The Impact of Anemia on Energy and Physical Functioning in Individuals With AIDS

Richard D. Semba, MD, MPH; Barbara K. Martin, PhD; John H. Kempen, MD, PhD; Jennifer E. Thorne, MD; Albert W. Wu, MD, MPH; for the Studies of the Ocular Complications of AIDS Research Group

**Background:** To our knowledge, the relationship between changes in hemoglobin level and energy and physical functioning in the anemic and “normal” ranges of hemoglobin among individuals with AIDS has not been well characterized.

**Methods:** In a multicenter, prospective, cohort study involving 19 clinics in the United States, 1406 individuals, 13 years and older, with AIDS were administered the Medical Outcomes Study HIV [human immunodeficiency virus] Health Survey (MOS-HIV) at baseline and at 3- to 6-month follow-up visits. Energy and physical functioning scores were the main outcomes.

**Results:** At baseline, a higher hemoglobin level was associated with a higher energy score and a higher physical functioning score \((P < .001 \text{ for both})\), after adjusting for CD4 lymphocyte count, sex, age, education, and HIV risk factor. In longitudinal analyses, increases in hemoglobin were associated with increases in energy and physical functioning scores \((P < .001 \text{ for both})\), after adjusting for CD4 lymphocyte count, sex, age, education, and HIV risk factor. Changes in the energy scales were, on average, 1.5 and 2.3 scale points per 1-g/dL change in hemoglobin level in the normal and anemic ranges, respectively. For the physical functioning scale, average changes were 2.7 and 2.6 scale points per 1-g/dL change in hemoglobin level in the normal and anemic ranges, respectively.

**Conclusions:** Higher levels of hemoglobin are associated with better quality of life among individuals with AIDS. Changes in hemoglobin level within the conventional normal range of hemoglobin are also significantly associated with changes in quality of life.

Arch Intern Med. 2005;165:2229-2236

---

**ANEMIA IS THE MOST COMMON morbidity of human immunodeficiency virus (HIV) infection and is associated with increased progression to AIDS and higher mortality.** The consequences of anemia include fatigue, a decreased sense of well-being, and an increased need for expensive human recombinant erythropoietin therapy, transfusions, and hospitalizations. Although the impact of anemia on the quality of life of patients with cancer has been well established, less is known about the effect of anemia on fatigue and quality of life in HIV-infected patients. The Anemia in HIV Working Group has recommended that the impact of anemia on energy/fatigue and anemia-related quality-of-life indicators needs further characterization. The energy and physical functioning scales of the Medical Outcomes Study HIV Health Survey (MOS-HIV), the most widely used quality-of-life instrument in HIV studies, are reliable and have discriminant validity in HIV-infected patients. Large increases in hematocrit among anemic patients who received recombinant human erythropoietin therapy were associated with substantial improvement in energy scales and physical functioning in HIV-infected adults. It is unclear if hemoglobin is associated monotonically with energy and physical functioning across the full range of concentrations or whether there is a threshold above which there is no subjective benefit of increasing the hemoglobin concentration. A recent study suggests that the relationship between hemoglobin and physical functioning may extend well into the range of what are conventionally defined as “normal” hemoglobin concentrations.

We hypothesized that hemoglobin, as measured in cross-sectional and longitudinal analyses, has a measurable and clinically significant association with health-
related quality of life that is independent of other markers of HIV disease severity. We also hypothesized that an important relationship between hemoglobin and quality of life would be apparent for smaller changes of hemoglobin within the range that is conventionally defined as a normal hemoglobin concentration and within the anemic range. To address these hypotheses, we examined quality of life as assessed by the MOS-HIV energy and physical functioning scales among individuals with AIDS participating in the longitudinal studies of the Ocular Complications of AIDS.

