

# Side-EFFECTS and ETI-Treatment: a multidisciplinary challenge

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# Conflicts of interest disclosure

- I have no conflicts of interest that relate to this presentation.

## BACKGROUND

- Belgium: ETI reimbursed:
  - >12 years: September 2022
- Side-effects: management guidelines were and are scarce

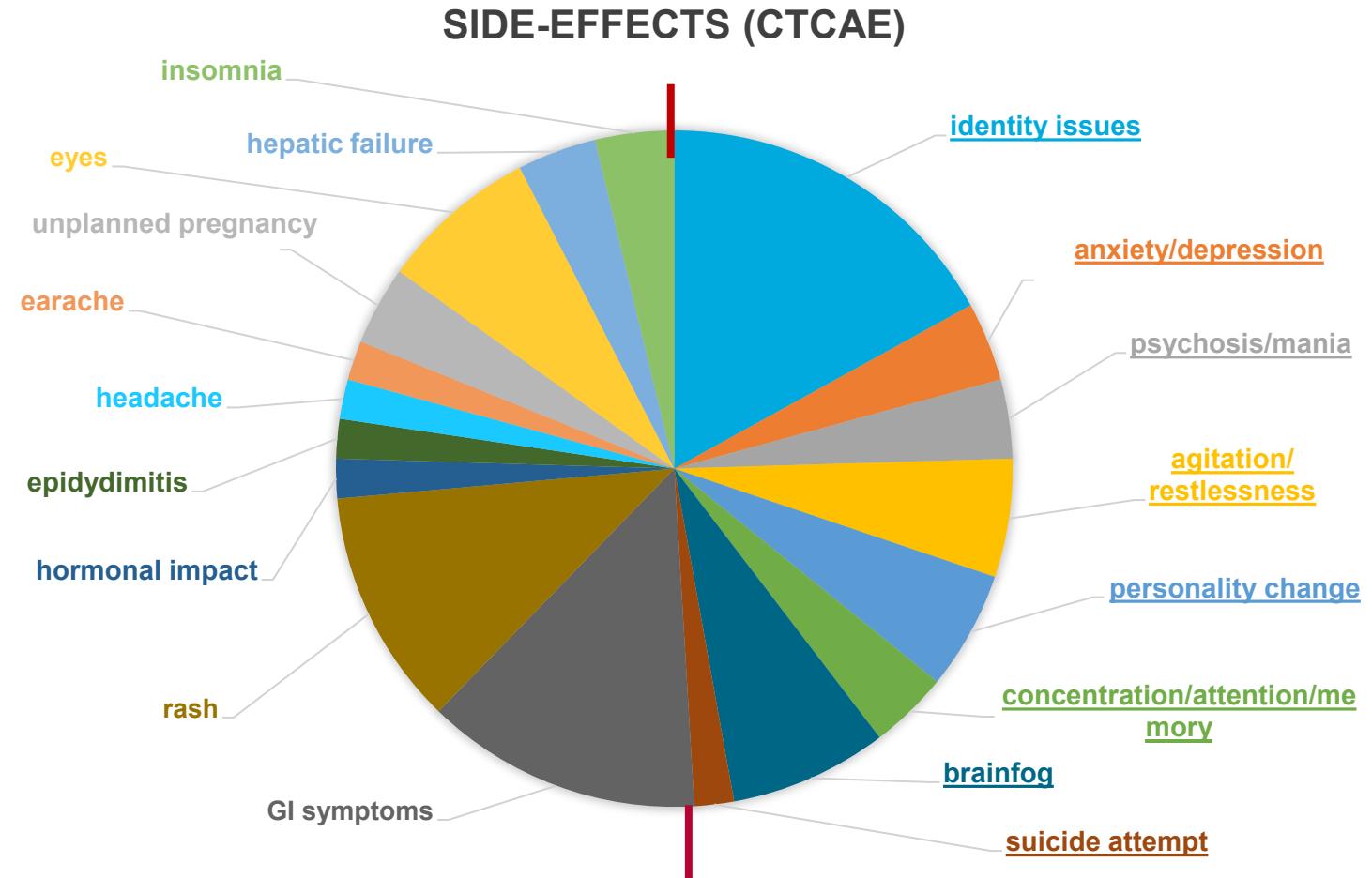
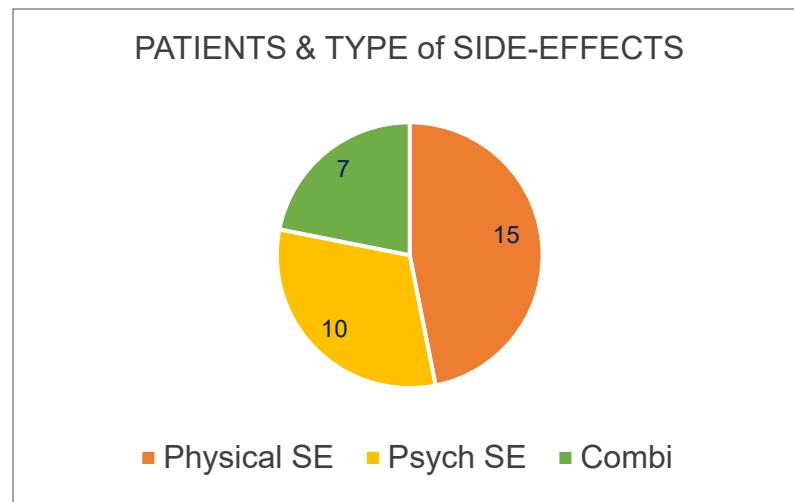
## AIMS

