Conceptualization and Measurement of Physiologic Health for Adults

Anemia

Bonnie Scott, George A. Goldberg,
Robert H. Brook, Kathleen N. Lohr

Rand

HEALTH INSURANCE EXPERIMENT SERIES

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Conceptualization and Measurement of Physiologic Health for Adults

Volume 6: Anemia

Bonnie Scott, George A. Goldberg,
Robert H. Brook, Kathleen N. Lohr

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PREFACE

The Rand Health Insurance Study (HIS), funded by a grant from the U.S. Department of Health and Human Services, is a large-scale social experiment designed to assess how varying the patient's cost of health services affects his or her use of services, quality of care, patient satisfaction, and health status. It is also designed to study how the provision of services in either the fee-for-service system or a prepaid group practice affects those same variables.

Nearly 8000 people in 2750 families were enrolled in the experiment in six sites across the United States: Dayton, Ohio; Seattle, Washington; Fitchburg, Massachusetts; Franklin County, Massachusetts; Charleston, South Carolina; and Georgetown County, South Carolina. The sites were chosen to represent the four Census regions of the country and an urban-rural mix, and to reflect variation in the amount of stress on the ambulatory medical care system (in terms of long or short delay for new and return appointments).

Families were enrolled in the HIS for either 3 or 5 years (approximately 70 and 30 percent, respectively). Low-income families were oversampled. Eligibility for participation in the HIS was broad; ineligible persons were mainly heads of households 61 years of age and older at the time of enrollment, members of the military, people confined to various institutions, and people eligible for Medicare. When families were enrolled, they agreed to assign their own health insurance benefits (if they were previously covered) to the HIS for the duration of their enrollment. Their policies were held in escrow and returned at the end of their participation. For persons who had not been previously insured, some coverage was obtained during the HIS and made available at the end of enrollment.

The families were assigned to one of 16 different insurance plans. For this purpose, a complex, unbiased allocation model was used to ensure that the assortment of families in each plan closely resembled that in every other plan in terms of 24 different demographic and socioeconomic variables. The 16 experimental plans were as follows:

One plan in which care is free to the family (i.e., 0-percent coinsurance).

Three plans with 25-percent coinsurance (i.e., the family pays 25 percent of its medical bills).

Three plans with 50-percent coinsurance.

Three plans with 50-percent coinsurance for dental and outpatient mental health services and 25-percent coinsurance for all other services.

Three plans with 95-percent coinsurance.

One plan with 95-percent coinsurance on outpatient expenditures up to a maximum out-of-pocket expenditure of $150 per individual ($450 per family) per year and no coinsurance above that; all hospital care is free on this plan.

One plan that assigns some Seattle participants to a prepaid group practice (Group Health Cooperative of Puget Sound).

One plan (a control group) that consists of a random sample of people already enrolled in the Seattle prepaid group practice who also meet the HIS eligibility requirements.

All plans except the first one and the last three have a ceiling on annual out-of-pocket expenditures by the family amounting to 5, 10, or 15 percent of annual family income. The maximum out-of-pocket expenditure per year per family is $1000 for the 50- and 95-percent coinsurance plans and $750 for the 25-percent plans. All plans have an identical, very comprehensive benefits package that covers ambulatory and hospital care, preventive services, all dental services except orthodontia, prescription drugs, certain over-the-counter drugs, most supplies and durable medical equipment, psychiatric and psychological services, and almost all other personal medical services, including those delivered by chiropractors and Christian Science healers.

Over the life of the HIS, data are collected on demographic and socioeconomic variables, health status, use of health services, satisfaction with and attitudes toward health care, and types of providers seen. The sources of health data include baseline interviews before enrollment, self-administered (or parent-completed) Medical History Questionnaires, biweekly Health Reports, annual Health Questionnaires, medical screening examinations, and claims submitted (chiefly by providers) for reimbursement for services rendered.

Comprehensive assessment of each person's health status occurs upon enrolling in the experiment, annually during the enrollment period, and upon leaving. As noted, a major HIS objective is to assess the effects of varying the cost of health services on the health status of individuals sampled from a general population. To this end, reliable, valid, and understandable measures are being specially developed or

adapted that will detect small but meaningful changes in the health status of enrollees.

HIS enrollment began in 1974. At the time of writing this Rand report series (R-2262-HHS), the HIS is still in progress. Enrollment data from all six sites are available and reported herein, but longitudinal (experimental) data are not yet available.

The volumes that constitute Rand report R-2262-HHS, which has the series title *Conceptualization and Measurement of Physiologic Health for Adults*, cover a wide variety of diseases and organ system defects, such as eyesight and hearing problems, cardiovascular and bronchopulmonary diseases (e.g., hypertension, chronic obstructive pulmonary disease), and surgery-related conditions (e.g., hernia, varicose veins). These are used to measure physiologic health, one of four conceptually distinct dimensions of health status defined for the HIS. The other three are physical, mental, and social health.

Volume 1 of this series is an overview of the HIS design. It includes a more detailed description of insurance plans and sites; a discussion of the health model adopted for the HIS, with particular emphasis on physiologic health; and notes on the statistical methods used to estimate the prevalence and level of effect of the various diseases and conditions in the HIS sample. The other, disease-specific, volumes of R-2262-HHS detail the suitability of these conditions as health status measures for the HIS, discuss important measurement issues, describe HIS techniques for determining the prevalence and personal impact of the conditions, give HIS enrollment results, and outline the disease-specific criteria for quality-of-care analyses for the HIS. These volumes report on enrollees aged 14 years and older. A companion series on the measurement of physiologic health among children under 14 years of age will also be published.

Different conditions have been selected for use in different age groups in the HIS population (see the list at the end of the Preface). For this reason, and because a few conditions have a relatively low prevalence in the general population under age 61, some findings and conclusions reported in the R-2262-HHS series are based on comparatively small numbers. Such conclusions should be generalized with caution.

Three other dimensions of health status—physical, mental, and social health—have been defined for the HIS, as has an integrative measure—general health perceptions. These measures are described in the eight volumes of R-1987-HEW, which has the series title *Conceptualization and Measurement of Health for Adults in the Health Insurance Study* and is a companion series to R-2262-HHS.

Detailed descriptive information about the Health Insurance Study, including site and sample selection methods, can be found in

Vol. I, Model of Health and Methodology, of the R-1987-HEW series, by John E. Ware, Jr., Robert H. Brook, Allyson Davies-Avery, Kathleen N. Williams, Anita L. Stewart, William H. Rogers, Cathy A. Donald, and Shawn A. Johnston. A synopsis of the health measurement strategy and enrollment results for these three health dimensions from the first site (Dayton, Ohio) appears in *Volume VIII, Overview,* by Robert H. Brook, John E. Ware, Jr., Allyson Davies-Avery, Anita L. Stewart, Cathy A. Donald, William H. Rogers, Kathleen N. Williams, and Shawn A. Johnston; this is also published as a Supplement to *Medical Care,* July 1979. Other volumes give more detailed methods and enrollment results for physical health in terms of functioning (Volume II), mental health (Volume III), social health (Volume IV), and general health perceptions (Volume V). More specialized analyses are covered in Volumes VI and VII on relations among health status measures and power analysis of the measures, respectively.

Measurement of these same health status dimensions for children under age 14 enrolled in the experiment is discussed in Marvin Eisen, Cathy A. Donald, John E. Ware, Jr., and Robert H. Brook, *Conceptualization and Measurement of Health for Children in the Health Insurance Study,* R-2313-HEW, May 1980.

Another Rand report series, *Conceptualization and Measurement of Health Habits for Adults in the Health Insurance Study,* contains information on two health habits being used by the HIS as proxy measures of future health status: smoking and overweight. These habits could conceivably be influenced by personal medical care, and the evidence strongly suggests that they have a serious effect on future morbidity and premature death. The series comprises two volumes, both by Anita L. Stewart, Robert H. Brook, and Robert L. Kane: Volume I, *Smoking,* R-2374/1-HEW, June 1979, and Volume II, *Overweight,* R-2374/2-HEW, July 1980.

A number of other Rand reports and publications discuss design and measurement issues related to the experiment. Currently the most up-to-date listing of HIS publications is given by Joseph P. Newhouse and Rae W. Archibald, *Overview of Health Insurance Study Publications,* P-6221, November 1978. The experimental design for estimating the effects of financing on demand for care is described in Joseph P. Newhouse, "A Design for a Health Insurance Experiment," *Inquiry,* 11:5–27, 1974; and in Joseph P. Newhouse, *The Health Insurance Study: A Summary,* R-965-1-OEO, March 1974. The structure of the experiment is reported in Lorraine Clasquin and Marie E. Brown, *Rules of Operation for the Rand Health Insurance Study,* R-1602-HEW, May 1977. Carl Morris describes the unbiased allocation model for assigning families to insurance plans in "A Finite Selection Model for Experimental Design of the Health Insurance Study," *Journal of*

Econometrics, 11:43–61, 1979. *The Health Insurance Study Screening Examination Procedures Manual,* R-2101-HEW, September 1978, by Lisa H. Smith, George A. Goldberg, Robert H. Brook, Laura Tosi, and Rae W. Archibald, presents a detailed description of all aspects of tests and procedures carried out in the enrollment and exit screening examinations.

DISEASES AND CONDITIONS FOR HEALTH STATUS AND QUALITY OF CARE MEASUREMENT

Diseases and Conditions	Applicable Age Group		
	0-4 Years	5-13 Years	14+ Years
Acne			X
Anemia	X	X	X
Angina pectoris and selected electrocardiographic abnormalities			X
Asthma		X	
Cancer	X	X	X
Chronic airway obstruction and shortness of breath			X
Colds	X		
Congestive heart failure			X
Convulsions	X	X	
Dental conditions	X	X	X
Diabetes mellitus			X
Eczema	X	X	
Enuresis (bedwetting)		X	
Growth and development disorders	X		
Hay fever		X	X
Hearing disorders		X	X
Hemorrhoids			X
Hernia			X
Hypercholesterolemia (high cholesterol)			X
Hypertension			X
Hyperthyroidism and hypothyroidism			X
Joint disorders			X
Lead poisoning	X	X	
Otitis media (middle ear infection)	X	X	
Stomach pain and peptic ulcer disease			X
Urinary tract infection		X	X
Varicose veins			X
Vision disorders		X	X

SUMMARY

INTRODUCTION AND DEFINITION

The Rand Health Insurance Study (HIS) will use data on the presence and adverse effects of anemia to study the effect of health insurance on health status and the quality of medical care among adults with different levels of health insurance. Anemia was selected as an appropriate indicator because (a) it is easy to diagnose and is amenable to treatment in most cases, (b) it is a common condition (especially among women), and (c) it affects a person's overall well-being.

Anemia is not a disease itself but, like fever, signals an underlying disease. It is usually defined as an abnormally low level of hemoglobin in the blood. Hemoglobin is the component of blood cells that contains iron, gives the blood its red color, and carries oxygen to all parts of the body through the bloodstream. A low level of hemoglobin can occur when blood is lost, when iron or other nutrients are insufficient to make new hemoglobin, when blood cells are destroyed within the body, or when disease prevents the body from making new hemoglobin.

Opinions vary about how low hemoglobin must be before it is called anemia. A "normal" level of hemoglobin, as with "normal" height, varies widely with each individual. A person can be defined as anemic by monitoring his or her hemoglobin level over a period of time, by observing his or her response to treatment, or by comparing his or her level with the normal levels established in the general population. The last method is most useful in screening large populations for anemia.

PREVALENCE AND DISEASE IMPACT

The prevalence of anemia in the United States is about 4 percent among adult men and between 6 and 14 percent among adult women, depending on the level of hemoglobin used to define anemia. Generally, the prevalence is higher among women than among men because of women's regular loss of blood through menstruation. Pregnancy and childbirth add to these losses. Over half of all anemia in both men and women is caused by iron deficiency, which usually begins with loss of blood. In women under age 50, the blood loss is almost always from

menstruation or pregnancy. In men, the blood loss may be from a hidden source, such as an ulcer in the small intestine.

Anemia produces very few symptoms unless it is severe (hemoglobin levels below 8 to 10 g/100 ml). Above these levels, the body can compensate for a lack of hemoglobin by increasing the rate of blood circulation. The symptoms of anemia are symptoms of low oxygen in the body—fatigue, breathlessness, dizziness, palpitations. They occur more frequently when the demand for oxygen is high, as during exercise, or when there is a sudden loss of blood and the body has not had time to adapt to the loss.

Although anemia itself is easily diagnosed by a simple blood test, its cause may not be obvious, as in the case of a slowly bleeding ulcer. If the cause of anemia is not diagnosed, not only will the underlying condition that is causing the anemia persist and progress, but the individual may experience worry or fear. However, some causes of anemia, once detected, are not amenable to treatment. Such causes include certain chronic diseases that prevent the body from making new hemoglobin, regardless of how much iron is present.

HEALTH INSURANCE STUDY METHODS

The HIS uses three sources of information to compare the prevalence and impact of anemia among groups of adults (14 years of age and older) having different kinds of health insurance. The Medical History Questionnaire (MHQ) is self-administered at the time of enrollment in the HIS and again at the time of exit, 3 or 5 years later. The MHQ gathers information on whether the individual has had anemia, on visits to a physician for anemia, and on treatments prescribed, plus recent worry, activity restriction, or days in bed attributed to anemia.

Second, a medical screening examination is given at enrollment and at exit. Blood samples taken during the screening examination are analyzed for hemoglobin and other hematologic components. At exit only, blood samples that are low in hemoglobin are further analyzed for iron deficiency by measuring the serum iron (SI) and total iron binding capacity (TIBC) of the blood.

Third, health insurance claim forms are filed during the HIS. These problem-oriented forms show the reasons for visiting a physician, the physician's diagnoses, and any prescribed medicines or laboratory tests, including those associated with anemia.

A person is defined as having had anemia at some time during the HIS if at least one of the following conditions is met:

1. The person has a low hemoglobin level at enrollment or exit screening.
2. A diagnosis of anemia of any type appears on at least two claim forms.

A person may also be defined as having iron deficiency anemia or macrocytic (large cell) anemia at the end of the HIS if, in addition to a low hemoglobin level, the blood meets further diagnostic criteria at the exit screening examination.

Adverse effects of anemia are measured by three questions on the MHQ about recent worry, activity restriction, and days in bed attributed to anemia.

Generally, after 3 or 5 years, both the prevalence of anemia and its impact are expected to be lower among persons with generous health insurance. Such individuals are expected to have more frequent visits to physicians and better technical medical care that will detect anemia more often or more quickly, and treat it more effectively, than individuals with less generous health insurance. However, because a person may be adversely affected simply by being told that he or she has anemia, generous insurance could also increase the impact from anemia by causing the person to worry about the condition.

HEALTH INSURANCE STUDY ENROLLMENT RESULTS

Among 5350 adults who completed an MHQ at the time of their enrollment in the HIS, 845 (16 percent) reported having anemia currently or having had it in the past; almost all (91 percent) of them were women. Six percent of all adults reported that they were currently taking some form of treatment for anemia, most often iron.

