

Inflammation, Chronic Diseases and Aging in a Developing Country Context: Evidence from a Biomarker Data Collection in Malawi

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Abstract

Virtually no large-scale socioeconomic survey data exist in sub-Saharan Africa that also provides a comprehensive biomarker-based assessment of respondents' health. In this paper, we present analysis of newly collected biomarker-based health indicators from rural Malawi that have been integrated into the Malawi Longitudinal Study of Families and Health (MLSFH). Our data includes the following biomarkers: high-sensitivity C-Reactive Protein, cholesterol, LDL, HDL, triglycerides, circulating glucose, urea, albumin, creatinine, total protein, uric acid, and HbA1c. For the first time in a sub-Saharan context, we will be able to study the factors associated with the distribution of biological markers for cardiovascular and/or metabolic risk factors, inflammation and aging and/or disease progression. We use these biomarkers to evaluate overall health status, estimate aging-related morbidity and mortality of the rural Malawian population, and examine the association of health with poverty, malnutrition and exposure to infectious diseases such as malaria, TB, HIV/AIDS, and other infectious/parasitic diseases.

1. Introduction

Biomarker-based indicators of health provide valuable insights into the biological functioning of individuals, critical information on pre-disease pathways proximate to a wide range of important health outcomes and the complex causal pathways between socioeconomic environments and health (Boerma et al. 2001; M. Weinstein and R. Willis 2001; T. McDade et al. 2007). Yet, biomarker measures that allow these analyses have only recently become integrated with extensive large-scale socioeconomic/demographic data⁵. Virtually no large-scale socioeconomic survey data exist in sub-Saharan Africa that also provides a comprehensive biomarker-based assessment of respondents' health. Such

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⁵ E.g., the Health and Retirement Study (HRS) and the English Longitudinal Study of Aging in the UK (ELSA)) are among the larger studies collecting biomarkers.

indicators, however, provide critical information on pre-disease pathways that proximate a wide range of important latent poor health outcomes.

These aspects are particularly important, but so far under-explored, in sub-Saharan Africa where populations bear a heavy burden of disease including malaria, TB, HIV/AIDS, and other infectious/parasitic diseases. For instance, in other contexts, numerous studies have established the pertinence of biomarker-based health indicators for assessing immune system functioning (Danesh et al. 2000; Kiecolt-Glaser et al. 1987; Ridkter et al. 2000), the biomedical consequences of poverty and malnutrition (Haltermann et al. 2001; Nokes et al. 1998; Va den Broek et al. 1998), and the effects of diabetes on morbidity and mortality (e.g., Rohlfing et al. 2000). While infectious diseases—such as HIV and Malaria—often attract the majority of research and are typically the focus of programs and interventions in sub-Saharan Africa (Behrman et al. 2006), there is a lack of knowledge on important health aspects such as *a*) risk factors associated with chronic/degenerative diseases typically accompanying the pace of aging, and *b*) how the immuno-infective environment in sub-Saharan Africa increases the risk for systemic assaults and thus influences the process of aging, morbidity and mortality.

In this paper, we present newly collected biomarker-based health indicators from rural Malawi that have been integrated into the longitudinal data collection from the Malawi Longitudinal Study of Families and Health (MLSFH). These data provide a unique possibility to address the existing important gap in the research literature discussed above. In addition, for the first time in a sub-Saharan context, these biomarker-based indicators allow to study the factors associated with the distribution of biological markers for cardiovascular and/or metabolic risk factors, inflammation and aging and/or disease progression. Moreover, we will be able to investigate—with biomarker-based health indicators that provide more accurate assessments than self-reported health assessments—how health conditions, as well as aging-related morbidity and mortality of the rural Malawian population are affected by poverty, malnutrition and exposure to infectious diseases such as malaria, TB, HIV/AIDS, and other infectious/parasitic diseases.

We use newly-collected innovative biomarker-based health indicators to describe and assess the overall health of 1,000 randomly-selected individuals living in the Southern region of Malawi, one of the poorest countries in the world. The biomarkers utilized in this research include high-sensitivity C-Reactive Protein (hsCRP), cholesterol, LDL, HDL, triglycerides, circulating glucose, urea, albumin, creatinine, total protein, uric acid, and HbA1c. Using these biomarker measures and MLSFH longitudinal survey data for these respondents will allow us to address a unique set of research goals for a rural population in sub-Saharan Africa.

