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DHPCs and aRMM – expectations, practice and opportunities from regulator's perspective

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Safety communication and aRMM materials

Main purpose:

Patient safety

- increase prescriber/patient awareness of risks
  adherence to recommendations /
  change in prescribing / treatment habits

- routine RMM – SPC/PIL
- additional RMM – materials, websites (as for valproate), videos, patient cards (in and out package)
- DHPC to communicate urgently safety information

Do these tools always work?

NO, not always

As important as content of the materials / DHPC, is the communication plan and dissemination (incl ways of dissemination and choosing right target group)

A well-thought-out communication plan is very important

Communication plan – approval by NCA

- There is no meaning
  in sending EMA communication plan to NCA

– it should be tailored, taking into account country specific issues.

EE Local PHV person - for products that have DHPC/aRMM in place.
The expectation is that PhV person is aware of the aRMM implemented for the medicinal product (incl the dissemination of the materials, training of HCPs, valid version of the materials, etc) and is aware of specific target audience.

Communication plan – questions to be asked

- How to reach all potential prescribers and not bother those who do not prescribe?
- Is it sufficient to send letter to specialist society only (asking to forward to members)?
  - Are all potential prescribers the members of the society - NO
- If only couple of specialists are using the product, is there any value in sending to all?
- If product is used in hospital only – dissemination namely or via department, include hospital pharmacy?
- Which is the best (accepted by HCPs) way of dissemination?
- How to guarantee, that the safety message really reaches the HCP (distinguish it from advertisement, misleading and confusing text in cover letter)?

Who is responsbile for dissemination and to whom

DHPC GVP XV Safety communication XV B.5.1

DHPC … is delivered **directly to individual healthcare professionals** by a marketing authorisation holder or a competent authority.

Educational materials [DIR 8(3)(iaa); DIR Art 104(3)(c)]; …

Running a RMS is MAHs **obligation** (RMM is part of RMS) it is implied that aRMM will be disseminated by MAHs
If a MS exceptionally wants to do this instead, this should be agreed locally.

Annex II D (CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT)

… Prior to prescribing **all healthcare professionals who intend to prescribe are provided** with …

1/3 Current practices in the Member States

All NCAs publish DHPCs /aRMMs on website

The approach is different as regards dissemination:

- EE, LV, LT: **accept dissemination via professional societies**, request sending (in specific cases) also to hospital departments, special clinics, hospital pharmacies, in case of specific products - namely
  In EE namely e-mails to certain Russian speaking family doctors are sent by NCA.

- In EE
  - current register or publicly available data is incorrect and incomplete
  - specialist societies not willing to share e-mail addresses of HCPs with MAHs
  - NOT all physicians are members of societies
  - we have to accept that not all physicians may receive the information

2/3 Current practices in the Member States

- NO: communication **needs to be directed at the individual physician**. In addition, professional societies may be informed.
- SE: dissemination by MAH by **regular mail directly** to individual prescribers (in additon , the MAH can be asked to also inform the concerned national societies via email
- FI: DHPCs directly to the target prescribers. Fimea informes the specialist societies. aRMM could be sent to the target prescribers directly and/or in some cases eg on clinic level depending on the type of material.
- Poland: DHPC and the educational materials are sent by MAHs to specified recipients

3/3 Current practices in the Member States

EE, LV: the **confirmation** is required

LT, PL: confirmation **not required**

(MAH should inform agency when distribution has taken place)

NO, SE, FI: confirmation **not required** (the MAH should archive the list of recepients which can be subject for PhV inspection).

1/3 Plans for future

All questioned MS are planning/working on integration of aRMM and DHCP in physicians prescription systems/e- health record systems

- Depends on IT providers + budget
- In EE it is now up to GPs / hospitals to request from their IT providers to enable the transfer of the data to prescriptions systems.

It is of importance to HCPs who the sender of a DHPC is:

It has been shown that HCPs would prefer to receive important new information on the safe use of medicines directly from the **agency**, as it would give the information high credibility and clearly distinguish it from advertising material.

The Danish solution (personal digital mailboxes of physicians mandatory) is an excellent model - all MS are waiting for this

EE: Currently no updated and correct registry of HCPs

There is understanding that HPCs register with updated e-mail list is **essential** (for safety communications, incl COVID-19).

2/3 Plans for future

NO: information accessible at the time when it is needed (in most cases when prescribing), is most useful for the physicians.

