

BIOMARKERS IN POPULATION BASED SURVEYS: EVIDENCE FOR ADVOCACY AND POLICY MAKING

*Alfredo Fort, MD, PhD¹, Dean Garrett, PhD, MPH, CLS¹, Jasbir Sangha, MS, MHS²,
Fred Arnold, PhD², and Monica Kothari, MS, MPH¹*

Introduction

Since the inclusion of anthropometry in 1986, the Demographic and Health Surveys (DHS) have generated a rich body of information related to the health of populations in the developing world through the collection of biomarker data. These data are critical to researchers and policy makers alike, and help to better understand the occurrence and distribution of a disease or human condition in a population, serve as a tool for advocacy, and guide the development of policies and programs to improve the health of these populations.

Traditionally, much of the data gathered in DHS surveys has been self reported. This method is the most direct and non-intrusive way of obtaining reasonably accurate information if questions are well designed and interviewers are trained with high standards of quality. However, it is well known that even under optimal conditions, some of the information collected may suffer from bias or recall problems. This is especially true for matters that are sensitive to the respondent or for situations occurring a long time before the interview. Some types of information (e.g., presence of a subclinical condition or an early pregnancy) may not be known to respondents. As countries become more interested in obtaining information about their populations, the addition of biomarkers to the arsenal of tools for data collection becomes imperative. Biomarkers complement reported health information by providing an objective profile of a specific disease or health condition in a population. Biomarker data also contribute to the understanding of behavioral risk factors and determinants of different diseases.

Biomarkers and their measurement

A biomarker may be thought of as a characteristic that can be independently measured and evaluated as an indicator of normal biologic processes, pathogenic processes, or pharmacologic response to a therapeutic intervention (Biomarker Definitions Working Group, National Institutes of Health, 2001). Biomarker measurements can serve as diagnostic tools to identify diseases in their early stages and can be used as surveillance tools to track changes in disease patterns or to evaluate intervention programs. In population-based surveys, biomarkers help assess the prevalence or occurrence of diseases or conditions and can also be used at a macro level to measure the long-term effect of policies and programs.

¹ PATH and the MEASURE Demographic and Health Surveys (DHS) project. MEASURE DHS is a USAID-funded project. Email address for correspondence: alfredo.fort@macrointernational.com

² ICF Macro and Demographic and Health Surveys (DHS).

As expected, tests for biomarkers in population based surveys have to be the least intrusive as possible and should preferably deliver results in a short period of time. The equipment or kits for the tests need to be rugged, portable, resilient to extreme temperatures and degrees of humidity, and relatively inexpensive. Meeting each of these conditions can be challenging. However, the confluence of advances in research and technology, increasing donor interest, and the capacity of DHS and other survey programs to implement biomarker tests in the increasingly make it possible to incorporate more biomarkers in survey operations.

The first consideration is intrusiveness. Although there are promising avenues for the collection of non-intrusive samples such as saliva, in the past results from these tests could only be obtained after analyses were completed in a central laboratory. Thus, samples had to be stored safely and transported as swiftly as possible, and the deterioration of samples was an important constraint.

Most tests require the collection of blood, which produces layers of complexities and considerations for survey operations. First, the intrusiveness of the method could reduce the response rate for the test and possibly for the overall interview as well. This concern is balanced with the population's eagerness to get a free test done in their own homes. Expert training of the interviewer/tester in how to approach the potential respondents in a sensitive manner, coupled with proficiency in the application of the test, has been critical in maintaining high response rates. Here, again, technology comes to the aid of measurement. For example, in the case of the measurement of hemoglobin for the determination of anemia, development of portable analyzers such as the HemoCue™ have made it possible to use a very small amount of blood from pricking a finger with a small lancet to produce reliable results within a few minutes.

When biomarkers cannot be tested directly in the field, the next consideration is the need to carefully plan the storage and transport of samples to a central laboratory. In the past, many tests required the collection of venous whole blood. This complicated the operation, making it necessary to have specially trained phlebotomists accompany the interviewers in the field. This makes the survey more expensive and adds layers of training and complicates the handling of logistics for the test kits. However, the main challenge in collecting venous whole blood is the preservation of the integrity of the blood components prior to analysis in a central laboratory. The preservation of venous whole blood samples requires having a "cold chain" in the field setting. A relatively large sample of blood needs to be collected in a tube and refrigerated immediately. The cold chain has to be maintained intact from the point of collection to its final storage and processing at the central laboratory, often across long distances and periods of time.

The increased application of tests based on the collection of dried blood spots (DBS) has revolutionized the capacity to obtain biomarkers in field settings. DBS samples have several advantages over venous blood (Parker and Cubitt, 1999; McDade et al., 2007). The use of DBS samples has eliminated the need for a cold chain and refrigeration of specimens in the field, reducing considerably the complexity of storage in remote areas and transport to the laboratory. Dried blood spots are obtained from the prick of a finger (or a heel in the case of very young children), thus reducing the need for syringes and needles, test tubes and racks, and reducing the invasiveness of the procedure. DBS samples are collected in pre-printed circles on a filter paper card, dried overnight, protected with glassine paper, sealed tightly in commercially available plastic bags with desiccants and humidity indicators, and then transported with relatively little effort to the central laboratory for testing. Many new tests, including those for HIV, micronutrients, infectious diseases, and those for tracking immunization coverage, are increasingly being validated for use with DBS.

