Describing the prices and market of anti-malarial medicines in Uganda

Study protocol

CONTENTS

Background and rationale

Objectives

Study Design

Study population, sample size, selection criteria

Data collection procedures, instruments & quality control

Data management and analysis

Ethical considerations

Study Protocol prepared by Martin Auton

For further information, contact

Renia Coghlan
Associate Director Global Access
Medicines for Malaria Venture
coghlanr@mmv.org

Martin Auton
Consultant, Management of Medicines
martinauton@mail.com

BACKGROUND AND RATIONALE

Medicines for Malaria Venture (MMV) is a public-private partnership whose mission is "to discover, develop and deliver new anti-malarial drugs through effective public-private partnerships". MMV has recently expanded its work from R&D to include access (post-registration delivery activities). MMV is "working with the Ministry of Health of Uganda and other stakeholders to ensure that strategies for improving access in the private sector are put in place….including the role of subsides in improving access in the private sector; how to deliver subsidised drugs to the rural poor; how to ensure sustainability and that any subsidy is not eaten up by the middle men and women."[1]

In order to design a program to improve the access to affordable and effective antimalarial medicines, baseline information regarding the demand (price, affordability, range and volumes) and the distribution network (outlet type and supply chains) of manufactured[2] antimalarial medicines in retail outlets/health facilities (public/private; formal/informal) is needed to assist in the determination of efficient channels of drug distribution, and the approach to achieve greatest accessibility and affordability of antimalarial medicines including new medicines coming to market in the next few years. This approach can then also be modified to monitor the scale up of Artemisinin Combination Therapies (ACT); extent of the presence of non-recommended antimalarials including monotherapy artemisinins on the market; as well as monitoring the effects of, and the interactions of, the launch of new medicines, the implementation of new malaria treatment policies, and price changes; especially any unintended consequences that may impact of the affordable access to effective antimalarial medicines.

It is intended gather solid baseline information systematically across a number of endemic countries in Africa starting with Uganda. Additionally in Uganda a more intensive study, with some additional aspects will be performed to act as a baseline in three districts of Uganda to monitor the implementation of interventions intended to (responsibly) improve access to subsidised ACT through retail outlets and to define the minimum package for subsidised ACTs (to facilitate scale-up).

The Uganda study will:
- Map the distribution channels for antimalarial medicines
- Describe price, affordability and availability data across a range of retail outlets/facilities (public/private; formal/informal); as well as at different stages of the supply chain
- Map all outlets selling antimalarial medicines in three areas (districts/counties/sub-counties) – where are they? What do they sell?

Separate, but related studies will:
- Present information on volumes and ex-factory prices of imported and locally manufactured medicines using National Drug Authority import approval data and information from local manufacturers to estimate the total number of courses of therapy as well as relative market share
- Describe health seeking and consumption behaviour through household surveys

The study will complement previous and ongoing studies and activities related to medicines prices being carried out by the Ministry of Health in collaboration with the World Health Organisation and HEPS, Uganda[3]. It also complements the (very) rapid assessment carried out by Dalberg Global Development Advisors in February 2006, by investigating price, affordability, availability and market situation in a systematic manner throughout the country including rural areas.

---

[1] Speech of the Minister of Health, Stakeholders Meeting on Improving Access to Artemisinin-based Combination Therapy (ACT) in the Informal Private Sector in Uganda; 20 February 2007
[2] Manufactured medicines as opposed to medicines prepared for example by traditional healers
[3] http://www.heps.org/

The proposed approach is an adaptation of the WHO/HAI Medicines Prices Methodology[4] after consideration of the objectives of MMV and the Ministry of Health of Uganda; and methods used in previous studies on the antimalarial medicines market. This has resulted in some modifications and the expansion of some aspects of the methodology especially with respect to the number and types of sectors sampled.

OBJECTIVES

The principal objective of the study is to understand the "supply-side" of the manufactured[5] antimalarial medicines market through characterisation of antimalarial outlets:
- public, private, formal, informal'
- mapping using GIS coordinates
- range of products (malaria and others)
- prices
- product flows
- sources of information

The survey will give insight into the antimalarial market to inform on the design of the MOH intervention and collect baseline information regarding the demand and the distribution network of antimalarial medicines in retail outlets/health facilities (public/private; formal/informal) to assist in the determination of efficient channels of drug distribution, and the approach to achieve greatest accessibility and affordability of antimalarial medicines including new medicines coming to market in the next few years. Specifically providing answers to the following questions:

Primary objectives
- What are the types, formulations and brands of antimalarial medicines are available for sale?
- What types of outlets are selling antimalarial medicines?
- What are the relative costs of different antimalarial medicines?
- How affordable are the different antimalarial treatments?
- What are the best selling[6] antimalarial medicines?
- What are the components of the final price – what are the factors that impact on the final price? (including manufacturing, wholesale and retail components)
- What guides which antimalarial medicines are stocked and which are sold by the various outlets?
- What proportion of outlets per sector stock the recommended first line treatments?
- Where do providers obtain their supplies of medicines?