- Identify treatment schedules for patients with physical and/or psychological side-effects

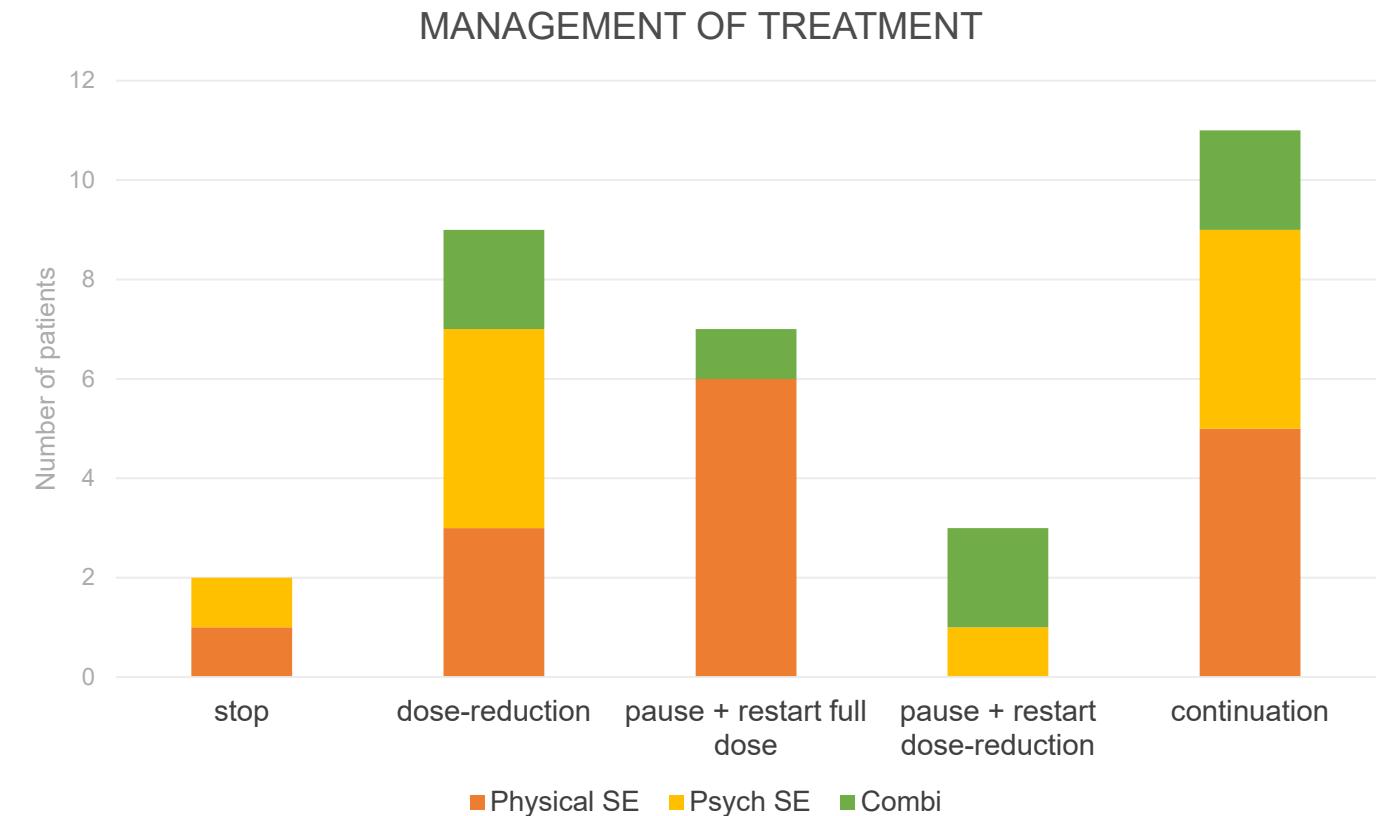


- Single center retrospective study
- Side-effects & changes in treatments: recorded over 1 year (01/09/2022-01/09/2023),
- Classified using Common Terminology Criteria for Adverse Events (CTCAE)
- Patients: short Mental Health Side-Effects Checklist (Graziano & Quittner)  
*(Headache, Sleep problems, Weight gain, Brain Fog, Mood, Anxiety, Concentration Problems)*

- 120 adult patients started ETI
- 32 patients → 53 side-effects



- Multiple medication schedules > individual approach
- Psychotropic medication (e.g. *anxiolytic, antidepressant, benzodiazepine*)
- Multidisciplinary follow-up
- Sweat test as pharmacodynamic parameter (3 cases)





