Strengthening the Quality of Clinical Pharmacokinetic Studies: Development and Validation of a Critical Appraisal Tool for Clinical Pharmacokinetic Research

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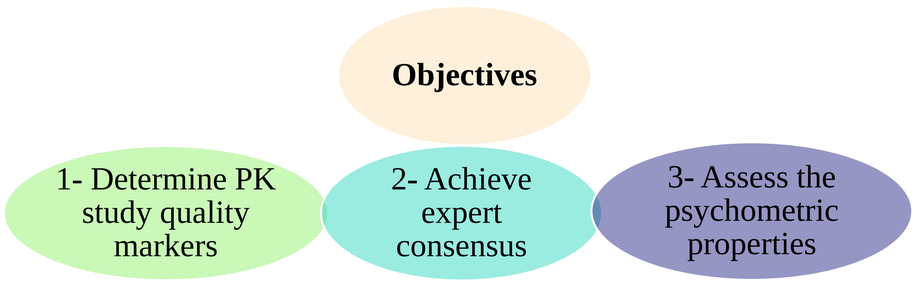
Background

- Application of knowledge from primary literature is accompanied by enhanced ability to critically apprise primary literature and determine whether it is conducted optimally[1].
- Quality of trials has several dimensions[1].
- 20% of the published trials did not specify basic pharmacokinetic (PK) parameters that are fundamental requirements for all drug dosing[2].
- Pharmacokinetic reporting guidelines were published:
  - To guide researchers in conducting pharmacokinetic studies[3]
  - To ensure the reporting of the required minimum basic information[3]
    - "Yes/No" checklist
      - The checklist was composed of 24 items

Objectives



Methods

Literature search

- Search of the literature published in English without years limit using Medline (via Ovid) (1946 to March 2018), EMBASE (1974 to March 2018), Cochrane databases of systematic reviews, Google and Google Scholar was conducted.
- Search terms encompassed three main search categories: pharmacokinetics, reporting guidelines/appraisal tools, quality markers.

Inclusion criteria:

- Primary, secondary, or tertiary levels of clinical pharmacokinetic scientific literature
- English language

Exclusion criteria:

- Cell or animal-based models

Data extraction

- Data extraction form was developed
- Protocol was registered with PROSPERO: CRD42018094571

Modified Delphi

Sampling method

- Purposeful sampling

Number of rounds

- Determined based on the agreement, disagreements and reconsideration

Consensus criteria

- **Inclusion criteria**

  ≥ 75% of participants select 4 or 5 on the 5-Point Likert scales.

  A median score of **≥** 4 and interquartile-range of ≤1.

- **Exclusion Criteria**

  < 75% of participants select 1 or 2 on the 5-Point Likert scales.

  A median score of ≤ 2 and interquartile-range of >1.

Questionnaire Development: through SurveyMonkey platform

Validity and reliability testing

- Content and face validity were tested
- Intra-rater and inter-rater reliability were tested

Limitations

- Data collection form was not validated
- Prevalence bias lead to undetectable Kappa Values

