Antimalarial drugs and diagnostic testing in the era of subsidies: multi-country findings

Stephen Poyer and Benjamin Palafox, on behalf of the ACTwatch Group
Presentation outline

• Overview of ACTwatch and methods

• Overview of multi-country results

• Country examples
  - Nigeria
  - Cambodia

• The future
ACTwatch: the original 7 countries

Objective
Provide policy makers with evidence on trends in availability, price, and use of antimalarials

Partnership
PSI, LSHTM and MoHs

5 year, 7 country project
Funded by the BMGF
3 Research components provide a comprehensive picture of the market

Outlet Survey (PSI)
What are the trends in the availability, market share and price of antimalarials?
- Trend data over the life of project

Household Survey (PSI)
What are the trends in the levels of use of different antimalarials. What are the determinants of use?
- Twice over the life of project (baseline and endline)

Supply Chain Research (LSHTM)
How is the private distribution chain structured? Wholesaler & market characteristics, mark-ups?
- Once over life of project
Outlet survey methods

- Clusters randomly selected proportional to population size
- Census of all outlets with the potential to stock antimalarials
- Over-sampling of public health facilities and pharmacies
- Audit of all antimalarials in stock:
  - generic name - brand name – formulation – strength - expiry date
  - price - volume (quantity) dispensed in the last 7 days
- Availability of diagnostic testing captured (RDT/microscopy)
- Data survey set and weighted to provide nationally representative estimates

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Household survey methods

- Cross-sectional household surveys
- Stratified multi-stage cluster samples
- Households nested within clusters selected for the outlet surveys
- Households with at least 1 child under 5 with fever in the last 2 weeks
- Caregivers of all eligible children invited to participate
- Data survey set and weighted for national estimates
Supply chain: Quantitative survey methods

- **Sampling frame** of wholesalers created by tracing the distribution chain starting from the bottom and working up:
  - From the outlet survey obtained name and address of top 2 antimalarial suppliers (terminal wholesalers)
  - Terminal wholesalers identified and interviewed and obtained name and address of top 2 antimalarial suppliers (intermediate wholesalers)
  - Process repeated with intermediate wholesalers, and so on, until top of the chain is reached

- **Data**:
  - From each wholesaler: business characteristics, licensing & regulation, audit of each antimalarial and RDT in stock and wholesale mark-ups
  - From the outlet survey: retail mark-ups
Supply chain: Qualitative methods

- Key Informant Interviews (KII) with public and private sector stakeholders situated at the top of the supply chain
  - identified through a comprehensive review of relevant documents and through consultation with actors familiar with the country’s supply chain

- In-Depth Interviews (IDI) with a sub-set of antimalarial providers sampled for the quantitative survey
  - Conducted at various levels of the supply chain (retail to the top of the supply chain), and across various settings (urban, rural, accessible, remote)

- Topics: Structure and composition of antimalarial and RDT supply chains; provider conduct (delivery, credit, marketing techniques, prices setting, stocking and supplier choices); perceptions of regulations; cost structure
ACTwatch methods used in 13 countries

* As part of Independent Evaluation of the AMFm
Additional funds from Global Fund

Ghana, DNDi/KATH; Niger, CRDH; Tanzania, IHI
Multi-country results
Diversity of outlet types with antimalarials in stock

Nigeria (n=2,113)

Benin (n=844)

DRC (n=1,375)

Madagascar (n=2,414)

Uganda (n=2,497)

Zambia (n=435)

Data from 2009/2010 outlet surveys
Diversity of outlet types with antimalarials in stock

- **Nigeria** (n=2,113)
- **Benin** (n=844)
- **DRC** (n=1,375)
- **Madagascar** (n=2,414)
- **Uganda** (n=2,497)
- **Zambia** (n=435)

Data from 2009/2010 outlet surveys
The private sector’s dominant role

Relative volume of antimalarials sold in the last 7 days in public/not for profit and private for-profit sectors (2011)

DRC data from 2009
Private sector availability of antimalarials

Availability of different antimalarial classes among private-sector outlets stocking antimalarials (2011)