# Casus monitoring sweat-chloride

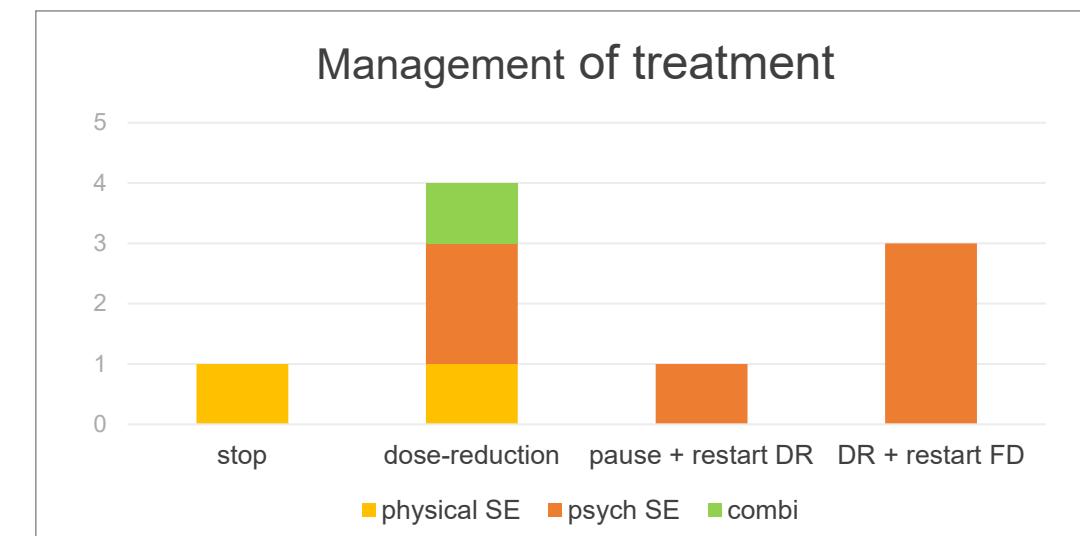
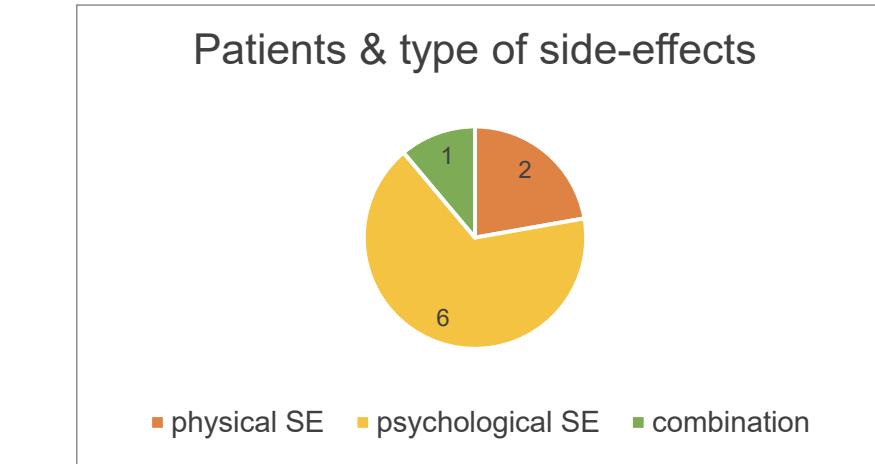
	Before ETI		Full dose ETI		Dose-adjustment 1		Dose-adjustement 2	
	Sweat Cl <sup>-</sup> (mmol/l)	FEV1%	Sweat Cl <sup>-</sup> (mmol/l)	FEV1%	Sweat Cl <sup>-</sup> (mmol/l)	FEV1%	Sweat Cl <sup>-</sup> (mmol/l)	FEV1%
Casus 1	111	85	37 (03/2023)	92	1 tabl Kaftrio daily no kalydeco (04/2024)		1 tabl Kaftrio / 2 days no kalydeco (04/2025)	
					26	91	33	95
Casus 2	116	74	40 (05/2023)	86	1 tabl Kaftrio daily no kalydeco (07/2023)		Full dose (02/2024)	
					66	91	23	89
Casus 3	104  (90 – symdeko)	70  83	? (only 10 days)		1 tabl Kaftrio daily (evening) no kalydeco (03/2023)		2 tabl Kaftrio Mon-Wed-Fri 1 tabl Kaftrio Tue-Thu-Sat-Sun no kalydeco (05/2023)	
					71,6	100	56	98



