

Side-EFFECTS and ETI-Treatment: a multidisciplinary challenge

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Conflicts of interest disclosure

- X 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

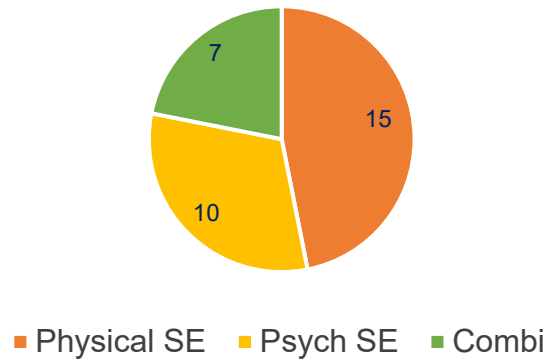
- Identify treatment schedules for patients with physical and/or psychological side-effects



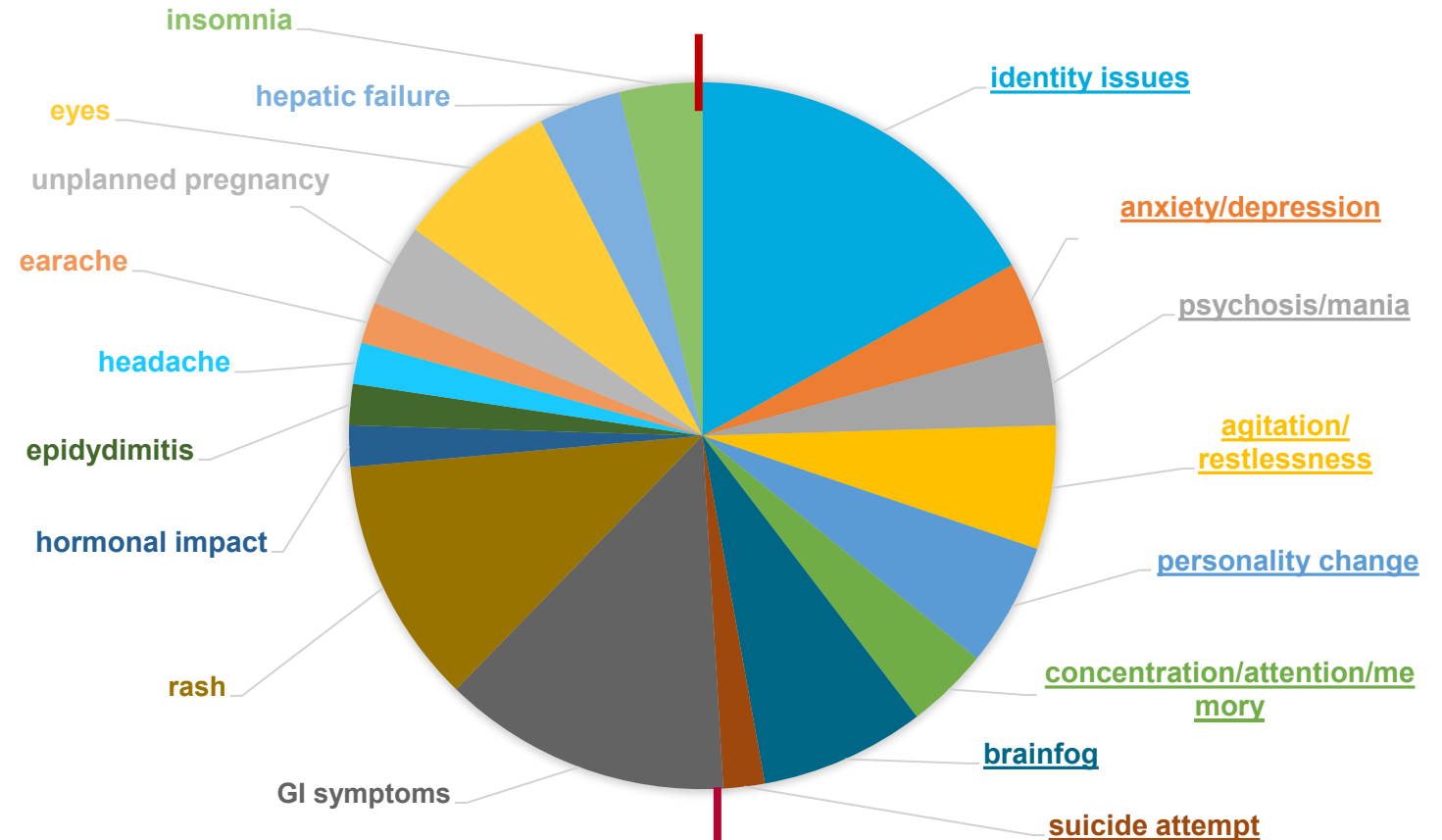
- Single center retrospective study
- Side-effects & changes in treatments: recorded over 1 year (01/09/2022-01/09/2023),
- Classified using Common Terminology Criteria for Adverse Events (CTCAE)
- Patients: short Mental Health Side-Effects Checklist (Graziano & Quittner)
(Headache, Sleep problems, Weight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