- a pilot where NOMA is in charge of sending out DHPCs and EMs to GPs via their electronic health record system/journal system (all GPs and pharmacies use a Prescribing and Dispensing Support System provided by NOMA). The GPs society will distribute the DHPC to the individual GPs via e-mail (as NOMA do not have access to the individual e-mail addresses.). This pilot will be evaluated, probably in 2021.
- In the future, NOMA hopes to be able to disseminate safety information through the electronic journal system to hospitals as well, as there is a ongoing project to create a data foundation for hospitals.

3/3 Plans for future

SE: Discussions are ongoing with the Swedish industry organisations regarding electronic distribution of DHPCs. A major concern is the MAHs' limited access to email addresses to HCPs, it varies largely and is in general low.

- DHPCs integrated in electronic prescribing support system (as described above) is of importance, however, it can not replace the MAH's obligation to distribute DHPCs.

Future:

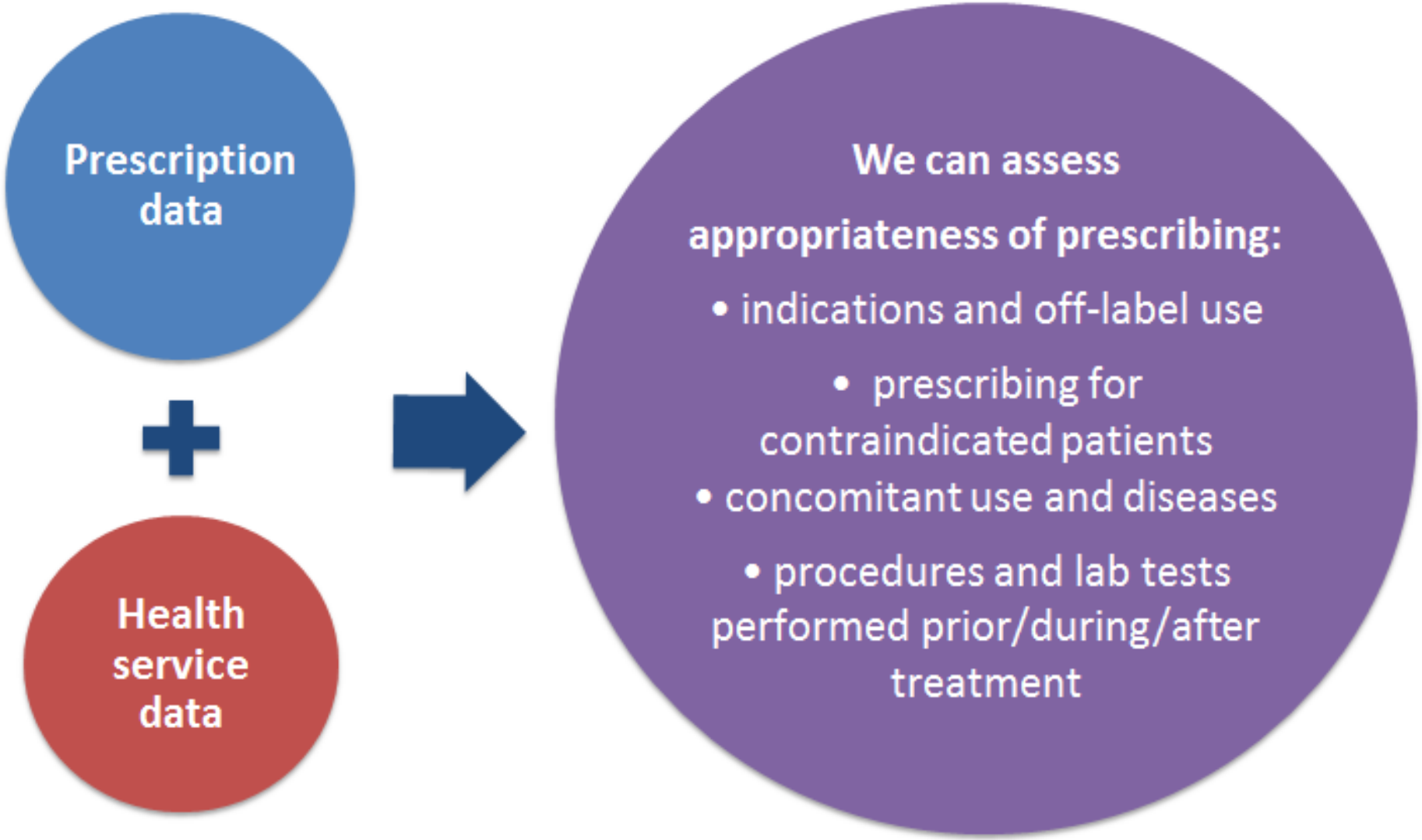
- To increase the number of physicians who could have access to materials, we publish the materials and DHPCs on agency's website and in the register of medicinal products.
  (depends on IT providers and budget).

