Assessment of the Prevalence and Impact of Anemia on Women Hospitalized for Gynecologic Conditions Associated With Heavy Uterine Bleeding

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OBJECTIVE: Women with heavy uterine bleeding often are untreated or inadequately treated for anemia. This study was conducted to estimate the prevalence and impact of anemia in women hospitalized for gynecologic conditions associated with heavy uterine bleeding.

STUDY DESIGN: The largest all-payer inpatient care database, the Healthcare Cost and Utilization Project's 2003 Nationwide Inpatient Sample, was queried using International Classification of Diseases, Ninth Revision, Clinical Modification *(ICD-9-CM) codes to identify and group women with gynecologic diagnoses associated with heavy uterine bleeding into 2 categories: those* with *or* without *anemia. Groups were evaluated for demographic characteristics, medical resource utilization and hospitalization costs using descriptive statistics.*

A disproportionate number of women hospitalized for gynecologic conditions associated with heavy uterine bleeding are anemic, require emergency department services and receive blood transfusions.

RESULTS: More than 25% of the estimated 300,589 women in the study had a diagnosis of anemia. Compared to patients without *a diagnosis of anemia, those* with *an anemia diagnosis were more likely to have a blood transfusion (24% vs. 0.7%, $p < 0.0001$), an emergency department admission (26.8% vs. 3.2%, $p < 0.0001$) and higher hospitalization costs ($5,631 vs. $5,101, $p < 0.0001$).*

CONCLUSIONS: Anemia and blood transfusions are common in women hospitalized for gynecologic conditions associated with heavy uterine bleeding. Greater patient and provider awareness of the prevalence and burden associated with anemia may increase opportunities to reduce blood transfusions and improve general health status and quality of life in this patient population. (J Reprod Med 2008;53:323–330)

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An estimated 10–15% of nonpregnant women experience heavy uterine bleeding (HUB) at some point in their lives.[1] HUB is associated with many debilitating sequelae, including iron deficiency, anemia, fatigue, discomfort, depression and disturbances in sexual functioning and social and occupational activities.[2-4] The most common diagnosis in women with HUB is dysfunctional uterine bleeding (DUB), a diagnosis of exclusion in which the etiology of bleeding is not related to underlying pelvic pathology, medication intake, iatrogenic causes, systemic disease or pregnancy.[5,6] Other known causes of HUB include local pelvic pathologic conditions and structural lesions such as uterine polyps, leiomyomas, endometrial hyperplasia, adenomyosis, infection and carcinoma, as well as systemic diseases, including coagulation disorders such as von Willebrand disease and thrombocytopenia.[1,2,4,5,7]

Current treatment strategies for HUB are aimed at reducing blood loss, correcting iron deficiency and anemia, improving quality of life and relieving patient anxiety.

In healthy, ovulating women, an average of 35–40 mL of blood is lost during a normal menstrual period.[2] Although a monthly menstrual blood loss of 80 mL is considered the upper limit of normal, women who routinely consume a typical Western diet (without iron supplementation) are susceptible to depletion of iron stores with menstrual blood loss volumes as low as 50 mL/month.[1,6,8] Of the more than 73 million women between the ages of 15 and 49 in the United States, 6.6 million to 10.3 million have HUB (menstrual blood loss >80 mL/cycle) and thus are at risk for iron depletion.[2,9,10] Anemia develops in as many as 20% (1.3 million to 2.1 million) of women with HUB.[11]

Current treatment strategies for HUB are aimed at reducing blood loss, correcting iron deficiency and anemia, improving quality of life (QOL) and relieving patient anxiety.[7,9] Although oral iron supplementation is recommended for preventing and treating iron depletion and iron deficiency anemia (IDA) in this patient population, currently available oral iron therapies have demonstrated limited effectiveness in correcting severe anemia due to poor compliance, suboptimal intestinal absorption and bioavailability.[12] As a result of inadequately treated or untreated anemia, many women with HUB remain at risk for experiencing functional and cognitive impairments, in addition to the deleterious physiological effects associated with iron deficiency and anemia.[4,13]

A better understanding of medical resource utilization, economic costs and burden of illness associated with anemia and its complications in women with HUB is essential for increasing provider and patient awareness, optimizing anemia management and improving health care outcomes in this patient population. A search of the National Library of Medicine's PubMed database found virtually no literature published on the clinical and economic implications of anemia in women hospitalized for gynecologic conditions associated with HUB. As an initial step to addressing this existing information gap, we used *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) diagnosis codes to query the largest all-payer, publicly available inpatient database to estimate the prevalence and impact of anemia in women hospitalized for gynecologic conditions associated with HUB, for the year 2003.

