Malaria Control in Emergencies

Mark Rowland
LSHTM
Aims

• Overview of complex emergencies
  – operational constraints
  – Transitions
• Situation analysis and planning
• Diagnosis and case management
  – drug resistance
• Malaria prevention
  – personal protection,
  – vector control
• Surveillance and epidemic response
• Research needs
Overview

- Malaria flourishes in conditions of crisis and displacement
- Operational differences conditions:
  - Unstable or no government
  - UN and NGOs provide health services
  - Insecurity and political flux
    - Long-term planning impossible
  - Breakdown of systems and infrastructure
- Strategies used in stable situations must be adapted for complex emergencies
Global distribution of *P. falciparum* and *P. vivax* in 2005. (Guerra et al 2006)

(a) *P. falciparum*

(b) *P. vivax.*
Factors contributing to the malaria burden in complex emergencies - differences from stable situations

• Lack of government
  – breakdown of health services
  – collapse of malaria control programmes
• Increased risk of epidemics
  – movement of people to areas of high transmission
  – increased vulnerability - famine and malnutrition
  – inadequate supply of drugs
• Environmental deterioration increases human-vector contact
• Problems of access
  – to refugee camps
  – to internally displaced populations
Malaria – emergency examples

• Refugees move to stable country
  – Burundians to Tanzania,
  – Afghans to Pakistan
• Refugees move to unstable country
  – Rwandans to DRC
• Internal displacement
  – South Sudan, Afghanistan
• Chronic conflict with no recognised government
  – Somalia, Myanmar
• Rapid transition to post-conflict conditions:
  – East Timor, Tajikistan
Transitions in emergencies

- Complex emergencies evolve from the acute to the post-emergency or chronic phase.

- Acute phase characteristics:
  - population displacement
  - change in authority
  - breakdown in infrastructure and services
  - impaired access
  - high mortality: >1 death per 10,000 population per day (definition of acute phase).
Post-emergency and chronic phases

- **Post emergency phase:**
  - mortality rates improve
  - basic food & health needs are met
  - Security improves

- **Chronic emergency countries = political deadlock**
  - conflict areas = acute phase
  - non conflict areas = post-emergency phase.

- Health provision and strategy differs between acute and post-emergency phase
Strategic planning

- **Situation analysis:**
  - Current or future problem
  - Local or imported malaria
  - Human/material resources available,
  - Expected future movements of refugees
- Develop a plan
  - Define objectives and strategy
  - Decide on activities, workplan, inputs/resources
  - Organisational framework
- Develop indicators for monitoring and evaluation, and plan how they will be measured
- Plan operational research, if there are gaps in information required to respond
- Develop a budget
Situation analysis

• Assess the causes or prospects of malaria
• Information needed on:
  – Local environment (geography, water, agriculture, rainfall & temp.)
  – Population (numbers, settlement pattern)
  – Epidemiology (disease prevalence, vectors and breeding sites, identify at risk communities or areas)
  – Security & access
  – Resources and logistics (human, health facilities, drugs, import practices)
• Plan the response
• Site planning (good selection may prevent malaria)
• Assessment team (skilled in disease control and operations)
Disease management

• Microscropy diagnosis
  – Not possible in acute phase if health system is weak
  – Diagnosis on clinical symptoms is inaccurate
    • In Africa, clinical diagnosis is the norm, overdiagnosis!
    • In Asia, parasitaemia associated with disease, but symptoms are non-specific:
      • Most suspected malaria is not malaria - SPR is < 25% in Asia

