Quantitative review of survey studies to assess the effectiveness of risk minimisation

Nawab Qizilbash *MBChB MRCP(UK) MSc DPhil(Oxon)*
OXON, Madrid & London
London School of Hygiene & Tropical Medicine
Hospital Cantoblanco, Madrid
n.qizilbash@oxonepi.com

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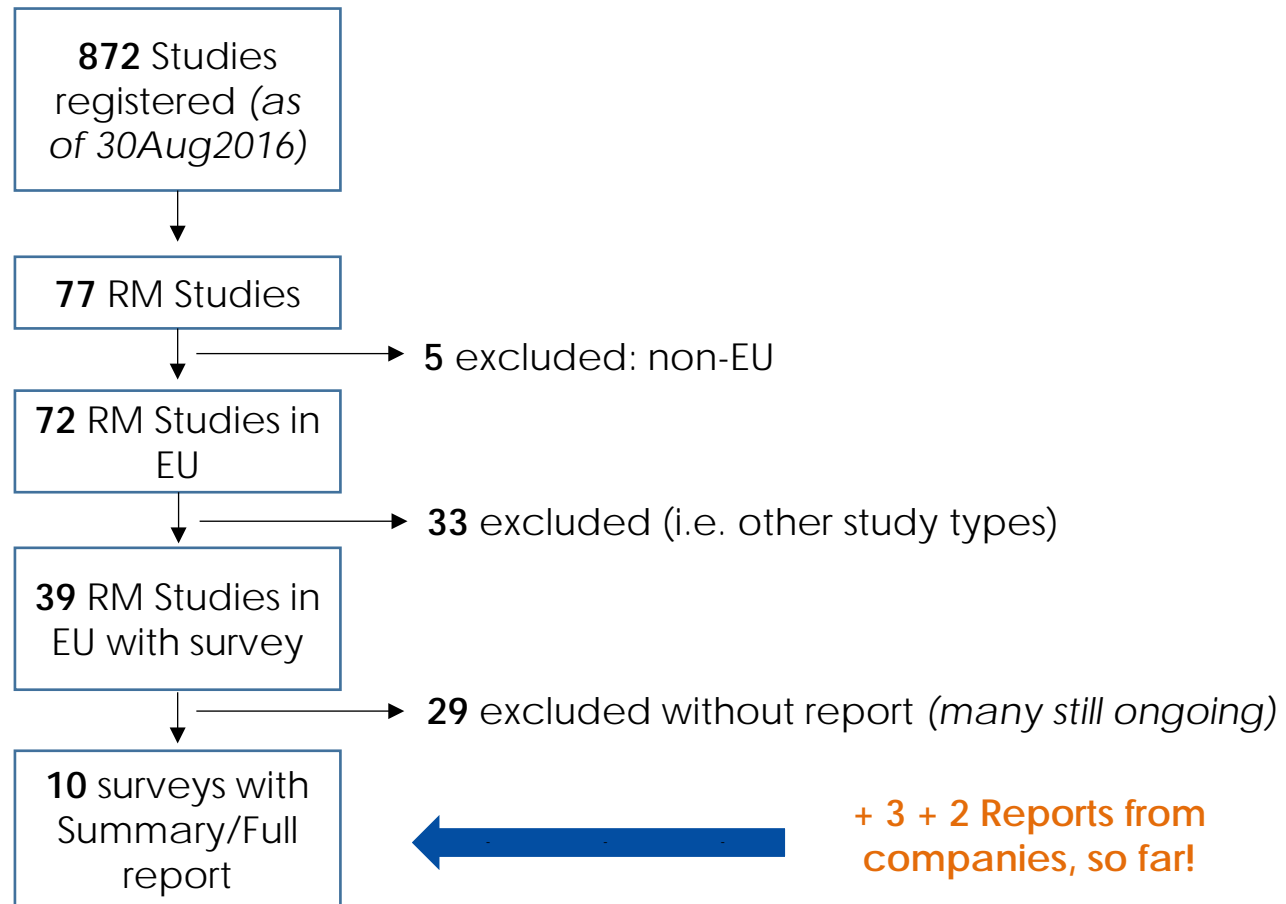
Bayer Epidemiology
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ENCePP SIG on Impact of PV Activities

Scope

→ **Aim**: A review of available survey studies to assess the effectiveness of risk minimisation measures (RMMs)

