ESF Exploratory Workshop on

Enhancing the quality and safety of pharmacotherapy in old age

Ghent (Belgium), june 12-14 2014

Convened by:

Monique Elseviers and Robert Vander Stichele

SCIENTIFIC REPORT

1. EXECUTIVE SUMMARY (approx. 2 pages)

Background

Quality of pharmacotherapy in old age needs to be appraised in the context of ageing taking into account multi-morbidity, disability, frailty and the higher importance of explicit care goals. A 'patient centered and tailored approach' has to be adopted including both explicit and implicit measures improving the quality of pharmacotherapy. In recent years, several new and revised tools were published to assess the use of potentially inappropriate medication (PIM) in old age (revised BEERS 2012; PRISCUS 2010; START-STOPP,2008). PIMs can be defined as "medications that have no clear evidence-based indication, and carry a substantially higher risk of adverse side-effects or are not cost-effective" (O'Mahony and Gallagher, 2008). Adaptation to national drug markets and applicability for automated electronic assessment form the main problems for a more generalized use of these tools in daily practice.

Objectives of the ESF workshop

An international multidisciplinary team of experts focused on the quality and safety of pharmacotherapy in old age aiming to define the requirements for an electronic assessment tool based on the European PIM lists.

Practical organization

Invitations for the meeting were sent out to the most important developers of European PIM lists (PRISCUS/P.Thürmann, START-STOPP/D.O'Mahony, BEDNURSE/S.Ruths, NORGEP/H.Salvesen-Blix), developers of more generalized assessment tools of poly-pharmacy (STRIPP/P.Jansen, SENATOR/D.O'Mahony+M.Petrovic), regular users of these lists (for general quality assessment (K.Johnell) as well as for assessment in individual patients(K.Taxis, H. Salvesen-Blix)) and experts in the field of risk/benefit assessment of medicines (J.Aronson), de-prescribing of medicines in old age (F.Haaijer-Ruskamp) and the development of prescribing quality indicators (P.Denig). A multidisciplinary approach was guaranteed by the profession of the participants ranging from geriatricians and general practitioners to clinical pharmacologists, clinical pharmacists, nurses and a pharmaco-epidemiologist.

On June 12-14, 2014, 15 experts from 8 European countries together with two rapporteurs and the two conveners assembled in Ghent, Belgium, for the ESF workshop. The meeting started on Thursday afternoon and ended on Saturday at noon. All participants actively contributed by presenting the state-of-the-art in their particular field of expertise or by sharing their experiences of the use of PIMs to evaluate the quality of pharmacotherapy at the individual as well as at the population level. Presentations were alternated with workshops and panel discussions introduced by literature reviews (terminology/T.Dilles, PIM lists/M.Azermai) or by clearly defined discussion points.

During the evenings in Ghent, all participants attended the diner and social program intending to facilitate individual contacts and networking.

Scientific content of the meeting

Participants started with a discussion of the general framework of the quality of prescribing, highlighting the potential hazards and harms of medicines and the confusing terminology of drug related problems (i.e. adverse drug reactions, adverse drug events etc.). De-prescribing should be considered as a valuable domain in quality of pharmacotherapy in a number of therapeutic areas, taking into account patients preferences and needs as well as (advanced) care planning in a multidisciplinary context.

From the presentations of the developers and the end-users of PIM lists, we learned that applications made from these tools varied considerably from general benchmarking purposes to clinical assessment for individual patients in preparation of a multidisciplinary medication chart review. The content of PIMs varied accordingly, from PIMs including only a particular drug name (e.g. do not use digoxin in old age) or a drug class (e.g. avoid anticholinergic drugs in the elderly) to complex descriptions including diagnostic and clinical information (e.g no β-blocking agents in patients with diabetes mellitus and frequent hypoglycemia).

Based on the variation between national drug markets, the experts decided that it seems more valuable to maintain multiple PIM lists instead of developing an overall European PIM list. International efforts should focus on producing and maintaining a publicly available inventory of existing PIM lists. There is a need to compose a catalogue of all active substances and drug groups mentioned in PIMs, classified according to the ATC system and grouped by physiological system. Although medication only PIMs data are valuable and need to be exploited to the maximum, many PIMs require the electronic availability of at least a limited set of clinical data.

Participants recommended that the evidence base for selection of PIMs should be documented and maintained in an international effort, with new methodologies to structure, synthesize and present safety information. Producers of PIMs need to join the e-health effort for semantic interoperability of the terminology, key concepts and clinical data standardized in a multilingual context. Additionally, the development of a validated set of quality indicators based on the explicit criteria as expressed in the available PIM lists is highly recommended.

Implications for future collaboration and research

As a direct result of the workshop, participants decided to start up four working groups to partly work out the recommendations formulated during the workshop:

a) A working group to clarify the conceptual framework and terminology
b) A working group to compose the International catalogue of PIMs and Quality Indicators
c) A working group on methodology to collect, synthesize, and present safety information
d) A collaboration with the interRAI group to explore the congruence of the interRAI clinical dataset with the requirements of the lists of PIMs.

Recommendations from the ESF workshop

During the workshop, the participants discussed a list of recommendations aiming to enhance the quality of pharmacotherapy in old age. After the workshop, the final version of these recommendations was distributed and approved by all participants (see enclosure).

2. SCIENTIFIC CONTENT OF THE EVENT

Abbreviations used: P=presentation, WS=workshop, PD=panel discussion

Session1: Conceptual framework of safety and quality of pharmacotherapy in old age

P: Introduction: Epidemiology and perspectives of the old age population, health profile, pharmacotherapy and drug related problems
Monique Elseviers (Ghent University, Belgium)
The workshop started with an overview of the demographic evolution of ageing and the associated health related problems. Polypharmacy in old age was highlighted and the specific consumption of medicines in nursing homes as well as in home care was documented.

