



QUANTITATIVE REVIEW OF EFFECTIVENESS OF RISK MINIMISATION MEASURES IN SURVEYS & OUTCOME STUDIES IN EUROPE

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CONFLICTS OF INTEREST

OXON Epidemiology: Conducts field & database observational studies for industry

- **Esther Artime, MSc**, Manager, Pharmacoepidemiology & Risk Management
Centre for Real World Field Studies, Madrid
- **Kirsten Rennie, MA(Cantab) MSc PhD**, Director of Epidemiology
Centre for Real World Database Studies, London

Stuart Pocock, Professor of Medical Statistics, London School of Hygiene & Tropical Medicine

Bayer AG, Epidemiology:

- **Montse Soriano Gabarro**, MD, MSc, Head of Epidemiology
- **Alex Asiimwe**, MSc, PhD, Director Epidemiology
- **Pareen Vora**, MSc, Epidemiologist

EMA: Thomas Goedecke

ENCePP S.I.G on Measuring Impact of PV Activities

AGENDA

1. SURVEY STUDIES

2. OBJECTIVES

3. METHODS

4. RESULTS

5. LIMITATIONS

6. CONCLUSIONS & RECOMMENDATIONS

7. OUTCOMES STUDIES

1

**SURVEY STUDIES
OBJECTIVES**



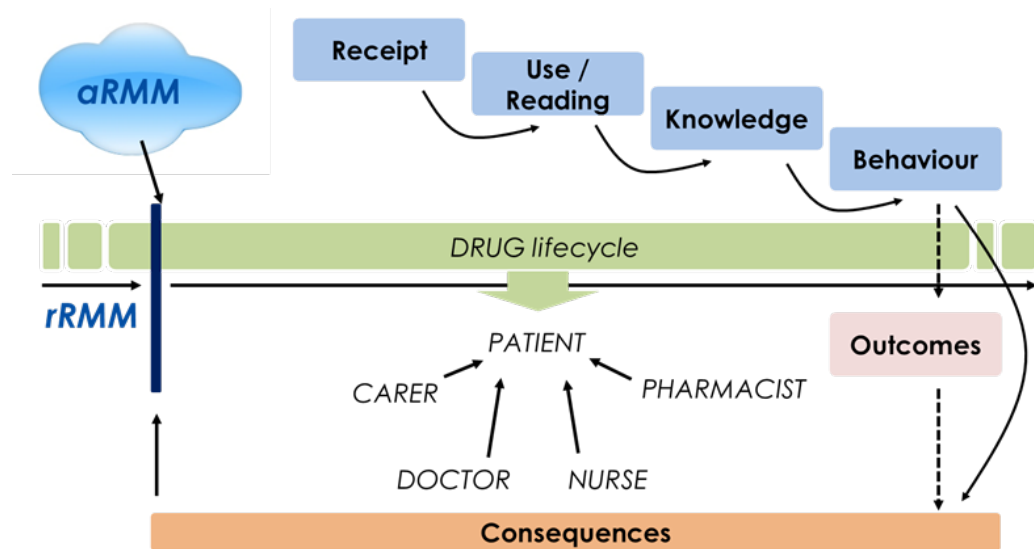
EU RM SURVEY STUDIES - GUIDANCE

- GVP XVI on Risk Minimisation – Annex 1 on Survey Methodology
- CIOMS Report 2014
- ENCePP Methods Guide – Section 4.1.1 on Surveys
- Standard survey texts

OBJECTIVES

1. To describe and analyse study characteristics and results of survey studies assessing the effectiveness of risk minimisation measures (RMMs)

- Participation
- Receipt
- Usage
- Knowledge
- Behaviour



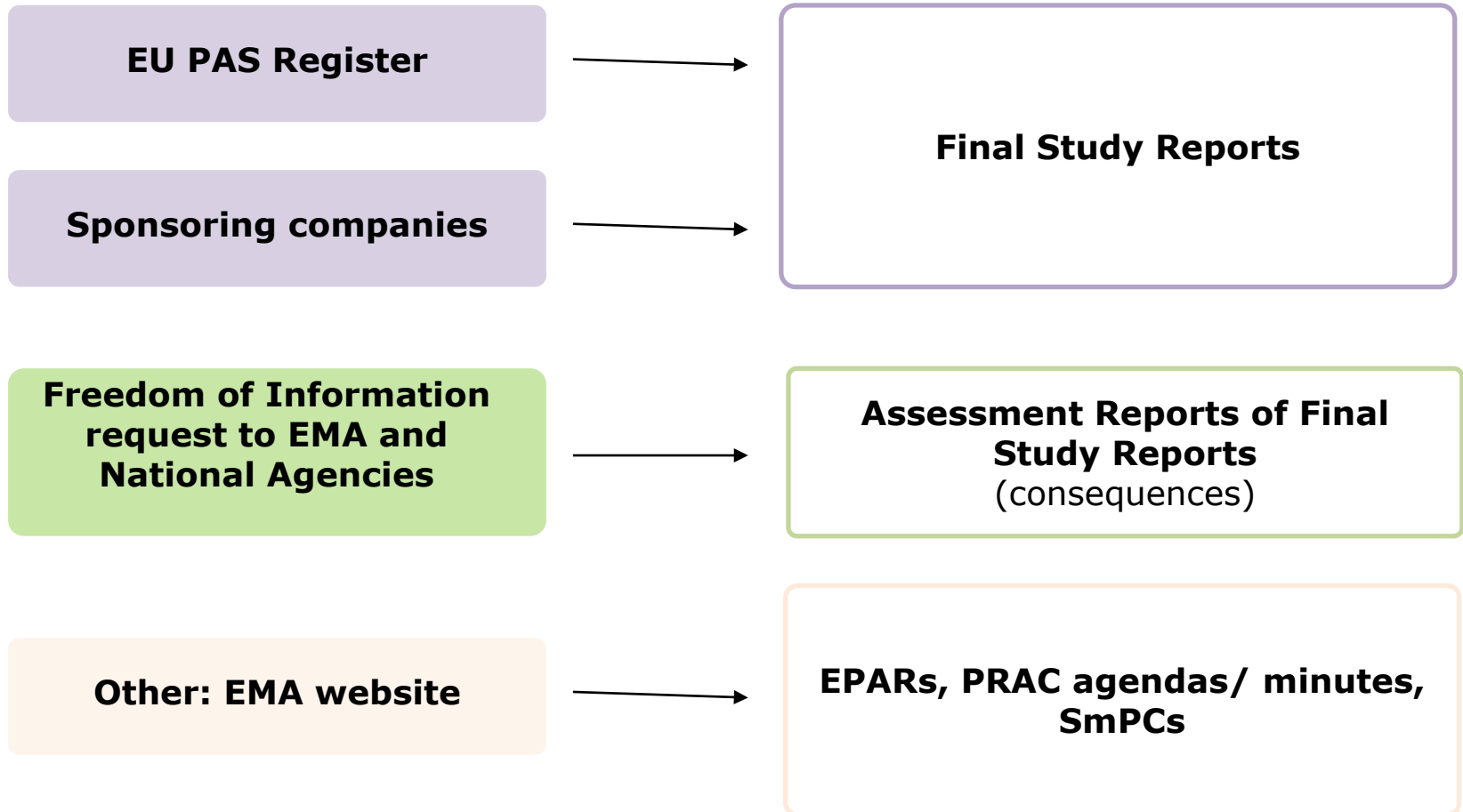
2. To describe regulatory consequences

2

SURVEY STUDIES METHODS



DATA SOURCES



STUDY INCLUSION CRITERIA

- **Survey** component assessing effectiveness of routine or additional RMMs
- In the **EU PAS Register** until *26 May 2017*
- Studies with **reports** (in the EU PAS Register/ from EMA/ from Pharma companies)
- Involvement of ≥ 1 **European country**