In Cambodia, the quality assured ACT category shows Any ACT

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## Variation in regulatory compliance by wholesalers (2009-2010)

<table>
<thead>
<tr>
<th>% of wholesalers that... (N)</th>
<th>Benin</th>
<th>Cambodia</th>
<th>DRC</th>
<th>Nigeria</th>
<th>Uganda</th>
<th>Zambia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Employed a staff member with health-related qualifications</td>
<td>28.7 (142)</td>
<td>63.4 (93)</td>
<td>92.8 (138)</td>
<td>62.8 (137)</td>
<td>100.0 (128)</td>
<td>97.6 (42)</td>
</tr>
<tr>
<td>Any up-to-date pharmacy license from the DRA was observed</td>
<td>0.9 (196)</td>
<td>29.5 (95)</td>
<td>19.9 (136)</td>
<td>8.7 (138)</td>
<td>82.0⁺ (128)</td>
<td>70.0 (40)</td>
</tr>
<tr>
<td>Reported they had been visited by an inspector in the past year</td>
<td>15.2 (189)</td>
<td>82.4 (91)</td>
<td>94.2 (138)</td>
<td>71.2 (132)</td>
<td>99.2 (123)</td>
<td>97.5 (40)</td>
</tr>
</tbody>
</table>

⁺ In Uganda this includes wholesalers who had a recently valid pharmacy license (i.e. Expired Nov or Dec 2008) as licences for 2009 were still being processed by the authorities at the time of data collection.
Diagnostics in the private for-profit sector

Availability of RDTs at the retail level (2011) and availability and sales volumes of RDTs among private sector wholesalers (2009-2010)

<table>
<thead>
<tr>
<th>Characteristic: Outlet/retailer RDT availability [%]</th>
<th>Benin</th>
<th>Cambodia</th>
<th>DRC</th>
<th>Nigeria</th>
<th>Uganda</th>
<th>Zambia</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1.1 (1079)</td>
<td>34.0 (777)</td>
<td>6.8* (1270)</td>
<td>1.4 (1415)</td>
<td>9.3 (2397)</td>
<td>9.3 (565)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Characteristic: Wholesaler RDT availability [%]</th>
<th>Benin</th>
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<th>Zambia</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>4.4 (204)</td>
<td>86.3 (95)</td>
<td>2.2 (138)</td>
<td>3.6 (138)</td>
<td>18.0 (128)</td>
<td>23.3 (43)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Characteristic: Wholesaler RDT sales volumes [median/week]</th>
<th>Benin</th>
<th>Cambodia</th>
<th>DRC</th>
<th>Nigeria</th>
<th>Uganda</th>
<th>Zambia</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0 (201)</td>
<td>0 (93)</td>
<td>0 (137)</td>
<td>0 (136)</td>
<td>0 (127)</td>
<td>0 (40)</td>
</tr>
</tbody>
</table>

* Data for DRC collected in 2009
Treatment-seeking behaviour for children with fever

Percentage of children under five with fever in the past two weeks who received an antimalarial, an ACT, a prompt ACT, and a diagnostic test (2010/2011)
Focus on Nigeria
Nigeria: country profile

Population: 158M
25% of malaria cases in Africa
Mainly *P. falciparum*
Oral artemisinin monotherapy controls introduced in 2006
Major external financing: WB, PMI, DFID & GF
AMFm phase 1 pilot country
# Nigeria: ACTwatch timeline

## Outlets

<table>
<thead>
<tr>
<th>Year</th>
<th>Period</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>2009</td>
<td>Sep/Oct</td>
<td>6,089 outlets approached, 2,210 met criteria</td>
</tr>
<tr>
<td>2011</td>
<td>Oct/Nov</td>
<td>8,507 outlets approached, 1,567 met criteria</td>
</tr>
</tbody>
</table>

## Households

<table>
<thead>
<tr>
<th>Year</th>
<th>Period</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>2009</td>
<td>Aug/Sep</td>
<td>4,649 households approached, 2,860 met criteria</td>
</tr>
<tr>
<td>2012</td>
<td>June/July</td>
<td>8,258 households approached, 1,312 met criteria</td>
</tr>
</tbody>
</table>