Materials and Methods

We performed a retrospective analysis of the Healthcare Cost and Utilization Project's 2003 Nationwide Inpatient Sample (HCUP-NIS) database, an all-payer, nationally representative survey of inpatient care in the United States.[14] Policymakers and researchers frequently use HCUP-NIS to evaluate, from a national perspective, health care utilization, charges, quality and outcomes. HCUP-NIS data capture information on inpatient stays from approximately 1,000 U.S. community hospitals, including nonfederal, short-term, general and specialty hospitals such as obstetrics and gynecology and pediatric facilities. The final sample for 2003 HCUP-NIS contains data for 7,977,728 patient discharges.

The study sample was selected using ICD-9-CM diagnosis codes[15] for the most common gynecologic conditions associated with HUB, including uterine leiomyoma (218), metrorrhagia (626.6), excessive or frequent menstruation (626.2) and premenopausal menorrhagia (627.0). HCUP-NIS does not contain

laboratory data (e.g., hemoglobin or iron values); therefore, we identified cases with anemia using ICD-9-CM diagnosis codes for IDA (280.0, 280.1 or 280.9). ICD-9-CM procedure codes were used to identify blood transfusion procedures, including perioperative autologous transfusion of whole blood or blood components (99.00), other transfusion of whole blood (99.03) and transfusion of packed cells (99.04).

All women, independent of age, were included in the study. We grouped women with a primary gynecologic diagnosis associated with HUB and a secondary diagnosis of anemia, as well as those with a primary diagnosis of anemia and a secondary gynecologic diagnosis associated with HUB, in a cohort labeled "heavy uterine bleeding *with* anemia." In a second cohort labeled "heavy uterine bleeding *without* anemia" we included only patients with a primary gynecologic diagnosis associated with HUB and no diagnosis of anemia.

To limit the impact of nongynecologic, anemia-causing complications and comorbid conditions on our analysis, we excluded records with the following ICD-9-CM diagnosis or procedure codes: maternal anemia (648.21, 648.22, 648.24); acute renal failure (669.92); pulmonary collapse (518.0); hematuria (599.7); hemoperitoneum (568.81); hemorrhage-complicating procedure (998.11); accidental puncture or laceration (998.2); hematoma-complicating procedure (998.12); continuous mechanical ventilation (96.71) and hemodialysis (39.95). Also excluded from the study were discharges with zero days recorded for length of stay (LOS). After all inclusion and exclusion criteria were applied, the study sample consisted of a total of 300,589 women, 222,600 *without* an anemia diagnosis and 77,989 *with* an anemia diagnosis.

The impact of race and age on the prevalence of anemia in women hospitalized for gynecologic conditions associated with HUB was assessed in this study. We also evaluated admission source, blood transfusions, average LOS, charges and costs to estimate inpatient care–related medical resource utilization and economic burden associated with anemia in this patient population.

Age was calculated from the birth date and the admission date. Race categories included white, black (African American), Hispanic, other or unknown. Not all participating states supply data on race; therefore, cases lacking race data were classified as "unknown." Sources of admission were categorized as emergency department, transfers from a hospital, "routine" (referrals from physician offices and clinics) and "other." LOS was calculated by subtracting the admission date from the discharge date.

The total charge variable contains edited total charges (e.g., values are rounded to the nearest dollar and zero charges are set to missing) and reflects the amount a hospital billed for the entire hospital stay. However, hospital charges typically do not include professional (physician) fees. Total cost was calculated by multiplying the total charge by the hospital-specific cost-to-charge ratio (CCR). For each facility, a hospital-wide CCR is used due to the lack of availability of detailed (department-level) costs and charges across all HCUP states. The hospital-specific CCR is based on cost and charge information contained in annual hospital-specific accounting reports available from the Centers for Medicare and Medicaid Services (CMS). In cases where a hospital-specific CCR was unavailable, a weighted group average CCR was used to estimate the cost of inpatient care for a discharge.