The availability of simpler tests, however, does not mean that conducting biomarker tests in the field is simple. Due consideration needs to be given to human subjects protection (including protection of the persons collecting samples), informed consent procedures, formal approval of the survey protocol by one or more Institutional Review Boards, procurement of all equipment and supplies and delivery in a timely manner (including attention to customs requirements and local laws), comprehensive training and field practice, preparation of detailed manuals for blood collectors and field supervisors, the logistics of getting needed supplies into the field, careful arrangements for the safe disposal of biohazardous waste, and assessments of laboratory capabilities and the preparation of lab protocols.

The Demographic and Health Survey program has been at the forefront of the movement to incorporate biomarker testing in large-scale national household surveys. To date, DHS has conducted biomarker tests on millions of respondents, measuring 16 different biomarkers in more than 80 countries (see Table 1). Measurements have been made for a wide range of health conditions, including infectious and sexually transmitted diseases, chronic illnesses such as diabetes, micronutrient deficiencies, and exposure to environmental toxins (e.g., lead). Specifically, biomarkers have been collected to measure anemia, HIV infection, stunting/wasting/underweight, blood pressure, hepatitis B and C, Herpes virus, measles, tetanus toxoid and malaria, to mention just a few.

Table 1
Biomarker tests done by the Demographic and Health Surveys (DHS)

BIOMARKER	YEAR TEST FIRST DONE	NUMBER OF SURVEYS INCLUDING TEST	POPULATION TYPICALLY TESTED¹	SAMPLING METHOD AND EQUIPMENT USED
Anthropometry (Weight, Height, Age)	1987	147	Women 15-49 years Children 0(6)-59 months Men 15-59 years	Non-invasive, measuring board and scale
Hemoglobin (for Anemia)	1995	62	Women 15-49 years Children 0-59 months Men 15-59 years	Capillary blood, HemoCue™ portable analyzer
HIV	2001	32	Women 15-49 years Men 15-59 years	Capillary blood, DBS ²
Blood pressure	1998	8	Women 15-49 years Men 15-59 years	Non-invasive, automatic cuff
Syphilis	1996	6	Women 15-49 years Men 15-59 years	Venous blood, RPR ³
Vitamin A	1996	4	Women 15-49 years Children 0(6)(12)-59 months	Capillary blood, DBS, HPLC ⁴ , RBP-EIA ⁵
Malaria	2006	3	Women 15-49 years Children 0(6)-59 months	Capillary blood, RDT ⁶ & thick/thin slides
<u>Other, less common tests:</u> Hepatitis B, Hepatitis C, Herpes, Measles, Tetanus, Chlamydia, Diabetes, Lipids, CRP, Transferrin				

¹ Varies by country e.g., Men 15-54 or 15-64; Children under 3 years

² DBS: Dried blood spots ³ RPR: Rapid Plasma Reagin ⁴ HPLC: High Performance Liquid Chromatography

⁵ RBP-EIA: Retinol binding protein enzyme immunoassay ⁶ RDT: Rapid Diagnostic Test

The use of findings from biomarker measurements for policy making is extremely difficult to monitor for several reasons. First, the time when decisions are made and policies and programs are modified varies enormously. Second, the venues where decisions are taken (e.g., directorate offices) and persons making those decisions may be different from those that the survey staff have usual contacts with. Third, it is not uncommon that policy decisions using these data do not fully cite the sources of information used in the decisions and often policy makers do not publicly admit that their decisions are based on survey results, precluding the ability to confirm a direct relationship between the two. Thus, the examples below of policies and programs in less developed countries that have been influenced by biomarker results from surveys should truly be considered the “tip of the iceberg.”

Salt Iodization

The DHS results from surveys conducted in Central Asia (from the mid to late 1990s) revealed that 50 percent or more of the sampled households lacked adequately iodized salt. These

findings had such a major impact on salt iodization programs in the region that by 2004, all of the Central Asian countries had adopted legislation mandating use of iodized salt. In 2001, Kazakhstan developed a five-year salt iodization plan after the 1999 survey reported high iodized salt deficiency figures. Similarly, the government of Turkmenistan committed itself to achieve universal salt iodization by 1994. The political will to ensure salt iodization resulted in very encouraging findings as the 2000 Turkmenistan DHS showed that 78 percent of the household salt tested had an iodine content of at least 15 parts per million (IDD News, 2005). Currently, there are plans by the government of Tanzania to collect baseline information on salt iodization as part of a planned food fortification program.

Anthropometry and Malnutrition

The measuring of height/length and weight in children and mothers over the years has provided a powerful tool for governments to gauge the levels and distribution of malnutrition within a country, and to plan sound nutrition policies and programs. The measurements of weight and height/length in children are compared with international child growth standards, such as the new WHO standards from 2006 (WHO, 2006). This comparison allows the calculation of the proportion of a population in specific nutrition categories. There are three standard anthropometric indices of physical growth for children: Height-for-Age, which is a measure of stunting or chronic malnutrition; Weight-for-Height, which is a measure of wasting or acute malnutrition; and Weight-for-Age, which takes into account both chronic and acute undernutrition. By convention, estimates that are more than two standard deviations below the median from the WHO standards reflect moderate malnutrition and measures more than three standard deviations below the median are equated with severe malnutrition (Gibson, 1990).

These anthropometric data have allowed governments to know the extent of acute and chronic malnutrition in their countries, and the particular regions, age groups, or population subgroups most affected. Guided by these data, broad food distribution campaigns in the 80s and 90s have been replaced or augmented by focused nutrition education and school, health center and community food supplementation programs (Meerman, 2008).