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<tbody>
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<td>population</td>
<td>3,237,805</td>
<td>2,542,696</td>
<td>1,953,547</td>
<td>1,929,767</td>
<td>1,238,690</td>
<td>1,048,107</td>
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<tr>
<td>TSE</td>
<td>677,857</td>
<td>568,856</td>
<td>459,513</td>
<td>384,509</td>
<td>277,325</td>
<td>186,142</td>
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<tr>
<td>vivax</td>
<td>111,425</td>
<td>91,527</td>
<td>73,406</td>
<td>50,471</td>
<td>31,792</td>
<td>21,235</td>
<td>31,277</td>
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<tr>
<td>falciparum</td>
<td>36,079</td>
<td>34,561</td>
<td>11,024</td>
<td>13,047</td>
<td>4,804</td>
<td>3,911</td>
<td>4,405</td>
</tr>
<tr>
<td>mix</td>
<td>4791</td>
<td>3686</td>
<td>503</td>
<td>176</td>
<td>170</td>
<td>94</td>
<td>55</td>
</tr>
<tr>
<td>SPR</td>
<td>22%</td>
<td>23%</td>
<td>18%</td>
<td>17%</td>
<td>13%</td>
<td>14%</td>
<td>16%</td>
</tr>
<tr>
<td>Pf / all malaria</td>
<td>24%</td>
<td>27%</td>
<td>13%</td>
<td>20%</td>
<td>13%</td>
<td>15%</td>
<td>12%</td>
</tr>
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</table>
Rapid diagnostic tests

- Improvement on clinical diagnosis
  - Histidine-rich protein II, a protein produced only by P. falciparum
  - Lactate dehydrogenase, non specific malaria antigen (all species)

- Kits containing LDH-II only can distinguish falciparum from vivax but not mixed infection

- Sensitivity is equal to microscopy - more than 90% of cases with parasitaemia test positive with RDT

- Below 100 parasites/ul sensitivity decreases

- Recent reports indicate sensitivities and specificities below operational requirements – problems with storage and transport (required 4-30 degree range cannot be achieved) and quality control

- Quick, reliable, low skill requirements, high case loads, cheap <$0.5 for PF, <$1 all species tests

- Used for confirmatory diagnosis, rapid surveys, malaria epidemics but HRP-II not suitable for drug resistance surveys
Treatment

- Base treatment on local drug resistance pattern
- Combination therapy (artesunate plus other antimalarial)
  ACT is WHO policy for falciparum but not universally used
  - Coartem (artemether-lumefantrine)
- Manage severe malaria with quinine - WHO guidelines
- Manage vivax malaria with chloroquine
  - Radical treatment of liver stage with primaquine for 14 days not routine
Multi-drug resistance in falciparum malaria

- Drug resistance causes increased morbidity and mortality
- On the Thai border with Myanmar, in Karen refugee camps, *P. falciparum* is resistant to most drugs.
- SE Asia is the “epicentre” from which resistance has spread
- The *in-vivo* response has been monitored over the last 25 years
Thailand/Myanmar border: in vivo cure rates

- Increasing resistance to chloroquine and then to SP in 1980s

- Mefloquine (MQ) introduced in 1984.

- By 1994 MQ cure rates <60%.

- The combination of MQ and artesunate gives cure rates > 95%.

- Until recently no decline in susceptibility to ACT/MQ
*P. falciparum* incidence fell 6 fold after the introduction of MQ-AS

- Rapid effect, gametocytocidal, reduced parasite reservoir.
Complex emergencies and epidemics
Burundi 2001 – case study for epidemic case management

Population 6.5 million
Civil war since 1993
IDPs 800,000, refugees 600,000
>2 million at risk, >1 million cases, thousands of deaths

Source: M. Barutwanato, LMTC, Burundi, 2000
Doubling of fever cases (Sept 00/Sept 99)
Chloroquine used
Paracheck RDT: 80% positive post-treatment
# Treatment debate during the epidemic

| National Protocol                          | 1- Chloroquine  
|                                          | 2- S/P          |
| WHO recommendation                       | S/P             |
| MSF suggestion                           | Artesunate + S/P|
| Compromise protocol used                 | Chloroquine + S/P|
Malaria Epidemic, Kayanza, Burundi
September 2000 – June 2001

Population: 579,606
515,994 cases
Incidence: 1,492/1,000/yr
In vivo drug efficacy – cure rates