Among the 3269 adults who received an enrollment screening examination, anemia (based on low hemoglobin values) was found among only 4.4 percent of them: 3.2 percent of the men and 5.4 percent of the women. These prevalence rates are comparable to those found in other large population surveys. Very few cases of anemia were severe; only 16 people had hemoglobin levels below 10 g/100 ml.

When measured on the Coulter Model S, hemoglobin values were more sensitive than hematocrit values for identifying people with microcytic (small cell) anemia. This is the most common kind of anemia and is usually caused by iron deficiency. Altogether, 41 percent of the participants in the HIS who were anemic had microcytic anemia.

Among the 143 persons identified as anemic based on hemoglobin

levels (not all of whom knew they were anemic), only 10 percent reported any kind of impact from the ailment. Worry was the most commonly mentioned effect (9 percent); only 4 percent reported any restriction of their activities. Among those 44 who correctly identified themselves as anemic (either currently or in the past), 32 percent reported some untoward effect of their condition: 30 percent reported worry; 14 percent, activity restriction; and 7 percent, days in bed. People who were taking some form of treatment for their anemia reported significantly more worry than those who were not under treatment.

The MHQ identified only 31 percent of the people who were in fact anemic. The remaining 69 percent were totally unaware of having anemia currently or of having had it at any time in the past.

QUALITY OF CARE

Quality of care for anemia will be assessed by criteria that outline good medical outcomes and processes. The data used to assess quality are from the MHQ and screening examinations at enrollment and exit, and from the health insurance claim forms filed during the HIS. Medical records are not examined. Good outcomes include absence of curable forms of anemia, little or no impact from anemia, and patient awareness of the diagnosis of anemia. Good treatment processes include use of appropriate diagnostic tests and appropriate therapy once the diagnosis has been made.

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Chapter 1

INTRODUCTION

Anemia is a condition of abnormally low concentration of hemoglobin in the blood. Hemoglobin is a molecule found within red blood cells; it contains iron, gives these cells their red color, and serves as the carrier of oxygen to all parts of the body via the bloodstream. People who are deficient in hemoglobin may also be deficient in the amount of oxygen being transported to their tissues.

The Rand Health Insurance Study (HIS) will use data on the presence and adverse consequences of anemia to study the effect of different levels of health insurance on the quality of medical care and health status. Anemia was selected for four reasons: (1) It is easily diagnosed and is usually easily treated; (2) it is a common condition in the United States, especially among women under age 50 and pregnant women; (3) when severe, it affects one's capacity for physical activity; and (4) it can result in serious complications in cases of misdiagnosis, incomplete diagnosis, or inappropriate treatment.

This volume presents the HIS definition of anemia, describes in detail why it is an effective measure of health status and quality of care, discusses issues of measurement and diagnosis, describes the HIS methods for measuring and studying anemia as an indicator of health status, presents results from HIS enrollment data, and outlines the HIS criteria for acceptable quality of care for persons with anemia.

Readers are referred to Volume 1 of this series for information about the overall design of the HIS and the analytic plan for studying the relationship of health insurance coverage to health status and quality of care. A separate publication will cover anemia in infants and children under 14 years of age.

Chapter 2

DEFINITION OF ANEMIA

Anemia, like fever, is not itself a disease; rather, it is a sign of underlying disease. It is usually defined as the condition in which the concentration of hemoglobin in whole blood falls below normal. Hemoglobin, the oxygen-carrying molecule inside red blood cells, commonly decreases in concentration because of one or more underlying conditions: (1) a relative lack of the necessary raw materials for making hemoglobin and red cells, such as iron and vitamins (nutritional or deficiency anemia); (2) a loss of blood at a greater rate than the body's capacity to replace it (through external or internal bleeding or destruction of blood cells); or (3) a general slowdown of the body's usual production of blood despite plentiful raw materials, most often because of concurrent infection or chronic disease.

It is important to detect anemia so that the underlying condition causing it can be identified and treated. Anemia itself, as will be described later, is not debilitating unless it is very severe, whereas the condition causing even mild anemia may occasionally become very debilitating, such as when a slowly bleeding ulcer suddenly ruptures and requires emergency surgery.

Anemia is defined as a low level of hemoglobin in the blood. A normal hemoglobin level can be determined by one of three methods: (1) by determining the level that is normal for the particular individual, (2) by the individual's response to treatment, or (3) by comparing the individual's level with the normal levels for a healthy population. Each method has its own assumptions, advantages, and disadvantages, and each may give a different answer to the questions "What level of hemoglobin is 'normal'?" and "When is the hemoglobin level low enough to be called anemia?"

(1) By the individual norms method of defining anemia, an individual can be labeled anemic if his or her "usual" hemoglobin level decreases by a significant amount—i.e., if the individual is anemic compared with his or her own usual state of health. By this method, a recent blood donor might be defined as anemic because a hemoglobin level taken within a few days after the donor has given blood would be (temporarily) lower than his or her usual one, even though it remains within the range of normal for the general population. Individual hemoglobin levels ordinarily do not fluctuate very much. In otherwise healthy people, the factors that affect the hemoglobin level

are sex, age, altitude, relative hydration or dehydration, posture when blood is drawn, time of day when blood is drawn, and pregnancy.[1]

Defining anemia on the basis of individual norms assumes that laboratory measures of hemoglobin are accurate. For hemoglobin values ranging from 12 to 18 g/100 ml, a significant change is typically taken to be a decrease of 1.0 or more grams of hemoglobin per 100 ml of whole blood (Wintrobe, 1974). The error in laboratory measurements has been determined to be 1 to 2 percent, or a difference of 0.12 to 0.36 g between separate measures on the same sample of blood (Koepke, 1977).

The use of individual norms provides the obvious advantage of detecting mild anemia in an individual before the hemoglobin level falls below population norms. It requires, however, that an individual's hemoglobin level be measured, recorded, and compared for changes at reasonably frequent intervals.

(2) By the second method for defining anemia—i.e., an increase in hemoglobin in response to treatment for anemia—people suspected of being anemic can be treated with nutritional supplements as if they actually are anemic; then, if their hemoglobin levels rise, they are defined as having been anemic. This method is most often used when the underlying cause of anemia is presumed to be a nutritional deficiency, usually iron.

However, when some people with normal hemoglobin levels (based on population norms) are treated with iron pills, their levels rise, even though they may report no change in symptoms (Elwood and Wood, 1966; Garby et al., 1969). This rise implies that such people had been anemic. The assumption underlying this method is that each

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[1]Henry (1979, pp. 911-912) describes these factors as follows:

Sex:	Men typically have higher hemoglobin levels than women.
Age:	Children typically have lower hemoglobin levels than adults.
Altitude:	Hemoglobin concentration increases with habitation at high altitude.
Hydration:	As the fluid portion of the blood changes relative to the red cell portion, the hemoglobin concentration of whole blood (fluid plus cells) changes accordingly. For example, dehydration may increase hemoglobin concentration.
Posture:	Hemoglobin concentration decreases by as much as 5 percent when a person is lying down.
Time of Day:	Diurnal variations of about 8 percent occur. Hemoglobin concentration is highest in the morning, lowest in the evening.
Pregnancy:	Hemoglobin concentration decreases in pregnancy because the increase in plasma volume is greater than the increase in the number of red cells.

person has an ideal or optimal hemoglobin level that the body naturally reaches when it is given plenty of raw materials (Garby et al., 1969).

Whether this ideal hemoglobin level is higher than prevailing population norms has become an important question in recent years. National and international health and nutrition groups, for example, have considered adding iron to all flour products to prevent iron deficiency anemia in the general population (WHO, 1968; AMA Council, 1972). Sweden has had such a supplementation program since the late 1940s; 42 percent of the average Swede's daily intake of iron comes from fortification iron (Olsson et al., 1978). However, evidence of a recent increase in the incidence of iron storage disease (hemochromatosis) in that country has cast doubt on the wisdom of excessive fortification of food with iron (Crosby, 1977, 1978; Olsson et al., 1978). Furthermore, epidemiologic studies have indicated that high hemoglobin levels are a risk factor in cardiovascular disease, although the reason for the association is not yet understood (Kannel et al., 1967).

The advantages of defining anemia by response to treatment are that the method is convenient and may avoid expensive or painful diagnostic tests. One disadvantage is that it may produce unnecessary iron loading. The effects of increasing hemoglobin levels on health are difficult to measure, because, as noted, no change in symptoms may be observed (Elwood and Wood, 1966). Also, if emphasis is placed on the process of treating the presumed anemia to confirm its presence, the detection and treatment of its underlying cause may be delayed, obscured, or neglected (Kingston, 1978; Reizenstein et al., 1979). For example, a slowly bleeding ulcer may go undetected if its only sign is anemia and if the anemia is treated without determining its cause.

(3) By the third method of defining anemia—i.e., by reference to average levels of hemoglobin in a healthy population—a person can be defined as anemic if his or her hemoglobin level, when compared with population norms, falls far below the average (usually two standard deviations below average, placing the person in the lower 2.5 percent of the population). This has been the most common method of defining anemia. Unfortunately, the precise level of hemoglobin that represents anemia can only be arbitrarily determined because hemoglobin, as with many other physiologic measures (height, for example), has a normal (bell-shaped) continuous distribution in the general population. Although there is a very slight preponderance of hemoglobin values toward the lower end of the distribution, there is no apparent value of hemoglobin that can be used to differentiate between low hemoglobin in healthy people and low hemoglobin in anemic people (Greendyke et al., 1962; NCHS, 1967; Koepke, 1977; Harwood and Cole, 1978).

The advantage of defining anemia by reference to hemoglobin levels in a healthy population is that large numbers of people can be screened for anemia without waiting to see how they respond to treatment or whether their individual hemoglobin levels remain stable over time. The disadvantages are the previously mentioned arbitrary determination of the level of hemoglobin that represents anemia and the difficulty of finding reference populations. One long-established authority based his reference values on a 1933 compilation of data from assorted populations in Europe and the United States, obtained by several investigators using various techniques (Wintrobe, 1933, 1974). Other investigators (Greendyke et al., 1962) have recommended revision of these older reference values.

Later studies of representative populations of healthy American men (Greendyke et al., 1962) and women (Judy and Price, 1958) have produced revised reference values for hemoglobin by employing modern and reliable laboratory techniques. The World Health Organization has avoided the issue of poorly established reference values by using arbitrary cutoff values for normal levels of hemoglobin (WHO, 1968).

Cook et al. (1971) attempted to solve the problem of an appropriate reference population by using discriminant analysis to separate the studied population into two populations, one anemic and one not anemic. They compared the hemoglobin values of the entire studied population with several thousand pairs of theoretical normal distributions (one anemic and one not anemic) until they found the pair of distributions that best fit the observed hemoglobin values. Still more recently, Harwood and Cole (1978) argued that hemoglobin does not follow a normal distribution. They recommend defining anemia as the lowest fifth or tenth percentile of hemoglobin levels in the population, rather than two standard deviations below the mean.

Table 1 summarizes the hemoglobin levels and prevalence rates of anemia that several investigators have found in sample populations. A comparison of these population surveys shows that the more recent results agree remarkably well with each other, considering the variety of the populations surveyed.

Table 1

Comparative Summary of Hemoglobin Values and Prevalence of Anemia

Samples	Measurement Methods	Level and Type of Measurement	Hemoglobin Values[a] and Prevalence of Anemia		
			Men	Women	Pregnant Women
Wintrobe (1933)					
Data from several studies in U.S. and Europe; 539 men, 403 women	Various	Mean 2 standard deviations Prevalence of anemia	16 14-18 Not reported	14 12-16 Not reported	
Judy and Price (1958)					
663 healthy women seen in general medical practice whose physical exam was normal; excluded women who were pregnant or who had any history of disease or menstrual irregularity	Alkaline hematin with Leitz-Rouey photometer (manual)	Mean 2 standard deviations Prevalence of anemia		12.55 10.2-14.8 Not reported	
Greendyke et al. (1962)					
950 army enlisted men, ages 17-29	Cyanmethemoglobin with Beckman spectrophotometer	Mean 2 standard deviations Prevalence of anemia	14.9 13.1-16.7 Not reported		
200 army enlisted men and officers, ages 30-63; both samples excluded men with a history of recent blood donation or illness	Cyanmethemoglobin with Beckman spectrophotometer	Mean 2 standard deviations Prevalence of anemia	15.4 13.7-17.1 Not reported		
World Health Organization (1968)					
Data from Poland, India, Israel, Mexico, and Venezuela; 327 men (none from Poland), 512 women (none from Poland), 739 pregnant women	Cyanmethemoglobin with manual hemoglobinometer	Arbitrary lower limits of hemoglobin Prevalence of anemia (depending on country)	13 1-14 percent	12 12-64 percent	11 27-80 percent

Samples	Measurement Methods	Level and Type of Measurement	Hemoglobin Values[a] and Prevalence of Anemia		
			Men	Women	Pregnant Women
Cook et al. (1971)					
Data from 7 Latin American countries; 304 men, 485 women, 899 pregnant women	Cyanmethemoglobin with Coulter Model S	Median 10th to 90th percentile Calculated prevalence of anemia[b] Prevalence of anemia by WHO limits	15.1 13.7-16.5 2 percent 3.9 percent	13.2 11.0-14.6 12 percent 17.3 percent	11.4 9.3-13.0 22 percent 38.5 percent
NCHS (1974)					
HANES random sample of persons ages 18-44; 1038 men, 2406 women, including pregnant women	Cyanmethemoglobin with automated hemoglobinometer	Median 10th to 90th percentile 5th to 95th percentile Prevalence of anemia by Wintrobe limits	15.9 14.6-17.5 14.1-17.8 4.2 percent	13.8 12.2-15.3 11.8-15.8 6.1 percent	
Cook et al. (1976)					
Washington state residents; 240 men, 18-45; 370 women, 18-45	Cyanmethemoglobin with Coulter Model S	Median 10th to 90th percentile Prevalence of anemia by WHO limits	15.2 13.8-16.6 4.2 percent	13.2 11.7-14.7 14.1 percent	
Harwood and Cole (1978)					
Over 13,000 hospital patients in Atlanta, Georgia; excluded persons under 12 years of age	Cyanmethemoglobin with Coulter Model S	Median 10th to 90th percentile 5th to 95th percentile Range Prevalence of anemia	15.2 13.2-16.8 10.4-17.1 6.3-18.8 Not reported	13.3 11.6-14.8 9.5-15.2 5.4-17.8 Not reported	

[a]Hemoglobin values in grams per 100 ml of blood.

[b]Prevalence calculated by statistical manipulation of the distribution into a "truly anemic" population. See original citation for explanation.

Chapter 3

JUSTIFICATION FOR SELECTING ANEMIA FOR HEALTH INSURANCE STUDY ANALYSES

PREVALENCE OF ANEMIA

Anemia is common in the United States, although it is much more so elsewhere in the world, particularly in poorer countries. In India, a survey of 4000 adult men and women found that 14 percent were severely anemic, having hemoglobin levels below 8 g/100 ml (Mehta, 1971). Even in England, 36 percent of a random sample of 100 adult clinic patients had hemoglobin levels below 12 g/100 ml (Watt, 1972).