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

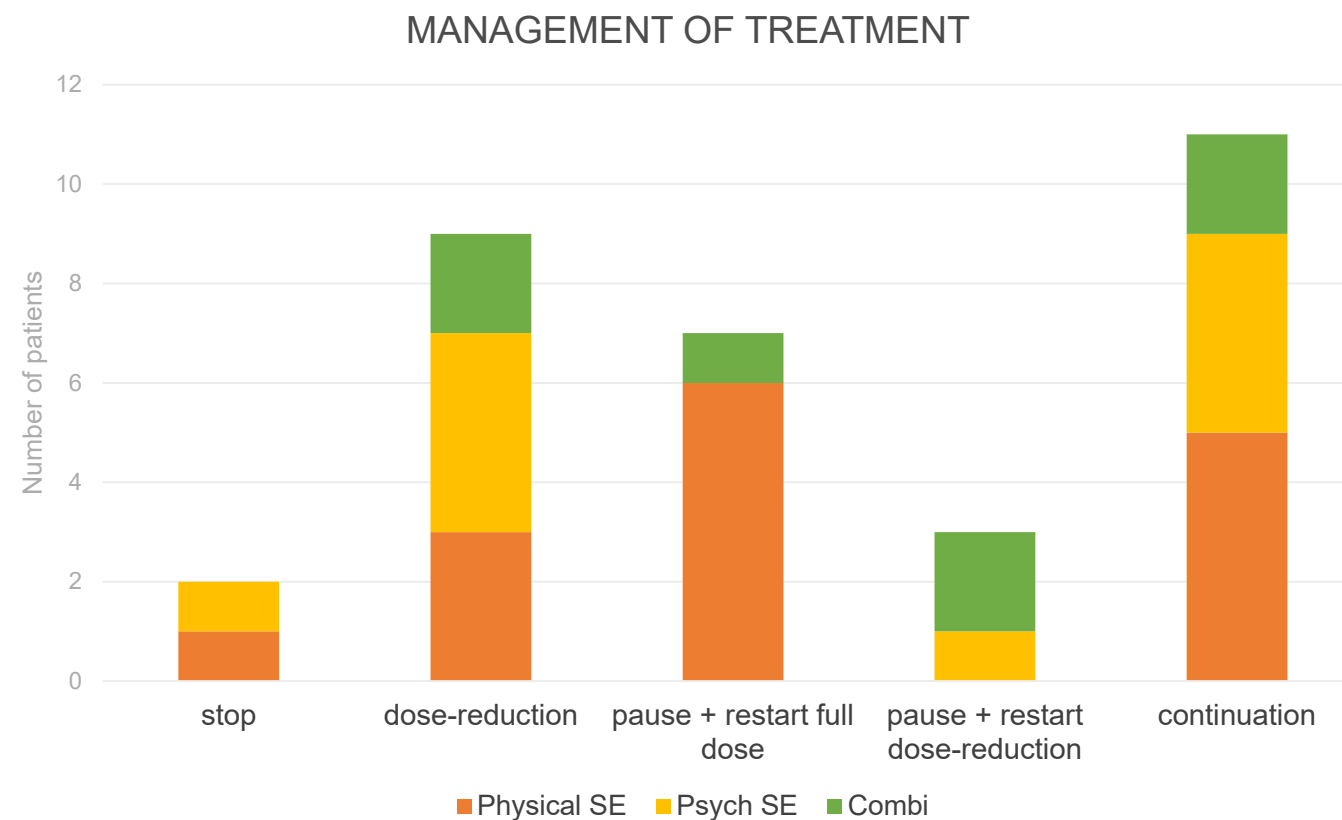
PATIENTS & TYPE of SIDE-EFFECTS



SIDE-EFFECTS (CTCAE)