P: Development of a conceptual framework of safety and quality
Robert Vander Stichele (Ghent University, Belgium)
The definition of the World Health Organization of rational prescribing was discussed, together with a model for the whole process of medication management (Bell et al., 2003).
Quality of prescribing can be looked at on from different words of reference (drug development (GCP), clinical pharmacology, drug utilization research, and medication management) and from different perspectives (Patients and caregivers, health care providers, policy makers, and health services). Assessment of quality may be directed at structure, process, or outcome. Assessment of quality can be made in a positive or negative way: (in)appropriate prescribing, % bad or good performers. Very often the qualifier "potentially" is used: potentially inappropriate medication (PIM), drug related problems which potentially or actually cause a drug-related hospital admission. The goal of quality assessment is to optimize the benefit of medicines, while minimizing the risk of medicines in the drug choice process and in the medication management process, at the right price to maximize "value".

P: Safety of pharmacotherapy in old age
Jeffrey Aronson (Oxford University, United Kingdom)
Jeffery Aronson (UK) laid the terminological groundwork for a discussion of the negative effects of medication. He posposed several theories to distinguish an adverse drug reaction from other concepts, namely on how it arises (EIDOS) and how it is classified based on dose relatedness, timing and patient susceptibility (DoTS). The application of this work could enhance adverse reaction prevention and prediction, as well as their management (i.e. decisions about licensing revocation).

WS-PD: Terminology in the field of drug related problems
Introduced by Tinne Dilles (Antwerp University, Belgium)
Tinne Dilles (Belgium) highlighted the inconsistent terminology used to describe problems with medication. In particular, she focused on the varied use of the terms drug-related problems, adverse drug effects and adverse drug reactions. She has identified 20 different classification systems, highlighting the need for standard terminology.

Workshop – Panel discussion: Terminology of drug related problems

The workshop members preferred during the meeting to only list the terms for which additional steps are required to precisely define the term or delineate the concept.
- Adverse drug effect (as defined by Aronson)
- Adverse drug reaction (ADR) (as defined by Aronson)
- Adverse drug event (ADE) (as used in the literature on medication errors or drug related problems)

- Adverse event (AE) (in GCP)
- Potential Hazard / Actual Harm
- Drug Related Problems
- Potentially Inappropriate Medicine / Potential Prescribing omissions / Potentially inappropriate Prescribing / Potentially Inappropriate Medication Management

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P: Quality of pharmacotherapy in old age
> **Petra Denig** (Groningen University, the Netherlands)

Petra Denig (Netherlands) emphasized the three primary domains of prescribing quality: initiation (i.e. timely, reduce omissions), optimal selection, and avoidance of overuse. Many of the tools available to enhance prescribing quality are only starting to address prescribing omission. Difficulty with ensuring prescribing quality arises in older people who have multi-morbidity and complex needs, and for whom limited evidence from clinical trials exists.

P: Deprescribing in old age
> **Flora Haaijer Ruskamp** (Groningen University, the Netherlands)

Flora Haaijer-Ruskamp (Netherlands) presented her experience with de-prescribing in older people through educational interventions and medication review. Several barriers among physicians (i.e. unclear how to prioritise medications to be stopped) and patients (i.e. insufficient support, fear of return of symptoms) were identified. Possible approaches are to involve patients and prescribers in medication review in order to address their concerns and goals of de-prescribing. She underlined the need for a comprehensive view of outcomes that places older patients' therapeutic goals (i.e. maintain independence or quality of life) at the centre of the therapeutic decision process.

PD: Defining a conceptual framework of safety and quality
> **Convenor: Robert Vander Stichele** (Ghent University, Belgium)

Panel discussion

Breaches of quality arise when the benefit of medicines (Disease treatment or cure, relief of symptoms, increased quality of life, or prevention of future risk) is not fully achieved, by the suboptimal use of available pharmacotherapy, or by the use of pharmacotherapy that entails unnecessary potential hazards (known possible adverse effects) or actual harms (occurring adverse drug reactions). The use of potentially inappropriate medications and potential prescribing omissions are aspects of quality that pertain to the drug choice process. The concept of medication error pertains to medication management (which, according to the definition may or may not include the drug choice process). A popular concept is the "drug related problem", which by definition may be restricted to actual outcomes or may also include process aspects (potentially inappropriate prescribing and/or distribution errors), and may or may not include elements of therapeutic failure by non-adherence, under dosing, or potential prescribing omissions.

It was agreed that the concepts "quality" and "safety" cannot be separated, and assurance of safety of drug use is an intrinsic part of assurance of quality.

A pragmatic way to describe domains of quality of the drug choice process is to list relevant questions: e.g. Are the actors well and independently informed ?; Is prescribing, dispensing and utilisation of medicines occurring in a good regulatory environment ?; Are the prescribers working with medicines with a good benefit / risk balance ? For each of these observed problems, the question can be asked: does the observed problem decreases the benefit and/or increases the risk of taking the medicine?

Similarly, a series of questions can be asked with regard to the quality of medication management: is it : e.g. free of transcription errors ?; free of dispensing errors ? dealing with non-adherence ? Again, for each of these problems, the question should be asked: Does the observed problem decrease the benefit and/or increase the risk?

Finally, it is also essential to assess the quality of dealing with actual harm from medicines? - Are prescribers, dispensers, nurses, caregivers, patients accurately dealing with adverse drug reactions or medication errors, resulting in harm?

