Poster #SA58

Approaches to Examine Treatment Adherence and Persistence Using German Claims Data – An Exemplary Analysis Using Oral Therapies for Prostate Cancer

Sophia Junker[1], Axel Dittmar[2], Sabrina Müller[2], Andreas Fuchs[3]

1. Cytel Inc., Potsdamer Straße 58, 10785 Berlin, Germany, 2. IPAM e.V., Alter Holzhafen 19, 23966 Wismar, Germany, 3. AOK PLUS, Sternplatz 7, 01058 Dresden, Germany

Treatment adherence and persistence analysis using claims data requires careful selection of analysis parameters depending on the research question, as they may exert a differential effect on outcomes. Nuanced consideration of applied methodologies is needed when interpreting results of such analyses.

Background/Objective

Different strategies have been described to identify treatment persistence and to determine the extent of treatment adherence based on claims data[1,2]. Several parameters, such as the definition of treatment discontinuation and the method of stock calculation, influence the calculation of treatment adherence and may be adjusted depending on the research question. This study investigated the effect of different parameters on the calculation of treatment persistence and adherence based on an example using oral novel hormonal agents (NHT) in prostate cancer (PC).

Methods

Using anonymized claims data from a statutory German sickness fund (AOK PLUS), male adult patients with PC followed by an incident NHT prescription, based on ATC codes, were identified in the period 01/01/2012-31/12/2020 (**Figure 1**) and followed up until 30/06/2022, death, or loss to follow-up. Persistence and adherence calculations were based on seven distinct parameters (**Table 1**). We altered one parameter at a time for a total of 16 scenarios. Non-persistence (NP) rates, time to discontinuation (TTD), % coverage, and non-adherence (NA) rates during persistent periods were analyzed for the first used NHT.

Table 1 definitions: coverage, period of time covered with medication by one or more prescriptions, basis for the calculation of persistent periods and % coverage within a time interval; **c.p.**, *ceteris paribus,* parameter as in base case; **d,** days; **DDD**, Daily Defined Dose as defined by the WHO and adjusted for Germany the WidO, used in the calculation of prescription coverage; **E.o.S.**, end of supply, calculated via DDD; **MPR**, medical possession ratio, measures the total supply of medication in possession over a specified period; **NA,** non-adherence; **PDC**, proportion of days covered, assesses the % of days a patient has medication available; **OPS**, operation and procedure code, hospital stays may only be considered covered by medication if an OPS code for the respective agent is documented; **stockpiling**, considers medication stock accumulated by prescription refills obtained ahead of schedule.

Table 1. Scenarios for the calculation of treatment adherence and persistence.

Parameter:	Min # prescript-tions	Coverage of 1 prescription	Stockpiling allowed	Method of % coverage calculation	% coverage truncation at 100%	Hospital coverage	Length of permissible gap for treatment discontinuation	Cut-off for defining NA
Relevant for:	Inclusion in calculation	Persistent period, % coverage	Persistent period	% coverage	% coverage	Persistent period, % coverage	Persistent period	% non-adherent
Base case	**1**	**DDD*1**	**Yes**	**PDC**	**No**	**Covered**	**45 d following E.o.S.**	**<80% coverage**
Scenario 1	**2**	c.p.	c.p.	c.p.	c.p.	c.p.	c.p.	c.p.
Scenario 2	c.p.	**DDD*0.5**	c.p.	c.p.	c.p.	c.p.	c.p.	c.p.
Scenario 3	c.p.	**DDD*2**	c.p.	c.p.	c.p.	c.p.	c.p.	c.p.
Scenario 4	**2**	**Individual**	c.p.	c.p.	c.p.	c.p.	c.p.	c.p.
Scenario 5	c.p.	c.p.	**No**	c.p.	c.p.	c.p.	c.p.	c.p.
Scenario 6	c.p.	c.p.	c.p.	**MPR**	c.p.	c.p.	c.p.	c.p.
Scenario 7	c.p.	c.p.	**No**	**MPR**	c.p.	c.p.	c.p.	c.p.
Scenario 8	c.p.	c.p.	c.p.	c.p.	**Yes**	c.p.	c.p.	c.p.
Scenario 9	c.p.	c.p.	c.p.	c.p.	c.p.	**OPS code**	c.p.	c.p.
Scenario 10	c.p.	c.p.	c.p.	c.p.	c.p.	c.p.	**30 d following E.o.S.**	c.p.
Scenario 11	c.p.	c.p.	c.p.	c.p.	c.p.	c.p.	**60 d following E.o.S.**	c.p.
Scenario 12	c.p.	c.p.	c.p.	c.p.	c.p.	c.p.	**60 d following last presc.**	c.p.
Scenario 13	c.p.	c.p.	c.p.	c.p.	c.p.	c.p.	**90 d following last presc.**	c.p.
Scenario 14	c.p.	c.p.	c.p.	c.p.	c.p.	c.p.	**180 d following last presc.**	c.p.
Scenario 15	c.p.	c.p.	c.p.	c.p.	c.p.	c.p.	c.p.	**<90% coverage**
Scenario 16	c.p.	**DDD*2**	c.p.	c.p.	c.p.	c.p.	**No permissible gap**	c.p.