→ **Type of RMMs:**
- o Routine: SmPC or PIL
- o Additional: e.g. educational materials

→ **Data sources:**
- o Reports from EU PAS Register
- o +/- Reports from pharma companies
- o +/- PRAC Minutes
- o +/- Data from EMA on consequences

→ **Standard methods** (with Bayer Epidemiology)

Study Selection

EU PAS Register

872 Studies registered *(as of 30Aug2016)*

↓

77 RM Studies

→ **5** excluded: non-EU

72 RM Studies in EU

→ **33** excluded (i.e. other study types)

39 RM Studies in EU with survey

→ **29** excluded without report *(many still ongoing)*

10 surveys with Summary/Full report

← **+ 3 + 2 Reports from companies, so far!**

Preliminary Results I

Study characteristics

Drug	Indication	RMMs	Safety concerns targeted	Target	Countries	Sampling
voriconazole	Fungal infections	PAC, Q&A brochure, HCP checklist	Phototoxicity, Squamous cell carcinoma of the skin, hepatotoxicity	Specialists	10	All identified prescribers approached
quetiapine	Antipsychotic	Educational materials	Extrapyramidal symptoms, somnolence, weight gain, lipid changes, hyperglycemia, metabolic risk factors	Specialists / GPs	8	Distribution list - random
dabigatran	Stroke prevention in AF	PAC, Prescriber Guide	Bleeding	Specialists / GPs **(3A)** / **patients (3B)**	8	Random
cyproterone acetate & ethinilstradiole	Acne / hirsutism in women	PAC, HCP brochure and checklist, DHPC	Indication dropped, thromboembolic complications	GPs	1	Unclear
retigabine	Epilepsy	Physician´s Guide	QT prolongation, voiding dysfunction	Specialists	7	Random
retigabine	Epilepsy	DHPC	Eve, skin and subcutaneous disorders	Specialists	7	Random
atomoxetine	ADHD	HCP leaflet, checklists, recording chart	CV and cerebrovascular disorders, need for BP and heart rate monitoring	Specialists	5	Unclear
atomoxetine	ADHD	HCP leaflet, checklists, recording chart	CV and cerebrovascular disorders, need for BP and heart rate monitoring	Specialists / GPs	5	Unclear
rilpivirine alone / combination	HIV-1	Routine i.e. SmPC	Development of resistance	Specialists / GPs / Nurses / Pharmacists	9	Unclear
denosumab	Bone metastases	Routine i.e. SmPC	Osteonecrosis of the jaw	Specialists	9	Random / stratified

Preliminary Results II

Variability: Participation data
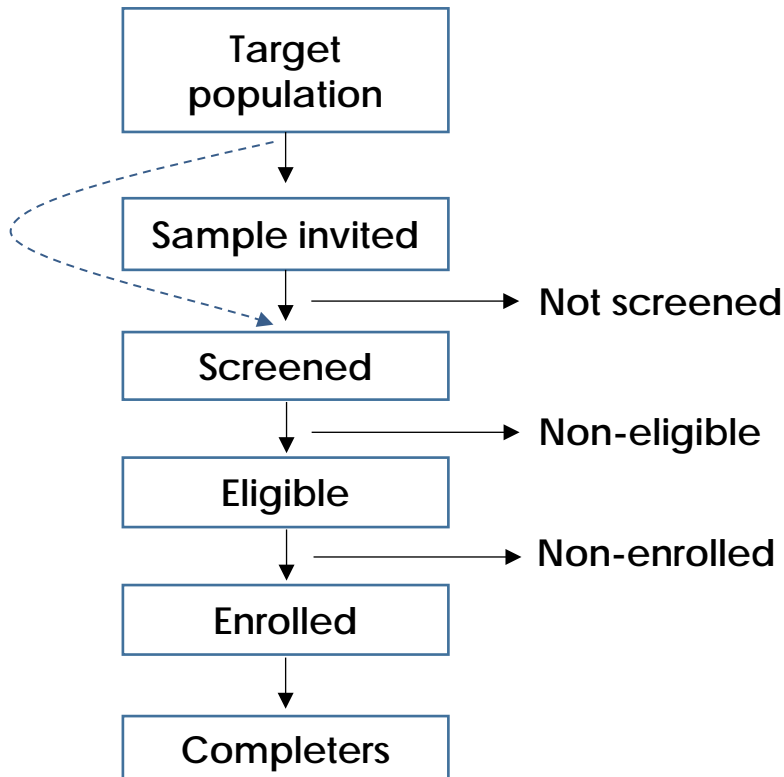
Variability in definition and terminology:

Response rate:
- Completers / eligible
- Screened / (Invited – undelivered)
- Responding or screened / Invited
- Agreeing to participate / contacted

Completion rate = Completers / eligible

Cooperation rate = completers / agreeing to participate

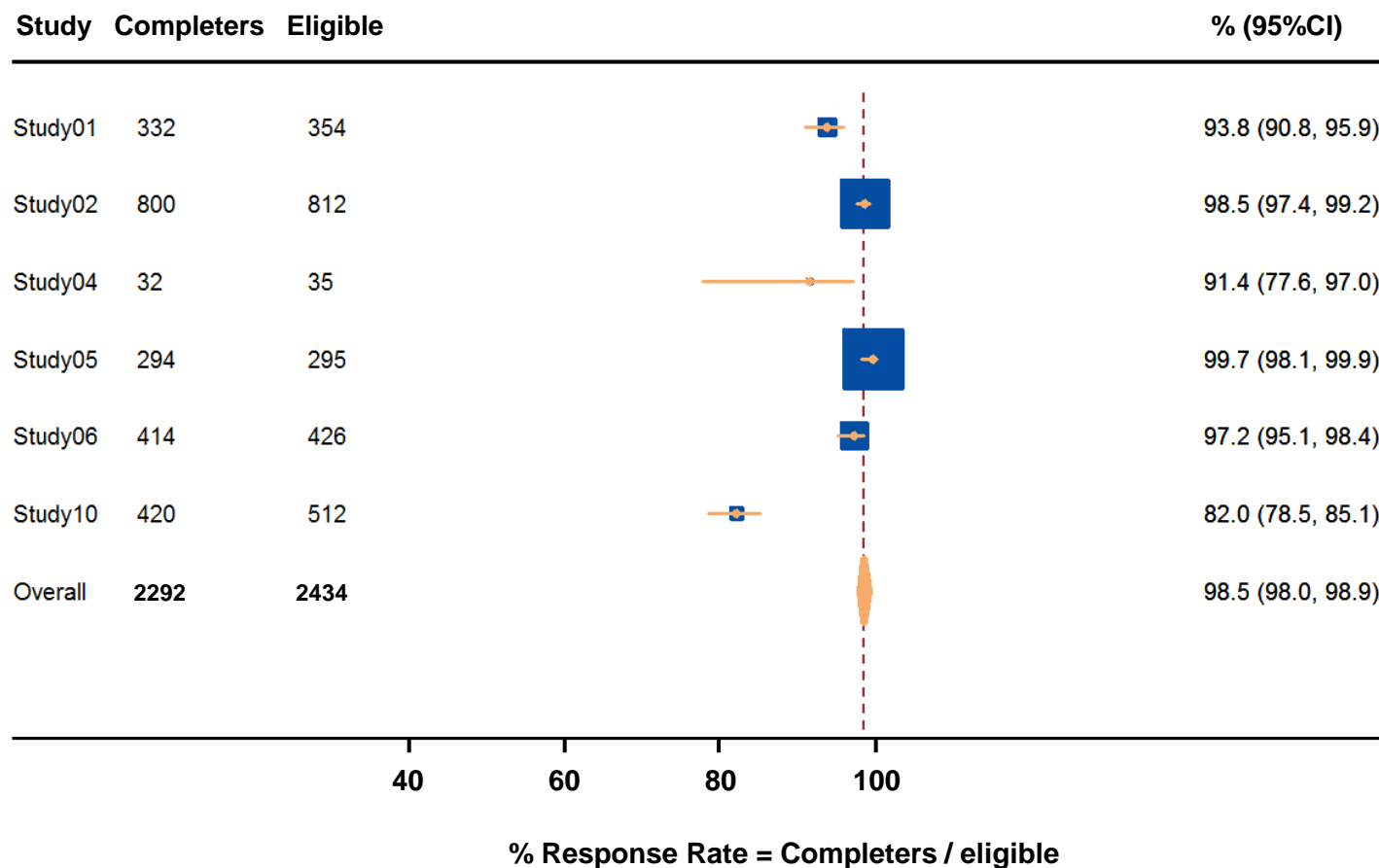Eligibility rate = Eligible / screened

Contact rate = contacted / targeted

Others:
- Completers / targeted
- Participation rate
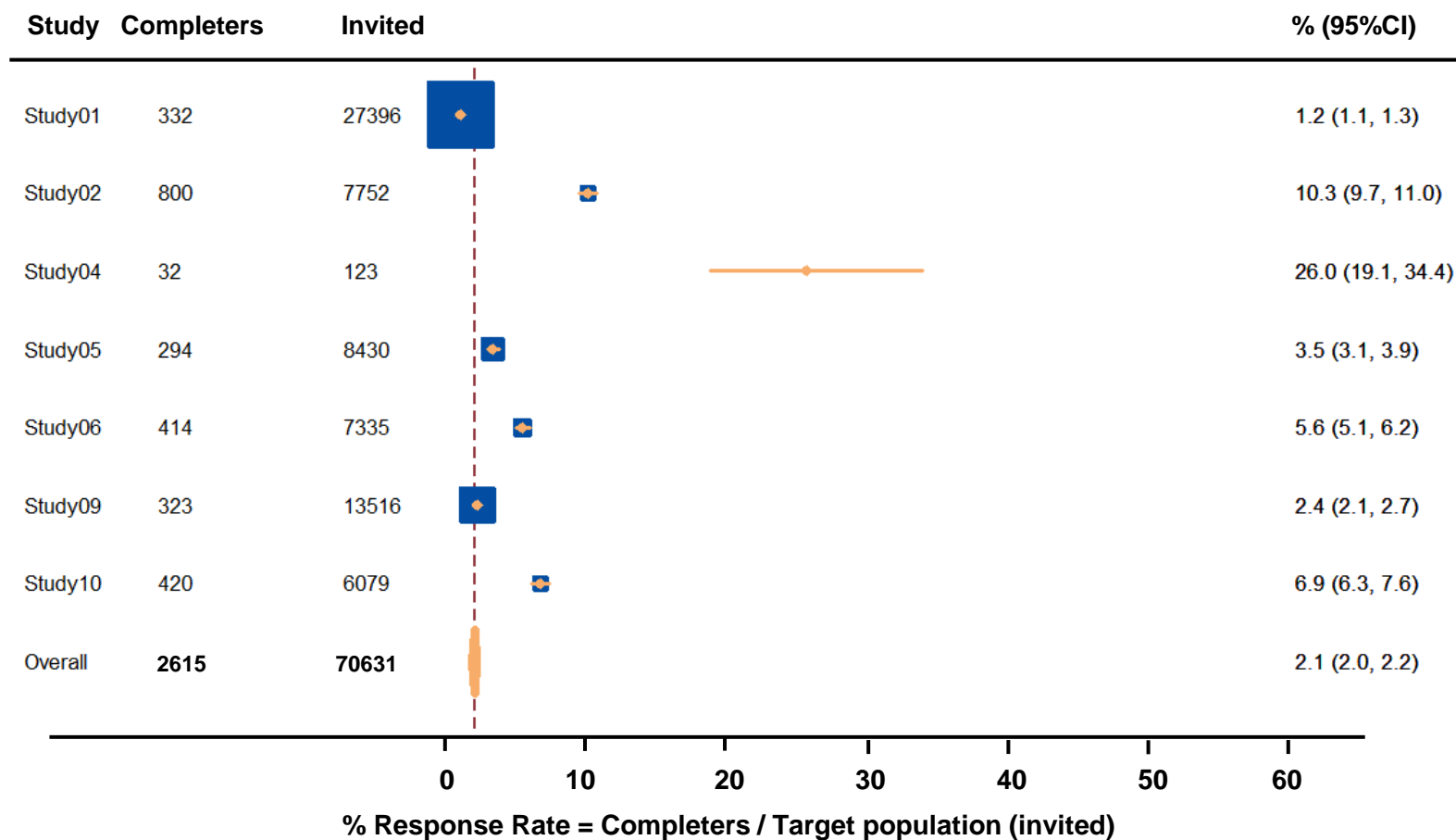- Refusal rate
- Non-response rate

Preliminary Results III

% Response rate (completers / eligible)

