# The Role of Baseline Body Temperature in Neutropenic Fever


Anthony Corsi, BS[1]; Madison Searles, MPH[1]; Christina Lupone, MPH[1], Ivayla I. Geneva, MD, PhD[2]

[1]State University of New York, Upstate Medical University; [2]Crouse Hospital


## Background

- While body temperature is a vital measurement used in all patient care, its value in certain contexts remains unclear[1-3]
- Previous studies indicate that body temperature may vary depending on patient age, temperature measurement site, and other less-studied factors, both in healthy and hospitalized patients[4,5]
- In some circumstances, such as in immunocompromised patients with neutropenia, body temperature serves as a crucial measure that guides treatment
- However, the simplistic definition of fever as a single oral temperature of 38.3°C or sustained temperature > 38°C for more than one hour fails to account for interpersonal variation in baseline body temperatures

## Objective

- To examine the relationship between the magnitude of body temperature deviation from the baseline in patients admitted for neutropenic fever and other features of their hospitalization, such as initial illness severity, fever persistence, neutropenia persistence, identification of infectious etiology causing fever, and the duration of hospital stay
- To propose a new and personalized definition of neutropenic fever

## Methods

- **Study Design:** retrospective chart review of patients admitted to Upstate Medical University (N=92)
- **Inclusion Criteria:**
  - Age ≥18 years
  - Hospital admission diagnosis of neutropenic fever
  - Availability of baseline outpatient body temperature readings
- **Exclusion Criteria:**
  - An infectious process identified prior to admission
  - Use of antibiotics for treatment or prophylaxis prior to admission
  - Absolute neutrophil count ≥1,500 cells/µL at time of admission
- **Definition of fever**
  - Tmax ≥ 38.0C or Tmax > 2SDs or > 3SDs from patients' personal baseline
- **Statistical Analysis:**
  - Descriptive statistics of cohort demographics, hospital course characteristics, and body temperature readings
  - Exact sign test for comparing Tmax on admission and patients' personal outpatient baseline body temperature
  - Linear Regression to study the effect of patients' age on the measured change in body temperature (ΔT)
  - Multiple logistic regression to model the length of stay based on ΔT, age, degree of neutropenia, ICU vs non-ICU level of care, persistence of fever at 72 hours after admission, and scheduled use of Tylenol
  - Multiple logistic regression to model the ability to identify a specific cause for fever based on the same variables listed above

## Results

**Table 1. Demographics and Features of Hospital Course**

| | | | |
|---|---|---|---|
| **Sex:** | | **Specific diagnosis accounting for fever:** | |
| Female | 47 (51.1%) | Pneumonia | 10 (10.9%) |
| Male | 45 (48.9%) | Bacteremia | 9 (9.8%) |
| **Age:** | | Gastroenterologic infection | 7 (7.6%) |
| Mean +/- SD | 54.9 +/- 17.9 years | Upper respiratory tract infection | 5 (5.4%) |
| Range | 20 to >90 years | Skin and soft tissues infection | 4 (4.4%) |
| **Acuity on admission:** | | Viremia | 1 (1.1%) |
| ICU admission | 10 (10.9%) | **Scheduled Tylenol use:** | |
| Non-ICU admission | 82 (89.1%) | Yes | 74 (80.4%) |
| **Primary Service:** | | No | 18 (19.6%) |
| Hematology-Onclogy | 45 (48.9%) | **As needed Tylenol use:** | |
| General Medicine | 13 (14.1%) | Yes | 59 (64.1%) |
| BMT unit | 10 (10.9%) | No | 33 (35.9%) |
| Medical ICU | 10 (10.9%) | **Discharge location:** | |
| Cardiothoracic | 4 (4.3%) | Deceased | 2 (2.2%) |
| Pediatric service (≥18 years old) | 4 (4.3%) | Home with self care | 55 (59.8%) |
| Surgery Transplant | 3 (3.3%) | Home with home health care | 27 (29.3%) |
| Neurosurgery | 3 (3.3%) | Skilled nursing facility | 3 (3.3%) |
| **Neutropenia level on admission:** | | Rehabilitation center | 1 (1.1%) |
| Mild (ANC < 1,500) | 4 (4.3%) | Short term hospital | 1 (1.1%) |
| Moderate (ANC < 1,000) | 10 (10.9%) | Home with hospice | 1 (1.1%) |
| Severe (ANC < 500) | 27 (29.3%) | Correction facility | 1 (1.1%) |
| Profound (ANC < 100) | 51 (55.4%) | Left against medical advice | 1 (1.1%) |
| **Reason for neutropenia:** | | **Length of stay (days):** | |
| Chemotherapy | 87 (94.6%) | ≤ 3 days | 40 (44.4%) |
| Transplant | 3 (3.3%) | > 3 days | 60 (66.7%) |
| SLE | 1 (1.1%) | Not included (deceased) | 2 (2.2%) |
| Unknown | 1 (1.1%) | **Survival:** | |
| **Reason for fever identified in 72 hours:** | | Alive on discharge | 90 (97.8%) |
| Yes | 44 (47.8%) | Deceased | 2 (2.2%) |
| No | 48 (52.2%) | | |

**Abbreviations:** SD: standard deviation, ICU: intensive care unit, BMT: bone marrow transplant, ANC: absolute neutrophil count, SLE: systemic lupus erythematosus.

