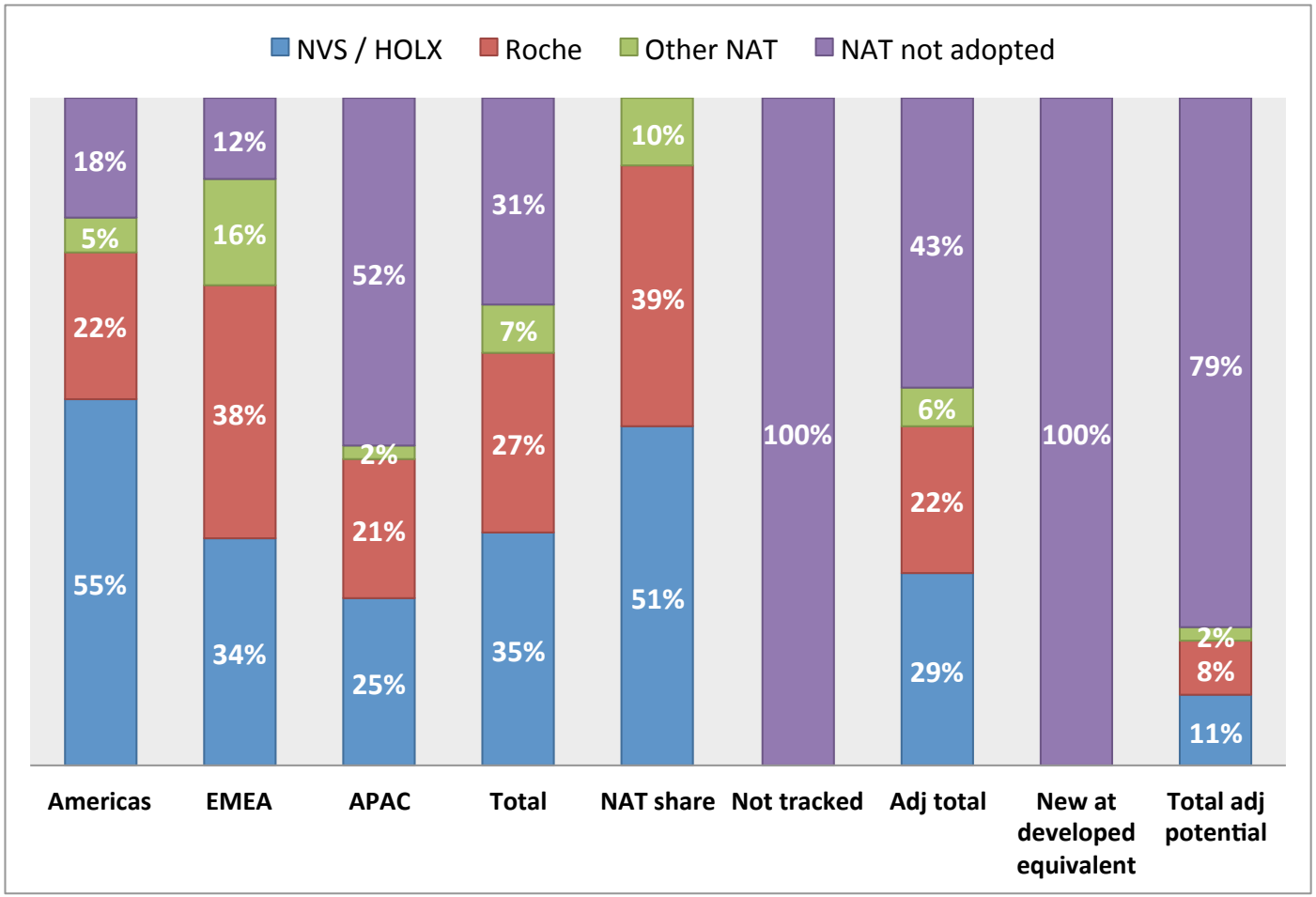
| Country | Population | HIV | HC / cap |
|---|---|---|---|
| Nigeria | 174,507,539 | 3.6% | $ 138 |
| Russia | 142,500,482 | 1.0% | $ 903 |
| Thailand | 67,448,120 | 1.3% | $ 390 |
| Tanzania | 48,261,942 | 5.6% | $ 102 |
| Ukraine | 44,573,205 | 1.1% | $ 585 |
| Sudan | 34,847,910 | 1.1% | $ 151 |
| Uganda | 34,758,809 | 6.5% | $ 126 |
| Ghana | 25,199,609 | 1.8% | $ 172 |
| Cameroon | 20,549,221 | 5.3% | $ 117 |
| Angola | 18,565,269 | 2.0% | $ 180 |
| Zambia | 14,222,233 | 13.5% | $ 100 |
| Rwanda | 12,012,589 | 2.9% | $ 147 |

Obviously other issues, such as political and regulatory considerations are also important

