Rebuild of catalogues survey – EU PAS Register

Project: Real World Metadata, Data Quality Framework and Catalogues

Presented by Ana Cochino – 18 November-2021 ENCePP Plenary meeting

Background: survey structure and objectives

- The survey was sent out to all ENCePP members with the purpose to:
  - Understand further points for improvement of the current existing EU PAS Register and ENCePP resources database building up on existing experience
  - Get feedback on the usefulness and feasibility of some data elements proposed in the current 'metadata list' of the MINERVA project
  - Collect requirements related to functionalities and common use scenarios
- The questionnaire was structured in three sections:
  - Data sources catalogue, from the point of view of the data user
  - Data sources catalogue, as a 'data owner'
  - Studies catalogue
- The results presented here focus on more challenging areas rather than an extensive summary of all responses received

Outline of the presentation

The slides show survey questions results along with the comments received, looking at fields such as

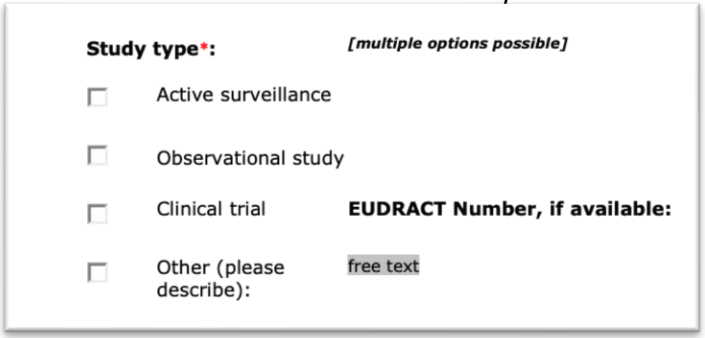
- Study type
- Study design
- Scope of the study
- Source of funding
- Coding of fields (dictionaries)
- Automatic checks for data accuracy
- Fields proposed to be added
- Data tables (suggested during MINERVA)

Study type – current EU PAS values

Study type

The current EU PAS register collects data on Study type with values: active surveillance, observational studies and clinical trial. The survey collected the following comments and proposals:

Current EU PAS questionnaire



Comments received:

- active surveillance and observational study are overlapping;

Suggestions for addition of new values:

- systematic reviews/meta-analysis of randomized controlled trials;
- questionnaire based surveys;

- sub-categories for clinical trials:
  - Expanded Access Programs
  - Pragmatic clinical trial

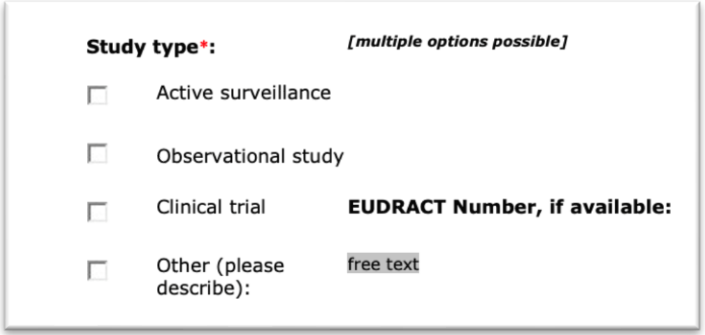
- sub-categories for active surveillance:
  - prescription event monitoring
  - intensive monitoring schemes

Proposals for 'observational study' refinement

Study type

The current EUPAS collects information structured as 'observational studies'. Further refinement of the category 'observational study' was proposed. During the survey the following values were suggested:

- prospective primary data study
- retrospective secondary data
- prospective secondary data
- systematic reviews and meta-analysis
- distinguish based on primary data collection
- questionnaire-based survey
- retrospective chart review
- ecologic study
- cohort, case-control, cross-sectional, self-controlled...
- non-interventional



Current EU PAS questionnaire

Study design – feedback received

The question on 'study design' values generated the following proposals:

