# **Eliminating Malaria Deaths**

Terrie E. Taylor, D.O. College of Osteopathic Medicine Michigan State University Blantyre Malaria Project, University of Malawi College of Medicine

# Pre-millennial malaria

- >400 million cases per year
- >1 million deaths per year
- Chloroquine resistant parasites
- Few new drugs on the horizon
- Diagnosis dependent on microscopy



COMBAT HIV/AIDS, MALARIA AND OTHER DISEASES



President's Malaria Initiative Fighting Malaria and Saving Lives



BILL& MELINDA GATES foundation



### A formidable and wily foe











TIDA

17

### A well population









#### And yet, there has been progress.



Noor AM et al... Lancet 2014:383:1239-47

#### Global, regional, and national incidence and mortality for HIV, (?) Tuberculosis, and malaria during 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013

Christopher J L Murray\*, Katrina F Ortblad, Caterina Guinovart, Stephen S Lim, Timothy M Wolock, D Allen Roberts, Emily A Dansereau, Nicholas Graetz, Ryan M Barber, Ionathan C Brown, Haidong Wang, Herbert C Duber, Mohsen Naghavi, Daniel Dicker, Lalit Dandong, Joshua A Salomon, Kyle R Heuton, Kyle Foreman, David E Phillips, Thomas D Fleming, Abraham D Flaxman, Bryan K Phillips, Elizabeth K Johnson, Megan S Coggeshall, Foad Abd-Allaht, Semaw Ferede Aberat, Jerry P Abrahamt, Ibrahim Abubakart, Laith J Abu-Raddadt, Niveen Me Abu-Rmeileht, Tom Achokit, Austine Olufemi Adeyemot, Arsène Kouablan Adout, José C Adsuart, Emilie Elisabet Agardht, Dickens Akenat, Mazin J Al Kahbourit, Deena Alasfoort, Mohammed I Albittart, Gabriel Alcalá-Cerrat, Miguel Angel Alegrettit, Zewdie Aderaw Alemut, Rafael Alfonso-Cristanchot, Samia Alhabibt, Raahib Alit, Francois Allat, Peter I Allent, Ubai Alsharift, Elena Alvarezt, Nelson Alvis-Guzmant, Adansi A Amankwaat, Azmeraw T Amaret, Hassan Aminit, Walid Ammart, Benjamin O Andersont, Carl Abelardo T Antoniot, Palwasha Anwarit, Johan Ärnlövt, Valentina S Arsic Arsenijevict, Ali Artamant, Rana J Asghart, Reza Assadit, Lydia S Atkinst, Alaa Badawit, Kalpana Balakrishnant, Amitava Banerjeet, Sanjay Basut, Justin Beardsley†, Tolesa Bekele†, Michelle L Bell†, Eduardo Bernabe†, Tariku Jibat Beyene†, Neeraj Bhala†, Ashish Bhalla†, Zulfigar A Bhutta†, Aref Bin Abdulhak†, Agnes Binagwahot, Jed D Bloret, Berrak Bora Basarat, Dipan Boset, Michael Brainint, Nicholas Breitbordet, Carlos A Castañeda-Orjuelat, Ferrán Catalá-Lópezt, Vineet K Chadhat, Jung-Chen Changt, Peggy Pei-Chia Chiangt, Ting-Wu Chuangt, Mercedes Colomart, Leslie Trumbull Coopert, Cyrus Coopert, Karen J Courvillet, Benjamin C Cowiet, Michael H Criquit, Rakhi Dandonat, Anand Dayamat, Diego De Leot, Louisa Degenhardtt, Borja Del Pozo-Cruzt, Kebede Deribet, Don C Des Jarlaist, Muluken Dessalegnt, Samath D Dharmaratnet, Uğur Dilment, Eric L Dingt, Tim R Driscollt, Adnan M Durranit, Richard G Ellenbogent, Sergey Petrovich Ermakovt, Alireza Esteghamati†, Emerito Jose A Faraon†, Farshad Farzadfar†, Seyed-Mohammad Fereshtehnejad†, Daniel Obadare Fijabi†, Mohammad H Forouzanfar†, Urbano Fra.Paleot, Lynne Gaffikint, Amiran Gamkrelidzet, Fortuné Gbètoho Gankpét, Johanna M Geleijnset, Bradford D Gessnert, Katherine B Gibneyt, Ibrahim Abdelmageem Mohamed Ginawit, Elizabeth L Glasert, Philimon Gonat, Atsushi Gotot, Hebe N Goudat, Harish Chander Guananit, Raieev Guptat, Rahul Guptat, Nima Hafezi-Nejadt, Randah Ribhi Hamadeht, Mouhanad Hammamit, Graeme | Hankeyt, Hilda L Harbt, Josep Maria Harot, Rasmus Havmoellert, Simon I Hayt, Mohammad T Hedavatit, Ileana B Heredia Pit, Hans W Hoekt, John C Hornbergert, H Dean Hosgoodt, Peter I Hotezt, Damian G Hoyt, John I Huangt, Kim M Iburgt, Bulat T Idrisovt, Kaire Innost, Kathryn H Jacobsent, Panniyammakal Jeemont, Paul N Jensent, Vivekanand Jhat, Guohong Jiangt, Jost B Jonast, Knud Juelt, Haidong Kant, Ida Kankindit, Nadim E Karamt, André Karcht, Corine