Quality of anticholinergic burden scales and their impact on clinical outcomes – a systematic review

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Introduction
Anticholinergic drug burden (ADB) is high in older people and increases with hospitalization. A practical way of assessing ADB is the application of an anticholinergic burden scale (ABS) usually ranking a specific drug into 4 levels, ranging from no (0) to high (3) anticholinergic activity. However, it is unclear how many of these scales are published, how they differ in quality and how they are associated with clinical outcomes.

Therefore, the aims of this systematic review were threefold:

1. To identify all published ABS and their validation studies
2. To compare the ABS systematically by using adapted tools
3. To evaluate associations with clinical outcomes in patients

Methods

1. Inclusion criteria for ABS:
   - Existence of a grading score for ADB
   - A list with medications with their scores available
   - ADB developed for adults (≥18 years)
   - Language: German, French, English

2. Exclusion criteria for ABS: Equation for ADB
   - Quality assessment of the ABS by using a self-adapted AGREE II tool.

3. Identification of validation studies using an ABS by calculating the cumulative ADB with any clinical outcome.
   - Assessment of their quality by using the Newcastle-Ottawa Scale I and the Cochrane Risk of Bias 2.0 tool and categorizing them into 6 different evidence levels with respect to their quality.

Results

1. 19 ABS and 104 validation studies.

(a) The AGB scale and GABS have the best and SCDL, the lowest quality (Table 1).

(b) 5 ABS have no validation studies (Figure 1, left).

(c) Mostly cohort (level 2a, 2b) and cross-sectional studies (level 5).

(d) Most investigated outcomes are cognition, delirium, falls, mortality with contradicting results (Figure 1, right).

2. Only 2 studies compared up to 8 ABS.

Great heterogeneity makes a meta-analysis impossible.

Conclusion
This review was able to identify all published ABS and their validation studies in order to assess their quality systematically by adapted tools. Though all ABS were recommended for use with modifications, they differentiate in quality. Though most ABS have been validated, we lack validation studies for newer scales and evaluation of the association for the four most investigated clinical outcomes showed contradicting results.

Hence, there is a need for good quality validation studies comparing multiple scales to define the best scale and to conduct a meta-analysis for the assessment of their clinical impact.

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2. Wells et al., The Newcastle-Ottawa Scale (NOS); for assessing the quality of nonrandomized studies in meta-analysis, available at: http://www.ohri.ca/programmes/clinical_epidemiology/oxford.asp

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**Table 1: Quality assessment of the included ABS by 3 researchers using a self-adapted AGREE II tool (numbers in %)**

<table>
<thead>
<tr>
<th>Domain</th>
<th>AAS</th>
<th>ABC</th>
<th>AGB</th>
<th>ACL</th>
<th>ADS</th>
<th>AES</th>
<th>AIS</th>
<th>ARS</th>
<th>ATS</th>
<th>BAADS</th>
<th>CABS</th>
<th>Chew</th>
<th>CI</th>
<th>PI</th>
<th>CRAS</th>
<th>DRS</th>
<th>DS</th>
<th>GABS</th>
<th>KABS</th>
<th>SCDL</th>
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**Figure 1:** Number of validations per ABS (left) and found association (∆ = positive, ▼ = negative) for the 4 most investigated clinical outcomes (right).

Evidence levels: 1 = good quality RCT, 2a/2b = good quality cohort studies (pro- and retrospective), 3 = good quality case-control studies, 4 = poor quality case-control and cohort studies, 5 = good and poor quality cross-sectional studies.

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