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Evaluation of the effect of methodological assumptions on estimates of adherence to antipsychotics: a real-world data study

Marina Fuente-Moreno; Antoni Serrano-Blanco; Maria Rubio-Valera; Alexandra L. Dima; Ignacio Aznar-Lou***

*marina.fuente@sjd.es
**Ignacio.aznar@sjd.es

Introduction

The use of **Real-World Data** holds great potential for ***medication adherence research*** as a non-invasive and low-cost approach. However, ***data inconsistencies*** (such as missing or outliers) may challenge adherence assessment.

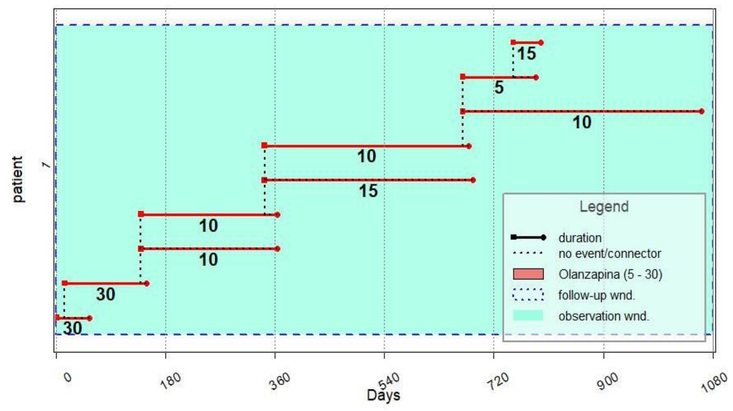
Antipsychotic (AP) treatments are complex. Frequent dose titration, combinations of APs and switching between APs result in ***complex prescription patterns,*** including:

- ↑ Number of overlapping prescriptions for the same patient and AP drug
- Coexistence of several doses within the overlapping prescription periods

What is the actual recommended dosing during these periods?

Would different assumptions affect adherence assessment?

Example of a patient's olanzapine prescription record



Objective

To assess the frequency of prescription periods with unclear recommended dosing and the **effect of four strategies** with several dosing assumptions on **adherence estimates** to antipsychotic treatments.

Methods

1 Patient identification criteria

Patients ≥ 18 years with ≥ 1 prescription of AP between 2015 and 2016 in a region of Catalonia, Spain.

Follow-up: 2015-2020

DB 1 - Prescription information

Prescription periods were grouped in Treatment Episodes (TE) by patient + AP active principle + AP dosage form.

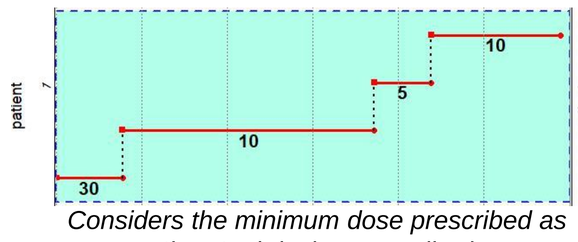
New TE - No registries for the same AP use in the previous 90 days

DB 2 - Dispensing information

2 Prescription data preparation strategies

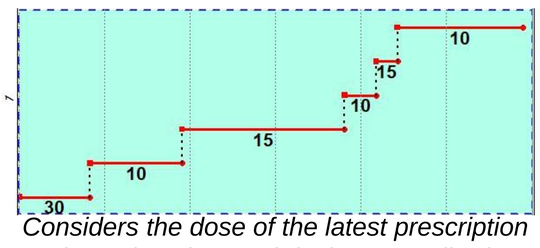
Proposed strategies for selecting the recommended dosing within overlapping prescription periods

The MINIMUM dosing assumption



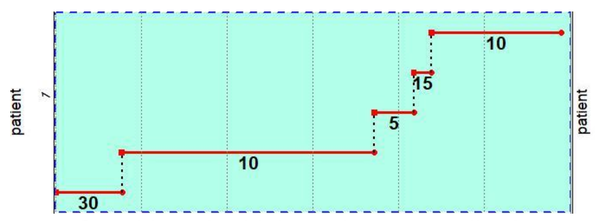
Considers the minimum dose prescribed as the atual dosing prescribed

The MOST RECENT dosing assumption



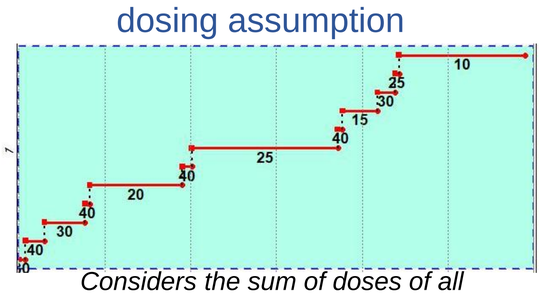
Considers the dose of the latest prescription issued as the atual dosing prescribed

The HIGHEST dosing assumption



Considers the highest dose prescribed as the atual dosing prescribed

The AGGREGATE dosing assumption



Considers the sum of doses of all prescriptions as the atual dosing prescribed

3 Study cohort

1st **new TE** identified per patient from 2016 that last ≥ 30 days

4 Adherence assessment

Observation Window (OW): up to 360 days.