OXON *epidemiology*

Study	Completers	Eligible		% (95%CI)
Study01	332	354		93.8 (90.8, 95.9)
Study02	800	812		98.5 (97.4, 99.2)
Study04	32	35		91.4 (77.6, 97.0)
Study05	294	295		99.7 (98.1, 99.9)
Study06	414	426		97.2 (95.1, 98.4)
Study10	420	512		82.0 (78.5, 85.1)
Overall	**2292**	**2434**		98.5 (98.0, 98.9)

40 60 80 100

% Response Rate = Completers / eligible

Preliminary Results IV

% Response rate (completers / target population)

Study	Completers	Invited	% (95%CI)
Study01	332	27396	1.2 (1.1, 1.3)
Study02	800	7752	10.3 (9.7, 11.0)
Study04	32	123	26.0 (19.1, 34.4)
Study05	294	8430	3.5 (3.1, 3.9)
Study06	414	7335	5.6 (5.1, 6.2)
Study09	323	13516	2.4 (2.1, 2.7)
Study10	420	6079	6.9 (6.3, 7.6)
Overall	**2615**	**70631**	2.1 (2.0, 2.2)

% Response Rate = Completers / Target population (invited)

Preliminary Results V

% Receipt

Study	Receivers	Completers		% (95%CI)
Study01	75	332		22.6 (18.4, 27.4)
Study02	299	800		37.4 (34.1, 40.8)
Study03A	279	411		67.9 (63.2, 72.2)
Study03B	445	802		55.5 (52.0, 58.9)
Study05	189	294		64.3 (58.7, 69.5)
Study06	174	414		42.0 (37.4, 46.8)
Overall	**1461**	**3053**		47.1 (45.4, 48.8)

% Receipt

OXON *epidemiology*
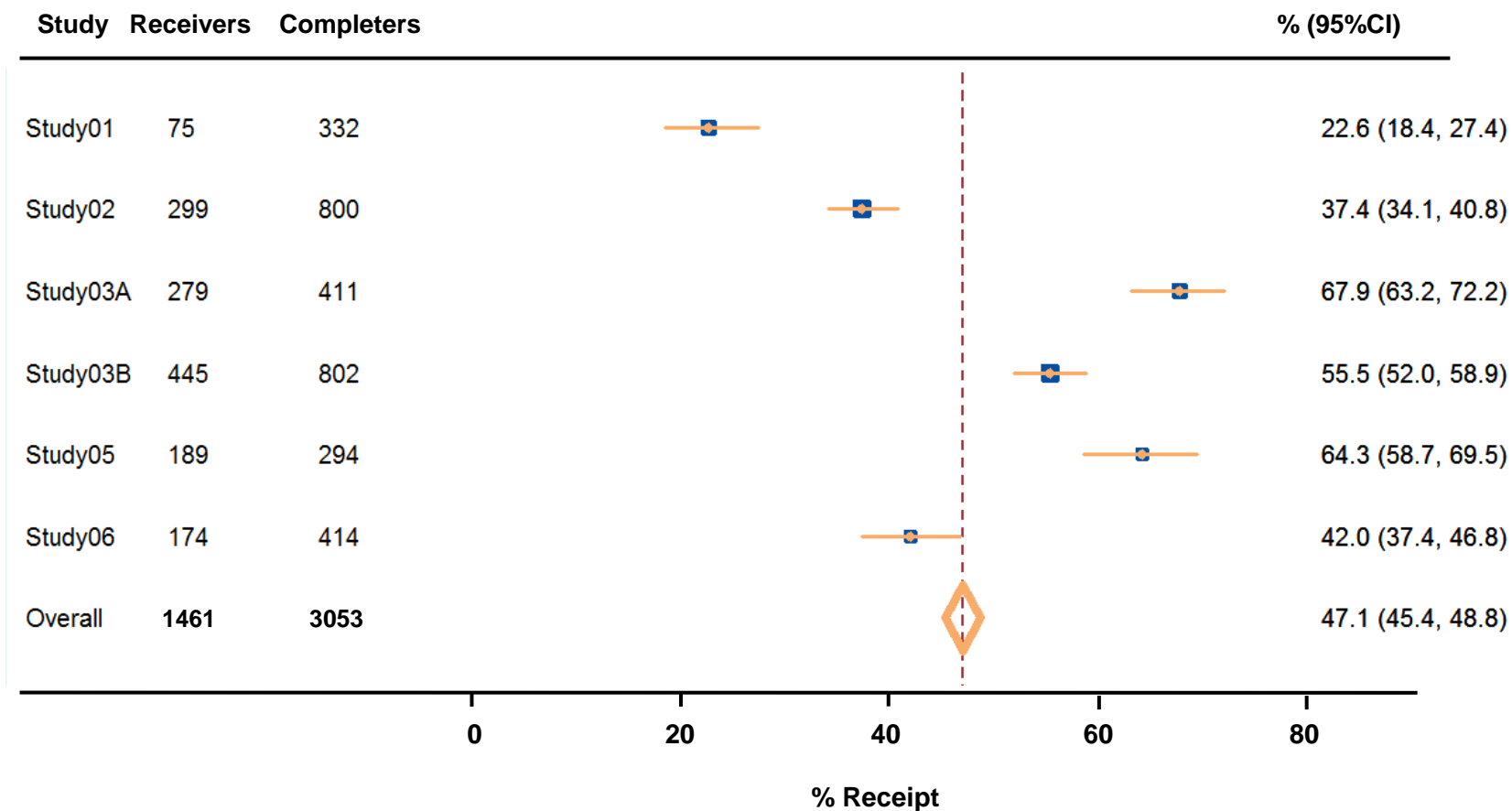
Correlation of receipt with response rates (completers / eligible)