Prevalence data on anemia in the United States are sparse and must be reviewed within the context that reported prevalence depends on the level of hemoglobin that is taken to be "normal." In its 1960-62 survey of 6672 U.S. adults aged 18 to 79, the National Center for Health Statistics (NCHS) used hematocrit levels to define anemia (NCHS, 1967). The lower limits of normal were taken from a 1933 reference standard of 40 ml/100 ml for men and 37 ml/100 ml for women; these hematocrit levels correspond to hemoglobin levels of 14 g/100 ml and 12 g/100 ml, respectively (Wintrobe, 1933, 1974). Using these cutoff limits, the NCHS reported a prevalence of anemia of 3.6 percent among men and 7.0 percent among women. Because the limits of normal were two standard deviations below the mean for the small reference population of Americans and Europeans described by Wintrobe in 1933, a prevalence of 2.5 percent was expected. Some researchers have contended, however, that the observed prevalence is higher because the 1933 limits were from an unrepresentative population and were probably too high (Judy and Price, 1958; Greendyke et al., 1962).

A subsequent national survey (NCHS, 1974) used hemoglobin as the measure of anemia. The same 1933 definition of anemia was retained (lower limits of normal of 14 g for men and 12 g for women). The observed prevalence among adults aged 18 to 44 was again higher than the expected 2.5 percent: 4.2 percent for men and 6.1 percent for women (including pregnant women).

Cook et al. (1976) surveyed a sample of 1564 lower-income Washington State residents, using hemoglobin limits of 13 g for men and 12 g for women. These limits, which are lower for men than the 1933

Wintrobe hemoglobin levels, were based on arbitrary levels adopted earlier by the World Health Organization (1968). Prevalence of anemia in the Washington sample, which included children, was 8.3 percent. For adults aged 18 to 45, prevalence was 4.2 percent among men and 14.1 percent among women (excluding pregnant women). Harwood and Cole (1978), reporting data from more than 13,000 hospital admissions of people 12 years of age and older in Atlanta, Georgia, found a 10 to 90 percentile range of hemoglobin values in this large population very close to what Cook et al. (1976) had found: 13.2 to 16.8 g for men and 11.6 to 14.8 g for women.

To summarize, in the United States, prevalence of anemia is about 4 percent among adult men and between 6 and 14 percent among adult women, depending on the level of hemoglobin used to define anemia. Women have a higher prevalence of anemia than men, and the variation with age is greater among women than among men.

The higher prevalence of anemia among women is believed to occur because of their lower iron stores. Women lose approximately 20 mg of iron each month in menstrual blood, and an additional 680 mg for each pregnancy (AMA Council, 1968). These iron losses are too great to be restored by the typical diet of many Americans. Women aged 14 to 54 consume only 60 percent of the U.S. Recommended Daily Allowance of 18 mg of iron (NCHS, 1977a) and therefore are much more likely to develop anemia because of nutritional iron deficiency (AMA Council, 1968). Nutritional iron deficiency is rare in adult men and is almost certainly caused by bleeding; anemia due to a dietary lack of iron is rare enough to warrant special attention (Rosenbaum and Leonard, 1964).

Lack of an essential nutrient is responsible for at least half the cases of anemia seen by physicians, and perhaps for as many as 70 percent (Wintrobe, 1974; Wallerstein, 1975). Of these nutritional causes of anemia, iron deficiency is much more common than that of vitamin B-12 or folic acid, which together account for only 2 percent of all diagnosed anemias. In general population surveys, the proportion of anemia caused by iron deficiency is even higher. Cook et al. (1976) found that 76 percent of the 130 persons in their sample of 1564 Washington State residents aged 5 years and older who were anemic by low hemoglobin levels were also iron deficient by one or more measures. In the 1973 NCHS Health Interview Survey, 74 percent of those persons who reported having anemia during the past year said it was iron deficiency anemia (NCHS, 1977b).

The remaining 20 to 30 percent of anemias are most often caused by concurrent infection or chronic disease. In these cases, a moderate chronic anemia develops in the presence of adequate iron and vitamins. Such anemia is believed to result from constant, low-grade

interference with production of red blood cells, although the exact mechanism is not understood (Bainton and Finch, 1964). An assortment of uncommon conditions accounts for a very small proportion of all cases of anemia in the United States, perhaps 2 percent at the most. These include genetic disorders of the hemoglobin molecule (sickle cell anemia, thalassemia) and disorders of the bone marrow (multiple myeloma, leukemia) (Wintrobe, 1974).

MORBIDITY AND MORTALITY

As mentioned earlier, anemia is not a debilitating condition unless it is very severe. Effects may not be noticeable if the anemia develops slowly, if the person is otherwise healthy, and if physical activity is minimal. When anemia develops slowly, compensatory mechanisms have time to develop in response to the blood's decreasing oxygen-carrying capacity. These mechanisms ensure that the amount of oxygen delivered to the body remains the same. Blood is circulated more rapidly by a more rapid heart beat and an increased volume per beat. Oxygen is extracted more easily from the blood into the tissues (the oxygen dissociation curve shifts to the right). These adaptations are directly proportional to the level of hemoglobin in the blood (Torrance et al., 1970; Woodson et al., 1978).

The effects of anemia become evident when compensatory adaptations are unable to keep pace with the demand for oxygen. An increase in physical activity, for example, demands more oxygen, and anemic people show a significantly decreased capacity for physical activity. When 75 women, aged 22 to 65, were tested by walking on a treadmill at various slopes, those with hemoglobin levels between 11.0 and 11.9 g/100 ml showed a 20-percent lower tolerance for the activity than women with hemoglobin levels above 13.0 g/100 ml. Tolerance was measured by heart rate, total time on the treadmill, and treadmill slope finally achieved. It was directly proportional to hemoglobin level (Gardner et al., 1975, 1977).

In addition to the physiologic adaptations that develop within the body in response to anemia, people who are anemic may voluntarily reduce their physical activity. Edgerton et al. (1979) measured the daily physical activity of more than 100 women working on a tea plantation in Sri Lanka, using continuous portable monitors similar to pedometers. After treatment with iron (ferrous sulphate, 200 mg daily for 30 days), physical activity increased compared with pretreatment levels. Hemoglobin levels and the amount of tea picked also increased. These changes did not occur in a placebo group matched for pretreat-

ment levels of hemoglobin, activity, and amount of tea picked. Initial average hemoglobin levels ranged from 10.2 to 11.4 g/100 ml, demonstrating that the effects of treatment are measurable, even when anemia is not severe.

The symptoms of anemia are those of low oxygen delivery to the body: fatigue, breathlessness, dizziness, and palpitations (Wood, 1971). They are usually not reported by persons with anemia until very low levels of hemoglobin are reached, less than 10 g/100 ml in women in one study (Elwood and Wood, 1966). Reported symptoms vary among people with the same hemoglobin level, both before and after treatment, but consistency of reported symptoms increases as hemoglobin levels drop (Elwood, 1970; Wood, 1971). Individual variations in symptoms are thought to be a function of individual variations in physical activity, cardiovascular adaptability, and awareness of body functioning. People who are physically active presumably report more symptoms, as do people whose coexisting heart or lung disease interferes with their capacity to compensate for anemia by increasing oxygen delivery to the body.

EFFECTS OF MEDICAL CARE

Medical care for anemia varies in its effectiveness, depending on the cause of the anemia. Nutritional anemias are quite responsive to treatment, whereas others, such as anemias caused by chronic disease, may be very unresponsive.

Medical care for nutritional anemia is highly effective once the cause has been determined. For anemia due to a deficiency of iron, vitamin B-12, or folate, initial therapy with supplements of the missing nutrients usually corrects the problem. Adjusting dietary habits or supplying the nutrient in a form usable by the body may then eliminate the need for continuing supplements, depending on the origin of the deficiency. For example, oral iron therapy results in a rise in hemoglobin of 2 to 4 g/100 ml after 3 or 4 weeks, provided the recommended dose of 60 mg of elemental iron three times daily is tolerated. Stomach upset is a frequent side effect of iron pills, and occasionally the dose must be adjusted downward to be tolerated. Although providing a more rapid correction of the anemia, intramuscular or intravenous iron therapy is rarely indicated because of the risk of serious side effects and the proven efficacy of oral therapy (*Medical Letter*, 1977, 1978).

For nonnutritional anemias, therapy is directed at the underlying cause, and its effectiveness varies with the nature of the condition. For

example, some chronic diseases such as rheumatoid arthritis are inherently more treatable than, say, sickle cell anemia or leukemia.

The underlying causes and the medical treatment of anemia can often contribute to morbidity and mortality in excess of the morbidity associated with anemia itself. A common problem in treating anemic patients arises from omissions in the diagnostic process: physicians fail to recognize anemia as a sign of more serious disease and thus overlook its underlying causes. For example, a bleeding cancer in the large bowel may go undetected if one of its first signs, iron deficiency anemia, is treated and the source of the blood (iron) loss is not sought. A retrospective survey of the medical records of 157 people 45 years and older for whom iron was prescribed during 1975 in Sweden, a country where commercial food has been fortified with iron since the late 1940s, found that nearly half (43 percent) of the records contained no evidence of a need for iron, either in laboratory tests for anemia or in reported symptoms (Reizenstein et al., 1979). The authors expressed concern that the indiscriminate prescribing of iron for older people may mask the presence of a bleeding tumor.

Empirical therapy with iron without proper diagnosis and follow-up can result in iron overload if the anemia is not caused by iron deficiency. Also, if combined nutritional anemia from vitamin B-12 and folate deficiencies is treated with folate only, neurological damage caused by lack of vitamin B-12 may progress. Finally, overuse of the convenient, injectable forms of iron can produce toxic effects not associated with oral therapy (Matthews and Casey, 1973; Savin, 1977).

Chapter 4

MEASUREMENT ISSUES

Anemia is usually measured by analysis of the blood for hemoglobin and/or hematocrit. This can be done manually, by visual comparison with standards for hemoglobin concentration, and by centrifuging the blood for hematocrit determination. Most often, however, these tests are performed by automated electronic equipment. The Coulter Model S, a widely used machine, combines automatic blood sample dilution with cell-counting apparatus and hemoglobinometry at the rate of two to three samples per minute. Since its introduction in the late 1960s, the accuracy, precision, and reproducibility of Coulter Model S determinations have been studied in detail and found to be a significant improvement over manual methods (Henry, 1979).

Measuring hemoglobin concentration in the blood is a good screening test for anemia because it is a direct measure of the oxygen-carrying capacity of the blood. In automated machines such as the Coulter Model S, hemoglobin is measured directly by a photoelectric cell that determines the optical density of the most stable hemoglobin pigment, cyanmethemoglobin. Repeated hemoglobin measures from the same blood sample, when done by automated equipment, vary by only 1 to 2 percent (Koepke, 1977). The manual method is less reliable and gives hemoglobin values that are consistently higher than automated measures by an average of 0.3 g/100 ml (Koepke, 1977).

With automation, the hemoglobin test for anemia has replaced the hematocrit test. It is considered more reliable because hemoglobin measurements have a smaller range of error than hematocrit determinations when done on automated equipment. Hematocrit is not measured directly; it is calculated by multiplying the red blood cell count (RBC) times the mean cell volume (MCV), each of which is measured by the impedance technique in the Coulter Model S.[1] Although the error in this technique is only about 1 to 2 percent (Henry, 1979, p. 879), it is present in both the RBC and the MCV measurements and its effect is additive in the hematocrit calculation.

Once anemia has been detected by a low hemoglobin level, other

[1]Briefly, the impedance technique involves passing uniformly suspended cells through an opening of fixed volume and fixed electrical conduction. As the cells go through the opening, they produce a measurable change in impedance that is proportional to their individual volumes. In this way, the cells are counted and their individual volumes are measured (Henry, 1979).

measures, such as the size of the red blood cells, sometimes help to determine the cause of the anemia. Before the introduction of automated laboratory equipment, manual microscopic examination of red cells was sometimes used to diagnose iron deficiency anemia. This was possible because in cases of long-standing severe iron deficiency, the red blood cells contain very little hemoglobin and appear small and pale. However, the manual method was difficult and not very reliable, even in expert hands. Fairbanks (1971) reported that hematologists examining red cells under a microscope diagnosed 6 percent of normal people as iron deficient and anemic. Moreover, they identified only 49 percent of those who really were severely iron deficient and anemic (i.e., men with hemoglobin levels of 4.0 to 11.6 g/100 ml and women with levels of 6.8 to 11.6 g/100 ml; both with low serum iron concentration).

Automated measures of cell size (MCV) and color (mean cell hemoglobin concentration; MCHC) are more reliable than the manual methods for detecting the small, pale red cells of iron deficiency anemia (Henry, 1979, p. 886). Except in severe cases, however, the MCV and MCHC measures may be only mildly abnormal. Of the two measures, the MCV is considered the more sensitive, but even the MCV fails to detect one-third of the patients with uncomplicated iron deficiency anemia (hemoglobin below 10 g/100 ml in men and 9 g/100 ml in women) (Bainton and Finch, 1964; Klee et al., 1976).

Transferrin saturation is the test most commonly used to establish the presence of iron deficiency anemia. It is calculated by dividing serum iron by total iron binding capacity (SI/TIBC). Normal values can range from 20 to 55 percent; SI is normally 60 to 160 micrograms/100 ml and TIBC, 250 to 350 micrograms/100 ml. Transferrin saturation cannot be used in place of a hemoglobin test in the first screening for iron deficiency anemia because the SI reliability is much lower than that of the hemoglobin test. Its coefficient of variation is 10 to 15 percent (Eastham, 1975) and its diurnal variation is as high as 40 percent (Bowie et al., 1963). Once the presence of anemia has been determined by a low hemoglobin concentration, however, transferrin saturation is very useful for determining whether the anemia is caused by iron deficiency.

In studying 300 hospital patients with anemia of various causes, Bainton and Finch (1964) found that a transferrin saturation of less than 16 percent reliably differentiated between those with iron deficiency anemia and those with anemia from other causes, especially when the TIBC was evaluated separately. For 115 patients with classical iron deficiency anemia (small, pale red cells), the transferrin saturation was between 2 and 16 percent (median of 7 percent). For another group of 17 patients with normal-appearing red cells but low

iron stores, the saturation was between 5 and 16 percent (median of 10 percent). For 122 patients with chronic disease anemia, the saturation was between 7 and 19 percent (median of 13 percent), and for 6 patients with combined iron deficiency and megaloblastic anemia, it was between 8 and 15 percent (mean of 11 percent). All patients with iron deficiency anemia had a transferrin saturation below 16 percent, as did most patients with chronic disease anemia. However, most patients with chronic disease anemia were distinguishable from those with iron deficiency anemia because their TIBC values were lower. They averaged 271 micrograms/100 ml and did not exceed 358 micrograms/100 ml, compared with an average TIBC of 346 micrograms/100 ml and a maximum of 460 micrograms/100 ml for the iron deficient group.