<table>
<thead>
<tr>
<th>Location</th>
<th>CQ efficacy</th>
<th>SP efficacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Karuzi</td>
<td>6.9%</td>
<td>33.6%</td>
</tr>
<tr>
<td>Kayanza</td>
<td>13.3%</td>
<td>58%</td>
</tr>
<tr>
<td>Cankuzu</td>
<td>36%</td>
<td>71.9%</td>
</tr>
<tr>
<td>Gitega</td>
<td>27%</td>
<td>50.9%</td>
</tr>
<tr>
<td>Bujumbura (1)</td>
<td>51%</td>
<td>87%</td>
</tr>
<tr>
<td>Bujumbura (2)</td>
<td>23.7%</td>
<td>60%</td>
</tr>
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</table>
Problems encountered implementing effective treatment

- first WHO request for support
- first MOH request
- WHO response: SP
- second Health Ministry request
- WHO confirmation: SP
- CQ: 90%
- SP: 54%
- In vivo resistance surveys
- Lancet Health Ministry: Recriminations
Conclusions

Government reluctant to change from chloroquine
WHO slow to support drug surveys
NGOs unable to control epidemic
Recriminations!
Led to MSF ACT Now! Campaign
ACT now universally recommended
Artesunate CT - issues

- Artesunate (AS) widely used as a single treatment
  - Split packs
- Expensive
  - Global fund subsidized treatment
- Counterfeit artemisinin widely available
- Artemisinin resistance in Cambodia
  - Can further selection/spread be prevented?
Prevention and control of malaria

• Insecticide Treated Nets - personal protection

• Indoor Residual Spraying - Mosquito control
Long lasting insecticidal nets LLIN

- Two types
  - Coated polymer binder (polyester)
    - PermaNet 2.0 (Vestergaard)
    - Interceptor (BASF)
    - DawaPlus (Bayer)
  - Incorporation LLIN (polyethylene)
    - Olyset (Sumitomo)
    - Duranet (Clarke)
- Long lasting treatment kits (insecticide plus binder)
  - KO-Tab-123 (Bayer)
  - IconMaxx (Syngenta)
Physical status of PermaNet 2.0 by age of net

6 country study: Angola, Ghana, Kenya, Madagascar, Togo, Zambia
Cross sectional survey results

<table>
<thead>
<tr>
<th>Year</th>
<th>No. nets</th>
<th>Mean number of holes per net</th>
<th>Percentage of holes per size$^1$</th>
<th>Percentage of holes per position$^2$</th>
<th>mean no. of open seams</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>small</td>
<td>medium</td>
<td>large</td>
</tr>
<tr>
<td>1</td>
<td>149</td>
<td>12.4</td>
<td>71</td>
<td>20</td>
<td>9</td>
</tr>
<tr>
<td>2</td>
<td>165</td>
<td>20.4</td>
<td>75</td>
<td>19</td>
<td>6</td>
</tr>
<tr>
<td>3</td>
<td>152</td>
<td>20.8</td>
<td>73</td>
<td>20</td>
<td>7</td>
</tr>
</tbody>
</table>
Durability of LLINs

WHO survey of PermaNet 2.0 (polyester)

<table>
<thead>
<tr>
<th>Year</th>
<th>No. nets</th>
<th>Mean number of holes per net</th>
<th>Percentage of holes per size(^1)</th>
<th>Percentage of holes per position(^2)</th>
<th>Mean no. of open seams</th>
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<td>3</td>
<td>152</td>
<td>20.8</td>
<td>73</td>
<td>20</td>
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LSHTM trial of Olyset (polyethylene) in occupied rooms

<table>
<thead>
<tr>
<th></th>
<th>1 years</th>
<th>7 years</th>
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<tbody>
<tr>
<td>Age of net</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mosquito mortality</td>
<td>73%</td>
<td>59%</td>
</tr>
<tr>
<td>% feeding on humans</td>
<td>16%</td>
<td>36%</td>
</tr>
</tbody>
</table>
Insecticide treated nets - constraints in acute phase

- High start up costs
- Suitable for epidemic control?
  - Delays in delivery.
  - Requires compliance, change in behaviour
- More likely to be used if
  - refugees previously used nets
  - shelter suited for hanging nets
- Less likely if
  - traumatised or social network breakdown
  - not used before
- More appropriate during chronic or post-conflict phases
Indoor residual spraying