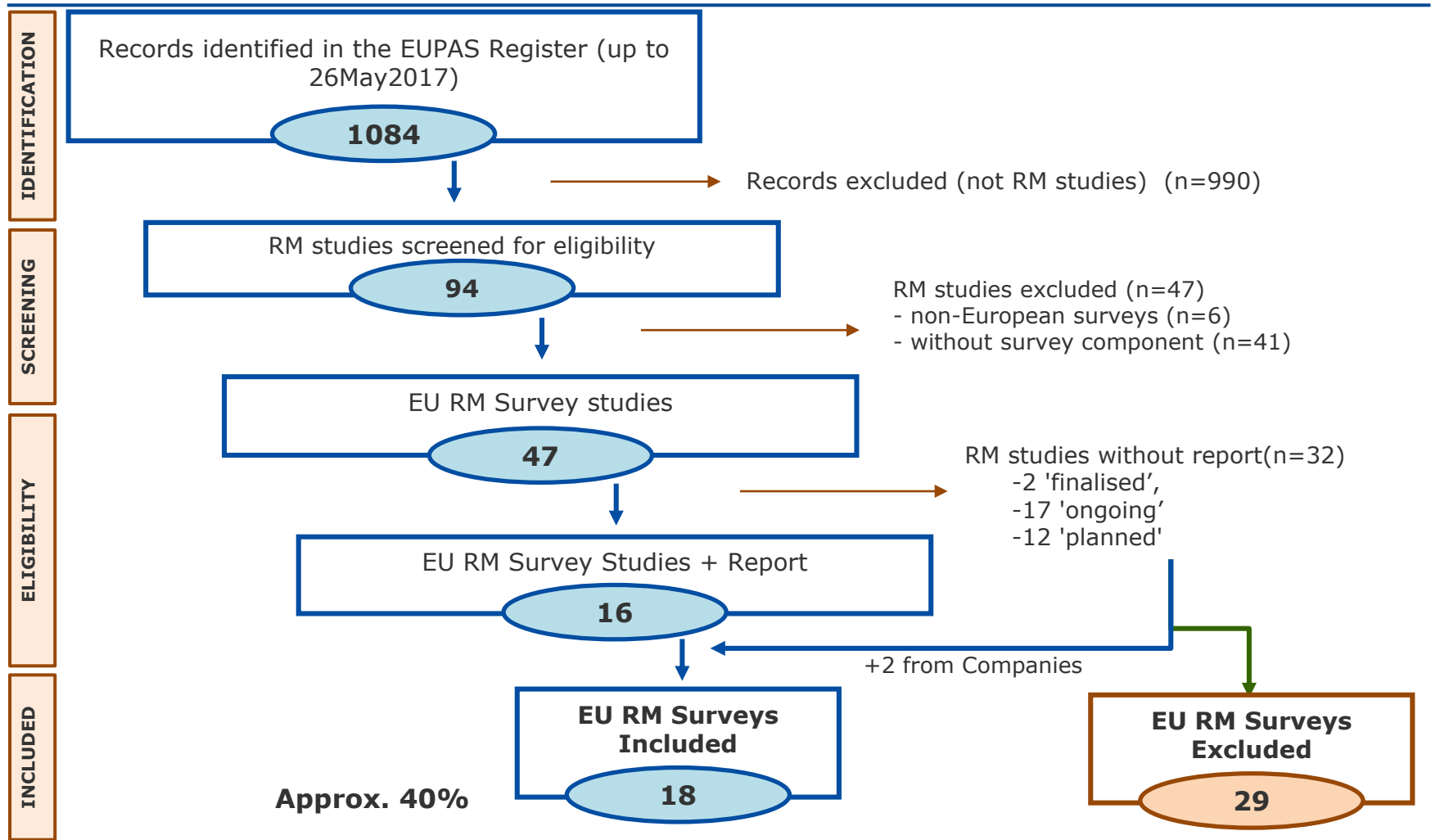
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SURVEY STUDIES

RESULTS:

- Study Selection & Characteristics
- Participation Data
- Receipt
- Use
- Knowledge
- Behaviour

SELECTION PROCESS



STUDY CHARACTERISTICS (I)

Population

- HCP: 14/18
- Patients: 1/18
- HCP and Patients: 3/18

DRUGS: ATC

- N-nervous system: 7/18
- L-antineoplastic and immunomodulating: 3/18
- Others: 8 /18

RMM TYPE

Additional: 16/18:

- PACs: 6/16
- DHPCs 5/16
- Brochures for HCPs 13/16
- Brochures for patients/caregivers 4/16

STUDY DESIGN

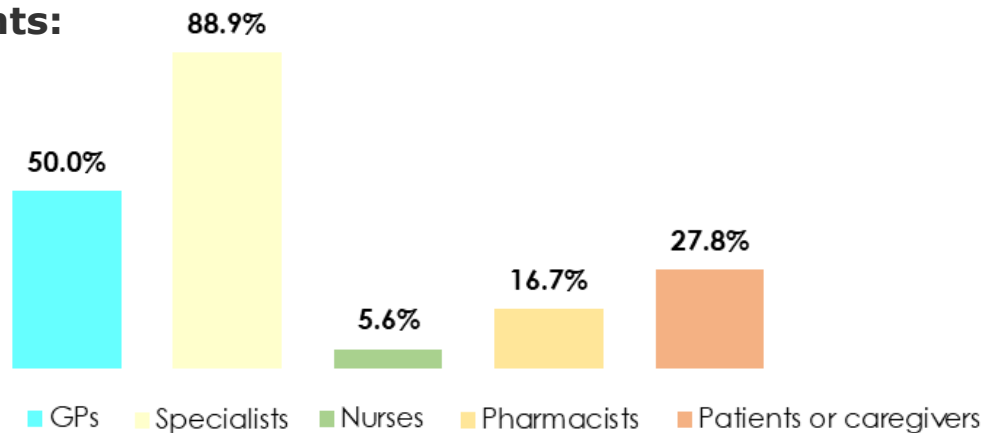
- One-wave X-sectional: 15/18
- Multi-wave design: 3/18

STUDY CHARACTERISTICS (II)

TARGET POPULATION

Number of countries: Median of 7.5; Range 1 - 12

Type of participants:



