Introduction or discontinuation of additional risk minimisation measures of medicines during the life cycle of medicines in Europe

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Declaration of interests

No conflicts of interest to declare

Background

Additional risk minimisation measures (aRMMs)

- Adequate patient selection
- Timely recognition of adverse drug reactions (ADRs)
- Appropriate management of ADRs
- Prevention of medication errors

Background

Types of aRMMs

- Educational materials
  - Healthcare providers
  - Patients caregivers
- Controlled access
- Controlled distribution
- Pregnancy prevention programme

Introduction

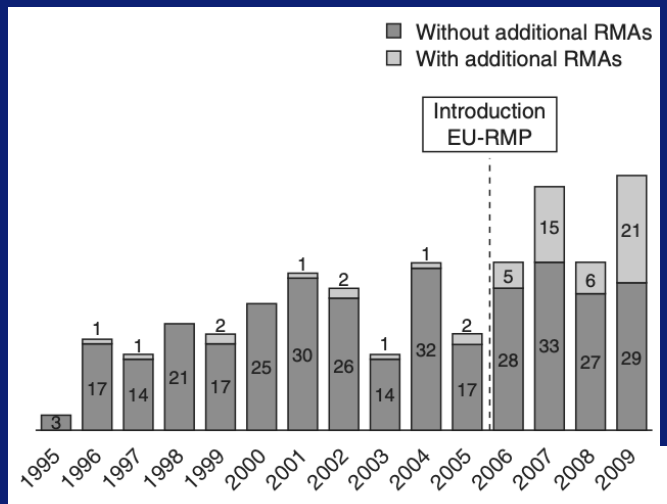
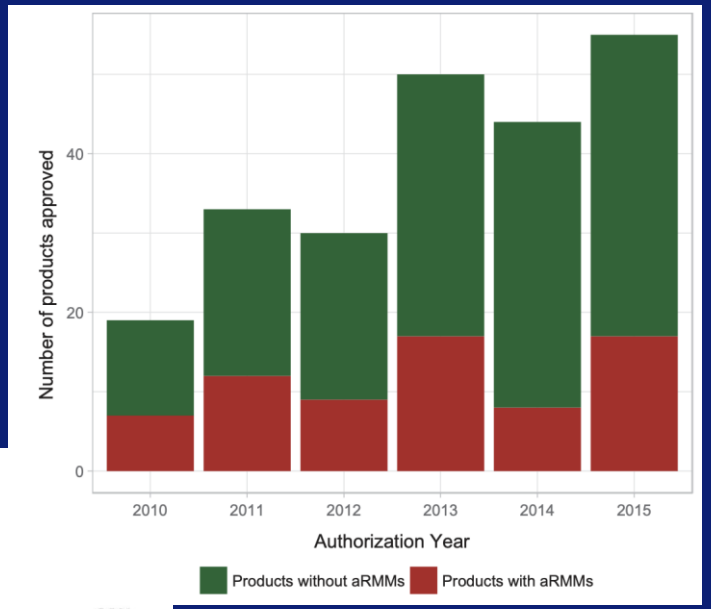
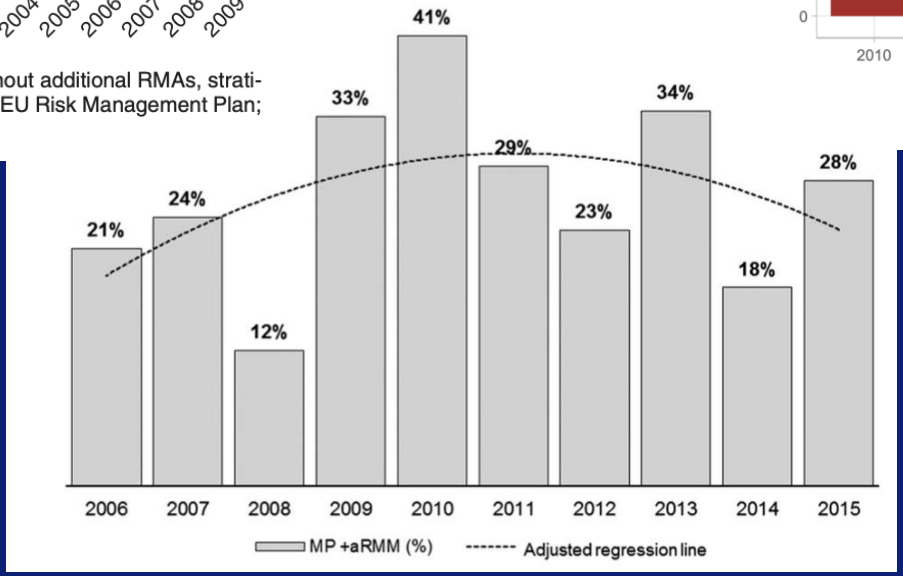


Fig. 1. Active substances with and without additional RMAs, stratified by year of authorization. **EU-RMP** = EU Risk Management Plan; **RMAs** = risk management activities.





From left to right:

1. Zomerdijk IM, Sayed-Tabatabaei FA, Trifiro G, et al. Risk minimization activities of centrally authorized products in the EU: a descriptive study. Drug Saf. 2012 Apr 1;35(4):299–314.