# Rough Donations and Testing by Healthcare Spending / Capita

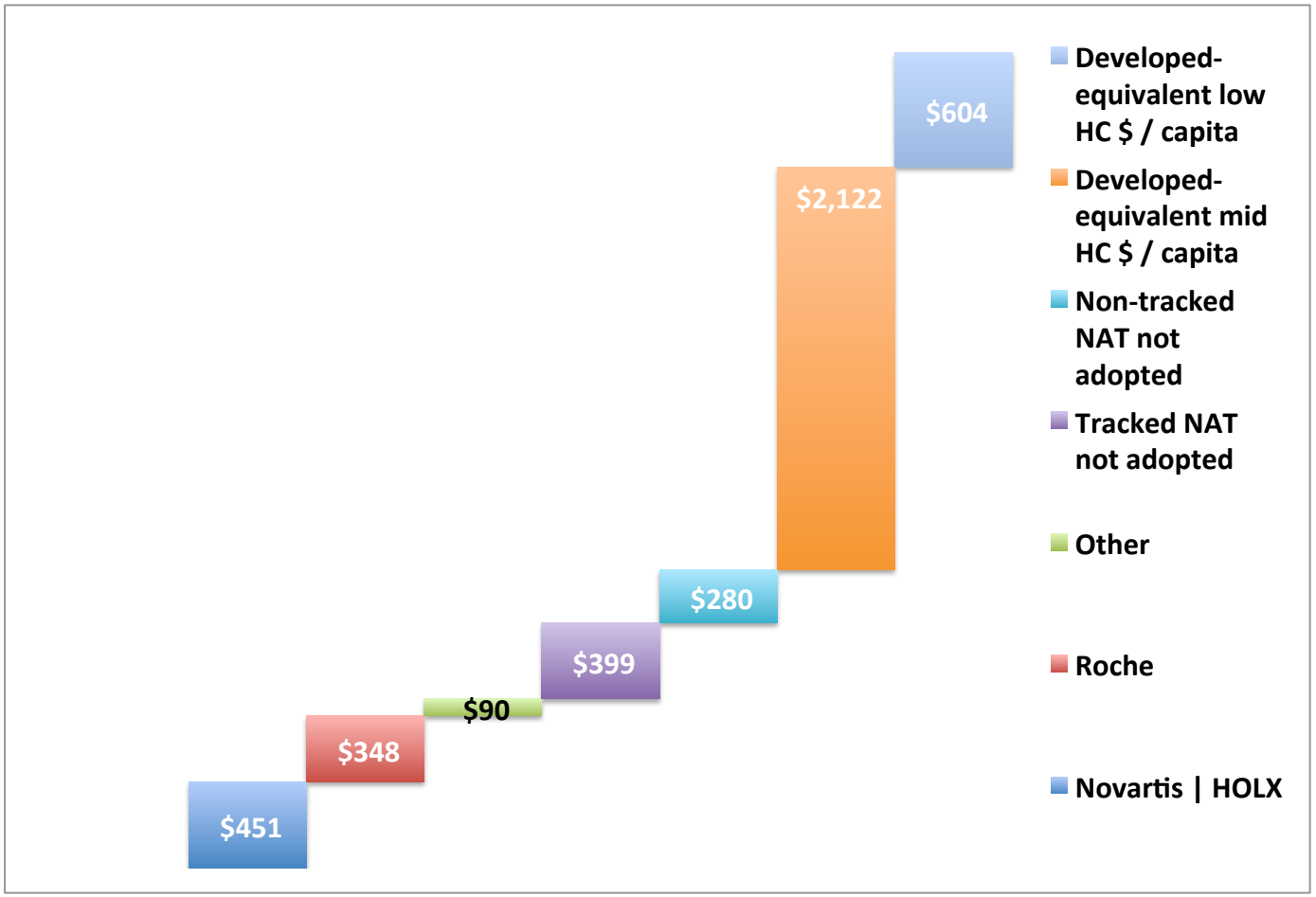


# Potential for New NAT Testing High




- Tracked: 92 million
- Not tracked: 20 million
- Potential at developed equivalent: 195 million

# NAT Potential Substantial at Current Equivalent Price of $14 per Donor



# Lever Potential Partners for POC Systems and Sales Forces

- NAT POC systems
  - Biofire
  - Cepheid
  - Nanosphere
  - Genmark
  - Great Basin
  - Meridian
  - Quidel
- Serology
  - Mainstream not Roche or Abbott
- POC Serology | IA
  - Alere
  - LRE/ Symbient / DCN consulting
  - Meridian
  - Orasure (saliva)
  - Quidel
  - Response Biomedical
- Blood processing
  - Fenwal / Fresenius
  - Haemanetics
  - Harvest