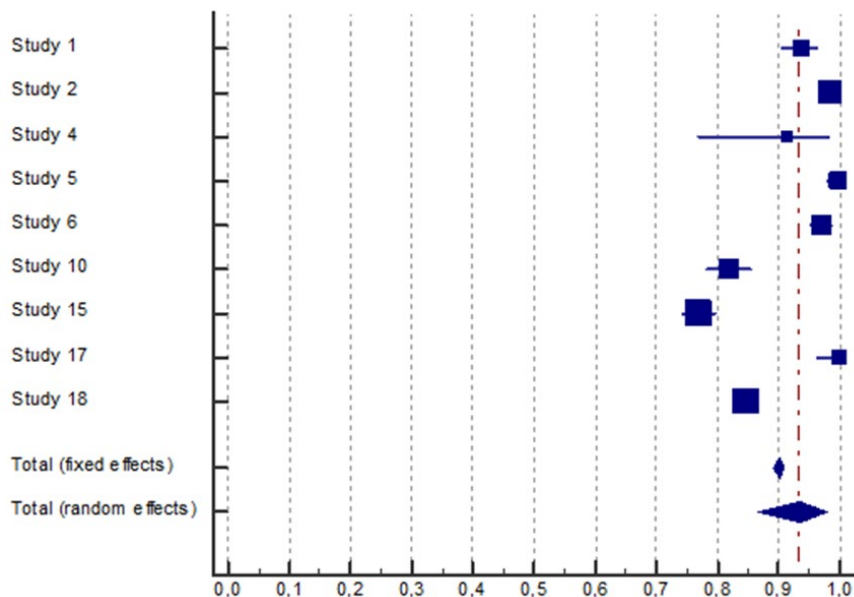
OUTCOMES

- Outcome evaluations alongside surveys in 5 of 18 (27.8%)
 - Drug utilization: 3
 - Monitoring: 1
 - ADRs: 1

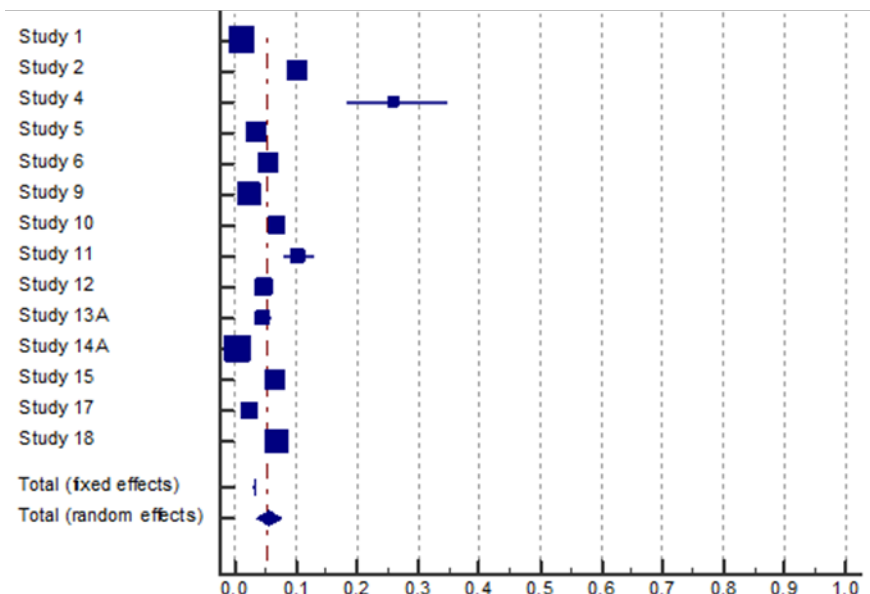
CALCULATED PARTICIPATION DATA

HCP Surveys

Completers / eligible: **93.4%** (86.8 - 97.9)

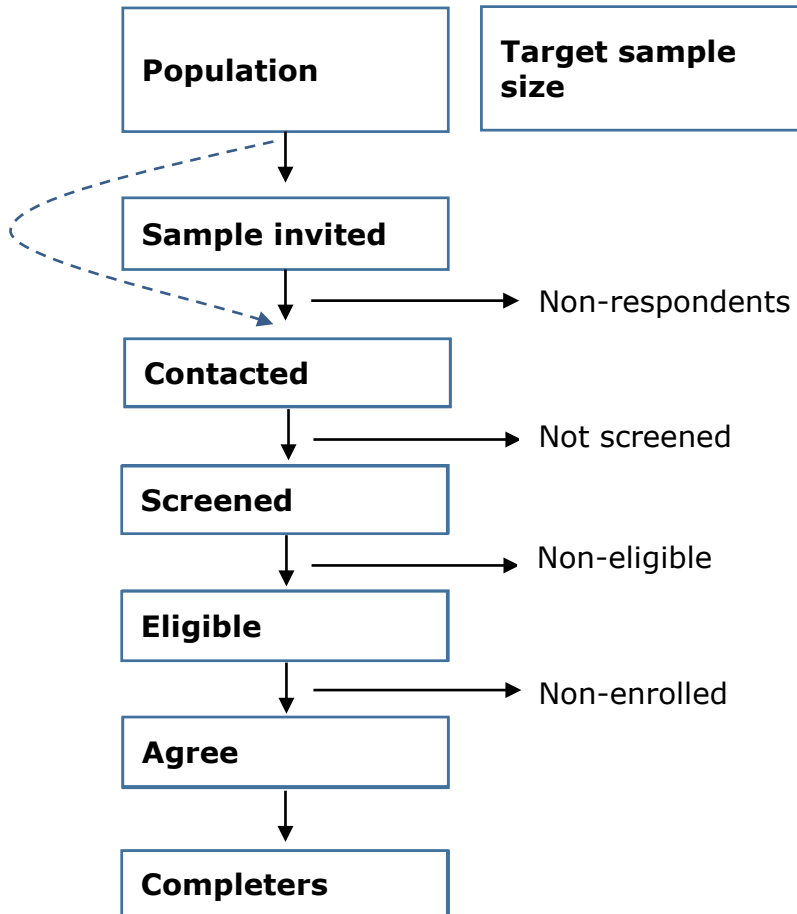


Completers / invited: **5.4%** (3.5 - 7.7)



