Individual Patterns of Objectively Measured Adherence to Growth Hormone Treatment and its Effect on Growth in Prepubertal Children with Growth Hormone Deficiency

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INTRODUCTION

- The easypod™ electromechanical injection device works in combination with the easypod Connect platform (EPC) to record and transmit real time data based on the time, date and dose of Growth Hormone (GH) injections, for patients with growth disorders receiving GH treatment. This limits the risk of misreporting and allows physicians to accurately monitor patient behavior relating to adherence to treatment.

OBJECTIVES

- To study individual patterns of adherence from start of treatment to 24 months and their effect on growth in prepubertal children with growth hormone deficiency (GHD).

METHODS

- Data on adherence (=100% x number of injections taken/number of injections prescribed) and growth uploaded to the easypod Connect platform or collected by the Easypod Connect Observational Study (ECOS; a 5-year, Phase IV open-label study) were included.[1,2]
- Inclusion criteria for both adherence and growth were age before onset of puberty (<10 years in girls and <12 years in boys). Additional inclusion criteria for growth were GHD and naïve to GH treatment (ECOS study).
- Latent class mixed models (LCMM) is a model-based clustering and classification technique applied in a wide range of fields including machine learning.
- In our study, LCMM were applied with longitudinal adherence as outcome and time and centered time squared in the model. This model groups the patients into classes based on their individual adherence pattern over time.
- Descriptive statistics for the adherence classes were provided in three categories (low ≤56%, medium >56–<85%, high ≥85%).[3]
- Linear regression analyses were performed to compare change in height standard deviation score (HSDS) between adherence classes from start of treatment up to 6–24 months. Figure 1.

RESULTS

Figure 1. Data sources for analysis
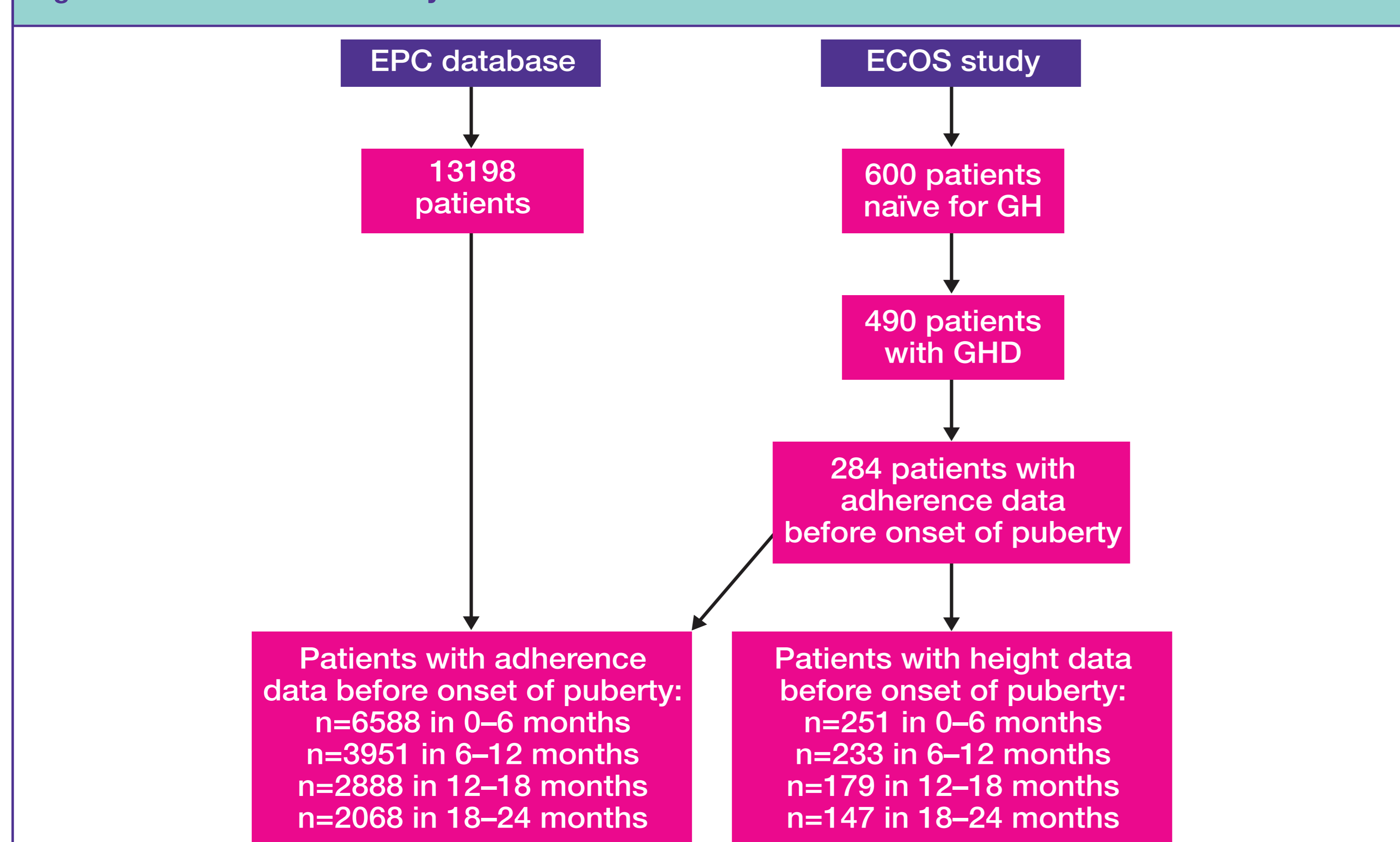
ECOS, easypod Connect Observational Study; EPC, easypod Connect; GHD, growth hormone deficiency