Session2: Potentially inappropriate medication (PIM) lists for the assessment of safety and quality of pharmacotherapy in old age

P: Presentations of established PIM lists: development, content, applications (3x20')
> **Petra Thürmann** (Helios Klinikum, Wuppertal, Germany)
> **Sabine Ruths** (University of Bergen, Norway)
> **Denis O'Mahony** (Cork University Hospital, Ireland)

In three sessions, the most important European PIM lists were presented by their developers: the PRISCUS list, BEDNURS and NORGEP as well as the START/STOPP criteria. Aim of these sessions was to introduce established PIM lists and to present the methodology, content, and applications. A comparison between these lists showed many similarities in the process of development, the content and the applications, but showed less uniformity in the medication listed in these PIM lists.
Petra Thurmann (Germany) presented the PRISCUS list. Priscus is latin for old, vulnerable. The Priscus list is a PIM list based on the Beers list and adapted to the German market, with 83 PIMs.
Sabine Ruths (Norway) presented the older Bergen District Nursing Home Study (BEDNURS), and the updated Norwegian General Practice Criteria (NORGEP). Both are PIM lists adapted to the Norwegian market.
Denis O'Mahony (Ireland) presented the START/STOPP criteria: Screening Tool to Alert doctors to Right i.e. appropriate, indicated Treatment and Screening Tool of Older People's potentially inappropriate Prescriptions.

PD: Inventory of published PIM lists
> **Introduced by Majda Azermai** (Ghent University, Belgium)

The panel discussion was introduced by a session on the inventory of other PIM lists not yet discussed. The focus was on medication only. The aim of this session was to illustrate with the inventory that the PIM lists have a certain level of agreement mainly on the underuse of certain drugs. The level of agreement between these lists on the overuse of drugs is lower, since these lists mention different symptoms (in anticholinergic or antihistaminic drugs), different reasons (in acid related drugs) or different outcomes (in antithrombotic drugs). This comparison led to the panel discussion, in which the need for an international PIM list was discussed and the implications for electronic monitoring.

Panel discussion

This part of the panel discussion focused on medication data used in PIM lists and resulted in the following conclusions: (see also recommendations of the ESF workshop in the annex)

- We do not need a new unifying PIM list. A new list would neither be necessary nor useful.
- Focus should be on existing European lists, including START/STOPP and PRISCUS, as well as LAROCHE, which are good starting points for Europe. NORGEP can be of added value because of its focus specific aspects of duration and dose, not included in other PIM lists.

- There is a need for an inventory of existing lists, which have undergone efforts of validation of their content.
- The inventory should be specific for the older population, adequately maintained and made publically available.
- In general, a detailed study of the overlap or gaps between all existing PIM lists would be useful.
- Existing PIM lists should demonstrate their relationship with desired (patient) outcomes through research.

P: Experiences with the regular use of PIM lists (3x20')

>> **Hege Salvesen Blix** (Norwegian Institute of Public Health, Norway).
>> **Katja Taxis** (University of Groningen, the Netherlands)
>> **Kristina Johnell** (Karolinska University, Stockholm, Sweden)

In three sessions, the experience with PIM lists in three countries was presented. The aim of this session was to compare implementation strategies and results of PIM lists. The presenters were chosen because of the different tools used, different settings and different approaches. The focus was on the richness of the clinical data.

Hege Salvesen Blix (Norway) presented a Norwegian safety programme that includes drug review in nursing homes and home care services. She also compared comprehensive chart review with applying PIM lists and concluded that NORGEP and START/STOPP are valuable tools but not enough to detect all problems with inappropriate prescribing in the elderly. Physicians are likely to address PIMs identified by PIM lists because they are pre-defined and evidence based.

Katja Taxis (Netherlands) shared her experience using PIM lists as part of medication reviews, especially in a nursing home setting. She concluded that BEERS and START/STOPP do not give representative picture of quality of prescribing in nursing homes. Clinically relevant problems are not covered by these lists when applied in people receiving end of life care.

Kristina Johnell (Sweden) shared her experience with the Swedish indicators, which are quality indicators, drug specific and disease specific for 11 diagnoses. Swedish national indicators for quality of drug use have already been used for the last 10 years.

PD: Published PIM lists: inventory of required associated clinical data

>> **Introduced by Majda Azermai** (Ghent University, Belgium)

The panel discussion was introduced with a similar comparison between existing PIM lists, with a focus on the clinical data, showing the incongruences.

Panel discussion

The starting point in the panel discussion was to identify the need for clinical data and the associated implications for electronic assessment. It resulted in the following conclusions (see also recommendations of the ESF workshop in the annex).

- Clinical data are needed. In an ideal world, the most detailed and recent information is available.
- Clinical data are required to fully appraise the quality of pharmacotherapy. However, medication-only PIMs are valuable and need to be exploited to the maximum.
- The richness of clinical data required to assess PIMs depends on data availability, the setting, the purpose of assessment, and the perspective of the assessor.
- The clinical data required to assess PIMs should be fully specified and operationalized for data collection. The terminology of key concepts should be standardized across languages and coding systems in order to ensure semantic interoperability.
- Producers of PIM lists need to join the e-Health effort for semantic interoperability

- The responsibility for this standardization partly lies with developers of PIMs.

The discussion revealed several problems. First, a consensus on coding for diagnosis should be reached. Currently problems arises when different pathologies are coded using different classifications. Secondly, the clinical data should be validated or methods should be developed for good medical record-keeping.

Different settings require different needs for clinical data. In the hospital setting, a full data set is available. In nursing homes however, there seems only sufficient medication data, but clinical data are not recorded systematically. Another problem in nursing homes is the amount of general practitioners, making validating clinical data harder.