Through the information generated by surveys, the government of Nepal has identified the glaring disparities that exist among the five regions of the country. The wealth of data obtained has generated the production of special reports and policies on child health and nutrition. For example, in 2002 a National Strategy for the Control of Anemia among Women and Children was developed by the Ministry of Health and Population, followed by a five-year plan with the same objectives in 2005 (MOHP, 2005). The fact that the nutritional status of children in the country continues to be inadequate is a cause of concern for policy makers. The 2006 Nepal DHS found that the overall underweight figure for the country (i.e., weight-for-age below two standard deviations from the median of the WHO standard) was 39 percent, a small 9 percent reduction from the 43 percent figure found in the previous five years. With information from these and other sources, the government has developed a National Nutrition Policy and

Strategy, which looks to promote exclusive breastfeeding and appropriate introduction of healthy feeding practices, train health workers on Infant and Young Child Feeding (IYCF), and continue iron supplementation and Vitamin A distribution in risk areas of the country (MOHP, 2006).

Another example of the use of nutrition status assessment for program planning and evaluation comes from Peru. After the latest round of DHS surveys in 2005 found that the prevalence of stunting had hardly decreased nationwide (from 31 percent to 30 percent since 2000), the government decided to embark on an ambitious poverty alleviation strategy, with the aggressive reduction of stunting by one percentage point per year as one of its indicators. The Peruvian Ministry of Economy then asked DHS to design supplemental sampling of its Continuous Survey in order to obtain estimates of stunting in children for the year 2007. The estimates to be obtained will be used as a baseline to monitor the intended malnutrition reduction through program interventions in impoverished rural areas.

A case in the opposite direction can be cited in the Dominican Republic. The 2007 DHS found that 8 percent of children under 5 years were overweight, a percentage that was as high as 12-13 percent in some regions and among children living in wealthier households. This finding was coupled with results depicting a worsening situation on breastfeeding in the country, placing the Dominican Republic among the countries in the world with the lowest prevalence of breastfeeding, and with extremely early introduction of bottle feeding among infants. The prevalence of exclusive breastfeeding among children under 6 months was only 8 percent (down from 10 percent in 2002), while before the first month of age nearly 70 percent of infants were bottle fed. The median duration of breastfeeding was a poor 7 months, contrasting with 17 to 21 months found in many neighboring South American countries (CESDEM and Macro International Inc., 2008).

These findings were deemed so critical that the Sub-Secretary for Health at his presentation during the dissemination of the DHS results for the country denounced the baby formula companies for their aggressive campaigns with doctors and nurses, who are seen as the main promoters of formula feeding of infants, and threatened to close the pharmacies that indiscriminately promoted formula feeding among clients.

A significant case of how repeat and consistent measurements affect perceptions and actions at high policy levels occurs in India. In setting up the goals for the Tenth Five Year Plan (2002-2007), India used the nutrition and child feeding data from the 1998-99 National Family Health Survey (NFHS-2). Based on the NFHS-2 estimates, one of the goals was to reduce severe undernutrition by half during the plan period.

Findings from the measurement of the nutritional status of children and the prevalence of anemia in the National Family Health Surveys have had a major impact on government nutrition programs at the national and state level. Evidence from these biomarker

measurements has highlighted four facts that have galvanized governmental and nongovernmental groups to urgently address nutritional problems:

- Indian children suffer from some of the highest levels of malnutrition in the world. Almost half of children under five years of age (48 percent) are stunted, 43 percent are underweight, and 20 percent are wasted.
- Anemia is extremely widespread among young children. Seven out of 10 children are anemic, including 43 percent who are moderately or severely anemic.
- There has not been any substantial progress in addressing nutritional deficiencies since the late 1990s. The prevalence of anemia in children actually increased substantially from the 1998-99 to the 2005-06 surveys.
- Although nutritional problems are widespread among children, they disproportionately affect disadvantaged groups. Even in households in the highest wealth quintile, however, more than half of young children are anemic and one-quarter of children are stunted.

Poor nutritional status is evident from a very early age. The previous focus of the government's flagship nutrition program almost entirely on children age 3-6 years was ill-advised since it did not cater to younger children. In response to these stark facts, there have been several policy and program responses at different government levels.

In January 2007, Prime Minister Manmohan Singh wrote a strongly worded letter to the Chief Ministers of all Indian states and union territories decrying the poor performance of government nutrition programs, urging them to carry out an evaluation of these programs, revamp the programs on an urgent basis, and report back to him every three months highlighting the steps they have taken and their effect. Excerpts from his letter are:

"I would like to share with you my concern over the implementation of the Integrated Child Development Services (ICDS) Scheme. A number of reports and surveys, including the **National Family Health Survey (NFHS-3)** [our bolding] and Focus on Children Under Six (FOCUS) seem to indicate a noticeable decline in the qualitative aspects of the programme...There is strong evidence that the programme has not led to any substantial improvement in the nutritional status of children under six...These are startling figures and the situation calls for urgent action...Recent judgements of the Honorable Supreme Court have also highlighted these problems."

"My own reading of these reports and surveys leads me to believe that proper implementation of the programme critically depends on political will, decentralized monitoring and meticulous attention to day-to-day operational issues. Otherwise, problems like irregular functioning of Anganwadi centres, inability to provide hot, cooked food, and leakage of food material meant for infants will persist...Also please lay special emphasis on program status in the areas of concentration of minority communities and preponderance of Scheduled Castes and Tribes...The core objective

of the ICDS in the 11th Plan should be universalization with quality.”