Kakizi Karemat, Anil Kault, Norito Kawakamit, Dhruv S Kazit, Andrew H Kempt, Andre Pascal Kengnet, Andre Kerent, Maia Kereselidzet, Yousef Saleh Khadert, Shams Eldin Ali Hassan Khalifat, Ejaz Ahmed Khant, Young-Ho Khangt, Irma Khonelidzet, Yohannes Kinfut, Jonas M Kinget, Luke Knibbst, Yoshihiro Kokubot, S Kosent, Barthelemy Kuate Defot, Veena S Kulkarnit, Chanda Kulkarnit, Kaushalendra Kumart, Ravi B Kumart, G Anil Kumart, Gene F Kwant, Taavi Lait, Arjun Lakshmana Balajit, Hilton Lamt, Qing Lant, Van C Lansinght, Heidi | Larsont, Anders Larssont, Jong-Tae Leet, James Leight, Mall Leinsalut, Ricky Leungt, Yichong Lit, Yongmei Lit, Graça Maria Ferreira De Limat, Hsien-Ho Lint, Steven E Lipshultzt, Shiwei Liut, Yana Liut, Belinda K Llovdt, Paulo A Lotufot, Vasco Manuel Pedro Machadot, Jennifer H Maclachlant, Carlos Maais-Rodriauezt, Marek Maidant, Christopher Chabila Mapomat, Wagner Marcenest, Melvin Barrientos Marzant, Joseph R Mascit, Mohammad Taufig Mashalt, Amanda J Mason-Jonest, Bongani M Mayosit, Tasara T Mazorodzet, Abigail Cecilia Mckayt, Peter A Meaneyt, Man Mohan Mehndirattat, Fabiola Meija-Rodriguezt, Yohannes Adama Melakut, Ziad A Memisht, Walter Mendozat, Ted R Millert, Edward J Millst, Karzan Abdulmuhsin Mohammadt, Ali H Mokdadt, Glen Liddell Molat, Lorenzo Monastat, Marcella Monticot, Ami R Mooret, Rintaro Morit, Wilkister Nyaora Moturit, Mitsuru Mukaigawarat, Kinnari S Murthyt, Aliya Naheedt, Kovin S Naidoot, Luigi Naldit, Vinav Nangiat, KM Venkat Naravant, Denis Nasht, Chakib Neijarit, Robert G Nelsont, Sudan Prasad Neupanet, Charles R Newtont, Marie Nat, Muhammad Imran Nisart, Sandra Noltet, Ole F Norheimt, Vincent Nowasebt, Luke Nyakarahukat, In-Hwan Oht, Takayoshi Ohkubot, Bolajoko O Olusanyat, Saad B Omert, John Nelson Opiot, Orish Ebere Orisakwet, Jeyaraj D Pandiant, Christina Papachristout, Angel J Paternina Caicedot, Scott B Pattent, Vinod K Pault, Boris Igor Pavlint, Neil Pearcet, David M Pereirat, Aslam Pervaizt, Konrad Pesudovst, Max Petzoldt, Farshad Pourmalekt, Dima Qatot, Amado D Quezadat, D Alex Quistbergt, Anwar Rafayt, Kazem Rahimit, Vafa Rahimi-Movaghart, Sajjad Ur Rahmant, Murugesan Rajut, Saleem M Ranat, Homie Razavit, Robert Quentin Reilly†, Giuseppe Remuzzi†, Jan Hendrik Richardus†, Luca Ronfani†, Nobhojit Roy†, Nsanzimana Sabin†, Mohammad Yahya Saeedi†, Mohammad Ali Sahraiant, Genesis May J Samontet, Monika Sawhneyt, Ione J C Schneidert, David C Schwebelt, Soraya Seedatt, Sadaf G Sepanlout, Edson E Servan-Morit, Sara Sheikhbahaeit, Kenji Shibuyat, Hwashin Hyun Shint, Ivy Shiuet, Rupak Shivakotit, Inga Dora Siafusdottirt, Donald H Silberbergt, Andrea P Silvat, Edgar P Simardt, Jasvinder A Singht, Vegard Skirbekkt, Karen Sliwat, Samir Sonejit, Sergey S Soshnikovt, Chandrashekhar T Sreeramareddyt, Vasiliki Kalliopi Stathopoulou†, Konstantinos Stroumpoulis†, Soumya Swaminathan†, Bryan L Sykes†, Karen M Tabb†, Roberto Tchio Talongwa†, Eric Yeboah Tenkorang†, Abdullah Sulieman Terkawit, Alan J Thomsont, Andrew L Thorne-Lymant, Jeffrey A Towbint, Jefferson Traebertt, Bach X Trant, Zacharie Tsala Dimbuenet, Miltiadis Tsilimbarist, Uche S Uchendut, Kingsley N Ukwajat, Selen Begüm Uzunt, Andrew J Vallelyt, Tommi J Vasankarit, N Venketasubramaniant, Francesco S Violantet, Vasiliy Victorovich Vlassov†, Stein Emil Vollset†, Stephen Waller†, Mitchell T Wallin†, Linhong Wang†, XiaoRong Wang†, Yanping Wang†, Scott Weichenthal†, Elisabete Weiderpasst, Robert G Weintraubt, Ronny Westermant, Richard A Whitet, James D Wilkinsont, Thomas Neil Williamst, Solomon Meseret Woldeyohannest, John Q Wongt, Gelin Xut, Yang C Yangt, Yuichiro Yanot, Gokalp Kadri Yenturt, Paul Yipt, Naohiro Yonemotot, Seok-Jun Yoont, Mustafa Younist, Chuanhua Yut, Kim Yun Jint, Maysaa El Sayed Zakit, Yong Zhaot, Yingfeng Zhengt, Maigeng Zhout, Jun Zhut, Xiao Nong Zout, Alan D Lopez‡, Theo Vos‡

