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BRIEF REPORT

TRANSFUSION

# Leading digit bias in hemoglobin thresholds for red cell transfusion

**Sheharyar Raza**[1,2] | **Malcolm Risk**[3] | **Christine Cserti-Gazdewich**[1,4]

[1]Division of Hematology, University of Toronto, Toronto, Canada

[2]Canadian Blood Services, Medical Affairs and Innovation, Canada

[3]Department of Biostatistics, University of Michigan, Ann Arbor, Michigan, USA

[4]Blood Transfusion Laboratory, University Health Network, Toronto, Canada

**Correspondence**
Christine Cserti-Gazdewich, Toronto General Hospital 3EC-306 200 Elizabeth Street, Toronto, ON M5G-2C4, Canada.
Email: christine.cserti@uhn.ca

**Funding information**
Department of Hematology, University of Toronto

## Abstract

**Background:** Leading digit bias is a heuristic whereby humans overemphasize the left-most digit when evaluating numbers (e.g., 9.99 vs. 10.00). The bias might affect the interpretation of hemoglobin results and influence red cell transfusion in hospitalized patients.

**Study Design and Methods:** Adults who received a red cell transfusion while registered at the University Health Network (Toronto, Canada) between January 1, 2016 and January 1, 2022 ($n = 6$ years) were included. The primary analysis excluded apheresis, red cell disorders, radiology suites, and operating rooms. The primary comparison was a regression discontinuity analysis of transfusion occurrence above and below the hemoglobin threshold of 79 g/L (local units). Additional analyses tested other leading digit and control thresholds (71, 81, and 91 g/L). Secondary analyses explored temporal covariates and clinical subgroups.

**Results:** A total of 211,872 red cell transfusions were identified over the study period (median pre-transfusion hemoglobin 76 g/L; interquartile range = 69–92 g/L), with 107,790 inpatient transfusions in the primary analysis. The 79 g/L threshold showed 815 fewer red cell units above the threshold (95% confidence interval [CI]: −1215 to −415). The 69 g/L threshold showed 2813 fewer transfused units (95% CI: −4407 to −1220), and 89 g/L showed 40 fewer units (95% CI: −408 to 328). The effect was accentuated during daytime, weekday, and May–June months, persisted in analyses including all transfusions, and was absent at control thresholds.

**Conclusion:** Leading digit bias might have a modest influence on the decision to transfuse red cells. The findings may inform practice guidelines and quasi-experimental study design in transfusion research.

**KEYWORDS**
leading digit bias, natural experiment, red cell transfusion, transfusion threshold

**Abbreviations:** CI, confidence interval; Hb, hemoglobin; IQR, interquartile range; PMH, Princess Margaret Cancer Center; RBC, red blood cells; SD, standard deviation; TGH, Toronto General Hospital; TWH, Toronto Western Hospital; UHN, University Health Network.

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## 1 | INTRODUCTION

Red cells are the most frequently transfused blood component, given to about one in seven hospitalized patients.[1–3] About a quarter of red cell transfusions are inappropriate when evaluated by guideline criteria.[4,5] Every transfusion originates from an individual physician's judgment and introduces the potential for errors in decision-making.[6]

Complex judgment under uncertainty, such as the decision to transfuse, may lead clinicians to use mental shortcuts as a substitute for the more complex task of synthesizing all available clinical information.[7] Prevailing guidelines recommend holistic patient assessment (complex task) and caution against overreliance on hemoglobin thresholds (mental shortcut).[8] Yet hemoglobin value is the strongest predictor of whether a patient will be transfused (second only to severe acute bleeding), indicating that clinicians inordinately rely on this test to guide transfusion.[9,10] However, the hemoglobin has a measurement error of 5 g/L and numeric evaluation can be prone to cognitive biases relating to the interpretation of numbers.[11]

Leading digit bias, also known as left-digit bias, is the tendency to place an unduly high weight on the first digit of numbers during evaluation (e.g., 9.999 feels unduly smaller than 10.000). The bias develops early in life, is relevant for multi-digit numbers, and is resistant to retraining.[12] Leading digit effects are employed in psychological pricing, sway college admissions, and affect stock markets.[13–15] Leading digit bias influences clinical judgment in diverse healthcare contexts, including organ transplantation, cardiovascular surgery, oncologic care, and cigarette consumption.[16–19]

We hypothesized that leading digit bias may affect the evaluation of pre-transfusion hemoglobin levels and trigger increased transfusions at clinically relevant leading digit thresholds. We tested our hypothesis by comparing the occurrence of transfusion above and below leading digit thresholds of pre-transfusion hemoglobin among hospitalized patients.