REFERENCES

1. Koledova E, et al. *Endocr Connect*. 2018;7(8):914-923.
2. van Dommelen P, et al. *PLoS One*. 2018;13(10):e0206009.
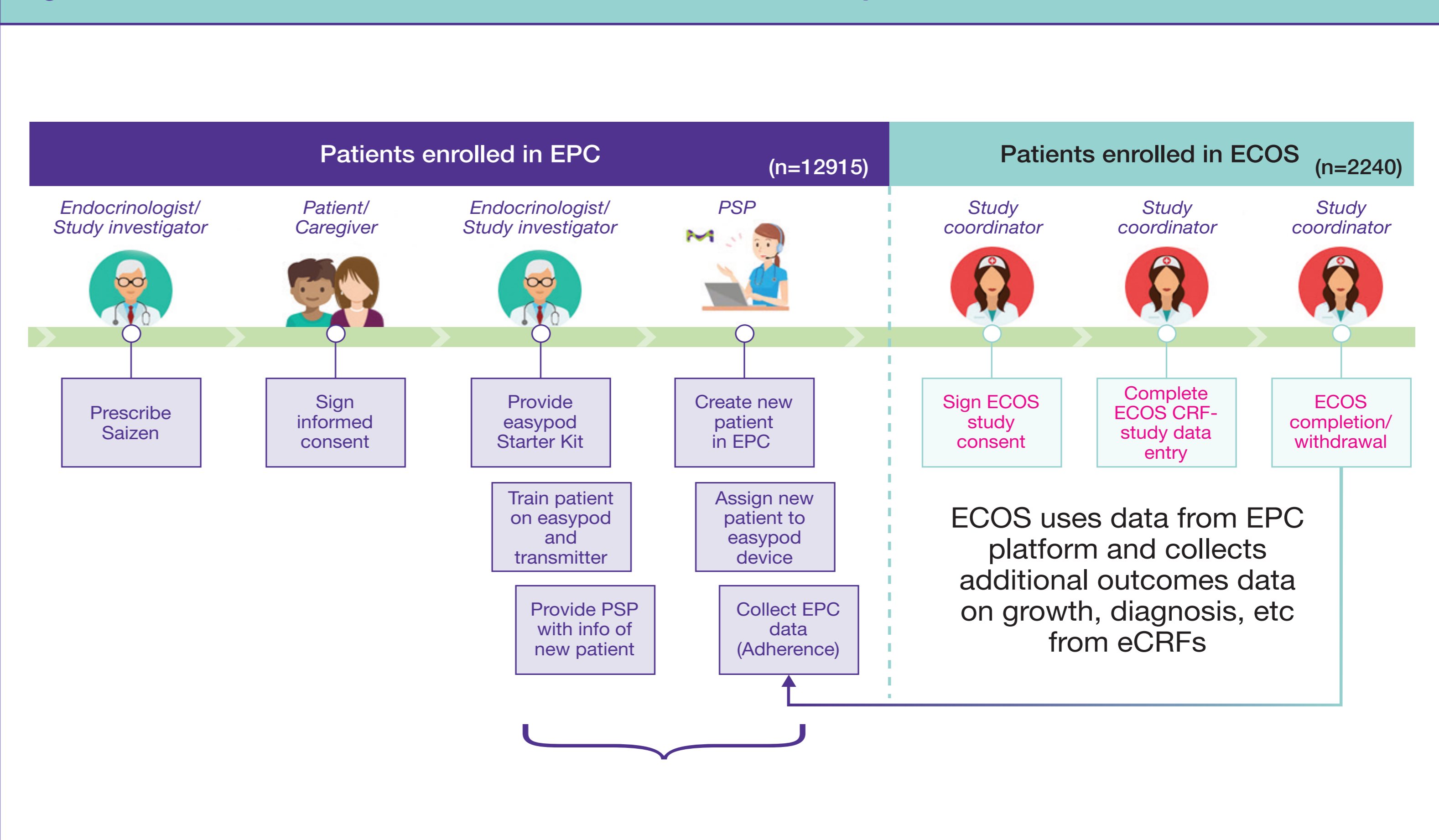3. Cutfield WS, et al. *PLoS One*. 2011;6:e16223.

