Malaria R&D in a time of global partnerships

David Reddy PhD, CEO MMV

Defeating Malaria Together

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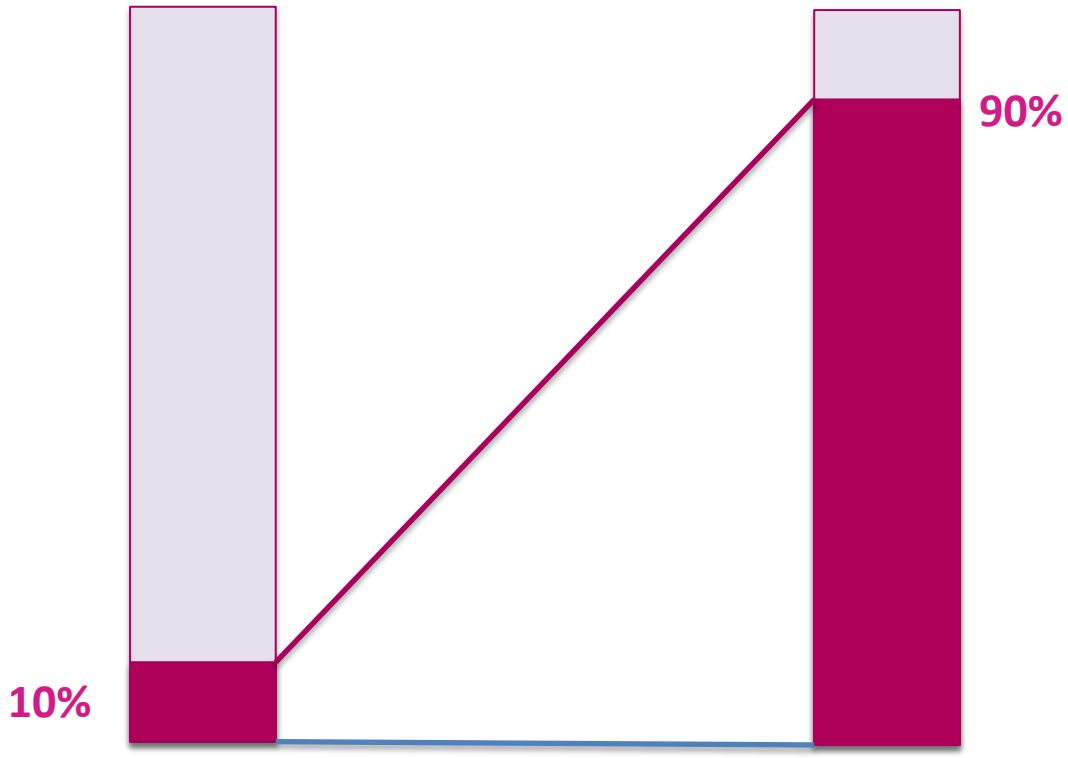
Medicines for Malaria Venture

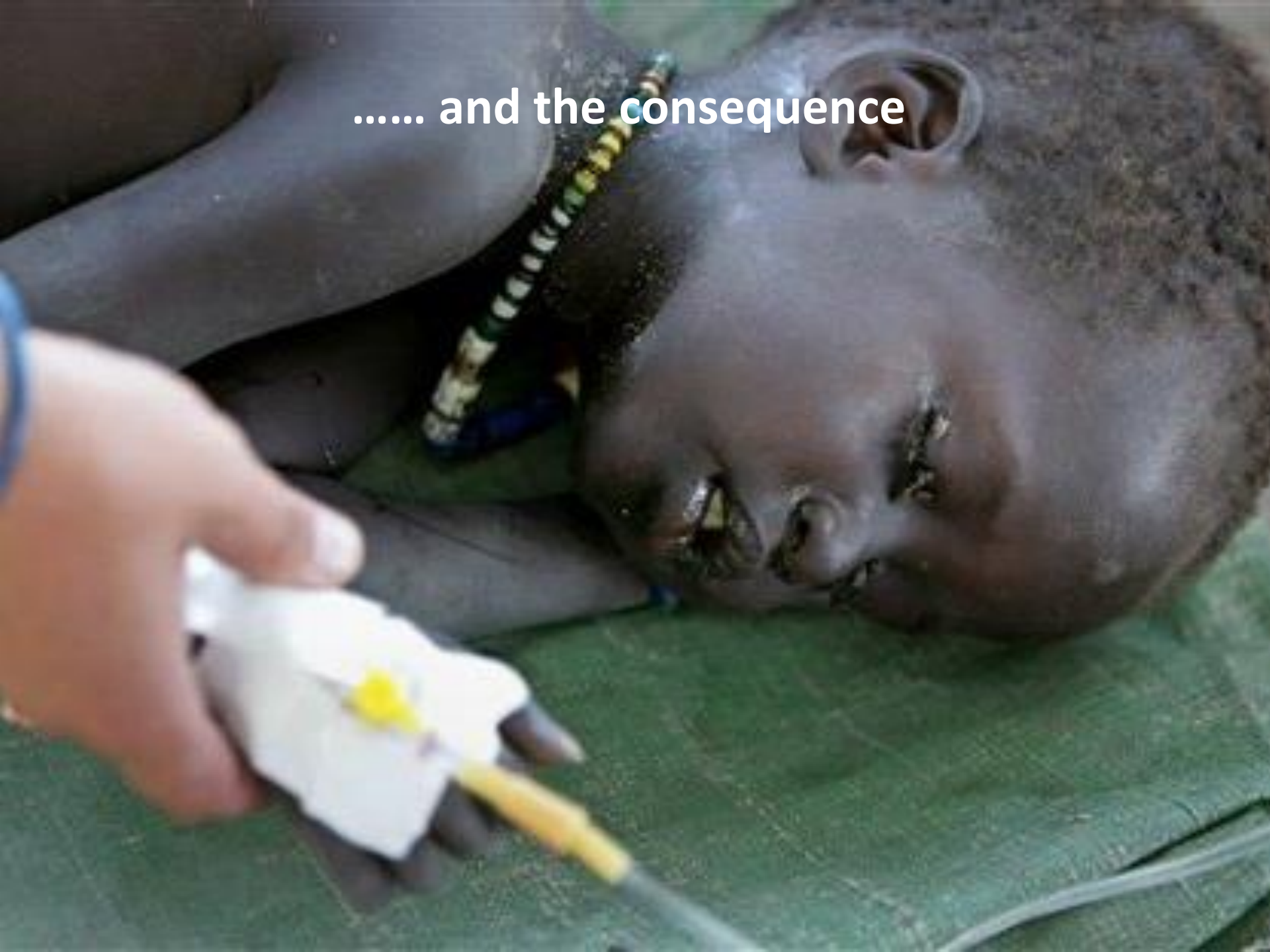
Here's the issue

10/90 gap: the fatal imbalance



Fatal Imbalance – a crisis in R&D – MSF report

http://www.msfaccess.org/sites/default/files/MSF_assets/NegDis/Docs/NEGDIS_report_FatalImbalance_CrisisInR&D_ENG_2001.pdf


…… and the consequence

EAS 2014 – 18 Leaders
55% of the global population

« We welcomed the Asia Pacific Leaders Malaria Alliance (APLMA) Task Force Progress Report 2014 and agreed to the goal of an ASIA PACIFIC FREE OF MALARIA BY 2030.