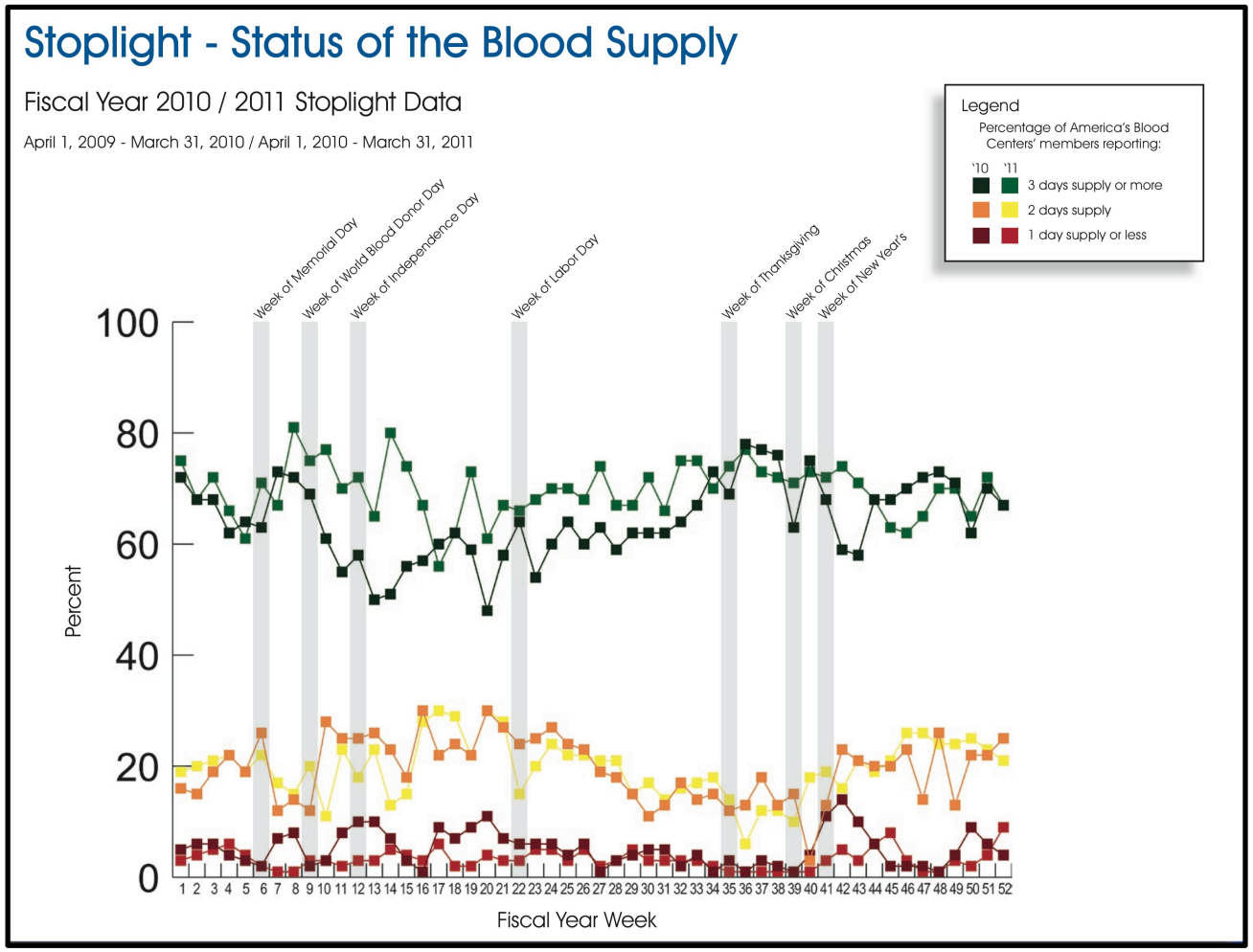
# US (DEVELOPED COUNTRIES) STILL HAS OPPORTUNITIES

# Donation in US Could still be Increased

- Donations
  - 10.8 million volunteers donate blood each year
  - 29 percent of which are first time donors
  - 17 million units of whole blood and red blood cells
- Who donates blood?
  - 38 % of the US population eligible
  - Less than 10 percent do so annually.
  - Patients scheduled for surgery may be eligible to donate blood for themselves(autologous blood donation)
- Where is blood donated?
  - Bloodmobiles
  - Community blood centers
  - Hospital-based donor centers

Source: AABB; 2009 National Blood Collection and Utilization Report

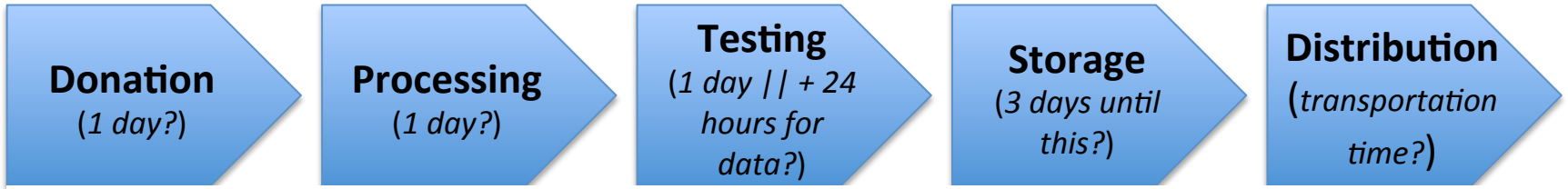
# Even Evolved Blood Donation Supply an Issue