Descriptive statistics (mean, median and range) were calculated for patient demographic characteristics, medical resource utilization components, total charges and total costs. All analyses accounted for the HCUP-NIS sampling design as described in the relevant HCUP publications.[14,16] Sample weights were applied to generate national estimates from the observed counts using a standard published algorithm to account for the cluster sampling methodology used to collect HCUP-NIS data.[14] SAS (Cary, North Carolina) survey procedure methods were used to perform statistical tests, including t tests for continuous variables and χ^2 tests for categorical variables, to assess the difference in means and proportions between women *with* an anemia diagnosis vs. those *without* an anemia diagnosis. The t test was used for total charges, total costs, age and LOS. The χ^2 test was used for payer mix, age group, race, median household income level and transfusion of packed cells.

This study, which involved an analysis of HCUP-NIS, a publicly available data set, was exempt from institutional review board approval per federal exemption category #4 (45 CFR 46.101(b)(4)).

Results

Study Sample Size and Clinical Characteristics

Based on our analysis of HCUP-NIS data, an estimated 300,589 discharges recorded an ICD-9-CM diagnosis code for a gynecologic condition associat-

ed with HUB. Nearly 26% (77,989) of these patients also had an ICD-9-CM diagnosis code for anemia (Table I). The two most common primary disorders in women *without* a diagnosis of anemia were uterine leiomyomas and menstrual-related bleeding, which accounted for 76.7% and 23.2% of cases, respectively. In the cohort *with* anemia, uterine leiomyomas (42.4%), menstrual-related bleeding (19.5%) and anemia (10.4%) were the most commonly reported primary disorders. "Leiomyomas of uterus, unspecified" (218.9), "intramural leiomyoma" (218.1), "submucous leiomyoma of uterus" (218.0) and "subserous leiomyoma" (218.2) accounted for 38.8%, 34.8%, 14.1% and 12.3% of the leiomyomas in the cohort *without* anemia and 36.8%, 33.0%, 20.4% and 9.8% of the leiomyomas in the cohort *with* anemia, respectively. In both groups more than 90% of the patients with menstrual-related bleeding had a diagnosis of "excessive or frequent menstruation" (626.2). IDA secondary to blood loss, chronic (218.0) accounted for nearly 60% of all women with an anemia-related primary diagnosis.

More than 85% of women *without* anemia and 59% of those *with* anemia reported a hysterectomy procedure (Table II). "Total abdominal hysterectomy" (68.4), "other and unspecified vaginal hysterectomy" (68.59), "laparoscopically assisted vaginal hysterectomy" (68.51) and "subtotal abdominal hysterectomy" (68.3) accounted for 68.2%, 15.4%, 10.3% and 6.1% of hysterectomy procedures performed in patients *without* anemia; and 72.6%, 13.5%, 8.5% and 6.4% of hysterectomy procedures performed in those *with* anemia, respectively. Nearly 25% of the women *with* anemia reported transfusion of packed cells (99.04), which was the third most common procedure in this cohort after hysterectomy and salpingo-oophorectomy.

Demographic and Socioeconomic Characteristics

Race and age were found to influence the prevalence of anemia in our study sample (Table III). African American and Hispanic women accounted for 37.5% of patients *with* anemia vs. 24% of patients *without* an anemia diagnosis ($p < 0.0001$). Women between the childbearing ages of 25 and 50 years represented 83% of the study population. Adolescent and young women between the ages of 12 and 24 years were 7 times more likely to have anemia (2.9%) than no anemia diagnosis (0.4%) ($p < 0.0001$).

Medical Resource Utilization

As shown in Figure 1, the emergency department was the source of admission for nearly 27% of women *with* anemia, but only 3.2% of women *without* an anemia diagnosis ($p < 0.0001$). Data on transfusion of packed cells are presented in Figure 2. Twenty-four percent of patients *with* anemia received a transfusion of packed cells during the course of hospitalization compared with only 0.7% of patients *without* a diagnosis of anemia ($p < 0.0001$). The average LOS for women *with* anemia was 25% longer than for women *without* a diagnosis of anemia: 3.0 days (95% CI 2.93–3.14) vs. 2.4 days (95% CI 2.33–2.43, $p < 0.0001$).