We tasked the APLMA co-chairs to submit to the 10th EAS in Malaysia a PLAN FOR ARCHIEVING THIS GOAL and to implement the recommendations of the APLMA Task Forces. »

ASIA PACIFIC LEADERS MALARIA ALLIANCE

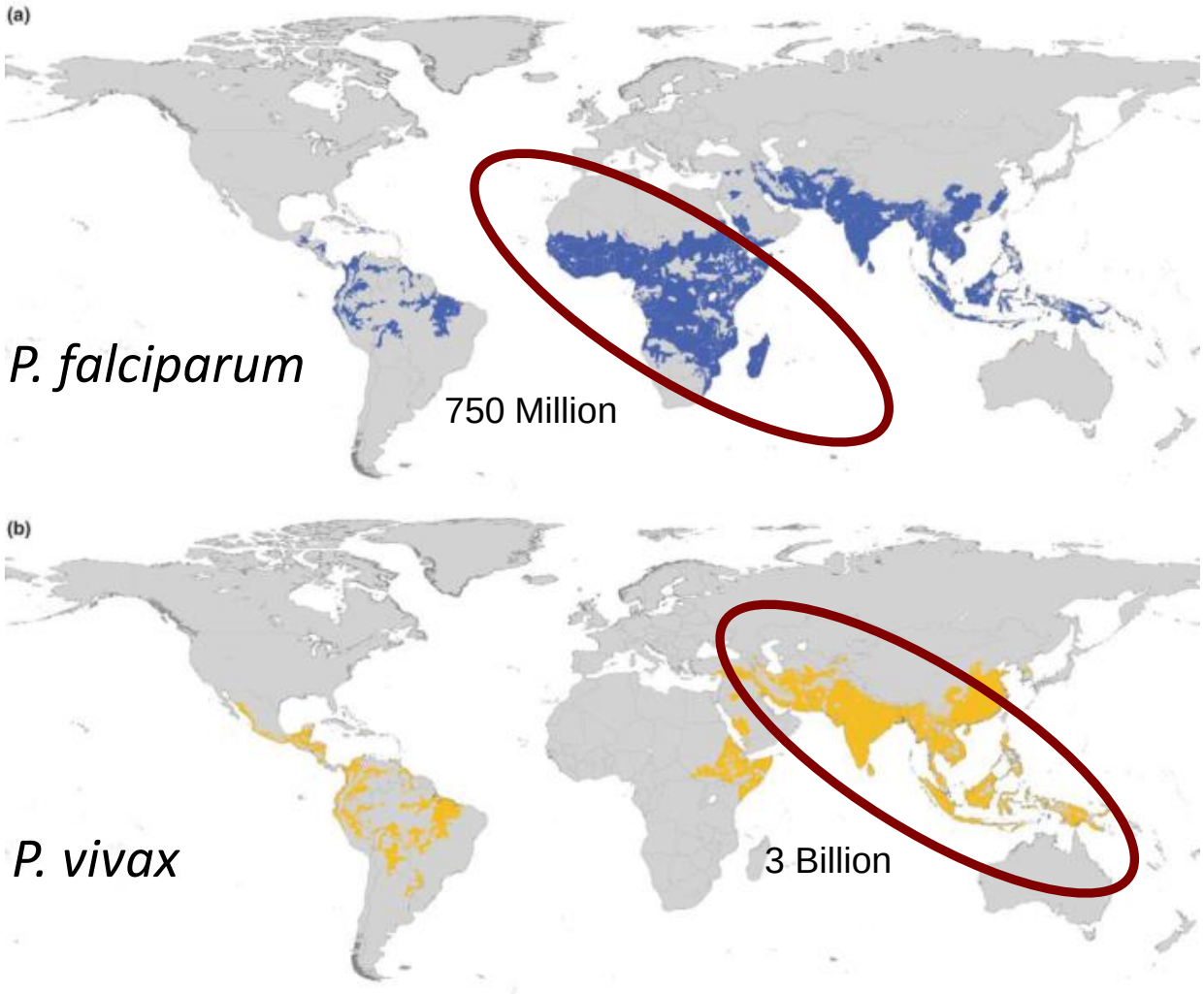
Malaria burden

90% reduction from 2015 levels by 2030

15% year on year reduction in mortality

Compares with 4% year on year currently

Malaria burden



45% of all malaria is in SEARO (India / Indonesia)

50% due to *P. vivax*

map malaria atlas project

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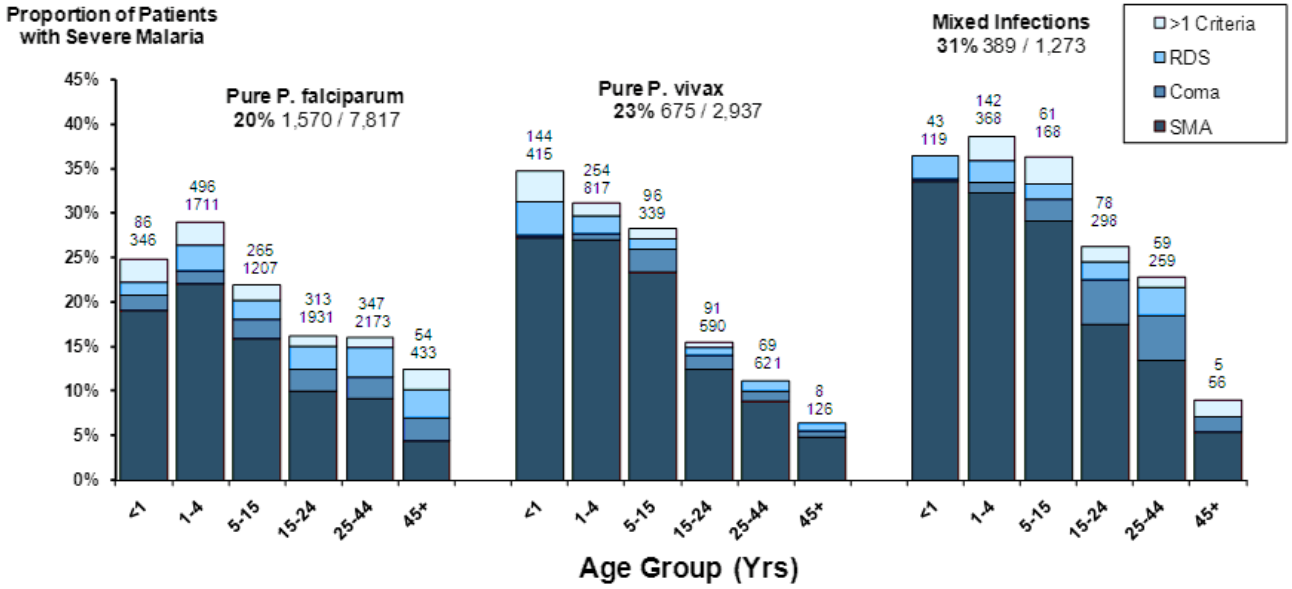
Severe and fatal *P. vivax* malaria

