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Conducting Investigator Initiated Trials in low Resource Settings – the Southern perspective

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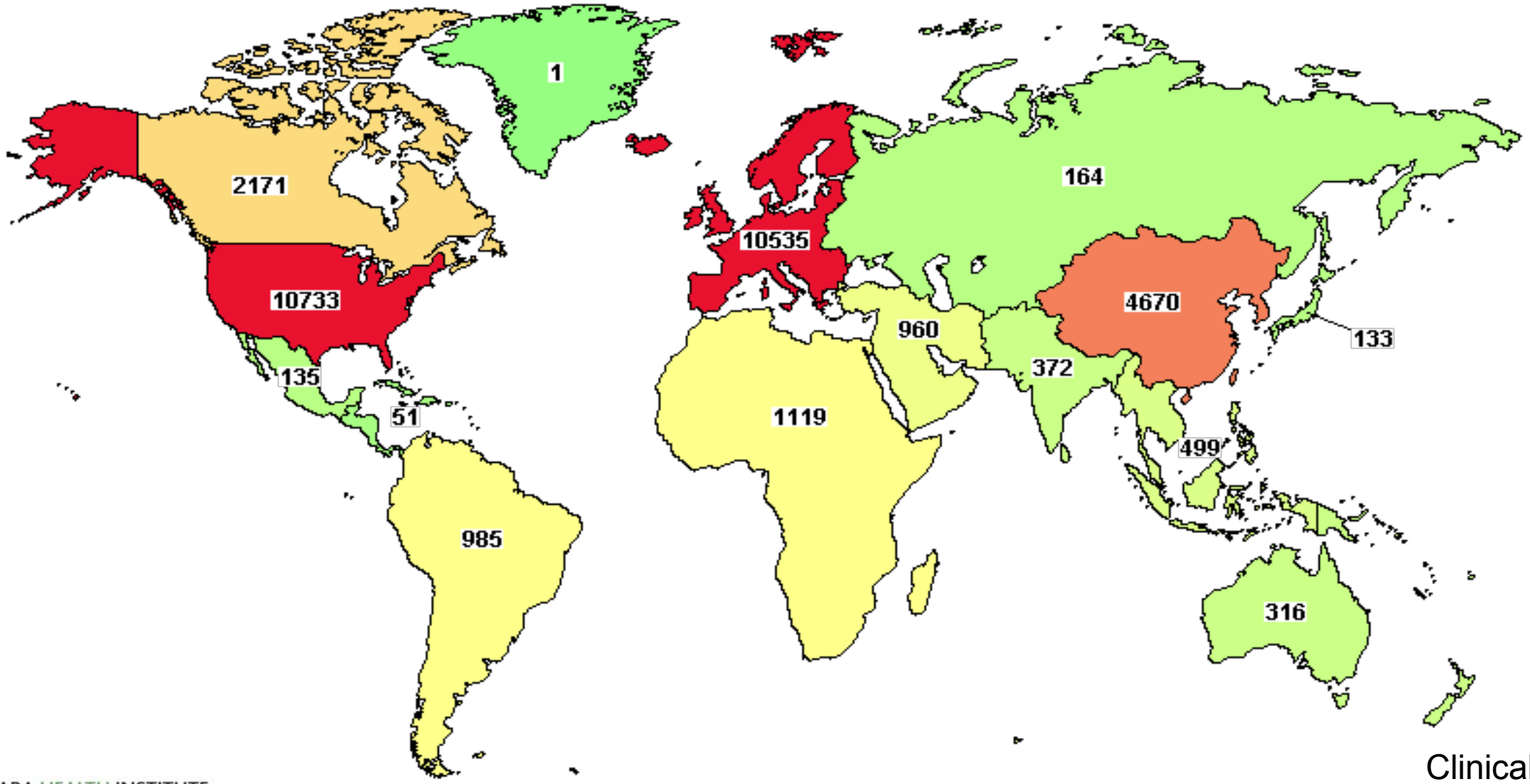
Basel, Switzerland

Definition of Investigator's initiated trials (ITT)

- Trials developed and sponsored by an independent investigator or academic sponsor.
- Industry support
  - Funding
  - Investigational Product/diagnostic
  - *Monitoring?*
- Funding source can be from other non-industry sources

Non-industry initiated trials



ClinicalTrials.gov

THE UTILITY OF ITT IN AFRICA

ITTs expand product knowledge

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JUNE 30, 2016 VOL. 374 NO. 26