Economic Cost

On average, patients *with* anemia incurred total hospitalization charges that were 13.3% higher ($15,315 [95% CI $14,198.66–$16,431.71] vs. $13,523 [95% CI $12,788.81–$14,257.77], $p < 0.0001$) than patients *without* an anemia diagnosis. After the costs of services were derived from charges, the average

Table I *Top ICD-9-CM Diagnosis Codes in Study Sample*

ICD-9-CM diagnosis code	Diagnosis description	% *With* anemia diagnosis (N = 77,989)	% *Without* anemia diagnosis (N = 222,600)
626.2	Excessive menstruation	17.7	22.0
218.9	Uterine leiomyoma, NOS	15.6	29.7
218.1	Intramural leiomyoma	14.0	26.7
218.0	Submucous leiomyoma	8.6	10.8
218.2	Subserous leiomyoma	4.1	9.4
280.0	Chronic blood loss, anemia	6.1	0
617.0	Endometriosis of uterus	3.2	0.5
280.9	Unspecified iron deficiency anemia	2.6	0
626.8	Other disorder of menstruation and other abnormal bleeding from female genital tract	1.8	<0.5
285.1	Acute posthemorrhagic anemia	1.7	0

NOS = not otherwise specified.

Table II *Top ICD-9-CM Procedure Codes in Study Sample*

ICD-9-CM procedure code	Procedure description	% *With* anemia diagnosis (N = 77,989)	% *Without* anemia diagnosis (N = 222,600)
68.4	Total abdominal hysterectomy	42.3	58.2
99.04	Transfusion of packed cells	24.5	0.7
65.61	Other removal of both ovaries and tubes at same operative episode	24.4	36.1
54.59	Other lysis of peritoneal adhesions	9.8	12.0
68.59	Other and unspecified vaginal hysterectomy	8.0	13.1
68.29	Other excision or destruction of lesion of uterus	5.4	10.4
69.09	Other dilation and curettage of uterus	5.2	2.2
68.51	Laparoscopically assisted vaginal hysterectomy	5.0	8.8
65.49	Other unilateral salpingo-oophorectomy	4.9	6.7
68.3	Subtotal abdominal hysterectomy	3.8	5.2

cost of hospitalization for patients *with* anemia was $5,631 (95% CI $5,393.01–$5,869.91) compared to $5,101 (95% CI $4,918.92–$5,282.21, $p < 0.0001$) for patients *without* an anemia diagnosis.

Discussion

Untreated or inadequately treated anemia continues to adversely affect the functional status and QOL of a disproportionate number of women, including those with HUB.[17] Several recent reports by the Quality Subcommittee of the Committee on Practice for the American Society of Hematology have acknowledged that anemia poses a major public health problem and that increased patient and provider awareness is central to improving health outcomes in this patient popualtion.[1,18] Nationally

Table III *Study Sample Demographic and Socioeconomic Characteristics*

Patient characteristic	Heavy uterine bleeding *without* anemia diagnosis	Heavy uterine bleeding *with* anemia diagnosis	p Value[a]
Sample size	222,600	77,989	
Age (yr)			<0.0001
Mean (95% CI)	43.37 (43.18–43.56)	42.44 (42.16–42.72)	
Median (range)	43.00 (13.00–93.99)	43.00 (12.00–89.00)	
Age (yr), n (%)			<0.0001
12–24	847 (0.4)	2,256 (2.0)	
25–34	23,737 (10.7)	8,258 (10.6)	
35–44	102,807 (46.2)	35,658 (45.7)	
45–49	58,455 (26.3)	21,085 (27.0)	
≥50	36,465 (16.4)	10,732 (13.8)	
Race, n (%)			<0.001
White	96,628 (43.4)	24,041 (30.8)	
Black	36,630 (16.5)	21,651 (27.8)	
Hispanic	16,765 (7.5)	7,597 (9.7)	
Other	8,939 (4.0)	3,400 (4.4)	
Unknown	63,638 (28.6)	21,300 (27.3)	
Median household income, n (%)			≤0.001
$1-35,999	47,316 (21.3)	22,847 (29.3)	
$36,000-44,999	54,666 (24.6)	21,119 (27.1)	
$45,000-59,999	58,740 (26.4)	17,726 (22.7)	
≥$60,000	57,702 (25.9)	14,612 (18.7)	
Payer mix, n (%)			<0.001
Medicare	6,102 (2.7)	2,790 (3.6)	
Medicaid	16,263 (7.3)	11,068 (14.2)	
Private insurance	187,868 (84.4)	54,719 (70.2)	
Self-pay/no charge/other	11,858 (5.3)	9,275 (11.9)	

[a] *t* Test used for age; χ^2 test used for payer mix, age group, race and median household income.