Secondary objectives
- What is the overall product mix of other commodities sold at the various types of outlet?
- Are the antimalarial medicines displayed on open display?
- Are there expired antimalarial medicines on the shelves?
- Are the medicines stored appropriately?
- Do customers ask for antimalarial medicines by name or ask for a recommendation for something for fever/malaria?
- Which medicines do the outlets recommend for customers with fever/malaria? (anti-pyretics, antimalarials or other medicines) How much would a "package" of treatment cost?
- To what proportion of customers are incomplete courses of antimalarial medicines sold?
- Are there advertising materials for antimalarial medicines displayed in facilities/outlets?

---

[4] http://www.haiweb.org/medicineprices/
[5] Manufactured medicines as opposed to medicines prepared for example by traditional healers
[6] By volume

- What information sources and where do the outlets obtain information about the antimalarial medicines stocked
- What are the legal restrictions for commonly used malaria medicines?

STUDY DESIGN

There are 5 aspects to the study which are a mixture of quantitative and investigative descriptive (qualitative) approaches:

1. Collating relevant information on the medicines and malaria situation in Uganda

Relevant information on the medicines and malaria situation in Uganda will be collated and documented.

2. Developing a map of the distribution channels for antimalarial medicines

A descriptive as well as diagrammatic representation of the flow of medicines in the public/private; formal/informal sectors will be developed from reference materials and through interviews with key informants.

3. Locating retail outlets selling antimalarial medicines

In the MOH (access) intervention and control geographic areas, all outlets selling antimalarial medicines will be located and described. The information will be presented descriptively and through GPS/GIS[7] spatial maps.

4. Measuring medicine prices and availability; collating other relevant information at the outlet level

Data collectors will collect information on the price and availability of medicines; additionally information on the management and sources of medicines will be collected.

5. Collating information on the components of the prices of selected antimalarial medicines

Interviews with key informants will be used to determine the components of the price the patient paid in different sectors including the manufacturer's selling price and amongst others costs for freight, import tariffs, taxes, mark-ups, distribution and dispensing fees. This aspect will be carried out after the preliminary analysis of the data from the preceding items as these will inform on the approach.

Timing

As the moderate/high transmission areas in Uganda do not have significant periods of time with lower levels of malaria, it can be expected that outlets stock medicines for malaria year round, therefore the timing of the survey should not be influenced by season.

Personnel

The survey will require the involvement of the following personnel: survey coordinator, survey manager, task force, area supervisors, data collectors and data entry personnel. The role of the task force regarding this study is particularly important to add local knowledge to the survey planning and interpretation in:
- Advising on the sectors and medicines to be surveyed
- Advising on any matters that arise during survey preparation, data collection and data analysis, including how to solve any problems that may be encountered
- Reviewing the survey report and making recommendations on policy options and possible lines of action

---

[7] GIS = Geographic Information System

The preliminary findings and analysis should be presented to a wide stakeholder group for their buy-in and inputs to the final report, findings and recommendations.

Details of the role and characteristics of the other personnel can be found in annex 1.

STUDY POPULATION, SAMPLE SIZE, SELECTION CRITERIA

1. Collating relevant information on the medicines and malaria situation in Uganda

The WHO/HAI Medicines Prices National Pharmaceutical Sector Form[8] will be adapted as a tool to collate secondary background information on national malaria and medicines policies, previous related studies (especially treatment seeking behaviour studies), medicines procurement and distribution in the government and private sectors, antimalarial medicines registered in the country, legal levels of use of each antimalarial; information on the financing of medicines and other relevant information. A preliminary compilation can be found in annex 2.

2. Developing a map of the distribution channels for antimalarial medicines

Information will be collated from reference sources and interviews with key informants.

3. Locating retail outlets selling antimalarial medicines

In three geographic areas, data collectors, ideally from the same or close-by locality being studied will use existing lists of health facilities, pharmacies and "drug shops", as well as interviews on arrival with the village leader and other informants in the locality to find all outlets and persons selling medicines. The three geographic areas will be selected by the Ministry of Health (MOH) as intervention (2) and control (1) areas for the implementation of interventions intended to (responsibly) improve access to subsidised Artemisinin Combination Therapy. These three areas were selected according to a number of criteria including: being areas of high transmission, have no shared border with other countries, have no other pilots occurring, have mapped malaria dynamics, and have efficacy data available.

The three district/district groupings selected are in the Eastern Region of Uganda: Palisa/Budaka; Kamuli/Kaliro and Soroti. Within these district grouping, 20 parishes plus the parishes of the district capital (Town Council or Municipality) will be sampled

Sampling will be carried out in collaboration with the health seeking behaviour household survey. In that survey 40 parishes will be selected using probability proportional to size using population census data for each of the 3 district groupings.

For the pricing and market outlet survey, the parishes of the district capital will be purposively selected plus 20 other parishes randomly selected from the list of 40 sampled for the household survey. This will allow some analysis of health seeking behaviour to be made with the pricing and market data from the outlets in those same areas.

In the pricing and market outlet survey, all outlets in those parishes will be identified and visited and GIS coordinates collected and the prices and other details measured as described below.

