

## **Systematic Review: Differences in Complete Blood Count Component Rhythms**

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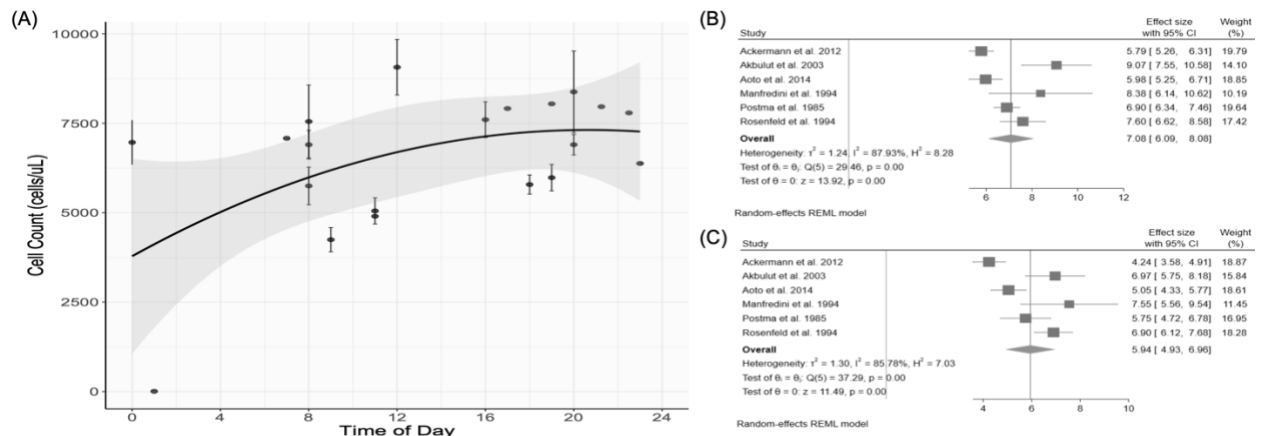
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**Supplemental Table 2. Summary of fitted Peak Time and Values from Polynomial Function**

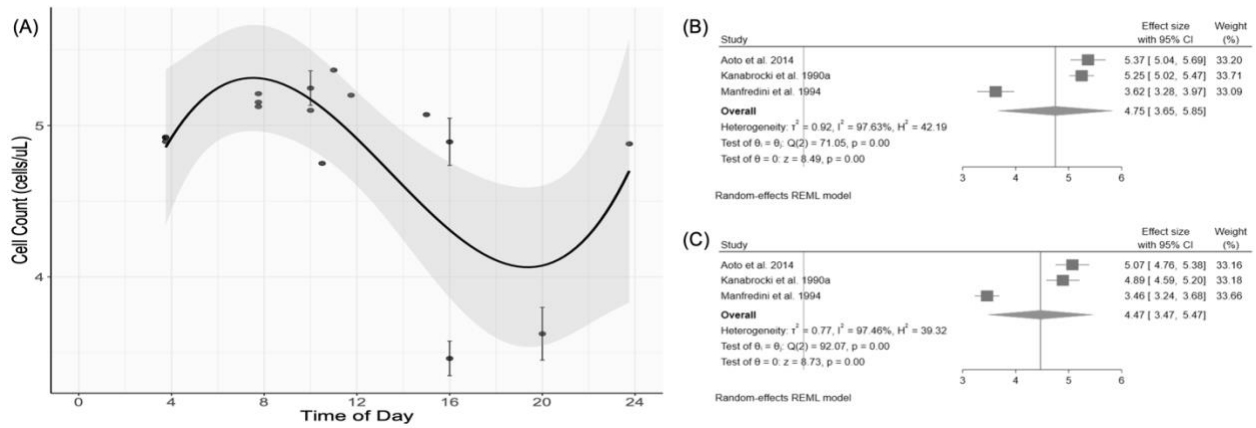
**Analysis.** Polynomial function analysis was conducted using the ggplot2 package in the R statistical environment. Peak values were not calculated for cell types with second-degree polynomial fits that yielded a minimum value or with unreliable polynomial fits. Of note, monocytes were poorly fit with each model likely due to insufficient data. Monocytes remained included in the analysis to demonstrate the lack of rhythmicity captured in previous studies.