Continuous Medication Availability - **CMA-7**

$$\frac{\textit{Proportion of days covered with medication in the OW}}{\textit{Total number of days in the OW}}$$

STATA 17

Results

Characteristics and CMA-7 estimates for patients and TE by prescription data preparation strategies

	MINIMUM				Most RECENT				HIGHEST				AGGREGATE			
	Patients		CMA-7		Patients		CMA-7		Patients		CMA-7		Patients		CMA-7	
	n	%	mean	SD	n	%	mean	SD	n	%	mean	SD	n	%	mean	SD
TE	**18,292**	100%	**60.2%**	0.38	**18,303**	100%	**59.9%**	0.38	**18,339**	100%	**59.5%**	0.38	**18,536**	100%	**57.1%**	0.37
Sex																
Male	8,419	46.0%	57.8%	0.38	8,423	46.0%	57.4%	0.38	8,443	46.0%	57.0%	0.38	8,527	46.0%	54.4%	0.37
Female	9,873	54.0%	62.3%	0.37	9,880	54.0%	61.9%	0.37	9,896	54.0%	61.6%	0.37	10,009	54.0%	59.3%	0.36
Age*																
< 65 years old	9,751	53.3%	55.4%	0.38	9,758	53.3%	55.1%	0.38	9,778	53.3%	54.7%	0.38	9,873	53.3%	52.2%	0.37
≥ 65 years old	8,541	46.7%	65.6%	0.36	8,545	46.7%	65.2%	0.36	8,561	46.7%	65.0%	0.36	8,663	46.7%	62.6%	0.35
Patients CMA-7 ≤ 10%	3,435	18.8%	-	-	3,450	18.8%	-	-	3,462	18.9%	-	-	3,555	19.2%	-	-
Patients CMA-7 ≥ 90%	6,581	36.0%	-	-	6,450	35.2%	-	-	6,354	34.6%	-	-	5,242	28.3%	-	-
Dosage form																
Oral-solid	15,669	85.7%	61.1%	0.38	15,681	85.7%	60.8%	0.38	15,718	85.7%	60.4%	0.38	15,912	85.8%	57.8%	0.37
Oral-liquid	2,141	11.7%	51.9%	0.37	2,140	11.7%	51.4%	0.37	2,140	11.7%	51.2%	0.37	2,144	11.6%	49.6%	0.36
LAI**	482	2.6%	68.0%	0.35	482	2.6%	67.8%	0.36	481	2.6%	67.8%	0.35	480	2.6%	65.9%	0.34
Polytherapy***	5,625	30.8%	-	-	5,576	30.5%	-	-	5,567	30.4%	-	-	5,585	30.1%	-	-
Therapeutic approach******																
Oral-Mono	12,553	68.6%	58.0%	0.38	12,553	68.6%	57.6%	0.38	12,599	68.7%	57.2%	0.38	12,776	68.9%	54.9%	0.37
LAI-Mono	174	1.0%	61.4%	0.38	174	1.0%	61.5%	0.38	173	0.9%	61.4%	0.38	175	0.9%	60.1%	0.37
Oral-Poly	4,822	26.4%	69.5%	0.32	4,830	26.4%	69.1%	0.31	4,820	26.3%	68.8%	0.32	4,836	26.1%	65.5%	0.31
Combined-Poly	743	4.1%	69.9%	0.29	746	4.1%	69.3%	0.3	747	4.1%	68.9%	0.3	749	4.0%	66.0%	0.3

Abbreviations: CMA-7, Continuous Medication Availability version 7; TE, treatment episode; LAI, Long-acting injectable

*At the start of the observation window. **AP drugs included as LAI: aripripazole, paliperidone, risperidone. *** Polytherapy: Concomitant AP during ≥ 30 days within the OW

**** Therapeutic approach: Oral monotherapy: 1 oral AP prescribed; LAI monotherapy: 1 LAI AP prescribed; Oral Polytherapy: ≥ 2 oral AP prescribed; Combined polytherapy: ≥ 2 AP prescribed being one a LAI

Conclusions

- Four data preparation strategies were proposed to account for the gradual increase in the recommended dosing when prescriptions overlap.
- The strategies described had a small effect on final adherence estimates.
- Considering the clinical setting and prescription practices The HIGHEST dosing assumption provided the most accurate estimate of adherence.

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