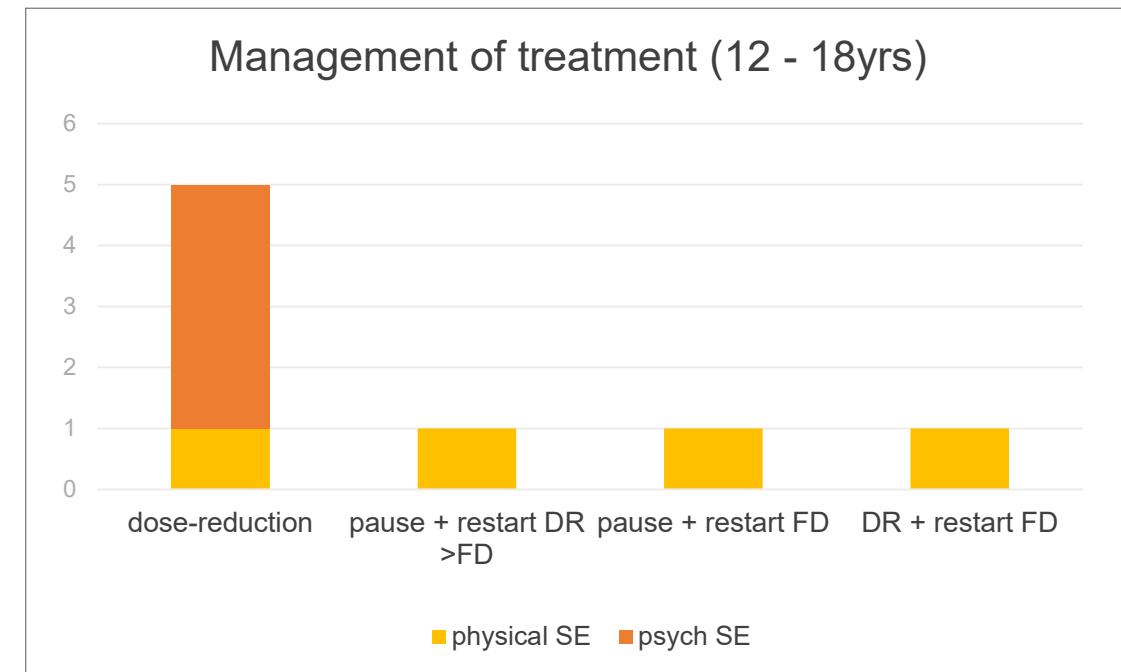
- A wide range of physical and psychological side-effects were observed, fluctuating in frequency, intensity, impact, ...
- Resulting in a wide variety of treatment adaptations,
- needing intense follow up
- Treatment optimization = a multidisciplinary challenge
- Liaison with psychiatric services was crucial for severe psychological side-effects