## Supply Chain

<table>
<thead>
<tr>
<th>Year</th>
<th>Period</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>2009</td>
<td>July/Aug</td>
<td>Quantitative: 140 wholesalers interviewed, Qualitative: 9 key informants and 30 in-depth</td>
</tr>
</tbody>
</table>

*1st AMFM drugs arrived in-country Jan 2011*
A complex and competitive supply chain

- Considerable domestic manufacturing capacity
- Sophisticated business practices
  - diverse marketing practices
  - vertically integration
  - specialised logistics companies
- Unlicensed wholesaling is also common
  - PPMVs in traditional markets

Traditional markets are key centres for both the wholesale and retail of antimalarials

Data collected in 2009
Availability in PHFs and the private sector

Availability of different antimalarial classes by sector, 2009 and 2011

*Among outlets stocking at least one antimalarial drug
Availability in PHFs and the private sector

Availability of different antimalarial classes and RDTs by sector, 2009 and 2011

* Among outlets stocking at least one antimalarial drug
1 in 3 private sector outlets continue to stock oral artemisinin monotherapy

Availability of oral artemisinin monotherapy in private sector outlets with antimalarials in stock, 2009 and 2011

<table>
<thead>
<tr>
<th>Type</th>
<th>Private For Profit</th>
<th>Pharmacy</th>
<th>Drug Store (PPMV)</th>
<th>General Retailers</th>
<th>Itinerant Drug Vendor</th>
<th>Total Private</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>358/88</td>
<td>403/37</td>
<td>990/1163</td>
<td>103/64</td>
<td>10/28</td>
<td>1864/1380</td>
</tr>
<tr>
<td>2009 Percentage of outlets</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Private For Profit</td>
<td>53</td>
<td>18</td>
<td>47</td>
<td>34</td>
<td>19</td>
<td>46</td>
</tr>
<tr>
<td>Pharmacy</td>
<td>97</td>
<td>100</td>
<td>36</td>
<td>19</td>
<td>17</td>
<td>35</td>
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<tr>
<td>Drug Store (PPMV)</td>
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</table>

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Nigeria 2009 & 2011 Outlet Survey Results
Which outlets are selling/distributing what types of antimalarials?

Market share of adult equivalent treatment doses (AETDs) of antimalarials sold/distributed in the past 7 days (2011)

- Private health facilities
- Pharmacies
- Drug shops (PPMVs)
- General retailers
- Itinerant drug vendors
Which outlets are selling/distributing what types of antimalarials?

Market share of adult equivalent treatment doses (AETDs) of antimalarials sold/distributed in the past 7 days (2011)

- Public/Not for Profit Sector
- Total Private

- Quality-assured ACTs
- Non quality-assured ACTs
- Non-oral artemisinin monotherapy
- Oral artemisinin monotherapy
- Non-artemisinin therapy

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Which outlets are selling/distributing what types of antimalarials?

Market share of adult equivalent treatment doses (AETDs) of antimalarials sold/distributed in the past 7 days (2011)
What antimalarials do children receive?

Proportion of children under five who received a given antimalarial class, among children who received an antimalarial, 2011 (n=565)

- Non-artemisinin therapy: 69%
- Chloroquine: 55%
- Any ACT: 30%
- Artemisinin monotherapy: 6%
Focus on Cambodia
Cambodia country profile (2011)

Very low transmission

*P.f.* 1st line: DHA-Pip (zone 1), AS+MQ

ACT & RDT private sector subsidy since 2004

CNM – Designated Three Zones:

- **Zone 1** Containment Program
- **Zone 2** [2½ years – BMGF]
- **Zone 3** “No Zone”

Dynamic policy/strategy environment aimed at containing drug resistance
**Cambodia: ACTwatch timeline**