Availability of blood in US

- Varies among regions
- Fluctuates throughout the year.
- Holidays / travel schedules, inclement weather and illness are factors
- Historically, blood collections can be low during the winter and summer months
- Guidance by FDA can eliminate, or defer donors
- Apheresis donation takes longer than whole blood
  - 1 to2 hours depending on the blood component(s) versus
  - 10 to 20 minutes

# Even Developed Process has Some Potential Left




**Donation** (*1 day?*)

- Donor registers
- Health history and mini physical
- 1 pint of blood and several small test tubes collected
- Bag, test tubes and the donor record labeled with identical bar code
- Donation stored in iced coolers until transported to a center

**Processing** (*1 day?*)

- Donated blood scanned into database, and test tubes sent for testing in parallel
- Most blood centrifuged into transfusable components – red cells, platelets, and plasma
- Primary components like plasma, can be further manufactured into components such as cryoprecipitate
- Red cells leuko-reduced
- Single donor platelets leuko-reduced and bacterially tested

**Testing** (*1 day || + 24 hours for data?*)

- Test tubes received (*one of five Red Cross National Testing Laboratories*)
- Dozen tests performed on each unit of blood – establishes blood type, and tests for infectious diseases
- Test results transferred electronically to manufacturing facility within 24 hours
- If test result positive, unit discarded and donor notified. Results confidential and shared with donor, except as required by law

**Storage** (*3 days until this?*)

- When test results received, units suitable for transfusion labeled and stored
- Red Cells stored in at 6º C up to 42 days
- Platelets stored room temperature in agitators up to 5 days (*2 days, or 5 days more?*)
- Plasma and cryo frozen and stored in freezers up to 1 year

**Distribution** (*transportation time?*)

- Blood is available to be shipped to hospitals 24 hours a day, 7 days a week

Source: US Red Cross

# Apparent Opportunity for Platelet Donation Efficiency

**Table 4-2. Outdated Components as a Percentage of the Total Number of Units of Each Type, Processed for Transfusion in 2008**

| | WB/RBCs | Whole-Blood-Derived Platelets | Apheresis Platelets | Plasma | Cryopre-cipitate | All Components |
|---|---|---|---|---|---|---|
| **Outdated Total** | 447,000* | 480,000 | 270,000 | 103,000 | 46,000 | 1,346,000 |
| **Processed/ Produced** | 17,402,000* | 1,964,000 | 2,130,000* | 5,700,000 | 1,462,000 | 28,658,000 |
| **Percent Outdated** | 2.6% | 24.4% | 12.7%* | 1.8% | 3.1% | 4.7% |

*Numbers reported as processed or produced by an institution; this may differ from the number reported as collected, but not significantly.

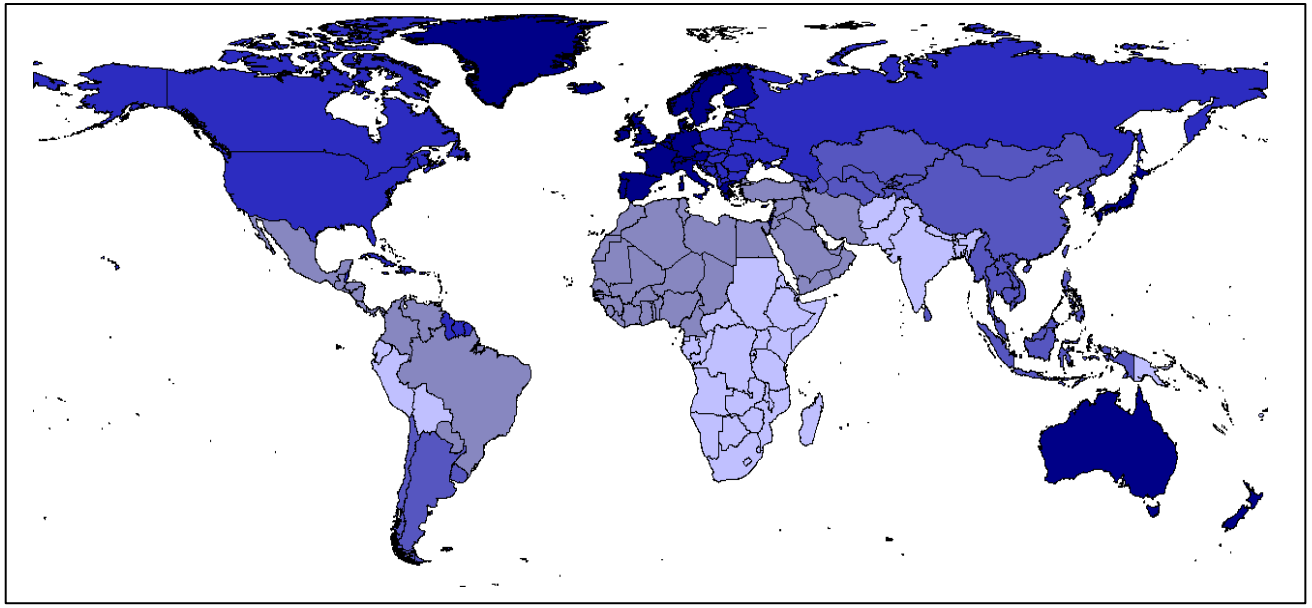
Source: 2009 National Blood Collection and Utilization Survey Report