4. Measuring medicine prices and availability; collating other relevant information at the outlet level

The ideal national survey would collect data from a large number of health facilities and other medicine outlets scattered around the country. However this would require a great deal of time and resources. To make the survey feasible, therefore, it is based on small samples of geographic areas and medicine outlets. Bias from the small sample is minimise by careful survey design by minimising amendments to tried and tested methodology (WHO/HAI

---

[8] http://www.haiweb.org/medicineprices/manual/NationalPharmaceuticalSectorform.doc

Medicines Prices Methodology) and by careful sampling, these study sites can adequately represent the situation in the country as a whole.

In total 6 geographic areas will be surveyed as part of a national survey of pricing and availability of antimalarial medicines; 3 of the areas will be those described above in as MOH intervention/control districts; the other 3 districts will be selected according to criteria described below to complement a present the national situation of areas with moderate/high transmission of malaria.

Described below (in the following order) are:
- Identification of sectors
- Sample size
- Selecting geographical areas
- Selection of outlets
- Selection of medicines to be studied

5. Collating information on the components of the prices of selected antimalarial medicines

The information will be collated from reference sources and interviews with key informants based on the findings in items 1-> 4 above. Interviews with different key informants will be used to validate the information obtained. WHO/HAI is in the late stages of re-fining the methodology to better describe the components of the final patient price for a medicine. MMV should seek permission to utilize the new methodology. The components study will be carried out after the main survey by a separate small team of data collectors and should include examination of the data on "FOB[9]" prices held at the National Drug Authority.

Identifying the sectors

One key issue in planning of the study is to decide is which and how many sectors to include in the survey. Each sector represents a conceptually different source of medicines or prices to be assessed and compared, a fuller background describing a wide generic categorisation of sectors can be found in annex 1.

For practical logistical reasons of data collection and data entry; as well as to not overcomplicate the data analysis, a national survey should try to limit the number of distinct sectors to eight[10]; although more than six could be accommodated with some extra resources.

Once the conceptual sectors are selected, they need to be characterised to assist the data collectors to assign each outlet a designation.

For Uganda it is proposed to study:

Public sector
1. Public health facility patient prices and Government procurement prices
2. Community-directed distributors[11]

Private sector
3. Retail pharmacies[12]
4. Drug shops[13]
5. Private clinics/dispensing doctors[14]

---

[9] Free-on-board; http://www.iccwbo.org/incoterms/id3045/index.html?cookies=no

[10] The revised standard WHO/HAI medicines prices surveys survey the patient prices for up to four sectors; the workbook facilitates the analysis of 4 sectors. A maximum of eight sectors is to enable the analysis to be manageable using no more than 2 workbooks.

[11] Community-directed distributors distribute HOMEPAK as part of Home Based Management of Fever/Malaria - pre-packaged unit doses with a combination Sulphadoxine/Pyrimethamin (SP) and Chloroquine (CQ) are administered to all febrile children by Community-directed distributors; there are pilots where the SP/CQ is being replaced by ACTs

[12] Licensed –using a list of licensed premises or license being produced - unlicensed will be treated as a retail

[13] Licensed –using a list of licensed premises or license being produced - unlicensed will be treated as a retail

6. Retail stores and general provisions stores/ kiosks (fixed structures)

7. Market stalls/mobile hawkers and other informal distribution points (temporary structures/mobile)

Not-for profit sector

8. NGO/mission health facilities and Joint Medical Stores procurement price

Sample size

The standard WHO/HAI methodology now[15] recommends that there are 30 outlets per sector for a survey to achieve enough data points for analysis; this is normally 5 outlets per sector in each of 6 geographic areas across a country.

a) Intervention/control districts for ACT access interventions

For each the three geographic areas selected by the Ministry of Health as intervention (2) and control (1) areas for the implementation of interventions, a "full survey" needs to be carried out with at least the minimum sample size - to allow each of the 2 intervention districts to be compared with the control district. As it is the intention to perform a census and to spatially map all the outlets in a given area, all of the outlets in a sector should be surveyed.

Sampling will be carried out in collaboration with the health seeking behaviour household survey. In that survey 40 parishes will be selected using probability proportional to size using population census data for each of the 3 district groupings.

For the pricing and market outlet survey, 20 parishes will be parishes randomly selected from the list of 40 sampled for the household survey; in addition any other parishes that are part of the district capital which have not been randomly selected will be added to the 20 parishes studied. This will allow some analysis of health seeking behaviour to be made with the pricing and market data from the outlets in those same areas.

It is intended to achieve around 30 outlets per sector (for at least for the most important sectors) so that there are sufficient data points for analysis. It is likely that there will be many more shops and vendors selling medicines than there are public health facilities and licensed pharmacies/drug shops and hence as long as all the outlets within these areas are visited, then 30 need not be achieved per area where 30 do not exist.

b) The three other geographic areas

For the national survey, the WHO/HAI methodology recommends that 30 outlets per sector are required; this being 5 outlets in each of 6 geographic areas.

As the data from 5 facilities per sector in each of the 3 geographic areas (total 15 per sector) described in the intervention control districts [a) above] can be utilised, an additional 15 facilities per sector should be selected from the 3 other geographic areas selected (5 outlets/sector/geographic area); in order to better describe the diversity and represent the urban poor of Kampala, 10 outlets per sector will be surveyed. The criteria of which outlets to select in all 6 districts will be the same, as described below.