Issues & challenges
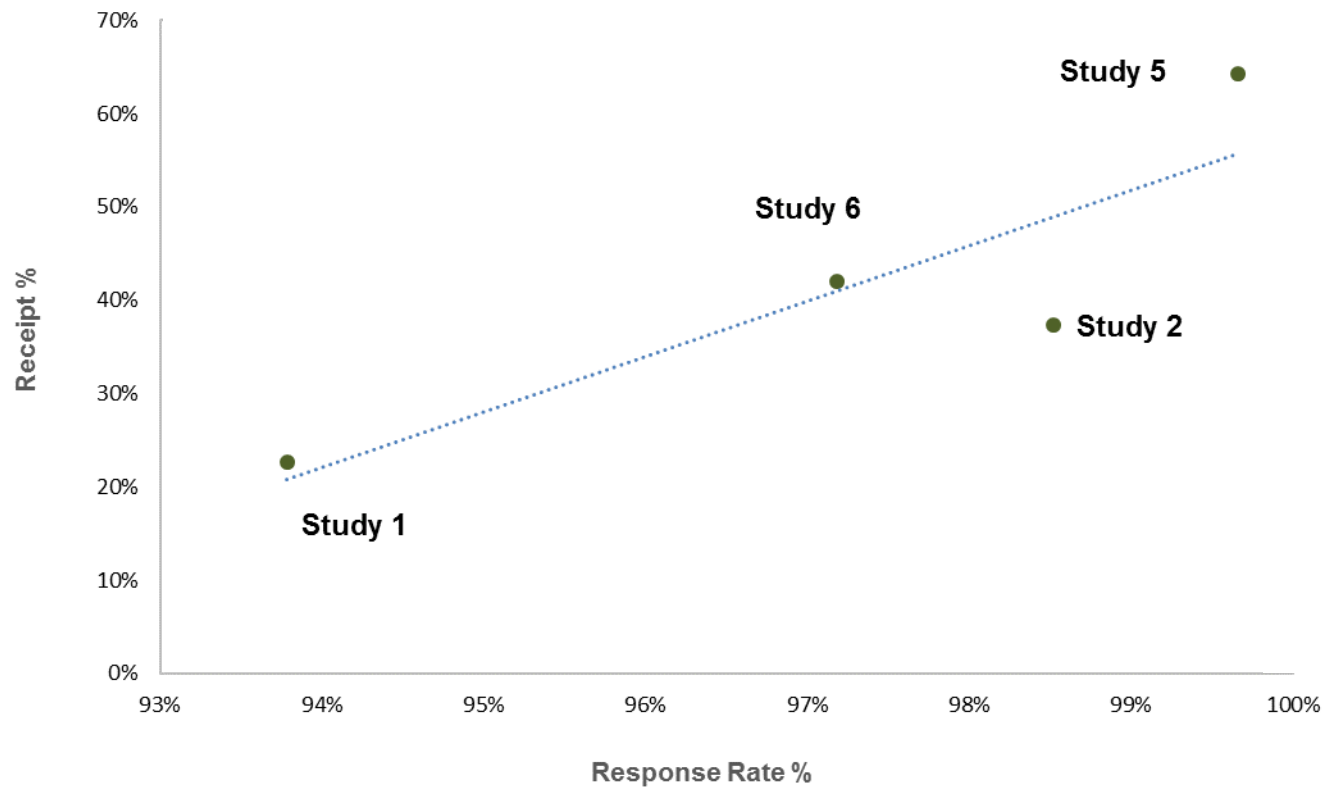
→ **Immense variation in reporting and conduct of studies:**