- Even if new HCPs register with updated and correct e-mail addresses will be ready and available for authorities, it will not be for MAHs

- MS willingness to disseminate DHPCs (& EMs)

Do RMM tools work?

Studies based on Estonian data show – NO, not always



Estonian Prescription Centre

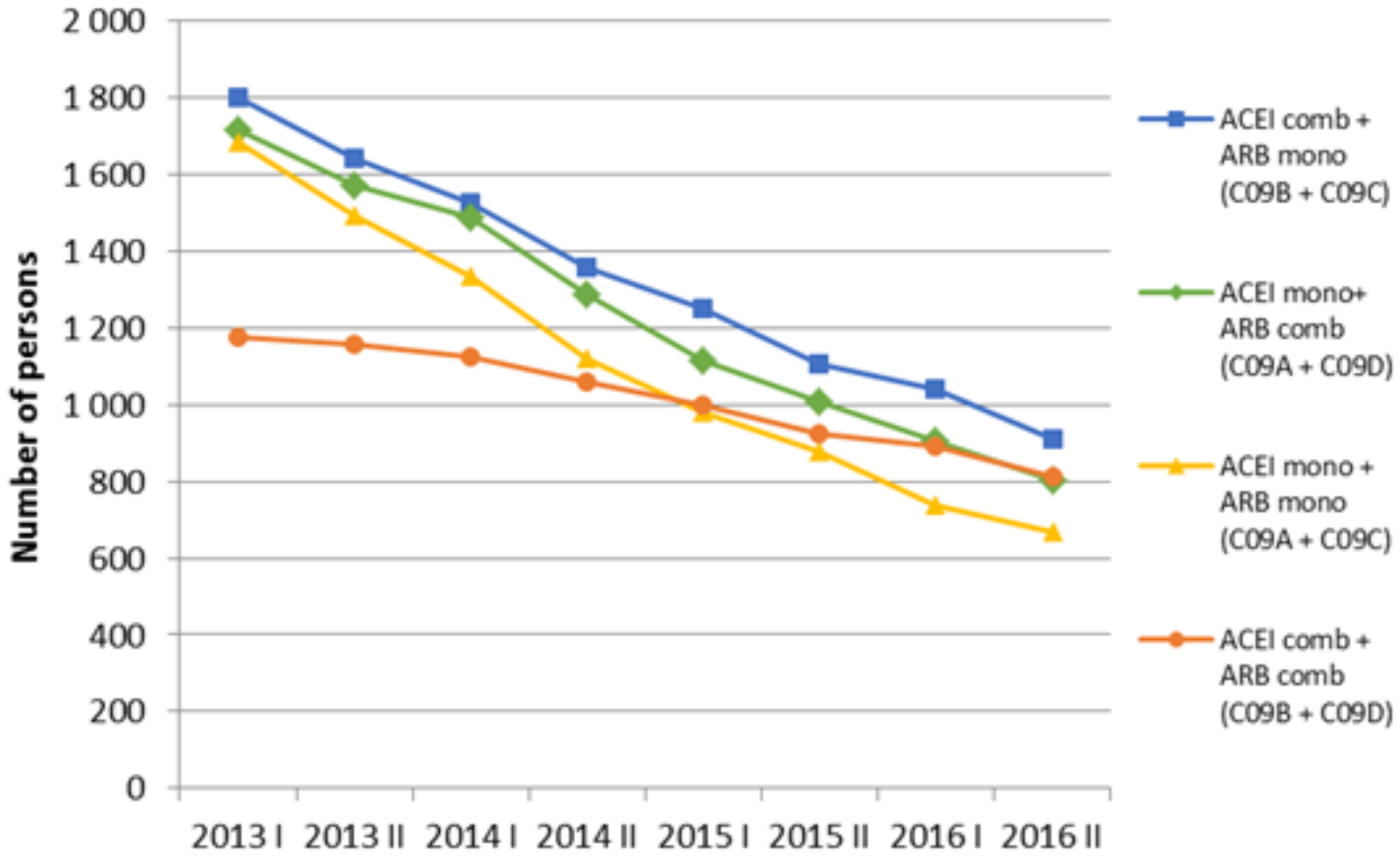
- Nationwide, paperless system for prescribing and dispensing medical prescriptions since 2010
- Comprises all out-patient (incl. uninsured) prescriptions