Seven-Year Efficacy of RTS,S/AS01 Malaria Vaccine among Young African Children

Ally Olotu, Ph.D., Gregory Fegan, Ph.D., Juliana Wambua, M.Sc., George Nyangweso, B.Sc., Amanda Leach, M.R.C.P.C.H., Marc Lievens, M.Sc., David C. Kaslow, M.D., Patricia Njuguna, M.Med., Kevin Marsh, F.R.C.P., and Philip Bejon, Ph.D.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Genetic Diversity and Protective Efficacy of the RTS,S/AS01 Malaria Vaccine

D.E. Neafsey, M. Juraska, T. Bedford, D. Benkeser, C. Valim, A. Griggs, M. Lievens, S. Abdulla, S. Adjei, T. Agbenyega, S.T. Agnandji, P. Aide, S. Anderson, D. Ansong, J.J. Aponte, K.P. Asante, P. Bejon, A.J. Birkett, M. Bruls, K.M. Connolly, U. D'Alessandro, C. Dobaño, S. Gesase, B. Greenwood, J. Grimsby, H. Tinto, M.J. Hamel, I. Hoffman, P. Kamthunzi, S. Kariuki, P.G. Kremsner, A. Leach, B. Lell, N.J. Lennon, J. Lusingu, K. Marsh, F. Martinson, J.T. Molel, E.L. Moss, P. Njuguna, C.F. Ockenhouse, B. Ragama Ogutu, W. Otieno, L. Otieno, K. Otieno, S. Owusu-Agyei, D.J. Park, K. Pellé, D. Robbins, C. Russ, E.M. Ryan, J. Sacarlal, B. Sogoloff, H. Sorgho, M. Tanner, T. Theander, I. Valea, S.K. Volkman, Q. Yu, D. Lapierre, B.W. Birren, P.B. Gilbert, and D.F. Wirth

OPEN ACCESS Freely available online PLoS one

Duration of Protection Against Clinical Malaria Provided by Three Regimens of Intermittent Preventive Treatment in Tanzanian Infants

Matthew Cairns[1]*, Roly Gosling[2], Ilona Carneiro[2], Samwel Gesase[3], Jacklin F. Mosha[4], Ramadhan Hashim[3], Harparkash Kaur[2], Martha Lemnge[3], Frank W. Mosha[4], Brian Greenwood[2], Daniel Chandramohan[2]

1 Department of Epidemiology and Population Health, London School of Hygiene & Tropical Medicine, London, United Kingdom, **2** Department of Infectious and Tropical Diseases, London School of Hygiene & Tropical Medicine, London, United Kingdom, **3** National Institute for Medical Research, Tanga Centre, Tanga, Tanzania, **4** Kilimanjaro Christian Medical College, Moshi, Tanzania

The Journal of Infectious Diseases

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Volume 200, Issue 11
1 December 2009

Selection of Parasites with Diminished Drug Susceptibility by Amodiaquine-Containing Antimalarial Regimens in Uganda FREE

Fatima Nawaz, Samuel L. Nsobya, Moses Kiggundu, Moses Joloba, Philip J. Rosenthal

The Journal of Infectious Diseases, Volume 200, Issue 11, 1 December 2009, Pages 1650–1657, https://doi.org/10.1086/647988

Published: 01 December 2009 **Article history** ▾

Identify new indications/regimens of existing medical interventions.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Azithromycin to Reduce Childhood Mortality in Sub-Saharan Africa

J.D. Keenan, R.L. Bailey, S.K. West, A.M. Arzika, J. Hart, J. Weaver, K. Kalua, Z. Mrango, K.J. Ray, C. Cook, E. Lebas, K.S. O'Brien, P.M. Emerson, T.C. Porco, and T.M. Lietman, for the MORDOR Study Group*

Articles

Comparative efficacy of low-dose versus standard-dose azithromycin for patients with yaws: a randomised non-inferiority trial in Ghana and Papua New Guinea

Michael Marks, Oriol Mitjà, Christian Bottomley, Cynthia Kwakye, Wendy Houinei, Mathias Bauri, Paul Adwere, Abdul A Abdulai, Fredrick Dua, Laud Boateng, James Wangi, Sally-Ann Ohene, Regina Wangnapi*, Shirley V Simpson, Helen Miag, Kennedy K Addo, Laud A Basing, Damien Danavall, Kai H Chi, Allan Pillay, Ronald Ballard, Anthony W Solomon, Cheng Y Chen, Sibauk V Bieb, Yaw Adu-Sarkodie, David C W Mabey, Kingsley Asiedu, on behalf of the study team*