The expert group showed mixed feelings in using national recording systems. The reliability, completeness and accuracy of these recording systems are not optimal. A good national recording system requires lots of support to be well registered.

In nursing homes, we would like a minimal data set, to carry out analysis on quality and safety, that will make us able to evaluate the results of interventions.

The expert panel showed interest in developing a small data set with a set of geriatric symptoms or diagnosis, that will cover almost all problems in the old. The use will be intended for settings where a good medical recording system is not available or reliable.

Session3: Assessment of safety and quality of pharmacotherapy in old age

P: Presentations of established assessment tools: development, content, applications (2x20')
Paul Jansen (University Medical Centre, Utrecht, the Netherlands)
Mirko Petrovic (University of Ghent, Belgium)

In this session global assessment tools with the integration of the assessment of PIMs were presented
Paul Jansen (the Netherlands) presented the development of an electronic prescription optimization method: the STRIP assistant i.e the Systematic Tool to Reduce Inappropriate Prescribing.
Mirko Petrovic (Belgium) presented the development and clinical trial of a Software ENgine for the Assessment & optimization of drug and non-drug Therapy in Older peRsons (SENATOR), funded by the European Commission.

WS: Selection of PIM criteria for the regular electronic assessment of safety and quality
Introduced by Monique Elseviers (University of Ghent, Belgium)

This workshop intended to confront the participants with the data requirements of all PIMs included in the revised BEERS, ACOVE and START/STOPP list. Participants were divided in 3 groups according to the main settings where PIMs are used (primary care, nursing home, hospital). Each group evaluated 3 PIM lists, presented on posters, by using stickers to indicate what kind of data is necessary to apply each PIM in their setting:

- *Red sticker: not useful for electronic assessment*
- *Blue sticker: Full dataset needed*
- *Yellow sticker: Minimal dataset needed*
- *Green sticker: No clinical data needed*

PD: Requirements, strengths and limitations of PIM criteria for the regular electronic assessment in the different settings
Convenor Robert Vander Stichele (University of Ghent, Belgium)

In this panel discussion the experiences of the practical exercise of the workshop were discussed. This discussion formed the base to formulate the requirements, strengths and limitations of the different lists of PIMs for the development of an electronic application in the different settings.

Panel discussion

Particularly in settings were clinical data are frequently lacking (home care, nursing homes), medication-only PIMs are valuable and need to be exploited to the maximum. In these settings, the use of a limited set of clinical data is highly recommended for a more complete assessment of the quality of drug therapy.   On the other hand, a limited clinical data set will be unnecessary in settings with good medical record-keeping practices and sophisticated electronic health care records. (see also recommendations of the ESF workshop in the annex)

Session4: Defining prescribing quality indicators in advanced age

P: Prescribing quality indicators: theoretical background and specific requirements in vue of safety and quality in advanced age
Petra Denig, Flora Haaijer Ruskamp (University of Groningen, the Netherlands)
Petra Denig (the Netherlands) presented prescribing quality indicators. She discussed how to go from individual criteria to quality indicators. This process has to deal with indicator requirements such as content validity, concurrent and predictive validity, and taking the availability of data into account.

WS+PD Selection of prescribing quality indicators in advanced age
Convenor Robert Vander Stichele (University of Ghent, Belgium)

Workshop – Panel discussion

Finally, the members of the ESF workshop discussed the difference between explicit criteria for inappropriate prescribing and quality indicators.
Explicit criteria for inappropriate prescribing are quality rules (taken from guidelines with graded specific practice recommendations), applicable to individual patients, suitable for Individual Medication Review, expressed as a logical algorithm, and grouped in a list. This list may or may not be researched for impact on outcome (as whole). An example of an explicit criterion of inappropriate prescribing is : If a patient uses an obsolete medication, then avoid continuing treatment, because the medication is ineffective and hence, the benefit/risk balance is unfavourable.
Prescribing Quality Indicators are tools to evaluate the quality of health services, suitable for benchmarking, quality assurance programmes, prescriber feedback, pay for performance, evaluation of interventions, expressed as ratio (A/A+B with a standard and a cut-off), validated as a single item, and possibly grouped in a set, which may or may not be researched for impact on outcome.
An example of a prescribing quality Indicator is: In 90 % of our nursing homes, 80 % of the residents do not have one obsolete drug on their medication list.
Participants recommended that funding for validation research regarding structural, process, and outcome quality indicators should be extended. The development of a validated QI set for population-based prescription databases should be fostered, while exploring the possibilities of record linkage with epidemiological patient registries with more detailed clinical content. (see also recommendations of the ESF workshop in the annex).

Session5: Future perspectives

P: Integration of the assessment of quality and safety of pharmacotherapy in the RAI data collection
Daniela Fialová (Charles University, Prague, Czech Republic)

Daniela Fialová (Czech Republic) presented the integration of the assessment of quality and safety of pharmacotherapy in the RAI data collection. She concluded that there are several advantages of RAI assessments: the link between CGA and pharmacotherapeutic data; standardized and validated approach, quality measurements; and important feedback to prescribing practice and regulatory bodies.

WS+PD Dissemination of the results and future research perspectives
                 Convenor Monique Elseviers (University of Ghent, Belgium)
In the last panel discussion, future perspectives were discussed. Participants expressed the need to start up several working groups aiming to continue the work done during this ESF workshop and to fulfil the practical requirements formulated in the recommendations of the workshop. For the concrete initiatives taken during the panel discussion see section 3.Dissemination of the results…

P Closing remarks
                 Robert Vander Stichele (University of Ghent, Belgium)
In his closing remarks, Robert Vander Stichele expressed his gratitude for the ESF granting of this workshop. He thanked all participants for their active and valuable contributions and announced a follow-up workshop in spring 2015, in Stockholm.