### METHODS

The subjects were participants in the longitudinal Studies of the Ocular Complications of AIDS, an ongoing, multicenter, epidemiological study of the ocular complications of AIDS. Subjects were enrolled and followed up at 19 AIDS-related ophthalmology clinics in the United States from September 1, 1998, through August 31, 2002. Inclusion criteria included being 13 years or older and being diagnosed as having AIDS, based on the 1993 Centers for Disease Control and Prevention revised surveillance case definition. Patients were seen semiannually unless they had a major ocular complication of AIDS, such as cytomegalovirus retinitis, in which case they were seen quarterly. At enrollment and follow-up visits, demographic and medical information was recorded using standardized questionnaires, and laboratory studies were performed. A complete blood cell count was obtained using a hematology analyzer. The CD4 lymphocyte count was measured by flow cytometry. Plasma HIV RNA was measured locally at each center.

Quality of life was measured at baseline and at every follow-up visit. Measurements were obtained before the ophthalmological examination, to avoid immediate effects of examination results on self-report of quality-of-life status. The MOS-HIV was used to assess the relationship between hemoglobin level and health-related quality of life. The MOS-HIV includes questions on self-perceived energy and functioning. The survey includes questions such as, “Does your health now limit you in these activities?”, “If so, how much?”, “Walking one block?” and “Walking uphill or climbing (a few flights of stairs)?” (Answers were as follows: Yes, limited a lot. Yes, limited a little. No, not limited.) The energy and physical functioning scales of the MOS-HIV quality-of-life instrument were transformed into a 0 to 100 scale, with higher scores reflecting...
better health status. The Cronbach α11 was used to measure the internal consistency reliability of the 2 scales in this population. Multitrait analysis12 was used to assess the convergent and discriminant construct validity of these scales with respect to other scales in the MOS-HIV. The distributions of the scales were checked for floor and ceiling effects.

The presence of anemia at baseline was examined by demographic characteristics (age, sex, education, race, and HIV risk factors) and by indicators of HIV disease progression (CD4 lymphocyte count and plasma HIV RNA level). Anemia was defined as a hemoglobin level of less than 12 g/dL for women and less than 13 g/dL for men, as defined by the World Health Organization.13 Age, education, CD4 lymphocyte count, and plasma HIV RNA level were categorized as shown in Table 1. The CD4 lymphocyte count categories reflect cut points used in clinical care; plasma HIV RNA categories are approximate quartiles of the distribution. P values were obtained using the χ² test. Energy and physical functioning scores also were examined by demographic characteristics and indicators of HIV disease severity, and by the presence of anemia. P values were obtained using the Kruskal-Wallis test.

Among those not anemic at baseline, the incidence of anemia during follow-up was analyzed by demographic characteristics and by indicators of HIV disease severity. The time to development of anemia in 25% of those not anemic at baseline was estimated, and P values were obtained using the Kaplan-Meier method. The incidence per person-year of observation also was calculated.

Multivariate linear regression models were created to examine the association of hemoglobin level with energy and physical functioning scores at baseline, adjusted for age, sex, education, race, HIV risk factor, and CD4 lymphocyte count. Alternative models also were created, in which plasma HIV RNA category was used in place of and in addition to CD4 lymphocyte category. Secondary multivariate longitudinal analyses, alternative models were created in which plasma HIV RNA level were categorized as shown in Table 1. The CD4 lymphocyte count categories reflect cut points used in clinical care; plasma HIV RNA categories are approximate quartiles of the distribution. P values were obtained using the Kaplan-Meier method. The incidence per person-year of observation also was calculated.

Multivariate linear regression models were created to examine the association of hemoglobin level with energy and physical functioning scores at baseline, adjusted for age, sex, education, race, HIV risk factor, and CD4 lymphocyte count. Alternative models also were created, in which plasma HIV RNA category was used in place of and in addition to CD4 lymphocyte category. Secondary multivariate longitudinal analyses, alternative models were created in which plasma HIV RNA level were categorized as shown in Table 1. The CD4 lymphocyte count categories reflect cut points used in clinical care; plasma HIV RNA categories are approximate quartiles of the distribution. P values were obtained using the Kaplan-Meier method. The incidence per person-year of observation also was calculated.