Summary

The NEW ENGLAND JOURNAL of MEDICINE

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Mortality after Fluid Bolus in African Children with Severe Infection

Kathryn Maitland, M.B., B.S., Ph.D., Sarah Kiguli, M.B., Ch.B., M.Med., Robert O. Opoka, M.B., Ch.B., M.Med., Charles Engoru, M.B., Ch.B., M.Med., Peter Olupot-Olupot, M.B., Ch.B., Samuel O. Akech, M.B., Ch.B., Richard Nyeko, M.B., Ch.B., M.Med., George Mtove, M.D., Hugh Reyburn, M.B., B.S., Trudie Lang, Ph.D., Bernadette Brent, M.B., B.S., Jennifer A. Evans, M.B., B.S., James K. Tibenderana, M.B., Ch.B., Ph.D., Jane Crawley, M.B., B.S., M.D., Elizabeth C. Russell, M.Sc., Michael Levin, F.Med.Sci., Ph.D., Abdel G. Babiker, Ph.D., and Diana M. Gibb, M.B., Ch.B., M.D., for the FEAST Trial Group*

Increase local knowledge of diseases.

eLIFE elifesciences.org

RESEARCH ARTICLE

A micro-epidemiological analysis of febrile malaria in Coastal Kenya showing hotspots within hotspots

Philip Bejon[1,2*], Thomas N Williams[1,3], Christopher Nyundo[1], Simon I Hay[4], David Benz[4], Peter W Gething[4], Mark Otiende[1], Judy Peshu[1], Mahfudh Bashraheil[1], Bryan Greenhouse[5], Teun Bousema[6,7], Evasius Bauni[1], Kevin Marsh[1,2], David L Smith[8], Steffen Borrmann[1,9,10]

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Contents lists available at ScienceDirect

Papillomavirus Research

journal homepage: www.elsevier.com/locate/pvr

HPV serostatus pre- and post-vaccination in a randomized phase II preparedness trial among young Western Cape, South African women: The evri trial

Staci L. Sudenga[a], B. Nelson Torres[a], Matthys H. Botha[b], Michele Zeier[c], Martha E. Abrahamsen[a], Richard H. Glashoff[d], Susan Engelbrecht[d], Maarten F. Schim Van der Loeff[e], Louvina E. Van der Laan[b], Siegfried Kipping[b], Douglas Taylor[f], Anna R. Giuliano[a,*]

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[b] *Department of Obstetrics and Gynaecology and Unit for Gynaecological Oncology, Tygerberg Hospital, Stellenbosch University, Cape Town, South Africa*
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[e] *Department of Infectious Diseases, Public Health Service of Amsterdam, Amsterdam, the Netherlands*
[f] *FHI 360, Durham, NC, USA*

An evaluation of clinical indicators for severe paediatric illness

L.A. Paxton,[1] S.C. Redd,[2] R.W. Steketee,[3] J.O. Otieno,[4] & B. Nahlen[5]

Brain swelling and ischaemia in Kenyans with cerebral malaria

C R J C Newton, N Peshu, B Kendall, F J Kirkham, A Sowunmi, C Waruiru, I Mwangi, S A Murphy, K Marsh

Compliment industry-sponsored clinical trial data to inform policy change considerations.

Wellcome Open Research

Wellcome Open Research 2018, 2:100 Last updated: 16 JAN 2018

Check for updates

STUDY PROTOCOL

REVISED Children's Oxygen Administration Strategies Trial (COAST): A randomised controlled trial of high flow versus oxygen versus control in African children with severe pneumonia [version 2; referees: 2 approved]

Kathryn Maitland [1,2], Sarah Kiguli[3], Robert O. Opoka[3], Peter Olupot-Olupot[4,5], Charles Engoru[6], Patricia Njuguna[2], Victor Bandika[7], Ayub Mpoya[2], Andrew Bush[1,8], Thomas N. Williams [1,2], Richard Grieve[9], Zia Sadique[9], John Fraser[10], David Harrison[11], Kathy Rowan[11]

Mbuagbaw *et al. Trials* 2011, **12**:5
http://www.trialsjournal.com/content/12/1/5