Acknowledgement

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Results

Figure 1. Flowchart describing study selection

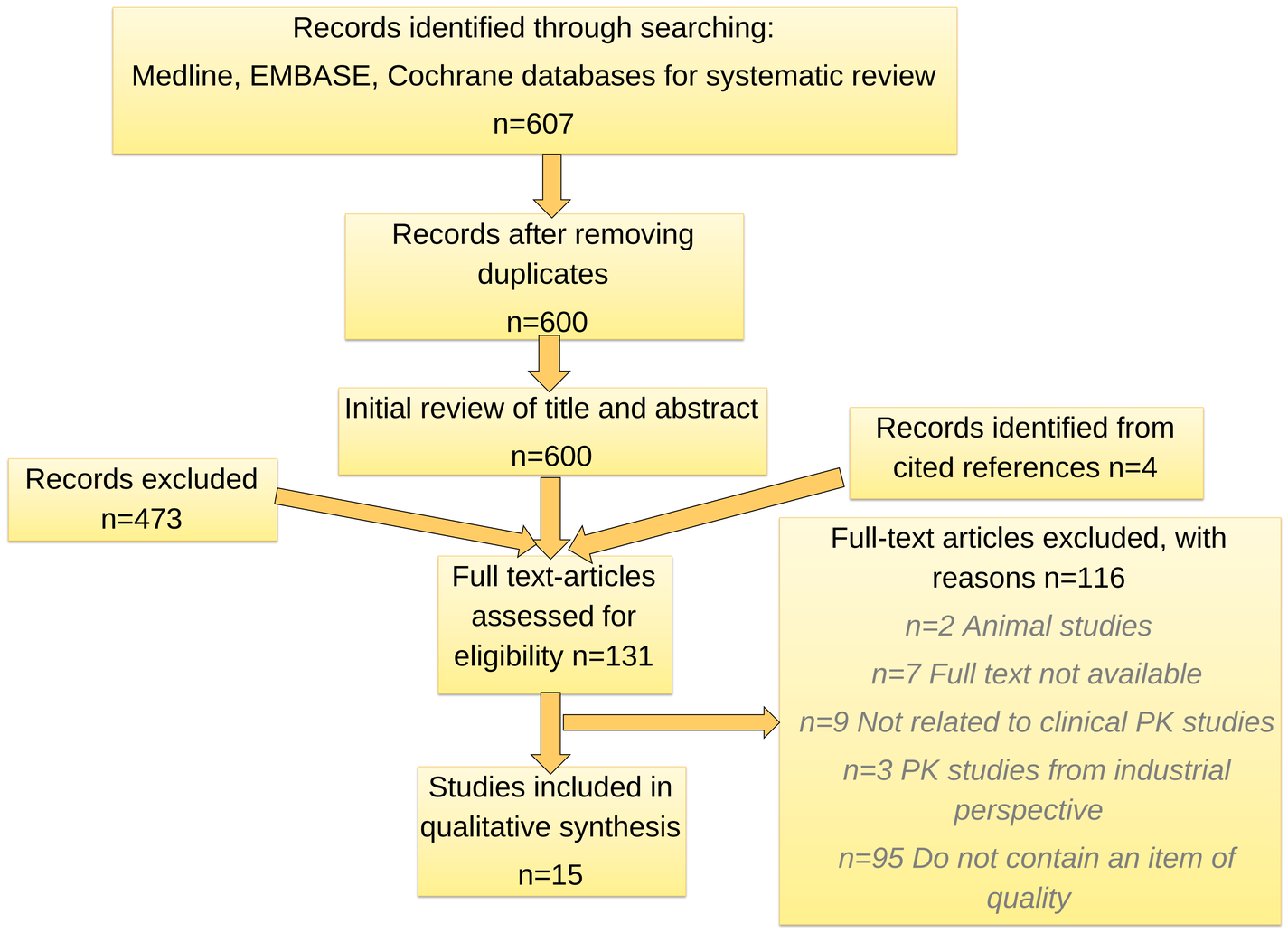

Figure 2. The Modified Delphi flow chart

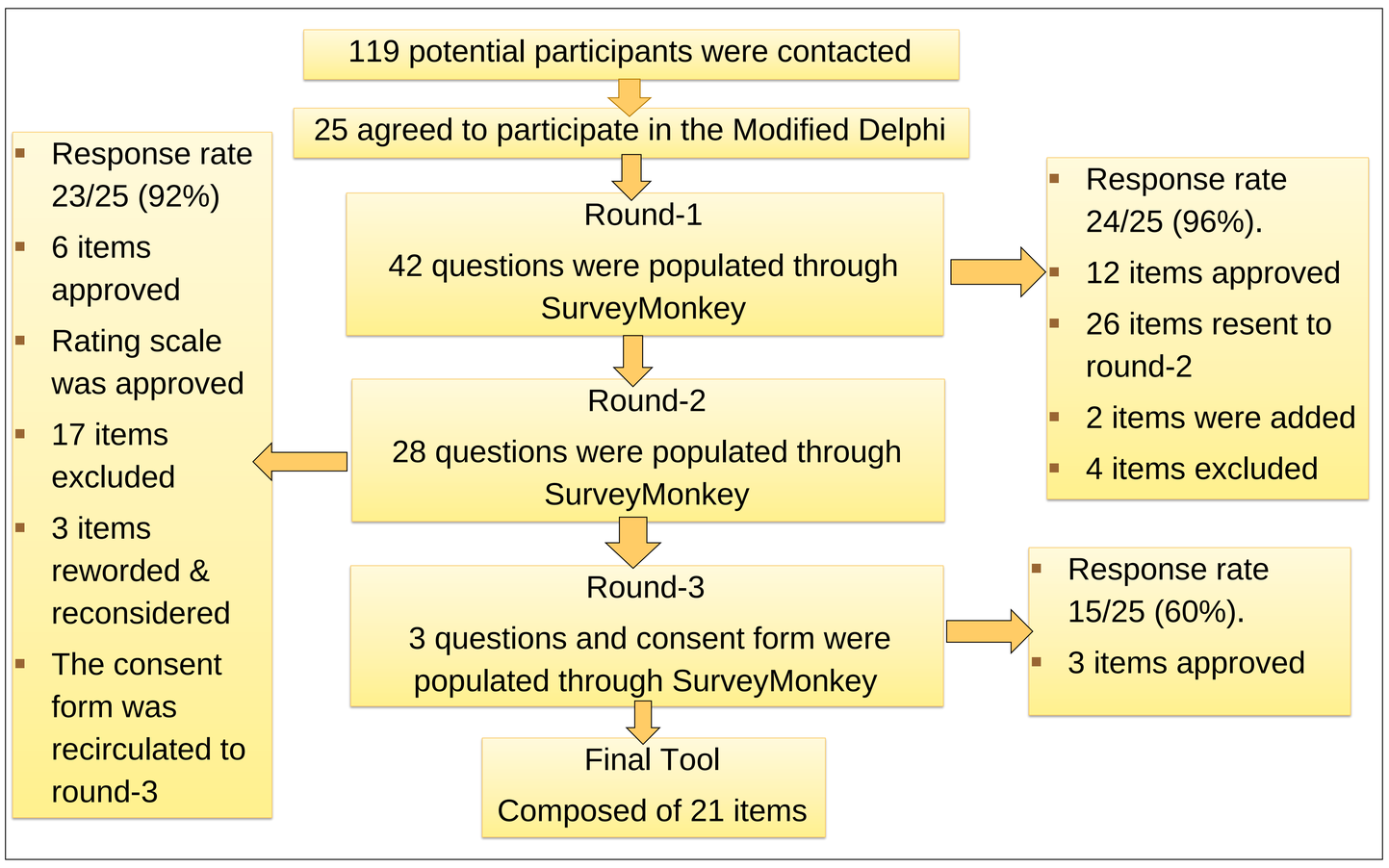

Table 1. Inter- reliability testing

Level of agreement	Questions (Q)
Less than a chance of agreement (< 0)	Q3, Q10
Slight agreement (0.01 - 0.20)	Q15
Fair agreement (0.21 - 0.40)	Q7, Q8,Q9,Q12, Q14, Q19
Moderate agreement (0.41 - 0.60)	Q6, Q11, Q17
Substantial agreement (0.61 - 0.80)	Q1, Q4,Q16, Q18, Q20
Almost perfect agreement (0.81 – 0.99)	Q13, Q21

Discussion/Conclusion

- Inventory of quality markers related to clinical pharmacokinetic studies was developed
- This critical appraisal tool will aid in enhancing the quality of the published clinical pharmacokinetic studies

Future Direction

- Further modification and psychometric testing should be done on the developed clinical pharmacokinetic critical appraisal tool to convey the dynamic evolution in the medical field.

References

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3. Kanji S, Hayes M, Ling A, et al. Reporting guidelines for clinical pharmacokinetic studies: The ClinPK statement. Clin Pharmacokinet. 2015; 54:783-95.