The level of significance in this study was P<.05.

**RESULTS**

Between September 1, 1998, and August 31, 2002, there were 1422 subjects enrolled, of whom 1406 (98.9%) had baseline hemoglobin and quality-of-life measures. Of 1112 with follow-up data collected on or before August 31, 2002, 1092 (98.2%) had hemoglobin and quality-of-life measures. At enrollment, 34.2% (95% confidence interval, 32.7%-36.7%) of subjects were anemic. The relationships of the prevalence and incidence of anemia to demographic characteristics (age, sex, education, race, and HIV risk factors) and to indicators of HIV disease progression (CD4 lymphocyte count and plasma HIV RNA category) are shown in Table 1. The prevalence of anemia was higher among younger subjects, black subjects, women, and those with a lower level of education. Of the risk factors for HIV infection, the lowest prevalence of anemia was among men who had sex with men. The prevalence of anemia was higher among those with lower CD4 lymphocyte counts and higher plasma HIV RNA levels. The overall time to 25% incidence of anemia in the study was 1.61 years. The time to 25% incidence of anemia is shown in Table 1, and was lower among black subjects, women, those with a lower level of education, injection drug users, individuals with lower CD4 lymphocyte counts, and those with a high plasma HIV RNA level.

The mean energy and physical functioning scores at enrollment are shown by demographic characteristics, CD4 lymphocyte count, plasma HIV RNA level, and anemia status in Table 2. There were no significant differences in energy score by age category or HIV risk factor, but borderline associations were found with race and sex. Energy scores were increasingly higher with higher education, higher CD4 lymphocyte category, and lower HIV RNA level.
RNA category, and were lower in subjects with anemia compared with those without anemia. Physical functioning scores were not significantly related to age, but were lower in black subjects and women, and were increasingly higher with increasing CD4 lymphocyte category and decreasing HIV RNA category. Physical functioning scores were higher among men who had sex with men and among those who were not anemic compared with those with anemia.

The relationships of hemoglobin concentrations, in deciles, with energy and physical functioning scores at enrollment are shown in the Figure. Energy and physical functioning scores were positively correlated with increasing decile of hemoglobin concentration (P < .001).

Estimates from multivariate models of the relationship of hemoglobin level with energy and physical functioning scores at enrollment are shown in Table 3. Hemoglobin level remained associated with energy score after adjusting for CD4 lymphocyte category, sex, age, education, HIV risk factor, and race. Hemoglobin level remained positively associated with physical functioning score after adjusting for these same factors. In alternative models in which plasma HIV RNA level was used in place of CD4 lymphocyte count, change in hemoglobin (per 1 g/dL) remained significantly (P < .001) associated with change in energy score (mean [SE], 1.46 [0.39]) and physical functioning score (mean [SE], 2.92 [0.42]).

Estimates from multivariate models of the relationship between longitudinal change in hemoglobin and change in energy and physical functioning scores are shown in Table 4. Change in hemoglobin level remained positively associated with change in energy score after adjusting for CD4 lymphocyte count, sex, age, education, HIV risk factor, and race. Similarly, change in hemoglobin level remained positively associated with change in physical functioning score after adjusting for the same factors. In alternative models in which plasma HIV RNA level was used in place of CD4 lymphocyte count, change in hemoglobin (per 1 g/dL) remained significantly (P < .001) associated with change in energy score (mean [SE], 2.04 [0.39]) and physical functioning score (mean [SE], 2.57 [0.40]).