Other researchers have confirmed these findings. In both iron deficiency anemia and anemia of chronic disease, transferrin saturation falls below 16 percent. Although it usually falls lower in cases of iron deficiency, the overlap is considerable. The overlap can be decreased, but not eliminated, when the TIBC values for both groups are compared. In iron deficiency anemia, TIBC usually rises above 300 micrograms/100 ml, whereas in chronic disease anemia TIBC usually remains below 350 micrograms/100 ml (Wintrobe, 1974).

In summary, after anemia has been diagnosed by a low hemoglobin level, a combination of a transferrin saturation of less than 16 percent plus a TIBC value above 350 micrograms/100 ml will very often identify those cases of anemia caused by iron deficiency. This is especially true for general population surveys because, as discussed earlier (Chapter 3), the proportion of anemia in the general population caused by iron deficiency greatly exceeds that caused by chronic disease. Therefore, any case of low hemoglobin and low transferrin saturation found in a general population survey such as the HIS screening examination is much more likely to be from iron deficiency anemia than from chronic disease anemia. For example, the predictive value of the transferrin saturation test alone was 87 percent among 1564 Washington State residents aged 5 years and older who were evaluated for both hemoglobin and transferrin saturation (Cook et al., 1976). Of the people with both low hemoglobin and low transferrin saturation (below 15 percent), 87 percent were found to be truly iron deficient by other measures. In the HIS, the use of the TIBC level to separate these two causes of anemia provides an added refinement to the already high discrimination obtained by the transferrin saturation test.

Similar results are found among pregnant women with iron deficiency anemia. Because anemia during pregnancy is most often caused by iron deficiency, transferrin saturation would be expected to

be below 16 percent in most pregnant women who are anemic, if the test is valid for measuring iron deficiency. Among 53 pregnant women in San Francisco who had been diagnosed as anemic (hemoglobin levels below 11 g/100 ml), Carr (1971) found that all had transferrin saturations below 16 percent; established normal values in other pregnant women who were not anemic were 25 to 35 percent. Specimens were drawn in the morning, when serum iron is highest, so the transferrin saturation was biased toward higher values. Even with this bias, all 53 anemic women had transferrin saturations below 16 percent, and transferrin saturation was found to be directly proportional to hemoglobin level.

Newer assays of iron availability by serum ferritin or free erythrocyte protoporphyrin (FEP) are less useful than the transferrin saturation test for determining whether anemia is due to iron deficiency. The test for increased FEP is nonspecific, because FEP rises in anemias caused by lead intoxication and in chronic disease anemia as well (Wintrobe, 1974). The serum ferritin test is a measure of iron stores (Lipschitz et al., 1974). It is useful for differentiating causes of iron deficiency anemia after the condition has already been established by other tests (Sheehan et al., 1978).

Anemia due to deficiency of vitamin B-12 or folate, like iron deficiency anemia, produces blood cells of an unusual size, in this case unusually large cells (macrocytosis). Developing red blood cells (precursors) need both B-12 and folate to divide; when one of these nutritional elements is missing, they cannot do so. Once anemia has been detected by a low hemoglobin concentration, the size of the red blood cells, the MCV, can sometimes be used to help determine whether the anemia is caused by vitamin B-12 or folate deficiency.

MCV is useful for detecting anemia due to vitamin B-12 or folate deficiency only after a low hemoglobin level has established the existence of the disease, because only about half of all people with large blood cells have either B-12 or folate deficiency. A Canadian study of 140 persons with MCV greater than 99 cubic microns found that 46 (33 percent) had folate deficiency and 16 (11 percent) had B-12 deficiency, as determined by subsequent blood tests (Thong et al., 1977). The remaining high MCV values were caused mainly by liver disease or alcoholism (in 36 patients, or 26 percent) or cytotoxic drug therapy for malignant disease (in 25 patients, or 18 percent). Of the 140 persons with macrocytosis, 37 (26 percent) were also anemic, when anemia was defined as hemoglobin below 11.5 g/100 ml in men and below 10.5 g/100 ml in women. The association between macrocytosis and liver disease or alcohol abuse is well known, although the exact cause is not well understood. Many drugs used to treat malignant disease cause macrocytosis by interfering with cell division.

In a study of 100 people with a greater degree of macrocytosis (MCV above 114 cubic microns), half were deficient in B-12 or folate or both; of these, 60 percent were also anemic (hemoglobin below 14 g/100 ml for men and below 12 g/100 ml for women) (McPhedran et al., 1973). Of a subgroup with very low levels of B-12 (below 100 picograms/ml) or erythrocyte folate (below 100 nanograms/ml), 80 percent were anemic. Most of the remaining 50 people with macrocytosis had liver disease or alcoholism (26 people) or had received drugs that are known to cause macrocytosis (13 people); the others (11 people) had macrocytosis without apparent cause.

Chapter 5

HEALTH INSURANCE STUDY METHODS

PREVALENCE OF ANEMIA

Two sources were used by the HIS to measure the prevalence of anemia at enrollment among its adult participants: a Medical History Questionnaire (MHQ) and a medical screening examination. The first source, the MHQ, was a self-administered questionnaire that included questions about anemia (reproduced in Appendix A). It was completed by adults (14 years of age and older) at the time of their enrollment in the HIS and again at the end of their participation in the Study, 3 or 5 years later. The MHQ had two parts, Form A and Form B. For all sites except the first one (Dayton, Ohio), all adult participants completed both forms. In Dayton (enrollment only), Form A was completed by all adults and Form B by a random subsample. At exit, all participants complete both forms of the MHQ.

The Anemia batteries (on Form B) contained questions pertaining to previous diagnosis of anemia; use of various therapies; and amounts of worry, activity restriction, and days in bed attributable to anemia. Two versions of the battery are reproduced in Appendix A. One was used at enrollment in Dayton; the other was used at enrollment at all other HIS sites and at exit at all sites. Differences in the two forms are the result of minor changes in the Dayton form to provide better information on the timing of medical care for anemia.

The battery is introduced by the question, "Has a doctor ever said you had anemia?" Persons who responded "yes" continued on to complete the battery and those who responded "no" "skipped out" to the next disease-specific battery.

The second source of information used to measure the prevalence of anemia was a medical screening examination given at enrollment to a randomly selected group of participants, generally between 50 and 75 percent of all participants, depending on the site.[1] At the Dayton site, a random sample of 204 adults who completed Form B at home did not receive a screening examination because of enrollment schedule constraints. Smith et al. (1978) describe screening examination procedures in detail.

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[1]This random sample will be used to study the effect of the screening examination on the participants' subsequent health status and use of medical services.

At the screening examination, blood samples were taken from all adults and later analyzed on the automated Coulter Model S (described in Chapter 4) for hemoglobin, hematocrit, red blood cell count, mean cell volume, mean cell hemoglobin, and mean cell hemoglobin concentration. In addition, the blood sample taken at exit from the HIS was analyzed for serum iron and total iron binding capacity for all adults whose hemoglobin level fell below the normal limits defined below, and transferrin saturation (SI/TIBC) was calculated.

Whenever any initial measurement fell outside the normal range of values for that measure, the test was repeated; in such cases, the second measurement was used for all analyses. In addition, a random selection of approximately 5 to 10 percent of all screening examination participants had extra blood drawn, and these extra samples were sent to the laboratory for testing in different batches so that laboratory reliability could be determined.

As discussed in Chapters 3 and 4, earlier reference standards for the lower limits of normal hemoglobin (e.g., Wintrobe, 1933) were probably too high or were drawn from populations that were unrepresentative of the general population in the United States. More recent sources (summarized in Henry, 1979, pp. 912, 2099), based on values obtained with electronic counters and on larger populations of healthy people, suggest that lower reference values might be preferred, especially for men. In particular, for a general population such as that enrolled in the HIS, the following values for the lower bound of normal hemoglobin are considered appropriate: men, 13.5 g/100 ml; women, 12.0 g/100 ml; and pregnant women, 10.5 g/100 ml.

The values adopted for use in the HIS depart from these reference values in two ways. First, separate limits were defined for adolescent boys aged 14 through 17, because boys typically have lower hemoglobin levels than adult men. Hemoglobin values in adolescent boys are increasing from the average childhood level of 13 g to the adult level of 16 g. These values have been found to correlate more with measures of sexual maturity than with age, presumably because androgenic hormones increase red blood cell production (Daniel, 1973). Such differences are not evident between adolescent girls and adult women, so no adjustment was necessary for girls.

Second, the lower limits of normal hemoglobin were defined as 0.5 g/100 ml (about 4 percent) lower than the reference limits given above, to allow for the effect of diurnal variation in hemoglobin concentration. Hemoglobin concentration is usually higher in the morning than in the evening. Diurnal variations have been found to be as much as 15 percent, when blood drawn in the morning is compared with blood drawn in the evening from the same person; average differ-

ences are 8 percent (Stengle and Schade, 1957; Dacie and Lewis, 1975). All the HIS blood samples were drawn after 11:00 A.M., and half were drawn between 6:00 P.M. and 10:00 P.M. Thus, in the HIS population, a slight systematic bias downward in hemoglobin values might be expected when these values are compared with those for blood samples drawn earlier in the day.

Adjustments for altitude were unnecessary because all the HIS sites are within 250 meters of sea level. No adjustments were made for race; the HIS adult population is about 85 percent white. A few recent studies suggest that the lower levels of hemoglobin (on average, 0.5 g lower) found among blacks compared with income-matched whites cannot be entirely explained by different prevalence rates for hemoglobinopathies or iron deficiency (Dallman et al., 1978; Meyers et al., 1979). However, these studies are preliminary, and other explanations that would make these differences clinically meaningful—lead exposure, for example—have not been tested.

A third source of information about the prevalence of anemia was the insurance claim forms filed for medical care during the years covered by the HIS. These forms show the patient's reason for visiting a physician, the physician's diagnoses, any laboratory tests or procedures performed, and any medications dispensed or prescribed.

In summary, an adult (14 years of age and older) will be defined as having had anemia at some time during the HIS if at least one of the following conditions is met:

1. Diagnosis of anemia of any type on at least two claim forms.
2. A hemoglobin level at the enrollment or exit screening examination that falls below the following limits (in grams per 100 ml of blood):

Boys, 14-17	12.5
Men, 18 and older	13.0
Girls, 14-17	11.5
Women, 18 and older	11.5
Pregnant women, all ages	10.0

As noted above, these limits were defined to be 0.5 g lower than standard reference limits to account for the effect of diurnal variation on hemoglobin concentration.

A person will also be defined as having had iron deficiency anemia or macrocytic (large cell) anemia if his or her hemoglobin level at the exit screening examination is less than the HIS limits and he or she meets the following criteria:

1. Iron deficiency anemia if transferrin saturation (SI/TIBC) at

exit is below 16 percent and total iron binding capacity (TIBC) is above 350 micrograms/100 ml.
2. Macrocytic anemia if mean cell volume (MCV) at exit is above 100 cubic microns.

DISEASE IMPACT

At least three factors contribute to the effect of anemia, all of which are measured in the HIS. First, capacity for physical activity drops when anemia is severe (Gardner et al., 1975, 1977); this capacity improves with therapy. Second, people labeled as anemic may experience mental distress. Third, inappropriate treatment can have serious consequences, such as iron overload in a person who is not iron deficient (Matthews and Casey, 1973; Kingston, 1978).

To assess the adverse effects of anemia, three questions on the MHQ were asked of all people who reported that they currently had anemia or had had it in the past. Specifically, capacity for physical activity is measured by two questions that ask what amount of activity restriction or how many days in bed have been caused by anemia. Worry about anemia is assessed by a third question. (See Table 13 or Appendix A for the exact wording of the questions.)

Responses to the worry and activity restriction questions ranged from "none" to "a great deal" (worry) or to "all of the time" (restriction). The question of bed days required only that the respondent write either zero or the specific number of days spent in bed because of anemia. A composite measure called "any impact" was also constructed; a person was assigned a positive score for "any impact" if he or she gave a positive response to at least one of the three questions.

Inappropriate treatment is measured by criteria developed to evaluate the quality of care for anemia. These criteria are described more fully in Chapter 7 and are specified in detail in Appendix C.

The three impact questions are part of a standard set of questions that appear repeatedly in the MHQ in association with various diseases and conditions. They were not specifically constructed to measure the symptoms or adverse consequences of anemia (or any other particular condition) but to facilitate comparisons of similar kinds of impact among several diseases and conditions. As just noted, however, they are meaningful with respect to two major consequences of anemia itself: reduced physical activity and higher levels of worry and concern.

To compare disease impact between groups of people, we calculated the percentages of responses at each level from "none" to "a great

deal" and of specific numbers of bed days. Disease impact was assessed both for persons who actually responded to the questions and for those who did not. Members of the latter group who did not answer the questions because they had answered "no" to the first MHQ question ("Has a doctor ever said that you had anemia?") had skipped the remaining questions about anemia; for these questions, scores equal to no impact were assigned. The rationale for this scoring rule was that people who report not having anemia should, if asked, logically report no impact from it.

These disease impact measures are expected to be affected by the level of health insurance in several ways. People with generous insurance coverage may be more likely to see a physician, be diagnosed and treated for their anemia, and be cured of it; this could reduce the prevalence of anemia among generously insured groups, compared with others, at the end of the HIS. Moreover, people often have anemia without knowing that they do. Unless anemia is severe, it has very few symptoms. Therefore, most cases of anemia are discovered by routine screening tests, the kind of tests that people with generous health insurance are more likely to get. Women are screened for anemia more often than men, because they are known by physicians to have a higher risk for developing anemia. Thus, men, especially, may benefit from generous health insurance by being screened and treated for anemia earlier than would otherwise occur.

Generous insurance may also be associated with a patient's receiving more sensitive and thoughtful care (better art of care), which may serve to minimize the worry or concern the patient may have about the condition. More generous insurance could also help to alleviate some of the physical limitation attributed to anemia, because treatment may be started earlier and followed more closely. Technical medical care (e.g., diagnostic and therapeutic procedures) may improve with the generosity of the insurance; this could lead to fewer incidents of inappropriate management among the more generously insured groups.

Conversely, expanded use of medical care prompted by more generous insurance may lead to undesirable results. Increased diagnostic efforts and nonspecific treatment among generously insured participants may, for example, result in greater worry or concern. Being labeled as anemic (perhaps erroneously) may prompt undue restriction of activity or other forms of unwarranted sick role behavior. Inappropriate or excessive use of medications may be observed.

Chapter 6

HEALTH INSURANCE STUDY ENROLLMENT RESULTS

The HIS enrolled a total of 5835 adults (14 years and older) at six sites. Just over 50 percent were women, and about 15 percent were nonwhite. The mean number of years of schooling completed by those 18 and older was 12, and the average family income (in 1973-74 dollars) was about $13,000. The entire experimental population was under age 62 at enrollment, so that no individual would reach age 65 during the experiment (the control population included two people over age 62). The Preface and Volume 1 contain additional information about the HIS sample and enrolled population.