- Belgium: ETI reimbursed:
  - 6-12 years: February 2023
  - 2-6 years: February 2025
- Monitoring side-effects by doctors, nurses, psychologist, ... added to recommended mental health screening program
- Short Mental Health Side-Effects Checklist (Graziano & Quittner)
  - 1x year
  - observations of mental or physical problems
  - weekly, if needed or in case of dose adjustment
- Clinical individual follow-up
- Sweat test

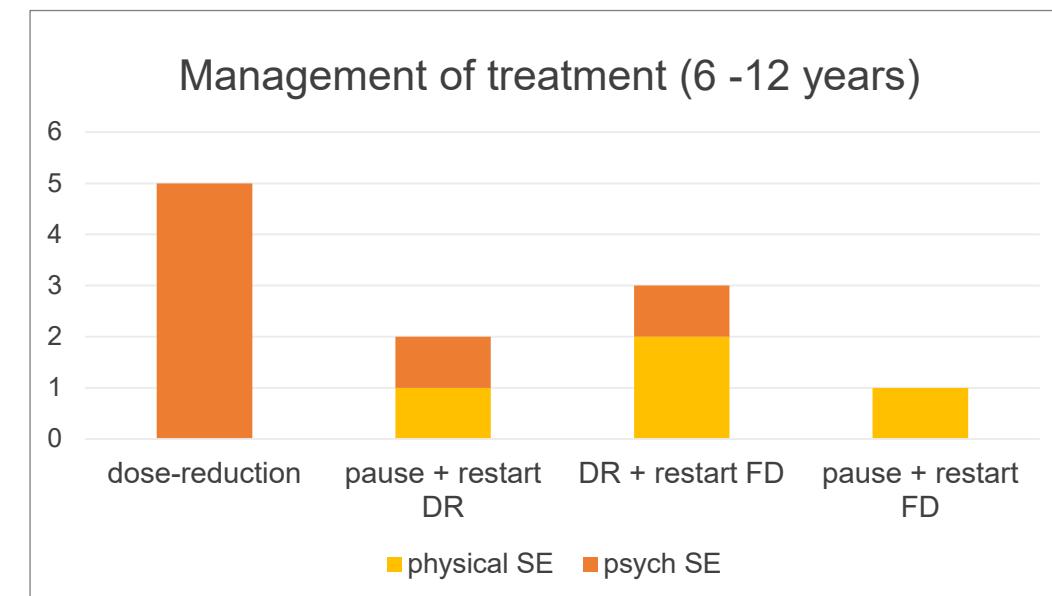
- n=9 > 4 physical SE, 7 psych SE
- Physical SE: headache, sleep, weight, hungry
- Psych SE: identity, anxiety/depression, concentration, brainfog, personality change
- Side-effects: 12-24 months after start ETI



- 40 patients, 12-18 years, started ETI
- 9 patients → side-effects:
  - 4 physical SE: rash, headache, insomnia/nightmares
  - 5 psychological SE: personality change, concentration
- Time after start ETI
  - Rash, headache: immediately
  - Others: 14 – 30 months after start ETI



- 31 patients, 6-12 years, dose= weight-related
- 11 patients → side-effects:
  - 4 physical SE: hepatic failure, headache, insomnia
  - 7 psychological SE: behavioural change, concentration, agitation
- Time after start ETI
  - Rash, headache: immediately
  - Others: 6 – 20 months after start ETI