When interaction terms were also added into the models to provide separate estimates of the effects of hemoglobin and CD4 lymphocyte count changes on energy and physical functioning score changes when hemoglobin measures were in the anemic and normal ranges, changes in the energy scale were, on average, 1.5 and 2.3 scale points per 1-g/dL change in hemoglobin in the normal and anemic ranges, respectively. Average energy scale changes were 0.5 and 2.0 scale points per 100/µL change in CD4 lymphocyte count in the normal and anemic ranges, respectively. For the physical functioning scale, average changes were 2.7 and 2.6 scale points per 1-g/dL change in hemoglobin in the normal and anemic ranges, respectively, and 0.5 and 1.5 scale points per 100/µL change in CD4 lymphocyte count in the normal and anemic ranges, respectively.
This study demonstrates that anemia has an important impact on quality of life in patients with AIDS, and that increasing levels of hemoglobin are associated with increasing energy and physical functioning scores across a wide range of hemoglobin concentrations. The association between hemoglobin concentration and energy and physical functioning scores was consistent in cross-sectional analyses at enrollment and in longitudinal analyses. The relationship also was consistent after adjusting for HIV disease severity, age, race, sex, and social and demographic factors.

Previous studies have shown that large changes in hemoglobin, as may accompany treatment with recombinant erythropoietin therapy, improve quality of life. However, our observations suggest that energy and physical functioning improve even as hemoglobin increases within the low end of the normal range, rather than identifying a threshold level beyond which increased energy and physical functioning no longer occurred. In the present study, for every 1-g/dL change in hemoglobin, there were changes of 1.5 to 2.3 points on the energy scale and 2.6 to 2.7 points on the physical functioning scale. Are these differences clinically important? Initial studies using the MOS-HIV suggested that there was a difference of 7 points on the energy scale and 10 points on the physical functioning scale between asymptomatic and symptomatic HIV disease. In a clinical trial involving patients with AIDS, there were differences of 6.7 points on the energy scale and 8.8 points on the physical functioning scale between those who developed adverse events in the first 4 weeks of the trial compared with those who did not have any adverse events. For patients with Pneumocystis pneumonia of mild to moderate severity, a 10–mm Hg change in A-a gradient was associated with a 5-point increase in the energy scale. These data suggest that changes of 2 to 3 g/dL in hemoglobin concentration and perhaps less would be important to an average patient.

This observation suggests that treatment of anemia may have potential benefit, perhaps particularly in terms of

### Table 3. Multivariate Model for the Association of Hemoglobin With the Energy and Physical Functioning Scores at Enrollment

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Energy Data</th>
<th>Physical Functioning Data</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Score Estimate (SE)</td>
<td>P Value†</td>
</tr>
<tr>
<td>Intercept</td>
<td>30.11 (6.06)</td>
<td>NA</td>
</tr>
<tr>
<td>Hemoglobin (per 1 g/dL)</td>
<td>1.42 (0.38)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>CD4 lymphocyte count/µL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>51-200</td>
<td>2.33 (1.65)</td>
<td>.16</td>
</tr>
<tr>
<td>201-350</td>
<td>4.27 (1.87)</td>
<td>.02</td>
</tr>
<tr>
<td>≥351</td>
<td>6.80 (1.91)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Female sex</td>
<td>−0.48 (1.98)</td>
<td>.81</td>
</tr>
<tr>
<td>Age (per year)</td>
<td>−0.05 (0.08)</td>
<td>.52</td>
</tr>
<tr>
<td>Education (college)</td>
<td>4.50 (1.43)</td>
<td>.02</td>
</tr>
<tr>
<td>Men having sex with men</td>
<td>0.96 (1.62)</td>
<td>.55</td>
</tr>
<tr>
<td>Black race</td>
<td>6.74 (1.48)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

Abbreviation: NA, data not applicable.
*Reference category for human immunodeficiency virus risk factor is all categories together, except men having sex with men; and for race/ethnicity, white race.
†Calculated using generalized estimating equation regression to obtain robust variance estimates for repeated measures.