PARTICIPATION DATA

Reporting scheme



→ Contact Rate = Contacted / Targeted

→ Response Rate = Completers / Invited

→ Completion Rate = Completers / Eligible

→ Respose Rate = Agreed / Contacted

→ Cooperation Rate = Completers / Agreed

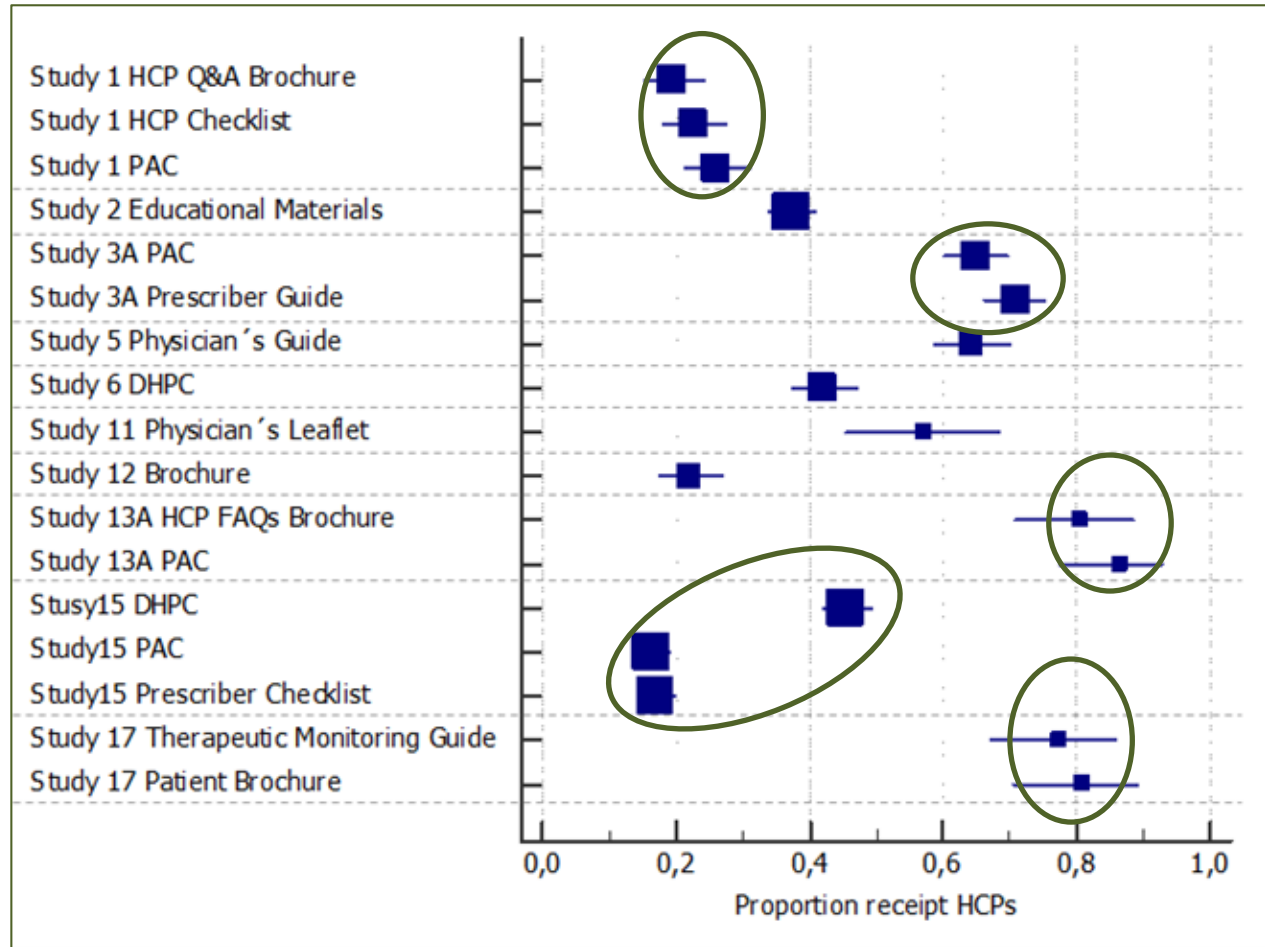
→ Eligibility Rate = Eligible / Screened

→ Completers / Screened

RECEIPT

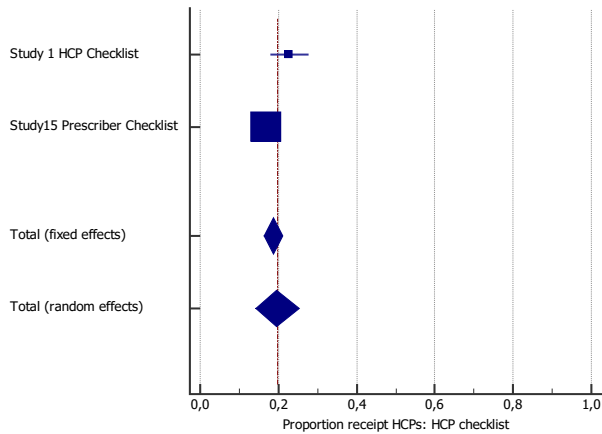
HCP Surveys - Overall

10 studies
with **17**
educational
materials

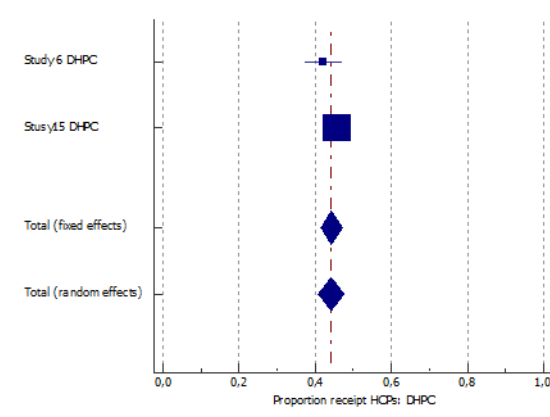


HCP Surveys - by Type of Educational Material

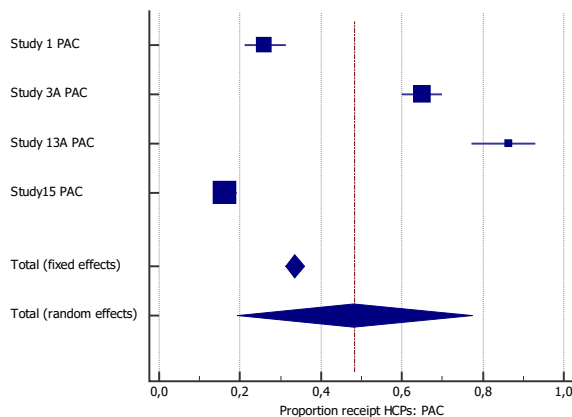
HCP CHECKLIST: 19.5% (14.2 – 25.4)



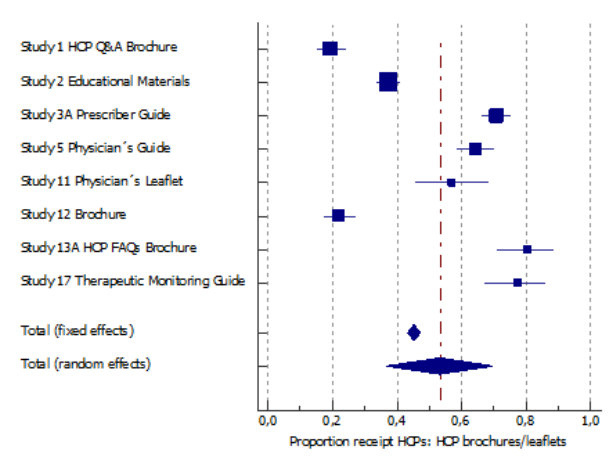
DHPC: 44.2% (40.9 - 47.5)



PACs: 48.1% (19.4 - 77.4)