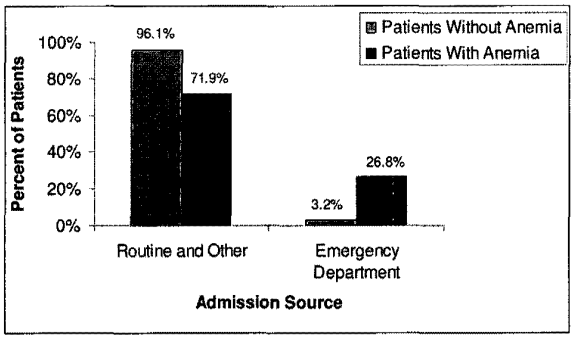

Figure 1 Source of hospital admission for patients with heavy uterine bleeding based on anemia status. Patients with a diagnosis of anemia were 8 times more likely to be admitted through the emergency department than patients without a diagnosis of anemia.

representative data on the prevalence of anemia and its impact on women hospitalized for gynecologic conditions associated with HUB are currently lacking. In this study, we set out to address this existing data gap by conducting a descriptive analysis of 2003 HCUP-NIS. Select ICD-9-CM diagnosis and procedure codes were used to estimate prevalence and to identify demographic characteristics, medical resource utilization and hospitalization costs associated with anemia in this patient population.

We found anemia to be prevalent in more than 25% of the women in our study population, particularly among adolescents as well as Hispanic and African American women. Although this prevalence estimate is based on ICD-9-CM diagnosis codes for anemia, rather than actual hemoglobin values, our estimate is consistent with previously reported data on the prevalence of anemia in women with leiomyomas and abnormal uterine bleeding.[3,11] More important, our estimate is likely to be conservative given the demographic composition and inpatient status of our study population. Twenty-seven percent of our study population was composed of Hispanic or African American women; national survey data suggest that the prevalence of iron deficiency is twice as high or greater in minority women compared with Caucasian women.[19] In contrast to our study, the Maine Women's Health Study, a prospective cohort study of 418 women ages 25 to 50 undergoing hysterectomy for nonmalignant conditions, involved a study population that was 98% Caucasian. In the Maine study, 21% of patients with leiomyomas and 4% of patients with abnormal uterine bleeding were found to have anemia, defined as a hemoglobin level ≤10 g/dL or a hematocrit value ≤32%, within the year before study entry.[3]

In our study, women in the anemia cohort were 8 times more likely to be admitted from the emergency department than women *without* an anemia diagnosis. Although we were unable to directly determine poverty status using HCUP-NIS data, women *with* anemia consistently had a lower median household income than women *without* an anemia diagnosis. Data suggest that impoverished women with HUB are particularly susceptible to iron deficiency and anemia because they are less likely to receive routine gynecologic examinations[20] and more likely to delay seeking care for gynecologic symptoms. Unfortunately, these women are at significant risk for developing advanced disease, symptomatic anemia and other complications that frequently require prompt assessment and intervention in the emergency department.

Blood transfusion therapy represents an effective intervention for rapidly correcting profound or symptomatic anemia.[17] However, blood transfusion is associated with serious adverse events such as transfusion reactions and the transmission of infectious agents.[12,17] In our study population, nearly 25% of patients *with* anemia received a transfusion of packed cells compared with <1% of patients *without* an anemia diagnosis. Although data regarding laboratory and/or clinical triggers for blood transfusion are not available in HCUP-NIS, it is highly unlikely that transfusions were administered to correct acute anemia in our study sample.

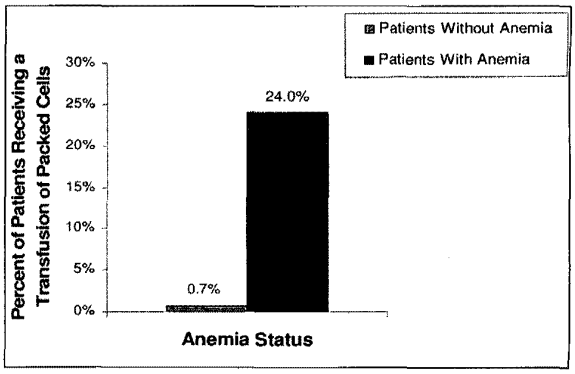

Figure 2 Percent of women with a diagnosis suggestive of heavy uterine bleeding receiving a transfusion of packed cells. During an inpatient stay, nearly 1 in 4 patients with a diagnosis of anemia received a transfusion of packed red cells.