Between August 12-14, 2007, a National Nutrition Conclave was convened in Chennai, with the theme “A Nutrition Secure India: How do we get there?” At the end of the conclave, the Chennai Declaration stated that:

“Sixty years after independence, national survey data (such as NFHS-3) show that the nutrition situation has not improved as desired in some areas in India, with almost 50% of our children underweight and more than 70% of our women and children with serious nutritional deficiencies such as anemia. The level of malnutrition in India today is morally unacceptable and has enormous costs in terms of social and economic development.”

The Chennai Declaration became a call for action among different government agencies, which included a comprehensive program, including:

- Setting up a National Nutrition Authority
- Establishing a Parliamentary Committee on Nutrition
- Developing a Citizen’s Charter on Nutrition
- Formulating a *national strategy for nutrition* for children under two years of age focusing on vulnerable and marginalized groups.

Later that year, the Union Minister of Health and Family Welfare, Dr. Anbumani Ramadoss, stated that:

“The results emanating from the latest National Family Health Survey (NFHS-3) indicate that malnutrition and anemia continue to be the two major health problems in the country. The timing of NFHS-3 is very appropriate as the findings of this round can be utilized to make appropriate interventions in the National Rural Health Mission. I hope State Governments would give due attention to address these grave issues.”

In India, comparable findings from two national Family Health Surveys helped the government realize the lack of effectiveness of child development schemes in the country and initiate a revamp of the government’s child nutrition programs. Statements came from the highest levels of government and have been translated into specific program orientation and planning. The call to action has also been spurred by hundreds of news articles and TV broadcasts decrying the fact that children are suffering from serious problems of malnutrition in spite of the economic boom in the country.

Another use of the anthropometric data is the development of age-based fixed dose treatment regimens based on weight-for-age data from DHS surveys. New dose presentations derived from such analyses could reduce under and over-dosage, particularly in children, and in the long run also contribute to the reduction of drug resistance in many countries. These analyses were done in a 2006 trial with a combined artesunate-amodiaquine (AS/AQ) treatment regimen

for *p. falciparum* malaria, using pooled DHS data (Taylor et al., 2006). The resulting new fixed doses for the drugs were compared against loose dosing in a recent randomized control study by Sirima and others (2009). The study found similar efficacies and adverse effects with both regimens but a better therapeutic fit of the fixed-dose regimen, thus supporting its future use. This type of standardization using anthropometric reference data from DHS surveys could prove invaluable for improved treatment of malaria and other diseases.

Anemia and micronutrient deficiencies

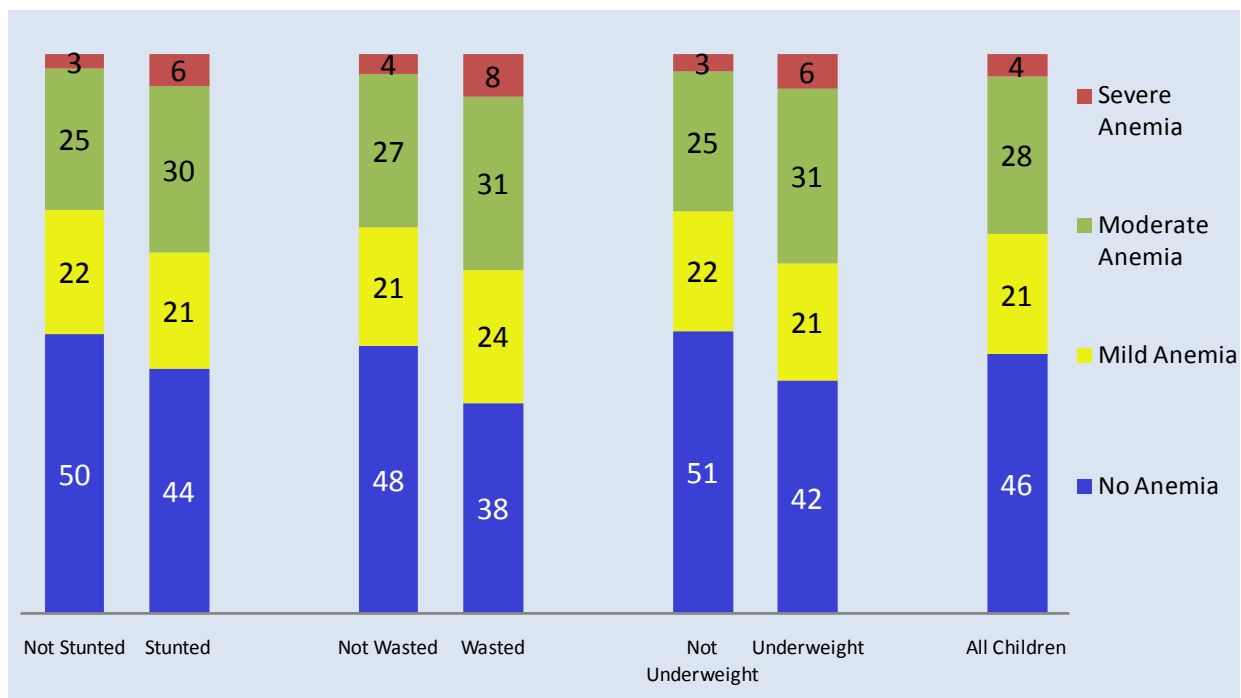
The advent of anemia testing in 1995, especially among children and pregnant women, added a powerful tool for the implementation of micronutrient and food supplementation campaigns, specifically focused on the distribution of iron and folate pills during antenatal care in most countries.