Estonian Health Insurance Information System

- Invoices data of provided services (in- and out-patient)
- Electronic invoicing since 2004
- For each provided service (examination, laboratory tests, procedures) the following can be identified
    - invoice date, amount paid
    - date, code and name of service
    - patient identification code, age, gender
    - main indication and comorbid diagnoses (ICD-10)
    - type of care
    - HCP speciality

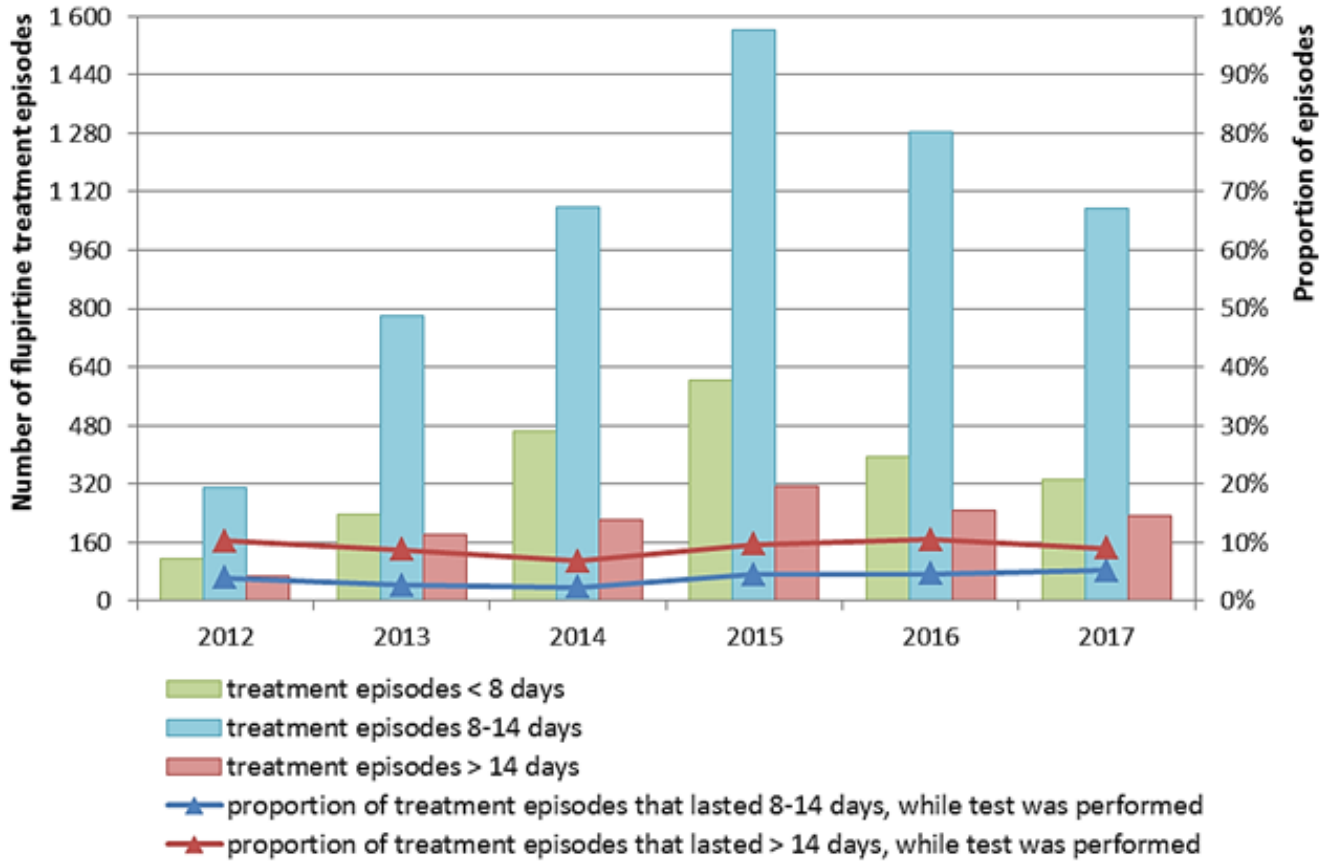
Study on co-prescribing of ACEI & ARB 2013-2016

- **Within 4 years, patients who received ACEI and ARB concomitantly decreased 50%.**
- The decreasing trend of patients co-prescribed shows that awareness of the restriction is increased over time.