OPEN ACCESS Freely available online

PLOS MEDICINE

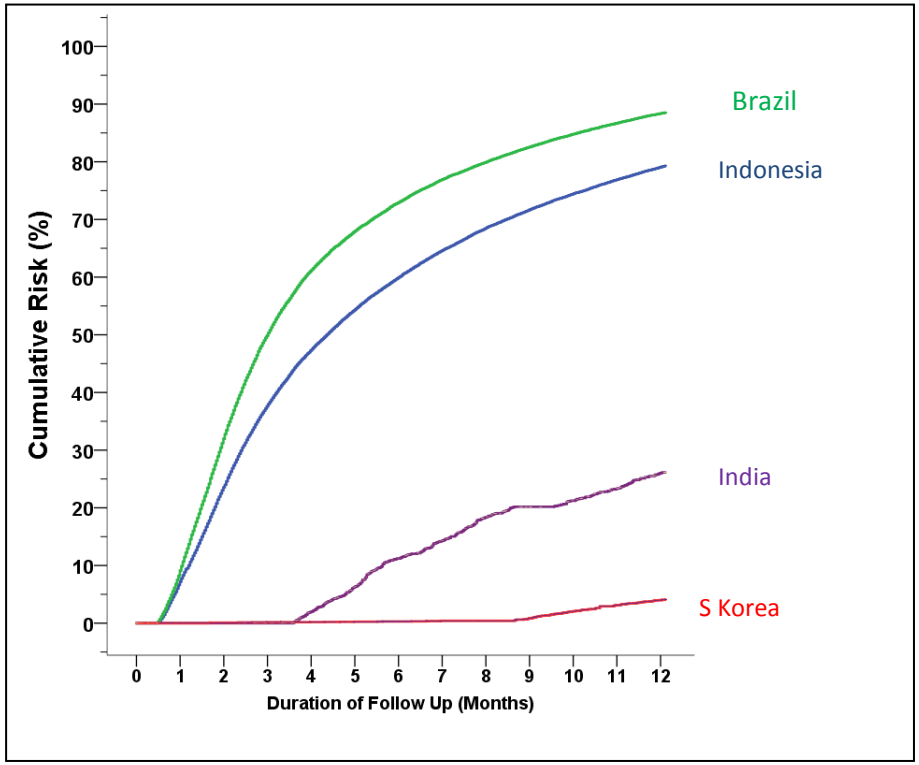
Multidrug-Resistant *Plasmodium vivax* Associated with Severe and Fatal Malaria: A Prospective Study in Papua, Indonesia

Emiliana Tjitra[1], Nicholas M. Anstey[2], Paulus Sugiarto[3], Noah Warikar[4,5], Enny Kenangalem[4,6], Muhammad Karyana[1], Daniel A. Lampah[4,6], Ric N. Price[2,7*]



The predominent morbidity and mortality of *P. vivax* is related to its propensity to recur

Risk of recurrence



Clinical disease, anaemia, coinfections/sepsis, miscarriage, stunting, malnutrition, late mortality, increased transmission…

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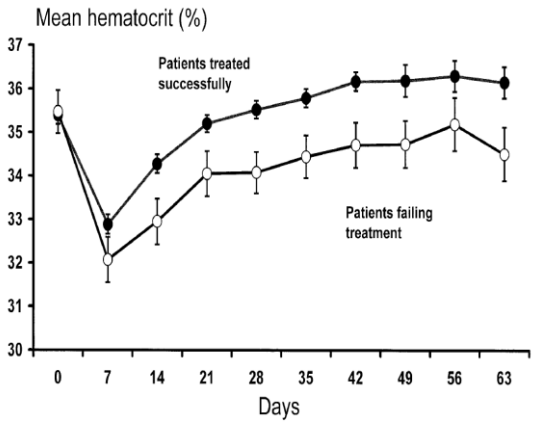
Recurrent malaria and anaemia