From 1995-97, three DHS surveys in central Asia (Kazakhstan, Uzbekistan and the Kyrgyz Republic) found high levels of anemia in women and children: 49 and 69 percent in Kazakhstan; 60 and 61 percent in Uzbekistan; and 40 and 50 percent in the Kyrgyz Republic, respectively. As a result of these findings, the UNICEF Office of the Central Asian Republics and Kazakhstan requested donor support and proposed strategies to combat anemia in the region. The proposed strategy included national and area-wide education, fortification of cereal flour, iron supplementation for women of reproductive age, pregnant women and children 6-24 months, and continued treatment practices for severe anemia and monitoring studies (Gleason and Kartoglu, 1997). Based on the Anemia Prevention and Control (APC) guidelines, one oblast (region) in each of the countries started the interventions in August 1998.

In 2001, each of the countries assessed the impact of interventions at the oblast level. The interventions were found to be successful and led to a “national commitment” in each of the countries to lower anemia and iron deficiency (Gleason, 2001). Despite initial commitments to reduce anemia in the region, some high levels of anemia persist. Increased donor involvement and commitment are required to sustain developments made in curbing iron deficiency and anemia (Gleason and Sharmanov, 2002).

Collection of diverse biomarker data is making it possible to conduct specialized analyses, such as the correlation of anemia and malnutrition at the national level, as in the case of Ethiopia, using data from the 2005 survey (see Figure 1). This analysis is part of a chartbook requested by the country for in-depth examination of results from the original data set (Macro International Inc. 2008).

Figure 1
Stunting, wasting and underweight among children under five, by anemia status
Ethiopia 2005 DHS



Another example of the use of biomarkers comes from Vitamin A deficiency (VAD). As a result of findings from the 2006 Uganda DHS that showed high levels of VAD in the population, the government started a pilot food fortification strategy to improve the vitamin A status in the country. With funding from USAID, the MOST micronutrient project is providing technical assistance in vitamin A supplementation, food-based activities, and anemia prevention and control in the country.

In collaboration with the USAID DISH project, MOST provides technical and logistical assistance in information campaigns and training workshops for distribution of vitamin A capsules in high risk areas. MOST and the Department of Food Science and Technology of Makerere University are working with local manufacturers of cereal, oil, sugar and dairy products to fortify locally consumed foods. According to MOST, "NARO (National Agricultural Research Organization), and VEDCO (Volunteer Efforts for Development Concerns) are implementing a project that promotes the growth and utilization of vitamin A-rich, orange-fleshed sweet potatoes. The aim of the project is to improve the nutritional status of children and women, household food security, and income. MOST is working with the MOH to develop an anemia prevention and control advocacy plan" (MOST Project, 2009).

Malaria

The Malaria Indicator Survey (MIS) is a relatively new survey that is designed to collect information on key malaria interventions, including use of insecticide-treated mosquito nets, prompt and effective treatment of fever in young children, indoor residual spraying and intermittent preventive treatment against malaria during pregnancy. The survey also collects information on the prevalence of malaria and anemia among children age 6-59 months. The Tanzanian 2007-08 HIV and MIS included rapid testing of malaria and the 2006-07 Angola MIS, the 2007 Rwanda Interim Survey, and the 2008 Senegal and Liberia MIS surveys included both rapid testing for malaria and microscopy.

Findings from the Angola survey on ownership and use of mosquito nets and on prevalence of malaria are being used in the present campaigns to increase the distribution of insecticide-treated nets (ITNs). For example, during the last World Malaria Day, the Minister of Health, Dr. José Van-Dúnem, spoke of renewed efforts by the government to abate the high number of deaths due to malaria—estimated at about 10,000 in 2008—which peaked in 2005 at 12,000 deaths (see <http://www.jornaldeangola.com>). The Angola MIS found that only 18 percent of children under 5 used an ITN (COSEP, Consaúde, and Macro International, 2007). It is too early to say what impact the malaria data for several countries will have in shaping policies in the region, but it is likely that levels found will be used as baseline indicators to monitor trends over time and to set goals for the reduction of malaria.

Human Immunodeficiency Virus (HIV)

Before the inclusion of HIV testing in DHS surveys, sentinel surveillance systems were the recognized source of data for estimating national HIV prevalence. The data primarily reflected pregnant women attending selected antenatal care (ANC) clinics in urban or peri-urban settings and therefore did not represent the general country population. DHS and AIDS Indicator Surveys (AIS) started adding HIV biomarker data in 2001, based on testing dried blood spots (DBS) and backed by a three-tier algorithm of enzyme-linked immunoassay (ELISA) and polymerase chain reaction (PCR) tests. These data were obtained from nationally representative samples from households, thus representing true estimates of the prevalence of HIV. To date, DHS has conducted HIV testing in more than 30 countries, mostly in Sub-Saharan Africa, providing a comprehensive picture of the prevalence of the disease in the continent (see Figure 2).

The addition of HIV testing in DHS signaled a powerful new tool in countries' efforts to combat the epidemic. Tanzania, for example, used the results of the 2003-04 HIV/AIDS Indicator Survey for the design of the Health Sector HIV/AIDS Strategy and the National Care and Treatment Plan, which focuses on VCT, home-based care and support, and treatment with antiretrovirals.