- 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 ⁻ (mmol/l)	FEV1%	Sweat Cl ⁻ (mmol/l)	FEV1%	Sweat Cl ⁻ (mmol/l)	FEV1%	Sweat Cl ⁻ (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-Son no kalydeco (05/2023)	
					71,6	100	56	98

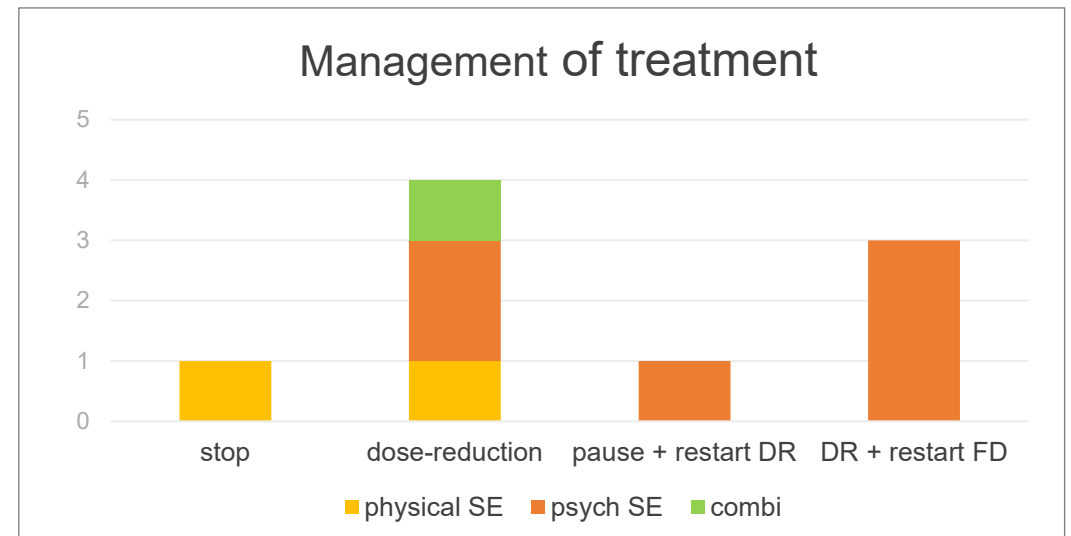
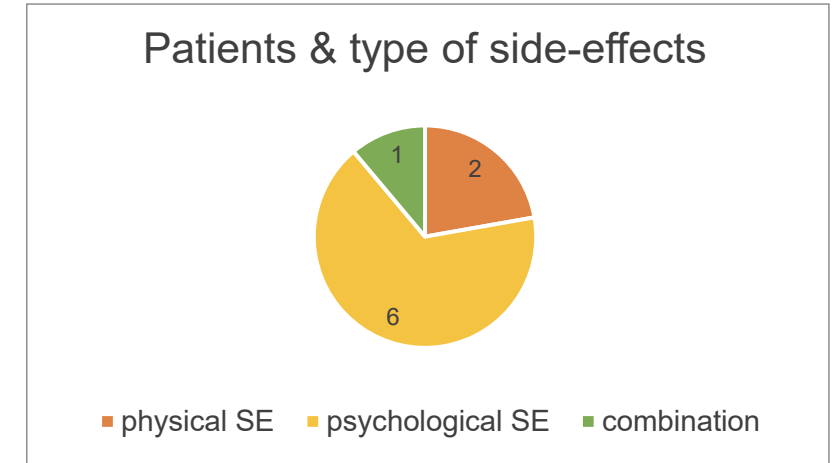


Conclusion after 1 year treatment (09/2023)