# TEST MENU

# Screening Test Panel Should be Set by Risk and Region

- NAT for HIV-1, HCV, and WNV
- NAT for HBV,HAV, HEV, dengue fever (e.g., India, Latin American and Africa), and parvo virus
- Other regional NAT and serology
- Hepatitis B surface antigen (HBsAg) / core antibody (anti-HBc)
- Hepatitis C virus antibody (anti-HCV)
- HIV-1 and HIV-2 antibody (anti-HIV-1 and anti-HIV-2)
- HTLV-I and HTLV-II antibody (anti-HTLV-I and anti-HTLV-II)
- Anti-CMV
- Serologic test for syphilis
- Antibody test for Trypanosoma cruzi (Chagas' disease)

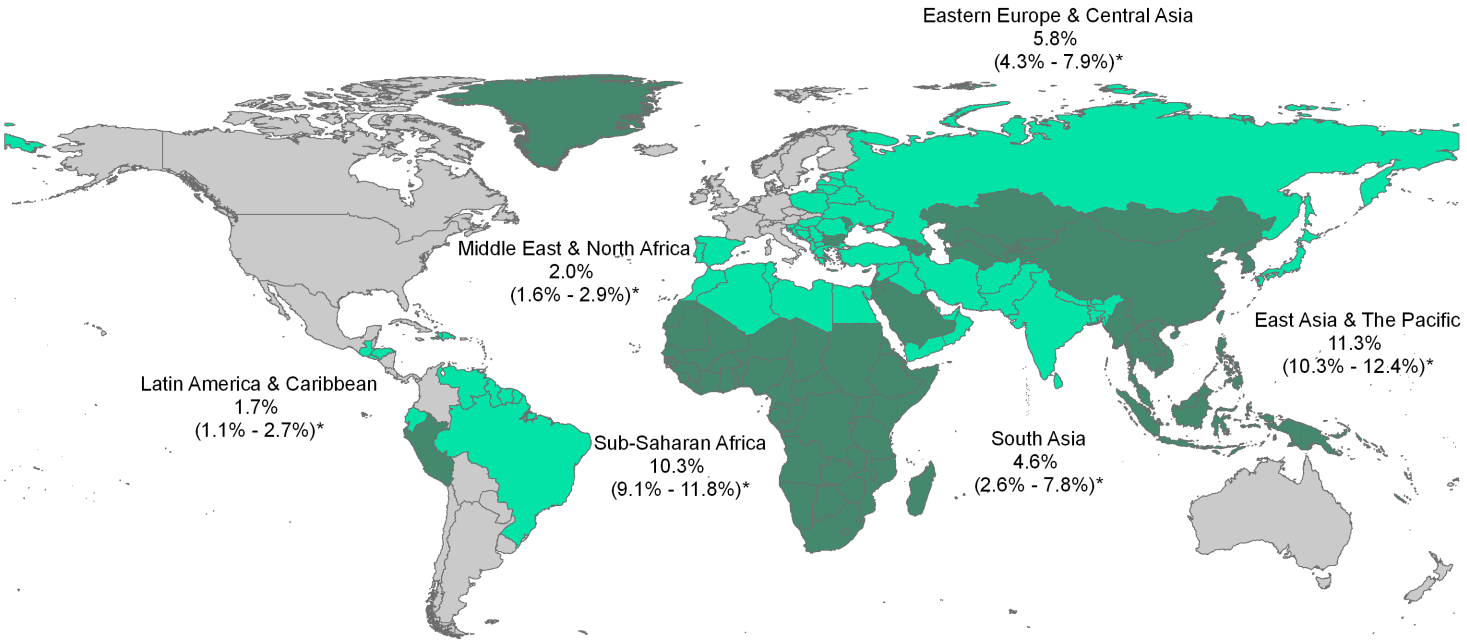
# Example - WHO Estimate of Adult HAV Prevalence



Darker shades indicate a greater proportion of at-risk adults.