P. falciparum clinical Trials

SMRU Thailand

N= 4,007

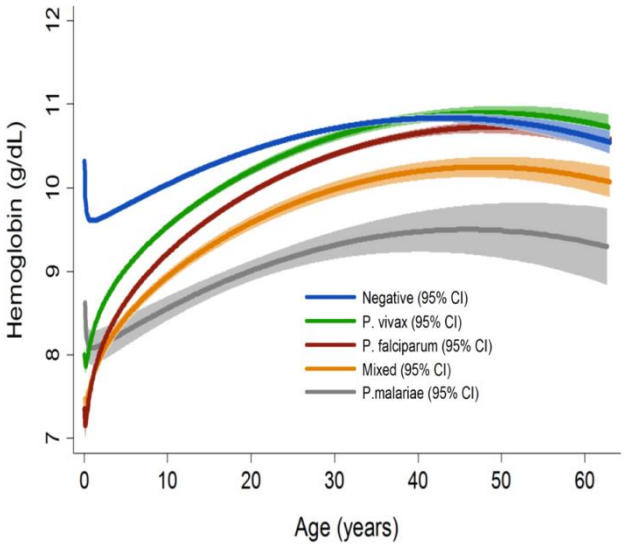


Price et al AJTMH 2001

Anaemia age relationship

Papua, Indonesia

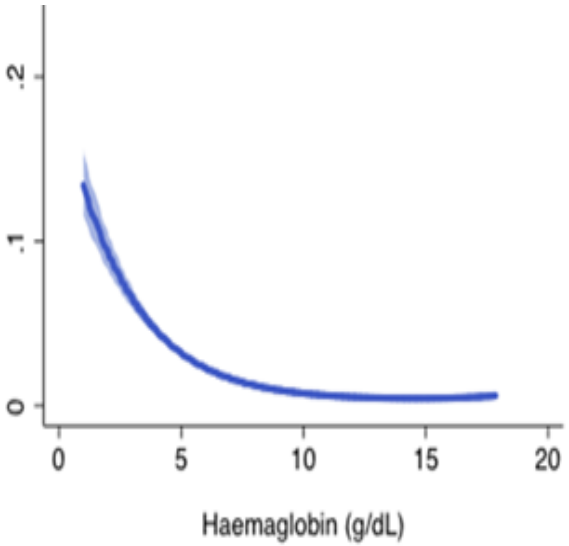
N= 219,845



Douglas et al PLoS Med 2013

Anaemia and risk of mortality

1.3% 2,781 / 219,845

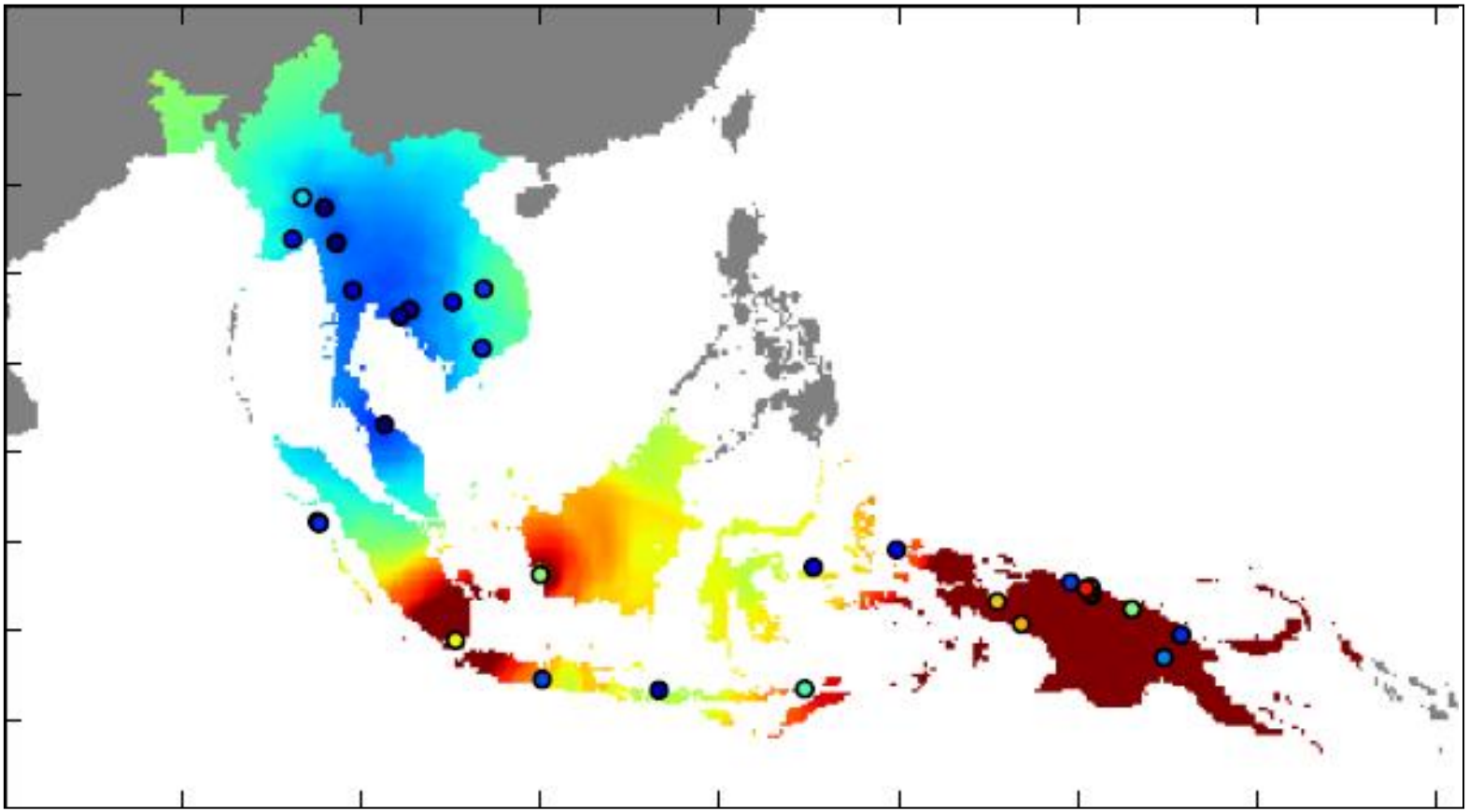


Risk of death = $1/(1+\exp(-(-1.44-0.4146*hb+0.0006*hb^3)))$

Douglas et al PLoS Med 2013

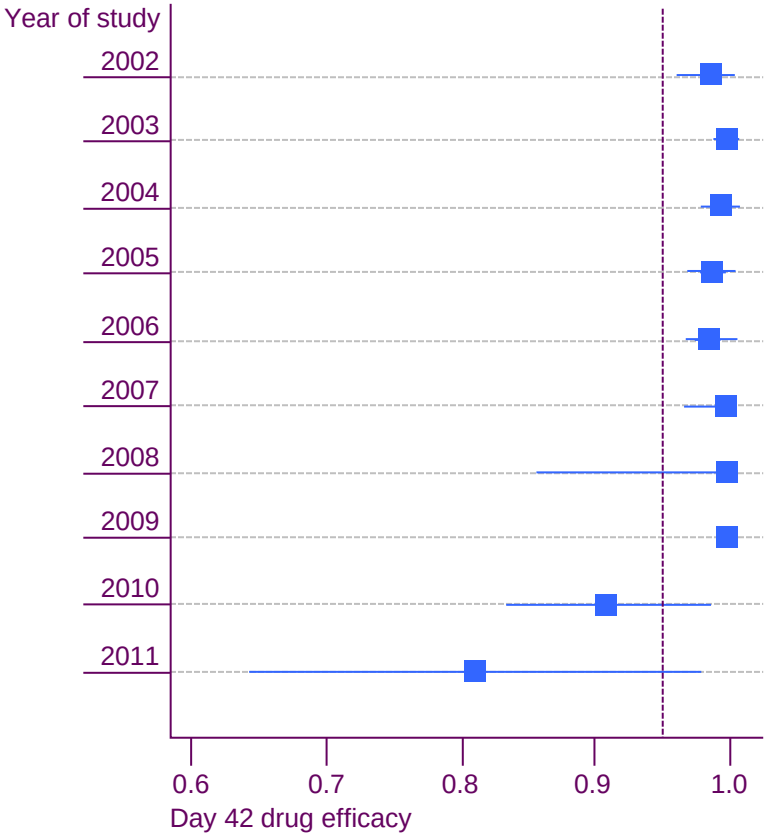
Emerging drug resistance: *Pf* and *Pv*

CQ resistant P. vivax

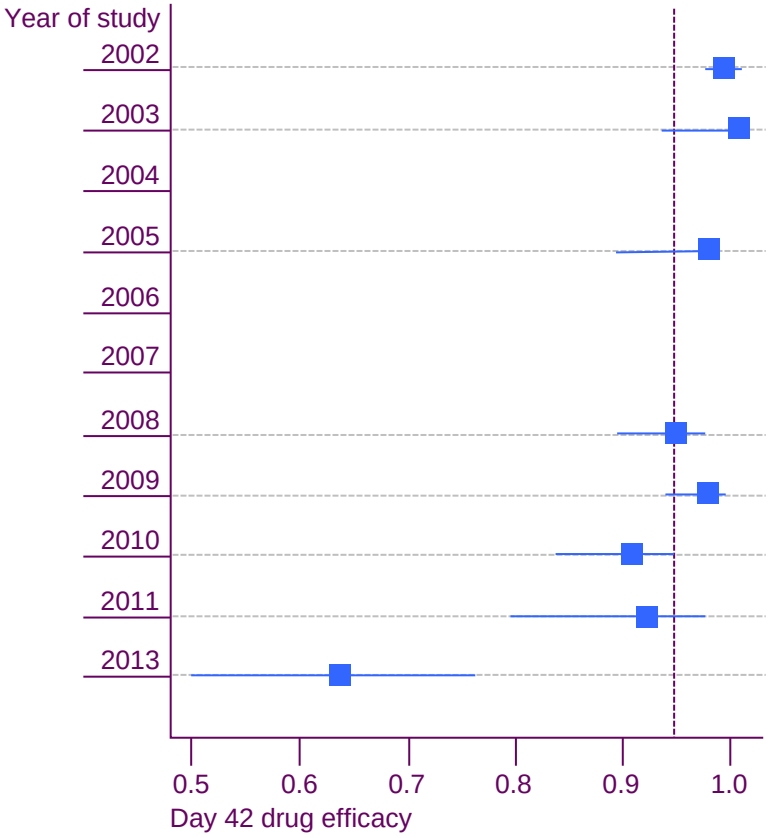


Clinical efficacy of DHA-piperaquine

DHA+PQP in rest of Asia



DHA+PQP in Cambodia



 Courtesy of WWARN 2015

MMV

Reducing the burden of malaria in disease-endemic countries, by DISCOVERING, DEVELOPING & DELIVERING new, effective and affordable antimalarial drugs