### Table 4. Multivariate Model for Association of Change in Hemoglobin Level With Change in Energy and Physical Functioning Scores

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Energy Data</th>
<th>Physical Functioning Data</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Score Estimate (SE)</td>
<td>P Value†</td>
</tr>
<tr>
<td>Intercept</td>
<td>2.52 (3.88)</td>
<td>NA</td>
</tr>
<tr>
<td>Hemoglobin (per 1 g/dL)</td>
<td>2.10 (0.41)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>CD4 lymphocyte count, change in 100/µL</td>
<td>1.10 (0.37)</td>
<td>.002</td>
</tr>
<tr>
<td>Female sex</td>
<td>−2.47 (2.21)</td>
<td>.26</td>
</tr>
<tr>
<td>Age (per year)</td>
<td>−0.04 (0.09)</td>
<td>.63</td>
</tr>
<tr>
<td>Education (college)</td>
<td>−0.86 (0.61)</td>
<td>.59</td>
</tr>
<tr>
<td>Men having sex with men</td>
<td>−2.29 (1.96)</td>
<td>.24</td>
</tr>
<tr>
<td>Black race</td>
<td>−1.45 (1.72)</td>
<td>.40</td>
</tr>
</tbody>
</table>

Abbreviation: NA, data not applicable.
*Reference category for human immunodeficiency virus risk factor is all categories, except men having sex with men; and for race/ethnicity, white race.
†Calculated using generalized estimating equation (GEE) regression to obtain robust variance estimates for repeated measures. The SEs are from the GEE model.
Baylor College of Medicine, Cullen Eye Institute, Houston, Tex: Richard Alan Lewis, MS, MD (Director); Pamela Frady, COMT; Ronald Gross, MD; Silvia Oreno-Nania, MD; Laura Shawver, COT; James W. Shigley, CRA; Benita Slight, COT; Steven Spencer, BA, COMT. Former members: Richard C. Allen, MD; Stephen P. Travers, CRA.

Emory University Eye Center, Atlanta, Ga: Daniel F. Martin, MD (Director); John Closek, COT; Alex DeLeon; David Furukawa, PA; Deborah Gibbs, COMT; Bob Myles, CRA; James P. Steinberg, MD. Former members: Denise Armenger; Antonio Capone, Jr; James Gilman, CRA; Baker Hubbard MD: Sandra Strittman.

Indiana University, Indianapolis: Mitchell Goldman, MD (Director); Janice Brown; Thomas Ciuilla, MD; Jean Craft, RN, CS; Hua Gao, MD; Paul Fry; Janet Hernandez, RN; Linda Pratt, RN; Tim Steffens, CRA; Beth Zwickl, RN, CS, MSN. Former members: Ronald Danis, MD; Debra Poe; James D. Richardson, MD; L. Joseph Wheat, MD.

The Johns Hopkins University School of Medicine, Baltimore, MD: J. P. Dunn, MD (Director); Patricia Barditch-Crovoo, MD; Stephen G. Bolton, CRNP; Joseph B. Brodine; Diane M. Brown, RN; Lisa M. Brune, RN, BSN; Dennis Cain; David Emmert; Douglas A. Jabs, MD, MBA; John H. Kempen, PhD; Laura G. Neisser, COT; Richard D. Semba, MD, MPH; Jennifer E. Thorne, MD. Former members: Rebecca Becker, PA-C; Jared Christopher, RN, BSN; Terry George; Susan Salavzbia, RN; Paul A. Latkany, MD; Quan D. Nguyen, MD; Armando L. Oliver, MD; George B. Peters III, MD; Faqir A. Qazi, MD; Aruna Subramanian, MD.

Louisiana State University Medical Center, New Orleans: Bruce Barron, MD (Director); Robin Bye, RN; Rebecca Clark, MD; Larry Dillon, COT; Christine Jarrott, RN. Former members: John Bennett, COT; Mandi Conway, MD; Gholam Peyman, MD. Former boarder: Eileen Buroff.