| | Region | *Population Seroprevalence* | | *Data Sources* (adjusted for the total number of countries in region) | |
|---|---|---|---|---|---|
| | | Child Immunity Rate | Adult Susceptibility Rate | Total Articles Available | Recent Articles Available |
| 1 | High income Asia Pacific | Low | High | ▲▲▲ | ▲ |
| 2 | Central Asia | Medium | Low-Medium | ▽▽ | ▽▽ |
| 3 | East Asia | Low-Medium | Low-Medium | ▲▲▲ | ▲ |
| 4 | South Asia | High-Medium | Very Low | ▲▲▲ | ▲ |
| 5 | Southeast Asia | Low-Medium | Low-Medium | ▲ | ▽▽ |
| 6 | Australasia | Low | High | ▲▲ | ▲ |
| 7 | Caribbean | Low-Medium | Medium | ▽▽ | ▽▽ |
| 8 | Central Europe | Low-Medium | Medium | ▲ | ▲ |
| 9 | Eastern Europe | Low-Medium | Medium | ▲ | ▽▽ |
| 10 | Western Europe | Low | High | ▲▲▲ | ▲ |
| 11 | Andean Latin America | High-Medium | Very Low | ▲ | ▽▽ |
| 12 | Central Latin America | High-Medium | Low | ▽ | ▽▽ |
| 13 | Southern Latin America | Medium | Low-Medium | ▲▲ | ▲ |
| 14 | Tropical Latin America | Medium | Low | ▲▲▲ | ▲▲▲ |
| 15 | North Africa / Middle East | Medium | Low | ▲▲ | ▲ |
| 16 | High income North America | Low | Medium | ▲▲▲ | ▲▲▲ |
| 17 | Oceania | Medium | Very Low | ▽▽ | ▽▽▽ |
| 18 | Central sub-Saharan Africa | High | Very Low | ▽▽ | ▽▽▽ |
| 19 | East sub-Saharan Africa | High | Very Low | ▽▽ | ▽▽ |
| 20 | South sub-Saharan Africa | High | Very Low | ▽ | ▽▽ |
| 21 | West sub-Saharan Africa | High-Medium | Low | ▽▽ | ▽▽▽ |