In countries with medium to high HIV prevalence rates or large populations, new figures of HIV prevalence based on nationally representative household surveys have led to a downward revision of their HIV estimates obtained from surveillance sites. For example, results from the Kenya 2003 and Ethiopia 2005 HIV surveys prompted the governments to adjust their official HIV figures and include them in their programmatic efforts.

A direct consequence of this redressing of HIV estimates is that countries have a more realistic picture of the epidemic and the ability to identify the most affected subpopulations. These data are being used to calibrate the HIV estimates made by country governments and international agencies. For example, according to UNAIDS and WHO (2006), approximately 5.7 million people in India were infected with HIV in 2005. However, after the 2005-06 National Family Health Survey (NFHS-3) estimated HIV prevalence to be 0.28 percent among men and women age 15-49 years based on almost 100,000 DBS samples collected throughout India, UNAIDS and the Government of India revised their estimate of persons living with HIV downwards to 2.5 million (less than half of the previous estimate).

The emergence of DHS HIV prevalence estimates in a large number of countries contributed to the decision by UNAIDS to reduce the global estimate of persons living with HIV from 39.5 million to 33.2 million (UNAIDS and WHO, 2007). This decision was based largely on HIV prevalence estimates from DHS surveys. Even for countries with generalized HIV epidemics that have not conducted a national population-based HIV survey, UNAIDS recommends that HIV data from antenatal clinic attendees should be adjusted downward on average by a factor of 0.8 (UNAIDS Reference Group on Estimates, Modelling and Projections, 2006). The 0.8 adjustment is based on the fact that HIV prevalence measured in population-based surveys is approximately 80 percent of the prevalence among antenatal clinic attendees in both rural and urban areas.

As more practical tests that can measure the incidence of new infections become available and are applied to population-based surveys, a more complete picture of the life history of HIV and AIDS will be pieced together.

For example, further analysis of HIV prevalence data from surveys has produced new evidence of the association of the infection in relation to people's behavior. Analyses of data from eight national surveys from sub-Saharan Africa indicate that HIV prevalence does not exhibit the same pattern of association with poverty as that seen with other infectious diseases or per traditional epidemiological pathways. Data reveal that adults in the wealthier quintiles have higher prevalence of HIV than those in the poorer quintiles (see an example in Figure 3). These findings hold true even for cohabiting couples, where the likelihood that one or both partners are infected with HIV still increases with wealth. These findings have revolutionized the way we think about HIV, and how to tailor programs to prevent and combat HIV (Bradley and Mishra, 2008).