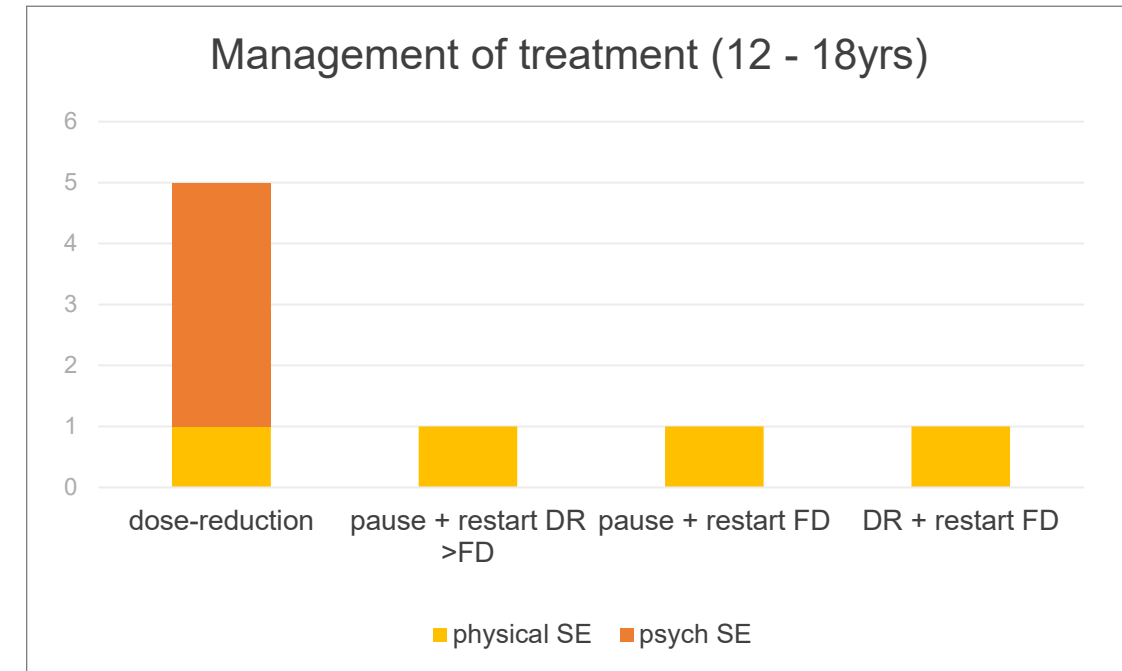
- A wide range of physical and psychological side-effects were observed, fluctuating in frequency, intensity, impact, ...
- Resulting in a wide variety of treatment adaptations,
- needing intense follow up
- Treatment optimization = a multidisciplinary challenge
- Liaison with psychiatric services was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

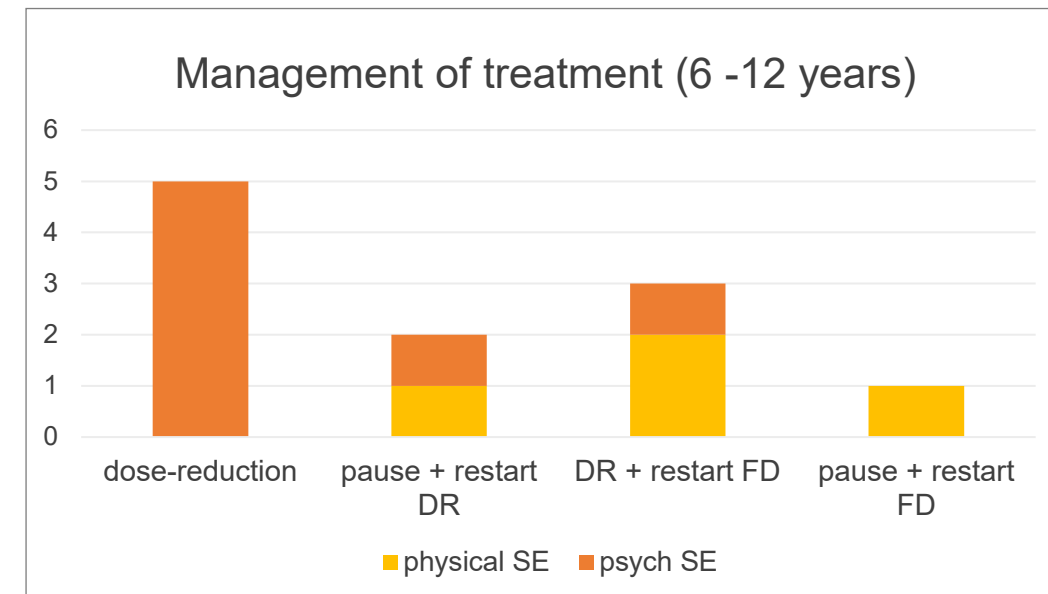
- n=9 > 4 physical SE, 7 psych SE
- Physical SE: headache, sleep, weight, hungry
- Psych SE: identity, anxiety/depression, concentration, brainfog, personality change
- Side-effects: 12-24 months after start ETI