- 'cross-sectional study':
  - To add 'questionnaire-based survey' here (and not as a specific type of 'observational study')
- 'cohort study':
  - To be further split in prospective cohort and retrospective cohort
  - To add registries (although are not a "design" per se)
- 'case control study':
  - include nested-case control study;
- Recommend to have only one category "Case-only...", but not then split by possible types
- 'case series' correspond to 'non-comparative cohort studies' and are not 'self-controlled'

Good agreement

Least agreement

Study design

Question 3 'study design'	👍	👎
Cross-sectional study	16	0
Cohort study	16	0
Case control study	15	0
Case-only (self-controlled) design - case-series	13	2
Case-only (self-controlled) design - self-controlled case series	14	1
Case-only (self-controlled) design – case-time-control	12	3
Case-only (self-controlled) design - case-case-time control	12	3
Randomised controlled trial	14	2
Non-randomised controlled trial	14	2

Study design (continued)

- Randomised trial:
  - should be limited to pragmatic trials
- Add pragmatic clinical trial separately, although they are falling under randomised controlled trial category (Large Simple trial)
- Non-randomised controlled trial:
  - Redundant with "observational study”
  - Should be further refined in: single arm or not
- Add: ecologic study

Study type vs study design – discussion points

- There is a level of overlap and confusion between what should go in 'study type' vs 'study design'

- To move forward, the proposal is to:
  - Limit 'study type' to the values 'interventional' and 'non-interventional' (only)
  - Structure further the 'study design' in taking specific set of values, depending on the 'study type' selected
  - Add more options to 'interventional' studies than currently available (in line with proposals received)
  - Collect more feedback and agreement on values in a dedicated WG1 meeting in December

Discussion on proposed values for 'study design' to follow (Slido)

Scope of the study

- Impact of regulatory actions: too specific and quite redundant with above categories depending on what aspect will be evaluated. Does it include RMM effectiveness? it may overlap drug utilization and effectiveness
- Effectiveness evaluation: to clarify as "assessment of risk minimization measure effectiveness/implementation”
- Drug interaction study - Too specific, quite redundant with "drug utilization study”

Disease epidemiology	✓ 15	0
Safety evaluation	✓ 15	0
Drug utilisation study	✓ 15	0
Efectiveness evaluation	✓ 15	✗ 0
Pharmacokinetic studies	✓ 12	✗ 2
Pharmacodynamic studies	✓ 11	✗ 3
Drug interaction study	✓ 12	✗ 3
Impact of regulatory action	✓ 13	✗ 2

Survey question: current values in EU PAS register

<u>Suggestions received to add values:</u>

- Natural history of disease studies
- hypothesis generation through AI
- validation studies,
- methods
- feasibility

Discussion on proposed values following (Slido)

Study's source of funding

(Question 5) In the current EU PAS Register The 'source of funding' lists the following values:

- Pharmaceutical companies
- Charities Government
- Body Research councils
- EU funding scheme

Other suggestion for 'source of funding':

- Institutional funding e.g. research funding of my hospital which is a public hospital.
- Academics, non-EU funding scheme, others
- Own funding/independent funding by institution
- Institutional internal funding
- EMA/National competent authorities

Coding of fields, dictionaries

(Question 6) The current EU PAS Register collects the information on 'study drug' as follows

- Substance class (ATC code)
- INN
- brand name

Are there any other values that are useful to be added to the above ones?

- 5 replies indicated agreement with the above values, two additional comments:

- Let's make sure this is a repeatable field in case multiple drugs have to be entered
- Mode of application (topical, systemic, etc.)

(Question 7) The medical condition is collected in the current EU PAS Register using MedDRA terminology. Is there another terminology that you find to be better suited/more useful (e.g.: SNOMED)?