Of the 5835 adults enrolled, 5715 (98 percent) completed Form A, the first half of the Medical History Questionnaire (MHQ). They included all adults enrolled in any experimental HIS plan, the Dayton control group, and a "pre-enrollment group" in South Carolina. Of the 5715 adults who completed Form A, 5350 (94 percent) received and completed Form B, the second half of the MHQ. As noted in Chapter 5, only a random sample of the enrollees at the Dayton site was asked to complete Form B; at all other sites, all adults were expected to complete it. Altogether, 5472 adults were eligible to complete Form B; thus, the true completion rate for Form B was 98 percent (5350 of 5472 enrollees).

The screening examination was administered to 3321 persons at the six sites. Those who received the examination represented a random sample of about 60 percent of the entire sample. Two additional people were examined without completing Form B of the MHQ. As mentioned earlier, not everyone was examined at enrollment; this was deliberate, in order to study how the fact of having been examined affected later use of medical services and health status.

PREVALENCE OF ANEMIA ACCORDING TO THE MEDICAL HISTORY QUESTIONNAIRE

The distribution of responses to the MHQ questions about medical diagnosis of and care for anemia is shown in Table 2. Those people

Table 2

Distribution of Responses to Questions about Anemia from the MHQ: Presence, Doctor Confirmation

Question[a]	Response	Number	Percent[b]
†*Has a doctor told you that you currently have anemia (sometimes called low blood) or are you currently under treatment for it?*	Yes, I have it or am under treatment for it.	19	2
	Yes, I had it, but it is now cured.	27	3
	No, I do not have anemia.	767	94
		813	99
**Has a doctor ever said that you had anemia or low blood?*	Yes	799	18
	No	3736	82
		4535	100
	Skipped this question	2	
	No questionnaire	365[c]	
†*Are you currently under a doctor's care or supervision for your anemia?*	Yes	12	26
	No	34	74
		46[d]	100
**When was the last time you saw a doctor about your anemia?*	Within past 3 months	88	11
	3-6 months ago	53	7
	7-12 months ago	78	10
	More than 1 year ago	576	72
	Never saw one	1	(e)
	Missing	3	(e)
		799	100

[a] Items marked with a dagger (†) appeared on the version of the MHQ used only in Dayton. Items marked with an asterisk (*) appeared on the version used at all other sites.

[b] Percentages may not sum to 100 because of rounding.

[c] By design, a portion of the sample population in Dayton did not receive the questionnaire (see text).

[d] The remainder of this table refers only to those persons who responded "yes" to the first question about anemia.

[e] Less than 0.5 percent.

who answered "yes" to the first question[1] were classified as having anemia currently or in the past. At the first site, Dayton, Ohio, where the question was worded "Has a doctor told you that you currently have anemia or are you currently under treatment for it?" only 46 of 813 (5.7 percent) answered "yes." At the remaining sites, where the question was "Has a doctor ever said that you had anemia?" the "yes" response rate was three times as high, 799 of 4535 (17.6 percent). Altogether, 845 of the 5350 people who completed the questionnaire (16 percent) said that they had anemia now or at some time in the past. Of these, 100 (12 percent) were currently under a doctor's care or had seen a doctor in the past 3 months for their anemia.

Of the 845 people with a current or past history of anemia, about one-third (6 percent of the total sample) were currently taking one or more treatments for it (see Tables 3 and 4). The percentages of respondents reporting that a doctor had prescribed a special diet, iron pills, and blood transfusions were slightly higher than those reporting that they currently followed such therapies (see Table 3); conversely, the percentage reporting that they used vitamin pills or shots was higher than the percentage who claimed that a physician had prescribed such therapy.

Most of the current treatment was with iron (see Table 4), and over half of those taking iron were taking nothing else. The next most common treatments were vitamins alone and vitamins plus iron, together accounting for half of all current treatments. Four of the respondents were receiving blood transfusions (in addition to their other treatments).

Although expected, the most striking finding among the responses to questions about anemia is that almost all (91 percent) of those who reported having anemia now or in the past were women. Table 5 shows the prevalence of anemia according to sex, based on responses to questions about current treatment.

PREVALENCE OF ANEMIA ACCORDING TO SCREENING EXAMINATION FINDINGS

Hematology data were available for 3269 of the 3321 people who were screened (98 percent). Of the 52 who did not have blood tests, 43 refused to have blood drawn and 9 blood samples either could not be obtained or were not analyzable.

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[1]The Anemia Battery from the MHQ is reproduced in Appendix A.

Table 3

DISTRIBUTION OF RESPONSES TO QUESTIONS ABOUT ANEMIA FROM THE MHQ: TREATMENTS PRESCRIBED BY PHYSICIAN OR CURRENTLY BEING USED

Question	Response	Number	Percent[a]
In the past 12 months, has a doctor prescribed any of these treatments for your anemia?			
Special diet	Yes	40	5
	No	784	93
	Missing	21	2
		845	100
Iron pills or shots	Yes	240	28
	No	598	71
	Missing	7	1
		845	100
Vitamin pills or shots	Yes	112	13
	No	713	84
	Missing	20	2
		845	99
Blood transfusions	Yes	13	2
	No	805	95
	Missing	27	3
		845	100
Do you currently take any of the following treatments for anemia, whether or not a doctor prescribed them?			
Special diet	Yes	26	3
	No	796	94
	Missing	23	3
		845	100
Iron pills or shots	Yes	209	25
	No	628	74
	Missing	8	1
		845	100
Vitamin pills or shots	Yes	162	19
	No	665	79
	Missing	18	2
		845	100
Blood transfusions	Yes	4	(b)
	No	814	96
	Missing	27	3
		845	99

[a]Percentages may not sum to 100 because of rounding.

[b]Less than 0.5 percent.

Table 4

CURRENT TREATMENTS FOR ANEMIA

Current Treatment	Number	Percent
Iron or transfusions	211	25
Iron alone	118	
Iron plus vitamins	72	
Iron plus special diet	6	
Iron plus diet and vitamins	11	
Transfusions	4	
Special diet or vitamins	81	10
Vitamins alone	73	
Special diet alone	3	
Vitamins plus special diet	5	
No treatment	553	65
Total	845	100

Table 5

STATUS OF ANEMIA ACCORDING TO SEX; BASED ON RESPONSES TO THE MHQ

MHQ Response[a]	Number	Percent		
		Men and Women	Men	Women[b]
Anemia currently being treated with iron or transfusions	211	4	3[c]	97[c]
Anemia currently being treated with diet or vitamins	81	2	6	94
Anemia in the past, no current treatment	553	10	11	89
Never had anemia	4503	84	54	46
Missing data (skipped questions)	2	(d)	50	50
Total	5350	100	47	53

[a]Based on a "yes" response to the first question and responses to questions about current treatment for anemia (see text).

[b]Includes pregnant women.

[c]Row percent.

[d]Less than 0.5 percent.

Hemoglobin and Hematocrit

Tables 6 and 7 show the distribution of hemoglobin and hematocrit values, respectively, according to sex and age. Hemoglobin and hematocrit values in the HIS population were approximately normally distributed; mean and median values coincided for all groups except pregnant women. The mean values for boys 14 to 17 years old were lower than for men because of differences in hemoglobin concentration related to sexual maturity, as discussed earlier. Differences between girls 14 to 17 years old and adult women were negligible. For pregnant women, the mean values were lower than for other women; this was expected, because of increased plasma volume during pregnancy.

The sensitivity of prevalence rate to the choice of a lower limit of normal hemoglobin or hematocrit is shown in Tables 6 and 7. For example, in men 18 and older, if the normal hemoglobin limit is chosen as 13.5 g, then the prevalence of anemia in that group is 5.9 percent, but if the limit is 14.0 g, the prevalence rate will increase to 14.9 percent.

Because of diurnal variation in hemoglobin and hematocrit concentrations, with lower values in the afternoon and evening, the HIS mean values are lower than would be expected in the general population. The average hemoglobin for adult men is usually 16 g; in one large survey (NCHS, 1979), it was reported to be 15.7 g for more than 2000 men in the 18 to 44 age group. The HIS average, by contrast, was closer to 15 g (14.9 g). All the HIS blood samples were drawn between 11:00 A.M. and 10:00 P.M. (half between 6:00 P.M. and 10:00 P.M.), when hemoglobin and hematocrit values are lower than they would have been in the morning. To correct for this slight systematic bias, as discussed in Chapter 5, HIS prevalence rates for anemia are based on normal limits that have been defined as 0.5 g (about 4 percent) lower than standard reference limits.

Table 8 shows the prevalence rates for anemia according to age and sex, based on the hemoglobin limits outlined in Chapter 5. The rate for the entire adult sample was 4.4 percent; 3.2 percent among men, 5.4 percent among women, and 3.7 percent among pregnant women. Very few of the 143 cases of anemia were severe; only 16 people had hemoglobin levels below 10.0 g.

As expected, the rates were lower for men than for women in every age group except adolescence, when hemoglobin values in boys are increasing from the average childhood level of 13 g to the adult level of 16 g; the average hemoglobin level in girls does not change much during adolescence. The prevalence rate for men 45 and older is slightly higher than for younger men; the older group is represented

Table 6

DISTRIBUTION OF HEMOGLOBIN VALUES ACCORDING TO SEX AND AGE

(g/100 ml)

	Adolescent Boys 14-17		Adult Men 18 and Older		Adolescent Girls 14-17		Adult Women 18 and Older		Pregnant Women	
Number screened (n = 3269)	214		1283		219		1499		54	
Median	14.1		14.9		12.9		13.1		11.7	
Mean	14.1		14.9		12.9		13.1		12.0	
2 standard deviations	12.1-16.1		12.9-16.9		11.1-14.7		11.0-15.2		9.6-14.4	
5th to 95th percentile	12.4-15.7		13.3-16.5		11.6-14.3		11.4-14.7		10.1-14.1	
10th to 90th percentile	12.8-15.5		13.7-16.1		11.9-14.0		11.8-14.3		10.7-13.3	
Hemoglobin Limit	Distribution[a]									
Below 10.0	--	--	0.1	0.1	0.5	0.5	0.8	0.8	3.7	3.7
10.0-10.4	--	--	0.1	0.2	0.5	0.9	0.6	1.4	3.7	7.4
10.5-10.9	--	--	0.1	0.2	1.8	2.7	1.1	2.5	5.6	13.0
11.0-11.4	--	--	0.0	0.2	1.4	4.1	3.1	5.6	16.7	29.6
11.5-11.9	0.9	0.9	0.2	0.5	6.4	10.5	6.0	11.6	29.6	59.3
12.0-12.4	4.7	5.6	0.5	0.9	17.8	28.3	13.5	25.2	5.6	64.8
12.5-12.9	7.0	12.6	1.9	2.8	26.0	54.3	19.1	44.3	16.7	81.5
13.0-13.4	10.3	22.9	3.1	5.9	20.1	74.4	20.9	65.2	11.1	92.6
13.5-13.9	19.6	42.5	9.0	14.9	13.7	88.1	17.4	82.6	3.7	96.3
14.0-14.4	19.2	61.7	16.5	31.4	7.8	95.9	9.7	92.3	3.7	100.0
14.5-14.9	13.5	75.2	21.0	52.4	2.7	98.6	3.9	96.2	--	--
15.0-15.4	14.5	89.7	19.4	71.8	0.5	99.1	2.5	98.7	--	--
15.5-15.9	8.9	98.6	14.6	86.4	0.9	100.0	1.0	99.7	--	--
16.0 and above	1.4	100.0	13.7	100.0	--	--	0.3	100.0	--	--

[a]Percentage and cumulative percentage.

Table 7

Distribution of Hematocrit Values According to Sex and Age
(ml/100 ml)

	Adolescent Boys 14-17		Adult Men 18 and Older		Adolescent Girls 14-17		Adult Women 18 and Older		Pregnant Women	
Number screened (n = 3269)	214		1283		219		1499		54	
Median	41.3		43.4		38.0		38.5		34.3	
Mean	41.3		43.5		38.1		38.6		35.1	
2 standard deviations	35.6-46.9		37.8-49.1		33.2-43.1		32.7-44.4		28.6-41.6	
5th to 95th percentile	36.7-45.6		39.1-48.1		34.5-41.8		34.1-43.4		29.9-39.3	
10th to 90th percentile	37.5-44.9		40.1-47.1		35.3-40.8		35.0-42.2		31.3-38.6	
Hematocrit Limit	Distribution[a]									
Below 31.0	--	--	0.2	0.2	0.5	0.5	0.9	0.9	7.4	7.4
31.0-32.9	--	--	0.1	0.2	1.4	1.8	1.9	2.7	18.5	25.9
33.0-34.9	1.4	1.4	0.1	0.3	5.5	7.3	7.0	9.7	31.5	57.4
35.0-36.9	4.7	6.1	0.9	1.2	21.0	28.3	18.0	27.8	11.1	68.5
37.0-38.9	16.8	22.9	3.4	4.6	34.7	63.0	28.6	56.4	24.1	92.6
39.0-40.9	22.0	44.9	12.8	17.4	27.9	90.9	25.2	81.5	3.7	96.3
41.0-42.9	26.6	71.5	26.3	43.6	6.8	97.7	11.6	93.1	0	96.3
43.0-44.9	18.7	90.2	28.7	72.3	0.9	98.6	4.9	98.1	3.7	100.0
45.0-46.9	8.9	99.1	17.0	89.3	1.4	100.0	1.5	99.6	--	--
47.0-48.9	0.5	99.5	8.0	97.4	--	--	0.1	99.7	--	--
49.0 and above	0.5	100.0	2.7	100.0	--	--	0.3	100.0	--	--

[a]Percentage and cumulative percentage.

Table 8

PREVALENCE RATES OF ANEMIA, BY AGE AND SEX, BASED ON HEMOGLOBIN VALUES[a]

Age Group (years)	Men		Women		Pregnant Women		Total	
	Cases Per Sample	Rate	Cases Per Sample	Rate	Cases Per Sample	Rate	Cases Per Sample	Rate
14-17	12/214	5.6	9/219	4.1	1/4	25.0	22/437	5.0
18-24	5/229	2.2	14/290	4.8	1/23	4.4	20/542	3.7
25-34	13/452	2.9	30/515	5.8	0/21	0	43/988	4.4
35-44	6/306	2.0	18/298	6.0	0/6	0	24/610	3.9
45-54[b]	10/186	5.4	17/254	6.7	--	--	27/440	6.1
55-61[b]	2/110	1.8	5/142	3.5	--	--	7/252	2.8
14-61[b]	48/1497	3.2	93/1718	5.4	2/54	3.7	143/3269	4.4

[a]Anemia was defined as hemoglobin (in grams/100 ml) below certain values, adjusted for age, sex, pregnancy, and diurnal variation; see text.