## 2 | METHODS

### 2.1 | Setting

University Health Network (UHN; Toronto, Ontario) is Canada's largest hospital network, with 1.2 million discrete adult patient visits and 40,000 red cell transfusions annually. UHN is comprised of three hospitals (Toronto General Hospital—TGH, Toronto Western Hospital—TWH, and Princess Margaret Cancer Center—PMH). Clinical services include emergency department (TGH and TWH), surgical services (TGH, TWH, and PMH), general medicine, critical care (TGH and TWH), cancer center (PMH), inherited red cell disorders (TGH), and transplant facilities (TGH). UHN guidelines suggest transfusion thresholds of less than 60 g/L for asymptomatic patients with iron deficiency, 70 g/L in low-risk patients, and 80 g/L in patients with acute coronary syndromes.[20] Blood products in Ontario are supplied by Canadian Blood Services, funded by the Ontario Health Insurance Plan, and administered through hospital transfusion services.

### 2.2 | Pre-transfusion hemoglobin

We identified all red cell transfusions at UHN from January 1, 2016 to December 31, 2021 (missing data detailed in Appendix S1) from an existing transfusion database containing data on ordering hospital site (TWH, TGH, and PMH), issue date, issue location (e.g., cardiology ward), clinical grouping (e.g., all cardiology units), and last available pre-transfusion hemoglobin in grams per liter. These data are extracted quarterly in automated reports from the laboratory information system (WellSky®), following pre-scripted retrievals of the most recent pre-transfusion hemoglobin value (within 24 h) from the electronic medical record (EPR Quadramed® via Mediware®; Appendix S1). We computed summary statistics (median and interquartile range [IQR]) for pre-transfusion hemoglobin. For some transfusions, the location was indeterminate (coded as "Other") and reflected either those orders made by telephone, or units dispensed from automated blood refrigerators. The extracted transfusion data did not contain information on post-transfusion increment, physician characteristics, admitting diagnosis, transfusion indication, massive hemorrhage, transfusion reactions, or hospital outcomes.

### 2.3 | Measured hemoglobin baseline

We identified all hemoglobin testing performed at UHN hospital sites over a 1-year period (January 1, 2020–January 1, 2021) to verify that the baseline distribution of hemoglobin values at our institution did not have leading digit anomalies. We plotted measured hemoglobin values by hospital, laboratory, and patient category (inpatient or outpatient) to identify discontinuities that might produce false positive results in leading digit analyses related to frequency of exposure (Appendix S1). We also performed regression discontinuity analyses to rigorously detect any leading digit effects in the distribution of hemoglobin results.[21]

## 2.4 | Leading digit effect

The primary outcome assessed the effect of the leading digit on the occurrence of red cell transfusion at hemoglobin 79 versus 80 g/L in a quadratic regression discontinuity design (regression bandwidth = ±5 g/L).[21–23] Although 69 g/L is the more common transfusion threshold in hospitalized patients, we chose 79 g/L as this threshold is only recommended in a small subset of hospitalized patients (those with active cardiac ischemia).[24] Hemoglobin 69 g/L might show threshold effects due to our transfusion guidelines rather than numeric bias, and 89 g/L might not provide sufficient sample size. A regression bandwidth of ±5 g/L was chosen as it approximates the error range for hemoglobin testing and excludes flanking thresholds.[25,26] Effect size is defined as the difference in a number of red cell units transfused associated with being above the threshold. Statistical inference on the threshold effect was conducted using linear regression controlling for local (i.e., within-bandwidth) quadratic trend with $p$ values determined using the $t$-test. Primary analysis included all transfusions given on inpatient clinical wards, and excluded transfusions given in operating rooms, apheresis, red cell disorders, and radiology, as these transfusions are performed in response to active hemorrhage or other specialized criteria not covered by general institutional guidelines. All excluded subgroups were later included in sensitivity analyses.