Wholesale sources[16]

---

[14] There is a significant number of retail stores run as private clinics, many of which appear analogous to drug stores. Licensed –using a list of licensed premises or license being produced - unlicensed will be treated as a retail

[15] Revised approach for 2007 Manual (not yet in published)

[16] Wholesale sources mean any business that is operating as a "wholesale" business selling products in bulk to retailers for onward sale to customers. It may be identified in the mapping of the supply chains that some retailers obtain their supplies from normal retail outlets – whilst this is relevant for the mapping of supply chains, it is not considered as a wholesale sector in terms of measuring prices and availability.

A question will be asked of retail outlets as to whether they sell medicines on a "wholesale" basis. As part of the components study, the supply chain including the wholesale sector will be investigated; information of sources collecting during the main data collection will inform the components study.

Selecting geographical areas

National procurement price data can usually be collected centrally from the office of the procurement officer or central medical stores; likewise for the NGO/mission sector. Data on patient prices and availability are obtained by data collectors in the field. Data will be collected in a systematic way in order to ensure that the findings are representative of the country or region in which the survey is being conducted.

The sampling approach will be select six geographical areas (districts) of the country and then at least five outlets selected from each of these (more in the intervention/control districts).

Three of the geographic areas will be selected based on being intervention/control districts for the MOH access intervention work. The three district/district groupings selected are in the Eastern Region of Uganda: Palisa/Budaka; Kamuli/Kaliro and Soroti.

The other three should be selected as described below, whilst at the same time considering the inclusion of the characteristics of the three pre-selected districts already selected:

Below are some criteria for selecting the six geographic areas, not necessarily in the order of consideration and their inclusion/exclusion may depend upon the precise aims of the study:

- If there are varying conditions in different parts of the country that may influence the way malaria medicines are managed or used - e.g. high, moderate and low transmission areas; malaria endemic, non-endemic, areas with seasonal transmission, areas with different first line drugs. – in which case organise the geographic areas into groups and select the study areas from these

- If the country is relatively homogeneous, geographically and epidemiologically, simply choose the capital city/ main population centre and the other geographical areas randomly

- The capital city and the main population centre (if different) should be selected (unless for example, the survey is restricted to presenting the situation in rural communities)

- Urban/peri-urban/rural distribution representing the national situation – in which case organise the geographic areas (e.g. districts) into groups and consider whether the areas selected reflect the urban/peri-urban/rural split

The three other districts selected to complement the intervention control districts were selected by the MOH as Kampala, Kabarole and Apac.

Characteristics for national survey

	Intervention/control district/district groupings	"Other" districts
Capital city		• Kampala
Northern		• Apac
Eastern	• Palisa/Budaka • Kamuli/Kaliro • Soroti	
Southern		
Western		• Kabarole

Selecting outlets

For the three intervention/control studies, the parish containing the district capital plus 20-30 parishes will be selected from each district by probability proportional to size sampling using population census data- all outlets will be studied as part of the approach in each of the parishes selected.

For the national study for each of the other three districts (non intervention/control districts), five outlets per sector will be surveyed.

The same criteria will be used to select which outlets' data to include in the national study dataset from the intervention/control studies. If the selection process yields areas or outlets not studied, the nearest one should be selected.

Lists of public health facilities, pharmacies and licensed drug shops have been obtained and prepared for the data collectors at the central level; however, accurate lists of other retail outlets probably do not exist and the sample frame may need to be compiled in the field.

<u>Selecting public sector facilities</u>

For convenience, public health facilities are used to anchor the sample, with other types of medicine outlet chosen by their proximity to these facilities. From a list of all public health facilities in each survey area that are within a 3 hours drive[17] of the main government health facility in that district.

Most countries have several levels of facilities, from hospitals down to health centres or dispensaries. Lower level facilities are often more widely dispersed than upper level ones. Generally, both upper and lower level facilities should be included if they are expected to stock most of the medicines included in the study.

- Choose at least five public health facilities in each survey area, as follows.
- Select the main public hospital[18] in the area (outpatient/primary health care services, not inpatient or specialist clinics). If there is more than one "main" facility, select randomly.
- Select four facilities from the ones remaining on your list:
- If there is only one level of facilities on the list, choose four at random
- If there are two or more levels on the list: divide the list by level and select 4 facilities proportionally across those levels
- If there are fewer than two facilities on any list, increase the number selected from the other lists accordingly
- If there are fewer than five public health facilities in any of the administrative areas chosen for the survey, extend the lists to include the closest facilities in a neighbouring area.

- Select an additional 2 public medicine outlets in each survey area, as back-up outlets in case you fail to access any of the public facilities[19]. For each public medicine outlet in the sample, select the nearest public medicine outlet for use as a back-up outlet. To the extent possible, back-up outlet should represent the same level of care as the sample outlet.

<u>NGO/mission health facilities</u>

The same process above can also be followed for the mission sector.