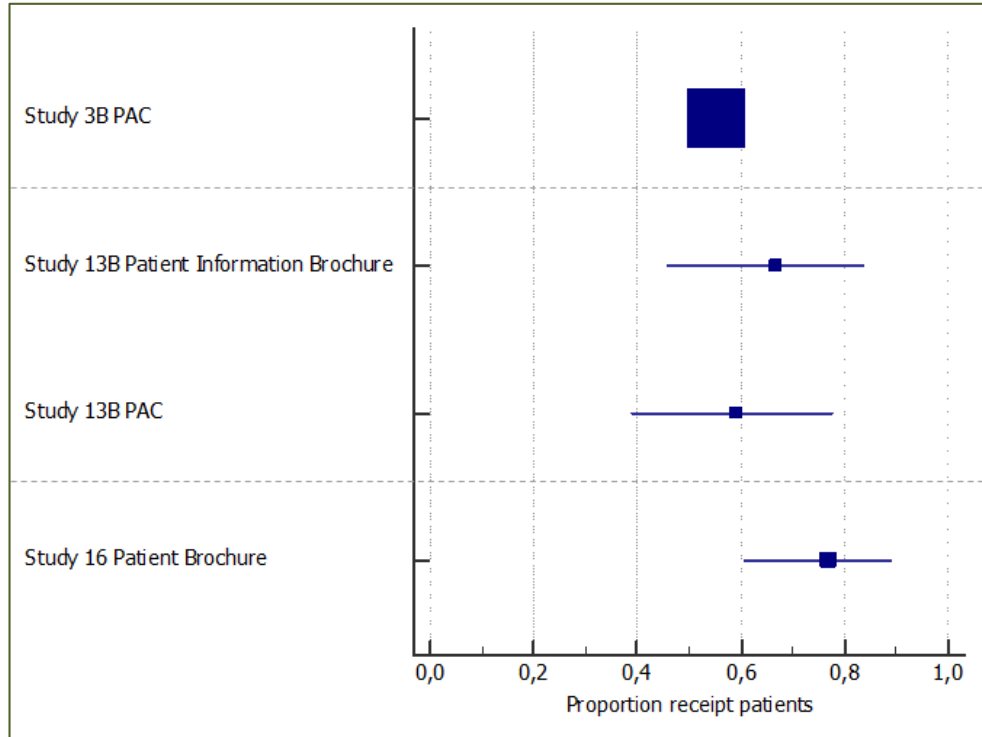
HCP BROCHURES: 53.4% (36.8 – 69.6)



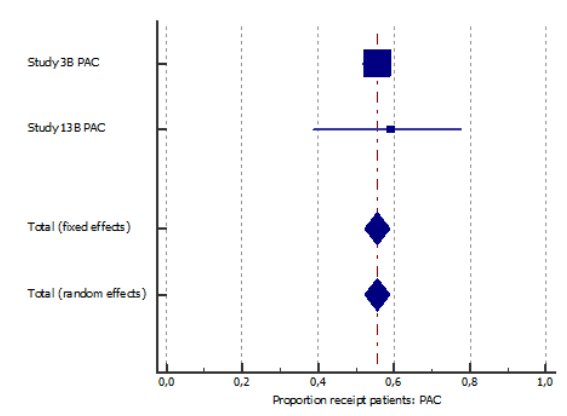
Patient Surveys - Overall and by Type of Educational Material

Receipt by patients of 4 educational materials in 3 studies → 50% - 80%

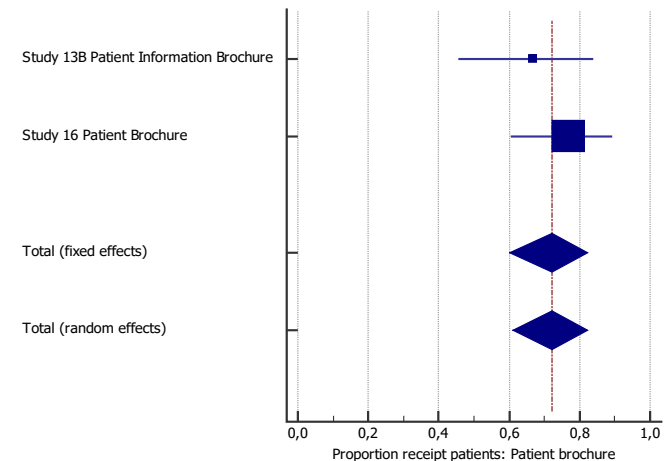
RECEIPT OVERALL



PACs: 55.6% (52.2 – 59.0)



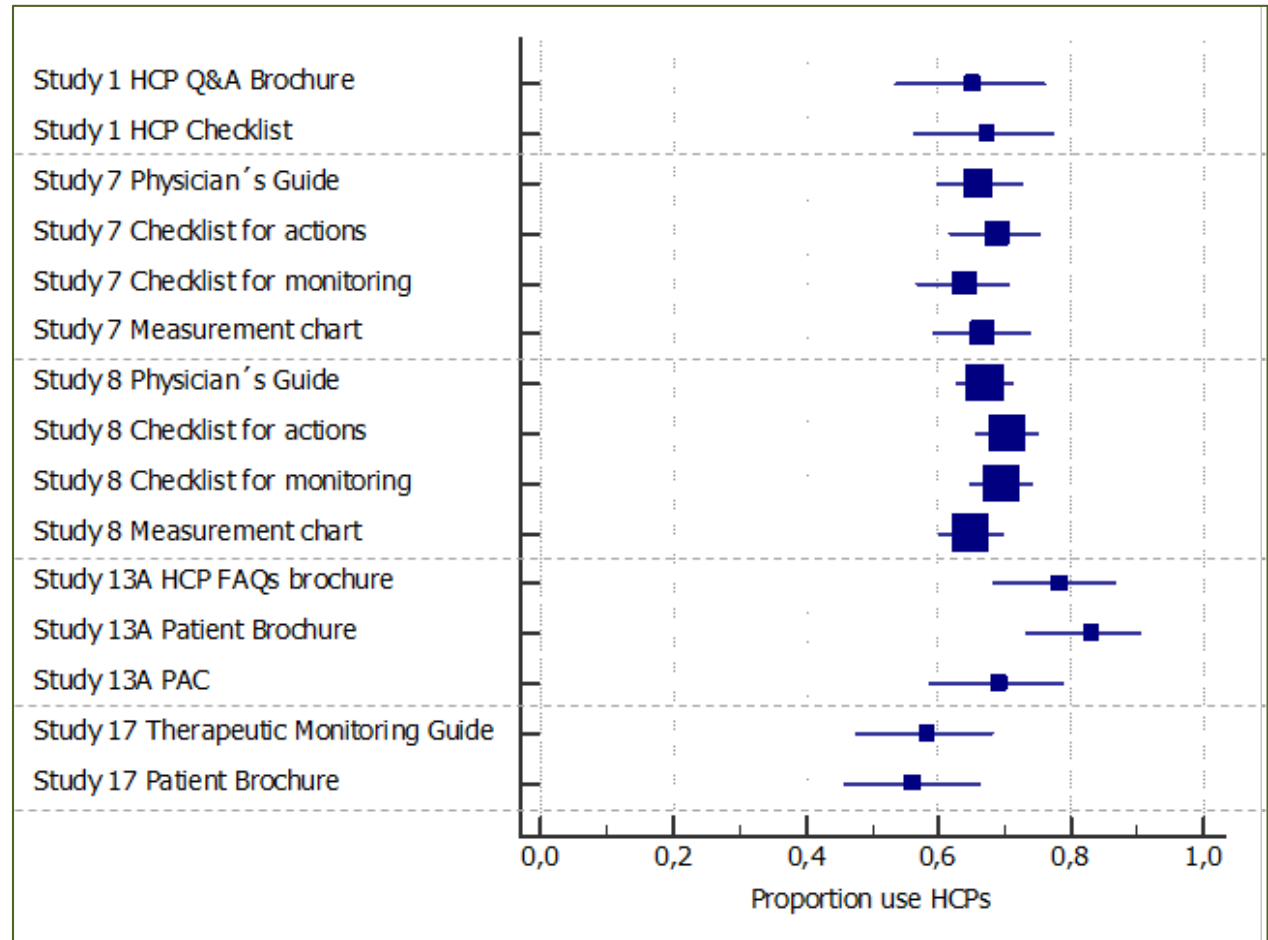
BROCHURES: 72.9% (61.0 – 82.1)