Additional analyses examined other leading digit pairs (69 and 89). Control thresholds were chosen based on Benford numbers (where a leading digit effect would not be expected), which are naturally occurring numeric patterns seen in some healthcare contexts (71, 81, and 91 g/L).[27] Covariate analyses explored the effect of time of day (day or night), July effect (May/June vs. July/August), and weekend effect (weekend or weekday).[28–30] Sensitivity analyses examined all patients and other regression bandwidths (±7 and ±9 g/L; Appendix S1). Analyses were performed using R (version 4.2.2), visualization with ggplot2, and analyses with dplyr package (version 1.1.3).

# 3 | RESULTS

## 3.1 | Pre-transfusion hemoglobin

A total of 211,872 red cell transfusions were identified over the study period, with 107,790 inpatient transfusions (50.9%) included in the primary analysis. The median pre-transfusion hemoglobin of the full dataset was 76 g/L (interquartile range [IQR] 69–92 g/L) and remained stable during the study period with substantial variability between clinical groups (Table 1). A majority of transfusions occurred during daytime hours (8:00 a.m. to 5:00 p.m.; $n = 146{,}766$, 69.3%). The three largest clinical subgroups were inpatient oncology ($n = 33{,}462$), red cell disorders ($n = 33{,}785$), and other ($n = 30{,}224$).

**TABLE 1** Summary of transfusions during the study period by hospital site, clinical grouping, and year.

| Category | Sample size | Pre-transfusion Hb g/L median (IQR) |
|---|---|---|
| Overall | 211,872 | 76 (69–92) |
| Site | | |
| PMH | 60,875 | 71 (68–76) |
| TGH | 138,666 | 83 (70–99) |
| TWH | 12,331 | 70 (65–82) |
| Clinical group | | |
| Apheresis | 22,304 | 103 (93–111) |
| Cardiology | 10,542 | 75 (69–82) |
| Critical care | 13,819 | 69 (65–74) |
| Dialysis | 981 | 68 (64–72) |
| Emergency | 3775 | 64 (57–71) |
| General medicine | 5125 | 67 (63–69) |
| Inpatient oncology | 33,462 | 69 (67–73) |
| Neurology | 1103 | 71 (66–80) |
| Operating room[a] | 21,641 | 89 (78–107) |
| Other | 30,224 | 71 (67–79) |
| Outpatients[a] | 26,091 | 75 (70–79) |
| Radiology[a] | 261 | 86 (73–100) |
| Red cell disorders[a] | 33,785 | 96 (88–104) |
| Surgery | 5005 | 70 (66–75) |
| Transplant | 3754 | 68 (65–71) |
| Year | | |
| 2016 | 32,900 | 77 (69–91) |
| 2017 | 32,385 | 76 (69–93) |
| 2018 | 35,015 | 75 (68–89) |
| 2019[b] | 11,618 | 75 (68–89) |
| 2020 | 54,307 | 76 (68–94) |
| 2021 | 45,647 | 76 (68–93) |

Abbreviation: IQR, interquartile range.
[a]Subgroups excluded from primary analysis.
[b]Data only available for the first and second quarters of 2019.

## 3.2 | Institutional hemoglobin testing

During the available testing period (January 1, 2020–January 1, 2021), a total of 462,276 hemoglobin

tests were performed with a median value of 110 g/L (IQR = 88–130 g/L; mean = 110 g/L, SD = 26.0). Median hemoglobin among inpatients was lower compared with outpatients (95 vs. 123 g/L) and highest among patients seen in the Emergency Department (129 g/L, IQR 113–142 g/L). Regression discontinuity analyses at hemoglobin results of 69, 79, and 89 g/L were not statistically significant (all $p > .05$; Appendix S1).

### 3.3 | Leading digit thresholds

The primary regression discontinuity analysis at 79 g/L threshold found that values above the threshold were associated with 815 fewer red cell units ($n = 19{,}335$; 95% confidence interval [CI]: −1215 to −415) than expected given the local quadratic trend, amounting to 27 additional monthly red cell transfusions below the threshold over the study period (Figure 1). Analyses at 69 g/L showed an effect