<u>Selecting other medicine outlets</u>

In the standard WHO/HAI methodology, all the other medicine outlets are sampled by their proximity to the public health facilities selected. In this study, it is intended to go further into the rural areas and to the informal sector which poses challenges to this approach. In this study, for each sector:

- Construct a sample frame by listing all possible providers/outlets/trading centres- to be included in the survey in each survey area that are within a 3 hours drive[20] of each public health facility selected[21]; then select 5 randomly; this may cover the whole district.

---

[17] WHO/HAI standard methodology

[18] Other than the outpatient department at the main hospital in each geographic area – if hospitals are important, then hospitals should be treated as a separate sector

[19] In the standard WHO/HAI methodology, a back-up facility is used to collect price data if <50% medicines on the list are available. For the malaria medicines study, it is not desirable for the outlets to stock all the antimalarial medicines and hence these criteria wouldn't make sense.

[20] The standard WHO/HAI methodology takes the closest private pharmacy or other outlet to the public health facility

- For some sectors such as a licensed sector, this may be relatively easy by obtaining the list of registered premises – for others there will probably be no list. Lists should be updated by the area supervisor from their local knowledge and from enquiring from local informants; then select 5 randomly. The local parish administrative council will be able to provide guidance on the identification of trading centres within the parish where it would be expected that there is a concentration of business outlets.
- For sectors in relatively well defined and small localities where it is relatively easy to construct a list of outlets by asking local informants, then such a list should be constructed; then select 5 randomly
- For a sector where a list of outlets does not exist and for which it is impractical to construct a list locally, the outlet/distribution point/hawker identified or found closest to one of the outlets selected randomly should be selected.
- If there is no outlet within 3 hours drive of a remote facility, another outlet in another location should be selected.

This process will result in a sample of at least five outlets in each survey area. However some areas may not have all the outlet types in which case the numbers can be made up from the larger sample in the intervention/control study districts.

In addition to the outlets selected for inclusion in the survey, two back-up facilities should be identified in advance for each team of data collectors each day. Data collectors should visit a pre-selected back-up facility if the facility or outlet will not give permission for data collection or that location is not accessible because of extreme conditions or political instability.

<u>Time of day for data collection</u>

Data collection will take place at all times of the day; however although the public and NGO/mission facilities will be targeted in the late mornings when they are likely to be open, but over the main rush period and small private outlets targeted in the afternoon when previous studies have found that the owner is most likely to be present[22].

Selecting medicines

This survey is examining the prices, availability and affordability of medicines for malaria. Preliminary searches regarding the different medicines registered and available in 3 African countries has resulted in a list of more than 100 entity, dosage form and strength permutations included co-formulated and co-packaged combination therapies; however within each country between 35 and 46 permutations were found. When different brands/manufacturers of the same permutation were considered each country had between 64 and 200 items[23].

A number of studies, especially those carried out in the non-licensed and informal sector have shown that a significant proportion of patients requiring antimalarial medicines are sold analgesics/antipyretics or even antibiotics in place of antimalarial medicines; whilst these medicines will not be included in the list of medicines surveyed, questions will be asked of the outlet personnel about the use and cost of these medicines.

In all the districts being surveyed all products found will be recorded – that being each entity, dosage form, strength and manufacturer. The data collection form will contain all medicines registered in Uganda as separate entries and the data collectors will add any other medicines that they find.

---

[21] In some countries, the statistical department or finance ministry may conduct periodic retail surveys that include price and availability information for a wide range of commodities to calculate the consumer price index and other statistics – such surveys may have a well established sampling frame that may be useful as well as a source of the price of basic commodities to use in the affordability calculations

[22] Uganda Monitoring the PSI Rural Condom Distribution Strategy in 4 districts, PSI Uganda, December 2006

[23] Other studies have identified in Senegal 13 "compounds" sold in 89 presentations, forms and dosages; and in Zambia >100 different brands, presentations and forms representing 14 "compounds" (Saving, Lives Buying Time (Shretta and Guimier)

In the analysis for the national study, a shorter list of 50 medicines will be analysed, this being composed of 16 core list antimalarials, 14 other medicines from the WHO/HAI core list and 20 supplementary antimalarials selected for Uganda For each medicine, the list contains one-dosage form, one-strength, and up to two products to measure: the highest price version and the lowest price version of that item[24]. The number of generic versions of each entity will also be recorded.

<u>Core list of medicines</u>

It is important to use the core list of medicines as the basis for the survey as this will enable you to compare prices with those in other countries, where they are available. The 30 medicines contained in the core list have been selected because they meet the following criteria:
- Availability: they are available in standard formulations and are widely used in many countries
- Global malaria treatment guidelines and/or number of countries adopting as first line therapy
- Have an MSH International reference price[25]
- Most common adult and paediatric formulations and strengths (alternate strengths can be in the supplementary list)
- Representing medicines which are available as single sources and multi-source supplier/manufacturer

14 medicines from WHO/HAI global core list medicines (not for malaria) will be also surveyed to serve as a comparator of how malaria medicine prices change over time compared to all medicines, as well a comparator to link with previously carried medicine prices surveys.

For the intervention/control districts the list of 14 "global core medicines" will be added to the data collection form. Data for the 50 core and supplementary medicines from these intervention control districts will then be extracted from the larger data set for analysis in the national survey findings.