	Studies Included (#)	Estimated Maximum Value (cells/uL)	Estimated Maximum Time	Best Fit polynomial (1 <sup>st</sup> / 2 <sup>nd</sup> / 3 <sup>rd</sup> degree)	Best Fit p-value	Best Fit R <sup>2</sup> value	AIC / BIC
<b>Leukocytes</b>	12	7313.31	20:27	2 <sup>nd</sup> -degree	0.067	0.273	361 / 365
<b>Erythrocytes</b>	6	5.31 * 10 <sup>6</sup>	07:31	3 <sup>rd</sup> -degree	0.024	0.531	22.7 / 26.5
<b>Hemoglobin</b>	5	--	--	2 <sup>nd</sup> -degree	0.513	-0.024	115 / 120
<b>Hematocrit</b>	5	42.47%	11:05	2 <sup>nd</sup> -degree	0.172	0.122	159 / 165
<b>Platelets</b>	11	--	~22:00 +/- 2 hours*	2 <sup>nd</sup> -degree	0.043	0.310	219 / 223
<b>Neutrophils</b>	9	5160.98	17:21	3 <sup>rd</sup> -degree	0.135	0.286	336 / 341
<b>Lymphocytes</b>	11	2532.19	23:47	3 <sup>rd</sup> -degree	0.010	0.383	424 / 431
<b>Monocytes</b>	5	--	--	1 <sup>st</sup> -degree	0.916	0.0002	96.4 / 96.6
<b>Eosinophils</b>	13	--	--	1 <sup>st</sup> -degree	0.393	0.026	378 / 383
<b>Basophils</b>	6	--	--	1 <sup>st</sup> -degree	0.177	0.192	99.2 / 100

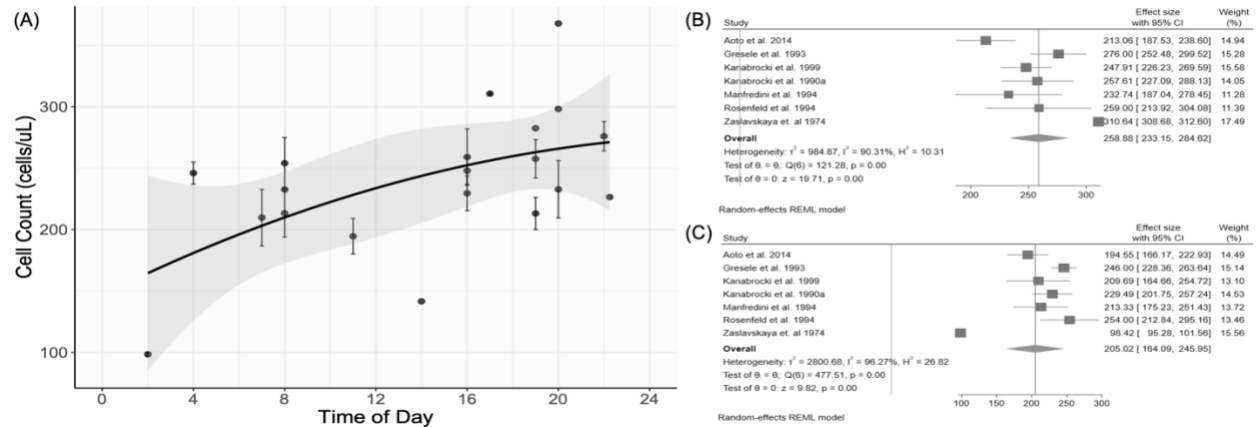
\* Estimated time range of peak based on the fit. Resolution of +/- 2 hours based on available data points. Highest density of data points in this range (n = 4)



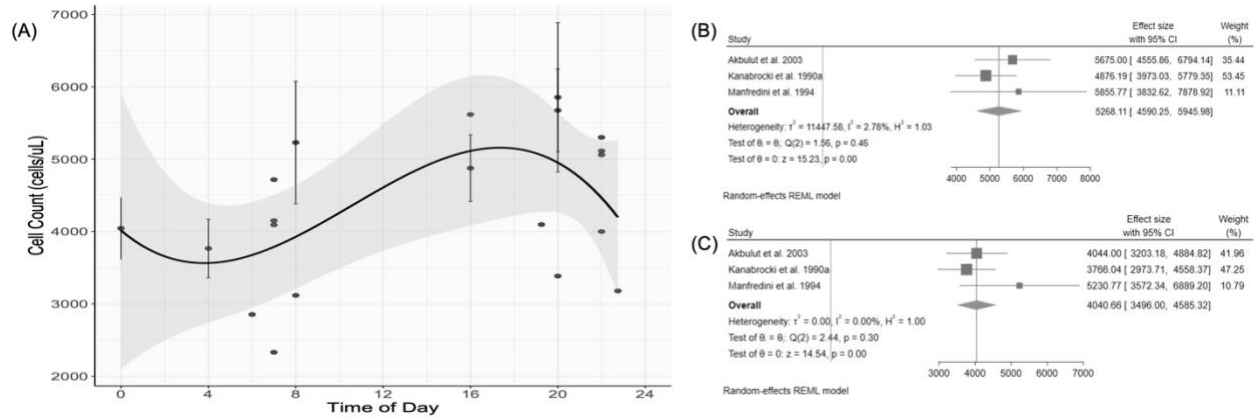
**Supplemental Figure 1. Rhythm of Leukocytes.** (A) Leukocytes values fitted with a second-degree polynomial generated via R statistical analysis. Standard error of the fit is shaded in grey around the line of best fit. For studies that reported standard error data, error bars are plotted with the associated data point ( $p=0.067$ ,  $R^2=0.273$ ,  $n=12$ ) (B) Forest plot of leukocyte peak values created with Stata SE software. Seven studies were not included in the Forest plot of peak values due to lack of error data.[2, 23-25, 32, 34, 35] (C) Forest plot of leukocyte trough values created with Stata SE software. Seven studies were not included in the Forest plot of peak values due to lack of error data[2, 23-25, 32, 34, 35]