First, data suggest that women with gynecologic bleeding are often anemic before surgery.[17] Second, we excluded patients with acute anemia-inducing complications and comorbid conditions from the study population. Finally, we did not identify a correlation between an anemia diagnosis or transfusion procedure and frequency or type of surgical procedure (e.g., hysterectomy).

Surgical blood loss has the potential to exacerbate preexisting anemia and influence the need for blood transfusion. Eighty-five percent of women *without* anemia reported a hysterectomy procedure compared with 59% of women *with* anemia. A clinical rationale that may account for this finding is that hysterectomy is typically performed as an elective procedure and, therefore, anemia is corrected preoperatively to optimize surgical outcomes. A higher number of hysterectomy procedures, in the cohort *without* anemia, were expected given that nearly 77% of women in this cohort had leiomyomas compared to only 42% of women in the anemia cohort. Also, adolescent and young women with anemia who have menstrual-related bleeding are generally not considered candidates for hysterectomy.

In a recent study of elderly patients with chronic kidney disease, hospitalization-related costs accounted for the largest driver of cost differences between anemia and non-anemia periods.[21] In our study, the average cost per hospitalization was higher in women *with* anemia than in women *without* an anemia diagnosis. Increased hospitalization costs associated *with* anemia is likely attributable to greater medical resource utilization and longer average LOS in this patient population. Although hospitalization-related costs can be significant, since anemia may persist or worsen in untreated or inadequately treated patients who continue to have some degree of uterine bleeding, it is important to recognize that these women also may incur substantial post–hospital discharge direct and indirect costs.

There are limitations to conducting this type of study, including the use of ICD-9-CM diagnosis codes to identify patients hospitalized for disorders such as anemia or gynecologic conditions associated with HUB. ICD-9-CM diagnosis codes may not capture all relevant cases, resulting in an underestimation of the actual prevalence of disease, which can affect other important outcome measures, such as admission source, LOS and blood transfusion procedures. Also, data are limited to information collected in HCUP-NIS, which is derived from discharge record abstractions; therefore, detailed and precise information is not available to validate the recording of diagnoses and comorbid conditions of interest. For example, in our study, we could not determine the severity of anemia or hemoglobin level at admission or at the time of transfusion.

The aim of this study was to perform a descriptive analysis of HCUP-NIS, the most reliable source of U.S. inpatient stay data, to raise provider awareness about the prevalence and impact of anemia in women hospitalized for gynecologic conditions associated with HUB. Our approach is consistent with the methodology and statistical analyses described in *HCUP Statistical Briefs*, which use simple descriptive statistical analyses to analyze prevalence, general characteristics and trends associated with hospitalization stays for a variety of specific conditions and topics.[22-25]

Our findings suggest that a disproportionate number of women hospitalized for gynecologic conditions associated with HUB are anemic, require emergency department services and receive blood transfusions. These findings warrant further investigation. Cross-sectional survey databases such as HCUP-NIS do not provide preadmission or post–hospital discharge data, thus making temporal or causal relationships difficult or nearly impossible to establish. In women with HUB who have low-grade chronic bleeding, anemia is likely to be present before hospitalization and persist after discharge if left untreated or inadequately treated.[17] Future studies in this patient population should assess preadmission and post–hospital discharge data using chart reviews, prospective studies or a longitudinal database. Also, it is important to identify admission and transfusion triggers in this patient population, including clinical status, hemoglobin values and iron indices (percent transferrin saturation and ferritin). Without this level of data, the cause and duration of anemia, reason for blood transfusion and post–hospital discharge medical resource utilization cannot be accurately determined.

Increased provider awareness and recognition of anemia in women with HUB along with more aggressive anemia management is likely to yield significant benefits at the individual patient level, including fewer hospitalizations, emergency department visits, blood transfusions and outpatient utilization of medical services. Most important, these steps can improve the general health and functional status of many women who experience

chronic blood loss and anemia due to HUB.

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