The various pack sizes of the same co-packaged and co-formulated combination therapies for different ages of will need to be treated as separate medicines in the list of medicines surveyed to be able to measure amongst other measures varying availabilities.

---

[24] The normal WHO/HAI methodology measures the innovator brand and lowest priced generic. As many African countries are largely generic markets and many of the ACT co-packaged products do not really have an innovator brand, it is proposed to measure the highest priced version of that item and the lowest priced version of that item. The ratio of the two will provide an indication as to the degree of market segmentation; for each case the manufacturers name will be recorded on the data collection form for subsequent analysis for example when there is a big difference between the highest and lowest priced equivalent. Where innovator brands are found and where that product is the most expensive, it will be recorded as the highest priced generic equivalent and the manufacturers name will allow it to be identified as the innovator brand.

[25] Reference prices are used to facilitate national and international comparisons. Summary measures of the medicine prices found during the survey can be expressed as ratios relative to a standard set of reference prices. The Management Sciences for Health (MSH) reference prices have been selected as the most useful standard; the MSH reference prices are the medians of recent procurement or tender prices offered by both not-for-profit and for-profit suppliers to developing countries for multi-source products.

Medicines for Malaria Venture

Proposed (draft) core list of antimalarial medicines[26]

	Name	Dosage form	Strength	Number of units for one course of therapy[27]	MSH 2006 price available
1	Amodiaquine	SYRUP/SUSP	50 mg/5 ml (base)		Y
2	Amodiaquine	TAB-CAP	150-200mg (base)		Y
3	Artemether	AMPOULE	80mg/ml		Y
4	Artemether	SUPPOS /RECTAL TAB	40mg		Y
5	Artemether	SYRUP/SUSP	15mg/5ml		Y
6	Artemether	TAB-CAP	50 mg		Y
7	Artemether + Lumefantrine	TAB-CAP	20mg + 120mg		Y
8	Artesunate	TAB-CAP	100 mg		Y
9	Artesunate	TAB-CAP	50 mg		
10	Artesunate + (Sulfadoxine + Pyrimethamine)	TAB-CAP	100mg + 250mg + 12.5mg		Y
11	Artesunate + Amodiaquine	TAB-CAP	50mg + 153mg		Y
12	Halofantrine	TAB-CAP	250mg		Y
13	Mefloquine	TAB-CAP	250mg (base)		Y
14	Quinine dihydrochloride	AMPOULE	250-300mg/ml		Y
15	Sulfadoxine + Pyrimethamine	SYRUP/SUSP	250mg + 12.5mg / 5ml		Y
16	Sulfadoxine + Pyrimethamine	TAB-CAP	500mg + 25 mg		Y

WHO/HAI (new) global core list

	Disease	Name	Strength	Dosage form	Number of units for one course of therapy	MSH-2005 price available
1	Asthma	salbutamol	0.1 mg/dose	inhaler		Y
2	Diabetes	glibenclamide	5 mg	cap/tab		Y
3	Cardiovascular disease	atenolol	50 mg	cap/tab		Y
4	Cardiovascular disease	captopril	25 mg	cap/tab		Y
5	Cardiovascular disease	simvastatin	20 mg	cap/tab		Y
6	Depression	amitriptyline	25 mg	cap/tab		Y
7	Infectious disease	ciprofloxacin	500 mg	cap/tab		Y
8	Infectious disease	co-trimoxazole	8+40 mg/ml	suspension		Y
9	Infectious disease	amoxicillin	500mg	cap/tab		Y
10	Infectious disease	ceftriaxone	1 g/vial	injection		Y
11	Infectious disease	fluconazole	150mg	cap/tab		Y
12	Pain/inflammation	diclofenac	50mg	cap/tab		Y
13	Pain/inflammation	paracetamol	24mg/ml	suspension		Y
14	Ulcer	omeprazole	20mg	cap/tab		Y

---

[26] Starting point for discussion - based on number of products registered/available in mini-analysis of 3 countries. Core medicines should have an MSH International Reference Price
[27] For calculation of affordability of a course of therapy and number of courses of therapy found in-stock

Uganda proposed (draft) supplementary list of antimalarial medicines

Up to 20 supplementary medicines (plus more if any core list medicines are deleted) can be added to bring the total to a maximum of core and supplementary of 50 medicines. From an analysis of medicines registered in Uganda there are an additional 19 medicines/dosage form combinations. Reviewing the list below, MMV has decided to survey all antimalarials registered or available on the Ugandan market.