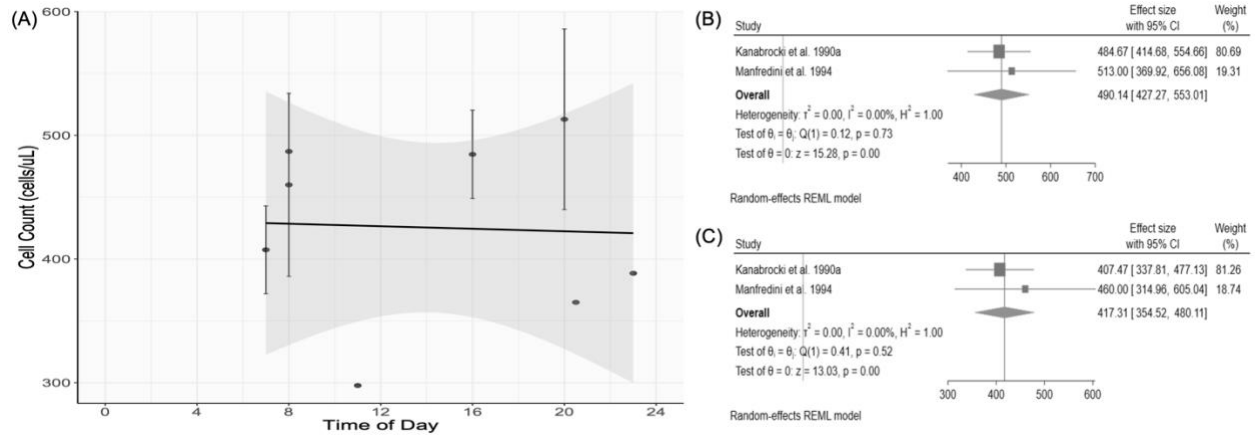
**Supplemental Figure 2. Rhythm of Erythrocytes.** (A) Erythrocyte values fitted with a third-degree polynomial generated via R statistical analysis. Standard error of the fit is shaded in grey around the line of best fit. For studies that reported standard error data, error bars are plotted with the associated data point. ( $p=0.024$ ,  $R^2=0.531$ ,  $n=6$ ) (B) Forest plot of erythrocyte peak values created with Stata SE software. Four studies were not included in the Forest plot of peak values due to lack of error data.[2, 25, 32, 45] (C) Forest plot of erythrocyte trough values created with Stata SE software. Four studies were not included in the Forest plot of peak values due to lack of error data[2, 25, 32, 45]