Key References

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3. DISSEMINATION OF THE RESULTS, CONTRIBUTION TO THE FUTURE DIRECTION OF THE FIELD, OUTCOME

Participants of this ESF workshop realized that the existing updated European lists of PIMs are currently mainly used in research settings or in preparation of an in-depth medication chart review of individual patients. The requirements for an automated electronic use of PIMs for the regular screening of the quality of pharmacotherapy in old age are rarely fulfilled and only available at the national level in a few countries (Sweden, Germany). A lot of work still have to be done, preferably at the European level, before a more generalized utilisation of this assessment tool can be promoted.

Therefore, the participants of the workshop decided to start up four working groups to focus on the main gaps in the knowledge and the practical requirements needed to obtain a useful tool for the regular automated assessment of the quality of drug therapy. They will assemble again in Stockholm, spring 2015, for a follow-up meeting of their activities. Initiatives for the working groups will be taken by the participants indicated on the list below. Other participants already expressed their willingness to join.

Working groups for follow up
1. Conceptual framework and terminology
   First: definitions, boundaries of concepts.
   Jeffrey Aronson, Robert Vander Stichele, Tinne Dilles.
2. International catalogue of PIMs and Quality Indicators
   Medication (ATC codes, dose duration, qualifier)
   Clinical data (small clinical data set, no clinical information needed)
   Majda Azermai, Maarten Wauters, Daniela Fialova, Mirko Petrovic, Monique Elseviers, Petra Denig, Hege Salvesen-Blix
3. Working group on methodology to collect, synthesize, and present safety information and evidence base for each PIM
   Petra Thurman (with help from someone from the Oxford group), Jeffrey Aronson, Robert Vander Stichele
4. Congruence between the interRAI and PIM lists
   Daniela Fialova , Petra Denig

The intermediate results of these working groups will be distributed go to all participants of the ESF meeting and will be discussed during the planned meeting in Stockholm.

Additional future perspectives

- A follow meeting is planned for April 2015, in Stockholm, Sweden, in collaboration with the Karolinska University of Stockholm (part workshop, part congress).
- Proceedings of the meeting with a focus on the recommendations approved by all participants (see Recommendations of the ESF workshop in annex) will be published with Majda Azermai as the first author
- We shall consider applying for a follow up grant from ESF.
- We shall consider applying for a EU research project grant.

- Intentions for bilateral collaboration were discussed at the meeting
  - Karolinska Institutet – Heymans Institute of Pharmacology
  - UZ Groningen and Department of Epidemiology, Norway
  - InterRAI and Heymans Institute
  - Semantic Health Net

4. FINAL PROGRAMME

Thursday, 12 June 2014

Morning	*Arrival*
12.30-13.30	*Lunch – informal welcome at conference place*

13.30-13.40	**Welcome by Convenors** **Monique Elseviers and Robert Vander Stichele** (Ghent University, Belgium)
13.40-14.00	**Presentation of the European Science Foundation (ESF)** **Roger Bouillon** (KULeuven, Belgium, Scientific Review Group for the Bio-Medical Sciences)
14.00-18.00	**Session1: Conceptual framework of safety and quality of pharmacotherapy in old age**
14.00-14.20	**P: Introduction: Epidemiology and perspectives of the old age population, health profile, pharmacotherapy and drug related problems** **Monique Elseviers** (Ghent University, Belgium)
14.20-14.40	**P: Development of a conceptual framework of safety and quality** **Robert Vander Stichele** (Ghent University, Belgium)
14.40-15.00	**P: Safety of pharmacotherapy in old age** **Jeffrey Aronson** (Oxford University, United Kingdom)
15.00-15.20	*Coffee / tea break*
15:20-16:20	**WS-PD: Terminology in the field of drug related problems** **Introduced by Tinne Dilles** (Antwerp University, Belgium)
16:20-16:40	**P: Quality of pharmacotherapy in old age** **Petra Denig** (Groningen University, the Netherlands)
16:40-17.00	**P: Deprescribing in old age** **Flora Haaijer Ruskamp** (Groningen University, the Netherlands)
17:00-18:00	**PD: Defining a conceptual framework of safety and quality** **Convenor: Robert Vander Stichele** (Ghent University, Belgium)
19.00	*Dinner*

Friday 13 June, 2014

09.00-12.30	**Session2: Potentially inappropriate medication (PIM) lists for the assessment of safety and quality of pharmacotherapy in old age**
09.00-10:00	**P: Presentations of established PIM lists: development, content, applications (3x20')** **Petra Thürmann** (Helios Klinikum, Wuppertal, Germany) **Sabine Ruths** (University of Bergen, Norway) **Denis O'Mahony** (Cork University Hospital, Ireland)
10.00-10.40	**PD: Inventory of published PIM lists** **Introduced by Majda Azermai** (Ghent University, Belgium)