The main objective this paper, which will be the first to present results of this biomarker-based study, is to identify factors associated with the distribution of biological markers for cardiovascular or metabolic risk factors and markers of disease and/or disease progression. We are particularly interested in the variability of these biomarkers and

possible interactions with age and sex, socioeconomic and environmental variables, HIV status in the context of poor and high infectious environment.

2. Background and Data

Data used for this research comes from the Malawi Longitudinal Study of Families and Health (MLSFH; formerly, Malawi Diffusion and Ideational Change Project), a longitudinal panel survey with survey waves in 1998, 2001, 2004, 2006 and 2008 that is implemented in three sites in rural Malawi: Rumphi (in the north), Mchinji (centre), and Balaka (south). Since 2004, the MLSFH has also conducted repeated tests of HIV for MLSFH respondents, revealing a HIV prevalence of about 9% in the MLSFH study population, with considerable regional variation: 2006 HIV prevalence among MLSFH respondents is 6.6% in Rumphi, 7.7% in Mchinji and 12.6% in Balaka. In 2008, the most recent data collection, the MLSFH conducted surveys with about 4000 male and female respondents age 28 and older, including also HIV tests and anthropometric measurements.

An innovative component of the 2008 MLSFH data collection is the inclusion of biomarkers for about 1,000 randomly-selected respondents in Balaka that provide measures for inflammation, chronic diseases and aging. These biomarkers include high-sensitivity C-Reactive Protein (hsCRP), cholesterol, LDL, HDL, triglycerides (a lipids panel), circulating glucose, urea, albumin, creatinine, total protein, uric acid, (collectively a measure of renal function and infection), HbA1c (a 3-month average of blood glucose, a measure of glucose control), and hemoglobin.

These biomarkers are currently being collected using the Demecal test kit, a innovative and newly available test kit that allows the extraction of blood plasma from blood drops collected via a simple finger prick from respondents at the home. The Demecal kit offers an ideal combination of viable blood for analysis and non-invasive means of blood collection. As such, the Demecal method offers several advantages over the other common means of collecting blood samples such as dried blood spots (DBS), which are vulnerable to damage or loss of viability of the blood sample; or intravenous blood collection, which is much more invasive than finger prick blood drops.

While MLSFH 2008 survey and HIV testing data is already available, the collection of biomarker data is currently ongoing, and is expected to be available by mid-November 2008.

3. Methods and Research Hypotheses

The analyses presented in this paper are the initial analyses of these newly-collected biomarker data. The methods that will be used for the analyses in this paper include descriptive statistics and explorative data analyses, as well as regression analyses exploring the association of the collected biomarkers with various demographic, socioeconomic and health characteristics.

A particular focus of our analyses will be the presence of high levels of hsCRP, which has been clinically recognized risk factor linked to the progression of acute infections, but also chronic diseases associated with aging. As a reliable serum indicator for systematic inflammation (Finch and Crimmins 2004), CRP increases with age, often to levels implicated in arterial degeneration and immunosenescence (Gurven, Kaplan, Whiking, Finch and Crimmins 2008). A substantial proportion of the population in Malawi suffers conditions that chronically elevate inflammatory markers. While there has been considerable research on levels of hsCRP in individuals known to be infected with HIV (see for example de Maat and Kluft 2001), very few studies have examined the distribution of inflammatory biomarkers within the general population in sub-Saharan Africa.

Two main hypotheses guide the present analyses:

a) We expect to find that biomarkers of inflammation, chronic diseases, and poor health are substantially elevated in the rural Malawian population as compared to developed countries. We hypothesize that this is particularly true with respect to indicators such as C-reactive protein that signals stress to the immune system. As a corollary, the rural Malawian population experiences substantially higher and more rapid rates of aging as reflected by biological markers of body functioning.

b) Direct exposure to infectious diseases, specifically HIV/AIDS, substantially diminishes individuals' health as reflected by the biomarkers.

4. Expected Findings and Conclusions

The biomarker data are in the process of being collected and will be available to conduct this research by mid-November 2008. Thus, in the current abstract we are not able to present any preliminary analysis based on these innovative data. However, we believe that this analysis will make an important contribution for understanding the health dynamics of a rural population in sub-Saharan Africa.