- 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



Pediatric casus: monitoring sweat-chloride

	Before ETI		Full dose ETI		Dose-adjustment 1		Dose-adjustement 2	
	Sweat Cl ⁻ (mmol/l)	FEV1%	Sweat Cl ⁻ (mmol/l)	FEV1%	Sweat Cl ⁻ (mmol/l)	FEV1%	Sweat Cl ⁻ (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		

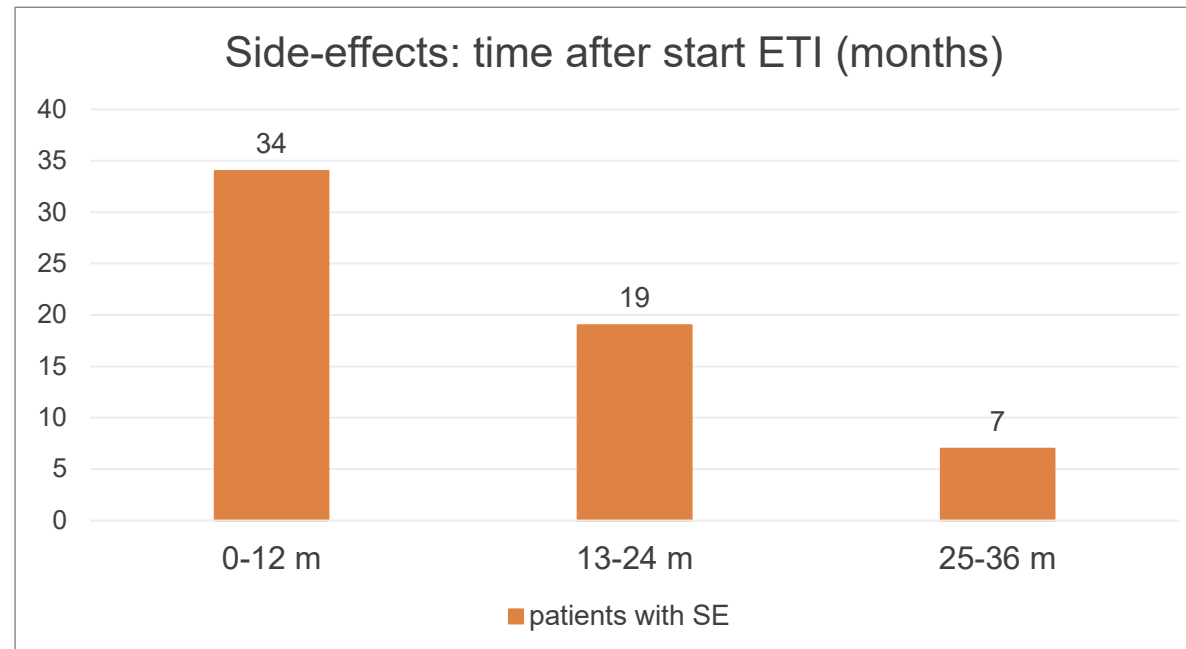
- 13 patients, 2 – 5 years, dose= weight-related
- 4 patients → side-effects (reported by parents):
 - 2 physical SE: GI-symptoms, insomnia, sleeping problems
 - 2 psychological SE: behavioural problems
- Management:
 - Dose-reduction (n=3)
 - Pause + restart dose-reduction (n =1)

