The patients’ adherence pattern, considering the regular filling of their prescribed therapy, is a key factor of therapeutically effectiveness of medication treatments, applied in case of chronic diseases. The therapy effectiveness, increased in course of appropriate patient-adherence, may grant direct or indirect advantages for all stakeholders of the health care system. These advantages may occur from the patients’ aspect in the positive changes in the disease status, just as in the medication cost or in other operational costs, avoided costs from the financial perspective in the cost burden of avoided episodes, from the manufacturers’ point of view in the increased brand loyalty and higher sales indicators. The extent of medication adherence can be measured in course of the analysis of part share of medication therapy covered period within a given time interval. [1].

In international practice it can be observed in general, that 80% or over therapy-covered period ratio is mentioned by professionals as adequate adherence pattern and the patients’ individual indicators are compared to this threshold value. [2] Regarding adherence analysis numerous ratios can be found in international scientific literature with simpler or more complex methodology. In our analysis we tend to reveal, that choosing an adequate ratio is not sufficient, because we are facing a set of pitfalls of the data management and methodology in the objective assessment of the chosen ratio. The chief aim of our study to demonstrate factors in course of practical examples in three indication areas, which may substantially influence the results and the right conclusions, if these factors are modified.

**Methods**

The adherence analysis is based on prescription filling data of database of the Hungarian Health Fund in the field of the following indications: diabetes, COPD, prostate cancer. Drug medications are not available in the database, so the 100% full fill ratio results to the adherence ratio in 2013 from the reimbursed pharmacy agents in case of an ultra-long-acting beta-adrenocceptor agent (indacaterol) in COPD, in case of a GLP-1 agent (exenatide) in diabetes, and in case of a CRH agent (goserelin) in prostate cancer. From the ratios available in scientific literature, the methodology PDC (Proportion of Days Covered) was chosen as a basis, which is such a ratio, which compares the number of therapy-covered days to the days that can be spent theoretically in therapy in a given period: [3, 4]. The PDC ratio is ranging between 0 and 1, where 1 means complete therapy coverage. In course of the indications a basic setting was established to calculate PDC ratio, then after changing each specified parameter or adding or dropping one criterion, the ratio was recalculated.

In course of the basic setting, number of therapy-covered days, then the PDC ratio of the patients were determined as follows. We examined the blood analysis dates (second period, whether it was covered by filed DDD (Days Therapy) or not. If yes, the given day was considered as a therapy-covered day. If not, the given day was not considered as a day spent on therapy. The DDDs were set as a basis for the calculation. In case of a PDC of 1 it means, that the unit from products belonging to a given agent were filled (same day filled), then the DDD values were considered as additive.

In case of a PDC if another refilling was observed yet within the period covered by the first filled (“monotherapy”), then the part of the therapy vector (the length of the therapy covered period based on the filled DDD of the first filled) was considered.

In course of the modified settings considering indacaterol (Figure 1.), the therapy coverage was examined only in case of new patients in 2013 (no indicaterol filled observed in 2012), the index period was from the period first fill + 364 days (or death, if it occurred within the 364 days). It is displayed on Figure 1., that more than 22% point difference can be observed between the two median PDC ratios calculated by the two approaches, in case of basic setting the PDC ratio is close to 60%, while with the modified setting it is 33.1%. The chief cause of the difference, that the new patients starting indacaterol therapy in the second half of 2013 have less theoretically chance to drop out or switch off until the end of the index period, thus they pull up aggregated median value. The result calculated based on the modified parameter reflects the practical and real therapy coverage ratio better compared to the basic setting, based on the results implementation of this modification in course of calculation PDC ratio is adequate. In course of examination of the first filled, which overlapped the second filled, was truncated. Therapy-length of each patient is the sum of days covered by therapy. As it is a real phenomenon in practice that the patients’ next fill occurs after the end of the therapy vector of the previous fill some days later, we allowed a 1-day grace period (furthermore Gap). According to the applied Gap, if a fill occurred within 1 day after the end of the previous therapy vector, the therapy was considered as continuous. In course of the study we applied a dynamic approach, thus both the beginning and the end of the index period was considered, if it was needed. In case of a new patient (who appears later than the first day of the period, for instance 01.01.2013), only the number of days that can be spent theoretically on the therapy are considered in the denominator of PDC ratio instead of the whole period. In the same way, in case of death within the index period, also only the number of days that can be spent theoretically on the therapy are considered in the denominator instead of the whole period, thus number of days between death and index date is excluded from the value of the denominator. After the calculation if the patients’ individual PDC ratio, the median value of the ratio is applied from the descriptive statistical indicators.

In case of settings different from the basic setting the following parameters we examined as influencing factors: in case of COPD the patient inclusion and exclusion criteria (364-day PDC ratio calculated from first fill of new patients in 2013); in case of diabetes the Gap (15-day, 30-day and 60-day grace period); in case of prostate cancer the mortality (no censor applied in case of death). In course of the analysis the PDC ratio was calculated based on SPC DDD values in each case.

**Results**

(Figure 2.) the grace period was modified, the strict 1 day value based on the basic setting was eased to 15, 30 and 60 days. The PDC ratio resulted a value above 80% in case of the basic setting, by softening the Gap with 15, 30 and 60days the ratio increased to 85% and 90%, then reached the 100% median value. Modifying the Gap we eased the strictness requirements, it is worth determining the level of strictness based on the specificities and characteristics of the indication area in course of PDC calculation. In case of prostate cancer (Figure 3.) the mortality parameter was modified, if a patient died within the index period, then neither the part of the therapy vector overlapping after death (nominator), nor the period between death and the end of index period (denominator) was truncated. Based on the results the mortality as a parameter should be managed in course of PDC calculation, concerning the time period after death is required in course of calculation both numerator and denominator. [6]

**Conclusions**

In course of the study it was proven, that value of the chosen PDC ratio is influenced by several parameters, and the ratio can not be compared to sensitivity of three parameters, both analysis can be achieved with the same analogy in course of the other parameters. In order to draw conclusions based on the results as correct as possible, if the parameters, influencing the adherence are set properly and consistently in accordance with the aim of the study and characteristics of the problem it is easier to be measured. This is one of the reasons for the effort of evaluating results of comparative studies. For instance comparing the results of studies with the same methodology (or even the same parameter setting), but concerning different therapeutic areas, or even comparing results concerning the same therapeutic area or a given agent, but from studies with different methodology.

**References**


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