Favoured method of control if
• permanent structures (mud huts or houses)
• mosquito species are indoor resting
• Infrastructure able to plan and supervise a spray campaigns

Common problems
• delays in delivery of insecticide and pumps
• poor organisation
• poorly trained spray teams
• pump failure & poor maintenance

Local outbreaks justify spraying . . . but epidemic conditions over before operations are mounted if malaria is seasonal!
Pyrethroids favoured but pyrethroid resistance is increasing!
A. Spraying with malathion in a group of Afghan camps in July 1992 at the start of the transmission season prevented most transmission.

B. Late spraying in a group of neighbouring camps in Sept-Oct 1992 failed to curb the outbreak (which came to a natural end in the winter). This illustrates the importance of correct timing of spray campaigns at the onset of the transmission season.

The importance of timing – logistical constraints (Rowland 1991)
Burundi epidemic – failure of IRS (Coosemans 2007)

<table>
<thead>
<tr>
<th>Survey Zone 1</th>
<th>Prevalence % (No.)</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention</td>
<td>60.0% (51)</td>
<td>48.8 - 70.5</td>
<td>0.6</td>
</tr>
<tr>
<td>Control</td>
<td>56.5% (48)</td>
<td>45.3 - 67.2</td>
<td></td>
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<tr>
<td>Survey Zone 2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intervention</td>
<td>28.2% (24)</td>
<td>19.0 - 39.0</td>
<td>0.4</td>
</tr>
<tr>
<td>Control</td>
<td>34.1% (29)</td>
<td>24.2 - 45.2</td>
<td></td>
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</table>
Successful house spraying in Afghan camps (Rowland 2000)
Prevention and control of malaria

Personal protection and Mosquito vector control:

• Acute phase
  Choice of intervention is not prescriptive

• The key local factors are:
  1. Type of shelter - housing, tents, plastic sheeting
  2. Human behaviour - sleeping practices, mobility
  3. Vector behaviour - biting times, indoor/outdoor resting
Spraying tents with pyrethroid

- Inner surfaces sprayed with pyrethroid against indoor resting mosquitoes.
- Insecticide persists for:
  - 6 months on single sheeted tents
  - >12 months on double sheeted tents
- Suitable for refugees or nomads
- Demonstrated 60-80% reduction in falciparum malaria in Afghan nomads in Waziristan
Plastic sheeting for refugee camps in Africa

Rationale: NGOs not expert in malaria control, so adapt the materials commonly distributed in emergencies

- Plastic sheeting impregnated with insecticide in factory
The design

**Insecticide + UV protectant:** control of flies and mosquitoes

- **outside**
  - Plastic tarpaulin

- **inside**
  - Core woven fabric, HDPE
  - LDPE laminated film
  - LDPE laminated film

**Insecticide:** control of mosquitoes (including malaria vectors)
Evaluation of tarpaulins and tents on outdoor testing platform - tent enclosed in giant net for trapping mosquitoes

- Testing using overnight platform bioassay
- Host seeking mosquitoes caught and released into trap net with two men sleeping under plastic tarpaulins
- Also used to test houseflies
Outdoor platform tests - insecticide treated plastic sheeting

Anopheles spp mortality

Mean % mortality of all anophelines (42.75)

- Untreated UNHCR sheeting
- UNHCR sheeting sprayed with deltamethrin
- Treated Tent
- Vestergaard treated sheeting
24hr mortality after 3 minute exposure
(all bioassays on the inside surface)

Number of weeks weathering

% 24hr mortality
ITPS finite lifespan in harsh conditions – does it matter?