[b]Except for two people, everyone who was screened was 61 years of age or younger.

by 12 anemic men, aged 47 to 54, who had hemoglobin values between 7.4 and 12.8 g. For most women, the prevalence of anemia is between 5 and 6 percent; it is slightly lower among adolescents and slightly higher among women between the ages of 45 and 54. Hemoglobin values are known to decrease with age, but usually only after age 55 or 60 (NCHS, 1979), so the slightly higher rates for both sexes in the 45 to 54 age group is an unexpected finding; it is, however, based on a small number of cases. The 3.7 percent prevalence rate among the 54 pregnant women who were screened is unexpectedly low.

The HIS prevalence rates for anemia, based on hemoglobin values, are compared with those for a national sample in Table 9. To make the HIS data comparable to the national data, pregnant women were included with other women, as in the NCHS analysis. Also, for this comparison only, the same lower limits of normal hemoglobin were used to define anemia in the HIS population as were used by NCHS, 14.0 g for men and 12.0 g for women, respectively. These limits were adjusted by 0.5 g to 13.5 g and 11.5 g to account for the effect of diurnal variation presumed to be present in the HIS values. The NCHS oversampled certain groups expected to be at high risk for malnutrition; however, they adjusted their rates to the age, sex, and income distribution in the entire U.S. population.

The HIS observed prevalence was similar to the U.S. rates for people 18 through 44 years. The observed prevalence rate in the HIS was higher for people between 45 and 59 years, primarily because of a high rate among men, 8.5 percent. Similarly, the total rate for all adults in the HIS, after age adjustment to the U.S. population,[2] was 7.3 percent, slightly higher than the observed U.S. rate of 6.4 percent. Both of these differences may reflect the effect of diurnal variation on hemoglobin or true differences produced by different sampling strategies or different populations sampled.

Hemoglobin versus Hematocrit

The HIS uses hemoglobin rather than hematocrit values to define anemia because hemoglobin can be measured with greater reliability on the Coulter Model S, as noted in Chapter 4. To determine the

[2]Age adjustment was done by the indirect method. This technique begins with a calculation of the overall prevalence of anemia that would be expected if the reported U.S. rates in each age group were applied to the HIS population. The indirect adjusted rate for the HIS is then computed as the overall rate for the standard (U.S.) population adjusted by the ratio of the crude prevalence rate observed for the HIS to the expected HIS prevalence rate. See Fleiss (1973) for a description of this method, which is the most commonly used technique for such adjustments.

Table 9

PREVALENCE RATES OF ANEMIA, BY AGE AND SEX: HIS, 1974-76; UNITED STATES, 1971-72

Age Group (years)	Men			Women[a]			Total		
		HIS			HIS			HIS	
	U.S. Rate[b]	Cases Per Sample	Rate	U.S. Rate[b]	Cases Per Sample	Rate	U.S. Rate[b]	Cases Per Sample	Rate
18-44	4.2	52/987	5.3	6.1	76/1153	6.6	5.5	128/2140	6.0
45-59	(c)	23/272	8.5	(c)	22/371	5.9	4.9	45/643	7.0
59 and older	(c)	1/24	4.2	(c)	0/25	0	8.8	1/49	2.0
Total	--	76/1283	5.9	--	98/1549	6.3	6.4	174/2832	7.3[d]

[a] Includes pregnant women.

[b] United States rates are from the 1971-72 NCHS survey of 6525 persons aged 18 and older (NCHS, 1974; Tables 37-39), where anemia was defined by threshold limits for hemoglobin, 14.0 g for men and 12.0 g for women. The HIS threshold limits were adjusted to 13.5 g and 11.5 g to allow for the effect of diurnal variation (see text).

[c] Not available.

[d] The total prevalence rate was adjusted by age for comparison with the United States rate, using the indirect method of adjustment. The observed prevalence was 6.1 percent.

sensitivity and specificity of the two measures, we compared the prevalence of anemia according to each measure. For the comparison, equivalent lower limits of normal were chosen (see Table 10), based on a plot of hemoglobin by hematocrit values for the HIS sample. As shown in Table 11, the hemoglobin and hematocrit measures agree on 99 cases of anemia (low values) and 3098 diagnoses of no anemia (normal values), for a total of 98 percent of the 3269 people sampled. Only 72 cases, or 2 percent of the total, remain doubtful.

Table 10

LOWER LIMITS OF NORMAL FOR HEMOGLOBIN AND HEMATOCRIT VALUES

Group	Hemoglobin (g/100 ml)	Hematocrit (ml/100 ml)
Adolescent boys, 14-17	12.5	35.5
Adult men, 18-61	13.0	38.5
Adolescent girls, 14-17	11.5	34.0
Adult women, 18-61	11.5	34.0
Pregnant women, all ages	10.0	31.0

Table 11

NUMBER OF PERSONS WITH AND WITHOUT ANEMIA, BASED ON HEMOGLOBIN AND HEMATOCRIT VALUES

Anemia Status, Based on Hemoglobin Values	Anemia Status, Based on Hematocrit Values		Total
	Anemic	Not Anemic	
Anemic	99	44	143
Not anemic	28	3098	3126
Total	127	3142	3269

To confirm the choice of hemoglobin over hematocrit as the preferred screening measure for prevalence of anemia in the HIS, the 72 doubtful cases were examined. Among the 44 people with low hemoglobin values and normal hematocrit values, half (22 people) had small cells (mean cell volume [MCV] less than 80 cubic microns), a finding that is consistent with iron deficiency anemia. The other half had normal MCV values but below-normal red blood cell counts (RBC), as did almost all of the 28 people with low hematocrit values and normal hemoglobin values.

The most likely explanation for these findings is that the Coulter Model S does not measure hematocrit directly. Rather, it calculates the hematocrit value as the product of RBC times MCV, each of which is susceptible to small errors of measurement. If either (or both) is only marginally abnormal, the calculation may still produce a hematocrit value that falls within the normal range. This is evidently what happened in the case of the 22 people with small cells (low MCV) and normal RBC values, who were judged anemic by hemoglobin measurement but had a normal hematocrit value by calculation.

In summary, the HIS originally selected hemoglobin instead of hematocrit as its screening measure for anemia because it is measured directly on the Coulter Model S and is therefore more reliable than the calculated hematocrit value. Analysis of the 72 cases (2 percent of the total screened) in which hemoglobin and hematocrit values disagreed showed that hemoglobin is also a more sensitive screening measure for anemia; it identified 22 cases of small cell or iron deficiency anemia that would not have been detected by a screening hematocrit alone.

Cell Size (Mean Cell Volume)

Table 12 shows the distribution of red blood cell size (MCV) in the HIS population, by anemia status. As discussed earlier, mean cell volume by itself is an unreliable indicator of anemia; its usefulness is in differentiating among causes of anemia. Generally, large MCV values (larger than 100 cubic microns) suggest megaloblastic anemia; small MCV values (smaller than 80 cubic microns) suggest iron deficiency anemia. Of the total of 187 people with abnormally large or small cells, 60 (32 percent) were anemic; of these, all except one had small cells.

The 59 anemic people with small cells represented 41 percent of the 143 people in the HIS who were anemic, which is consistent with the finding that a large proportion of anemia is iron deficiency anemia. Among the 109 people with small cells who were not anemic, all but one had normal hematocrit values and normal hemoglobin

Table 12

DISTRIBUTION OF CELL SIZE IN THE HIS POPULATION, BY ANEMIA STATUS

Anemia Status[b]	Distribution of Cell Size[a]				
	Very Small, $<75\mu^3$	Small, $75-79\mu^3$	Normal, $80-100\mu^3$	Large, $101-110\mu^3$	Very Large, $>110\mu^3$
Anemic (n = 143)	36 (25)	23 (16)	83 (58)	1 (1)	0 (0)
Not anemic (n = 3126)	28 (1)	81 (3)	2999 (96)	17 (1)	1 (c)

[a]Mean cell volume (MCV) in cubic microns. Percentages are shown in parentheses.

[b]Based on hemoglobin value (see text for definition).

[c]Less than 0.5 percent.

values. In addition, the percentage of individuals who had MCV values below 75 cubic microns was much smaller for those who were not anemic (26 percent) than for those who were (61 percent).

Among the total of 19 people with large cells, 7 (37 percent) had abnormal liver function tests (SGOT above 43 units/ml), which is consistent with the observation that liver disease is associated with macrocytosis (Thong et al., 1977; McPhedran et al., 1973). Of the remaining 12 people with large cells, 11, including the single anemic person, had only marginally increased MCV values, from 101 to 105 cubic microns.

DISEASE IMPACT

To assess the impact of anemia among those who had or believed they had anemia, three questions were asked on the MHQ concerning (a) the amount of recent worry about anemia, (b) the restriction of activity due to the disease, and (c) the number of days in bed attributed to anemia. (See Appendix A for the exact wording of the questions.) All persons who responded positively to the initial question in the Anemia battery (regarding whether a doctor had said they had anemia now or had had it in the past) responded to these questions, regardless of whether they were anemic according to the screening examination test for hemoglobin.

The distribution of responses to these questions is given in Table 13. Worry was the most common adverse effect reported by the MHQ respondents: 16 percent reported at least a little worry about their illness. Only about 7 percent reported that they had restricted their activities because of the condition, and approximately 1 percent claimed to have spent one or more days in bed because of their anemia. Altogether, 18 percent of the respondents reported at least one adverse effect of anemia (see also Table 14).

Based on the responses to these three questions, Table 14 compares the adverse effects of anemia for three groups of people: those who were currently taking iron or transfusions for anemia, those who were taking vitamins or a special diet for anemia, and those who had had anemia at some time in the past but were not currently taking any treatment for it. The respondents are further categorized as to whether they had anemia according to the hemoglobin test done at the screening examination or were not screened. Table 14 shows the percentage of persons in each group who responded positively (answered something other than "none") to each of the three questions. Table B.1

Table 13

DISTRIBUTION OF RESPONSES TO QUESTIONS ABOUT ANEMIA FROM THE MHQ: DISEASE IMPACT

Question	Response	Number	Percent[a]
During the past 3 months, how much has your anemia worried or concerned you?	A great deal	12	1
	Somewhat	28	3
	A little	103	12
	Not at all	701	83
	Missing	1	(b)
		845	99
During the past 3 months, how often has anemia kept you from doing most of the kinds of activities other people your age do?	All of the time	1	(b)
	Most of the time	6	1
	Some of the time	14	2
	A little of the time	41	5
	None of the time	781	92
	Missing	2	(b)
		845	100
During the past 30 days, how many days has your anemia kept you in bed all or most of the day?	20 days	2	(b)
	10 days	1	(b)
	4 days	2	(b)
	2 days	2	(b)
	1 days	3	(b)
	0 days	833	99
	Missing	2	(b)
		845	99

[a]Percentages may not sum to 100 because of rounding.

[b]Less than 0.5 percent.

in Appendix B shows the detailed distribution of responses to these questions.

Persons whose MHQ assessment of themselves as being anemic now or in the past turned out to be correct, based on their low hemoglobin values at the screening examination, were more likely to report disease impact than those who believed themselves, incorrectly, to be anemic (see Table 14). Of the 44 persons who were truly anemic, 32 percent had a positive score for "any impact." Thirty percent reported worrying about their condition, 14 percent reported restricting their activities, and 7 percent reported spending time in bed because of the ailment.

People who reported on the MHQ that they were currently taking some form of treatment for anemia (whether or not the screening tests showed they were anemic) were also more likely to report adverse

Table 14

Percentage of HIS Enrollees Reporting Worry, Activity Restriction, and Days in Bed Due to Anemia,[a] by Anemia Status: Enrollees Answering Disease Impact Questions on the MHQ

Anemia Status	Number of Enrollees Answering Questions About Anemia	Percentage Reporting Worry[b]	Percentage Reporting Activity Restriction[b]	Percentage Reporting Days in Bed[b]	Percentage with Any Kind of Impact
Anemia present--low hemoglobin					
Taking iron or transfusions	17	29	6	6	29
Taking vitamins or diet	5	40	60	20	60
No current treatment	22	27	9	5	27
Total	44	30	14	7	32
Anemia not present					
Taking iron or transfusions	98	38	14	2	40
Taking vitamins or diet	40	18	5	0	18
No current treatment	302	8	4	1	9
Total	440	15	6	1	16
Not screened for anemia					
Taking iron or transfusions	96	41	16	1	41
Taking vitamins or diet	36	11	8	0	14
No current treatment	229	9	4	1	10
Total	361	17	8	1	19
Grand total	845	17	7	1	18

[a] Among those who answered the questions about disease impact of anemia.

[b] The distribution of responses to the disease impact questions is given in Appendix B, Table B.1.

effects from the disease than those who were not taking treatment. This finding suggests that anemia's impact is related to the perception of its presence: If a person believes that he or she currently has anemia and requires treatment for it, then that person is more likely to report adverse effects than if he or she perceives the anemia as having been cured or as not requiring treatment.

Table 15 shows the distribution of responses to the three impact questions for all persons who completed the MHQ, regardless of whether they actually answered the questions. For this comparison, scores equal to no impact were assigned to all persons who did not answer the three questions, as was described in Chapter 5. Therefore, the impact shown in Table 15 is the same as that shown in Table 14 except that it is expressed as a percentage of the total population of 5350 people who completed the MHQ. The proportion of people reporting any adverse effects of anemia was compared among three groups: those with low hemoglobin, those with normal hemoglobin, and those who were not screened for hemoglobin. People who were physiologically anemic were more likely to report some untoward effects of anemia than those who were not anemic, but the absolute numbers were small. Only 10 percent of people with anemia reported any kind of impact, most often worry (see Table 15); only 4 percent reported activity restriction. These results were not unexpected because unless anemia is severe, it has very few symptoms. Anemia in the HIS was not severe; only 11 percent of those who were anemic had hemoglobin levels below 10 g. Therefore, most people with anemia were probably not aware of its presence and did not attribute any effects to it.

The two preceding tables (Tables 14 and 15) have shown the proportion of persons who reported any adverse effects of anemia. Another dimension of the self-perceived effects of anemia is their magnitude or severity. This dimension is reflected in Table 16, which shows the median categories of responses to the impact questions among those persons who actually gave a positive response (i.e., a response other than "none"). For example, among anemic people taking iron, the median level of worry reported was "a little." The median level of worry reported did not differ between people who were physiologically anemic and those who were not. People who were taking some form of treatment for anemia, whether or not they were in fact anemic, reported a higher median level of activity restriction from anemia than those with no current treatment, i.e., "some" or "most of the time" compared with "a little of the time." The median levels of days in bed were not meaningful because only 10 people (1 percent of the 845 people who answered the questions) reported any days in bed.

Table 15

Percentage of HIS Enrollees Reporting Worry, Activity Restriction, and Days in Bed Due to Anemia,[a] by Anemia Status: Enrollees Completing the MHQ

Anemia Status	Number of Enrollees Completing the MHQ	Percentage Reporting Worry[b]	Percentage Reporting Activity Restriction[b]	Percentage Reporting Days in Bed[b]	Percentage with Any Kind of Impact
Anemia present--low hemoglobin	143	9	4	2	10
Anemia not present	3124	2	1	(c)	2
Not screened for anemia	2083	3	1	(c)	3
Total	5350	3	1	(c)	3

[a]Among all those who completed or should have completed the MHQ, regardless of whether they answered the questions about disease impact of anemia.