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Operating model

Syndicated investment
Governments, philanthropic

Global partnership
Funders, industry, academia, NMCPs, UN agencies, CROs

Virtual drug pipeline
R&D and portfolio management

Independent expert scientific review
Supports clinical candidate selection and stage-gating

Strong contractual framework
Increases access and good governance

Creating value for patients, partners & funders

evaluating our contribution through 6 lenses

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Value through competencies

Integrating malaria drug R&D

- R&D / malaria strategy
- Strong contractual framework
- Effective resource allocation
- Cost containment
- Staged financing & milestones
- Syndication of investment
- Portfolio management
- Controlling & reporting

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Value through competencies

Applying accumulated knowledge

30 R&D scientists and physicians

464 years R&D experience

414 years Pharma experience

172 years malaria experience

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Value through competencies

Coordinating a broad malaria medicine R&D network

130 active partners including 28 Pharma and 13 Biotech companies

47 countries

60% of global malaria development projects

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Value through competencies

Forging an integrated global effort

- 28 pharmaceuticals companies
- 13 biotech companies
- 56 universities
- 38 research institutes
- 72 clinical sites
- 50 government agencies

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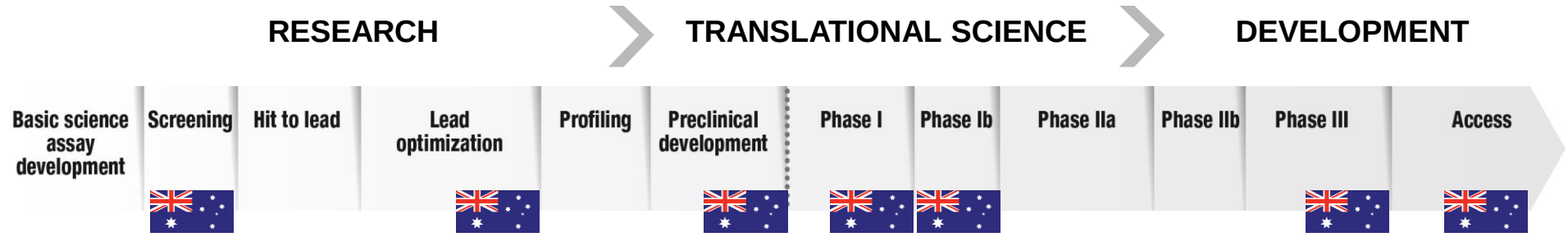
MMV / Australia R&D Continuum



e.g. Eskitis
- Blood stage
- Gametocytes stages

e.g. CDCO, Monash University
- Pharmacokinectics

e.g. Menzies
- Clinical isolates

e.g. QIMR/QPharm
- FIH, human blood-stage challenge model, transmission blocking

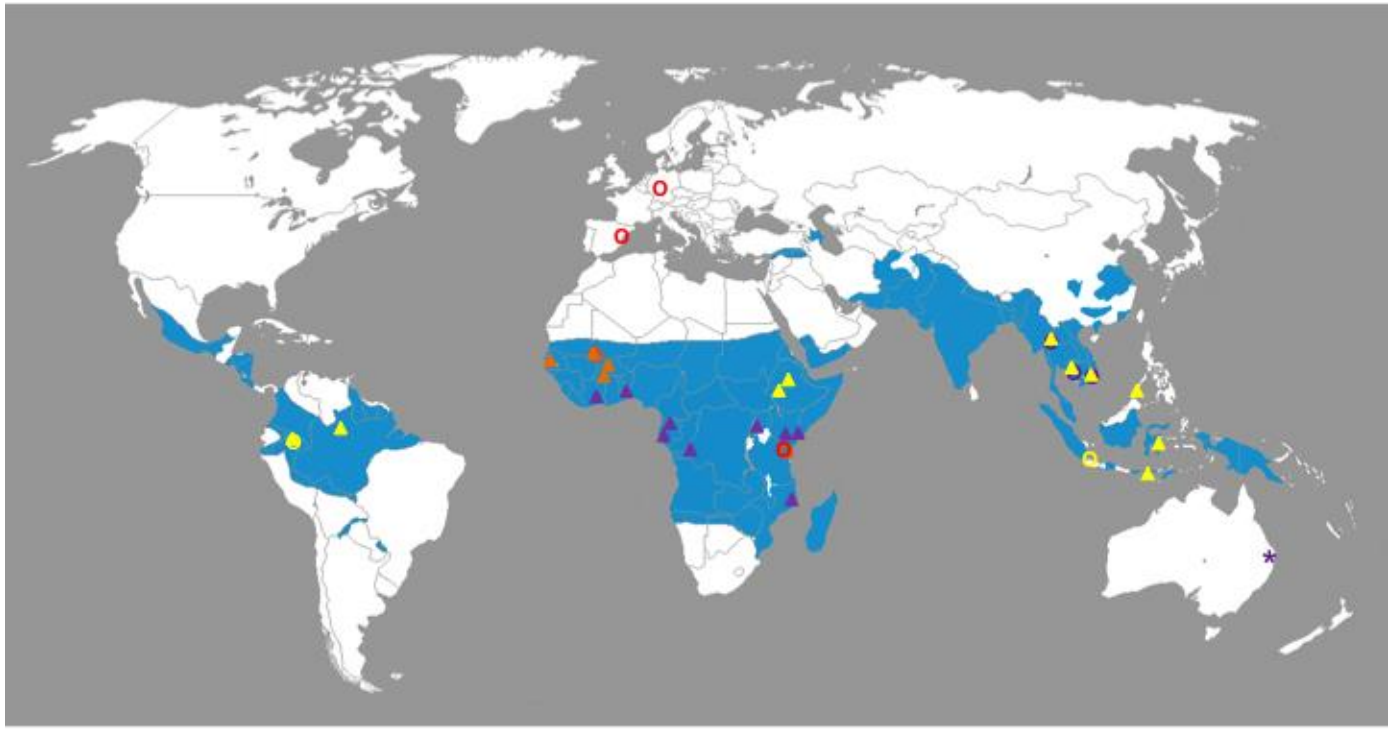
e.g. Australian
- Army Research Institute

e.g. Newcrest Mining, Oil Search

e.g. d3 Medicine
- Strategic planning
- Translational science

WEHI
Burnett Institute
PNG IMR
APMEN

Clinical trial sites



TCP1/TCP2: blood-stage

- ✱ Human *Pf* infected blood challenge
- ▲ PoC study sites
- O Phase III study sites