- Physical lifespan of ITPS was 6 months
- Refugees build permanent shelters ASAP
- Most useful in the first weeks or months
Tobana camp – Sierra Leone
Village trial of ITPS – roof & ceiling treatment

INSECTICIDE TREATED PLASTIC SHEETING (ITPS):
EVALUATION TO USE, FROM AN INTER-SECTORAL DECISION MAKING PROCESS
Phase III Crude Trends: Parasitological Findings

Mean Monitoring Cycle RDT positivity rates; Tobana Refugee Camp [Plastic Only Roof](N=117)

- ITPS (n=53)
- UPS (n=64)

JOHNS HOPKINS UNIVERSITY
For Presentation Off-prints and ITPS / Phase III Related Information »» mburns@jhsph.edu
Largo camp – ITPS on 4 walls and ceiling

### Phase III Crude Trends: Parasitological Findings

<table>
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<tr>
<th>Monitoring Cycle Day</th>
<th>ITPS (n=49)</th>
<th>UPS (n=50)</th>
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<tr>
<td>0</td>
<td>10%</td>
<td>15%</td>
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<tr>
<td>1</td>
<td>20%</td>
<td>25%</td>
</tr>
<tr>
<td>2</td>
<td>30%</td>
<td>35%</td>
</tr>
<tr>
<td>3</td>
<td>40%</td>
<td>45%</td>
</tr>
<tr>
<td>4</td>
<td>50%</td>
<td>55%</td>
</tr>
<tr>
<td>5</td>
<td>60%</td>
<td>65%</td>
</tr>
<tr>
<td>6</td>
<td>70%</td>
<td>75%</td>
</tr>
<tr>
<td>7</td>
<td>80%</td>
<td>85%</td>
</tr>
<tr>
<td>8</td>
<td>90%</td>
<td>95%</td>
</tr>
<tr>
<td>9</td>
<td>100%</td>
<td>100%</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Largo</th>
<th>Tobanda</th>
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<tbody>
<tr>
<td>ITPS</td>
<td>UPS</td>
</tr>
<tr>
<td>All</td>
<td>49%</td>
</tr>
<tr>
<td>Under 3y</td>
<td>59%</td>
</tr>
<tr>
<td></td>
<td>47%</td>
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<td>55%</td>
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ITPS trial inside mud houses (Diabate 2006)

- ITPS used as
  - ceiling lining
  - Wall lining

Results:

- Ceiling only treatment did not kill mosquitoes
- Killed mosquitoes when all resting surfaces covered with ITPS
ITPS conclusions

- Valuable in acute phase emergency
- Effectiveness < 1 year
- Limited value for chronic emergencies except during the transitional phase
- No substitute for conventional vector control tools where these work well
Acute phase preventive interventions
Treating blankets/top-sheets with permethrin solution

Blankets are also standard issue in emergencies

15% households treated with permethrin
15% household treated with placebo solution
Cases of malaria recorded at BHU
Incidence by age group in the treated top-sheet trial

- Personal protection in the younger age groups: 0-20 years
- Adults immune, less impact observed
- Treatments reduced mosquito biting rates by 70% and killed 30% of mosquitoes
- Effective against indoor and outdoor resting mosquitoes
- Treatments lasted 3 months
Anthroponotic cutaneous leishmaniasis (*L. tropica*)
Afghanistan
Trial of 3 interventions against leishmaniasis over 1 year

Household randomised trial in Kabul:

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Incidence</th>
<th>% protection</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Placebo</td>
<td>7.2%</td>
<td>-</td>
</tr>
<tr>
<td>2. ITNs</td>
<td>2.4%</td>
<td>67%</td>
</tr>
<tr>
<td>3. Treated blankets</td>
<td>2.5%</td>
<td>66%</td>
</tr>
<tr>
<td>4. Indoor spraying</td>
<td>4.4%</td>
<td>39%</td>
</tr>
</tbody>
</table>

Efficacy: Blankets = ITN

Popularity: ITN > Blankets

Conclusion: Blankets for epidemic control, ITN for long-term protection
Permethrin treated blankets or top-sheets

- protection against falciparum and vivax for 3 months
- Suitable for acute phase emergencies and disasters
- Cost-effective, fewer logistical problems
- Also protects against cutaneous leishmaniasis
Future vision & next steps