Results

SAMPLE SELECTION

Of 52,437 individuals with PC, 3,438 had a prescription claim for an NHT and fulfilled all other selection criteria (**Figure 1**). The first received NHT was abiraterone (ABI) in 2,045 cases, enzalutamide (ENZ) in 1,265 cases, apalutamide (APA) in 124 cases, and darolutamide (DAR) in 4 cases (**Table 2**).

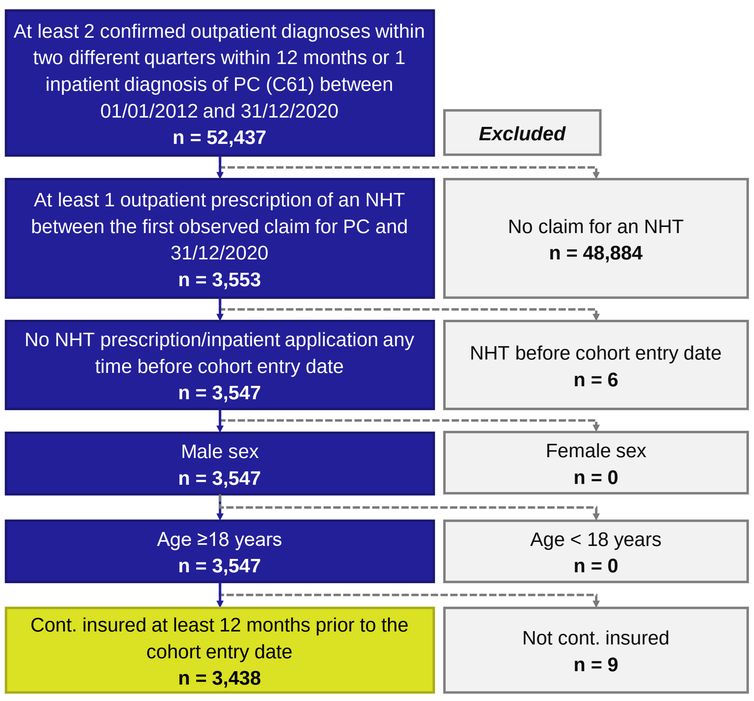

Figure 1. Attrition chart.

CHARACTERISTICS

The mean age among all included patients was 76.3 years, with a Charlson Comorbidity Index of 9.2 (**Table 2**). The most common comorbidity was hypertension (83.8%). Patients were observed for an average of 24.5 months.

ADHERENCE & PERSISTENCE OUTCOMES

The % of patients who displayed NP during the observational period varied between 30.1% and 65.9% across all NHTs (Scenario 3 [S3] and S9, respectively), while TTD ranged from 11.1 to 55.1 months (S12, S3). The average % of days covered with medication during the persistent periods ranged from 59.8% to 101.2% (S2, S16), translating into NA rates of 0.1% to 86.8% (S16, S2). Increases in the coverage of one prescription (i.e., DDD multiplied by a factor of 2) and extensions of the permissible gap for discontinuation calculation drastically reduced NP rates and led to a higher observed TTD (**Figure 2**). Mean % coverage was high in scenarios with high coverage of one prescription and low for scenarios with prolonged permissible gaps. Accordingly, the same scenarios had a differential effect on NA rates. Changes in the coverage calculation method (PDC/MPR) and consideration of stockpiling affected the % coverage to a different extent, depending on the type of NHT.