TCP3a: relapse prevention

- O PoC study sites
- ▲ Phase III study sites

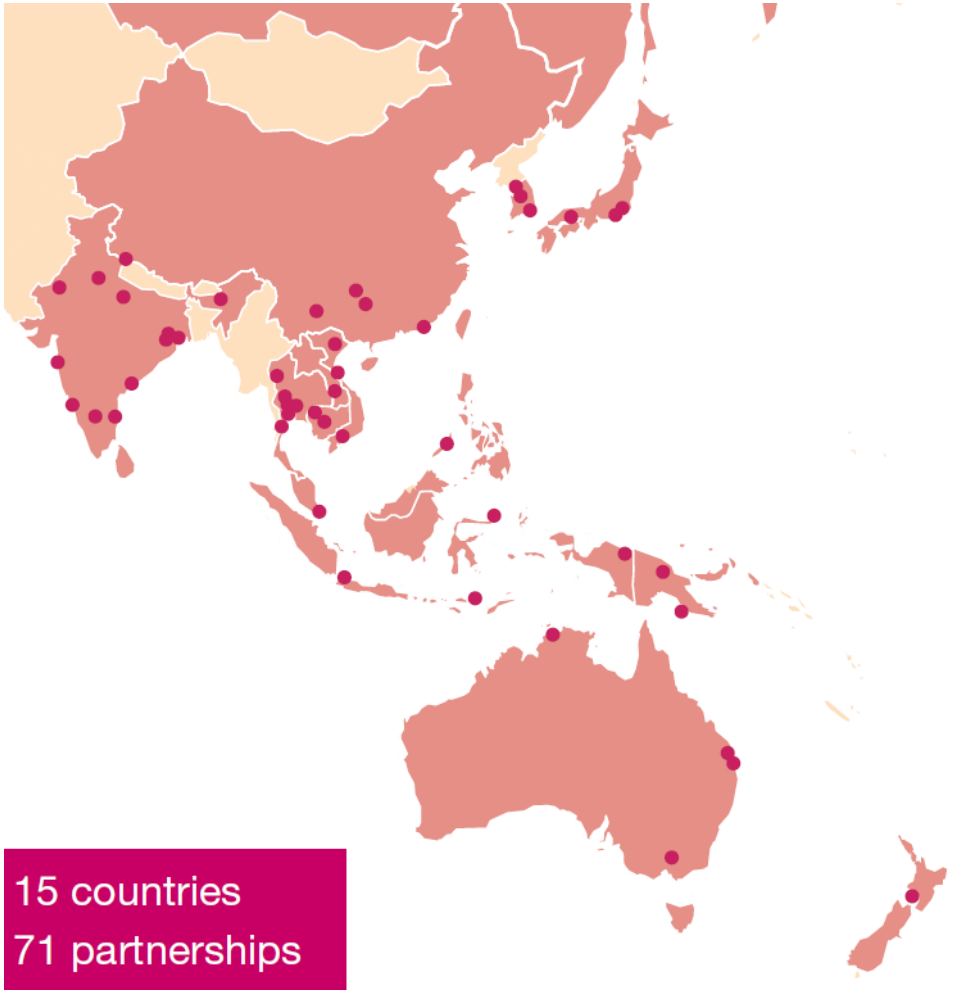
TCP3b: transmission blocking

- O PoC study sites
- ▲ Phase III study sites

TCP4: chemoprotection

- O PoC study sites

Broad regional network of partners



Value through competencies

Experience in drug registration processes

- EU orphan drug status
- EU article 58
- Swissmedic
- US FDA
- WHO pre-qualification
- National registrations

Value through competencies

Ensuring governance & compliance

Board of Directors

WHO, UN, donors, endemic countries, academia, public health, ex-Pharma

Advisory Committees

ESAC and APMAC: international experts in drug discovery, development, registration, manufacturing, commercialization, program implementation and public health

Financial Compliance

Swiss GAAP compliant – annual audit by KPMG.
Specific NIH, UNITAID, USAID, DFAT, Norad audits
5 GCP audits, 2 GMP audits, 1 Good Distribution Practice audit