**Table 2. Recorded Body Temperature Readings**

| | | | |
|---|---|---|---|
| **Outpatient baseline body temperatures, N=92** | | **Maximal temperature 25-48 hours, N=87** | |
| Mean +/- SD | 36.71 +/-0.30C | Mean +/- SD | 37.60 +/- 0.79C |
| Range | [35.8-37.5] | Range | [36.28-39.61] |
| **Self-reported fever before admission, N=55** | | **Maximal temperature 49-72 hours, N=78** | |
| Mean +/- SD | 38.72 +/- 0.45C | Mean +/- SD | 37.43 +/- 0.69C |
| Range | [37.83-40.00] | Range | [36.61-39.61] |
| **Maximal temperature on admission, N=91** | | **Persistence of fever (defined as T ≥ 38C), N=88** | |
| Mean +/- SD | 38.14 +/- 0.82C | 22 (23.9%) | |
| Range | [36.87-39.70] | **Persistence of fever (1 SD above baseline), N=87** | |
| **ΔTemperature, N=90** | | 73 (79.3%) | |
| Mean +/- SD | 1.45 +/- 0.87C | **Persistence of fever (2 SD above baseline), N=87** | |
| Range | [-0.22-3.81] | 50 (54.3%) | |
| | | **Persistence of fever (3 SD above baseline), N=87** | |
| | | 31 (33.7%) | |

**Note:** All body temperatures are standardized to oral measurement site.
**Abbreviations:** SD: standard deviation.

**Table 3. Modeling Length of Hospital Stay**

| | P-values | | | | | | |
|---|---|---|---|---|---|---|---|
| | **Age** | **ANC on admission** | **ANC at 72 h** | **ICU vs non-ICU level of care** | **Δ T** | **Persistence of fever at 72 h** | **Scheduled Tylenol use** |
| **Model A - Generic fever cutoff (Tmax ≥ 38.0C)** | 0.249 | 0.379 | 0.922 | 0.999 | **0.010** | **0.009** | 0.185 |
| **Model B - Personalized fever cutoff (Tmax > 2SDs)** | 0.503 | 0.632 | 0.609 | 0.999 | **0.023** | 0.497 | 0.547 |
| **Model C - Personalized fever cutoff (Tmax > 3SDs)** | 0.405 | 0.588 | 0.708 | 0.999 | **0.033** | **0.040** | 0.275 |

**Abbreviations:** Tmax on admission: the highest body temperature measured during the Emergency Department stint and the first 8 hours following hospitalization, SD: standard deviation, ICU: intensive care unit, ANC: absolute neutrophil count.

**Table 4. Modeling Ability to Identify Fever Etiology**

| | P-values | | | | | | |
|---|---|---|---|---|---|---|---|
| | **Age** | **ANC on admission** | **ANC at 72 h** | **ICU vs non-ICU level of care** | **Δ T** | **Persistence of fever at 72 h** | **Scheduled Tylenol use** |
| **Model A - Generic fever cutoff (Tmax ≥ 38.0C)** | 0.477 | 0.555 | 0.989 | 0.261 | 0.689 | 0.347 | 0.457 |
| **Model B - Personalized fever cutoff (Tmax > 2SDs)** | 0.672 | 0.558 | 0.942 | 0.272 | 0.768 | 0.527 | 0.459 |
| **Model C - Personalized fever cutoff (Tmax > 3SDs)** | 0.572 | 0.493 | 0.935 | 0.250 | 0.757 | 0.696 | 0.376 |

**Abbreviations:** Tmax on admission: the highest body temperature measured during the Emergency Department stint and the first 8 hours following hospitalization, SD: standard deviation, ICU: intensive care unit, ANC: absolute neutrophil count.

- **Maximum body temperatures at admission were significantly higher than patients' baseline**
- **Patients' age did not correlate with the deviation from baseline temperature at admission**

### Modeling the hospital length of stay

**General fever cutoff (Tmax ≥ 38°C):**
- This model correctly classified 80.8% of cases
- An increase in body temperature by 1°C correlated with a 2.90x increased risk of hospital stay longer than 4 days (OR=2.90, p<0.05, 95% CI 1.29, 6.51), while controlling for age, ANC, admission service, persistence of fever at 72h, and scheduled Tylenol use
- Patients with a persistence of fever were at a 10.47x increased risk of hospital stay longer than 4d (OR=10.47 p<0.05, 95% CI 1.78, 61.63), while controlling for Tmax, age, ANC, admission service, and scheduled Tylenol use

- **Baseline body temperature +2 SD from personalized baseline fever cutoff:**
  - This model correctly classified 74.0% of cases.
  - An increase in body temperature by 1°C correlated with a 2.28x increased risk of hospital stay longer than 4 days (OR=2.28, p<0.05, 95% CI 1.12, 4.65)
- **Baseline body temperature +3 SD from personalized baseline fever cutoff:**
  - This model correctly classified 76.7% of cases.
  - An increase in body temperature by 1°C correlated with a 2.19x increased risk of hospital stay longer than 4 days (OR=2.19, p<0.05, 95% CI 1.01, 4.49)
  - Patients with a persistence of fever were at a 3.97x increased risk of hospital stay longer than 4d (OR=3.97 p<0.05, 95% CI 1.07, 14.76)

### Modeling the ability to identify fever etiology

- Results of models were not significant

## Conclusions

- Given the average outpatient baseline body temperature of 36.7 +/- 0.3°C, at 2 SDs above this baseline, only 3% of patients would be above the traditional 38°C cutoff for fever. At 3 SDs, still only 20% would qualify. This renders the standard 38°C cutoff too high to be useful in identifying many neutropenic fever cases
- Our data supports the utility of using personalized fever cutoffs derived from each patient's baseline temperature
- The magnitude of temperature deviation from patients' baseline body temperature could serve as a predictor for hospital length of stay

## References


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