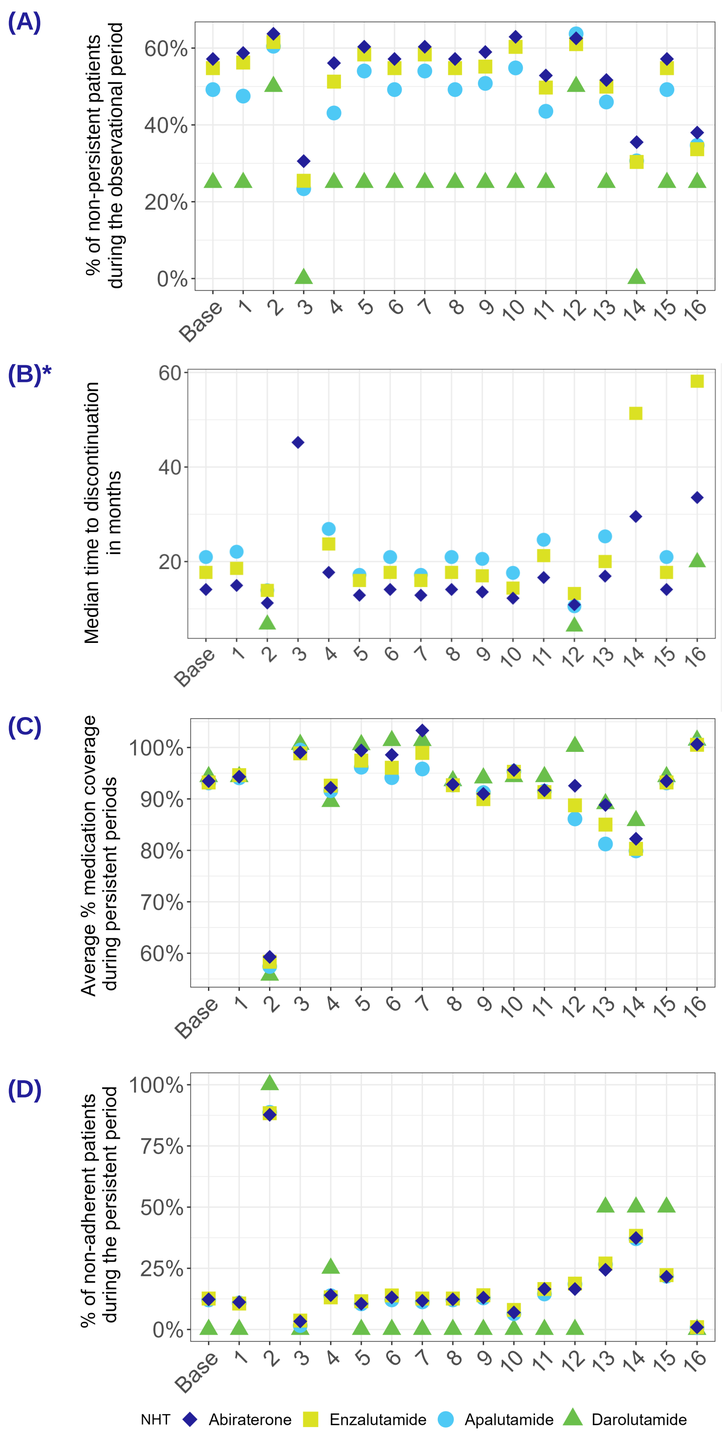

Figure 2. (A) % NP, (B) TTD, (C) Mean % coverage, and (D) % NA calculated based on the parameter definitions outlined in Table 1, among PC patients initiating an NHT.

NA, non-adherence; NHT, novel hormonal therapy; NP, non-persistence; PC, prostate cancer; TTD, time to discontinuation
* Missing values equal median TTD not reached.
Please note that values for darolutamide are based on 4 patients and are therefore not representative.

Table 2. Characteristics of patients with PC at the time of incident NHT prescription.