HCP Surveys - Overall

5 studies with 15 educational materials

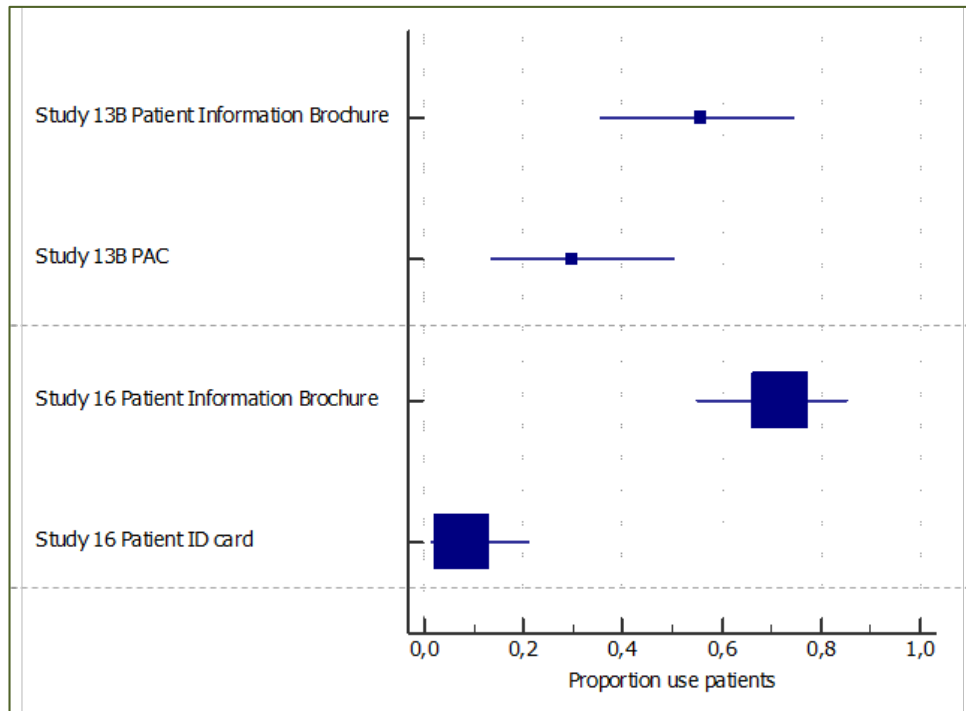
80% of educational materials had use levels of 50-70%



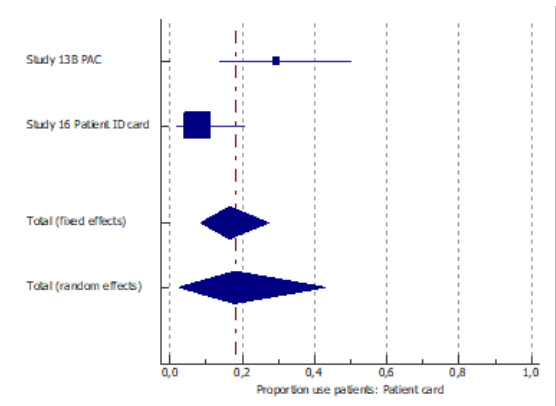
Patient Surveys - Overall and by Type of Educational Material

Reported use in 2 studies of 4 educational materials: < 30% for 2 items

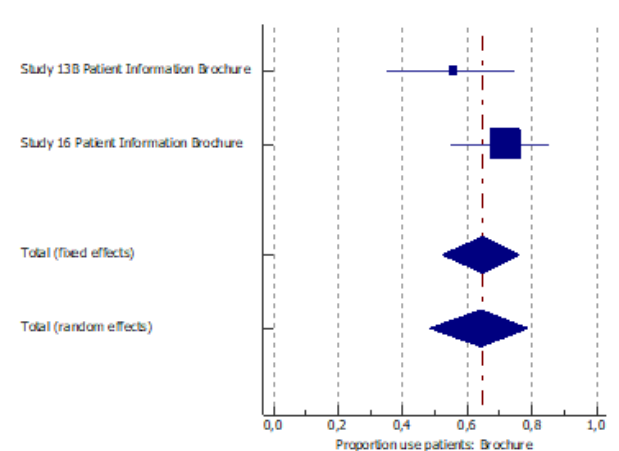
USE



PACs: 17.9% (2.5 – 43.0%)



BROCHURES: 64.3% (48.3 – 78.8)



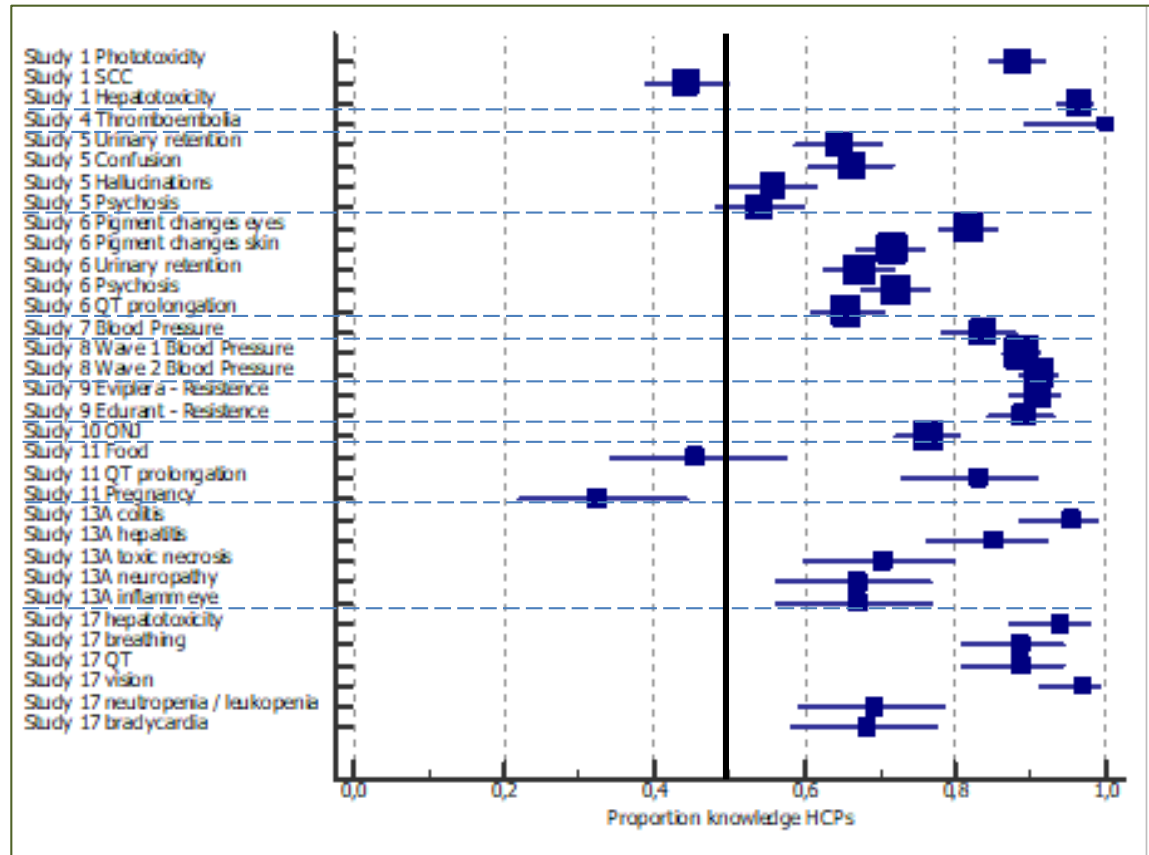
HCP Surveys

13 studies with knowledge of 46 safety concerns

Knowledge of 33 safety concerns:

- > 80% for half of safety concerns
- > 50% for 90% of safety concerns

KNOWLEDGE



KNOWLEDGE

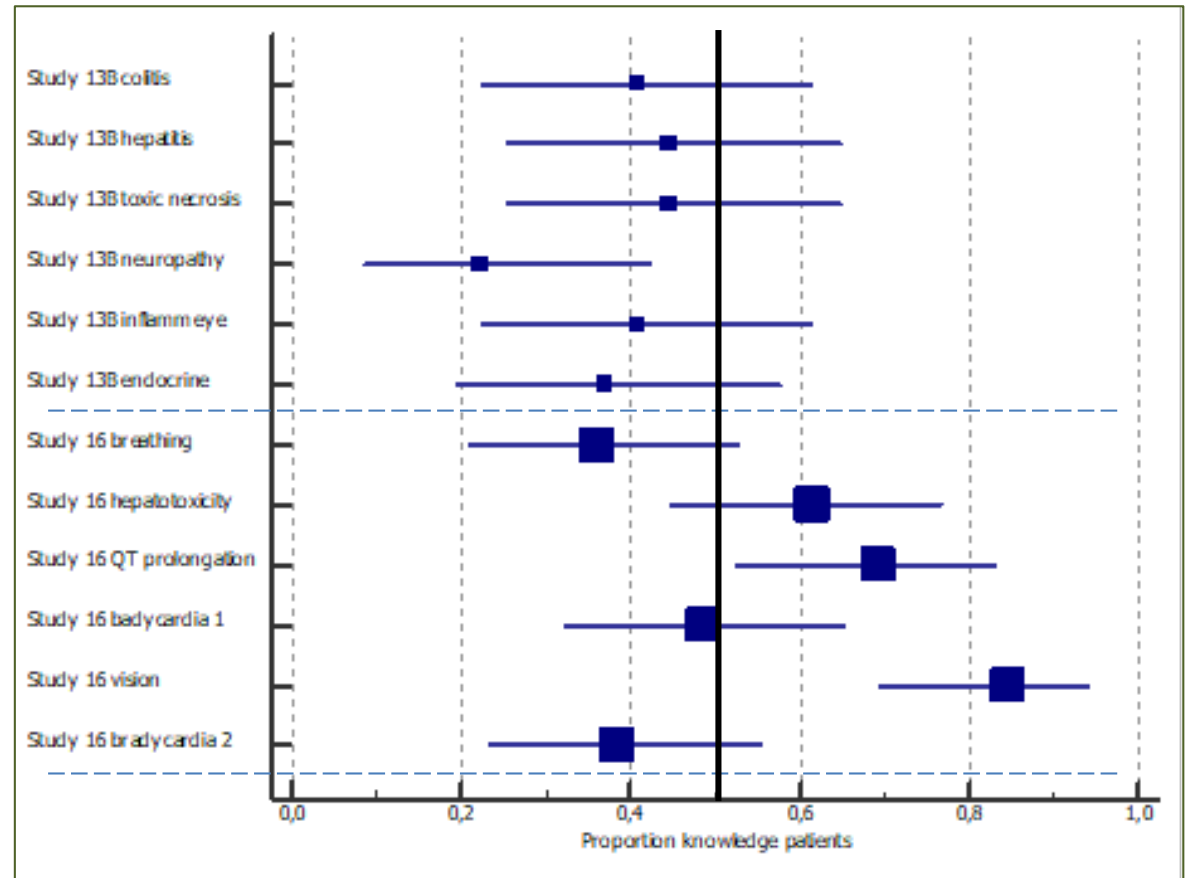
Patient Surveys

2 Studies with 13 safety concerns

Knowledge < 50% for 60% of safety concerns

Knowledge 50 – 70% for 31% of safety concerns

KNOWLEDGE

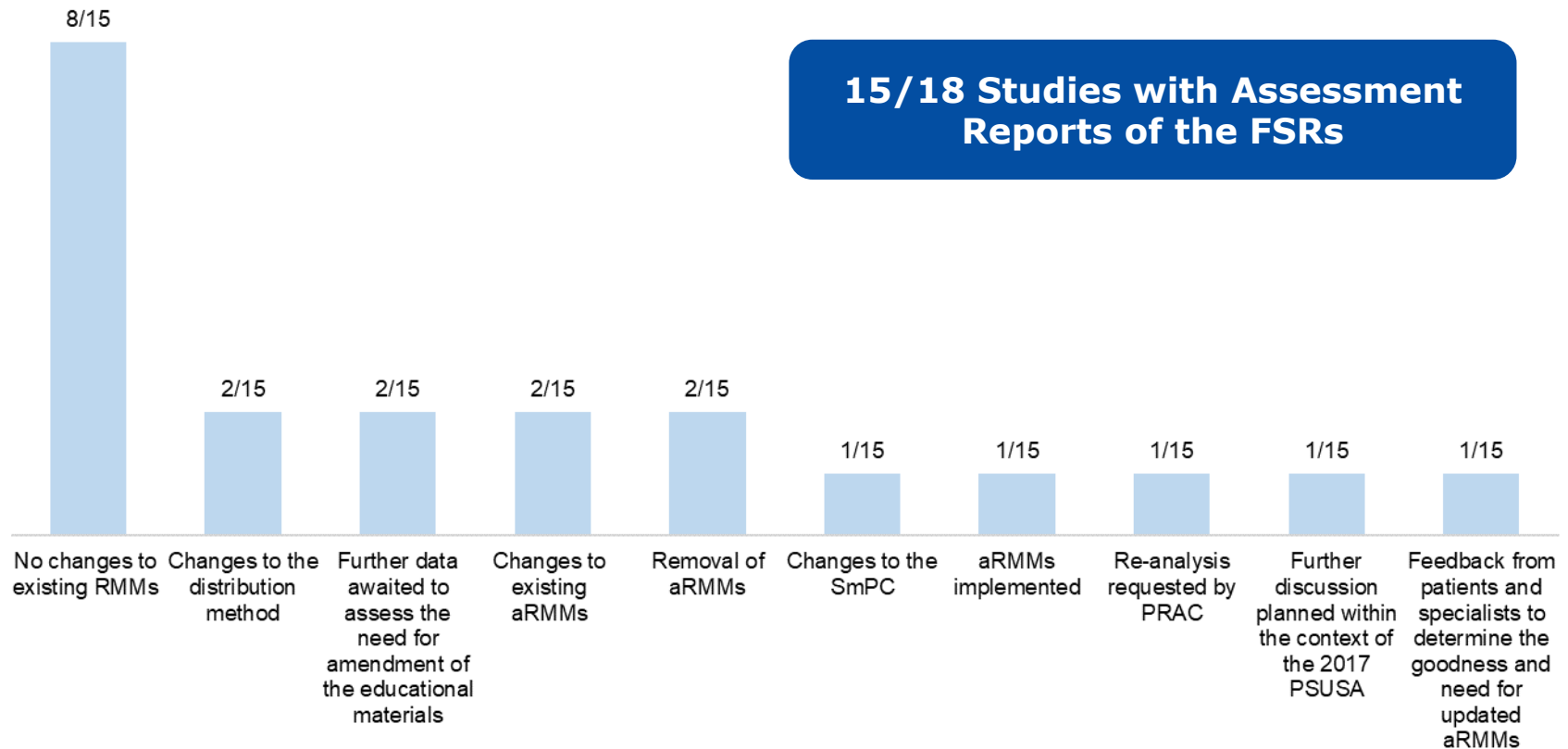


Work in progress

- Reported in **8/18**
- Data extractable for 25 items in only **4 studies:**
 - All 25 items > 50% correct responses
 - 9/25 items >80% correct responses