[b]The distribution of responses to the disease impact questions is given in Appendix B, Table B.2.

[c]Less than 0.5 percent.

Table 16

MEDIAN CATEGORIES[a] OF WORRY, ACTIVITY RESTRICTION, AND DAYS IN BED, BY ANEMIA STATUS

Anemia Status	Worry (n = 143)	Activity Restriction (n = 62)	Days in Bed (n = 10)
Anemia present--low hemoglobin			
Taking iron or transfusions	Little	Most	20
Taking vitamins or diet	Little/some[b]	Most	20
No current treatment	Little	Little	2
Anemia not present			
Taking iron or transfusions	Little	Little/some[b]	1/2[b]
Taking vitamins or diet	Little	Little	(c)
No current treatment	Little	Little	4
Not screened for anemia			
Taking iron or transfusions	Little	Some	10
Taking vitamins or diet	Little	Some	(c)
No current treatment	Little	Little	1
Total	Little	Little	2/4[b]

[a]Medians are based on the positive responses (i.e., excluding "none") to questions about disease impact of anemia. The distribution of responses is shown in Appendix B, Table B.1.

[b]Dual median.

[c]There were no enrollees in this category who responded positively to this item.

The medians shown in Table 16 summarize the perceived severity of the effects of anemia. To find out whether the apparent differences in severity were statistically significant, we analyzed all the responses (including "none") by using the Wilcoxon Two-Sample test.[3] We found that the responses of people who were physiologically anemic did not differ greatly from those of people who were not anemic, but the responses of people who were currently under treatment for anemia showed significantly more worry than those not under treatment ($p < .0001$). This finding is consistent with the impression noted earlier

[3]This procedure compares answers to a question between two groups by ranking responses from lowest to highest among all members of the population and then summing the ranks for each group. It is equivalent to the Mann-Whitney U test.

(Table 14) that the adverse effects of anemia are related more to the perception of its presence than to its actual presence.

RELIABILITY OF HEMATOLOGY MEASUREMENTS

Reliability refers to the ability of a measurement to produce the same results when the same object is measured. In the HIS, a repeat test of randomly selected blood samples was used to evaluate the reliability of the screening examination measurements. Of the 3269 blood samples taken at the screening examination, 264 (8.1 percent) were randomly selected to be retested. Each sample was divided in two, and the new samples were independently labeled and sent to the laboratory at different times of day, so that they would not be processed in the same batch. Comparison of the first and second measurement of these 264 split samples provides an estimate of their reliability. The difference between the first and second measurement of hemoglobin ranged from -3.3 to $+1.5$ g/100 ml, with an average difference of $+0.02$ g, standard deviation 0.34 g. For hematocrit, the difference between the first and second measurement ranged from -9.2 to $+5.9$ ml/100 ml, with an average difference of $+0.02$ ml, standard deviation 1.12 ml.

VALIDITY OF THE MEDICAL HISTORY QUESTIONNAIRE

Validity refers to the extent to which a measure assesses what it purports to assess. One indication of the validity of the MHQ questions about anemia is how well the answers agree with hemoglobin values from the screening examination.

In Table 17, anemia status based on answers to MHQ questions about anemia is compared with anemia status based on screening hemoglobin values. Of the 3265 people who answered the anemia questions and were screened for hemoglobin, 142 were classified as anemic because of a low hemoglobin. Of these 142, only 22 had reported on the MHQ that they were currently under treatment for anemia. Thus, the sensitivity of the MHQ, the proportion of those who really were anemic who had also answered on the MHQ that they were under treatment for anemia, was only 15 percent (22 of 142 persons). The sensitivity increases to 31 percent (44 of 142) if we include the 22 people who answered that they had had anemia in the past but were not currently taking any treatment for it.

Table 17

NUMBER OF PERSONS WITH AND WITHOUT ANEMIA, BASED ON MHQ RESPONSES AND HEMOGLOBIN VALUES

Anemia Status Based on Responses to MHQ	Anemia Status Based on Screening Hemoglobin Value[a]		Total Number Screened
	Anemic	Not Anemic	
Anemia currently being treated with iron, transfusions, diet, or vitamins	22	138	160
Anemia in the past, no current treatment	22	302	324
Never had anemia	98	2683	2781
Total	142	3123	3265[b]

[a]Anemia was defined as hemoglobin values (g/100 ml) below certain lower limits of normal, adjusted for age, sex, pregnancy status, and diurnal variation (see Chapter 5).

[b]Excludes 4 persons who were screened, one of whom was anemic. Two of the 4 skipped the anemia questions, and the other 2 did not receive the MHQ.

The specificity of the MHQ, the proportion of truly nonanemic people who answered that they were not under treatment for anemia (302 persons) or had never had anemia (2683 persons), was 96 percent (2985 of 3123 persons). Some of the remaining 4 percent (138 persons) may have answered that they were under treatment for anemia because they were under preventive treatment or were just finishing a course of treatment, not because they believed that they were currently anemic. Specificity decreases to 86 percent (2683 of 3123) when the 302 people who answered that they were not currently under treatment for anemia are classified as being currently anemic.

The sensitivity and specificity of the MHQ for identifying people with anemia depends on how the people who are not currently under treatment for anemia are classified. If they are considered not to have anemia, the sensitivity of the MHQ is 15 percent, with a specificity of 96 percent. If the same people are considered as having anemia, sensitivity is increased to 31 percent, but the specificity drops to 86 percent.

Of the 142 people in the HIS with anemia, 98 (69 percent) were totally unaware of it, probably because the disease has few symptoms unless it is very severe. Thus, asking people if they are currently under treatment for anemia is not a good way to determine if they are actually anemic. Blood tests, particularly hemoglobin tests, are needed to screen for the presence of anemia.

PREVALENCE OF ANEMIA ACCORDING TO THE HIS INSURANCE PLANS

Table 18 shows the distribution of persons with anemia among the HIS experimental insurance plans. The 16 plans, described in more detail in the Preface, have been grouped into four kinds of fee-for-service plans, based on their levels of coinsurance or maximum deductible expenditure. The two prepaid group practice plans are both located at the Group Health Cooperative of Puget Sound (GHC), in Seattle, Washington. Only the 2865 persons who were assigned to one of these plans[4] *and* who could be classified as to the presence of anemia on the basis of screening examination data are included in the analyses.[5] Anemia was defined as a screening hemoglobin value below certain normal limits, adjusted for age, sex, pregnancy, and diurnal variation, as outlined in Chapter 5.

Differences in prevalence of anemia among the four types of fee-for-service plans were not statistically significant. This is as expected, and reflects the unbiased assignment of people to plans at the time of enrollment into the HIS, before data from the MHQ or the medical screening examination were collected. Not shown in Table 18 is the prevalence of anemia among people assigned to the fee-for-service plans in Seattle, counted separately from other locations. It was 3.4 percent (14 of 413 persons screened), which is not significantly different from the 3.9 percent prevalence in the prepaid experimental plan in Seattle. The prepaid control plan is not strictly comparable to any other HIS plan, even in Seattle, because it was composed of people who had already been participating in the GHC before the HIS began at that site. The difference in prevalence of anemia between the experimental and control GHC plans (3.9 and 3.3 percent, respectively) was not significant.

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[4]For more information on the assignment of families to plan, see Morris, 1979.

[5]Of the original 3321 individuals who received the screening examination, 410 were not assigned to an HIS experimental plan; they were left over from a large pool of possible participants from which the unbiased assignments to plan were made. An additional 46 persons were not classifiable because of missing hemoglobin data.

Table 18

PREVALENCE OF ANEMIA, BY HEALTH INSURANCE PLAN

HIS Experimental Health Insurance Plan[a]	Number of Persons Classifiable[b]	Number of Persons with Anemia	Percent with Anemia
Fee-for-service (all sites)			
Free care	771	31	4.0
25 or 50 percent coinsurance	556	20	3.6
95 percent coinsurance	431	20	4.6
Individual/family deductible	501	22	4.4
Prepaid group practice (Seattle only)			
Experimental	364	14	3.9
Control	242	8	3.3
Total	2865[c]	115	4.0

[a]See Preface for details of insurance coverage.

[b]Includes only those screened for hemoglobin at enrollment.

[c]Includes only persons who were assigned to an experimental health insurance plan.

These findings demonstrate that the assignment of families to the HIS experimental health insurance plans was not biased at enrollment with respect to the presence of anemia. Thus, the Study should be able to determine whether the course of the disease—among those who truly are anemic—differs as a function of differences in the amount or type of care associated with the various levels of insurance coverage.

POTENTIAL EFFECTS OF HEALTH INSURANCE ON ANEMIA

More generous health insurance could have positive effects on anemia at several points in the diagnosis and treatment process. First, the percentage of anemic persons who knew they were anemic was very low among HIS participants. This is not entirely surprising, because unless anemia is severe, it has very few symptoms that would alert a person to its presence. Most cases of anemia, therefore, are

discovered by routine screening tests. Better and more frequent medical care in general, an expected result of more generous insurance, could increase the likelihood that screening tests for anemia would be performed, which, in turn, could improve the detection and recognition of anemia among HIS participants with generous health insurance. In general medical practice, women are more often screened for anemia than men, largely because women are known by physicians to have a higher risk for developing anemia. Thus, having generous health insurance may especially benefit men, insofar as they will then be more likely to visit a physician, have a more thorough examination, including screening for anemia, and receive appropriate treatment.

Second, anemic persons with more generous insurance might visit physicians more often than those with less generous insurance, so their condition might be treated more promptly. More frequent visits to a physician might also be associated with better advice about diet (e.g., consumption of iron or other nutrients associated with deficiency anemias) and with greater attention to possible side effects of medications, such as iron overload or stomach upset caused by iron preparations. With more prompt and effective treatment, persons with generous health insurance might also show less restricted activity or worry about their condition.

Finally, and perhaps most important, generous insurance is expected to result in greater attention to the underlying causes of anemia, with earlier diagnosis and treatment of potentially serious illness (a bleeding ulcer, for example).

Generous health insurance might have negative effects as well. Persons with such coverage who visit their physicians more frequently (for anemia or for other conditions), and whose hemoglobin values are only borderline, may erroneously be diagnosed as anemic. This could produce needless worry, unnecessary consumption of medications, and further diagnostic procedures that may be expensive, risky, or painful. Also, depending on a person's innate propensity to adopt the sick role, it could lead to unnecessary disability in the form of restricted activity or even bed days.

Chapter 7

QUALITY OF CARE CRITERIA FOR ANEMIA

The HIS criteria for judging the quality of care for anemia (Appendix C) are based on the use of relevant laboratory tests to establish the diagnosis of anemia and on rules for therapy, once a specific diagnosis has been made. These criteria cannot take into account the results of laboratory tests ordered by a physician, results that might heavily influence the amount and direction of further diagnostic procedures. The HIS does not collect data on laboratory test results, nor does it examine medical records. Some criteria dealing with therapy assume that a specific and correct diagnosis has already been made, an assumption that cannot be verified or confirmed with the limited information available through HIS claim forms and questionnaires.

The HIS data sources include detailed medical history questionnaires and screening examination results at enrollment and at exit. Also, problem-oriented insurance claim forms filed during the HIS provide information on physicians' diagnoses, laboratory tests, procedures, and medications dispensed or prescribed. Pharmacy claim forms provide information on prescriptions filled.

With the restrictions noted above in mind, the criteria listed in Appendix C will be used to test hypotheses regarding the relationship between insurance level and quality of care. Favorable outcomes in the criteria include the absence of curable forms of anemia, little or no disability from the condition, and patient knowledge of its presence. Good processes of care include appropriate diagnostic tests, therapy, and followup. The criteria are expressed in a form that assumes that the level of quality of care has been high.

APPENDIX A

ANEMIA BATTERY FROM THE MEDICAL HISTORY QUESTIONNAIRE

ENROLLMENT MEDICAL HISTORY QUESTIONNAIRE[1]

ANEMIA

165. HAS A DOCTOR EVER SAID THAT YOU HAD ANEMIA (a-NEE-mee-a) OR LOW BLOOD? 16/

Yes ..... 1 —*Answer 166*
No ..... 2 —*Go to 172, page 44*

166. IN THE PAST 12 MONTHS, HAS A DOCTOR PRESCRIBED ANY OF THESE TREATMENTS FOR YOUR ANEMIA? (Circle one number on each line.)

	Yes	No	
A. Special diet	1	2	17/
B. Iron pills or shots	1	2	18/
C. Vitamin pills or shots	1	2	19/
D. Blood transfusions	1	2	20/

[1]Used in all HIS sites except Dayton at enrollment and in all sites upon exit. Revisions incorporated in this version were based on experience with the initial Dayton battery.

DO NOT WRITE IN THIS SPACE

167. DO YOU CURRENTLY TAKE ANY OF THESE TREATMENTS FOR ANEMIA, WHETHER OR NOT A DOCTOR HAS PRESCRIBED THEM? (Circle one number on each line.)

	Yes	No	
A. Special diet	1	2	21/
B. Iron pills or shots	1	2	22/
C. Vitamin pills or shots	1	2	23/
D. Blood transfusions	1	2	24/

168. WHEN WAS THE LAST TIME YOU SAW A DOCTOR ABOUT YOUR ANEMIA?

(Circle one)

Within past 3 months 1 25/
3 - 6 months ago 2
7 - 12 months ago 3
More than 1 year ago 4

169. DURING THE PAST 3 MONTHS, HOW MUCH HAS YOUR ANEMIA WORRIED OR CONCERNED YOU?

(Circle one)

A great deal 1 26/
Somewhat 2
A little 3
Not at all 4

170. DURING THE PAST 3 MONTHS, HOW MUCH OF THE TIME HAS YOUR ANEMIA KEPT YOU FROM DOING THE KINDS OF THINGS OTHER PEOPLE YOUR AGE DO?

(Circle one)

All of the time 1 27/
Most of the time 2
Some of the time 3
A little of the time 4
None of the time 5

171. DURING THE PAST 30 DAYS, HOW MANY DAYS HAS YOUR ANEMIA KEPT YOU IN BED ALL OR MOST OF THE DAY? (If none, write in "0.")