	Name	Dosage form	Strength	# units for one course of therapy	MSH 2006 price available
1	Artemether	AMPOULE	100 mg/ml		Y
2	Artemether	AMPOULE	20mg/ml		Y
3	Artesunate	TAB-CAP	200 mg		Y
4	Artesunate + Amodiaquine	TAB-CAP	100 mg + 200mg		Y
5	Artesunate + Amodiaquine	TAB-CAP	50mg + 200mg		Y
6	Chloroquine	AMPOULE	40mg/ml (base)		Y
7	Chloroquine	SYRUP/SUSP	75mg/5 ml (base)		Y
8	Chloroquine	TAB-CAP	250mg (base)		Y
15	Chloroquine	SYRUP/SUSP	100mg/5ml (base)		N
16	Dihydroartemesinin	TAB-CAP	60mg		N
9	Halofantrine	TAB-CAP	250mg		Y
10	Primaquine	TAB-CAP	15mg		Y
11	Proguanil	TAB-CAP	100mg		Y
12	Quinine bisulfate	SYRUP/SUSP	100mg/5ml		Y
13	Quinine dihydrochloride	SYRUP/SUSP	100mg/5 ml		Y
14	Quinine sulfate	TAB-CAP	300-310mg (sulfate/bisulfate)		Y
17	Sulfadoxine + pyrimethamine + Chloroquine [Homapak - half strength]	TAB-CAP	250mg /12.5mg + 125mg		N
18	Sulfadoxine + pyrimethamine + Chloroquine [Homepak – adult]	TAB-CAP	500mg /25mg + 250mg		N
19	Sulphamethopyrazine (Sulfalene) + pyrimethamine	TAB-CAP	500mg + 25mg		N
20					

DATA COLLECTION PROCEDURES, INSTRUMENTS AND QUALITY CONTROL

Data collection

Data collectors will work in teams of two coordinated by an area supervisor and survey manager. Each data collection team on arrival in a locality will spend some time exploring the vicinity and asking the local community for information on where medicines are sold. Background information will be obtained from the local District Director of Health and the NDA drug inspector; additionally local guides will be used. This information, in addition to any official lists of outlets, will be used to construct the sampling frame. In the MOH intervention/control areas, all facilities will be visited and in the 3 other geographic areas, sampling will be performed as described previously.

The data collection forms for the recording of all of the outlet and facility based information can be found in annex 3; the information is recorded by interviewing the owner or employee in the outlet; the data collectors will ask to be shown things as well.

Additional tools for survey planning, budgeting as well as characteristics of personnel required have been developed in Excel as part of the work on the standard medicine prices surveys which were further developed for the initial budgeting of costs for MMV, effects of changing the number of geographic areas and number of facilities per area can be observed.

It is estimated for the Uganda study that the 24 data collectors and 6 area supervisors will be required for around 16 working days for the training, data collection and travel. Additionally there will be 4 data entry personnel.

Medicine prices and availability

For each medicine included on the data collection form, the price will be collected. For medicines which are unlabelled, information will be attempted to be recorded based on the description of the seller; if no name can be identified, no price information will be recorded, however it will be recorded that "x" number of different unidentifiable antimalarial medicines were available for sale.

Inventory of medicines

In order to capture medicines not on the data collection form (which contains all the registered antimalarial medicines in Uganda), a blank data collection form will be provided for the data collector to record information about any medicines, combinations, dosage forms or strengths not listed. It is anticipated that there will perhaps be a very few permutations found that are not registered with the National Drug Authority. It needs to be determined through the pilot testing the precision with which the data collectors fill this information to enable it to be analysed.

Medicines registered with the National Drug Authority

After the data collection during the data entry stage, details of each medicine found will be checked against the list of antimalarial medicines registered with the national drug authority.

Volumes of medicines in stock

The number of packs of each medicine where price information is collected that are in the outlet will be recorded. This will be used to calculate the number of treatment courses available. Standard regimens will need to be determined for each antimalarial medicine for adults and children as applicable will need to be developed. If multiple pack sizes are found the comments column will be used to record all the varieties. Additionally at each outlet, information about the number of customers acquiring antimalarial medicines per day/per week will be explored

Top selling/most dispensed products and main wholesale sources

Questions relating to wholesale sources will be asked by the data collectors, largely to inform the design of the subsequent components study. As part of that study, estimations of the best selling antimalarials by volume will be investigated. Estimations of sales and volumes of drugs should be converted into the number of courses of therapy.

Expired medicines and storage conditions

For each medicine where price information is collected, it will be recorded if there were any packs of this item on the shelf or stores area (but not put aside for destruction) that are expired. If there is no information on expiry date, this will be recorded as n/a (not available) and this can be used to calculate the proportion of medicines available without expiry date information. Additionally an assessment of the storage conditions will be made, especially relating to the exposure of the medicines to sunlight and heat.

"Buying-terms" and selling decisions

In order to further understand what medicines are stocked, the potential influence of special "Buying-terms" (e.g. credit) and the decision involved on which medicines are sold to patients; questions will be asked during the main outlet survey and during the component study. Issues around selling choices will be elucidated during the outlet survey and questions around buying terms during the components survey.

Other issues explored

What other commodity items are stocked by the outlet – what is the product mix?

Are the antimalarial medicines on display or "under-the-counter" or hidden?

What are the sources of information on the medicines sold?

Data entry and analysis tools

Data entry and analysis will take place at central level largely using the WHO/HAI International Medicine Price Excel Workbook which consolidates the findings and summarizes the results..

Additional data being collected as part of the malaria medicines prices surveys will be analysed in parallel using a custom made Excel workbook.

Data will be entered into separate sets of workbooks for each of the intervention districts, the control district and as a national data set separately to produce 4 sets of analysed data.