	Before ETI		Full dose ETI		Dose-adjustment 1		Dose-adjustement 2	
	Sweat Cl <sup>-</sup> (mmol/l)	FEV1%	Sweat Cl <sup>-</sup> (mmol/l)	FEV1%	Sweat Cl <sup>-</sup> (mmol/l)	FEV1%	Sweat Cl <sup>-</sup> (mmol/l)	FEV1%
Casus 1 10 years	103  (96 – orkambi)	103  110	47,5  (03/2023)	120	02/2024: stop  03/2024: restart 1 tabl kaftrio daily no kalydeco		10/2024:  1 tabl kaftrio daily 20u start 1 tabl kalydeco daily 8u	
					65	120	?	117
Casus 2 9 years	104	75  (92 – orkambi)	38	113	02/2024  1 tabl kaftrio 1 tabl kalydeco			
					50	119		

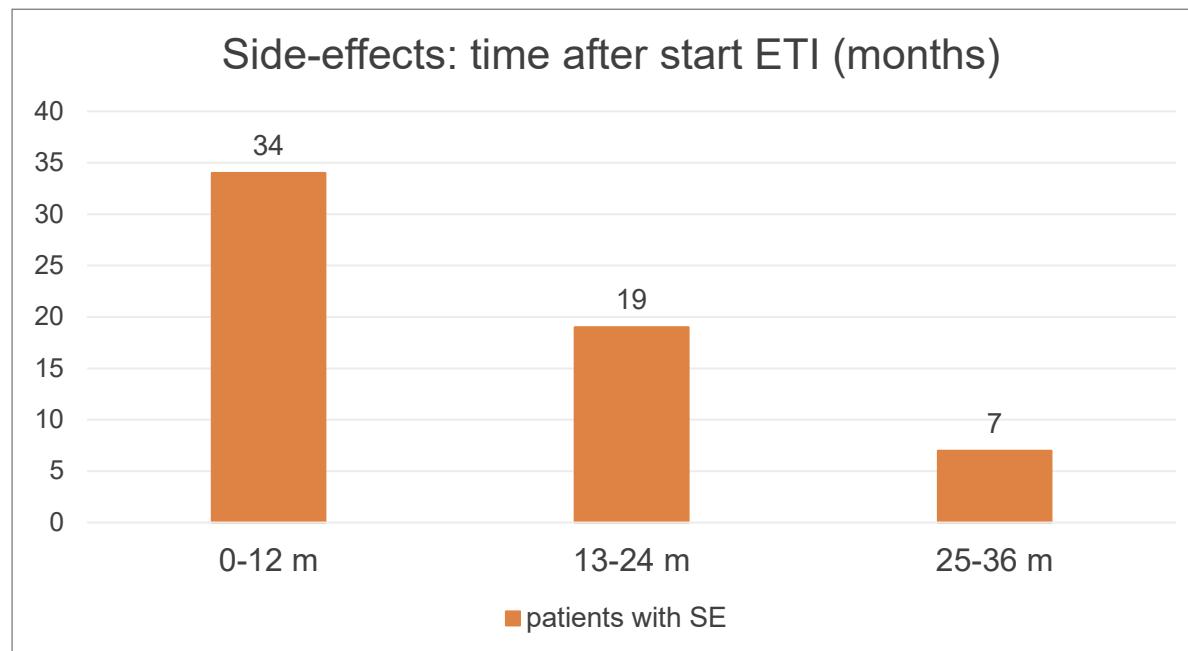
- 13 patients, 2 – 5 years, dose= weight-related
- 4 patients → side-effects (reported by parents):
  - 2 physical SE: GI-symptoms, insomnia, sleeping problems
  - 2 psychological SE: behavioural problems
- Management:
  - Dose-reduction (n=3)
  - Pause + restart dose-reduction (n =1)