10.40-11.00	*Coffee / Tea Break*
11.00-12.00	**P: Experiences with the regular use of PIM lists (3x20')** **Hege Salvesen Blix** (Norwegian Institute of Public Health, Norway). **Katja Taxis** (University of Groningen, the Netherlands) **Kristina Johnell** (Karolinska University, Stockholm, Sweden)
12.00-12.30	**PD: Published PIM lists: inventory of required associated clinical data** **Introduced by Majda Azermai** (Ghent University, Belgium)
12.30-14.00	*Lunch*
14.00-18.00	**Session3: Assessment of safety and quality of pharmacotherapy in old age**
14.00-15:00	**P: Presentations of established assessment tools: development, content, applications (3x20')** **Paul Jansen** (University Medical Centre, Utrecht, the Netherlands) **Mirko Petrovic** (University of Ghent, Belgium)
15.30-16.00	*Coffee / tea break*
16.00-17.30	**WS: Selection of PIM criteria for the regular electronic assessment of safety and quality** **Introduced by Monique Elseviers** (University of Ghent, Belgium)
17.30-18.00	**PD: Requirements, strengths and limitations of PIM criteria for the regular electronic assessment in the different settings** **Convenor Robert Vander Stichele** (University of Ghent, Belgium)
19.00	*Dinner*

Saturday 14 June 2014

09.00-10.30	**Session4: Defining prescribing quality indicators in advanced age**
09.00-09.30	**P: Prescribing quality indicators: theoretical background and specific requirements in vue of safety and quality in advanced age** **Petra Denig, Flora Haaijer Ruskamp** (University of Groningen, the Netherlands)
09.30-10.40	**WS+PD Selection of prescribing quality indicators in advanced age** **Convenor Robert Vander Stichele** (University of Ghent, Belgium)
10.40-11.00	*Coffee / Tea Break*
11.00-12:30	**Session5: Future perspectives**
11.00-11.20	**P: Integration of the assessment of quality and safety of pharmacotherapy in the RAI data collection** **Daniela Fialová** (Charles University, Prague, Czech Republic)
11:20-12.20	**WS+PD Dissemination of the results and future research perspectives** **Convenor Monique Elseviers** (University of Ghent, Belgium)
12:20-12.30	**P Closing remarks** **Robert Vander Stichele** (University of Ghent, Belgium)
12:30	*End of Workshop and departure*

5. FINAL LIST OF PARTICIPANTS

	Country	Participants	Affiliation
CONVENERS			
1	BE	Monique Elseviers	Ghent University, Heymans Institute of Clinical Pharmacology
2	BE	Robert Vander Stichele	Ghent University, Heymans Institute of Clinical Pharmacology
ADMINISTRATION AND REPORTING			
3	BE	Maarten Wauters	Ghent University, Heymans Institute of Clinical Pharmacology
4	BE	Katrina Perehudoff	Ghent University, Heymans Institute of Clinical Pharmacology
PARTICIPANTS			
5	BE	Mirko Petrovic	Ghent University Hospital, Department of Geriatrics Universitair ziekenhuis Gent
6	BE	Majda Azermai	Ghent University, Heymans Institute of Clinical Pharmacology
7	BE	Tinne Dilles	University of Antwerp, department Nursing Sciences Antwerp, Belgium
8	CZ	Daniela Fialová	Charles University in Prague, 1st Faculty of Medicine, Dept. of Geriatrics and Gerontology, Prague, Czech Republic
9	DE	Petra A Thürmann	University of Witten/Herdecke, Philipp Klee-Institute for Clinical Pharmacology. HELIOS Klinikum Wuppertal, Germany
10	IE	Denis O'Mahony	Cork University Hospital , Department of Medicine, University College Cork & Consultant Geriatrician, Wilton, Cork, Ireland.
11	NL	Katja Taxis	University of Groningen, department Pharmacotherapy and Pharmaceutical patient care Groningen, the Netherlands
12	NL	Flora Haaijer Ruskamp	Department of Clinical Pharmacy and Pharmacology University Medical Center Groningen, the Netherlands
13	NL	Petra Denig	Department of Clinical Pharmacy and Pharmacology University Medical Center Groningen, the Netherlands
14	NL	Paul Jansen	Universiteit Utrecht, Department of Geriatric Medicine, Utrecht, The Netherlands
15	NO	Hege Salvesen Blix	hege.salvesen.blix@fhi.no Norwegian Institute of Public Health, Department of Pharmacoepidemiology, Oslo, Norway
16	NO	Sabine Ruths	University of Bergen, Department of Global Public Health and Primary Care, Bergen, Norway
17	SE	Monica Bergqvist	Karolinska Institutet, Institutionen för neurobiologi, vårdvetenskap och samhälle,Sektionen för omvårdnad, Huddinge, Sweden
18	SE	Kristina Johnell	Karolinska Institutet and Stockholm University: Aging Research Center, Department of Neurobiology, Care Sciences and Society,Stockholm, Sweden
19	UK	Jeffrey Aronson	Oxford University; Nuffield Department of Primary Care Health Sciences, Radcliffe Observatory Quarter, Oxford, UK
20	BE ESF	Roger Bouillon ESF representative	KULeuven, emeritus professor of medicine endocrinology, Leuven, Belgium

6. STATISTICAL INFORMATION ON PARTICIPANTS

Apart from the two conveners (BE) and the two rapporteurs (BE), the 15 participants of the ESF workshop came from 8 European countries:

- Belgium: 3
- Czech Republic: 1
- Germany: 1
- Ireland: 1
- Netherlands: 4
- Norway: 2
- Sweden: 2
- United Kingdom: 1

The age of the 19 attendees ranged from 25 to 65 years, including 6 male and 13 female participants.

Scientific specialties ranged from geriatricians (4), and general practitioners (1) to clinical pharmacologists (3), clinical pharmacists (5), nurses (4) and pharmaco-epidemiologists (2).

Enclosure:

RECOMMENDATIONS FROM THE ESF WORKSHOP

On June 12-14, 2014, an international multidisciplinary team of experts assembled in Ghent, Belgium, for an ESF workshop focusing on the quality and safety of pharmacotherapy in old age and aiming to define the requirements for an electronic assessment tool.