# Example – PLoS Estimate of Adult HBV Prevalence (note contrast with HAV)

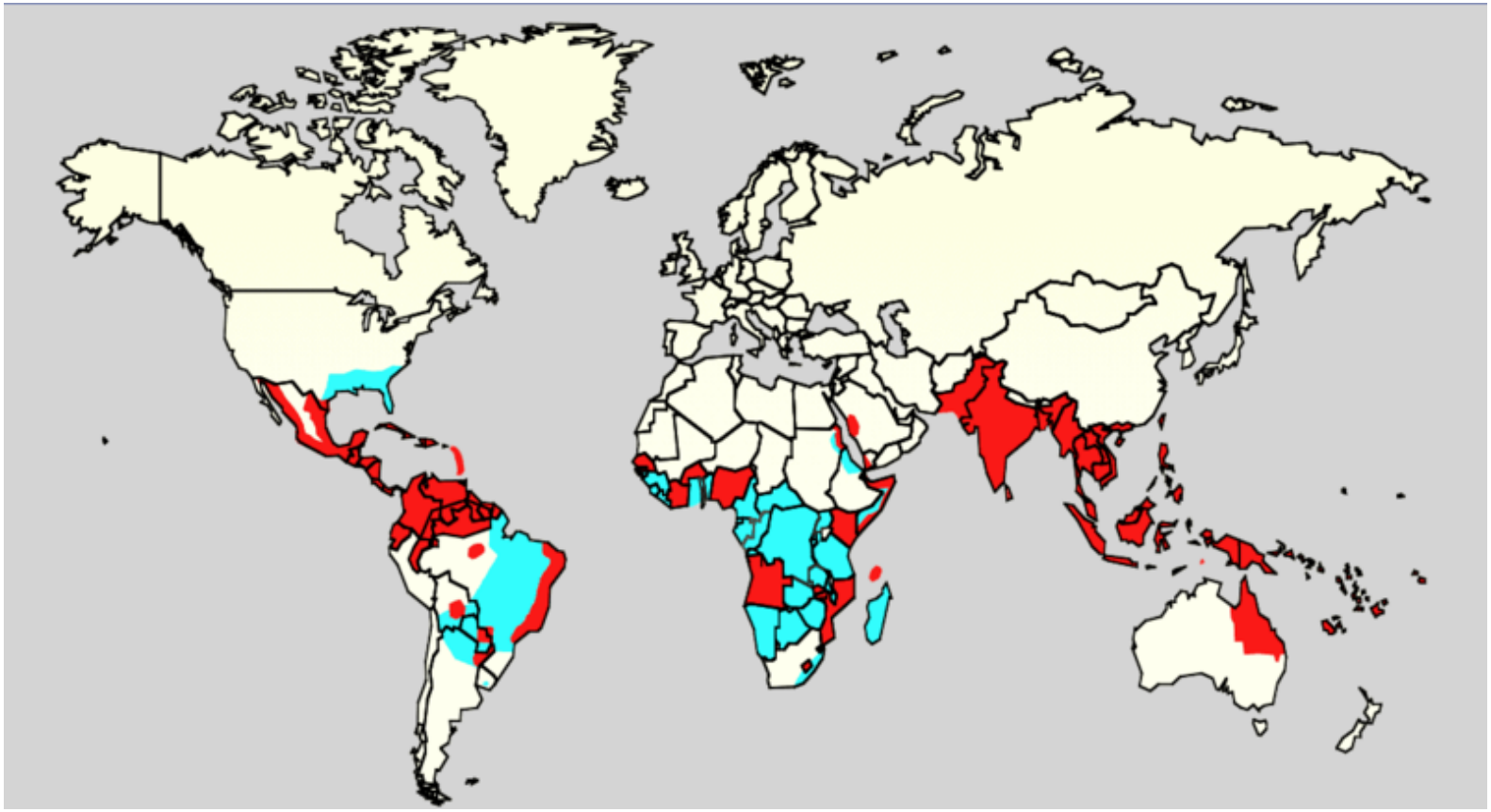



**Global Categories of Chronic Hepatitis B Endemicity**

- Low < 2% (Latin America & Caribbean and Middle East & North Africa)
- Intermediate 2% - 7% (Eastern Europe & Central Asia and South Asia)
- High ≥ 8% (Sub-Saharan Africa and East Asia)

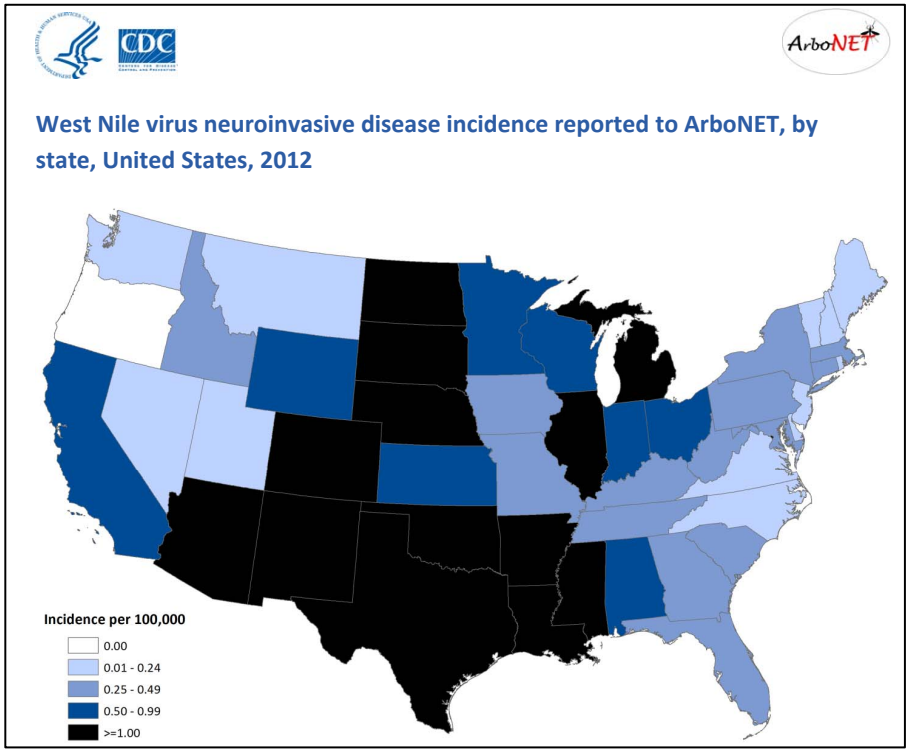
* Estimates from our random-effects meta-analysis (95% Confidence Interval)

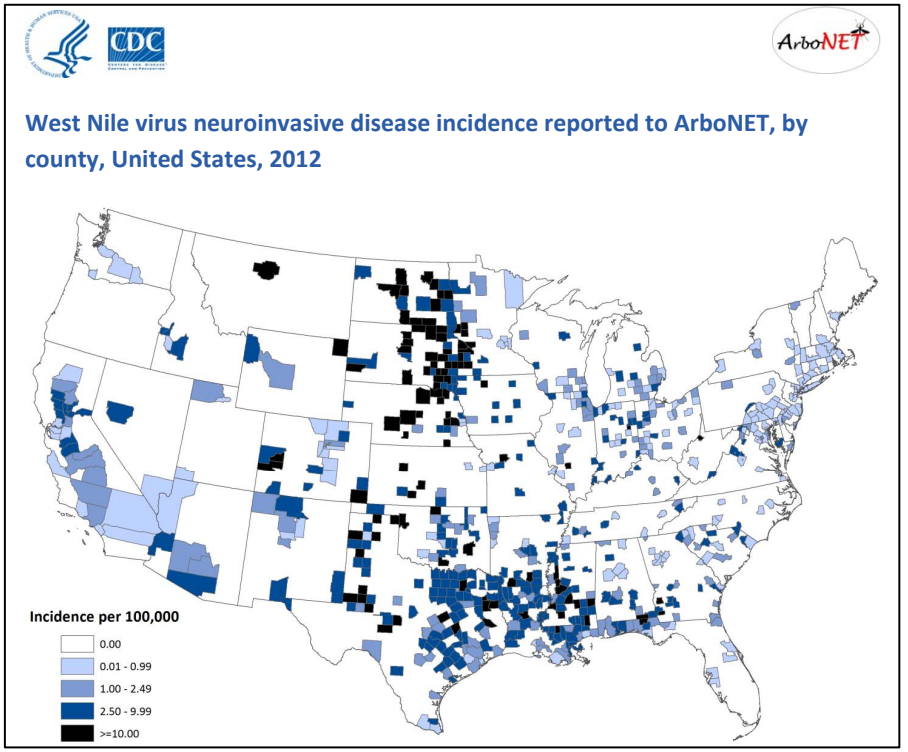
# Dengue Fever Incidence Varies Widely, Affecting NPV from History and Testing