Value through innovation

Validating new targets and discovering new molecules

Molecules targeting each step of malaria parasite lifecycle

21 new series and **12** novel candidates

compounds against **6** novel targets in the parasite lifecycle

origin of molecules split equally between industry & academia

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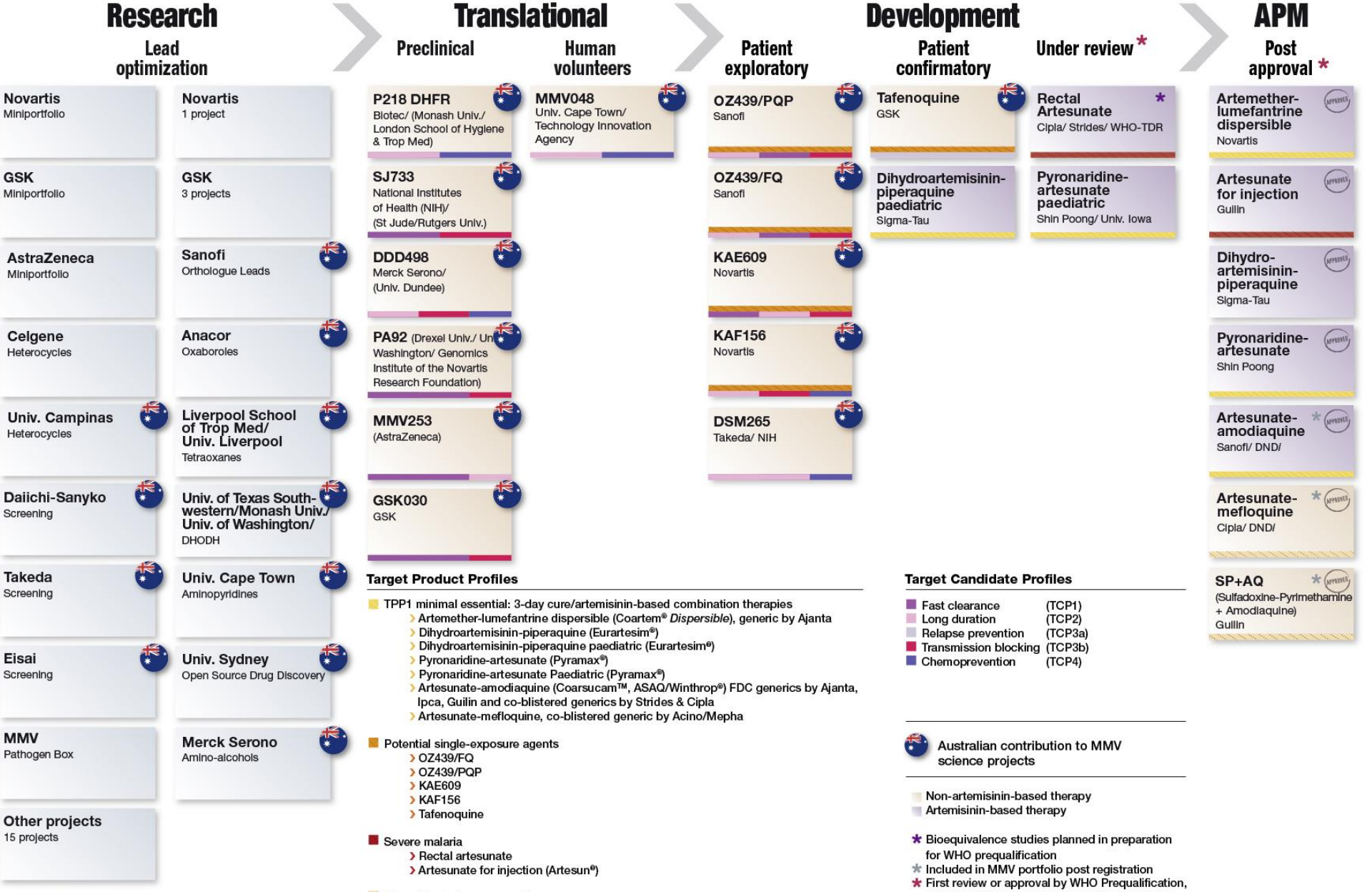
Research
Lead optimization
Novartis
Miniportfolio
GSK
Miniportfolio
AstraZeneca
Miniportfolio
Celgene
Heterocycles
Univ. Campinas
Heterocycles
Daiichi-Sanyko
Screening
Takeda
Screening
Eisai
Screening
MMV
Pathogen Box
Other projects
15 projects
Novartis
1 project
GSK
3 projects
Sanofi
Orthologue Leads
Anacor
Oxaboroles
Liverpool School of Trop Med/ Univ. Liverpool
Tetraoxanes
Univ. of Texas South-western/Monash Univ./ Univ. of Washington/
DHODH
Univ. Cape Town
Aminopyridines
Univ. Sydney
Open Source Drug Discovery
Merck Serono
Amino-alcohols
Translational
Preclinical
P218 DHFR
Biotec/ (Monash Univ./ London School of Hygiene & Trop Med)
SJ733
National Institutes of Health (NIH)/ (St Jude/Rutgers Univ.)
DDD498
Merck Serono/ (Univ. Dundee)
PA92 (Drexel Univ./ Un Washington/ Genomics Institute of the Novartis Research Foundation)
MMV253
(AstraZeneca)
GSK030
GSK
Human volunteers
MMV048
Univ. Cape Town/ Technology Innovation Agency
Development
Patient exploratory
OZ439/PQP
Sanofi
OZ439/FQ
Sanofi
KAE609
Novartis
KAF156
Novartis
DSM265
Takeda/ NIH
Patient confirmatory
Tafenoquine
GSK
Dihydroartemisinin-piperaquine paediatric
Sigma-Tau
Under review *
Rectal Artesunate
Cipla/ Strides/ WHO-TDR
Pyronaridine-artesunate paediatric
Shin Poong/ Univ. Iowa
APM
Post approval *
Artemether-lumefantrine dispersible
Novartis
Artesunate for injection
Guilin
Dihydro-artemisinin-piperaquine
Sigma-Tau
Pyronaridine-artesunate
Shin Poong
Artesunate-amodiaquine *
Sanofi/ DND/
Artesunate-mefloquine *
Cipla/ DND/
SP+AQ *
(Sulfadoxine-Pyrimethamine + Amodiaquine)
Guilin
Target Product Profiles
TPP1 minimal essential: 3-day cure/artemisinin-based combination therapies
Artemether-lumefantrine dispersible (Coartem® Dispersible), generic by Ajanta
Dihydroartemisinin-piperaquine (Eurartesim®)
Dihydroartemisinin-piperaquine paediatric (Eurartesim®)
Pyronaridine-artesunate (Pyramax®)
Pyronaridine-artesunate Paediatric (Pyramax®)
Artesunate-amodiaquine (Coarsucam™, ASAQ/Winthrop®) FDC generics by Ajanta, Ipca, Guilin and co-blistered generics by Strides & Cipla
Artesunate-mefloquine, co-blistered generic by Acino/Mepha
Potential single-exposure agents
OZ439/FQ
OZ439/PQP
KAE609
KAF156
Tafenoquine
Severe malaria
Rectal artesunate
Artesunate for injection (Artesun®)
Intermittent chemoprevention
Sulfadoxine-pyrimethamine + amodiaquine (SP+AQ)
Target Candidate Profiles
Fast clearance (TCP1)
Long duration (TCP2)
Relapse prevention (TCP3a)
Transmission blocking (TCP3b)
Chemoprevention (TCP4)
Australian contribution to MMV science projects
Non-artemisinin-based therapy
Artemisinin-based therapy
* Bioequivalence studies planned in preparation for WHO prequalification
* Included in MMV portfolio post registration
* First review or approval by WHO Prequalification, or by regulatory bodies who are ICH members or observers

Value through innovation

Increasing the scientific knowledge base

218 scientific publications between 2008 – end 2014

25 scientific publications in 2014

Value through innovation

Accelerating malaria R&D

MMV's malaria box

providing researchers with

400 anti-malaria compounds

to further R&D in NTDs

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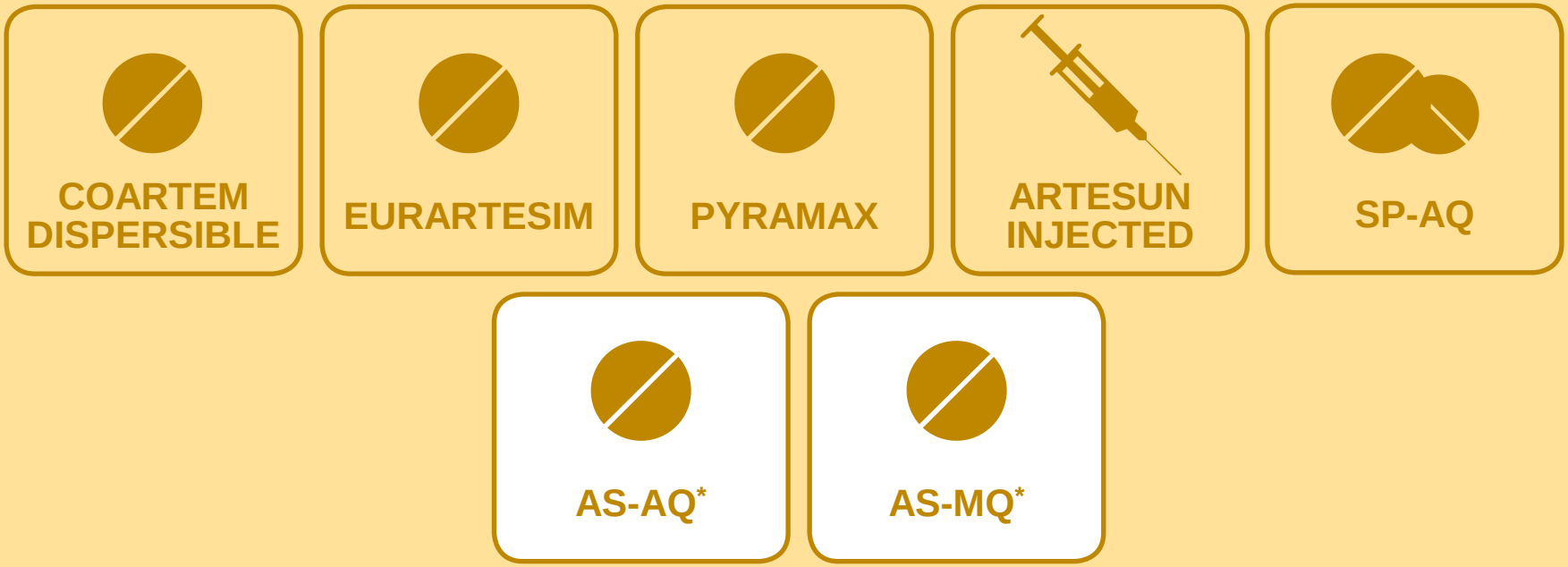
Delivering value through productivity