In recent years, several new and revised tools were published to assess potentially inappropriate medication (PIM) in old age (revised Beers2012; Priscus 2010; Start-Stopp,2008). PIMs can be defined as "medications that have no clear evidence-based indication, and carry a substantially higher risk of adverse side-effects or are not cost-effective" (O'Mahony and Gallagher, 2008).

The content of PIMs varied considerably, from PIMs including only a particular drug name (e.g. do not use digoxin in old age) or a drug class (e.g. avoid anticholinergic drugs in the elderly) to complex descriptions including diagnostic and clinical information (e.g. avoid non-selective β-blocking agents in patients with diabetes mellitus and frequent hypoglycemia). Lists of PIMs are applied for general benchmarking purposes as well as for clinical assessment of individual patients in preparation of a multidisciplinary medication chart review.

Adaptation to national drug markets and applicability for automated electronic assessment form the main problems for a more generalized use of these tools in daily practice.

The members of the ESF workshop formulated the following recommendations

2) Reflections on the quality of pharmacotherapy in old age

a) Quality needs to be appraised in the context of the problems that attend old age, including multi-morbidity, disabilities and frailty.

b) A patient-centred approach in older people is needed, including both explicit and implicit measures that improve the quality of pharmacotherapy. In assessing and managing the quality of drug therapy at both the population and individual levels, lists of PIMs play an important role in assuring the quality of pharmacotherapy.

c) Outcomes should be well defined
   i) Therapeutic failure should also be considered as an undesired outcome.
   ii) Symptomatic burden is also very important and should be adequately documented.
   iii) Quality of life must be assessed and documented (pain, discomfort, depression, dyspnoea): optimizing the benefit-harm balance.
   iv) Outcomes should include the patient perspective (QoL) and the societal view (less hospitalisation).
   v) Realistic goals of care must be set.
   vi) Advanced care planning could be incorporated in the perspective of achievement of care goals.

d) De-prescribing should be considered in a multidisciplinary context as a valuable domain in quality of pharmacotherapy in a number of therapeutic areas, taking into account patients preferences and needs, life expectancy as well as (advanced) care planning.

e) Underuse should also be considered

3) How can we improve the quality of pharmacotherapy in old age?

a) Improvement can be considered at each stage of the complete medication management system, starting with the prescription of a medicine, then the dispensing, preparation and administration and ending with monitoring.

b) Improvement can additionally be considered by the observation of (lack of) therapeutic effects, adverse drug reactions and drug-drug and drug-disease interactions.

c) Improvement can be obtained by stimulating a multidisciplinary multistep approach with the organisation of medication chart reviews involving prescribers as well as (clinical) pharmacists and nurses.

d) Pharmacotherapy in old age needs a frequent follow-up with a regular re-evaluation of the therapeutic effect, dosage and benefit-risk profile, particularly when new medicines are prescribed/de-prescribed or new symptoms/pathology arise.

e) Lists of PIMs are considered as a valuable tool
   i) to improve the quality of prescribing in individual patients (in caring for the individual patient)

   ii) to follow-up the impact of interventions to improve prescribing (in health care research projects)
   iii) to evaluate the quality of pharmacotherapy at different health care levels and in different settings (primary care, home care, nursing home, hospital).

f) Populations of palliative older adults, severely demented older adults and persons with short life expectancy are specific groups with different care goals, where the general criteria are no longer valid and cannot be applied. .

4) Could PIMs be assessed electronically?

a) So far, PIMs have mainly been applied to survey data extracted from:
   i) the medical charts of individual patients
   ii) existing health care databases (such as reimbursement data, dispensing databases).

b) PIMs can be assessed electronically for a broad and regular evaluation of the quality of pharmacotherapy in old age. Particularly PIMs based on medication only can be easily adapted for broad screening programs. More difficulties can be expected for the adaption of PIMs where additional information on diagnoses and clinical data is required.

c) Prerequisites for electronic assessment are
   i) Medications should be coded (ATC, …)
   ii) Clinical data should be coded (ICPC, ICD, SNOMED-CT)
   iii) Decision rules (explicit criteria) should be fitted into an operational algorithm.

d) For regular application of PIM lists, secondary use of routinely collected data is highly recommended.

e) Developers of lists of PIMs should consider the suitability of the second data collection method throughout the development cycle.

f) Electronic medical records should respect a uniform coding system for medicines, clinical diagnosis, and symptoms, enabling automated screening for PIMs.

5) Is a new unifying list of PIMs required?

a) No. A new list would neither be necessary nor useful.

b) Focus should be on existing European lists, including the recently introduced START/STOPP and PRISCUS, and LAROCHE, which are good starting points for Europe. NORGEP can be of added value because of its emphasize on additional items related to duration of therapy and dose. Also the updated Beers list as 'the international standard' can be considered as a valuable approach for improvement of prescribing practices.

c) There is a need for an inventory of existing lists, which have undergone efforts of validation of their contents.

d) The inventory should be specific for older people, adequately maintained and made publically available.

e) In general, a detailed study of the overlap or gaps between all existing lists of PIMs would be useful.

f) Existing lists should demonstrate their relationship to desired (patient) outcomes through research.