Dengue distribution in 2006.
Red: Epidemic dengue and A. aegypti
Aqua: Just A. aegypti

# West Nile Incidence Varies Widely, Affecting NPV from History and Testing



# Neglected Parasitic Infections include

- Top 5
  - Chagas Disease
  - Cysticercosis
  - Toxocariasis
  - Toxoplasmosis
  - Trichomoniasis
- Other
  - Babesiosis
  - Malaria
  - African trypanosomiasis
  - Leishmaniasis

# Neglected Tropical Diseases (NTDs)

- Buruli ulcer
- Chagas disease
- Cysticercosis
- Dengue fever
- Dracunculiasis (Guinea Worm Disease)*
- Echinococcosis
- Fascioliasis
- Human African Trypanosomiasis (African Sleeping Sickness)
- Leishmaniasis
- Leprosy (Hansen's disease)
- Lymphatic filariasis*
- Onchocerciasis*
- Rabies
- Schistosomiasis*
- Soil-transmitted Helminths (STH) (Ascaris, hookworm, and whipworm)*
- Trachoma*
- Yaws

# Clinical need beyond blood banking to identify patients with Chagas

- CDC estimates 300,000 or more Trypanosoma cruzi-infected individuals of Hispanic origin currently live in the United States.
- Since blood donor screening began, the number of requests to CDC for consultation and drug release for Chagas disease has increased markedly
- Only approximately 11% of Chagas seropositive blood donors have contacted CDC for consultation regarding treatment.
- Chagas disease is endemic throughout much of Mexico, Central America, and South America, where an estimated 8–11 million persons are infected

# Dengue Fever – High Burden and Need for both NA and IA Tests

Burden

- Mortality is 1–5% without treatment, and < 1% with treatment
- Severe disease carries mortality of 26%
- Dengue endemic in > 110 countries
- Infects 400 million people worldwide annually, with 100 million manifesting disease
- Leads to ½ million hospitalizations, and 25,000 deaths.

Testing

- PCR and viral antigen detection more accurate in the first seven days, but only of diagnostic value during this acute phase
- Tests for dengue antibodies, can be useful in confirming a diagnosis in later stages of infection.
  - IgM
    - In a person with symptoms, is considered diagnostic.
    - Becomes undetectable 30–90 days after a primary infection, but earlier following re-infections.
  - IgG
    - Is a useful indicator of past infection.
    - After primary infection, reaches peak levels in blood after 14–21 days.
    - In re-infections, peaks earlier and titres usually higher.
    - Detection alone is not considered diagnostic unless blood samples collected 14 days apart, and greater than 4x increase in levels.
  - Test for IgG and IgM can cross-react with other flaviviruses, and may result in a false positive after recent infections or vaccinations with yellow fever virus or Japanese encephalitis.

## Table 3. Priority Needs for Enhanced Surveillance, Treatment, and Prevention Efforts for the High Priority Neglected Infections of Poverty.

| Disease Category | Disease | Expanded Active Surveillance and Treatment | Newborn Screening and Treatment | Epidemiological Transmission Studies | New Diagnostics | New Drugs | New Vaccines |
|---|---|---|---|---|---|---|---|
| **Helminth Infections** | Ascariasis | + | | + | | | |
| | Toxocariasis | + | | + | + | | |
| | Strongyloidiasis | + | | + | + | | |
| | Cysticercosis | + | | + | + | + | |
| **Protozoan Infections** | Giardiasis | + | | | | | |
| | Cryptosporidiosis | + | | + | | + | |
| | Trichomoniasis | + | | | | | |
| | Chagas disease | + | + | + | + | + | + |
| | Leishmaniasis | + | | + | + | + | |
| | Congenital toxoplasmosis | + | + | + | + | + | + |
| **Bacterial Infections** | Congenital syphilis | | + | + | | | |
| | Brucellosis | + | | + | | | |
| | Bovine tuberculosis | + | | + | | | |
| | Trench fever | + | | + | | | |
| | Leptospirosis | + | | + | | | |
| **Viral Infections** | Dengue fever | + | | + | | + | + |
| | Congenital CMV | + | + | + | | + | + |

doi:10.1371/journal.pntd.0000256.t003

Hotez PJ (2008) Neglected Infections of Poverty in the United States of America. PLoS Negl Trop Dis 2(6): e256. doi:10.1371/journal.pntd.0000256
http://www.plosntd.org/article/info:doi/10.1371/journal.pntd.0000256

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