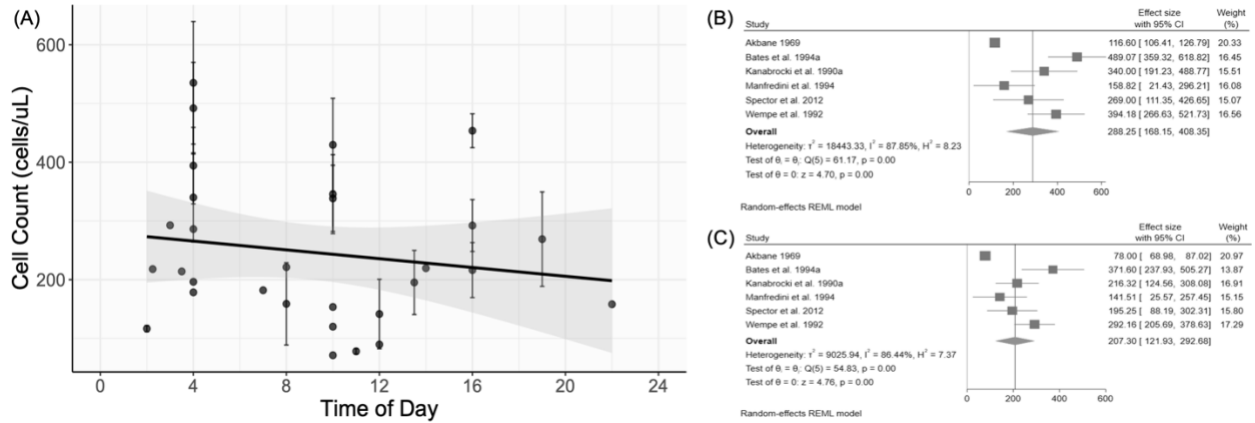
**Supplemental Figure 3. Rhythm of Platelets.** (A) Platelet values fitted with a second-degree polynomial generated via R statistical analysis. Standard error of the fit is shaded in grey around the line of best fit. For studies that reported standard error data, error bars are plotted with the associated data point. ( $p=0.043$ ,  $R^2=0.310$ ,  $n=11$ ) (B) Forest plot of platelet peak values created with Stata SE software. Five studies were not included in the Forest plot of peak values due to lack of error data[2, 20, 25, 32, 44]. (C) Forest plot of platelets trough values created with Stata SE software. Five studies were not included in the Forest plot of peak values due to lack of error data[2, 20, 25, 32, 44]



**Supplemental Figure 4. Rhythm of Neutrophils.** (A) Neutrophil values fitted with a third-degree polynomial generated via R statistical analysis. Standard error of the fit is shaded in grey around the line of best fit. For studies that reported standard error data, error bars are plotted with the associated data point. ( $p=0.135$ ,  $R^2=0.286$ ,  $n=9$ ) (B) Forest plot of neutrophil peak values created with Stata SE software. Eight studies were not included in the Forest plot of peak values due to lack of error data.[2, 24, 25, 32, 34, 41, 42, 47] (C) Forest plot of neutrophil trough values created with Stata SE software. Eight studies were not included in the Forest plot of peak values due to lack of error data[2, 24, 25, 32, 34, 41, 42, 47]

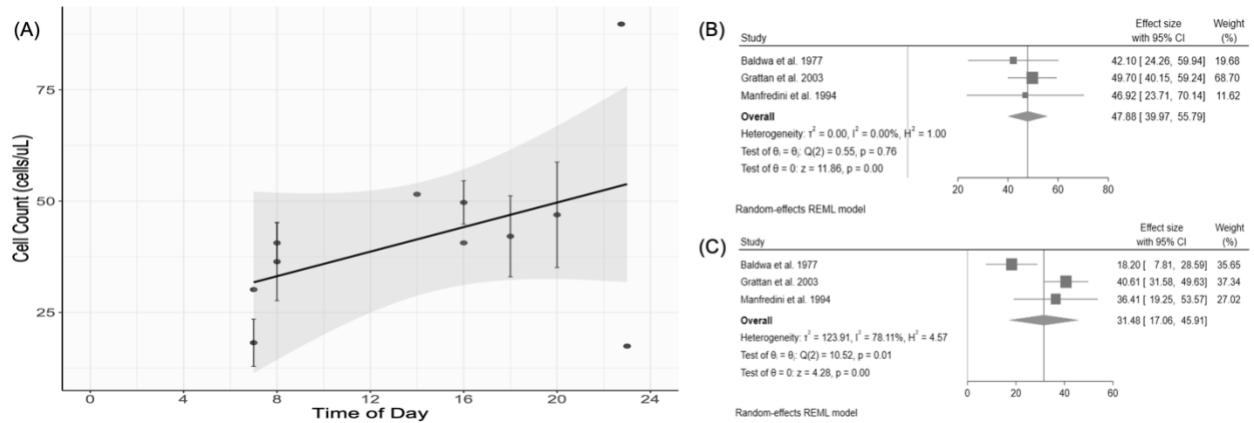


**Supplemental Figure 5. Rhythm of Monocytes.** (A) Monocytes values fitted with a linear function generated via R statistical analysis. Standard error of the fit is shaded in grey around the line of best fit. For studies that reported standard error data, error bars are plotted with the associated data point. ( $p=0.916$ ,  $R^2=0.002$ ,  $n=5$ ) Of note, monocytes were poorly fit with 1<sup>st</sup>, 2<sup>nd</sup>, and 3<sup>rd</sup> degree models, likely due to insufficient data. Monocytes remained included in the analysis to demonstrate the lack of rhythmicity captured in previous studies. (B) Forest plot of monocyte peak values created with Stata SE software. Five studies were not included in the Forest plot of peak values due to lack of error data[2, 17, 24, 25, 32] (C) Forest plot of monocyte trough values created with Stata SE software. Five studies were not included in the Forest plot of peak values due to lack of error data[2, 17, 24, 25, 32]