References

- Anglewicz, P., J. Adams, F. Obare, S. Watkins, and H.-P. Kohler (2007). The Malawi Diffusion and Ideational Change Project 2004–06: Data collection, data quality and analyses of attrition. Unpublished working paper, Population Studies Center, University of Pennsylvania, Philadelphia, PA. Available online at <http://www.malawi.pop.upenn.edu>.
- Behrman, J. R., J. A. Behrman, N. Perez (2006) Out of Sync? Social Science Research on Health and Development and Health Conditions in Developing Countries *Unpublished working paper*, University of Pennsylvania.
- Bignami-Van Assche, S., G. Reniers, A.A. Weinreb (2003). An Assessment of the KDICP and MDICP Data Quality. *Demographic Research* 5(1):29-76.
- Boerma, J.T., E. Holt, and R. Black (2001). Measurement of Biomarkers in Surveys in Developing Countries: Opportunities and Problems. *Population and Development Review* 27: 303-314.
- Danesh, J., P. Whincup, M. Walker, L. Lennon, A. Thomson, P. Appleby (2000) Low grade inflammation and coronary heart disease: Prospective study and updated meta-analysis. *British Medical Journal*, 321, 199-204.
- De Maat, M.P. and C. Kluft (2001). Determinants of C-Reactive Protein Concentration in Blood. *Ital Heart J* 2(3): 189-195.
- Finch, C.E. and Grimmins, E.M. (2004). Inflammatory Exposure and Historical Changes in Human Life-Spans. *Science* 305(5691): 1736-1739.
- Gurven, M., H. Kaplan, J. Winking, C. Finch, and E.M. Grimmins (2008). Aging and Inflammation in Two Epidemiological Worlds. *J Gerontology A Biol Sci Med Sci* 63(2): 196-199.
- Halterman, J. S., J. M. Kaczorowski, C. A. Aligne, P. Auinger, P. G. Szilagyi (2001) Iron deficiency and cognitive achievement among school-aged children and adolescents in the United States. *Pediatrics*, 107(6), 1381-1386.
- Kiecolt-Glaser, J. K., L. Fisher, P. Ogrocki, J. C. Stout, C. E. Speicher, R. Glaser (1987) Marital quality, marital disruption, and immune function *Psychosomatic Medicine*, 49, 13-34.
- McDate, T.W., S. Williams, and J.J. Snodgrass (2007). What a Drop Can Do: Dried Blood Spots as a Minimally Invasive Method for Integrating Biomarkers into Population-Based Research. *Demography* 44(4): 899-925.

- Nokes, C., C. van den Bosch, D. A. P. Bundy (1998) The Effects of Iron Deficiency and Anemia on Mental and Motor Performance, Educational Achievement, and Behavior in Children: A Report of the International Nutritional Anemia Consultative Group Washington, D.C.:USAID.
- Obare, F., P. Fleming, P. Anglewicz, S. Watkins, and H.-P. Kohler (2006). HIV prevalence and HIV Incidence in rural Malawi: Evidence based on the Malawi Diffusion and Ideational Change Project, 2004–06. Unpublished working paper, Population Studies Center, University of Pennsylvania, Philadelphia, PA.
- Ridker, P.M. (2001). High-Sensitivity C-Reactive Protein: Potential Adjunct for Global Risk Assessment in the primary Prevention of Cardiovascular Disease. *Circulation* 103(13): 1813-1818.
- Rohlfing, C. L., R. R. Little, H. M. Wiedmeyer, J. D. England, R. Madsen, M. Harris, K. Flegal, M. Eberhardt, D. Goldstein (2000) Use of GHb (HbA1c) in screening for undiagnosed diabetes in the US population. *Diabetes Care*, 23, 187-191.
- Thornton, Rebecca, Agatha Bula, Kondwani Chavula, Simona Bignami-Van Assche, and Susan C. Watkins. (2005). [Reactions to Voluntary Counseling and Testing in Rural Malawi](#). Submitted for publication.
- Watkins, S., Behrman, J.R., Kohler, H.P., and Zulu, E.M. (2003). Introduction to research on demographic aspects of HIV/AIDS in rural Africa. *Demographic Research*, S1(1), 1-30.
- Weinstein, M. and R.J. Willis (2001). Stretching Social Surveys to Include Bioindicators: Possibilities for the Health and Retirement Study, Experience from the Taiwan Study of the Elderly. In: C.E. Finch et al.(2001). *Cells and Survey: Should Biological Measures be Included in Social Science Research?* National Research Council (U.S.). Committee on Population: National Academy Press. pp: 250-275.
- Van den Broek, N. R., S. A. White, J. P. Neilson (1998) The association between asymptomatic HIV infection and the prevalence and severity of anemia in pregnant Malawian women. *American Journal of Tropical Medicine and Hygiene*, 59, 1004-1007.