New York Hospital–Cornell Medical Center, New York: Mark-Hen Heim Heimann, MD (Director); Kenneth Boyd; Charles Cole, MD; Roberta Janis, RN, BSN; Jean Mamakos, RN, MSN; Joseph Murphy, MD; Diane (Iglesias) Rivera, COA; Kent Sepkowitz, MD. Former member: Firas M. Rahhal, MD.

New York University Medical Center, New York: Dorothy N. Friedberg, MD (Director); Adrienne Adessi, MA, RN, PhD; Douglas Dieterich, MD; Richard Hutt, RN; Monica Lorenzo-Latkany, MD; Maria Pei, COA. Former member: Alex McMeeking, MD.

Northwestern University, Chicago, IL: Alice Lyon, MD (Director); Pamela Hulvey; Lori Kaminski; Alice T. Lyon, MD; Annmarie Muñana, RN; Robert L. Murphy, MD; Jonathan Shankle; Michelle Till, MD. Former members: Daniel Andrews, MD; Steve Grohman, MD; Alexander Habib; Robert Hirshhstich, MD; Jill Koecher; Frank Palella, MD; Peter Pertel, MD; Jamie VonRoen; James Yuhr.

Rush University, Chicago: Mathew W. MacCumber, MD, PhD (Director); Bruce Gaynes, OD, PharmD; Harold Kessler, MD, Pauline Merrill, MD; Frank Morini; Denise Voisvull-Marre. Former members: Andrea Kopp; Nada Smith.

University of California, Irvine: Baruch D. Kuppermann, MD, PhD (Director); Marcia Alcouloume, MD; Donald N. Forthal; Jeff Grijalva, COT; Rosie Magallon; Santos Patel, MD; Bret Trup. Former members: Karen Lopez; Nader Moinfar, MD; Thomas Mark, CRA; Melody Vega, COA; Randy Williams.

University of California, Los Angeles: Gary N. Holland, MD (Director); Robert D. Almanzor; Margrit E. Carlson, MD; Suzette A. Chafey, RN, NP; Ann K. Johiro, RNC, FNP; Ardis A. Moe, MD; Susan S. Ransome, MD; Angela Sanderson; Robert Stalling, COA. Former member: Dennis Thayer, CRA.

University of California, San Diego: William R. Freeman, MD (Director); Tom Clark; Daniel Goldberg; Brian Kosobucki, MD. Former members: Sunan Chaidhawanqual, MD; Lingyun Cheng, MD; Mark Cleveland; Randall L. Gannon; Claudia Garcia, MD; Patricia Garoutte; Marietta Karavellas, MD; Nicole Reagan; Mi-Kyoung Song, MD; Francesca Torriani, MD; Dorothy Wong; Tekeena Young.

University of California, San Francisco: Alex Louie, MD (Director); Bruce Stieler, MD; Robert Biluich; Thomas Ciulla, MD; Jean Craft, RN, MSN; Joseph Murphy, MD; Diane (Iglesias) Rivera, COA; Kent Sepkowitz, MD; James O. O’Donnell, MD.

The University of North Carolina at Chapel Hill: Travis A. Meredith, MD (Director); Debra Cantrell; Kelly DeBoer; Sandy Jankowski; Angela Jeffries; Roje Kaemaz; Maurice B. Lander, MD; Kean T. Oh, MD; David Wohl, MD. Former members: Stephanie Betran; David Eifrig, MD; John Foley, MD; Jan Kylstra, MD; Barbara Longmire; Sharon Myers; Jeremy Pantell; Stephen G. Bolton, CRNP; Joseph B. Brodine; Diane (Iglesias) Rivera, COA; Kent Sepkowitz, MD; James O. O’Donnell, MD.

The University of Pennsylvania Medical Center, Philadelphia: Charles W. Nichols, MD (Director); Dr. Mark Bardsley, BSN; Cheryl C. Devine, MD; Albert Johnson; Jay Kostman; Rob Roy MacGregor, MD; Albert M. Maguire, MD; William Nyberg; Leslie Roman, RN, BSN. Former members: Christopher Helker, RN, MSPH; Karen McGibney, RN; Keith Mickelberg, RN.