Adults

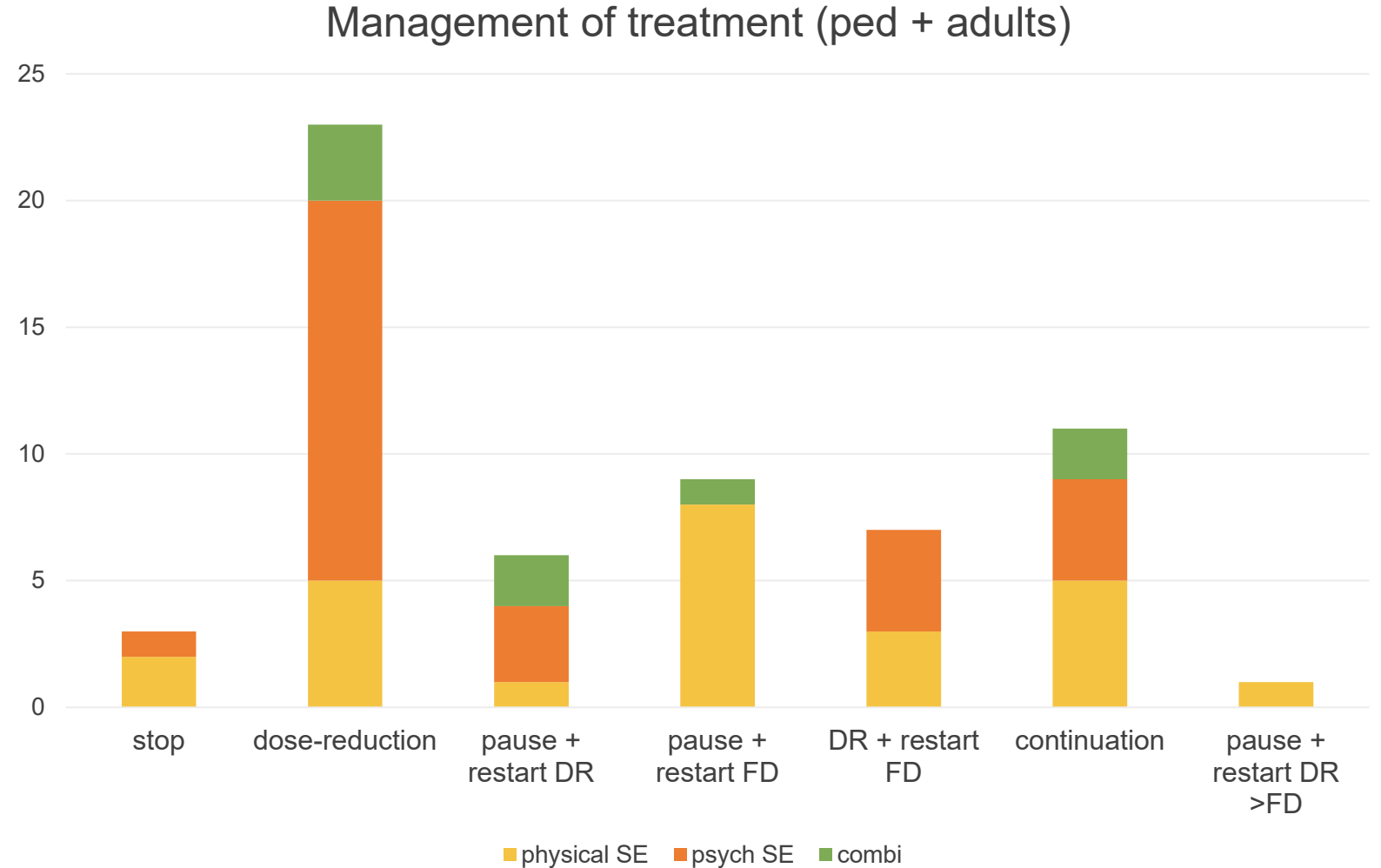
- 120 patients started ETI
- 41 patients > side-effects

Pediatric

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



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



- 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?

Never end on...

Thank You!