REGULATORY CONSEQUENCES

From PRAC and National Regulatory Reports



Not mutually exclusive categories

4

SURVEY STUDIES LIMITATIONS



LIMITATIONS

- **Incomplete:** 3 (+4?) studies recently acquired and being evaluated
- **Behaviour** remains to be further analysed
- **Questionnaire validation:** inadequate description 50% not reported

- **Non-systematic:** Limited to FSRs in EU PAS Register (+ some sponsors)
- **Publication bias?**
- **Generalizability?** → biased participant samples?

- **Heterogeneity** of studies by design, characteristics, and results → Case studies may be more relevant
- **Subgroup analyses/meta-regression** hindered by access to detailed data
- **Changes in reporting practices with time?** → More reports for time trends
- **Confounding?**
- **Lack of outcomes** - ~ a third have accompanying outcomes. but process outcomes also needed

5

SURVEY STUDIES CONCLUSIONS & RECOMMENDATIONS



SUMMARY & RECOMMENDATIONS

- **Regulatory consequence:** Most frequently no change to RMM
- **Receipt:** moderate and better for HCP/patient brochures
- **Use:** moderate in HCPs and lower in patients
- **Knowledge of AEs:** HCPs > patients

- **Variability in reporting** sampling, participation data, qualitative approaches to testing questionnaires and key endpoints

- **Lessons learned for study conduct (Case studies)**
- **Heterogeneity of results and evaluations** → results interpreted within the context of each evaluation

- **Need for more specific and detailed guidance**
 - Revise Methods Guide on Surveys
 - Reporting of surveys

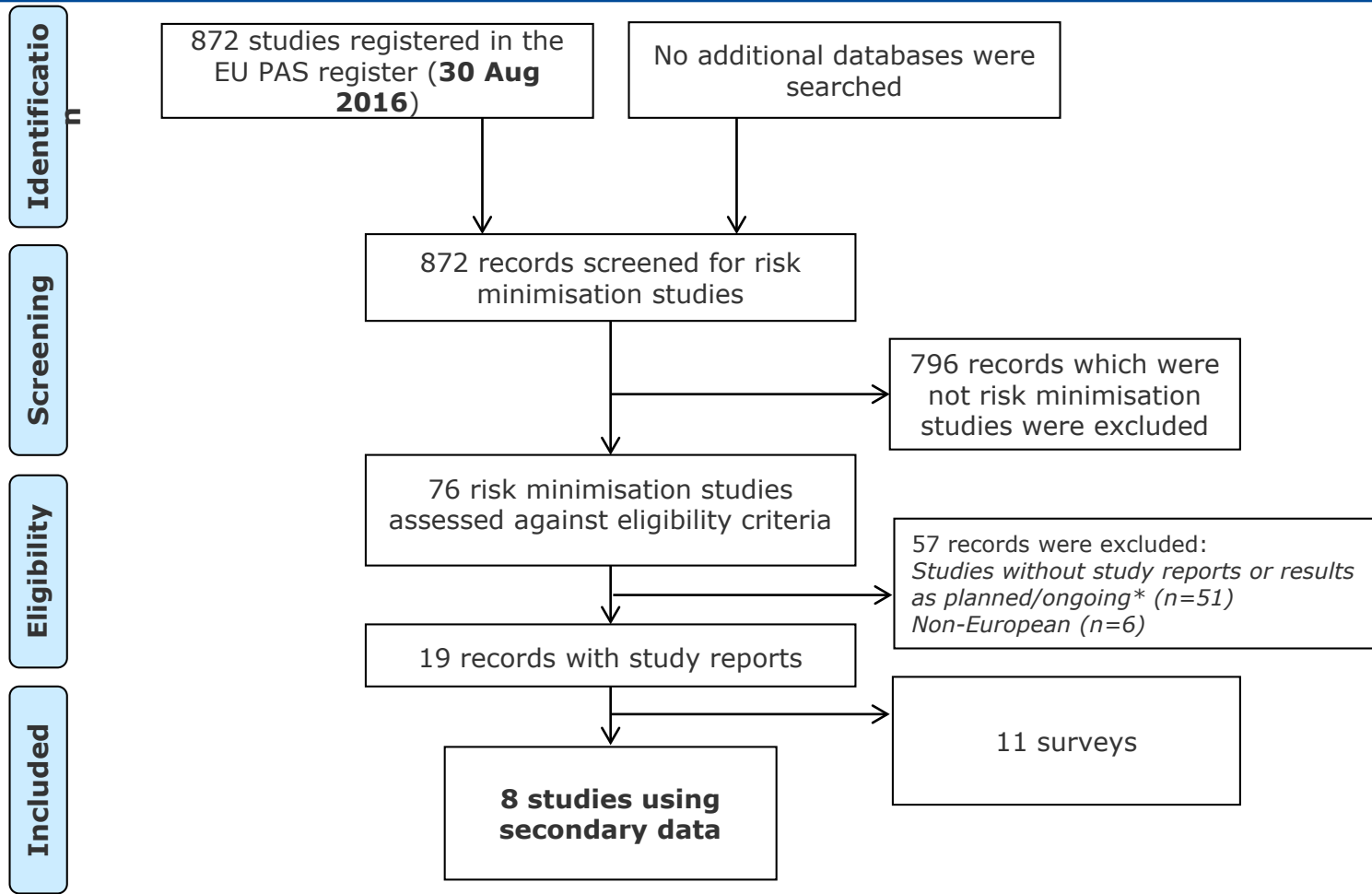
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STUDIES WITH 'OUTCOMES'



SELECTION PROCESS

Reports until Aug 2016



*Status for five out of 51 was completed

Eight studies

RMMs

- All aRMMs + 5/8 also rRMMs e.g. label changes

Study Design

Retrospective cohort studies: 7/8 → Drug Utilization Studies

- 3 with pre-post design (label changes , DHPC)

Cross-sectional study: 1/8

Data Sources

- 2/8 electronic/paper medical records
- 6/8 multiple healthcare databases

Outcomes

- Drug utilization
- Monitoring of laboratory parameters
- AEs

As reported

23 indicators in 8 studies:

- 'success': 8/23
- inconclusive: 1/23
- 1/23: success in one country but inconclusive in the other country
- Insufficient information: 13/23

Thank you!



**Additional information
and case studies:
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