First NHT → Characteristic ↓	Abi-raterone n = 2,045	Enza-lutamide n = 1,265	Apa-lutamide n = 124	Daro-lutamide n = 4	Overall n = 3,438
Age					
Mean (SD)	75.8 (8.4)	77.2 (8.2)	75.8 (9.7)	80.5 (6.8)	76.3 (8.4)
Median [min, max]	77 [44, 99]	78 [35, 99]	78 [48, 93]	82 [71, 87]	77 [35, 99]
CCI					
Mean (SD)	9.4 (3.4)	9.0 (3.5)	7.3 (3.5)	7.0 (2.9)	9.2 (3.5)
Median [min, max]	10 [2, 20]	9 [2, 19]	8 [2, 14]	8 [3, 10]	9 [2, 20]
Top-3 comorbidities*					
I10 Hypertension	1,710 (83.6%)	1,063 (84.0%)	104 (83.9%)	3 (75.0%)	2,880 (83.8%)
C79 Secondary malignant neoplasm	1,422 (69.5%)	729 (57.6%)	45 (36.3%)	0 (0.0%)	2,196 (63.9%)
E78 Lipidemias	1,009 (49.3%)	649 (51.3%)	58 (46.8%)	2 (50.0%)	1,718 (50.0%)
Follow-up time (months)†					
Mean (SD)	24.1 (20.1)	25.4 (18.2)	22.0 (7.6)	16.2 (6.8)	24.5 (19.1)
Median [min, max]	20 [0, 112]	22 [0, 99]	22 [2, 40]	19 [6, 21]	20 [0, 122]

CCI, Charlson Comorbidity Index based on Chae et al. 2013, not adjusted for age[3].
* Top-3 comorbidities in the overall cohort. † Follow-up time calculated from incident NHT prescription to death, end of insurance, or end of observational period.

Conclusions

- This study portrays the effect of specific parameters on NP and NA outcomes, which varied widely depending on the altered-parameter scenario. The extent to which analyzed NA and NP outcomes fluctuate between investigated agents can vary depending on the chosen parameters.
- Accordingly, treatment adherence and persistence analysis using claims data requires careful selection of analysis parameters depending on the research question, and nuanced consideration of applied methodologies is needed when interpreting results of adherence/persistence analyses.
- While this study investigated the effects of methodological changes on NA and NP outcomes of individual agents, defining NA of combination therapies using prescription data poses an additional challenge[4].

LIMITATIONS

The prescribed dosage of a medication is not documented in claims data. Accordingly, assumptions about the days covered by a prescription will over-/underestimate the true prescription coverage for included patients. This analysis aims to showcase the effect of parameter changes on NA/NP outcomes and should not be used to compare NA/NP between included NHTs. The analysis for darolutamide was based on a very small sample and thus, the reliability of results for this subsample is limited.

References

1. Wilke, T., Groth, A., Mueller, S. et al. How to use pharmacy claims data to measure patient nonadherence? The example of oral diabetics in therapy of type 2 diabetes mellitus. Eur J Health Econ 14, 551–568 (2013). https://doi.org/10.1007/s10198-012-0410-y; **2.** Ihle, P., Krueger, K., Schubert, I., Griese-Mammen, N., Parrau, N., Laufs, U. and Schulz, M. (2019), Comparison of Different Strategies to Measure Medication Adherence via Claims Data in Patients With Chronic Heart Failure. Clin. Pharmacol. Ther., 106: 211-218. https://doi.org/10.1002/cpt.1378; **3.** Chae, J.W., C.S. Song, H. Kim, K.B. Lee, B.S. Seo, D.I. Kim, Prediction of mortality in patients undergoing maintenance hemodialysis by Charlson Comorbidity Index using ICD-10 database. Nephron Clin Pract, 2011. 117(4): p. c379-84; **4.** Alfian, S.D., Pradipta, I.S., Hak, E., Denig, P. (2019), A systematic review of measures estimates adherence and persistence to multiple medications. J Clin Epidemiol, 108, pp. 44-53, 10.1016/j.jclinepi.2018.12.003

Disclosures

SJ is an employee of Cytel Inc. and has no conflicts of interest to declare. AD and SM participated in this study as members of IPAM e.V. and have nothing to declare. AF works for a statutory insurance fund (AOK PLUS), which provided the data used in this study.

Contact information

sophia.junker@cytel.com

www.cytel.com

IPAM INSTITUT FÜR PHARMAKOÖKONOMIE UND ARZNEIMITTELLOGISTIK AN-INSTITUT DER HOCHSCHULE WISMAR

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Contact information: www.cytel.com

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