## Adults

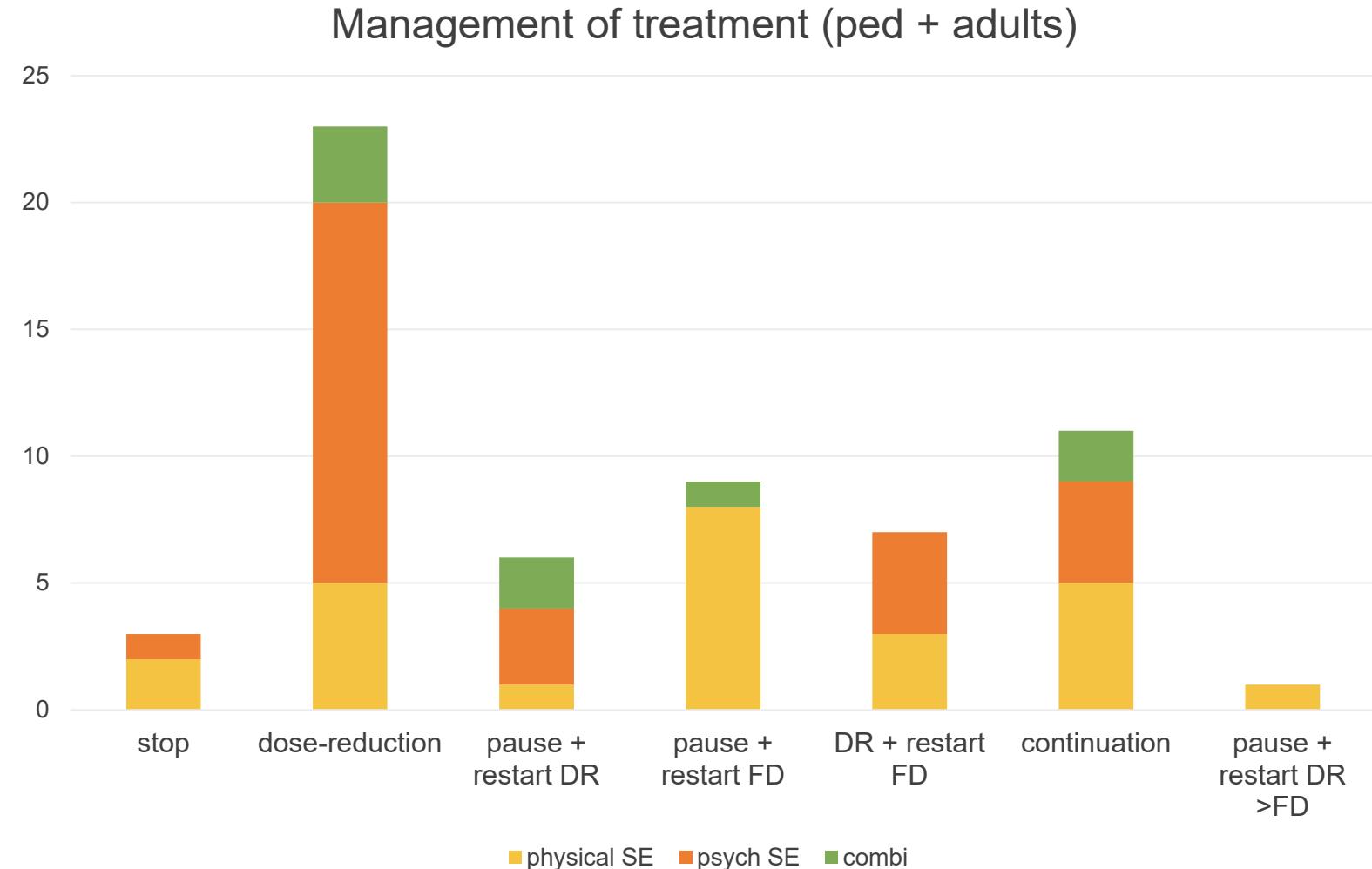
- 120 patients started ETI
- 41 patients > side-effects

## Pediatric

- 84 patients started ETI
- 24 patients > side-effects



- Trial and error
- Follow-up
- Therapeutic drug monitoring?



# Conclusion

- Side-effects > in adults and pediatric patients
- Stay alert, even after 1 or 2 years ETI
- Dose-adjustment often needed
- Needing intense follow up > checklist is helpful for both patient/parents and team
- Treatment optimization = a multidisciplinary challenge
- Liaison with psychiatric services is crucial for severe psychological side-effects, also for pediatric population.
- Future: therapeutic drug monitoring?