2. Annalisa Rubino & Esther Artime (2017) A descriptive review of additional risk minimisation measures applied to EU centrally authorised medicines 2006-2015, Expert Opinion on Drug Safety, 16:8, 877-884

3. Reynold D. C. Francisca, Inge M. Zomerdijk, Miriam C. J. M. Sturkenboom & Sabine M. J. M. Straus (2018) Measuring the impact of the 2012 European pharmacovigilance legislation on additional risk minimization measures, Expert Opinion on Drug Safety, 17:10, 975-982

Aims

To estimate

the probability of introduction of aRMMs during the life cycle for products without aRMMs at the time of authorisation

and

the probability of discontinuation of aRMMs during the life cycle for products with aRMMs at the time authorisation

Methods

Study design:	Cohort study
Drugs of interest:	New chemical entities authorised through EU central procedure between January 1st 2006 and December 31st 2017
Study period:	January 1st 2006 – July 1st 2018
Data source:	European Public Assessment Reports (EPAR) on www.ema.europa.eu

Methods

Outcomes:

1) introduction of aRMMs post-authorisation in medicines without aRMM

2) discontinuation of aRMMs post-authorisation in medicines with aRMM

Covariates:

- Type of marketing authorisation (MA)
- Orphan designation
- Authorisation status at the end of follow-up

Analysis:

- Survival analysis (Kaplan Meier)

Results

	Medicines without aRMMs at authorisation (N = 346)	Medicines with aRMMs at authoriation (N = 130)
Median follow-up time in months (range)	58 (8-150)	65 (8-150)
Type of MA (%) - Regular - Conditional - Exceptional	 320 (92%) 12 (3%) 14 (4%)	 111 (85%) 8 (6%) 11 (8%)
Orphan designation (%) *	54 (16%)	32 (25%)
Authorisation status at end follow-up (%) - Authorised - Withdrawn - Suspended	 316 (91%) 29 (8%) 1 (0%)	 117 (90%) 13 (10%) 0 (0%)

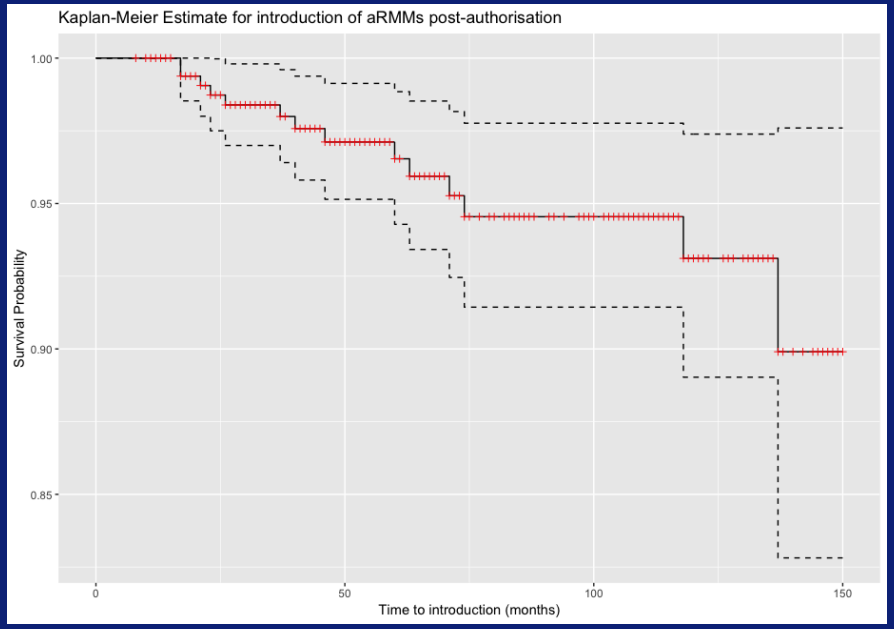
Results

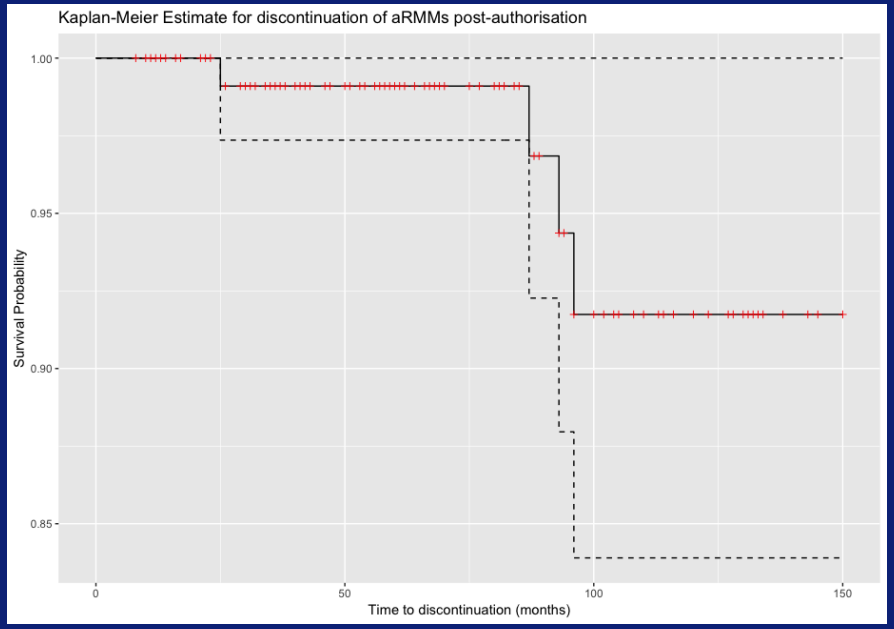
Probability of *introduction* of aRMMs:

- 5y after MA: 3.5% (95%CI 1.2%-5.7%)
- 10y after MA: 6.9% (95%CI 2.6%-11%)

Probability of *discont'* of aRMMs:

- 5y after MA: 0.9% (95%CI 0%-2.6%)
- 10y after MA: 8.3% (95%CI 0%-16.1%)





Conclusion

- Low probability of introduction of aRMMs for medicines without aRMMs at authorisation

- Low probability of discontinuation of aRMMs for medicines with aRMMs at authorisation

Erasmus MC

Questions?

The End

Thank you for your attention!