ACKNOWLEDGMENTS

DISCLOSURES

PvD is an advisor to Merck KGaA. JMW is a member of advisory boards of Merck KGaA, OPKO, Biomarin, Aeterna Zentaris, Ammonett and Agios. EK is an employee of Merck KGaA.
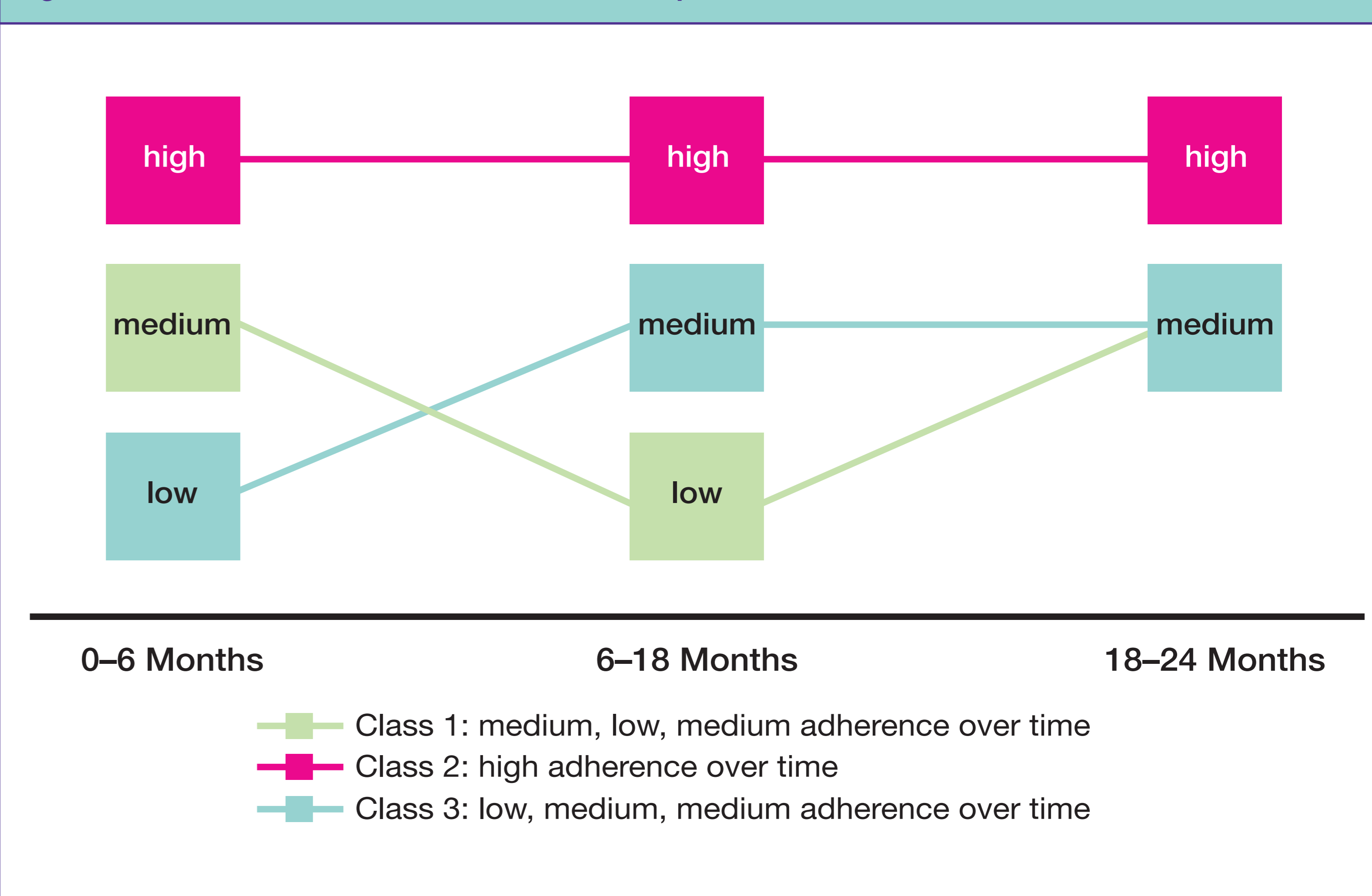
Figure 2. Patient flows in the EPC database and the ECOS study

eCRF, electronic clinical report form; EPC, easypod Connect; ECOS, easypod Connect Observational Study; PSP, patient support program

- We applied LCMM to patients enrolled in EPC database to group patients into classes based on their individual adherence pattern over time. Three classes were constructed. Figure 3.

Figure 3. Classes constructed based on adherence patterns

Class 1: medium, low, medium adherence over time
Class 2: high adherence over time
Class 3: low, medium, medium adherence over time

- Class 1 (n=342) had on average medium adherence between 0–6 months, low adherence between 6–18 months and medium adherence between 18–24 months. Class 2 (n=5968) maintained a high adherence. Class 3 (n=278) had on average low adherence between 0–6 months, and adherence consistently increased to medium adherence at 18–24 months.
- Significant differences in change in HSDS between 0–18 months (change HSDS= -0.52, p=0.002) and 0–24 months (change HSDS= -0.45, p=0.03) were found in class 1 (medium 0–6 months, low 6–18 months and then medium 18–24 months adherence) compared to class 2 (high adherence between 0–24 months). No other significant differences were found.

CONCLUSIONS

- **This is the first time that a clustering and classification technique has been applied to analyze the data collected in ECOS and EPC with adherence profiles and assessment of outcomes.**
- **Our study shows that monitoring patterns of adherence over time is important, because poor adherence, especially between 6 and 18 months after start of treatment, can lead to suboptimal clinical outcomes.**
- **The traditional approach to monitoring adherence is generally based on self-reported data, which is prone to recall and social desirability bias. New eHealth-based ecosystems with automatic adherence recording and data transmissions, such as the easypod™ connect system, allow proactive close monitoring of adherence, which may improve adherence and subsequent outcomes.**

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