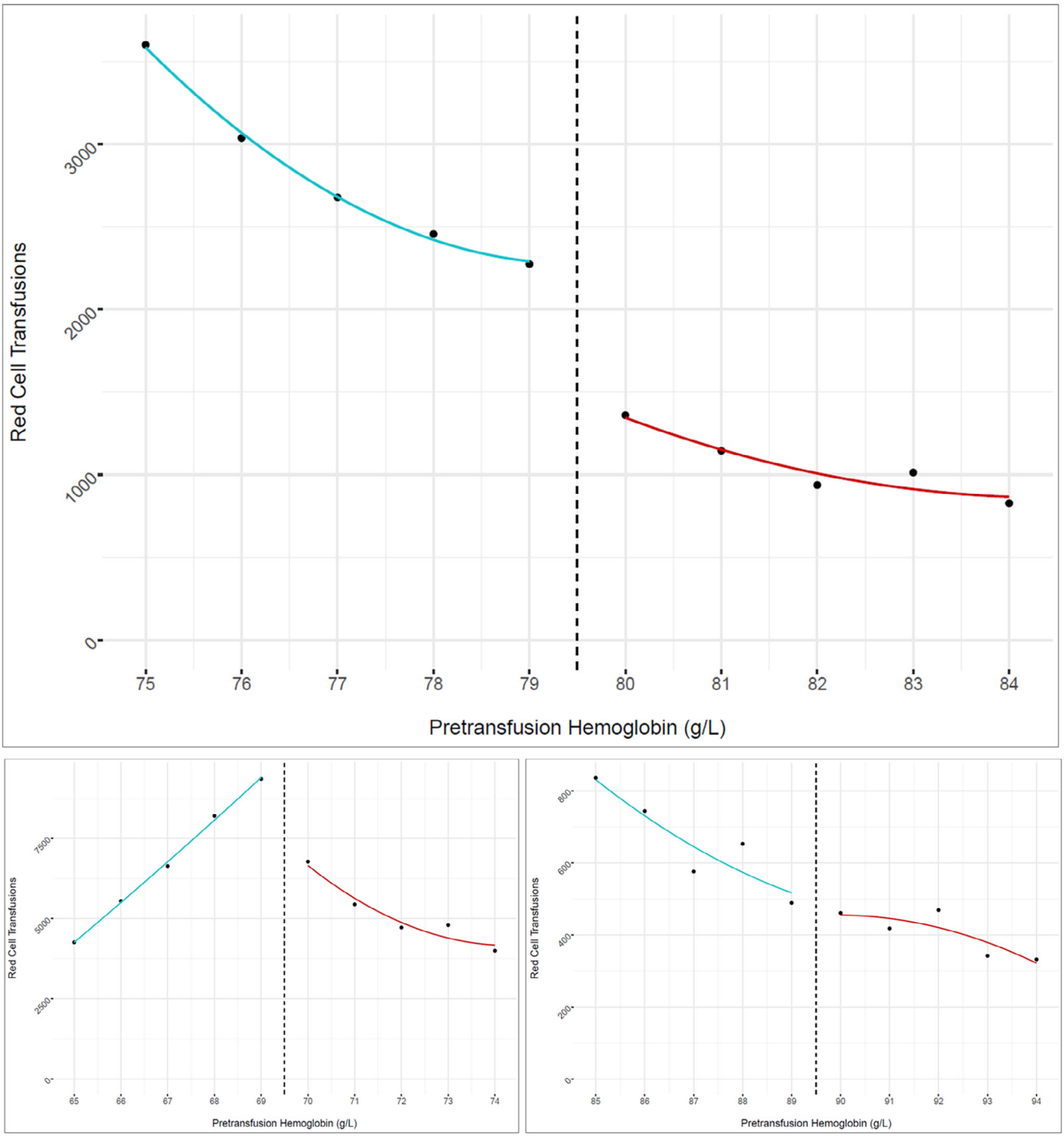



FIGURE 1 Plot depicting discontinuity analyses of transfusion occurrence at pre-transfusion hemoglobin thresholds of 69, 79, and 89 g/L in separate panels. Lines depicting regression trends above and below threshold. [Color figure can be viewed at wileyonlinelibrary.com]

**TABLE 2** Results of quadratic regression discontinuity analyses.

| Subgroup | Threshold | Effect size[a] (# of transfusions) | 95% Confidence interval | Analytic sample size |
|---|---|---|---|---|
| Threshold | 69 | −2813* | (−4407 to −1220) | 59,749 |
| | 79 | −815* | (−1215 to −415) | 19,335 |
| | 89 | −40 | (−408 to 328) | 5320 |
| | 71 | −700 | (−4736 to 3336) | 59,092 |
| | 81 | 89 | (−802 to 980) | 16,568 |
| | 91 | 22 | (−353 to 396) | 4798 |
| Day | 79 | −613* | (−970 to −255) | 11,835 |
| Night | 79 | −202 | (−421 to 17) | 7500 |
| May/June | 79 | −179* | (−274 to −83) | 3096 |
| July/August | 79 | −83 | (−293 to 127) | 3359 |
| Weekday | 79 | −504** | (−775 to −232) | 12,911 |
| Weekend | 79 | −311** | (−559 to −63) | 6424 |