Figure 2
HIV Prevalence from DHS surveys

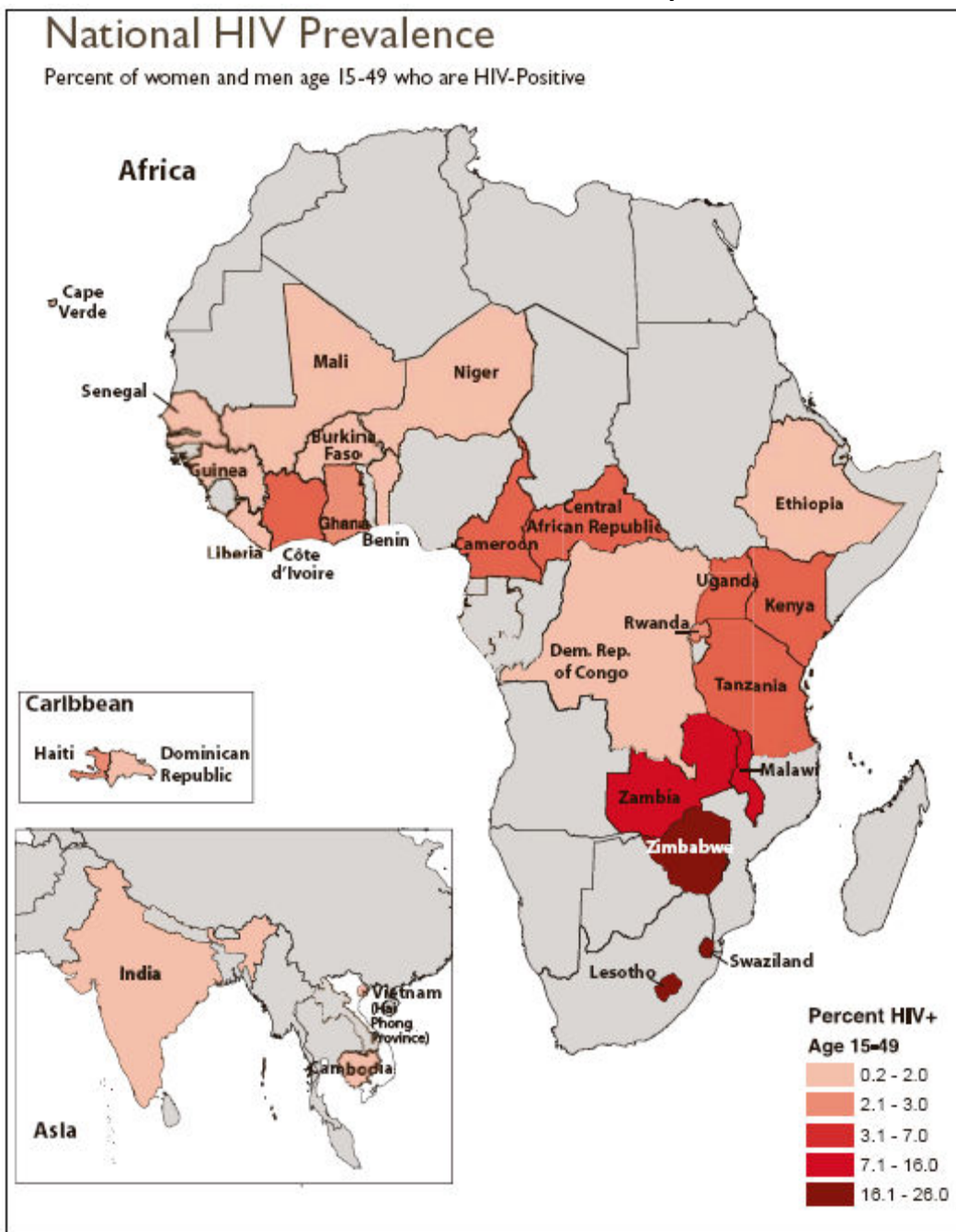
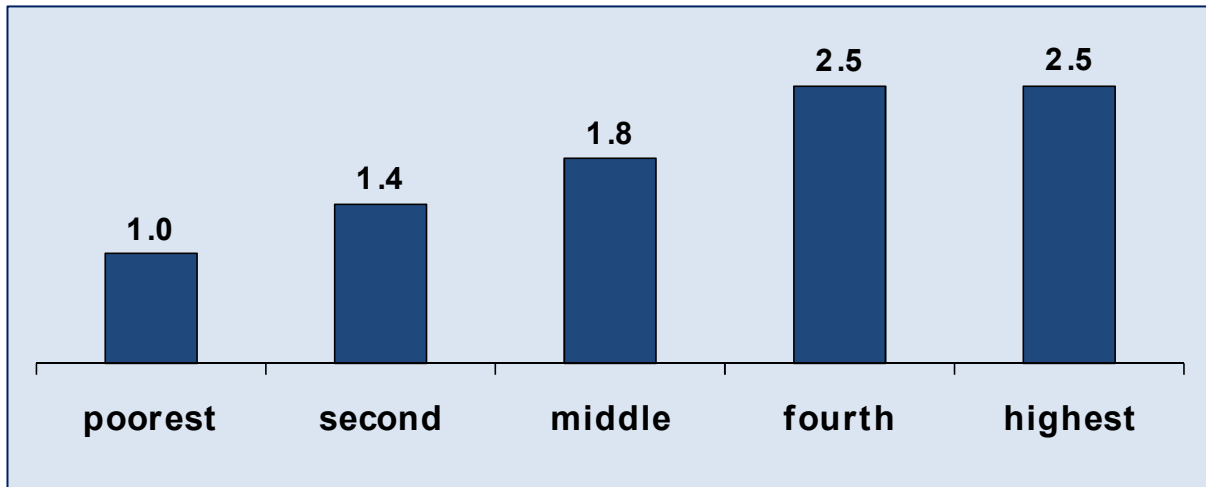


Figure 3
Prevalence of HIV Infection by Wealth Quintile – Kenya 2003 DHS



Findings such as these have helped create awareness among policy makers and planners of the need to include higher socioeconomic groups in their planning to combat the AIDS epidemic. Thus, traditional materials and media intended for the poor or illiterate have to be replaced or supplemented with those for more “savvy” audiences, and the messages need to be placed in more varied venues, such as youth and sports associations and cyber cafés.

Further analyses of other biomarker data have revealed interesting anomalies, such as the apparent positive association between overweight women and HIV in several sub-Saharan African countries. However, when controlled for wealth and other socio-demographic factors, the relationship reverses direction, producing positive associations between women who were underweight and positive HIV status (Mishra et al., 2007). More research, especially of a longitudinal nature, is needed to discriminate between these primary associations and causal or risk factors for the disease. Results from these studies should better guide programmers into targeting scarce and expensive HIV/AIDS interventions to well-defined risk populations.

Future tests and policy implications

Thanks to improvements in technology and the interest and needs of countries, other biomarkers are being incorporated in population-based surveys, and the use of biomarker data in more sophisticated analysis is expanding. For example, rapid diagnostic testing (RDT) for malaria is helping to confirm differing prevalence rates of deadly falciparum malaria in many African countries. Given the close correlation between climate and altitudes on the one hand and malaria infection on the other hand, a spatial repository of data on malaria is being constructed as more information from surveys is obtained. Other biomarkers currently included in DHS surveys include retinol-binding protein assay (for Vitamin A), tetanus toxoid, measles,

herpes virus, and lipid tests. Tests to be potentially included in the near future are prostate specific antigen, transferrin (for iron deficiency), human papilloma virus (HPV) and C-reactive protein. Less invasive sample sources are being explored, such as saliva and DNA from mucosal or other epithelial cells, which should ease anxiety over blood testing.

Future developments in the field of microfluidics may allow a battery of expanded tests (e.g., for infectious, chronic and genetic conditions) to be performed rapidly in the field, with just a fraction of the blood collected currently, and in a portable device the size of a credit card. Biomarkers will continue to be an important addition to the collection of valuable population-based survey data. Moreover, the ability to examine the relationship between biomarker results and a wide variety of demographic, attitudinal, and behavioral data collected in population-based surveys enhances the utility of the biomarker measurements.