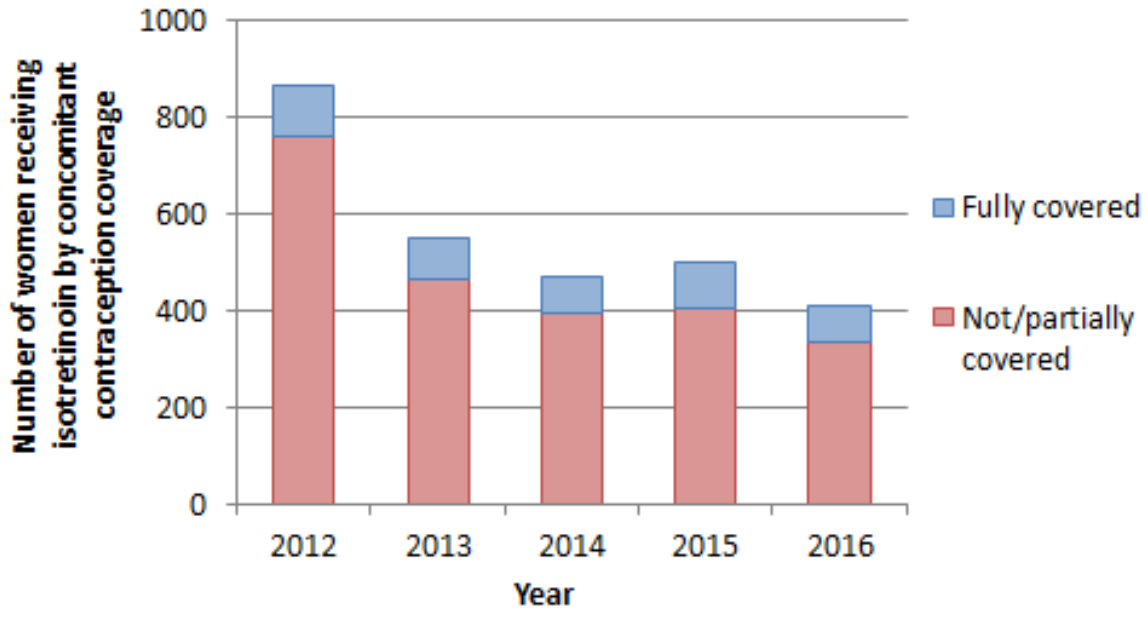
Flupirtin and liver monitoring 2012-2017

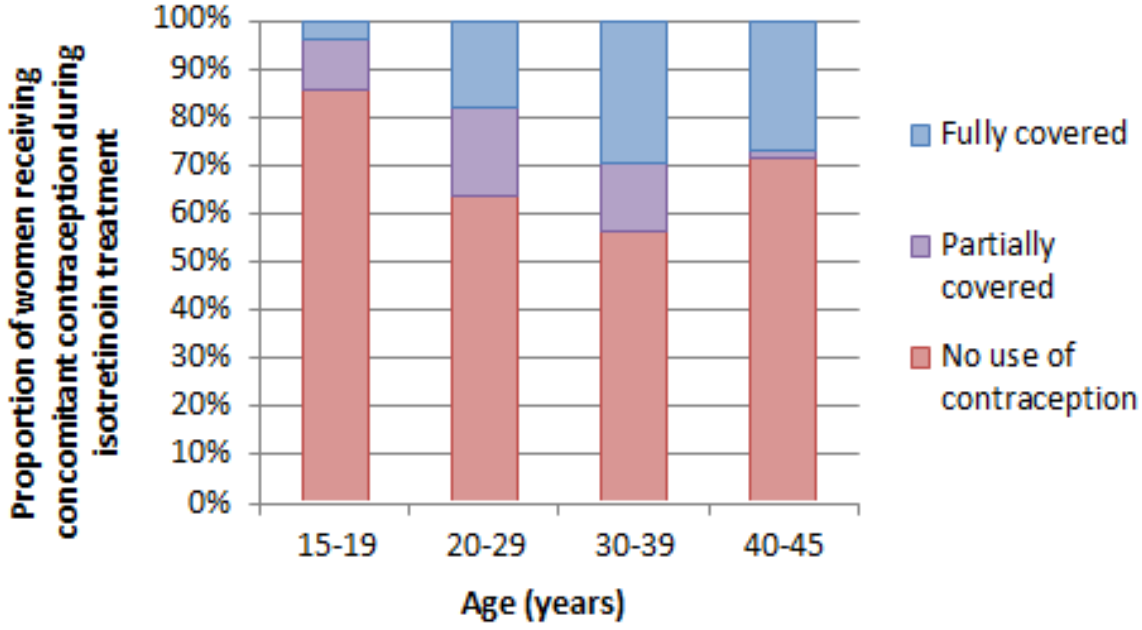
- In 4% of patients who took F for 8–14 days and in 9% who took F for more than 2 weeks liver enzyme tests were performed.
- 32% patients used F concomitantly with other hepatotoxic medicines (statins, diclofenac, paracetamol etc).