**ACT and RDT subsidy since 2004**

<table>
<thead>
<tr>
<th>Year</th>
<th>Outlet</th>
<th>Household</th>
<th>Supply chain</th>
</tr>
</thead>
<tbody>
<tr>
<td>2008</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>2009</td>
<td>Outlet</td>
<td>Household</td>
<td>Supply chain</td>
</tr>
<tr>
<td></td>
<td>2009: June/July</td>
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<tr>
<td></td>
<td>7,833 outlets approached</td>
<td>22,371 households approached</td>
<td>Quantitative: 95 wholesaler interviews</td>
</tr>
<tr>
<td></td>
<td>1,019 outlets met screening criteria</td>
<td>1,465 households met screening criteria</td>
<td>Qualitative: 19 semi-structured interviews</td>
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<td>2011: June/Aug</td>
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<td>18,584 outlets approached</td>
<td>20,895 households approached</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1,529 outlets met screening criteria</td>
<td>1,013 households met screening criteria</td>
<td></td>
</tr>
<tr>
<td>2011</td>
<td>Outlet</td>
<td>Household</td>
<td>Supply chain</td>
</tr>
<tr>
<td></td>
<td>2011: Nov/Dec</td>
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<td></td>
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<tr>
<td></td>
<td>20,895 outlets approached</td>
<td></td>
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<tr>
<td></td>
<td>1,013 outlets met screening criteria</td>
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</table>
What do people initially do when they think they have malaria?

- **Take some action at Home**: 54%
- **Do nothing**: 4%
- **Private Sector**: 33%
- **Public Facility**: 9%
- **Village Malaria Worker**: <1%

80% of people who initially seek treatment outside the home go to private sector.
Do initial actions differ by containment zone?

Zone 1
(n=491)

- Private facility: 20%
- Village Malaria Worker: 7%
- Public health facility: 3%
- Took some action at home or did nothing: 20%

Zone 2
(n=318)

- Private facility: 31%
- Village Malaria Worker: 2%
- Public health facility: 6%
- Took some action at home or did nothing: 31%

Zone 3
(n=203)

- Private facility: 33%
- Village Malaria Worker: 9%
- Public health facility: 9%
- Took some action at home or did nothing: 33%
What antimalarials did patients find in retail outlets in 2011, compared with 2009?

Availability of different antimalarial classes among outlets with antimalairals in stock, by sector in 2009 and 2011

Cambodia 2009 & 2011 Outlet Survey Results
...and which antimalarials are outlets selling?

Availability of different antimalarial classes among outlets with antimalairals in stock, by sector in 2009 and 2011

- ASMQ
- Other ACT
- Oral artemisinin monotherapy
- DHA+PPQ
- Non-artemisinin therapy
- Non-oral artemisinin monotherapy

Cambodia 2009 & 2011 Outlet Survey Results
Household survey data show a more complicated picture

Proportion of people who received antimalarial and/or cocktail treatment among those reporting they had malaria fever, 2011
What are ‘cocktails’?

- Typically contain 3-7 drugs
  - antipyretics, antihistamines, caffeine, vitamins, antibiotics
  - Not all contain antimalarials (quinine, chloroquine, artesunate)
- Made-to-order by dispenser, but also sold by wholesalers
- Patients often unaware contents

For retailers, the provision of cocktails was:
- More profitable than selling only other drugs
- Reflection of expertise and quality of treatment delivered

“Multiple symptoms require multiple medicines”
Diagnostic testing: are tests available?

Availability of any diagnostic test among outlets with antimalairals in stock in the past three months, (2011)

Although RDTs were available in many private businesses and perceived as easy to use, they were also considered less precise than microscopy and as not adding value to the services and products being offered.
Diagnostic testing: are patients being tested?

Proportion of people with *malaria fever* who report receiving a diagnostic test, by containment zone (2011)

Overall 44% of people with malaria fever were tested. 65% reported receiving an RDT; 27% reported microscopy; 12% couldn’t recall the type of test.
Impact and Future

Household survey, Uganda, 2012
Prompt parasitological confirmation by microscopy or by RDTs is recommended in all patients suspected of malaria before treatment is started.
Past and projected international funding for malaria control

Source: WHO World Malaria Report 2011
Acknowledgements

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Members of the ACTwatch Advisory Committee

- Mr. Suprotik Basu
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