REFERENCES

Biomarker Definitions Working Group, National Institutes of Health. 2001. Biomarkers and surrogate endpoints: Preferred definitions and conceptual framework. *Clin Pharm Therapeutics* 69(3): 89-95. Accessed on 6/9/2009 from www.ospp.od.nih.gov/biomarkers/ClinicalPharmacology.

Bradley, Sarah and Vinod Mishra. HIV and Nutrition among Women in Sub-Saharan Africa. 2008. *DHS Analytical Studies* No. 16. Calverton, Maryland, USA: Macro international Inc.

Centro de Estudios Sociales y Demográficos (CESDEM) and Macro International Inc. 2008. Encuesta Demográfica y de Salud 2007. Santo Domingo, República Dominicana: CESDEM and Macro International Inc.

Consultoria de Serviços e Pesquisas–COSEP Lda., Consultoria de Gestão e Administração em Saúde–Consaúde Lda. [Angola], and Macro International Inc. 2007. Angola Malaria Indicator Survey 2006-07. Calverton, Maryland: COSEP Lda., Consaúde Lda., and Macro International Inc.

Gibson, RS. 1990. *Principles of Nutritional Assessment*. New York and Oxford: Oxford University Press.

Gleason, GR and U Kartoglu. 1997. Anemia Prevention and Control Programme for the Central Asian Republics and Kazakhstan (CARK:APC). Iron Deficiency Project Advisory Service (IDPAS). IDPAS# 18.

Gleason, GR. 2001. Anemia Prevention in Four Republics in Central Asia and Kazakhstan. Forging Effective Strategies to Combat Iron Deficiency, Sponsored by ILSI, CDC, Emory University and MI, 7-9 May, Atlanta,. IDPAS #581.

Gleason, GR and T Sharmanov. 2002. Anemia prevention and control in four Central Asian republics and Kazakhstan. *Journal of Nutrition* 132: 867S-870S.

IDD News. 2005. IQ+Jagriti Vol. III (1), March 2005. Accessed on 2/10/2009 from <http://www.iqplusin.org/downloads/mar05.pdf>.

Macro International Inc. 2008. Nutrition of Young Children and Women, Ethiopia 2005. Calverton, Maryland, USA: Macro International Inc.

McDade T, S Williams, and JJ Snodgrass. 2007. What a drop can do: Dried Blood Spots as a minimally invasive method for integrating biomarkers in population-based research. *Demography* 44(4): 899-925; 2007.

Meerman, J. 2008. Making nutrition a national priority: Review of policy processes in developing countries and a case-study of Malawi. Manuscript funded by FAO. Available at http://www.fao.org/ag/agn/nutrition/docs/Meerman_%20MAKING%20NUTRITION%20A%20NATIONAL%20PRIORITY.pdf

Ministry of Health and Population (MOHP) [Nepal]. 2005. *Five Year Plan of Action for the Control of Anemia among Women and Children in Nepal 2062/63-2066-67 [2005/06-2009/2010]*. Kathmandu, Nepal: Nutrition Section, Child Health Division, Department of Health Services, Ministry of Health and Population.

Ministry of Health and Population (MOHP) [Nepal]. 2006. *Annual Report. Department of Health Services 2061/62 [2004/2005]*. Kathmandu, Nepal: Ministry of Health and Population.

Mishra, Vinod, S Bignami-Van Assche, R Greener, M Vaessen, R Hong et al. 2007. HIV infection does not disproportionately affect the poorer in sub-Saharan Africa. *AIDS* 21: S17-S28.

MOST Project. Description of the work in Uganda. Accessed on August 9, 2009 from <http://www.mostproject.org/countryprograms.htm#Uganda>.

Parker, SP and WD Cubitt. 1999. The use of the dried blood spot sample in epidemiological studies. *J Clin Pathol* 52: 633-639.

Sirima S, A Tiono, A Gansané, A Diarra, A Ouédraogo, A Konaté, J Kiechel, C Morgan, P Olliaro and W Taylor. 2009. The efficacy and safety of a new fixed-dose combination of amodiaquine and artesunate in young African children with acute uncomplicated *Plasmodium falciparum*. *Malaria Journal*: 8:48, 11 pp.

Taylor W, D Terlow, P Olliaro, N White, P Brousseau, F ter Kuile. 2006. Use of weight-for-age data to optimize tablet strength and dosing regimens for a new fixed-dose artesunate-amodiaquine

combination for treating falciparum malaria. *Bulletin of the World Health Organization* 84:956-964.

UNAIDS and WHO. 2006. AIDS Epidemic Update. December 2006. UNAIDS/06/29E. Geneva: UNAIDS and WHO.

UNAIDS and WHO. 2007. AIDS Epidemic Update. December 2007. UNAIDS/07/27E. Geneva: UNAIDS and WHO.

UNAIDS Reference Group on Estimates, Modelling, and Projections. 2006. Improving parameter estimation, projection methods, uncertainty estimation, and epidemic classification. Report of a meeting of the UNAIDS Reference Group on Estimates, Modelling, and Projections, Prague, Czech Republic, 29 November - 1 December. Available at: <http://data.unaids.org/pub/Report/2007/2006prague>.

World Health Organization. 2006. WHO Child Growth Standards: Length/height-for-age, weight-for-age, weight-for-length, weight-for-height and body mass index-for-age: Methods and development. Geneva: World Health Organization. Available at: http://www.who.int/childgrowth/standards/technical_report/en/index.html.