#### Summary

#### Lancet 2014; 384: 1005-70

Background The Millennium Declaration in 2000 brought special global attention to HIV, tuberculosis, and malaria through the formulation of Millennium Development Goal (MDG) 6. The Global Burden of Disease 2013 study provides a consistent and comprehensive approach to disease estimation for between 1990 and 2013, and an opportunity to assess whether accelerated progress has occured since the Millennium Declaration.

Published Online July 22, 2014 http://dx.doi.org/10.1016/ S0140-6736(14)60844-8



Murray CJL, et al. Lancet 2014;384:1005-70





#### There is still plenty of malaria...and death.





Murray CJL, et al. Lancet 2014;384:1005-70





Noor AM et al.. Lancet 2014:383:1239-47



# We have the tools, now.

- Malaria rapid diagnostic tests (RDTs)
  - 2000: Commercial development ramps up
  - 2005: 200,000 tests distributed
  - 2008: WHO-based evaluation/comparison
  - 2010: 88 million tests distributed
  - 2012: 205 million tests distributed



# We have the tools, now.

- Rapidly effective, affordable oral antimalarial drugs
  - 1983: *Qinghaosu* noticed by the West
  - 2000: Use of *qinghaosu* (artemisinin) endorsed
  - 2005: 11 million treatments delivered
  - 2006: WHO encourages combination chemotherapy
    - 2012: 331 million ACT treatments delivered

#### **Resource allocation**



Pipeline to Product: Malaria R&D Funding Needs into the Next Decade. PATH Malaria Vaccine Initiative, 2013

# In a perfect world, these could have a major impact.



Rafael ME, et al. Reducing the burden of childhood malaria in Africa: the role of improved diagnostics. Nature Publishing Group 2006. http://www.nature.com/diagnostics

## In the belly of the beast (Uganda), they do have a major impact.



#### Absolute numbers of malaria indicators among children admitted Jinja Hospital



#### Absolute numbers of malaria indicators among children admitted Tororo Hospital



# **Cohort studies in Tororo and Jinja**

- Dedicated study clinics open
  - 7 days a week
    - adjacent inpatient facilities available
- Parents/guardians instructed to bring their child to the clinic whenever ill



# **Cohort studies in Tororo and Jinja**

- Reimbursement for transport provided for all visits to the study clinic
- Every febrile participant was tested for malaria with a blood smear
- Patients were followed daily during treatment







# Cohort studies in Tororo and Jinja Proof of principle

- 2,135 children
  - birth to 10 years of age
- 5,041 person years of follow-up
- 16,258 treatments for malaria

# Cohort studies in Tororo and Jinja Proof of principle

- 80 patients (0.04%) with malaria danger signs
- 84 (0.04%) patients with severe malaria
  mostly severe anemia
- 39 deaths from all causes

# Cohort studies in Tororo and Jinja Proof of principle

#### ...only 2 malaria deaths



#### Feasibility



#### Success of ART roll outs across Africa



UNAIDS. Treatment 2015

#### Success of ART roll outs across Africa



Murray CJL, et al. Lancet 2014;384:1005-70



## **Drug resistance**



#### **MMV Portfolio 2001**



#### **MMV Portfolio: October 2008**



#### 2014 Portfolio



16 Projects

## Smart use of ACTs

• Pairing diagnosis to treatment will help to reduce rate of development of resistance



#### Potential pitfall: cost



White MT, et al. Mal J 2011;10:337

## Potential pitfall: cost



White MT, et al. Mal J 2011;10:337

#### Symptoms ≠ testing





# Testing ≠ treatment









- Extend prompt diagnosis and effective treatment to the periphery
- Nip each episode of uncomplicated malaria in the bud

Eliminating Malaria Deaths

# Acknowledgments

- Grant Dorsey, Moses Kamya and the Makerere University – UCSF Research Collaboration
- Jörg Mohrle, MMV
- Rick Steketee, Laura Newman, et al, PATH

- Photo credits: Aaron Dennis, Ryan Carroll, Quique Bassat
- MSU Communications (Kim Ward, Mackenzie Kastl, Anthony Siciliano, Kevin Epling)

# MICHIGAN STATE UNIVERSITY

Spartans Will.