From basic to advanced computerized IV to oral switch for paracetamol and antibiotics: an interrupted time series analysis

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BACKGROUND & IMPORTANCE

- **Early switch from intravenous (IV) to oral therapy** of bioequivalent drugs has major advantages, but **remains challenging**.
- Different strategies have been tested over the years to overcome **barriers as prescribers' misconceptions, practical and organizational concerns**.
- *We aimed to **develop, validate and investigate the effect of an advanced computerized algorithm for IV to oral switch (IVOS),** as part of a centralized pharmacist-led medication review service*.

Figure 1. ***Schematic overview of methods***

METHODS (Figure 1)

- The intervention targeted **paracetamol** and **10 bioequivalent antibiotics**.
- Based on a definite set of **criteria for IVOS**, obtained by a literature search and validated by a multidisciplinary expert panel, **2 clinical rules** were developed to identify patients with **potentially inappropriate IV prescriptions (PIVs)**.
- **Process validation** was performed determining the rule effectiveness and positive predictive value (PPV).
- Post-intervention, the clinical rule alerts were reviewed by **pharmacists who provided recommendations** to switch in case of eligibility.
- An **interrupted time series (ITS) study** was performed to compare the number of residual PIVs between the pre-intervention and post-intervention period.
- The **total number of recommendations, acceptance rate and financial impact** were recorded for the 8-month post-intervention period.

RESULTS

- Literature search & content validation revealed **13 switch criteria (Table 1)**.
- Process validation yielded a **PPV of 99% and rule effectiveness of 84%.**
- Figure 2 shows the **proportion of residual PIVs** during the ITS study period. At baseline, the median proportion of residual PIVs was 66% with a median number of 11 residual PIVs per day. After the intervention, the median proportion and median number dropped, respectively, to 17% and 3.
- **Post-intervention, the number of residual PIVs is 21%** (β_2=0.21; 95% CI 0.13-0.32) of the pre-intervention number. The advanced IVOS algorithm showed a **significant reduction of 79% (*p*<0.01)** in the number of residual PIVs (Table 2).
- Neither a significant underlying time trend was observed during both pre- (β_1, *p*=0.32) and post-intervention period (*p*=0.34), nor a significant difference when comparing pre- and post-intervention trends (β_3, *p*=0.38) (Figure 2, Table 2).
- During an 8-month period, **1091 recommendations** were provided of which **74%** were accepted, resulting in a **one-day cost saving of €4664.20.**
- Prioritizing the IVOS algorithm for paracetamol during the global **COVID-19 pandemic** was helpful in **preventing shortages of IV paracetamol**.

Table 1. ***Definite set of 13 criteria for IVOS grouped in 2 categories***

Category 1: Ability of oral absorption (applicable for paracetamol and antibiotics)	Category 2: Type of infection (only applicable for antibiotics)
1. Ability to swallow and take oral medications and/or food	8. Exclusion of endovascular infection (e.g. endocarditis)
2. Absence of nausea and vomiting	9. Exclusion of septic shock
3. Absence of severe diarrhea	10. Exclusion of meningitis
4. Absence of ileus or gastrointestinal obstruction	11. Exclusion of *Staphylococcus aureus* bacteremia
5. Absence of active gastrointestinal bleeding	12. Exclusion of central nervous system infection
6. Absence of a malabsorption syndrome	13. Exclusion of necrotizing fasciitis
7. Absence of gastric bypass surgery	

Table 2. ***Model summary***

	Estimate	Standard error	*p*-value
Intercept (β_0)	0.68	0.11	< 0.01
Pre-intervention trend (β_1)	1.00	< 0.01	0.32
Change in level after intervention (β_2)	0.21	0.23	**< 0.01**
Post-intervention trend	1.04		0.34
Change in trend after intervention (β_3)	1.04	0.04	0.38

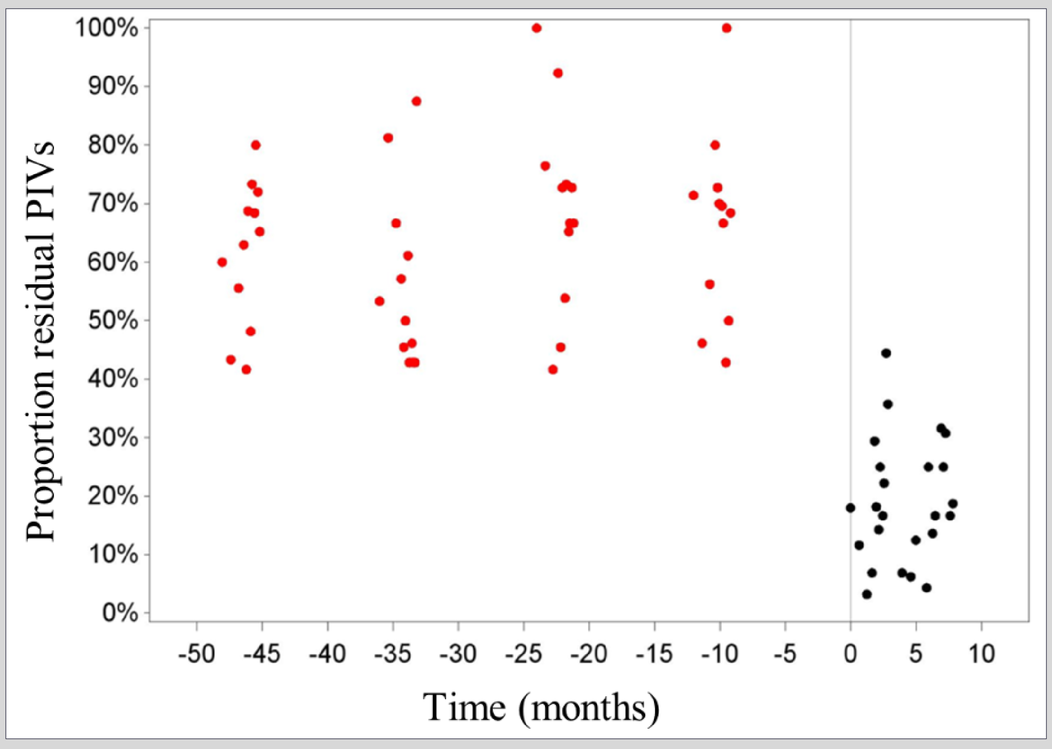

Figure 2. ***Observed proportions of residual PIVs over time***

CONCLUSION & RELEVANCE

- → Our study showed that the **advanced IVOS algorithm combined with a pharmacist-led medication review improved switch therapy** of bioequivalent drugs **impressively**.
- → The rules can easily be **transferred to or replicated in other Belgian hospitals**, to support a widespread use.
- → Given the almost perfect rule effectiveness and high PPV, the service may have the potential **to evolve as a stand-alone CDSS-feature** without pharmacist interference to realize switching at the actual moment of prescribing.