5(+2) quality products launched since 2009



* Transferred from DNDi-led partnership portfolio to MMV-led partnership portfolio 20th May 2015

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Delivering value through productivity

Addressing current and future medical needs

7 new medicines
in clinical development

- Drug resistance
- Single dose cures
- Children & pregnant women
- Prevention of relapse
- Chemo-prevention
- Transmission blocking

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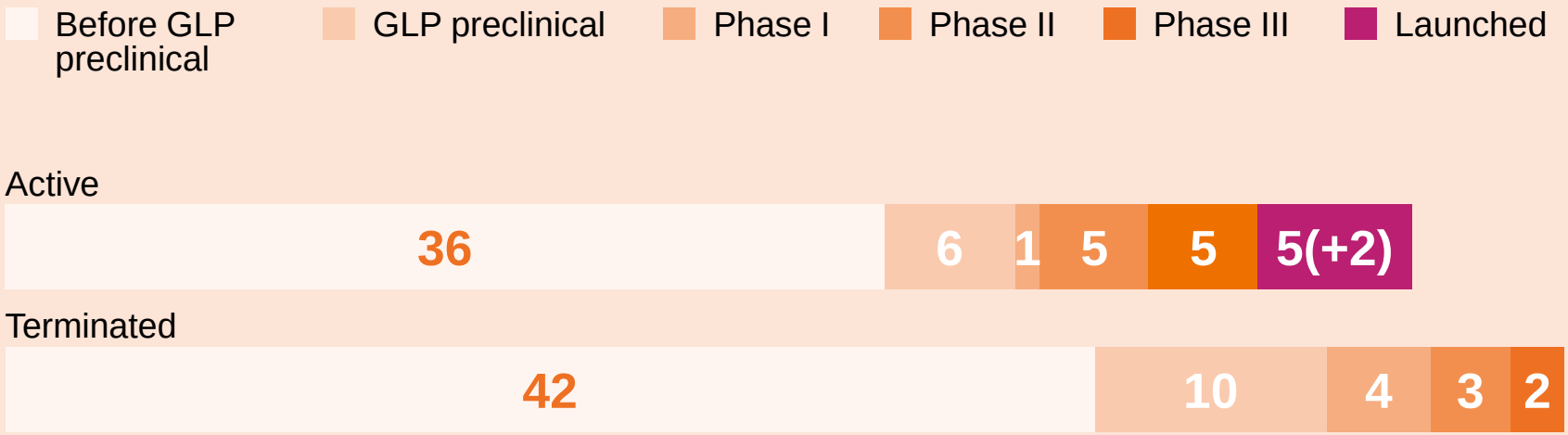
Value through efficiency

Providing rigorous portfolio management

Project progression and termination



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Value through efficiency

Reducing clinical development costs

Industry estimates for clinical development of an anti-infective (Tufts)

Industry: $180m

MMV: $53m

Total clinical development costs for pyronaridine-artesunate

Value through efficiency

Challenging costs

Example: non-clinical toxicology study

Initial cost proposal

CRO competitive bid	**73% reduction**
Final MMV share:	**50% of CRO bid** **13% of initial proposal**

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Value through efficiency

Cutting production costs

Improved routes of synthesis: eg mefloquine

Current cost API: $800 – 1000/kg

Improved synthesis: $400/kg

Value through efficiency

Leveraging donor funds

Pharma's 'in-kind' support

MMV donor funds $1.00	"Matched" Pharma funding $1.00	"In-kind" Pharma support $1.50	Total $3.50

Value through health impact

Saving lives

Coartem® Dispersible

250 000 000
treatment courses delivered

60 000 000 to 87 000 000*
children cured

340 000*
children's lives saved

* estimates based upon drug distribution data, epidemiology / testing data and clinical efficacy data (PCR-corrected 28-day cure rate for Coartem-dispersible) and observational data

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Value through health impact

Saving lives

Injected artesunate

36 300 000
vials delivered since WHO pre-qualification

55%*
reduction in mortality vs quinine in DRC

200 000 - 240 000**
children's lives saved

* Ferrari G, Ntuku H, *et al.* An operational comparative study of quinine and artesunate for the treatment of severe malaria in hospitals and health centres in the Democratic Republic of Congo: the MATIAS study. Malaria Journal, 14 :226 (30 May 2015)
** estimates based upon drug distribution data and clinical efficacy data

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Value through financial and economic impact

Increasing access by reducing prices

Qualifying generic producers
Example: injectable artesunate

Target price/vial: company A

Actual price/vial: company B
92% reduction

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Value through financial and economic impact

Impact of malaria on the workforce

Newcrest Mining's Lihir Island (PNG) mining site

Reduction in malaria cases and work days lost through LLINs & ACTs

Investment in malaria R&D

Support for Lihir malaria elimination effort

2500 cases

8000
work days lost in 2009

<500 cases by year-end 2012

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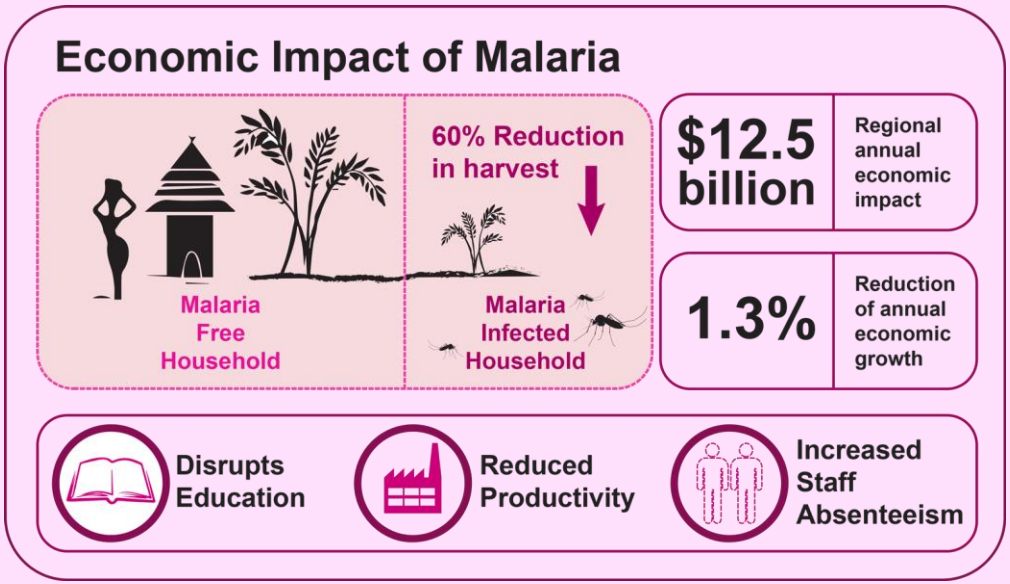
Value through financial and economic impact

Addressing a major barrier to economic development



$208.6 billion

NPV of malaria reduction & elimination during 2013-35

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MMV is grateful for the support of the following donors