TRIALS

STUDY PROTOCOL Open Access

The cameroon mobile phone sms (CAMPS) trial: a protocol for a randomized controlled trial of mobile phone text messaging versus usual care for improving adherence to highly active anti-retroviral therapy

Lawrence Mbuagbaw[1*], Lahana Thabane[2,3], Pierre Ongolo-Zogo[1], Richard T Lester[4,5], Edward Mills[6], Jimmy Volmink[7], David Yondo[1], Marie José Essi[1], Renée-Cecile Bonono-Momnougui[1], Robert Mba[1], Jean Serge Ndongo[1], Francois C Nkoa[1], Henri Atangana Ondoa[1]

Articles

Daily co-trimoxazole prophylaxis to prevent mortality in children with complicated severe acute malnutrition: a multicentre, double-blind, randomised placebo-controlled trial

James A Berkley, Moses Ngari, Johnstone Thitiri, Laura Mwalekwa, Molline Timbwa, Fauzat Hamid, Rehema Ali, Jimmy Shangala, Neema Mturi, Kelsey D J Jones, Hassan Alphan, Beatrice Mutai, Victor Bandika, Twahir Hemed, Ken Awuondo, Susan Morpeth, Samuel Kariuki, Gregory Fegan

oa OPEN ACCESS

Strengthen human & capacity infrastructure

Ideal IITs in Africa

- Be more applicable to local populations and build on local healthcare knowledge.
- Respond to local/regional needs and driven by a national agenda.
- Should influence policy and sustainably link research to action.
- Should involve local staff at all levels and stages of trial conduct,
  - Opportunity for ‘learning by doing’ and skill development

Barriers to Investigator Initiated trials in Africa

- Inadequate capacity for clinical research (human resources and infrastructure)
  - Lack of appropriately trained clinical scientists and career structure to support them.
  - Lack of motivation/incentives & competing interests.
  - Lack of appropriate facilities and infrastructure.
  - Operational barriers.
- Lack of adequate and appropriate funding
  - Inadequate funding for clinical trials and other types of clinical research

Barriers to Investigator Initiated trials in Africa

- Inadequate public engagement with clinical research.
  - Insufficient public promotion of clinical research by Government
  - Insufficient engagement by researcher with research participants and policy-makers.
- Lack of research planning, regulation and coordination.
  - Lack of a coordinated national plan to balance excellence on the world stage with relevance to local problems;
  - An inefficient regulatory framework for clinical trials and registration of new medicines hindering the conduct of innovative clinical trials.

Addressing the barriers to ITT in Africa

- Increase and maintain the supply of skilled clinical researchers.
  - Strengthening of biomedical research in universities and health care institutions.
  - Increase motivation and incentives.
- Increase funding in IIT and strengthening translational research.
  - Government, industry and non-industry funding.
  - Local and international collaborations.
- Close cooperation between researchers and health policy-makers.
  - Define priority areas that need ITT to address
  - Improves uptake into policy.

Addressing the barriers to ITT in Africa.

- Increase awareness of health research and its impact.
  - Secondary-school and tertiary-school science education.
  - Improved health research profile among policy makers, the media and the public.
- Improve the research infrastructure.
- Inclusive trial operations.
  - Research conducted within local institutions
  - Use of local staff
  - Financial and material resources routed through local institution.

Fig. 1.3. Regional ranking of leading causes of disease burden, measured in disability-adjusted life-years (DALYs), 2011

Cause	African	Americas	South-East Asia	European	Eastern Mediterranean	Western Pacific	Global
Lower respiratory infections	1	9	1	14	1	10	1
HIV/AIDS	2	19	15	16			6
Diarrhoeal diseases	3		3		3		4
Malaria	4						13
Preterm birth complications	5	13	4		2	15	5
Birth asphyxia and birth trauma	6		7		5	17	9
Protein-energy malnutrition	7				18		
Meningitis	8				20		
Congenital anomalies	9	12	10	19	9	14	11
Road injury	10	5	8	8	7	4	8
Neonatal sepsis and infections	11		20		13		
Iron-deficiency anaemia	12		11		11		15
Stroke	13	6	6	2	8	1	3
Endocrine, blood, immune disorders	14	16			17		
Maternal conditions	15						
Ischaemic heart disease	16	1	2	1	4	2	2
Tuberculosis	17				14	20	16
Unipolar depressive disorders	18	2	12	3	6	5	10
Interpersonal violence	19	3					
Epilepsy	20						

Ranking legend: 1–5; 6–14; 15–20; No ranking

THANK YOU