Development and Validation of a Critical Appraisal Tool for Clinical Pharmacokinetic Research

Background
- Application of knowledge from primary literature is accomplished by enhanced ability to critically appraise primary literature and determine whether it is conducted optimally.
- Quality of trials has several dimensions.
- Pharmacokinetic reporting guidelines were published:
  - To guide researchers in conducting pharmacokinetic studies
  - To ensure the reporting of the required minimum basic information
  - "Yes/No" checklist

Objectives
1. Determine PK study quality markers
2. Achieve expert consensus
3. Assess the psychometric properties

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

Results

Figure 1. Flowchart describing study selection
- Records identified through searching: Medline, EMBASE, Cochrane databases for systematic review
  - n=607
- Records after removing duplicates
  - n=600
- Initial review of title and abstract
  - n=600
- Records excluded
  - n=473
- Full text articles assessed for eligibility
  - n=131
- Studies included in qualitative synthesis
  - n=15
- Records identified from cited references
  - n=4
- Full text articles excluded, with reasons
  - n=116
  - n=2 Animal studies
  - n=7 Full text not available
  - n=9 Not related to clinical PK studies
  - n=95 Do not contain an item of quality

Figure 2. The Modified Delphi flow chart
- 119 potential participants were contacted
- 25 agreed to participate in the Modified Delphi

Table 1. Inter-rater reliability testing

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

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.

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References