The analysis plan can be found in annex 4.

Quality control

An area supervisor, preferably a pharmacist, in each of the geographical areas are responsible for dealing with queries and communicating with the country survey manager to ensure that any issues that arise during data collection are managed in the same manner. At the end of each day the area supervisor checks the data collection forms from the data collectors; the areas supervisors will also make spot check visits to a number of the outlets - 10% in the intervention/control districts and 20% in the other districts.

The workbook has built into it a double entry data entry function as well as a "check-data" function that identified potential outliers

Additional data being collected as part of the malaria medicines prices surveys will be analysed in parallel using a custom made Excel workbook using similar principles of double entry and identification of outliers.

External to the survey manager and survey coordinator, the medicine price workbooks should be reviewed by a third party for quality control purposes.

DATA MANAGEMENT AND ANALYSIS

Data entry and analysis will take place at central level largely using the WHO/HAI International Medicine Price Excel Workbook which consolidates the findings and summarizes the results. The analysis plan can be found in annex 4.

Data will be analysed for each of the intervention districts, the control district and as a national data set separately to produce 4 sets of analysed data.

The Medicine Prices Workbook also provides automatic summaries of data to permit four types of data analysis:
- Price and availability comparisons within any one sector
- Price and availability comparisons between different sectors
- Treatment affordability
- Price composition.
- The summaries calculated automatically by the Workbook can be used to analyse:
- Medicine price levels and variations in different sectors, geographical areas, medicine types and individual medicines

- Treatment affordability in relation to the daily wage of the lowest paid government worker
- Components of the prices of medicines paid by purchasers and consumers.

Other analyses that can will be performed:
- Price and availability comparisons within and between sectors by medicine/combinations of medicines
- Treatment affordability by sector and between sectors
- Proportion of outlets by sector stocking the first line recommended antimalarial medicine(s)
- Number of treatment courses of antimalarials available for sale
- Proportion of medicines that were expired; proportion of medicines found without expiry dates labelled
- Price composition by sector and between sectors
- Inventory of antimalarial medicines on the market
- Proportion of medicines found which are registered with the national drug authority including differences between sectors (total and by type of antimalarial)
- Proportion of medicines were not found and are registered with the national drug authority including differences between sectors (total and by type of antimalarial)
- Top selling/dispensed antimalarials by sector (by volume)
- Main wholesale sources by sector
- Volumes of top selling and first line recommended antimalarial medicines (probably aggregated); number of treatment courses
- Proportion of outlets selling antimalarial medicines with them on open display
- Proportion of outlets adequately storing antimalarial medicines
- Proportion of medicines sold without original packaging/labelling
- Qualitative description concerning decisions on which medicines to stock and which medicines are sold to customers

Comparing prices

Price will be compared in both Ugandan shillings and as a median price ratio.

Summary measures of the medicine prices found during the survey can be expressed as ratios relative to a standard set of reference prices (median price ratio). Reference prices are used to facilitate national and international comparisons. The Management Sciences for Health (MSH) reference prices have been selected as the most useful standard; the MSH reference prices are the medians of recent procurement or tender prices offered by both not-for-profit and for-profit suppliers to developing countries for multi-source products.

However MSH international reference prices (or any other source of international reference prices) do not exist for all the antimalarials on the market and for these medicines comparisons will be restricted to comparisons in Ugandan Shillings.

Assessing affordability

One of the best ways of illustrating the impact of medicine prices on the cost of health care for individual patients and society is to compare the cost of treatment with peoples' income.

For this survey, the daily wage of an unskilled government worker is used for comparison identifying the number of days an unskilled government worker would have to work in order to afford the cost of a defined course of treatment.

Additionally the results will be analysed to present affordability in terms of available discretionary expenditures for different levels of household expenditures/income as well as comparing to the price of basic commodity items such as sugar, rice, cooking oil, eggs etc.

Uganda census data from 2002 also contains estimations of household wealth nationally as well as by district and this data will be utilised to further describe the affordability of medicines.

The standard workbook contains 10 pre-set conditions and treatments however these can all be amended to calculate affordability of different malaria medicines. If the 10 (non-malaria) global medicines are included, the affordability of another disease or condition that uses one of the global medicines may be interesting for comparison purposes.

ETHICAL CONSIDERATIONS

There are no ethical issues of patient clinical confidentiality as the data collectors obtain price and availability information of the medicines available in the facility only. There are issues of the exploration of business practices related to the prices charged for medicines in the outlets; some of the outlets may not be legally licensed to sell medicines and some licensed outlets may sell medicines beyond the scope of their license.

There is potentially very limited or no harm to the data collectors or staff of the medicines outlets visited, nor to future patients to the outlets. However some of the outlets visited will be unlicensed and illegal.

Data will be stored and managed to ensure that neither the outlet nor the personnel could be neither identified either in the research documents or reported to the authorities.

Ethical clearance is probably unnecessary as there would be no issues of patient confidentiality as there will be no patient interactions from the data collectors, and no accessing of patient information.

Approval of the study will be obtained from the Ministry of Health and a verbal informed consent will be obtained before or the interview begins in each outlet.