University of Southern California, Los Angeles: Jennifer I. Lim, MD (Director); Tom S. Chang, MD; Alexander Charonis, MD; Robert Equi, MD; Jesus Garcia; Francoise Kramer, MD; Lori Levin, MPH; Tracy Nichols, BSN; Scott Paulter, MD; Wyatt Saxton; Nancy Walker, COA. Former members: Bonnie Hernandez, COT, JoAnn Leto, COT; Sharon Millard, RN, COT; Jeffrey Nadler, MD.

The University of Texas Medical Branch, Galveston: Helen K. Li, MD (Director); Wael M. Abdulghani, MD; Susan Busch; John Horna, BS; Wiline Jean; Zbigniew Krasow; BS; Lu-Chi Nguyen, COMT; David Paar, MD; Anne Stewart, MS. Former members: Robert Blem, MD; Celia Hutchinson; Vivian Keys; Beverly B. Mizell, RN; Michelle Onarato, MD; Sami H. Uwaydat, MD.

(Continued)
adults. However, the cumulative incidence of anemia reducing the prevalence of anemia among HIV-infected (CART), introduced around 1996, has had an impact on light the fact that anemia remains the most common mor-

Endurance, energetic efficiency, and maximum oxygen consumption are improved in athletes with ranges of

as with observational studies, potential biases that may have affected the observations should be considered in interpreting the results of this study. Participants with a better quality of life may have been more likely to receive CART, but the analyses were adjusted for effects of CART (CD4 lymphocyte count and plasma HIV load). Estimates of anemia prevalence may be biased by which patients were available and willing to participate in the parent study, and estimates of incident anemia could be similarly affected by incomplete follow-up. However, such bias would likely serve to underestimate the prevalence and incidence of anemia, if those who are anemic are less likely to contribute data to the study. This would not be expected to affect the relative estimates of the effect of different hemoglobin levels or changes in hemoglobin level on the energy and physical functioning scales. The study population consisted of individuals with AIDS who were seen at major academic medical centers in the United States. The findings from this study population may not be generalized to other populations if the level of medical care and use of antiretroviral medications are different, and if the association of hemoglobin level with energy and physical functioning is modified by these factors.

In summary, this prospective cohort study shows that increases in hemoglobin are associated with measurable increases in quality of life among individuals with AIDS, and that increases in hemoglobin, even within the normal range, are associated with increases in quality of life.
Funding/Support: This study was supported by grant R01 DA15022 from the National Institute on Drug Abuse, Bethesda, Md; by cooperative agreements U10 EY08052 (The Johns Hopkins University School of Medicine, Baltimore), U10 EY08057 (The Johns Hopkins University Bloomberg School of Public Health, Baltimore), and U10 EY08067 (University of Wisconsin, Madison) from the National Eye Institute, Bethesda; and by grants 5M01 RR00188 (Baylor College of Medicine, Houston, Tex), M01 RR00052 (The Johns Hopkins University School of Medicine), 5M01 RR05096 (Louisiana State University, New Orleans), 5M01 RR00865 (University of California, Los Angeles), 5M01 RR00046 (The University of North Carolina at Chapel Hill), 5M01 RR00043 (University of Southern California, Los Angeles), 5M01 RR00047 (Weill Medical College of Cornell University, Ithaca, NY), and R01 DA10252, R01 AI41956, K23 EY13707, and K23 EY00386 from the National Center for Research Resources through the General Clinical Research Center, Bethesda.

Role of the Sponsor: The funding bodies had no role in data extraction and analyses, in the writing of the manuscript, or in the decision to submit the manuscript for publication.

Acknowledgment: We thank The Johns Hopkins AIDS Clinical Trials Unit for assistance with this study.

REFERENCES