*Note*: Statistical inference on the threshold effect was conducted using linear regression controlling for local quadratic trends with $p$ values determined via the $t$-test.
[a]Units transfused associated with being above the threshold after controlling for local quadratic trend. Negative numbers signify fewer transfusions below threshold.
*$p < .01$; **$p < .05$.

size of 2813 units ($n = 59{,}749$; 95% CI: −4407 to −1220) and 89 g/L showed an effect size of 40 units ($n = 5320$; 95% CI: −408 to 328). Analyses at thresholds 71, 81, and 91 g/L did not demonstrate a statistically significant association with transfusion counts (Table 2). The findings were replicated with all patients (without subgroup exclusions) and alternate regression bandwidths (Appendix S1).

## 4 | DISCUSSION

We studied thousands of inpatient red cell transfusions across diverse subspecialty services and found a twofold increase in transfusions just below compared to just above the leading digit threshold of 79 g/L. The increase was modest and accounted for an additional 160 red cell transfusions per year in the selected inpatient cohort of 20,000 transfusions annually. The effect was accentuated during daytime, weekdays, and near the end of the academic residency year, suggesting that more experienced clinicians might disproportionately manifest this bias. The effect was not explained by the baseline distribution of hemoglobin results. Together our results suggest that leading digit bias might influence red cell transfusion in hospitalized patients.

### 4.1 | Limitations

Our study has several limitations. The data did not include details on patient or physician characteristics; patient factors, in particular, are unlikely to vary across hemoglobin change of 1 g/L (smaller than the test error margin). Missing data due to extraction errors could potentially create a selection bias (e.g., pre-transfusion hemoglobin might be systematically missing in patients with hyperacute bleeding), although this would not be conditional on leading digit thresholds. The analysis is based on single pre-transfusion hemoglobin values whereas transfusion decisions often incorporate trends. The available transfusion data lacked a denominator for all patients with hemoglobin of 79 or 80 g/L.

Furthermore, we cannot disambiguate the extent to which our findings are explained by providers following transfusion guidelines rather than being influenced by leading digit bias. Our institutional guidelines recommend 70 g/L for most patients and do not easily account for leading digit effects at 79 g/L (except for the cardiology wards where 80 g/L might be routine); however, guidelines at other institutions may vary. The study does not examine differences in nursing behavior (e.g., notifying on-call physician), resident turnover (e.g., rotating from institutions with differing guidelines), or laboratory result interfaces (e.g., emphasizing results below certain thresholds), albeit these factors could also reflect a leading digit bias. Shifting away from leading digit thresholds may be challenging because several large randomized trials implicitly endorse such thresholds. Our findings are based on grams per liter (whole numbers) and replication at centers using grams per deciliter (decimal numbers) may vary, although leading digit bias has been reported for decimals.[16] Our study was observational, cannot establish causality, and was based on a single hospital network.

## 4.2 | Implications

Our findings have several important implications. First, the results might inform guidelines on selecting thresholds less susceptible to a prevalent cognitive bias or discourage threshold-based decision-making in favor of holistic evaluation.[31] Second, the strength of the leading digit effect might be used as an indicator of physician overreliance on laboratory testing.[32] Third, leading digit thresholds might be used in a quasi-random design, such as using instrumental variable methods, linear structural equation models, and negative control analysis.[21] Fourth, leading digit bias might also be mitigated with counteracting behavioral nudges to reduce inappropriate transfusion.[14,33] Fifth, our study might motivate research on other psychological biases in the field of transfusion.[34] Finally, our study highlights an important pitfall in clinical reasoning because red cell transfusions should treat patients rather than numbers.

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## CONFLICT OF INTEREST STATEMENT

The authors have disclosed no conflicts of interest.

## DATA AVAILABILITY STATEMENT

Data may be available upon request.

## ETHICS STATEMENT

The study was approved by the Research Ethics Board at the University Health Network.

## ORCID

*Christine Cserti-Gazdewich* https://orcid.org/0000-0002-5297-6406

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## SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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