- Rates of: participation, receipt, knowledge, behaviour, usage
- Sampling
- Country selection
- Validation of questionnaires

- Designs: lack of clinical & safety outcomes
- Selection bias of studies? (→ EMA / Companies)

- Assessment, criteria for success & thresholds

→ **Additional guidance document on conduct and reporting to improve quality and consistency (→ ENCePP SIG):**
    - Conduct → Methodological standards
    - Reporting → Standardisation of terminology and presentation

What kind of guidance documents or initiatives would you find most useful?

(0=no need, 5=much needed) ■ 4-5 ■ 2-3 □ 0-1
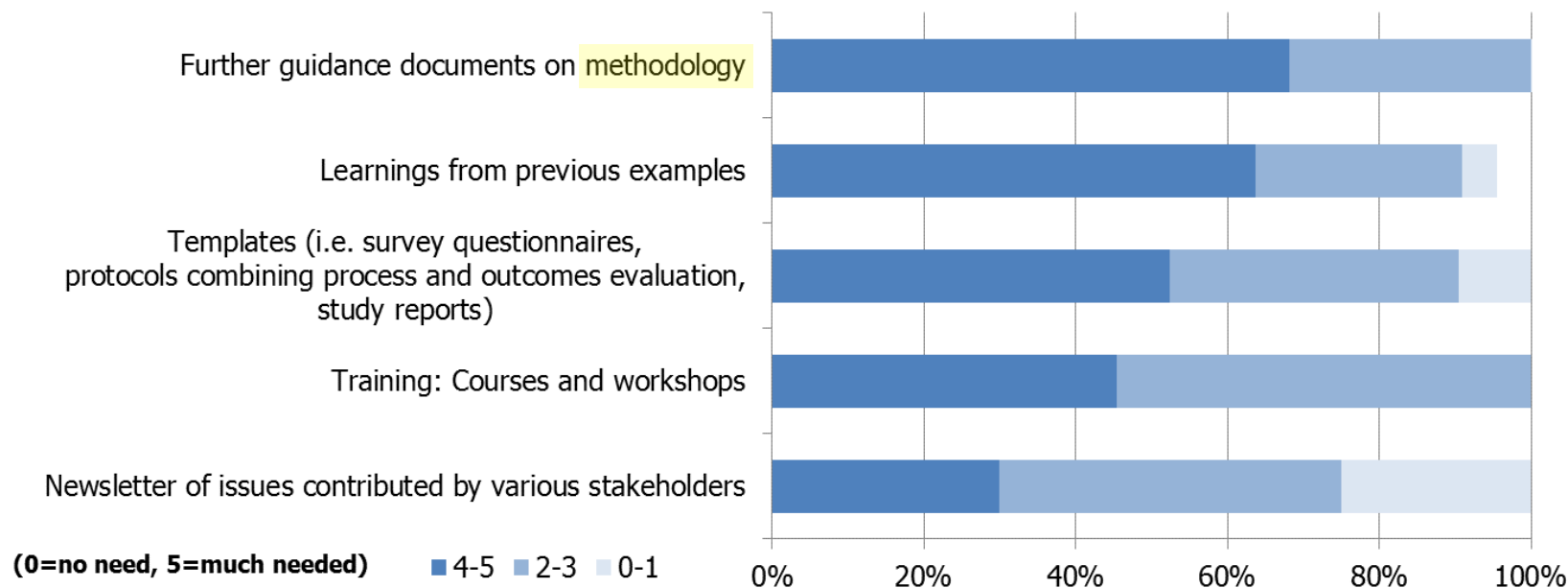
Thank you - More study reports/data please!

n.qizilbash@oxonepi.com