- Blankets are distributed in tens of thousands in acute emergencies
- Pre-treat with long-lasting formulation, e.g. permethrin during manufacture and stockpile
- No technical or operational requirements
- Treated blankets and ITPS together should give full protection

- Disease control trials of Deet (repellent) treated blankets currently underway in Tanzania
  - Multiple village trial
Construction of mud houses in post-acute or chronic phases allows increased use of ITN or indoor spraying
Treated nets

- Highly appropriate for
  - the post-conflict phase
  - returnees (repatriation package).
- Encourages self reliance if weak government unable to deliver malaria control.
- Distribution strategies
  - free or subsidized?
  - cost recovery or social marketing?
  - Delivery/sales?:
    - health sector clinics,
    - mobile teams,
    - community distribution or nets-for-work
Teaching the community about treated nets

- Good visual aids and trainers:
  - get the message across
  - improve proper use
Health information leaflet encourages proper use
ITN in Eastern Afghanistan - % coverage of population
Merits of different interventions

- ITNs, IRS, sprayed tents, are equally effective against malaria (giving >60% protection).
- IT blankets cheaper than ITN but effect is short-term.
- IT plastic tarpaulins for acute phase
- House spraying (IRS) for epidemics
- ITN in chronic emergencies and post conflict conditions

- Cost per person protected per year is:
  - ITN $1.5 in first year, $0.25 thereafter
  - IT blankets $0.25 (cost of blankets excluded)
  - IRS $0.5
  - Tent spraying $0.25
Surveillance 1

• Main risk factor that triggers epidemics:
  – Migration of non-immunes to an area with transmission
  – Creation of local breeding sites

• Passive surveillance through clinics
  – may spot epidemics initially,
  – monitoring progress of epidemic or control intervention.

• Cross sectional community surveys (all age groups) to monitor the course of the epidemic (prevalence - % positive)
  – Blood smears and microscopy
  – Rapid diagnostic tests v useful
**Surveillance 2**

- Important information to mount epidemic response
  - Species of malaria,
  - Transmission local or imported? (survey women & children – less mobile)
  - Seasonal transmission?
  - Mortality & morbidity rates (number with fever, confirmed malaria, severe malaria, deaths)
  - Active surveillance to confirm epidemic: cross sectional parasites surveys - use RDTs if microscopy unavailable
  - Drug resistance and % treatment failures
  - Passive surveillance (clinic based): number or proportion of fever due to malaria
  - Management (health staff expertise, availability of drugs)
  - Vector species and breeding sites
Epidemic response

- Active case detection or mass treatment of fever cases by mobile teams:
  - use RDTs and combination therapy
  - monitor trends using RDT or slide positivity
- Passive case detection at clinics is not adequate response to an emergency.
- Vector control and personal protection
  - ITN (delays, bulky, behavioural change? Cost?)
  - Not space spraying or aerosoling (anophelines fly at night)
  - Permethrin/DEET treated blankets or top sheets
  - pyrethroid treated tents or ITPS
  - Indoor spraying if houses and vectors feed/rest indoors
**Coordination**

- **Organisational framework**
  - UN umbrella or NGO coordination body.
  - Functions
    - improve efficiency
    - prevent duplication of activities
    - common logistic systems
    - negotiation with authorities
- **Division of responsibility**
  - NGO responsibility for specific area and running PHC services
  - NGO may specialise in malaria: advice, commodities, training, research, monitoring and evaluation for other agencies in malaria control
Research needs in complex emergencies

• Pregnancy
  ° Presumptive intermittent treatment - which drug or combinations?
• Vivax chemotherapy and radical cure
  ° New treatment regimens: 14 day or weekly primaquine
• Vector control
  ° Further studies of ITPS (plastic sheeting)
  ° Trials of ITPS with insecticide treated blankets in acute phase
  ° Repellents – easy to distribute but would they be used to good effect
Improving standards

- Malaria control in complex emergencies – an interagency field handbook (2005)
- How to
  - assess malaria in emergencies,
  - plan and implement responses (surveillance, diagnosis, case management, prevention, operational research, evaluation)
- Download from RBM website (www.who.int)