Isotretinoine, use of contraceptives and pregnancy 2012-2016

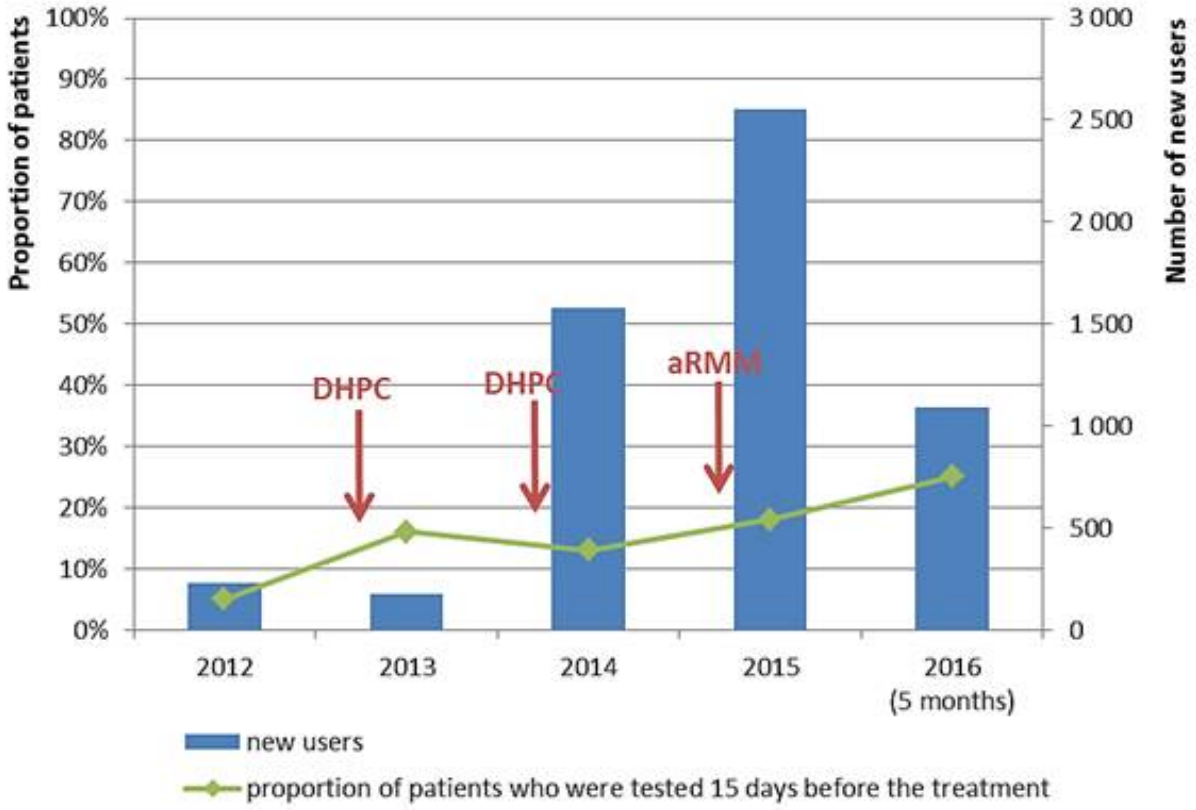
- Among women aged 15–45 years only 15.7% had full and 13.9% partial contraceptive coverage.
- There were 10 pregnancies during isotretinoin treatment.