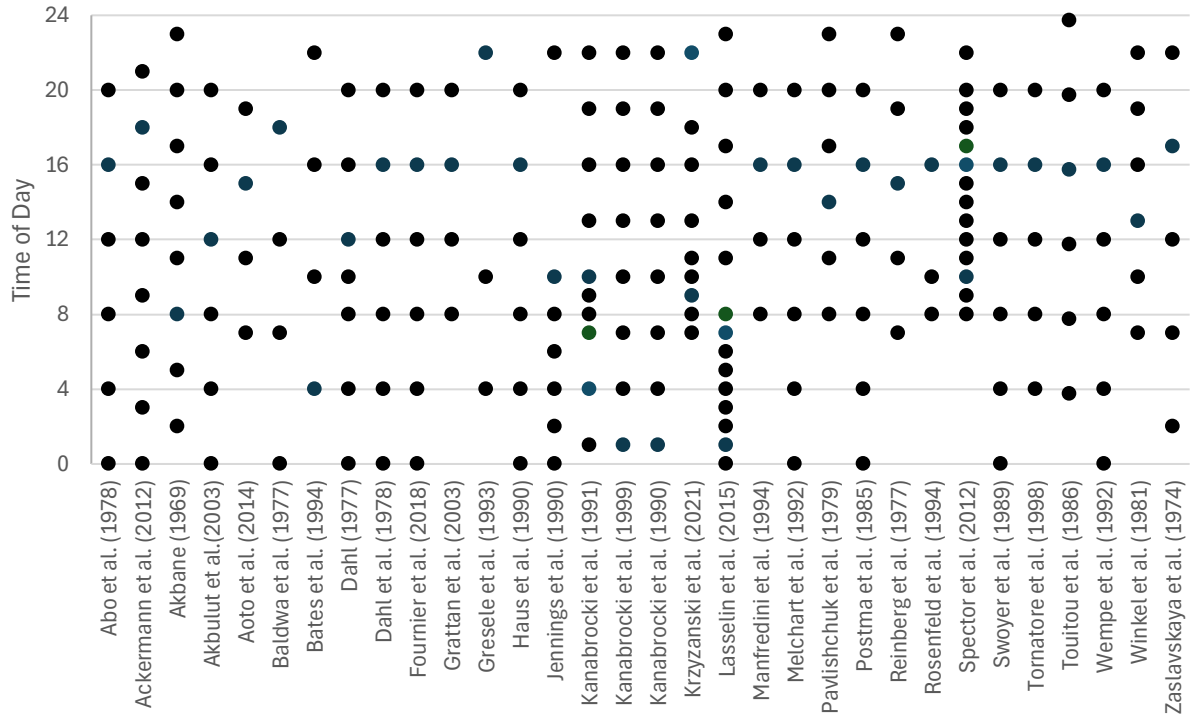


**Supplemental Figure 6. Rhythm of Eosinophils.** (A) Eosinophil values fitted with a linear function generated via R statistical analysis. Standard error of the fit is shaded in grey around the line of best fit. For studies that reported standard error data, error bars are plotted with the associated data point. ( $p=0.393$ ,  $R^2=0.026$ ,  $n=13$ ) (B) Forest plot of eosinophil peak values created with Stata SE software. Nine studies were not included in the Forest plot of peak values due to lack of error data.[2, 24, 25, 32, 34, 39-41, 47] (C) Forest plot of eosinophil trough values created with Stata SE software. Nine studies were not included in the Forest plot of peak values due to lack of error data[2, 24, 25, 32, 34, 39-41, 47]





**Supplemental Figure 7. Rhythm of Basophils.** (A) Basophil values fitted with a linear function generated via R statistical analysis. Standard error of the fit is shaded in grey around the line of best fit. For studies that reported standard error data, error bars are plotted with the associated data point. ( $p=0.177$ ,  $R^2=0.192$ ,  $n=6$ ) (B) Forest plot of basophil peak values created with Stata SE software. Five studies were not included in the Forest plot of peak values due to lack of error data.[2, 23, 32, 42, 44] (C) Forest plot of basophil trough values created with Stata SE software. Five studies were not included in the Forest plot of peak values due to lack of error data.[2, 23, 32, 42, 44]



**Supplemental Figure 8. Time Points per Article.** The included time points for each article are depicted over a 24 hour period across the y-axis.