- MedDRA (3 replies)
- ICD (6 replies)
- SNOMED (1 reply)

Discussion on terminology for medical condition following (Slido)

Coding of fields, dictionaries (Continued)

- *(Question 8)* The current EU PAS register collects the information on 'population' as follows: Preterm Newborns; Term Newborns (0-27 days) Infants and toddlers (28 days – 23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-44 years) Adults (45-64 years) Adults (65-74 years) Adults (75 years and older).
  - Agreement with the proposed categories (3 replies).
  - We would suggest to have only two adult categories 18-64 and 65+. Having more is confusing. (1 reply)
  - To also be more explicit when the target population is a population of "Health Care Providers" rather than patients (e.g risk minimisation surveys targeting HCP) (1 reply)
  - More granularity in the elderly population (1 reply)
  - 2-5 pre school children and 6-11 children (1 reply)
- *(Question 9)* The current EU PAS register collects the information on 'population of interest' as follows: Renal impaired, Hepatic impaired, Immunocompromised, Pregnant women, Lactating
  - The populations of interest are good but rather limited. It could be expanded with for instance paediatrics, elderly, people with intellectual disabilities etc.
  - Add institutionalized patients (e.g. residing in nursing homes), paediatric, neonates

Introduction of automatic checks

- *(Question 10)* A proposal to introduce consistency checks such as:
  - Where the scope of the study is 'disease epidemiology', then the type of study design 'clinical trial' would not be allowed
  - If the study information lists "an established data source = No" then "sources of data = claims database" should not be allowed

<u>Other suggestion of such checks:</u>

- None

<u>Comment</u>

- We would be cautious with implementation of automatic checks as they may be circumstances where multiple design and multiple type of data sources can be used under the same protocol/study

Fields to be added (proposals put forward during survey)

- Comparator (yes/no): There could be more than one comparator
- Orphan drug: Would rather use the ATC search for it
- Orphan drug should be identified through "study drug" or "medical condition"
- Adding cross-reference to Clinicaltrial.gov:
  - other registries (WHO) to be allowed?
  - is already captured in EUPAS register
  - Or any other registers as more are developed
  - avoid duplicating efforts and making the

"study catalog", a complement to "clinicaltrials.gov and not a duplicate

	✓	✗
Comparator (yes/no) - if 'yes' to be indicated	16	0
Orphan drug as exposure	12	3
Has the study been registered in clinicaltrial.gov (yes/no	14	2
For regulatory required studies, the 'marketing authorisation date' (if product based study) in the given indication studied	12	4
Information on Patient Reported Outcomes (PRO) and “Clinician Reported Outcome (ClinRO)	16	0
Use of informed consent	13	3
For PASS studies: Safety concerns to be addressed (MedDRA coded)	15	1

Proposals put forward by WG3, consulted during the survey

Fields to be added (continued)

- For regulatory required studies, the 'marketing authorisation date' (if product-based study) in the given indication studied
  - will be difficult if several marketing authorisations exist and for older INNs
  - why is this important? what if there are several products involved?
  - To add also: EPAR link or Risk Management Summary link
  - Require also 'regulatory procedure number' for the protocol assessment and results assessment of cat 1, 2 and 3 PASS in line with GVP V and VIII
- Use of informed consent:
  - Also, GPRD compliance of consent
- Instead of the 'PASS studies – safety concern to be addressed'
  - it would be more valuable to have the possibility to enter in a field a disease, or/and an event so that all studies done in one specific disease area and/or with a specific outcome event could be found

Proposals for areas of data collection in a future study catalogue

(Question 12) The below categories are suggested by MINERVA group to be collected as part of the 'study catalogue'

- Generally, there's an agreement that the broad categories are useful
- Less agreement on the information around Data characterization (to be further discussed in December)

	👍	👎
The institution that conducted the study (e.g.: contact details, affiliation to a network)	✓ 16	0
The study protocol (the upload of the document, the type of study, population, interventions, comparators, outcomes, timing, setting)	✓ 16	0
Data sources or data banks used (details on extraction and software	✓ 15	✗ 1
Data characterisation performed (completeness, conformance, stability, logical consistency, historical data)	✓ 12	✗ 3
Study results (data extraction procedure and results, summary results tables)	✓ 15	0
Study report and publications	✓ 14	0

Next steps: a dedicated meeting of WG1 will be held in December to look at the different suggestions presented and agree on a proposal for the categories of these fields

Any questions?

Further information

[Insert relevant information sources or contact details as applicable.]

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