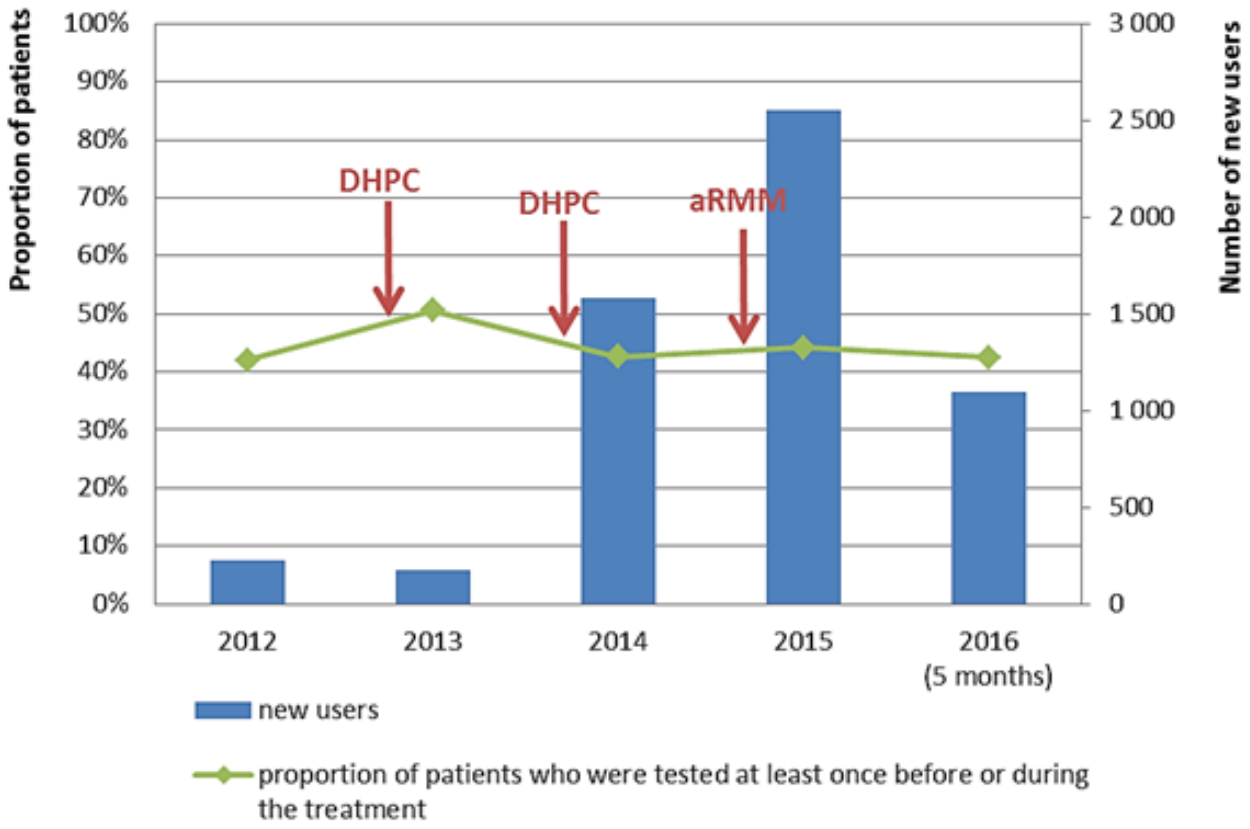




Agomelatine and liver monitoring 2012-2016

- In 17% of patients the test was performed prior to the treatment.
- Only 4% of patients were tested exactly as recommended (one test prior and 4 tests regularly during treatment).





Agomelatine and liver monitoring 2016-2019

- Only in **5%** of the patients tests were performed according to the liver function scheme. In the previous study - 4%.
- In 29% of the patients the test was performed before the initiation of the treatment. In the previous study - 17%.
- At least one test was performed before the initiation of or during the whole treatment course in 57% of patients. Compared to the previous study it is increased by 13%.

Is there any improvement in treatment habits?

Do the RMM tools serve the purpose?

In conclusion

- EC Decision/PRAC reccomendation ≠ acceptance
  of the information / change of habits by the HCPs

- Communication / dissemination and education play the key role

All RMM tools are to increase patient safety

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Thank you!

DHPC, aRMM and all other PhV questions:
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