_____ days in bed last month 28-29/

ENROLLMENT MEDICAL HISTORY QUESTIONNAIRE, DAYTON

ANEMIA

56. HAS A DOCTOR TOLD YOU THAT YOU CURRENTLY HAVE ANEMIA (SOMETIMES CALLED LOW BLOOD) OR ARE YOU CURRENTLY UNDER TREATMENT FOR IT? ("ANEMIA" PRONOUNCED "A-NEE-ME-A") 4315

NO, I DO NOT HAVE ANEMIA (LOW BLOOD) ..... 3 *(GO to q. 63, page 16)*

YES, I HAVE IT OR AM UNDER TREATMENT FOR IT 1

YES, I HAD IT, BUT IT IS NOW CURED .... 2 *(GO to q. 57)*

57. In the past 12 months, has a doctor prescribed any of these treatments for your anemia? CIRCLE YES OR NO FOR EACH.

Special diet	Yes 1	4316
	No 2	
Iron pills or shots	Yes 1	4317
	No 2	
Vitamin pills or shots	Yes 1	4318
	No 2	
Blood transfusions	Yes 1	4319
	No 2	

58. **Do you currently take any of the following treatments for anemia, whether or not a doctor prescribed them? CIRCLE YES OR NO FOR EACH.**

Special diet	**Yes** ..... 1 **No** 2	4320
Iron pills or shots	**Yes** ..... 1 **No** 2	4321
Vitamin pills or shots	**Yes** ..... 1 **No** 2	4322
Blood transfusions	**Yes** ..... 1 **No** 2	4323

59. **Are you currently under a doctor's care or supervision for your anemia?** 4324

Yes 1
No 2

60. **During the past 3 months, how much has your anemia worried or concerned you?** 4325

(Circle one.)

A lot 1
Somewhat 2
A little 3
Not at all 4

61. **During the past 3 months, how often has anemia kept you from doing the kinds of activities other people your age do?** 4326

(Circle one.)

All of the time 1
Most of the time 2
Some of the time 3
A little of the time 4
None of the time 5

62. **During the past 30 days, how many days has your anemia kept you in bed all or most of the day? (IF NO DAYS IN BED, WRITE IN "0".** 4327

_____ **Days in bed**

APPENDIX B

DISTRIBUTION OF RESPONSES TO DISEASE IMPACT QUESTIONS

The following two tables present the number and percentage of responses to three disease impact questions from the Medical History Questionnaire (MHQ) for the same categories of anemia status that were summarized earlier in Tables 14 and 15.

Table B.1 shows the responses of the 845 people who actually answered the questions. Table B.2 shows the responses of all 5350 people who completed Form B of the MHQ, regardless of whether they answered the questions about the adverse consequences of anemia. Responses equivalent to no impact were assigned to the 4505 people in Table B.2 who did not actually answer the questions because of negative answers to earlier items (see Chapter 5). In both tables, the number of people in each anemia category is shown in parentheses. The number of responses may not add to the subtotals for these categories, however, because missing responses are not shown (less than 1 percent of all responses). The entries in the "level of impact" column are given in abbreviated form. The questions and responses are shown in Table 13 and Appendix A.

Table B.1

Distribution of Responses to Disease Impact Questions on the MHQ, by Anemia Status

Anemia Status	Worry			Activity Restriction			Days in Bed		
	Level of Impact	No.	Percent	Level of Impact	No.	Percent	No. of Days	No.	Percent
Anemia present--low hemoglobin									
Taking iron or transfusions (n = 17)	Great	1	6	All	0	0	20	1	6
	Some	0	0	Most	1	6	0	16	94
	Little	4	24	Some	0	0			
	None	12	71	Little	0	0			
				None	16	94			
Taking vitamins or diet (n = 5)	Great	0	0	All	0	0	20	1	20
	Some	1	20	Most	2	40	0	4	80
	Little	1	20	Some	0	0			
	None	3	60	Little	1	20			
				None	2	40			
No current treatment (n = 22)	Great	1	5	All	0	0	2	1	5
	Some	0	0	Most	0	0	0	21	95
	Little	5	23	Some	0	0			
	None	16	73	Little	2	9			
				None	20	91			
Anemia not present--normal hemoglobin									
Taking iron or transfusions (n = 98)	Great	2	2	All	0	0	2	1	1
	Some	8	8	Most	0	0	1	1	1
	Little	27	28	Some	7	7	0	96	98
	None	61	62	Little	7	7			
				None	84	86			
Taking vitamins or diet (n = 40)	Great	1	3	All	0	0	0	40	100
	Some	1	3	Most	0	0			
	Little	5	13	Some	0	0			
	None	33	83	Little	2	5			
				None	38	95			

Anemia Status	Worry			Activity Restriction			Days in Bed		
	Level of Impact	No.	Percent	Level of Impact	No.	Percent	No. of Days	No.	Percent
No current treatment (n = 302)	Great	2	1	All	0	0	4	2	1
	Some	3	1	Most	1	(a)	0	299	99
	Little	18	6	Some	0	0			
	None	278	92	Little	11	4			
				None	288	95			
Not screened for anemia									
Taking iron or transfusions (n = 96)	Great	4	4	All	1	1	10	1	1
	Some	13	14	Most	2	2	0	94	98
	Little	22	23	Some	5	5			
	None	57	59	Little	7	7			
				None	81	84			
Taking vitamins or diet (n = 36)	Great	0	0	All	0	0	0	36	100
	Some	1	3	Most	0	0			
	Little	3	8	Some	2	6			
	None	32	89	Little	1	3			
				None	33	92			
No current treatment (n = 229)	Great	1	(a)	All	0	0	1	2	1
	Some	1	(a)	Most	0	0	0	227	99
	Little	18	8	Some	0	0			
	None	209	91	Little	10	4			
				None	219	96			
Total (n = 845)	Great	12	1	All	1	(a)	20	2	(a)
	Some	28	3	Most	6	1	10	1	(a)
	Little	103	12	Some	14	2	4	2	(a)
	None	701	83	Little	41	5	2	2	(a)
				None	781	92	1	3	(a)
							0	833	99

[a]Less than 0.5 percent.

Table B.2

Distribution of Responses to Disease Impact Questions, by Anemia Status: Enrollees Completing Form B[a] of the MHQ

Anemia Status	Worry			Activity Restriction			Days in Bed		
	Level of Impact	No.	Percent	Level of Impact	No.	Percent	No. of Days	No.	Percent
Low hemoglobin (n = 143)	Great	2	1	All	0	0	20	2	1
	Some	1	1	Most	3	2	2	1	1
	Little	10	7	Some	0	0	0	140	98
	None	130	91	Little	3	2			
				None	137	96			
Normal hemoglobin (n = 3124)	Great	5	(b)	All	0	0	4	2	(b)
	Some	12	(b)	Most	1	(b)	2	1	(b)
	Little	50	2	Some	7	(b)	1	1	(b)
	None	3056	98	Little	20	1	0	3119	100
				None	3094	99			
Not screened (n = 2083)	Great	5	(b)	All	1	(b)	10	1	(b)
	Some	15	1	Most	2	(b)	1	2	(b)
	Little	43	2	Some	7	(b)	0	2079	100
	None	2020	97	Little	18	1			
				None	2055	99			
Total (n = 5350)	Great	12	(b)	All	1	(b)	20	2	(b)
	Some	28	1	Most	6	(b)	10	1	(b)
	Little	103	2	Some	14	(b)	4	2	(b)
	None	5206	97	Little	41	1	2	2	(b)
				None	5286	99	1	3	(b)
							0	5338	100

[a]Among all those who completed the Medical History Questionnaire, regardless of whether they answered the questions about disease impact of anemia; those who did not complete the battery were scored as "none."

[b]Less than 0.5 percent.

APPENDIX C

ANEMIA QUALITY OF CARE CRITERIA

All criteria listed below, unless otherwise specified, refer only to enrollees who have anemia according to the HIS definition (see Chapter 5). Rarely, alternative criteria will also be tested to see if the insurance plan effects differ for slight variations in the threshold value of the criterion. "He" is used in the criteria to refer to both men and women. Numerical diagnostic codes are from the Hospital-International Classification of Diseases (HICDA-II), adapted for use in the United States (2d ed., 1973).

PATIENT OUTCOMES

1. If the enrollee had anemia at the time of the enrollment screening examination, then (a) the anemia is less severe at the exit screening examination; or (b) [alternative to (a)] the anemia is no longer present at the exit screening examination.

2. If the enrollee has had at least two visits to a physician during the HIS for a primary diagnosis of anemia of any type, then he reports that he has had anemia on the exit Medical History Questionnaire (MHQ).

3. If the enrollee has had two or more visits to a physician at least 6 months prior to exit from the HIS for a diagnosis of a treatable form of anemia (iron deficiency anemia, 280-280.9; other deficiency anemia, 281.0-281.9; acute hemorrhagic anemia, 285.1; unspecified anemia, 285.9), then the anemia is no longer present at the exit screening examination.

4. If the enrollee was treated with iron at least 3 months prior to exit from the HIS, then he does not have anemia at the exit screening examination.

5. If the enrollee was treated with vitamin B-12 or folate at least 3 months prior to exit from the HIS, then he does not have anemia at the exit screening examination.

6. If the enrollee has iron deficiency anemia at the exit screening examination, then, on the exit MHQ, he reports (a) "none at all" or "a little" worry about anemia; (b) restriction of activity "none of the time"; and (c) "zero" days in bed attributed to anemia.

7. If the enrollee does not have anemia at the exit screening examination but nevertheless reports on the exit MHQ that he has anemia, then he reports no worry, no activity restriction, and no days in bed attributed to anemia on the exit MHQ.

8. If an enrollee has iron deficiency anemia at the exit screening examination, then he reports on the exit MHQ that he (a) has anemia; (b) is taking iron; and (c) has seen a physician about anemia within the past 6 months.

9. If an enrollee has macrocytic anemia at the exit screening examination, then he reports on the exit MHQ that he (a) has anemia and (b) has seen a physician about anemia within the past 6 months.

PROCESS

The following criteria, unless otherwise specified, do not apply to pregnant women.

Anemia in General

1. If the enrollee had anemia at the time of the enrollment screening examination, but reported on the enrollment MHQ that he did not have anemia, then there is followup for the anemia within 3 months after the enrollment screening examination:

(a) A hematocrit, hemoglobin, or complete blood count (CBC) is performed.
(b) [Alternative to (a)] a diagnosis of anemia of any type (280-285.9) appears on at least one claim form.
(c) [Alternative to (a)] the enrollee writes "anemia" (or a similar term) as the reason for a visit to a physician on at least one claim form.

2. If the enrollee has had two or more visits to a physician during the HIS for a primary diagnosis of anemia, then on at least one of these visits the enrollee has written "anemia" (or a similar term) as the reason for the visit.

3. If the enrollee was diagnosed for the first time during the HIS as having anemia of any type (280-285.9), then the following tests were performed:

(a) A CBC within 1 month before or after the first appearance of the diagnosis (on the claim form).

(b) A reticulocyte count within 1 month before or after the first appearance of the diagnosis.
(c) A followup hematocrit, hemoglobin, or CBC within 3 months after the first appearance of the diagnosis.

4. If the enrollee has received transfusions of any kind of blood constituents while an outpatient and has not been hospitalized for anemia in the preceding 3 months, then he does not have a diagnosis of iron deficiency anemia (280-280.9), other deficiency anemia (281-281.9), or unspecified anemia (285.9).

5. If the enrollee has received steroid therapy for anemia, then he does not have a diagnosis of iron deficiency anemia (280-280.9), other deficiency anemia (281-281.9), hereditary hemolytic anemia (282-282.9), or unspecified anemia (285.9).

6. If the enrollee has had a diagnosis of anemia of any type (280-285.9), then he has not taken any of the following prescribed drugs without also taking folate since the diagnosis was made: phenytoin, phenobarbital, primidone, methotrexate, or other antineoplastic agents.

7. The enrollee has not received any unknown injections (drug name not specified) for anemia.

Iron Deficiency Anemia

8. If male enrollees of any age or female enrollees aged 50 years or older were diagnosed for the first time during the HIS as having iron deficiency anemia (280-280.9) or unspecified anemia (285.9), then the following tests were performed within 3 months after the diagnosis:

(a) Stool for occult blood (e.g., guaiac or Hemoccult).
(b) Serum iron and TIBC, or serum ferritin.
(c) [Alternative to (b)] serum iron.

9. If the enrollee was diagnosed for the first time during the HIS as having iron deficiency anemia (280-280.9), then the enrollee received the following:

(a) At least 3 months of iron therapy.
(b) At least one reticulocyte count within 21 days after therapy began.
(c) At least one hematocrit, hemoglobin, or CBC within 1 month after therapy began.
(d) [Alternative to (c)] at least two hematocrits, hemoglobins, or CBCs within 3 months after therapy began.

10. If the enrollee has received iron injections, then

(a) He has a diagnosis of iron deficiency anemia (280-280.9) on at least one claim form.
(b) He has already received at least a 1-month trial of oral iron.
(c) He has had at least two checks of hematocrit, hemoglobin, or CBC and at least one check of reticulocyte count before the first injection.
(d) [Alternative to (c)] he has had at least one check of hematocrit, hemoglobin, or CBC and at least one check of reticulocyte count before the first injection.
(e) He has had a followup hematocrit, hemoglobin, or CBC within 3 months after the first injection.
(f) The injections extend over a maximum period of 6 weeks.

Exclusion: If the enrollee has a diagnosis of disease of the esophagus, stomach, duodenum (530-537.9), or intestine (560-569.9), or has had an operation on the esophagus, stomach, or intestine (45-46.9), then criteria (b), (c), and (d) do not apply.

11. If the enrollee has received prescribed oral iron therapy, then

(a) He has a diagnosis of iron deficiency anemia (280-280.9) on at least one claim form.
(b) He has had at least one visit to a physician for anemia every 6 months while taking iron.
(c) He has had at least one check of hematocrit, hemoglobin, or CBC every 6 months while taking iron.

Macrocytic Anemia

12. If the enrollee was diagnosed for the first time during the HIS as having megaloblastic anemia, pernicious anemia, other vitamin B-12 deficiency anemia, or folate deficiency anemia (281-281.9), then the following tests were performed within 3 months after the diagnosis:

(a) Serum B-12 and serum folate.
(b) [Alternative to (a)] serum B-12.

13. If the enrollee was diagnosed for the first time during the HIS as having pernicious anemia (281.0) or other vitamin B-12 deficiency anemia (281.1), then

(a) He received vitamin B-12 therapy after the diagnosis was made.

(b) He received a check of hematocrit, hemoglobin, or CBC within 3 months after the start of vitamin B-12 therapy.

14. If the enrollee was diagnosed for the first time during the HIS as having folate deficiency anemia (281.2), then

(a) He received folate therapy after the diagnosis was made.
(b) He received a check of hematocrit, hemoglobin, or CBC within 3 months after the start of folate therapy.

15. If the enrollee has received vitamin B-12 injections, then

(a) He has a diagnosis of pernicious anemia (281.0) or other vitamin B-12 deficiency anemia (281.1) on at least one claim form.
(b) He has had at least one check of hematocrit, hemoglobin, CBC, or serum B-12 every 6 months while receiving vitamin B-12 injections.

16. If the enrollee has received prescribed folate therapy, then

(a) He has a diagnosis of folate deficiency anemia (281.2) on at least one claim form.
(b) He has had at least one visit to a physician for anemia every 6 months while taking folate.
(c) He has had at least one check of hematocrit, hemoglobin, CBC, or serum folate every 6 months while taking folate.

Anemia During Pregnancy

17. If the enrollee has a diagnosis of anemia during pregnancy, then

(a) She receives both folate and iron therapy throughout the pregnancy after the diagnosis has been made.
(b) She has had at least one check of hematocrit, hemoglobin, or CBC after the pregnancy.

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