6) Is there a need to create a repository of PIMs?

a) Yes, a complete repository of all available PIMs is needed, beginning with the building stones content of already established lists (PRISCUS, START/STOPP, NORGEP, LAROCHE, BEERS).

b) This repository should be for functional use, with regard to availability of data, setting, geographic area, purpose, perspective and therapeutic focus. Evidence used for selection of PIMs should be documented and maintained in an international effort.

c) The elements required for each PIM in the repository are:

    i) Data collection requirements for valid use of the PIM: Medication (name, unique identifier, ATC-code), duration, dose, patient ID, indication, clinical data, specific parameters.

    ii) An indication of whether longitudinal data are necessary or whether the PIM can be applied to cross sectional data only.

    iii) The relevant therapeutic area.

    iv) The evidence substantiating its designation as a 'PIM' (indicating the strength of evidence and of the recommendation).

    v) Its relationship to quality indicator(s)

        (1) Is it possible to determine the denominator?

        (2) Is validation research available for the status as quality indicator?

        (3) Is the QI part of a validated set of quality indicators?

    vi) Any epidemiological data on the prevalence of the PIM.

    vii) The source (i.e. the list from which the PIM originates).

d) We might develop new methods to structure, synthesize, and present evidence on PIMs. These methods could be inspired by the methods on collecting information of suspected adverse drug reactions developed by the Cochrane Collaboration and the critical appraisal tools developed by the Oxford Centre for Evidence Based Medicine.

7) Is an international catalogue of medication required?

a) A catalogue of substances and group names (as mentioned in any of the PIMS in the repository) should be used. It should be completed, maintained and made publically available.

    i) Single active substances do not pose a problem for the creation of an international catalogue, but attention to the presence of effects or inconsistencies (e.g. verapamil versus calcium channel blockers) is needed.

    ii) Group names should be agreed upon internationally and defined by combining ATC codes at different levels. (e.g. antihistamines).

    iii) Problems with combinations need to be addressed.

    iv) Qualifiers of active substances (route of administration, pharmaceutical form (e.g. extended release) should sometimes be considered.

b) Information technology should be used more to collect data on the indications of medications, using predefined drop-down lists with coded value sets.

c) The expression of the medication should be universally applicable to any therapeutic arsenal of any given country, provided this therapeutic arsenal is correctly linked to the ATC.

d) A basis for selection is frequency of use (pharmaco-epidemiology and drug utilisation research).

e) Medications should be grouped by physiological systems, which is already the case when using ATC.

8) Are clinical data required to assess the quality of pharmacotherapy?

a) Yes, clinical data are required to fully appraise the quality of pharmacotherapy. However, medication-only PIMs are valuable and need to be exploited to the maximum.

b) The richness of clinical data required to assess PIMs depends on data availability, the setting, the purpose of the assessment, and the perspective of the assessor.

c) The clinical data required to assess PIMs should be fully specified and operationalized for data collection. The terminology of key concepts should be standardized across languages and coding systems in order to ensure semantic interoperability.

d) Producers of lists of PIMs need to join the e-Health effort for semantic interoperability

e) The responsibility for this standardization partly lies with developers of PIMs.

9) Is a limited clinical data set required for routine data collection from medical records?

a) A limited clinical data set may be useful for specific settings and circumstances.

b) It can be useful for focused validation of clinical data collection systems that are not completely reliable.

c) It should be well motivated, with an explicit statement of its purpose and perspective.

d) A limited clinical data set will be unnecessary in settings with good medical record-keeping practices and sophisticated electronic health care records.

e) It is necessary to establish a working group on this topic.

f) Research on the development of new PIMs should also consider the content of the limited clinical data set.

10) Quality Indicators (QIs)

a) A PIM may or may not evolve from a QI, provided additional validation research has been performed. PIMs are but one source of QIs.

b) For the assessment of quality of prescribing in older people at a public health level, PIMs should first evolve to the status of QIs.

c) There is a need for an easily accessible catalogue of quality indicators for older people (which are sparse and often still being developed) to provide an overview. Australia made some headway in this regard (Basger BJ et al, 2008) and should be contacted.

    i) QIs for older people should be collected in a set, with additional information on what data are needed to apply them and how they should be evaluated.

    ii) QIs should be differentiated from structural indicators. The latter should be better developed, but are more difficult because they can be setting-specific. It is still unclear whether structural indicators only serve a descriptive function or whether they are related to outcomes.

d) Funding for validation research regarding structural, process, and outcome quality indicators should be extended.

e) The development of a validated QI set for population-based prescription databases should be fostered, while exploring the possibilities of record linkage with epidemiological patient registries with more detailed clinical content.

f) Development of explicit criteria and quality indicators should include steps to assure semantic interoperability on EU and global level with due respect for the international classifications and nomenclatures and the development of appropriate clinical models for selected clinical parameters. Active substance and medication group names should be expressed with the ATC classification system.

11) International collaboration

a) Collaboration should be established with the international interRAI Corporation (International Resident Assessment Instrument Corporation), to determine the fit between the data collection requirements and the need for clinical data to operate explicit criteria and quality indicators.

b) Collaboration must be intensified on a European level.

    i) Formal cooperation between scientific associations of primary care physicians, geriatricians, clinical pharmacologists, (clinical) pharmacists, nurses, and pharmaco-epidemiologists is needed to foster the field of quality assurance in pharmacotherapy.

    ii) Collaboration with the European Initiatives on e-HEALTH, Semantic Interoperability (SemanticHealthNet), and secondary use of clinical data for research (EHR4CR) is needed.

    iii) New support systems at the point of care for comprehensive decision support in treating older adults are under development. Collaboration with projects such as STRIP, SENATOR, and PRIMA should be intensified.

    iv) Collaboration on the European level is needed to maintain expertise in the pharmaco-therapeutic knowledge databases that underpin decision support systems. Contact with the Guidelines International Network (GIN) and the Cochrane Group is needed.

    v) Exchange of information should be fostered with CIOMS.