**SUPPLEMENTARY MATERIAL**

**Figure S1** Length of stay during the transition to the two-bag NAC regimen. The median (50%), 25% and 75% quantiles per month are shown.



**Table S1** Sensitivity analysis of two-bag regimen implementation date. Variables associated with development of anaphylactoid reactions requiring treatment.

|  |  |  |
| --- | --- | --- |
|  | Anaphylactoid |  |
|  | Crude OR (95% CI) | Adjusted OR (95% CI)a |
| Paracetamol concentrationb | 0.81 [0.73, 0.90] | - |
| * Two-bag regimen
 | 0.71 [0.60, 0.83] | 0.65 [0.55, 0.77] |
| * Three-bag regimen
 | 0.87 [0.76, 1.00] | 0.82 [0.70, 0.94] |
| Paracetamol concentration BLLQ | 1.43 [1.11, 1.84] | 0.94 [0.62, 1.46] |
| Two-bag regimen (n = 3,199) | 0.36 [0.28, 0.47] | 0.44 [0.32, 0.60] |
| Antihistamine overdose | 0.21 [0.02, 0.77] | 0.17 [0.02, 0.64] |
| Daily use of antihistamines  | 0.60 [0.40, 0.87] | 0.76 [0.50, 1.11] |
| Age, per 10-year increase | 0.89 [0.84, 0.95] | 0.85 [0.78, 0.91] |
| Age, 0-9 year of age | 0.36 [0.10, 0.89] | 0.15 [0.04, 0.38] |
| Length of stay, per day | 0.97 [0.93, 1.00] | 0.97 [0.92, 1.00] |
| Charlson Comorbidity index | 0.89 [0.80, 0.98] | 0.95 [0.85, 1.06] |

All treatments prior to January 1, 2013 was defined as following the three-bag regimen . BLLQ: Below the Lower Limit of Quantification, a Adjusted for NAC regimen, plasma paracetamol concentration, interaction between plasma paracetamol and NAC regimen, antihistamine poisoning, and age b Log2 transformed, i.e. the odds ratio corresponds to a doubling of the plasma concentration. Plasma concentrations BLLQ were set to 130 µmol/L

**Table S2** Sensitivity analysis of two-bag regimen implementation date. Variables associated with development of anaphylactoid reactions requiring treatment.

|  |  |  |
| --- | --- | --- |
|  | Anaphylactoid |  |
|  | Crude OR (95% CI) | Adjusted OR (95% CI)a |
| Paracetamol concentrationb | 0.81 [0.73, 0.90] | - |
| * Two-bag regimen
 | 0.60 [0.46, 0.75] | 0.55 [0.42, 0.69] |
| * Three-bag regimen
 | 0.87 [0.77, 0.98] | 0.81 [0.71, 0.91] |
| Paracetamol concentration BLLQ | 1.43 [1.11, 1.84] | 0.87 [0.57, 1.35] |
| Two-bag regimen (n = 2,391) | 0.38 [0.29, 0.50] | 0.44 [0.32, 0.60] |
| Antihistamine overdose | 0.21 [0.02, 0.77] | 0.19 [0.02, 0.69] |
| Daily use of antihistamines  | 0.60 [0.40, 0.87] | 0.75 [0.49, 1.10] |
| Age, per 10-year increase | 0.89 [0.84, 0.95] | 0.84 [0.78, 0.90] |
| Age, 0-9 year of age | 0.36 [0.10, 0.89] | 0.13 [0.04, 0.35] |
| Length of stay, per day | 0.97 [0.93, 1.00] | 0.97 [0.93, 1.00] |
| Charlson Comorbidity index | 0.89 [0.80, 0.98] | 0.96 [0.85, 1.06] |

All treatments prior to January 1, 2014 was defined as following the three-bag regimen . BLLQ: Below the Lower Limit of Quantification, a Adjusted for NAC regimen, plasma paracetamol concentration, interaction between plasma paracetamol and NAC regimen, antihistamine poisoning, and age b Log2 transformed, i.e. the odds ratio corresponds to a doubling of the plasma concentration. Plasma concentrations BLLQ were set to 130 µmol/L